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Dear readers,

We bring to your attention the next issue of our journal that is thematic and focuses on various issues of joint replacement.

The journal opens with the work of the authors from Novosibirsk (Aleksandrov et al.), who studied the survival rate of unconstrained ceramic wrist joint implants in 83 patients. Having analyzed the results, the authors state that the intermediate outcomes of total arthroplasty with an unconstrained ceramic endoprosthesis of the wrist joint are encouraging in terms of a lasting positive effect in achieving mobility of the wrist joint that is lost due to the degenerative process. An eleven-year follow-up demonstrates that the survival rate of an unconstrained ceramic wrist replacement is 88 %.

Kotelnikov et al. (Samara) analyzed the biomechanics of the proximal interphalangeal joint after its replacement in 42 patients. Using 3D modeling, a digital model of the endoprosthesis was created. The finite element method was applied to study the critical states of the developed digital model simulating stereotypical movements in the joint, and objective results were obtained and used in clinical practice. Based on the data obtained, the authors concluded that the load of up to 5 kg in the early postoperative period is optimal for the patient, while the range of flexion should not exceed 90°. The load in the range from 5 to 20 kg is possible, but the angle of flexion in the proximal interphalangeal joint should not exceed 30°. The load of 20 kg and the flexion angle of more than 30° may result in the dislocation of the endoprosthesis components; flexion angle of more than 60° may cause a periprosthetic fracture.

The first experience in robot-assisted knee arthroplasty in 10 patients was shared by authors from St. Petersburg (Airapetov et al.).Despite the high cost and the need for additional consumables, this technique has a number of advantages over the classical manual technique. Such advantages include accurate restoration of the limb axis even in extra-articular deformities, correct position of endoprosthetic components, reduction of intra-operative blood loss due to closed bone marrow canals, and safety for patients.

Authors from Kurgan (Teplenky et al.) assessed the impact of previous surgical treatment on the results of total hip replacement in young patients with dysplastic coxarthrosis. The paper presents a retrospective analysis of the outcomes of surgical treatment of 78 patients aged 14-30 years. Based on the results obtained, the authors came to the conclusion that prior reconstructive interventions in the hip joint increase the technical complexity and aggressiveness of subsequent total arthroplasty, contribute to an increased risk of late complications, but do not have a significant impact on the results of treatment.

Mitroshin et al. (Penza) compared the strength characteristics of a carbon-based friction pair of a hip joint endoprosthesis, including components made of monolithic or non-monolithic pyrolytic carbon. Based on the data obtained, the authors conclude that the designs of the head and liner of the hip joint endoprosthesis with a friction pair made of carbon material provide high reliability in the conditions of hip joint functioning at maximum loads. Mitroshin et al (Penza) compared the strength characteristics of a carbon-based friction pair of a hip joint endoprosthesis, including components made of monolithic or non-monolithic pyrolytic carbon. Based on the data obtained, the authors conclude that the designs of the head and liner of the hip joint endoprosthesis with a friction pair made of carbon material provide high reliability in the conditions of hip joint functioning at maximum loads.

Prevention of pain after arthroplasty in patients with fractures of the proximal femur is the topic of the publication by Han et al. (Kazan, Tashkent). The authors performed a comparative study of 60 clinical cases using the VAS pain scale in terms of assessing the effectiveness of postoperative multimodal pain relief using the author's method. Positive dynamics of pain disappearance were noted in patients with increased BMI of any grade, including those with BMI ≥ 40.

A comparative analysis of the results of using various surgical techniques in 94 patients with closed injuries to the sciatic nerve after total hip replacement was carried out by authors from Saratov (Bazhanov et al.). According to the authors, the most effective method of surgical treatment for this pathology is microsurgical neurolysis in combination with two-level electrical stimulation, which is characterized by a faster rate of pain regression as well as by positive dynamics of clinical and electrophysiological parameters in the affected lower limb.

The issues of diagnosis are discussed in two publications. Hematological markers of periprosthetic infection during revision hip arthroplasty were studied by authors from Kurgan (Matveeva et al). Patients with acute and chronic types of periprosthetic infection were screened for hematological parameters upon admission and during treatment in order to monitor the course of the purulent inflammatory process. It was observed that patients with acute PJI do not need additional clinical and laboratory examination; it is necessary to use integral laboratory indicators that allow a more accurate assessment of the inflammation in a purulent wound.

Aranovich et al (Kurgan, Yoshkar-Ola, Perm) studied the relationship between serotonin levels in the blood of children and adolescents with unstable flat and valgus foot deformity and confirmed the relationship between the level of serum serotonin and this type of deformity, which, according to the authors, confirms the involvement of the serotonergic system in the formation and progression of foot pathology.

Experimental studies are presented in two publications. Stogov et al (Kurgan, Yekaterinburg) conducted a comparative assessment of the osseointegration of new percutaneous implants made of ultrafine-grained Ti Grade 4 alloy in an experiment on 12 rabbits. Analysis of the results showed that the osseointegration of the percutaneous implant with a mixed nanocrystalline and ultrafine-grained structure was more effective relative to the comparison product. The authors conclude that the use of such implants promising for solving clinical problems in prosthetics.

Tsiskarashvili et al. (Moscow) also studied the effectiveness of polymer hydrogels impregnated with an antibacterial drug in chronic osteomyelitis in experiments on rabbits. A comparative analysis of the results showed that the hydrogel, unlike polymethyl methacrylate (PMMA), reliably relieves chronic osteomyelitis without additional systemic antibiotic therapy and does not cause material-associated bone resorption. At the same time, the clinical and laboratory picture fully corresponds to the data of microbiology, radiology and histomorphometry.

Three case reports of this journal issue describe examples of the use of an individual implant during revision hip arthroplasty in a 72-year-old patient with a Paprosky type IV bone defect (Kovaldov et al, Nizhny Novgorod), the combined use of elastic intramedullary reinforcement and Ilizarov apparatus in the treatment of pseudarthrosis of the hip and shoulder in a girl with osteogenesis imperfecta (Mingazov et al.; Kurgan; Leeds, UK) and a rare case of periprosthetic infection after total hip arthroplasty caused by Mycobacterium abscessus (Kasimova et al., St. Petersburg).

The literature review that finalizes this issue is devoted to the analysis of domestic and foreign publications on the undesirable phenomenon during hip replacement, “ceramic noise”, in the friction pair of the endoprosthesis. The authors note that the noise can be a predictor of problems in the endoprosthesis functioning. The accumulation of a database will lead to a deeper understanding of the noise, methods for its correction and timely prevention of the risk of ceramic cracking.

We hope that this thematic issue will be interesting and useful to specialists and will expand their knowledge in this orthopaedic field.

A.V. Burtsev, MD
Chief Editor of Genij Ortopedii

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Original article

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Survival of unconstrained ceramic wrist joint implants

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Abstract

Introduction Survival of implants is an important indicator of improvement in the patient's quality of life. In foreign literature, the issue of implant survival finds special attention. **The aim** of the work was to evaluate the efficacy and survival of an unconstrained ceramic wrist joint endoprosthesis. **Materials and methods** We analysed 83 cases of total wrist arthroplasty with an unconstrained ceramic implant at long-term follow-up. At the Novosibirsk RSITO, total wrist arthroplasty was performed in 81 patients with severe changes in the wrist joint from 2011 to 2021. Two patients underwent arthroplasty on two joints. A retrospective uncontrolled cohort study was conducted which divided the hospitalized patients into three groups according to the etiological cause of the disease. Radiological methods were used to control the state of the implant (radiography in two projections and CT-scans of the wrist joint). For binary indicators, the number, rates and 95 % confidence interval of frequencies were calculated according to the Wilson formula in the groups. Comparison was carried out by Fisher's exact two-sided test. The p-error was corrected using the Benjamini – Hochberg method. Kaplan – Meier curves were constructed for survival analysis. The groups were compared using a generalized chi-square test. **Results** Each case of repeated surgical intervention was evaluated from the standpoint of selected groups. Depending on the time elapsed from surgery to revision, we calculated the time frame for overall and group survival of the components of the wrist joint endoprosthesis. The causes and scope of surgical revision are presented. **Discussion** There are no data on the survival of unconstrained ceramic wrist joint implants in the foreign literature. Graphic images according to a proposal for the division of the orthopaedic postoperative period are presented. Conclusions 1. Intermediate conclusions in regard to total arthroplasty with an unconstrained ceramic endoprosthesis of the wrist joint inspire optimism in obtaining a stable positive effect of motion range lost due to the degenerative process in the wrist joint. 2. An 11-year follow-up period demonstrates that the survival rate of an unconstrained ceramic wrist endoprosthesis is 88 %.

Keywords: endoprosthesis, replacement, wrist joint, implant survival, postoperative period

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INTRODUCTION

The statistics of the early and late postoperative periods of a totally replaced wrist joint with an unconstrained ceramic implant was presented in our previous study [1]. Survival of implants is an important temporal indicator of improvement in the patient's quality of life [2]. In the Russian-language literature, there are a limited number of articles on the results of wrist joint arthroplasty [3, 4]. Therefore, there are gaps in the coverage of the problem: there are no data on the survival of implants. Foreign journals and scientific books pay special attention to the issue of implant survival, but there are no data on the use of ceramic implants [6-15].

Purpose To evaluate the efficacy and survival of an unconstrained ceramic wrist joint implant.

MATERIALS AND METHODS

The surgeons of the Tsivyan Novosibirsk Medical Research Institute for Traumatology and Orthopedics performed more than 120 surgical interventions to replace the wrist joint by the time of this study completion. Eighty-three cases of surgical treatment were analyzed at long-term follow-up. The protocol of the local ethics committee for the study approval is dated January 17, 2023, extract number 002/23, meeting minutes number 001/23. We recorded all cases of repeated surgical interventions, their causes and their results. We evaluated the time of re-hospitalization and the result of revision surgery. The Kaplan – Meier curve allowed us to assess the survival of the components of the wrist endoprosthesis (EP). From 2011 to 2021, total wrist arthroplasty was performed in 81 patients with severe degenerative changes in the wrist joint who voluntarily agreed to surgical treatment and agreed to the proposed treatment plan. Two patients underwent surgery on two joints.

A retrospective uncontrolled cohort study was conducted. The hospitalized patients were divided into three groups, according to the etiological cause of the disease.

The RA group included patients with rheumatic diseases of the wrist joint. The Trauma group included patients with consequences of injuries and surgical interventions. The small AVN group included cases of dysplasia and osteochondropathy of the wrist joint.

All patients underwent radiographic examination before surgery, at the end of the surgery and at follow-up appointments. If patients complained of pain, MSCT of the replaced joint was prescribed to assess the stability of the endoprosthesis components. Once the cause of the re-appearance was revealed, we determined the scope of revision operations.

The evaluation of implant survival had two time-points: the first point corresponded to the primary wrist arthroplasty, the second point was the date of repeated surgical intervention. All re-operations were recorded in a table indicating the time elapsed since the first operation. The results were subjected to statistical analysis. Patients who did not seek reoperation continued follow-up examinations.

Statistical methods For binary indicators of sex, involvement of an endoprosthesis, arthrodesis, operations without a prosthesis, positive dynamics, the number, rates and 95 % confidence interval (95 % CI) of frequencies were calculated using the Wilson formula in groups. To quantify differences between the groups, odds ratios (ORs) were calculated with 95 % CI. Comparison was carried out by Fisher's exact two-sided test. The correction of the error in multiple comparisons in the achieved significance levels *p* was carried out by the Benjamini – Hochberg method (Table 1). To analyze the freedom from reoperations, Kaplan – Meier curves were constructed. Endoprosthesis survival tables were compiled with estimates of freedom and 95 % CI. Groups were compared using a generalized chi-square test.

RESULTS

The reasons for repeated referral were periprosthetic fractures, dislocation of the component, dislocation of the endoprosthesis, arthrofibrosis of the totally replaced wrist joint, hand mal-position (maintenance and fixation of the hand in a mal-position versus the initial state), and aseptic instability of components. According to the types of orthopedic care, we divided the revisions into three subgroups: EP exchange, arthrodesis, and soft tissue interventions.

Radiographic study methods allowed us to evaluate clinical manifestations described by patients at follow-up examinations. The position of the endoprosthesis components, peri-implant osteolysis, and design defects were assessed. In cases of instability of the EP components or disintegrity of the peri-implant bone tissue (periprosthetic fracture), the surgical intervention was implant exchange (EP exchange arthroplasty). If it was impossible to reinstall the endoprosthesis component, we performed total arthrodesis of the wrist joint (arthrodesis). We never found any mechanical destruction of the implant components. If instability of the endoprosthesis components was not detected, surgical assistance was release of the articular surface of the implant from scar tissues and tendon transfer to achieve a balanced position of the hand. Comparative indicators of the results of the re-interventions, causes of revision and the scope of surgical care in regard to gender and age are presented in Table 1. Table 1 also shows the quantitative indicators of each study group that were included in the diagrams of the presented material.

To estimate the time of the active EP functioning, each operation was marked on the time curve, where the starting point is the time of the operation (Fig. 1). Depending on the time elapsed from the moment of the first to the second operation, the time frames were calculated. Based on the fact that the initial state of the patients and the cause of the degenerative change of the wrist joint were different, the results were combined into a specific group of patients. Combining the results enabled to determine the group survival of the endoprosthesis (Fig. 2, 3, 4).

Table 1

Comparison between the groups RA, Trauma, AVN

Parameters	RA (n = 26)	Travma (n = 48)	AVN (n = 9)	Comparison	
	n, % [95 % ДИ]	n, % [95 % ДИ]	n, % [95 % ДИ]	OR [95 % CI]	Two-tailed Fisher test, p-level, correction
Sex, males	1, 4 % [1 %; 19 %]	28, 58 % [44 %; 71 %]	5, 56 % [27 %; 81 %]	RA vs. Tavma: 33.5 [4.7; 1475] RA vs. AVN: 0 [0; 0.4] Travma vs. AVN: 1.1 [0.2; 5.9]	RA vs. Tavma: < 0.001*, < 0.001* RA vs. AVN: 0.002*, 0.004* Travma vs. AVN: > 0.999, > 0.999
Implant exchange	1, 4 % [1 %; 19 %]	6, 12 % [6 %; 25 %]	1, 11 % [2 %; 43 %]	RA vs. Tavma: 3.5 [0.4; 170.6] RA vs. AVN: 0.3 [0; 28.2] Travma vs. AVN: 1.1 [0.1; 59]	RA vs. Tr.: 0.410, > 0.999 RA vs. AVN: 0.454, > 0.999 Travma vs. AVN: >0.999, > 0.999
Arthrodesis	0, 0 % [0 %; 13 %]	3, 6 % [2 %; 17 %]	0, 0 % [0 %; 30 %]	–	RA vs. Tr: 0.548, > 0.999 RA vs. AVN: > 0.999, > 0.999 Travma vs. AVN: > 0.999, > 0.999
Interventions on soft tissues	2, 8 % [2 %; 24 %]	9, 19 % [10 %; 32 %]	2, 22 % [6 %; 55 %]	RA vs. Tavma: 2.7 [0.5; 28.1] RA vs. AVN: 0.3 [0; 4.9] Travma vs. AVN: 0.8 [0.1; 9.3]	RA vs. Tr.: 0.309, 0.803 RA vs. AVN: 0.268, 0.803 RA vs. Tr.: > 0.999, > 0.999
Positive dynamics	26, 100 % [87 %; 100 %]	45, 94 % [83 %; 98 %]	9, 100 % [70 %; 100 %]	–	RA vs. Tavma: 0.548, > 0.999 RA vs. AVN: > 0.999, > 0.999 Travma vs. AVN: > 0.999, > 0.999

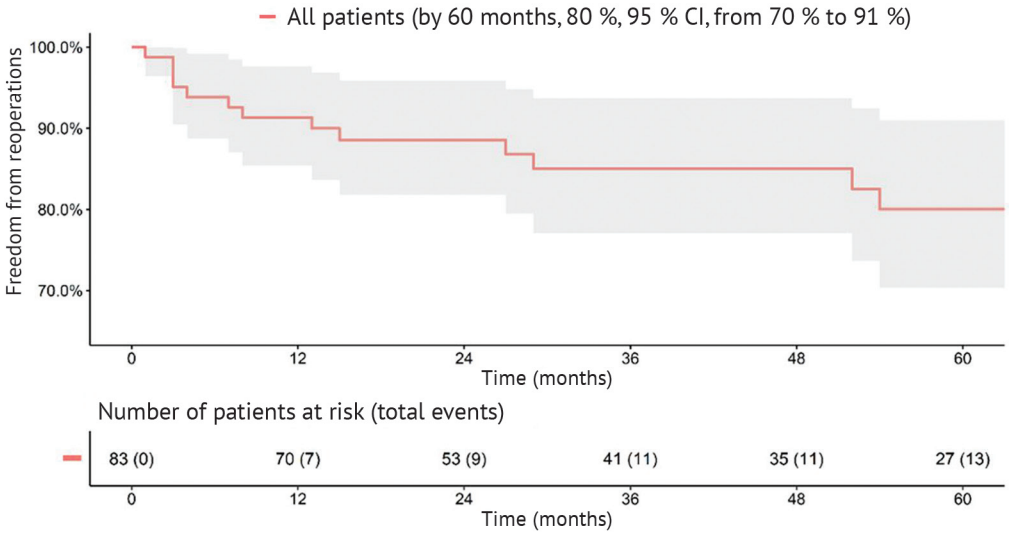

Fig. 1 Kaplan – Meier curve of freedom from reoperation in all patients

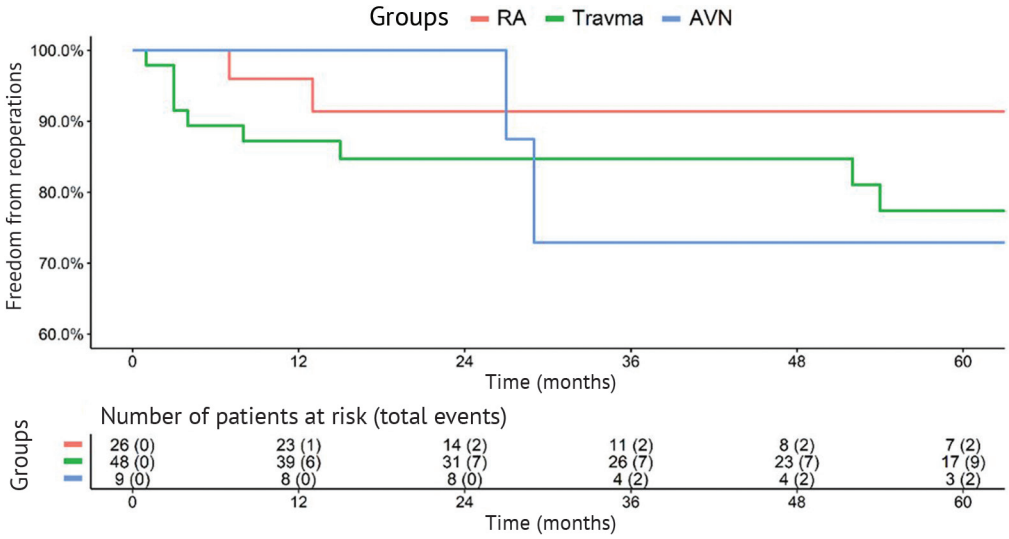

Fig. 2 Kaplan – Meier curve of freedom from reoperation risk in patients groups

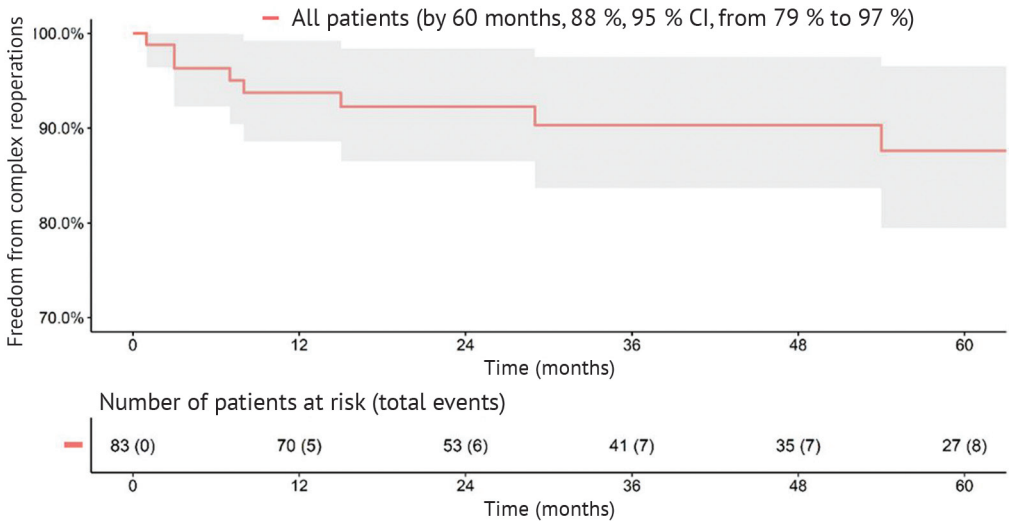

Fig. 3 Kaplan – Meier curve of freedom from reoperation risk with implant exchange in all patients

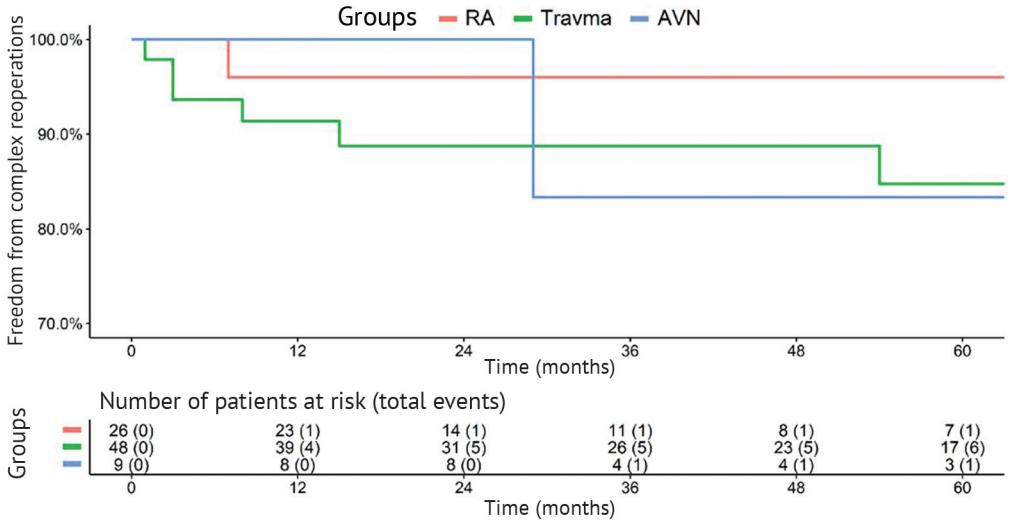

Fig. 4 Kaplan – Meier curve of freedom from reoperation risk with implant exchange in the groups

An important element of a satisfactory result of the restoration and preservation of the wrist joint motion is the interaction at all stages of orthopedic treatment with specialists from related fields. Rehabilitologists, rheumatologists and neurologists should be named among the main narrow specialists.

The assistance of rehabilitation specialists is an urgent need at the first stage of the postoperative period. A significant number of researchers point to the indispensability of the participation of rehabilitation specialists in the postoperative period. Controlled exercises for the joint assist in correcting wrong stereotypes of joint motion that persisted in patients over many years of illness [16-20]. The participation of rheumatologists is necessary for the selection of basic therapy, taking into account the common pathological mechanism of morphological changes in the joint [6, 17, 21]. The involvement of neurologists assists to correct the afferent-efferent connections of the upper limb what has a positive effect on the final result.

The reason for repeated surgical intervention in the RA group was the failure to compensate for the underlying disease. Clinical manifestations were reactive tendovaginitis of the flexor tendons of the fingers. Long-term reactive tendovaginitis aggressively affects the general well-being of the patient and the stability of the EP components. Such a pathological condition requires close interaction "rheumatologist-patient-traumatologist". In the initial stage of clinical manifestations, conservative correction of the pathological condition is possible. Primary total wrist arthroplasty is performed from the dorsal side, and upon the approach, synovectomy of the extensor tendons of the wrist and fingers is performed. It is for this reason that, in ineffective conservative treatment within a month, approach to the flexor tendons is necessary. A subtotal synovectomy of the flexor tendons of the wrist and fingers is required. It should be noted that the opening of the carpal tunnel with the release of the median nerve only is not enough. X-ray signs of instability of the endoprosthesis components are the basis for exchange of the components using bone cement.

After a total wrist replacement, it is very important for a person to return to social activities with an improved quality of life. There were cases when patients completely stopped feeling that the joint was subjected to the operation. Along with the positive characteristics after arthroplasty of the wrist joint, there were cases when the joint was subjected to an excessive physical activity. In a number of such cases, the performance of heavy physical labor limits the functionality of the operated joint in the absence of radiological signs of instability of the endoprosthesis components. Therefore, the attention of patients should be drawn to the fact that the joint replaced is an artificial one, and the force load on the joint should be limited.

In the group of patients with post-traumatic joint alterations, there were periprosthetic fractures, dislocations, and dislocations of EP components. Their reason was falling down on the involved arm. Despite the small size of the capitatum, it was necessary to exchange the distal component in several cases using the Pressfit method, followed by good osseointegration of the EP. Unfortunately, it was in this group that three cases were identified that ended in total arthrodesis of the wrist joint (Fig. 5).

Despite the small size of the AVN group, it should be noted that the greatest difficulties arose with the patients who were diagnosed with wrist joint dysplasia. The long-standing stereotype of movements minimized the efforts of rehabilitators and traumatologists. This group had instability

of the proximal EP component. During the revision surgery, individual components were exchanged using bone cement. Along with the implant component exchange, tendon transfer was performed to correct the position of the hand. The flexor and extensor tendons of the wrist underwent transposition that depended on the initial state of the hand. These measures were sufficient for stabilization and a long-term positive effect of the surgery.

The data obtained allow us to state that the survival rate of total arthroplasty with an unconstrained ceramic wrist joint implant was 88 %.

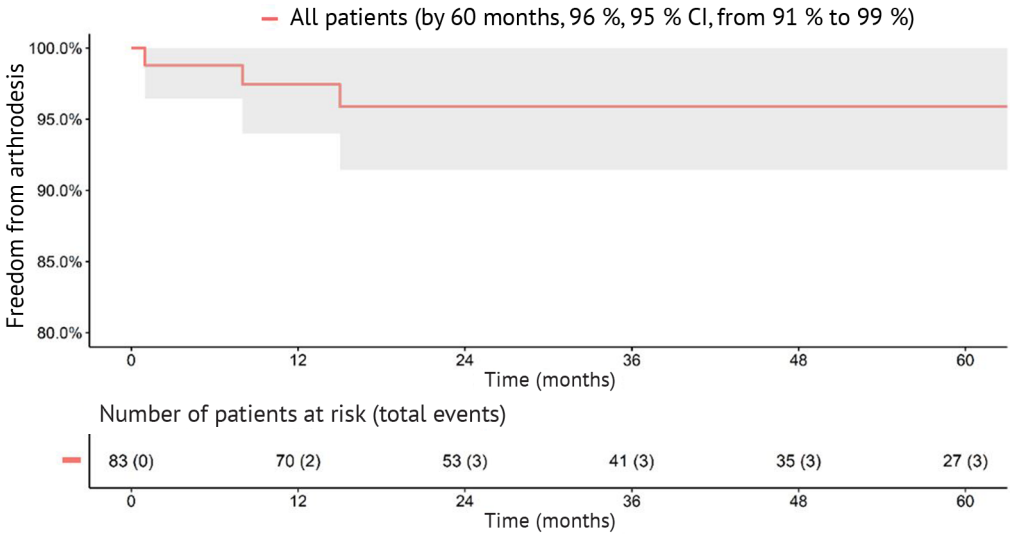

Fig. 5 Kaplan – Meier curve of freedom from arthrodesis in all patients

DISCUSSION

In the classical literature, the notion of the postoperative observation period has diverse characteristics. Many sources give the same names, but different time frames are implied. Scientific publications indicate time frames without explaining their meaning. A five- and ten-year assessment of the implant survival has been demonstrated [33-45]. We found the only definition of the postoperative period in the Big Medical Encyclopedia.

The postoperative period has two successive stages [5]. The immediate postoperative period begins from the completion of the operation and continues until the patient is discharged from the hospital. The late postoperative period runs outpatiently and is used for the final elimination of general and local disorders caused by surgical trauma.

In the Russian literature, there are no data on the survival of any types of wrist joint implants. In foreign publications, there is information about the complications of total wrist arthroplasty, reaching 35 %. Menon J reported a 33 % failure rate in wrist arthroplasty with Volz implants 40 months after implantation [6]. The failure rate in the study by Cooney et al. for the use of Meuli prostheses was 23 % after 5 years of follow-up [6]. Rademer et al. in 2003 revealed 80 % of poor results 52 months after implantation of APH endoprosthesis [46].

The rate of negative results described above is primarily associated with the search for the optimal shape and material for the implant. The rejection of the compromised implant attracted the designers to search for a new model. The negative effects of the tribological friction pair forced the search for modern materials for a new generation of endoprostheses. The demand for improving the quality of life and maintaining the mobility of the lost joint on the part of patients obliges researchers to look for the optimal shape and material.

The rate of positive results of ceramic endoprostheses in our study was 88 %. We did not find similar articles in terms of the chosen method of surgical treatment, devoted to the study of the survival of ceramic endoprostheses of the wrist joint, in the literature. We have made an attempt to interpret our results obtained in different time periods.

In joint arthroplasty, the foreign body in the human body is planned to be implanted for a long period of time. Dislocations, suppuration, persistence of pain and limitation of function, loosening of the endoprosthesis components are complication risks of joint arthroplasty [22-32]. These manifestations can occur at different times and for different reasons. Joint arthroplasty does not entail recovery, but only a long-term improvement in the quality of life.

Based on this thesis, the postoperative period is an important stage of observation and analysis. The results obtained by us are actually and statistically presented in Table 1. Their values were used in the graphs what allow us to determine the patterns that we propose for discussion.

Analyzing the literature data and the results of the study, we divided the orthopedic postoperative period into immediate (inpatient), early (up to 2 years), medium-term (from 2 to 8 years) and long-term (more than 8 years).

The immediate postoperative observation period is 6-8 days. It allows to regularly evaluate the postoperative suture, the position of the hand, radiological signs of the position of the components of the EP.

The early postoperative period must be distinguished due to possibility to detect disorders that can be corrected. In this time period, scar tissue is formed, the stereotype of movement in the replaced joint changes.

In the postoperative period from 2 to 8 years (mid-term), secondary changes in the components of the endoprosthesis may be observed. The most common symptom is periprosthetic osteolysis (aseptic instability). During this period, the social adaptation of patients has already been completed and patients use the hand without focusing on the artificial joint.

The long-term postoperative period serves one purpose: to determine the survival of EP.

This division of the postoperative period seems to us to be optimal and reasonable, unifying the notion of the implant function. This division allowed us to evaluate the results of the surgical method.

CONCLUSION

The results of the study demonstrate the positive dynamics in complex rehabilitation of patients after total wrist arthroplasty.

The analysis of the data obtained in the long-term period allows us to conclude that total arthroplasty with an unconstrained ceramic endoprosthesis of the wrist joint has a stable positive effect.

An eleven-year follow-up period demonstrates that the survival rate of an unconstrained ceramic wrist endoprosthesis is 88 %.

Due to insufficient literature data on this issue, there is a need to conduct further studies of the results of total wrist arthroplasty.

Conflict of interest *Not declared.*

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Biomechanics of the proximal interphalangeal joint after total joint replacement

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Abstract

Introduction Small joints arthroplasty of the hand including the proximal interphalangeal joint (PIPJ) is associated with the need to create anatomically adapted structures using optimal materials. Introduction of a new medical device requires comprehensive preclinical testing. **The objective** was to determine a range of loads allowed for the proximal interphalangeal joint after arthroplasty through analyzing the biomechanics to prevent critical conditions and complications. **Methods** A full-ceramic non-constrained anatomically adapted proximal interphalangeal joint implant was developed between 2016 and 2021 using an integrated approach with preclinical trials and a clinical study of 42 patients (25 males, 17 females) with PIPJ arthritis. A digital endoprosthesis was created with 3D-modelling. Critical conditions for the digital model imitating typical joint movements were explored with the use of finite element method and the findings to be employed in clinical practice. **Results** A stable biomechanical construct was intact with loads of 5 kilograms and a motion ranging from 0 to 60 degrees, with loads of 20 kilograms and a motion ranging between 0 and 30 degrees. Cortical bone could sustain loads up to 20 kilograms with a motion ranging between 0 and 60 degrees. Discussion Load capacity of the implant was explored considering the strength of bone tissue and zirconium ceramics as a material. The study set a vector for the development of the optimal mode of motor activity early after surgery and indicated the optimal range of motion to be applied after PIPJ arthroplasty. **Conclusion** The load up to 5 kg was optimal for the patient to be applied early after surgery with the range of flexion measuring less that 90°. The patient could use a load of 5 to 20 kg with flexion in the proximal interphalangeal joint measuring less than 30°. Endoprosthetic components were likely to get dislocated with a load of 20 kg and flexion angle of greater than 30°. Periprosthetic fracture could occur with flexion angle of greater than 60°.

Keywords: proximal interphalangeal joint replacement, finite element method, joints arthroplasty of the hand, digital modelling

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INTRODUCTION

Diseases and injuries of the proximal interphalangeal joint (PIPJ) including osteoarthritis of PIPJ occur in approximately 15.5 % of the population. Osteoarthritis of PIPJ is a degenerative disease that leads to a severe decrease in the quality of life, disability in various groups of population including those who are able to work in unavailability of adequate treatment [1, 2]. Arthrodesis in a functional position has long been the "gold standard" in the treatment of osteoarthritis of PIPJ providing reliable relief of pain and swelling, but the procedure is associated with restricted hand function [3]. Endoprosthetic replacement of PIPJ today is becoming the most preferred and promising solution for restoring the joint and the hand function. The procedure has evolved through a long evolution, starting from the 20^{s} of the last century and now PIPJ implants are presented in the form of constrained (silicone) and non-constrained constructs made of metal-polyethylene and pyrocarbon [4, 5].

Despite the diversity of products all implants have their own advantages and disadvantages affecting the inconsistent functional results of PIPJ arthroplasty [6]. In recent years, zirconium ceramics have attracted the attention of clinicians and medical reseachers. Major qualities of the material including wear resistance, biocompatibility and biointertness, corrosion resistance are perfectly employed in orthopedic and dental implantology. In the last decade, the first reports on the use of all-ceramic endoprostheses were published in the world scientific literature attracting the attention of hand surgeons [7, 8, 9]. World practice has been developing into personalized medicine, and endoprosthesis of small joints of the hand suggests an optimal design of anatomically adapted implants and the ideal material for the manufacture [10, 11].

Scientific and technological progress in medicine is characterized by new medical products entering the market, pharmacological drugs, treatment methods and technologies. An innovation goes through the thorny path of preclinical testing before being used by a wide network of medical institutions; in relation to various types of implants, these are toxicological studies on cell cultures, technical testing of samples in a laboratory certified in a specific field, preclinical

testing on laboratory animals and cadaver material [12].

Numerous reports on the severity of revision interventions during hand joint replacement initiated this digital study in order to protect the patient from additional physical and psycho-emotional injuries. Endoprosthesis of the PIPJ with non-constrained implants can be characterized by common complications including [13, 14]:

- dislocation in the implant;
- fracture of the stem;
- periprosthetic fracture of the phalanx.

The objective was to determine a range of loads allowed for the proximal interphalangeal joint after arthroplasty through analyzing the biomechanics to prevent critical conditions and complications.

MATERIAL AND METHODS

Forty-two patients with osteoarthritis of the PIPJ were examined by an orthopedic and trauma surgeon at the Samara State Medical University Hospital between 2016 and 2021. There were 25 male (59.5 %) and 17 female (40.5 %) patients with the mean age of 44 ± 2.71 years. The patients presented with pain, moderate swelling and severely limited movements in the PIPJ. The VAS scored 5 ± 1.4, and the average flexion in the PIPJ was 48.7 degrees. The patients underwent a comprehensive examination including collection of complaints and medical history, physical examination, radiography of the hand in two projections, and computed tomography (CT). 3D CT was performed for biomechanical examination of healthy and affected joints.

Dissection of 25 cadaveric hands was produced to explore the anatomy of the capsular-ligamentous apparatus of the PIPJ.

Based on the above research and analysis of the experience of foreign colleagues in the field of endoprosthesis of the PIPJ, the tendency to personalized medicine, we have developed the design of an all-ceramic unconstrained anatomically adapted endoprosthesis of the proximal interphalangeal joint (RF Patent for utility model No. 202476 dated 02/19/2021. Bull. No. 5) [15].

The product is a non-constrained endoprosthesis and is made of solid zirconium ceramics. The articular surfaces are made anatomically: the proximal component is represented by toroidal condyles and a groove between them, forming an arc of 210 degrees; the distal component has a concave surface, an ellipsoidal shape and a ridge antagonist of the groove in the middle. The design of the seating surfaces of the articular parts has two planes to ensure rotational stability with minimal resection of bone tissue. The stems have a conical shape and rounded at the tops for ease placement using the press-fit. The implant is presented in four sizes and supplied with a set of tools for placement. The endoprosthesis has undergone a full cycle of preclinical technical and toxicological tests: technical tests have been completed at the ANO Center for Quality, Efficiency and Safety of Medical Prescriptions, Moscow (Act No. 11/022.R-2021 dated November 10, 2021). Toxicological tests were performed in the physicochemical laboratory "Delma", Pushchino (program of toxicological studies of medical devices No. MI21-0208/02 dated August 2, 2021).

Medical science, which serves practical healthcare, involves the collective work of specialists of various specialties: doctors, design engineers, IT specialists, graphic designers. This effective tandem facilitates excellent results at the preclinical stage of research minimizing the risk of complications and other adverse events in clinical practice [16]. A database of CT scans in the DICOM format, 3D models generated with polygonal modeling, 3D sculpting, and automated modeling systems developed at the Institute of Innovative Development of SamSMU were used for the anatomical and biomechanical study of the PIPJ.

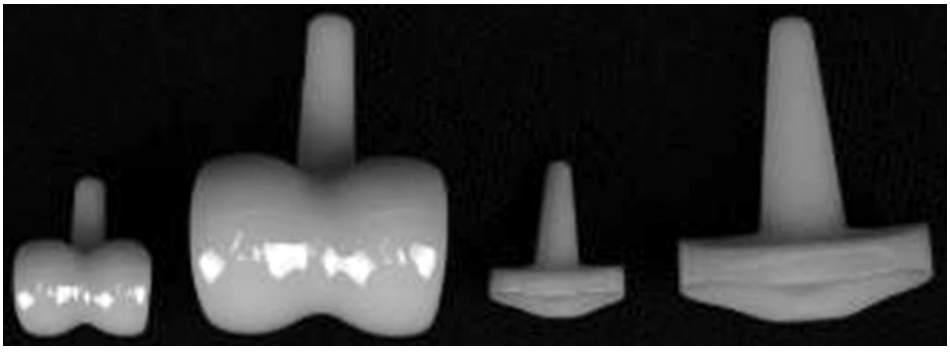

Fig. 1 All-ceramic, unconstrained, anatomically adapted proximal interphalangeal joint endoprosthesis, available in two sizes

ZBrush and Autodesk 3dsMax software systems were employed to obtain three-dimensional models of joints for a new endoprosthetic design. The finite element method was used for reproduction of critical conditions leading to complications. The finite element method (FEM) was the main method for analyzing the stress-strain conditions of the constructs, widely used in aircraft manufacturing, industry and construction. FEM is indispensable in the development of implants for orthopaedic use: it can be used to determine the effective loads on an endoprosthesis, a screw, plate, dental implant, etc. and on a musculoskeletal segment for prediction of the service life of the product at given loads and optimize the design at the preclinical stage. In this study, FEM was used in the Ansys software package [17, 18]. Major stereotypes were identified from a variety of hand movements and loaded as 3D models into the program. The ceramic properties presented in Table 1 were employed.

Table 1

Mechanical properties of ceramics

Property	Value
Density, g/cm^3	6
Average particle size, microns	< 1
Bending strength, MPa	900
Young's modulus, GPa	210
Vickers hardness, HV 0.1a	1200

Mechanical properties of cortical bone used to develop the digital model:

– Young's modulus 1.8 × 10^{10} Pa;

– tensile strength 146 MPa;

– specific gravity 1800 kg/m^3.

Cortical bone measurements were used for the digital model of PIPJ replacement using the Ansys software package, since modeling may suggest simplification and abstraction from the real scenario due to the complex reproduction of physiological and biomechanical processes in native bone. A solid model of the implant was integrated into the bone tissue, representing a biomechanical structure that was subjected to strength analysis. The purpose of the calculations was to analyze the stress of the construct, identify weaken areas in the bone and in the implant material to prevent destruction of the biomechanical components. Major stereotypes of movements were used to develop a digital finite element model which consisted of spherical gripping of objects with a flexion of 0, 30, 60 and 90 degrees in the PIPJ and compression of the object [19, 20]. The permissible working loads for joint flexion angles were determined based on the calculation of the stress condition of the biomechanical construct "implant – bone tissue".

Strength analysis was based on the finite element method. The biomechanical model was marked with Solid 45 finite elements with boundary conditions applied to the model: the bone tissue of the proximal phalanx was rigidly fixed along the surface of the end – the "rigid embedding" fastening, and forces were applied to the distal phalangeal element of the bone in the axial direction. The finite element model of the biomechanical construct is shown in Figures 2-5.

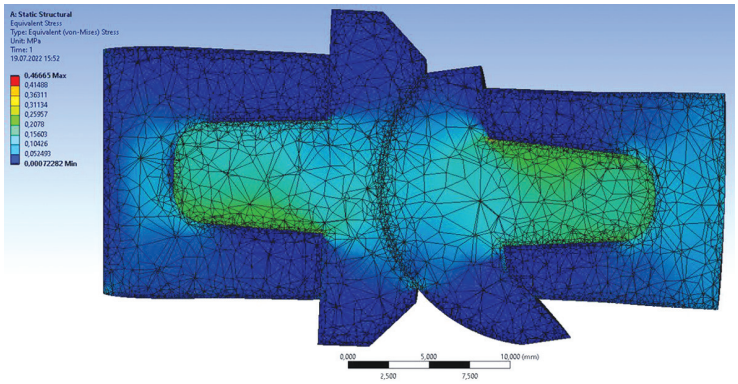

Fig. 2 Finite element model of an implanted PIP endoprosthesis. The model is shown with a load force of 1 kg with flexion of 0 in PIP 0º

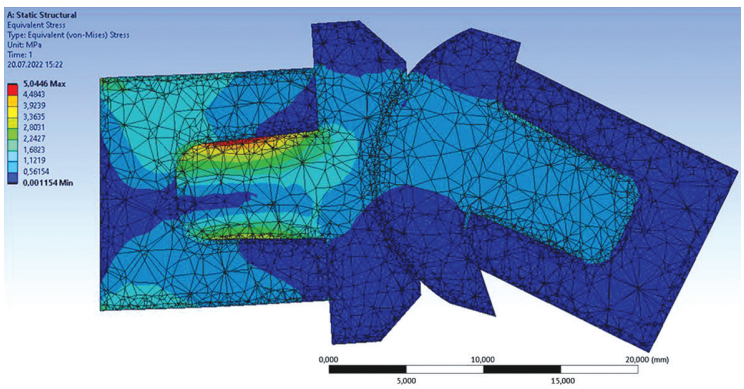

Fig. 3 Finite element model of an implanted PIP endoprosthesis. The model is shown with a load force of 5 kg. Flexion angle in PIP measuring 30º

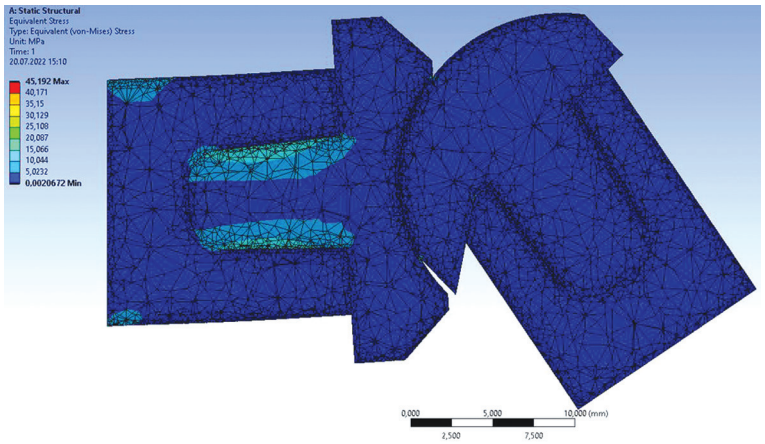

Fig. 4 Finite element model of an implanted PIP endoprosthesis. The model is shown with a load force of 10 kg. Flexion angle in PIP measuring 60º

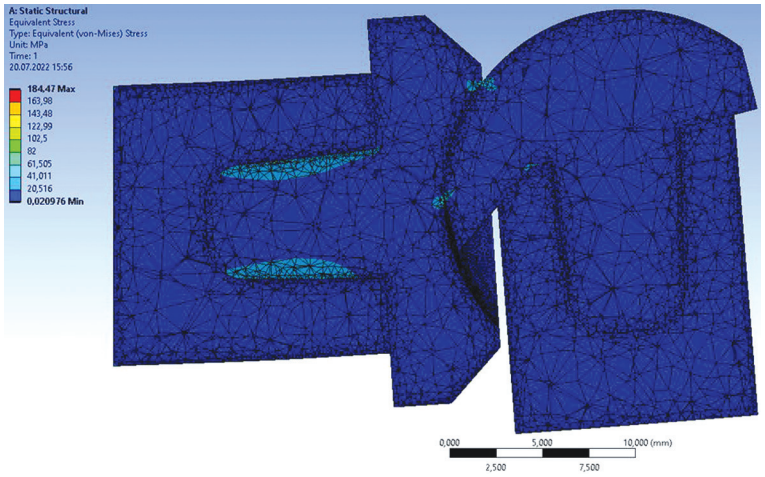

Fig. 5 Finite element model of an implanted PIP endoprosthesis. The model is shown with a load force of 20 kg. Flexion angle in PIP measuring 90º

Loading included a ball grip with a flexion of 0, 30, 60, 90 degrees in the PIPJ and compression of the object. The loads ranged between 1 kg and 20 kg. The magnitude of the load applied was chosen based on literature data showing the maximum loads at which critical conditions occurred in real clinical conditions [30]. For demonstration purposes, the figures show only one type of the load applied as an example.

The clinical picture and range of motion in the operated joint were evaluated in addition to digital modeling of critical conditions using the finite element method. Our series included 10 patients who underwent endoprosthesis of the proximal interphalangeal joint for post-traumatic arthritis; the maximum follow-up period was 6 months.

RESULTS

The correlation between stresses in bone tissue and the loads applied is shown in Figure 6.

Analysis of critical loads simulated in PIPJ showed:

– the stability of the biomechanical construct being not impaired at any flexion (0°, 30°, 60°), except 90° with a load of up to 5 kilograms;

– cortical bone tissue can withstand loads of up to 20 kilograms at any flexion (except for a flexion angle of 90°);

– the biomechanical construct remained stable at flexion of 0-30° with loads of up to 20 kilograms;

– the strength of the implant elements significantly (more than 2 times) exceeded the strength of the bone tissue in the "implant – bone tissue".

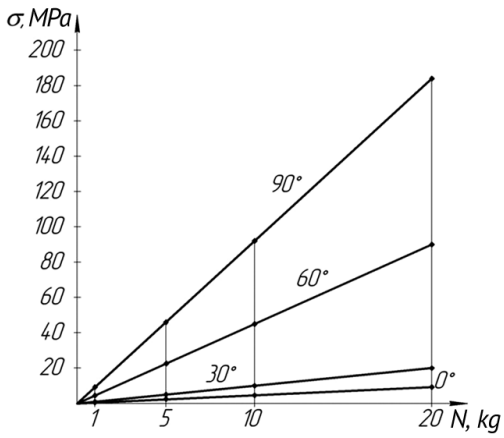

Fig. 6 Correlation between stresses in bone tissue and the loads applied

DISCUSSION

Trauma and orthopaedic surgery is a rapidly advancing and evolving branch of medicine with new methods of diagnosis and treatment of various pathologies being introduced daily. A number of technologies have changed the way that joint replacement surgeries are done: robot-assisted knee replacement has already become routine practice in the United States. Over 100,000 joint replacements are performed annually in Russia, and more than 90 % of the number include large joints: hip, knee, shoulder [21]. Modern lines of implants for large joints facilitate treatment of osteoarthritis of various stages, taking into account technical difficulties and patient comorbidity using arthroplasty as a routine, universal and absolutely accessible medical service [22, 23]. Despite the great successes achieved in surgery of large joints, replacement of small joints of the hand and foot fails to provide an optimistic picture. The complex geometry and biomechanics of the joints, the limited stock of bone and periarticular tissues, high demands placed on the hand by the patient make outcomes of hand joint replacement contradictory and debatable [24, 25]. The hand is one of the most complex organs with the largest representation in the central nervous system and high human demands. Restoring fine motor skills of the fingers, the need to perform strictly apportioned movements in everyday life is a real challenge for the team of specialists involved in the treatment of diseases and injuries of the hand. Finger replacement implant design continues to evolve as past implants have had variable success [26, 27, 28, 29]. An anatomically adapted PIP joint based on an analysis of biomechanics and radiological data from 42 patients with different degenerative diseases was simulated at SamSMU between 2016 and 2021. We simulated the biomechanics that occur in real clinical conditions in order to reduce the rate of complications associated with the use of endoprostheses. This is a pilot research in the industrial implantology in the Russian Federation.

Modeling of real biomechanics is essential to avoid critical clinical conditions and physical and psycho-emotional trauma. Simulation suggests an abstraction from the actual use of an endoprosthesis in a patient and gives us the opportunity to determine the boundary conditions for the use of the implant. The finite element analysis demonstrated the greatest stresses being experienced by the "implant – bone tissue" zones with the exception of the model having a flexion angle of 00 in the PIPJ. Greater stresses are observed at the flexion angle of 00 in the PIPJ of the endoprosthestic components. Bone tissue appeared to be the most loaded material and most susceptible to destruction. The prospects of the research can include the development of a "weak link" preventing bone destruction by stress concentrators introduced into the implant components. The endoprosthesis will be subject to destruction with the extreme loads.

Strength tests performed in patients after replacement of the proximal interphalangeal joint will be practical to avoid the risk of critical complications including dislocation of endoprosthetic components, fracture of the stem and periprosthetic fracture.

The digital model offered had drawbacks that were acceptable for experimental research and for the modeling process [30]. The Ansys software package could identify the implant as a simplified model to allow mathematical calculations and abstraction of the process from the real clinical scenario. The principle can be employed for complex preclinical trials with no clinical conditions provided at the stage. Nevertheless, we could achieve our goal and analyze the maximum loads on the implant measuring the strength characteristics of bone tissue and zirconium ceramics as a material. The study was aimed to develop an optimal mode of physical activity early after surgery and an optimal range of motion after PIPJ arthroplasty.

The interdisciplinary research is essential for developing a new endoprosthetic design using new materials and their combinations. We used the results of the study in the postoperative management of 10 patients with a maximum follow-up period of 6 months. Mathematically calculated loads allowed for 49 to 70 degrees of flexion achieved in the involved joint during rehabilitation. There were no complications associated with critical conditions of the endoprosthetic joint: fractures of the stem, periprosthetic bone fracture, joint instability.

CONCLUSION

A load of 5 kg or less applied early after surgery was shown to be optimal for the patient with flexion angle being 90° or less. The patient could use a load weighing 5 to 20 kg with the flexion angle of 30° or less in the proximal interphalangeal joint. The risk of endoprosthetic dislocation is greater with a load of 20 kg and a flexion angle of more than 30°, and a periprosthetic fracture can occur at a flexion angle measuring more than 60°.

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Doroganov S.O. – visualization, writing – editing.

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Original article

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Robot-assisted knee arthroplasty: first experience (a prospective randomized study)

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Abstract

Introduction Primary total knee arthroplasty has long been proven effective in the treatment of stage 3–4 knee osteoarthritis. It is well known that this intervention not only improves the quality of life, but also helps to restore the function of the joint and eliminate axial deformities. **Purpose** To compare early results of total knee arthroplasty using robot-assisted technology with conventional manual technique. **Materials and Methods** 20 patients diagnosed with stage 3 osteoarthritis of the knee joint and varus deformity of the knee joint axis were included in a prospective randomized study. Patients were divided into 2 representative groups, 10 subjects underwent robot-assisted knee arthroplasty, and the conventional manual technique was used in the other 10 patients. For clinical assessment, functional scales KSS, WOMAC, Lysholm Score were used, postoperative radiographs were evaluated. **Results** According to clinical functional scales, 10 days after surgery, there was an improvement in performance in the patients of both groups ($p < 0.05$); the duration of the operation in the patients of both groups did not differ in general; intra-operative blood loss in the group with robot-assisted arthroplasty was lower; and assessment of postoperative results by radiological imaging showed a better component positioning according to preoperative planning in the robotic group. **Discussion** When the operation is performed by experienced surgeons, one can expect the correct position of the components and the balance of the ligamentous apparatus in standard arthroplasty. However, the use of robot-assisted technology provides a secure intervention performance even at a hospital where a small number of such operations is performed. **Conclusion** Despite the high cost and the need for additional consumables, robot-assisted arthroplasty has a number of advantages over classical manual techniques. These advantages include: accurate restoration of the limb axis even in extra-articular deformities, correct position of the endoprosthesis components, reduction of intra-operative blood loss due to closed medullary canals, and safety for patients. However, the role of the surgeon in such operations remains paramount, as it is the surgeon who is responsible for planning the operation, performing it, and achieving soft tissue balance.

Keywords: robot-assisted arthroplasty, knee joint, osteoarthritis

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INTRODUCTION

Primary total knee replacement has long proven its effectiveness in the treatment of knee joint osteoarthritis in stages 3-4. It is well known that this intervention not only improves the quality of life, but helps restore joint function and eliminate axial deformities. About two million such operations are performed annually in the world [1, 2].

Robotic assistance in surgical interventions is a modern, actively developing area of scientific and practical studies, which covers many types of specialized surgical care for a variety of pathologies [3, 4, 5, 6]. Robotic surgery in surgical orthopedics was first described in 1993 [7]. In recent years, the use of robotic technologies in the treatment of diseases of the musculoskeletal system has received further development. The use of robotic assistance is considered one of the methods of knee replacement, in which the "robot arm" ensures resection of the femur and tibia and formation of the bone bed for the knee joint endoprosthesis under the supervision of a surgeon [8]. The operation of such a system includes two main stages [9]:

1) preoperative planning is performed on the basis of computed tomography data of the hip, knee and ankle joints with a preliminary calculation of the cutting angles of the bones to be resected, the size and position of the components;

2) bone resection with an active system (robot "arm") based on preoperative individual planning, implantation of endoprosthetic components and control of soft tissue balance under navigation control.

There are numerous publications in the literature in which the authors describe that the use of robotic assistance during implantation of an endoprosthesis helps to more accurately calculate the level of the distal femur and proximal tibia cuts, select the optimal sizes of the endoprosthesis components and align the mechanical axis of the limb under navigation control [10, 11, 12], which, in turn, ensures good balance of the ligaments [13, 14, 15]. The study of Hampp et al. showed that the accuracy of the bone cuts and positioning of the implant components in robot-assisted operations is higher compared to manual total knee arthroplasty [16].

Purpose: comparison of early results of robot-assisted knee joint arthroplasty with the conventional manual knee arthroplasty.

MATERIALS AND METHODS

A prospective randomized study was conducted from 03.04.2023 to 28.04.2023 at the Center for Bone and Joint Surgery of the St. Petersburg Research Institute of Phthisiopulmonology. The study included 20 patients diagnosed with stage 3 idiopathic osteoarthritis of the knee joint and varus deformity of the joint axis (varus deformity up to 8º was taken into account). The stage was determined according to the Kellgren-Lawrence classification. For the purpose of randomization, using a computer random number generator, patients were divided into 2 groups: ten patients underwent implantation of a knee joint endoprosthesis using robotic technology (group 1), 10 patients underwent joint replacement with standard manual technology (group 2). Patients in group 1 were informed about the advantages and disadvantages of robotic arthroplasty. The gender and age characteristics of the patients and clinical parameters of the knee joint function before surgery are presented in Table 1.

Table 1

Patients' data and knee functions

Parameter		Group 1	Group 2	p – value
Age, years , Me (Q1-Q2)		61.4 (48-72)	63.4 (47-75)	> 0.05
Males	Abs.	4	3	
	%	40	30	
Females	Abs.	6	7	
	%	60	70	
Left side	Abs.	5	6	
	%	50	60	
Right side	Abs.	5	4	
	%	50	40	
Implant type CR	Abs.	9	7	
	%			
Type of implant PS	Abs.	1	3	
	%			
KSS, points, Me (Q1-Q2)		60.5 (49-68)	59 (44-66)	> 0.05
Lysholm scale, Me (Q1-Q2)		57 (47-64)	56.5 (46-62)	> 0.05
WOMAC, points, Me (Q1-Q2)		31 (27-35)	33 (29-39)	> 0.05

The data presented in the table indicate the absence of statistically significant differences between the studied groups of patients and the possibility of subsequent correct analysis of the results obtained.

Preoperative preparation In the preoperative period, patients in group 1 underwent computed tomography of the hip, knee and ankle joints for preoperative planning of component sizes, calculation of the angles of deviation of the axis of the lower limb and final positioning of the components considering axis correction. Patients in group 2 underwent standard planning based on X-ray telescopic images.

Surgical technique All patients received antibiotic prophylaxis and administration of tranexamic acid according to a standard regimen before incision. All operations were performed by one surgeon. In all cases, a mechanical alignment philosophy was followed. Robot-assisted knee replacement also required the presence of an assistant to provide the computer part of the operation. The patients' limb was placed on a special fixator. Two pins with sensors for communication with navigation were installed in the distal femur and proximal tibia (Fig. 1).

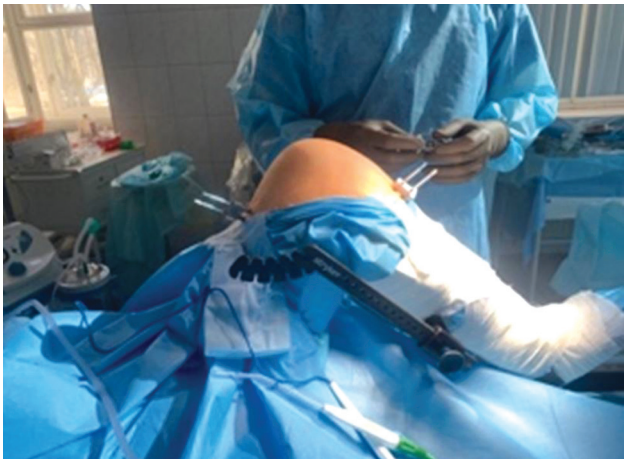


Fig. 1 Limb position with sensors for navigation

In all cases, a standard medial parapatellar approach was performed. Check points were installed in the area of the medial epicondyle of the femur and the medial part of the tibial tuberosity to synchronize data with the robot. Next, anatomical landmarks were registered with a comparison of the patient's 3D computed tomography model (Fig. 2).

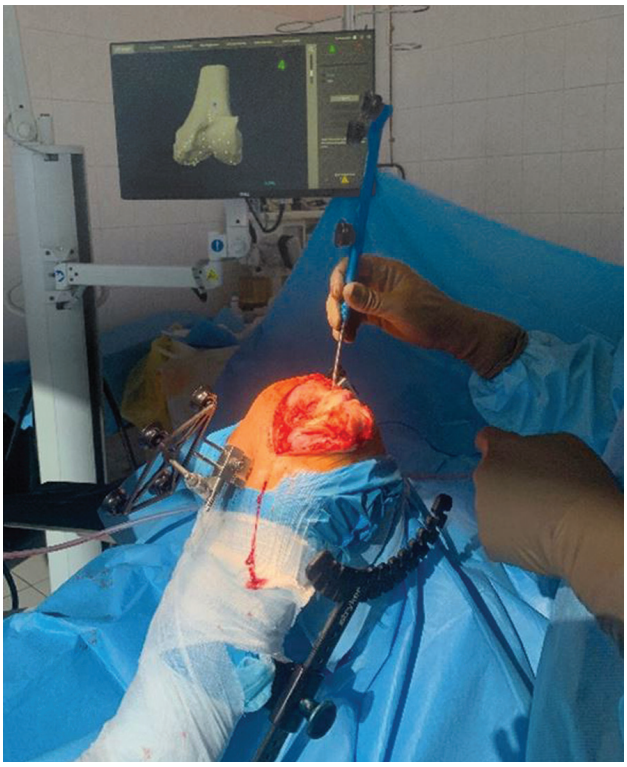


Fig. 2 Registration of anatomical landmarks

The next step was to position the robot's "arm" to make cuts of the femur and tibia. The cutting process was constantly shown on the monitor what was "unusual" when switching from the manual technique (Fig. 3, 4).

After cutting, the soft tissues were released; the tibial bed was processed for the endoprosthesis components, and the implant was installed using standard surgical techniques (Fig. 5).

Next, joint stability was assessed under navigation control and the tracking of the patella in the intercondylar groove was monitored (Fig. 6).

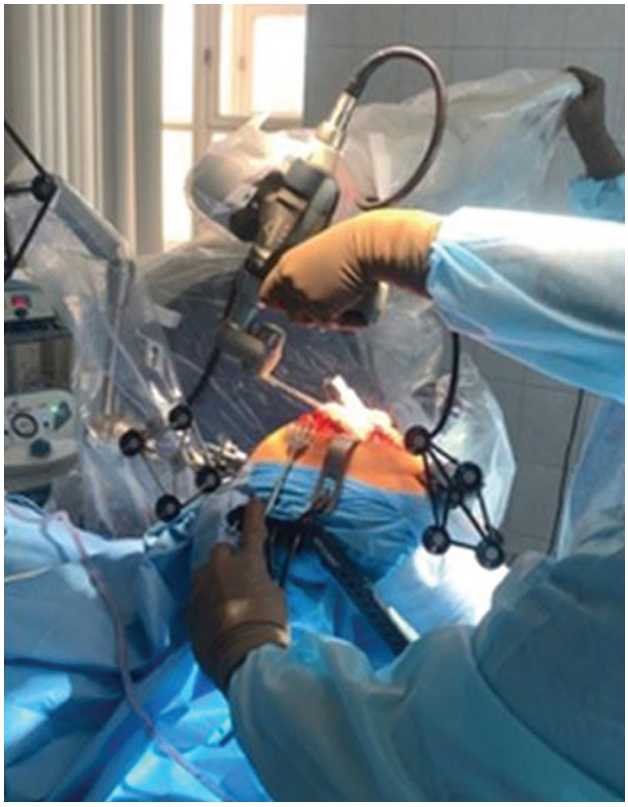


Fig. 3 Cutting of the distal femur

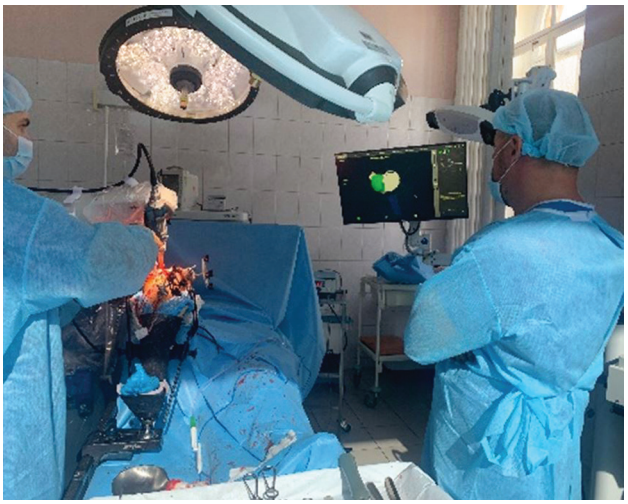
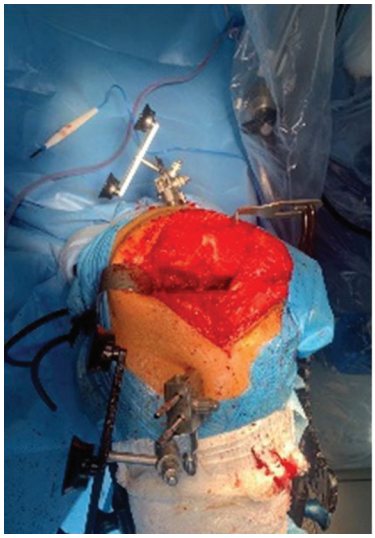


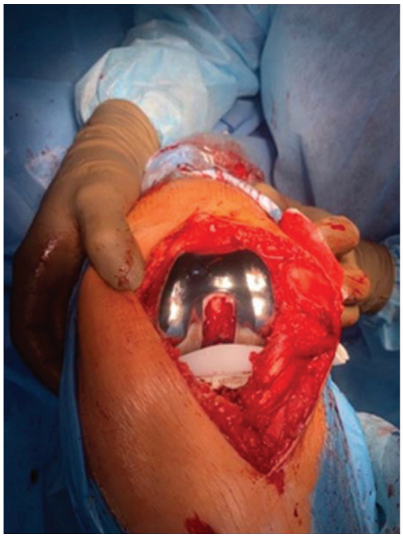
Fig. 4 Control of cutting on the monitor

In group 2, the conventional manual technique of knee arthroplasty using an extramedullary guide was performed. The postoperative period was similar in both groups, including the prevention of thromboembolic complications and a standard course of rehabilitation. The next day, radiographs were taken to monitor postoperative results and correctness of the installed components taking into account the restoration of the mechanical axis of the limb, the correspondence of the size of the components, and the possible filing of the femoral component into the anterior cortex. Patients were observed in the department for 10 days to assess early postoperative results.

Statistical analysis of the data obtained during the study was done in accordance with modern requirements of descriptive statistics in biomedical research [17]. We used specialized software: Statistica 13 and IBM SPSS® Statistics version 20.



a



b

Fig. 5 Intra-operative photo: *a* performance of the cut; *b* implant installed

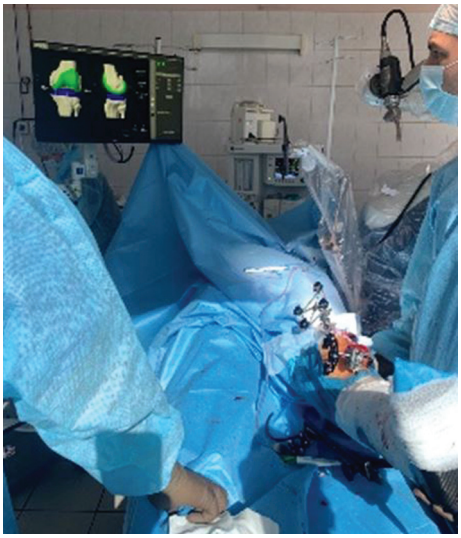


Fig. 6 Assessment of joint stability under navigation control

The normality of the distribution of quantitative characteristics was studied using the Shapiro-Wilk test; the distribution of the studied parameters was found to differ from normal. Therefore, further statistical analysis was carried out using nonparametric methods. The median (Me) and interquartile range (Q1-Q3) were calculated. For independent quantitative samples in study groups, determination of the significance of statistical differences in indicators using the nonparametric Mann – Whitney U test, differences were considered significant at $p \leq 0.05$. Comparison of indicators before and after treatment (dependent samples) was carried out using the Wilcoxon T-test; differences were considered significant at $p \leq 0.05$.

RESULTS

In both groups of patients, early postoperative functional results were comparable. The range of motion in the knee joint in patients of both groups increased significantly. In group 1, the results improved by an average of 20 points after analyzing Me indicators on the KSS scale on post-surgery day 10, on the WOMAC scale by 19.9 points, on the Lysholm scale by 18 points. In robot-assisted surgery, intra-operative blood loss was on average 60 ml lower, and the duration of the operation was 10 minutes longer on average. In control radiographs of patients in group 1, the position of the components fully corresponded to the preoperative planning, namely, the mechanical axis of the limb was restored, the dimensions of the implants corresponded to the anatomical dimensions of the bone in this location, and there was no "filing" of the femoral component. Among the patients of group 2, there was a slight filing of the femoral component into the anterior cortex in one case; the sizes of the components were selected correctly, but a residual varus of 2º was determined in 2 patients. Table 2 shows the dynamics of the studied postoperative parameters in both groups of patients.

Table 2

Postoperative parameters in both groups, Me (Q1-Q2)

Parameter		Group 1		p	Group 2		p – value
		Before surgery	After surgery		Before surgery	After surgery	
Knee range of motion	Flexion, degrees	108 (100-110)	127 (115-135)	< 0.01	111 (105-115)	126,5 (120-130)	< 0.01
	Extension, degrees	173 (165-175)	180 (180-182)	< 0.05	171.5 (165-175)	180 (180-180)	< 0.05
Varus deformity		5.3 (4-6)	0.8º (0-2)	< 0.01	4.5 (4-6)	1 (0-3)	< 0.01
KSS, points		60.5 (49-68)	81 (75-84)	< 0.01	59 (44-66)	76 (70-84)	< 0.01
Lysholm scale, points		57 (47-64)	77.5 (68-82)	< 0.01	56.5 (46-62)	73 (68-79)	< 0,01
WOMAC, points		31 (27-35)	10.1 (8-16)	< 0.01	33 (29-39)	13.3 (10-19)	< 0.01
Intra-operative blood loss, ml		250 (150-270)			310 (280-350)		< 0.05
Duration of intervention, minutes		75 (65-80)			65 (55-75)		> 0.05

DISCUSSION

Robot-assisted knee replacement has been actively introduced into orthopedic practice. Some authors believe that the advantages of using robots are leveled by the cost of consumables and the robot assistant itself [9]. After our clinical assessment, we observed comparable results in the increased range of motion and clinical outcome measures at 10 days. This, in our opinion, is explained by the fact that the operations were performed by one surgeon who has more than 100 similar operations per year and, accordingly, with one technique for working with soft tissues, as well as comparable patient parameters before surgery. It is evident that the assessment of the results after 10 days is preliminary in nature and does not present a complete picture of the function. This suggests the need for more in-depth studies.

According to some published data, the use of robots significantly increases the duration of the operation, and thereby the intra-operative blood loss may also increase [14]. Our data show that the volume of blood loss was insignificantly but reliably lower in the group of robotic assistance. In our opinion, this is due to the preservation of closed intramedullary canals during surgery, which can be a source of bleeding during the surgery. This will likely have a positive effect on the patient's future life due to the importance of preserving red bone marrow in the metaepiphysis of the bones and yellow bone marrow in the medullary canal. In some situations, maintaining closed medullary canals is extremely important if consequences of inflammatory processes remain present. It should be noted that robot-assisted knee replacement allows increasing the accuracy of implant positioning and limb alignment in case of extra-articular limb deformities [18, 19], as well as reducing iatrogenic damage to periarticular soft tissues [20].

As for the duration of the operation, it was comparable between the study groups. Additional time is spent on installing navigation sensors on the thigh and lower leg; however, in our opinion, the operating time should be

counted from the moment the incision in the knee joint area is made. No time is wasted on determining the size of components and their position (especially rotation), given that all this is performed at the preoperative planning stage.

It is clear that if the operation is performed by experienced surgeons, one can expect the correct position of the components and the balance of the ligamentous apparatus even in standard replacement; however, the use of robot-assisted technology ensures patient's protection even in the hospitals with a small number of similar operations. This is confirmed by our results of postoperative radiation control.

Additional advantages of robot-assisted technology include the possibility of correcting cuts, location of components and, accordingly, balance at any stage of the operation, as well as a certain safety for soft tissues, taking into account the shutdown of the blade in deviation from the specified parameters of the bone location.

CONCLUSION

Robot-assisted knee replacement, despite its high cost and the need for additional consumables, has a number of advantages over conventional manual techniques. Such advantages include accurate restoration of the limb axis even in extra-articular deformities, correct position of endoprosthetic components, reduction of intra-operative blood loss by preservation of closed medullary canals, and safety for patients. However, the role of the surgeon in such operations remains paramount, since it is the surgeon who is responsible for planning the operation, its execution and achieving soft tissue balance. Among the shortcomings of robotic assistance are the additional radiation exposure of the patient due to preoperative computed tomography, additional expensive equipment in the operating room, which also significantly reduces the working space for medical personnel.

Conflict of interest *The authors declare that there are no obvious or potential conflicts of interest related to the publication of this article.*

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Informed consent *Patients gave their voluntary written informed consents.*

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The effect of previous surgical treatment on the outcome of total hip replacement in young patients with dysplastic coxarthrosis

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Abstract

Introduction Hip dysplasia of various genesis is recognized as a common cause of coxarthrosis. Total hip replacement (THR) is the operation of choice for the patients with the final stage of the pathological process. There are different opinions on the impact of previous surgical treatment of hip dysplasia on THR. **The aim** of the study was to explore the effects of previous surgical treatment on the outcomes of THR in young patients with dysplastic and secondary coxarthrosis. **Material and methods** Surgical outcomes of 78 patients (58 females and 20 males; 91 joints) with dysplastic and secondary coxarthrosis (age 14-30 years, average age 24.3 ± 4.3 years) treated witrh THR were retrospectively reviewed. Patients were assigned to two groups. Group I (control) included 27 patients (33 joints) with dysplastic coxarthrosis primarily treated with THR. Group II (treatment group) included 51 patients (58 joints) who had previously undergone THR. **Results** Patients of group II demonstrated longer duration of surgery by 47.89 %, greater blood loss by 16.92 % and the higher complication rate by 42.1 %. **Discussion** The treatment group showed a significantly increased frequency of late complications in the form of implant instability. Patients of group II demonstrated better functional results estimated with HHS as compared to the outcomes of patients of group I. **Conclusion** Hip reconstructions performed earlier were associated with technical difficulties, aggressive THR procedure, a greater risk of late complications, but showed no significant effect on the outcomes.

Keywords: coxarthrosis, hip dysplasia, organ preservation surgery, osteotomy, total hip replacement

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INTRODUCTION

Hip dysplasia of various origin is recognized as a common cause of coxarthrosis. J. Aronson (1986) reported 76 % of secondary coxarthrosis caused by the initially distorted articular surfaces [1]. Total hip replacement (THR) is the operation of choice at the final stage of the pathological process in this cohort of patients. According to the literature, surgical intervention for dysplastic coxarthrosis is associated with greater trauma and a higher complication rate of arthroplasties performed for idiopathic coxarthrosis [2]. This is due to a loss of acetabulum bone, deformation, abnormal femoral anatomy, proximal dislocation of the femur and severe changes in the periarticular soft tissues [3, 4]. There are different opinions on the impact of previous surgical treatment of hip dysplasia on THR. Several authors report greater technical difficulties, aggressive intervention, higher complication rate and worse treatment outcomes [5, 6, 7]. Possible causes include changes in the acetabular orientation, deformity of the proximal femur and scars in the periarticular soft tissues. Other authors suggest no association between previous reconstructions and greater rate of complications and revisions [8, 9].

The objective was to explore the effects of previous surgical treatment on the outcomes of THR in young patients with dysplastic and secondary coxarthrosis.

MATERIAL AND METHODS

The work is a single-center retrospective study. An analysis of the results of surgical treatment of 78 patients (58 women and 20 men) (91 joints) with dysplastic and secondary coxarthrosis treated with total hip replacement at the National Medical Research Ilizarov Centre for Trauma and Orthopaedics between 2005 and 2020. Indications for THR included severe pain or the need to improve ambulation and daily physical activity. Inclusion criteria included stage III dysplastic coxarthrosis, developed as a result of hip dysplasia, age under 30 years. Exclusion criterion included age over 30 years. The mean age of the patients at the time of surgery was 24.3 ± 4.3 years (range, 14-30 years). There were 7.7 % patients aged under 18 years. Patients we assigned to two groups. Group I (control) included 27 patients (33

joints) with dysplastic coxarthrosis primarily treated with THR. Group II (treatment group) included 51 patients (58 joints) who had previously undergone THR. More than one hip surgery was performed for 28 cases. The groups showed no significant differences in gender and the mean age (Table 1). The patients aged under 18 years were included in group II. Severe hip pain was recorded in the patients of group I and was associated with physical activity. Preoperative Harris hip score (HHS) [10] scored 31.6 ± 1.8. The VAS pain syndrome scored 8.4 ± 0.14 [11]. Most patients used additional means of support (n = 24, 72.7 %). The relative shortening was more than 3 cm in 4 observations.

Severe pain associated with physical activity was observed in patients of group II. Preoperative HHS scored 36.5 ± 0.8. The VAS pain syndrome scored 8.30 ± 0.08. In this group, limited ROM was noted in all planes. Twenty-one patients (36.2 %) used a cane. The relative shortening measured more than 3.2 cm in 32 observations (55.2 %). Hip joints graded with the Crowe classification [12] are presented in Table 2.

More severe anatomical disorders caused by the hip displacement were observed in group II (Table 2). Patients in both groups underwent THR. For bilateral involvement, the procedures were performed at intervals of 4 to 6 months. Cementless THR was used for patients of group I. Cementless THR was performed for 49 (84.5 %) cases of group II. Hybrid fixation with cementless cup and cemented stem was used in nine patients.

Medical documentation was reviewed for technical and surgical details, postoperative care, errors and complications and mid-term treatment results. HHS and VAS were used to assess the outcomes. Statistical data processing was performed using the Attestat computer program, version 9.3.1 (certificate of registration No. 2002611109 with Rospatent). Data were presented as the mean and standard deviation. The Mann – Whitney test was used to test statistical hypotheses about differences in pairwise comparisons between the groups. The data were considered statistically significant at $p < 0.05$. The study was carried out in accordance with the ethical standards of the Declaration of Helsinki (as revised of October 2013), approved by the ethics committee (protocol No. 4 (68) of November 11, 2020). Voluntary informed consent was obtained from all patients for publication of the findings without disclosing the identity.

Table 1

Comparative characteristics of patients

		Gender		Age			
		male	female	Less than 18 years	19-30 years	mean	median
Group I	abs.	10	23	–	33	23.5 ± 3.6	24
	%	30.3	69.7	–	100		
Group II	abs.	17	41	7	51	24.2 ± 4.2	25
	%	29	70.6	12	43.2		

Table 2

Distribution of hip joints with dysplastic coxarthrosis graded with the Crowe classification

		Crowe type				Всего
		I	II	III	IV	
Group I	abs.	16	8	4	5	33
	%	48.5	24.2	12.1	15.2	100
Group II	abs.	13	24	11	10	58
	%	22.4	41.4	19.0	17.2	100

RESULTS

Anterolateral surgical approach was used in most cases. A posterior approach was used in four cases of group I (12.1 %) and in five cases in group II (8.6 %) with type IV involvement. Additional surgical interventions and complications of THR seen in 78 patients with dysplastic coxarthrosis are shown in Table 3. Acetabular plastic surgery was common for patients of group I (Fig. 1). There were more additional corrective hip surgeries in group II (Fig. 2). Shortening osteotomy was performed in one case of group I (3 %) and in four cases (6.9 %) of group II due to severely dislocated femoral head. Intraoperative complications in the groups were recorded in 4 (10.85 %) cases. They were more common for patients of group I. Intraoperative complications developed in 9.15 % (3/33) of group I and in 1.7 % (1/58) of group II.

Table 3

Surgical options and complications of THR in patients with dysplastic coxarthrosis

Description	Group I (n = 33)		Group II (n = 58)	
	abs.	%	abs.	%
Standard approach	29	88.0	53	91.4
Acetabular plastic surgery	10	30.3	10	17.2
Shortening/corrective osteotomy of the femur	1/1	6.1	4/6	17.2
Fracture of the femur	2	6.1	1	1.7
Acetabular fracture	1	3.05	0	0
Neurological disorder	1	3.05	1	1.7

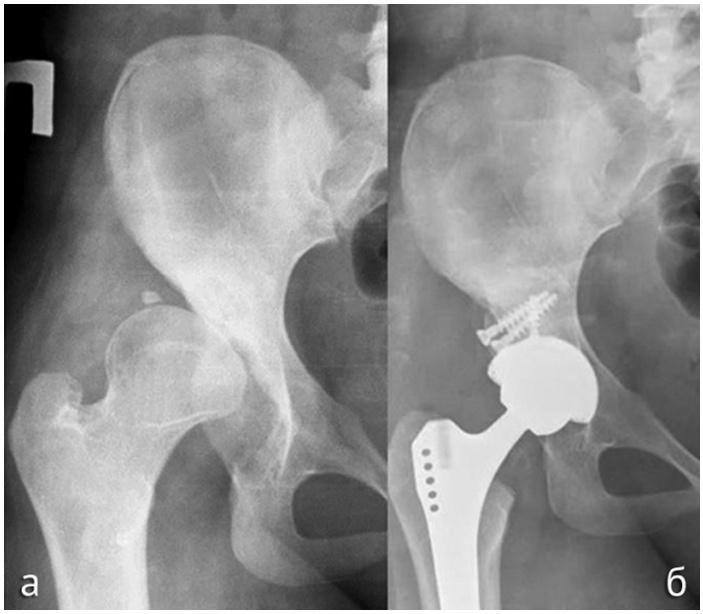

Fig. 1 AP view of the right hip joint Crowe type III in a 17-year-old patient: (a) prior to THR; (b) THR performed, acetabular roof plastic surgery, fixation with screws

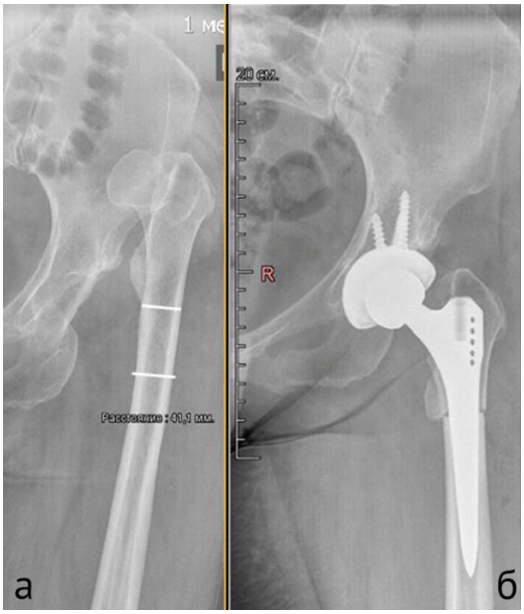

Fig. 2 AP view of the left hip joint Crowe type IV in a 29-year-old patient: (a) prior to THR; (b) THR performed, shortening subtrochanteric osteotomy of the proximal femur

The operation time was significantly longer in group II (Table 4), which was associated with severe anatomical disorders (Table 2). The operation protocols indicated a significant increase in the mean intraoperative blood loss in group II. There was a significant decrease in RBC in both groups after three postoperative days (Table 5). There was also a more pronounced decrease in hemoglobin levels. No statistically significant differences were observed in preoperative and postoperative parameters of both groups. Packed red blood cell transfusions were used postoperatively for two (6 %) patients in group I and 11 (19 %) patients in group II to treat anemia. The length of hospital stay was highly variable with the average length of stay being 30 % longer in group II as compared to group I (Table 4). HHS was used to evaluate short-term results within the period of six months. The mean HHS measured 91.4 ± 1.1 in group I and 93.6 ± 0.4 in group II. No poor outcomes were recorded. Long-term outcomes were assessed over a period of 2 to 17 years with the mean of 8.2 ± 1.7 years. The mean HHS measured 90.4 ± 1.4 with the VAS being 1.00 ± 0.06 in group I. The mean HHS measured 89.6 ± 1.3 with the VAS being 0.9 ± 0.08 in group II. Poor outcomes were observed in nine joints with implant instability diagnosed at a long term (after 4 years). Periprosthetic joint infection developed in one case of group II. A recurrent dislocation was seen in one patient of group I. Implant instability was associated with trauma in two cases of group II. Aseptic instability of the femoral component was diagnosed in five cases. The frequency of late complications and poor outcomes was higher in patients of group II (Table 6). There was no difference in the proportion of good and excellent results in the groups.

Table 4

Comparative characteristics of the groups

Description		Group I (n = 33)	Group II (n = 58)	Mann – Whitney U test
Duration of surgery, min.	mean	78.3 ± 4.3 (35-170)	115.8 ± 5.7 (35-275)	U = 574.5; p < 0.05
	median	70	105	
Duration of inpatient treatment, days	mean	17 ± 1.1 (9-42)	21.9 ± 1.3 (9-74)	U = 732.5; p = 0.05
	median	14	18	
Blood loss, mL	mean	413.6 ± 19.3 (200-1300)	483.6 ± 22.1 (100-1200)	U = 756.5; p < 0.05
	median	350	400	

Note: differences being significant at $p \leq 0.05$.

Table 5

Dynamics in RBC measured in 78 patients with dysplastic coxarthrosis

Description		Group I	Group II	Mann – Whitney U test
RBC, 10^{12}/л	pre-op	4.6 ± 0.1	4.4 ± 0.06	U = 790.5; p > 0.05
	post-op	3.5 ± 0.1	3.4 ± 0.06	U = 770; p > 0.05
HGB, г/л	pre-op	130.9 ± 3.6	129.2 ± 1.8	U = 747; p = 0.05
	post-op	103.2 ± 3.3	102.1 ± 1.7	U = 840.5; p > 0.05
HCT, %	pre-op	39.5 ± 0.7	37.8 ± 0.58	U = 774; p > 0.05
	post-op	32.44 ± 0.9	29.8 ± 0.6	U = 742.5; p > 0.05

Note: differences being significant at $p \leq 0.05$.

Table 6

HHS measured in 78 patients (91 joints) at a long term

Outcome	Group I		Group II	
	abs.	%	abs.	%
Excellent	26	78.8	42	72.4
Good	2	6.1	9	15.5
Fair	3	9.0	1	1.7
Poor	2	6.1	6	10.4
Total	33	100	58	100

DISCUSSION

THR performed for patients with dysplastic coxarthrosis is associated with technical difficulties due to affected articular surface anatomy, lack of bone tissue, shortened periarticular muscles and hip dislocation. This increases the risk of intraoperative and postoperative complications and worsens the treatment outcome in comparison with arthroplasty performed for primary coxarthrosis [13, 14, 15, 16]. V. Sakellariou (2014) reported inferior clinical and functional outcomes in patients with dysplastic coxarthrosis treated with THA as compared with those in patients with primary hip osteoarthritis [17]. This form of hip osteoarthritis can be caused by a congenital pathology or an articular disease of childhood treated either conservatively or surgically. The treatment seeks to restore articular relationships, stabilize the hip joint, improve the limb function and prevent early arthritis.

There are different opinions on the effect of previous pediatric and adolescent hip surgeries on subsequent arthroplasty. Several authors report greater technical difficulties, aggressive intervention, higher complication rate and inferior treatment outcomes [18]. Possible causes include changes in the acetabular orientation, deformation of the proximal femur and scars in the periarticular soft tissues [19, 20].

Prolonged operative time and substantial postoperative blood loss were reported in patients who had previously undergone interventions on the articular components [21, 22]. Patients could be at higher risk for intraoperative fractures of the articular components [2, 14]. Ferguson G.M. (1994) reported 23 % cases of intraoperative complications [23]. N. Boos (1997) reported a high level (8.1 %) of late infectious complications in patients who had undergone a previous hip surgery [7]. WH Rijnen reported the adverse event encountered in 12.5 % of the cases [24]. Previous pelvic osteotomy could suggest a greater risk of implant loosening with the incidence ranging between 7 and 23 % [2, 24]. C.L. Peters (2001) reported a greater dysfunction in young patients who underwent THA after a failed innominate osteotomy

evaluated with the HHS [25]. According to the opposite opinion, previous reconstructive operations on articular components were not associated with higher complication rate, revision interventions and inferior outcomes of arth roplasty [8, 9, 26, 27, 28, 29]. Supporters of the opinion suggested an increase in the operating time and technical complexity of the procedure in this cohort of patients.

The cohort of patients included young individuals aged under 30. Arthritis progressing after reconstructive operations in the third decade of life could be associated with an inadequate volume and inconsistent surgical option, and technical surgical errors. Repeated surgical interventions had a role and added to the inherent anatomy and functionality of the joint. Medical records indicated greater technical complexity and morbidity related to THR patients of the treatment group as compared to the controls. There were concerns of increased operating room time, increased blood loss, and extended patient length of stay at the hospital. The frequency of intraoperative complications was nearly identical in the comparison groups. Standard approach was used in the majority of cases. A greater proportion of hip surgeries was performed in the treatment group. Acetabular plastic surgery was common for the comparison group.

Higher rate of late complications in the form of implant instability was observed in the treatment group. The proportion of good functional results measured with the HHS was higher in patients of group II as compared with the outcomes of group I. To a certain extent, the data obtained contradict to the findings observed by C.L. Peters who reported a significant deterioration in the clinical outcomes after a previous pelvic osteotomy in THR patients with similar radiological parameters [25].

This work has limitations due to a small number of patients in the treatment and control groups, short follow-up periods, which does not allow an objective assessment of the survival rate of the THR in the cohort of patients.

CONCLUSION

Previous hip reconstruction procedures increase the technical complexity and aggressiveness of subsequent THR contributing to a greater risk of late complications and having no significant impact on the outcomes.

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Kaminsky A.V. – formal analysis.
Fozilov Dzh.T. – data collection, preparation of work for publication, writing – initial draft.

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Clinical evaluation and accuracy of mechanical axis alignment in robotic total knee arthroplasty

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Abstract

The first experience in robotic total knee arthroplasty (RoTKA) has been obtained resulting in the questions about clinical efficiency and accuracy of lower limb alignment. **Objective** To clarify clinical evaluation and accuracy of alignment of the mechanical axis of the lower limb in RoTKA. **Materials and methods** Twenty-nine patients with osteoarthritis of the knee of Kellgren-Lawrence stage 3-4 underwent RoTKA. The knee joint was assessed with VAS, WOMAC, FJS-12; the range of motion was measured. The changes in the axis of the lower limb were evaluated on the full limb length radiographs. **Results** Pain before the surgery according to VAS was 5.8 ± 1.5 points, on the first day after the surgery it was 8.5 ± 1.4, on day 3 – 5.9 ± 1.2, on day 12 – 2.9 ± 1.1. The range of motion on the first day after the surgery was 99.5° ± 1.4°, three months later – 115.1° ± 1.1°, six months later – 125.6 ± 1.5°, one year later– 127.5 ± 1.6°. The WOMAC score before the surgery was 32.7 ± 3.3, after the surgery 25.1 ± 2.1, three months later 7.3 ± 1.3, six months later 2.8 ± 0.2, and after one year – 1.3 ± 0.5. The FJS-12 score 3 months after the surgery was 68.2 ± 4.1, after 6 months 80.3 ± 2.9, after one year 94.0 ± 2.1. The analysis of postoperative full length roentgenograms in 72 % of cases (n = 21) did not reveal any deviation of the mechanical axis from the planned one and in 28 % of cases (n = 8) the deviation of the mechanical axis was up to 1° from the planned one. **Discussion** Neither technical difficulties nor complications inherent to RoTKA were found. According to the results of VAS, WOMAC and FJS-12 questionnaires, and the assessment of the range of motion, a positive dynamics was observed. According to the results of tele-roentgenograms, there was alignment of the limb axis and the accuracy of the position of the endoprosthesis components. **Conclusion** The study of this technology has demonstrated safety, accuracy of alignment of the mechanical axis, validity of indications and contraindications, and stable early clinical results.

Keywords: knee joint, robot, total knee arthroplasty, robotic total knee arthroplasy

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INTRODUCTION

Osteoarthritis is a chronic progressive disease that affects the joints and is characterized by degeneration of articular cartilage, structural changes in the subchondral bone and synovium [1]. Gonarthrosis (osteoarthritis of the knee joint (OAKJ) is a lesion of the knee joint, which manifests itself with pain, restriction of knee motion and axial disorders of the lower limb, leading to an impairment in the quality of life of the patient [2, 3]. Approaches to its treatment depend on the stage of the disease. The most common clinical and radiological classification was developed by Kellgren JH and Lawrence JS (1957), in which the authors proposed to distinguish four stages of the disease [4].

Gonarthrosis in stage 3-4 (K-L, 1957) is an indication for total knee arthroplasty (TKA) after failure of complex conservative therapy. This surgical intervention can relieve pain, eliminate deformity, restore the range of knee motion and quality of life [2, 3, 5-8].

The conventional (manual) technique of primary TKA is based on the use of an intra- and extramedullary guider. Its accuracy decreases in the absence of movements in the knee joint; rough extensive scars adhered to the underlying bone; ankylosis of the knee joint in the absence of pain; a history of previous injuries [9]. In gross deformities of the femur and tibia, anatomical landmarks change and make the alignment of the implant difficult. In such cases, computer navigation is used, but it is not feasible in ankylosis and severe contracture of the hip joint [10].

More than 20 years ago, robots were introduced into the clinical practice of arthroplasty to solve the problems of primary TKA. There are 2 groups of them: semi-active orthopaedic robots or surgical systems that help restore the axis of the lower limb by determining the levels and angles of corrective resections of the femur and tibia, but the resection itself is performed by the surgeon; and active orthopedic robots that perform resection autonomously according to the preoperative plan while the surgeon only controls the process. Autonomous work is visually controlled by the surgeon and the robot itself from undesirable effects, thereby ensuring the safety of the patient

during the operation. However, some surgeons doubt about the safety of using the robot [11-16].

The above facts, the inconsistency of the literature data, the uncertainty of indications and contraindications for various surgical methods, doubts about the safety and accuracy of lower limb axis alignment determined the relevance of studying these issues in our work.

Objective To determine the clinical efficacy and accuracy of mechanical axis alignment of the lower limb in robotic total knee arthroplasty.

MATERIALS AND METHODS

A prospective, uncontrolled single-centre study was conducted in the clinic of traumatology, orthopedics and joint pathology of the University Clinical Hospital No. 1 of the Department of Traumatology, Orthopaedics and Emergency Surgery of the First Moscow Sechenov State Medical University (Sechenov University) from 2019 to 2021.

Criteria for inclusion of patients in the study:

– age over 18 years, gonarthrosis in stage 3-4 according to the Kellgren-Lawrence classification with pain above 5 points on a 10-point VAS scale;

– risk of anesthesia on the ASA scale is not more than III;

– available written informed consent to perform the TKA operation according to the offered method.

Criteria for non-inclusion of patients into the study:

– risk of anesthesia on the ASA scale more than III (history of thromboembolic and infectious complications, uncorrectable diabetes mellitus, prednisolone-dependent systemic diseases, anemia and thrombophilia);

– BMI in accordance with the recommendations of the developer more than 35 kg/m^2;

– severe deformities of the knee joint (valgus > 15° or varus > 15°), primary bone defects;

– extensor contracture of the knee joint up to 90°;

– metal implants on the affected side.

Criteria for exclusion of patients from the study:

– refusal of the patient to further participate in the study;

– patient's non-compliance with the prescribed regimen.

Informed consent on the course of the study was obtained prior to enrollment in the study.

The clinical study enrolled 43 patients selected according to the inclusion and non-inclusion criteria, of which 14 patients were excluded from the study during the year. Twenty-nine patients were analyzed (82.76 % women (n = 24), 17.24 % men (n = 5), mean age was 67.1 ± 2.7 years, mean BMI (kg/m^2) was 31.2 ± 3.4, the mean range of motion was 86.03 ± 3.7°, the mean mechanical axis before surgery was 170 ± 1.8°. RoTKA using the TSolution One® robotic orthopedic system (THINK Surgical Inc., USA) was performed under spinal anesthesia using a medial parapatellar approach. Cemented knee endoprostheses Zimmer® Persona with preservation of the posterior cruciate ligament (Cruciate Retaining (CR)) with a fixed liner were used. Patellar plasty was not performed, but removal of osteophytes and circular denervation was part of the operation.

The following issues were studied in the process of preparation, planning of the operation, postoperative period and rehabilitation:

1) validity of indications and contraindications recommended by the manufacturer (range of motion of the knee joint less than 90°, varus or valgus deformity more than 15°, presence of metal on the affected side of the knee joint, BMI > 35 kg/m^2);

2) complications;

3) the level of pain in patients according to VAS, WOMAC scores, range of motion (ROM) of the knee joint before and after surgery, FJS-12 scores after surgery;

4) changes in the axis of the lower limb and positioning of implants based on CT scan before and after surgery.

Statistical processing of clinical material consisted of grouping data, calculating intensive and extensive indicators, determining the average error of relative values, determining the reliability of the difference between the compared values (t), the correspondence criterion K, the Pearson coefficient (Chi-square), the correlation coefficient of multifactorial systems using the IBM SPSS Statistics 22.0 (SPSS Inc., Chicago, Illinois) – Windows 10 Pro, computer – Asus UX 434, Intel Core i7 2.7 GHz processor, RAM – 16 GB. For true numeric (scale) variables (VAS, WOMAC, FJS-12, mechanical axis), frequency histograms and values of statistical parameters were calculated, including arithmetic mean (M), standard deviation (Б), statistical error of the mean (m), minimum and maximum value and median (Me). To analyze changes in indicators over time, Student's t-test was used, and a two-sided Student's test was used before and after surgery. Differences were considered significant statistically at $p < 0.05$.

The RoTKA technology consists of 3 stages: 1) CT examination of the lower extremities; 2) planning on TPLAN; 3) operation using the TCAT system (Fig. 1).

At stage 1, the patient undergoes a CT examination of the ower extremities with the capture of the hip and ankle joints in the supine position with a hollow calibration rod, which was fixed to the affected limb (Fig. 2).

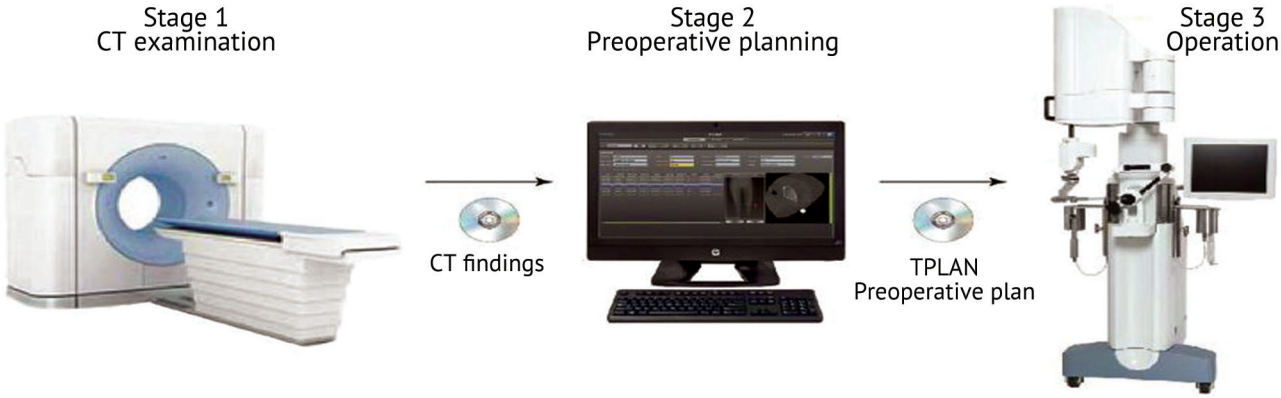

Fig. 1 Technological diagram of robotic orthopaedic system TSolution One® (THINK Surgical Inc., USA) operation

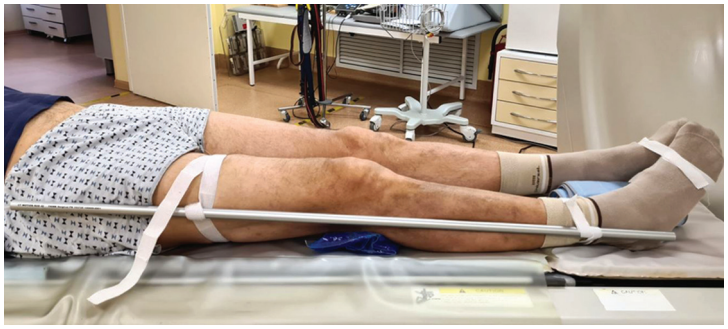

Fig. 2 Position of the patient with the calibration rod during CT-study

The calibration rod is included in the delivery of the robotic unit and must be displayed on all slices of the CT examination. The slice pitch is 1 mm; the number of slices is not fewer than 440 and not more than 1300. Patient movements during the CT examination are strictly prohibited.

At stage 2 (planning), the CT scan data (CD) is loaded into the TPLAN computer planner, step-by-step image analysis is performed: segmentation of the axial sections of the femur and tibia, marking bone growths (osteophytes). The computer converts images of separate sections into a 3D model of the patient's knee joint, on which it applies anatomical landmarks, builds axes, resection level, selects the size and position of the implant, which is evaluated and approved by the surgeon; and after which the operation plan is recorded on a CD (Fig. 3).

Surgical stage 3 begins with loading the CD plan into the TCAT Surgical System, and the robot systems and surgical instruments are tested. Non-sterile calibration of the robotic system is performed with the participation of an assistant and a robotic engineer, then the assistant and operating nurse perform draping and sterile calibration of the surgical instruments of the robot, after which the patient is delivered to the operation room.

After surgical field treatment, the limb is placed in a special holder fixed to the table in the position of 90-100° flexion. Anteromedial approach to the knee joint is performed and the patella is freely dislocated outwards. Osteophytes on the femur and tibia are not removed until bone registration. The lower limb of the patient is fixed in the position of flexion 90° to the TCAT system with special fixators and the calibration pin buttons and pin screws are installed in the femur and tibia (Fig. 4).

Upon lower limb fixation, bone motion sensors (Bone Motion Monitors (BMM's)) are installed to the femur and tibia; registration is performed using a special program in the robot's computer. Computed tomography points are combined with the corresponding virtual prototype of the femur and tibia, which were created during the planning of the operation, after which the robotic unit begins to "see" the real bone. In case of any inaccuracies, failures, movement of the patient or limb to more than 1 mm, the system stops the work and requires repeated bone registration using a pin button and a pin screw (Fig. 5, 6).

The program is designed in such a way that it is impossible to miss or incorrectly mark these landmarks; if the system does not see the anatomical landmarks, it will not switch. After the preparation of the robot (fixation and calibration) is completed, the resection stage is started.

Resection is performed with a cylindrical cutter (8 mm) at a speed of 8000 rpm and constant irrigation with saline to cool the surface of the bone and cutter (Fig. 7).

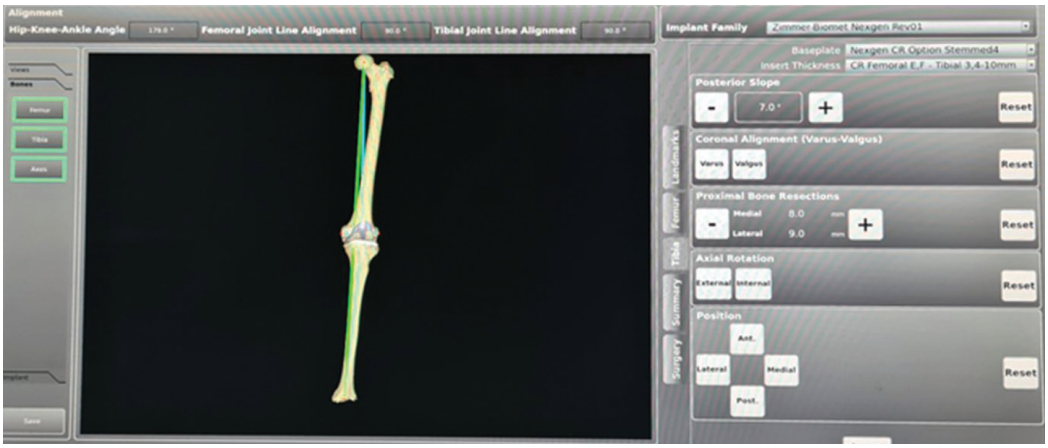

Fig 3 3D-model of the lower limb with the positioned components of the implant

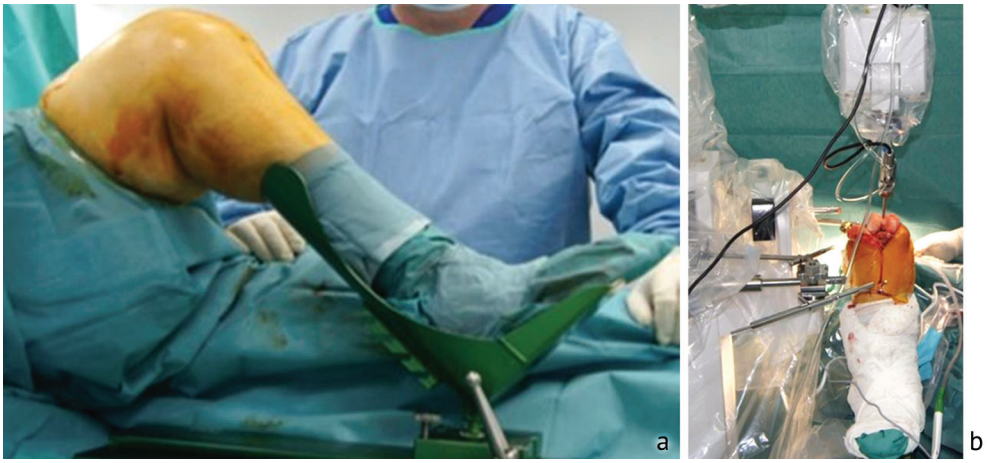

Fig. 4 Lower limb fixation: a into the holder; b to the robot

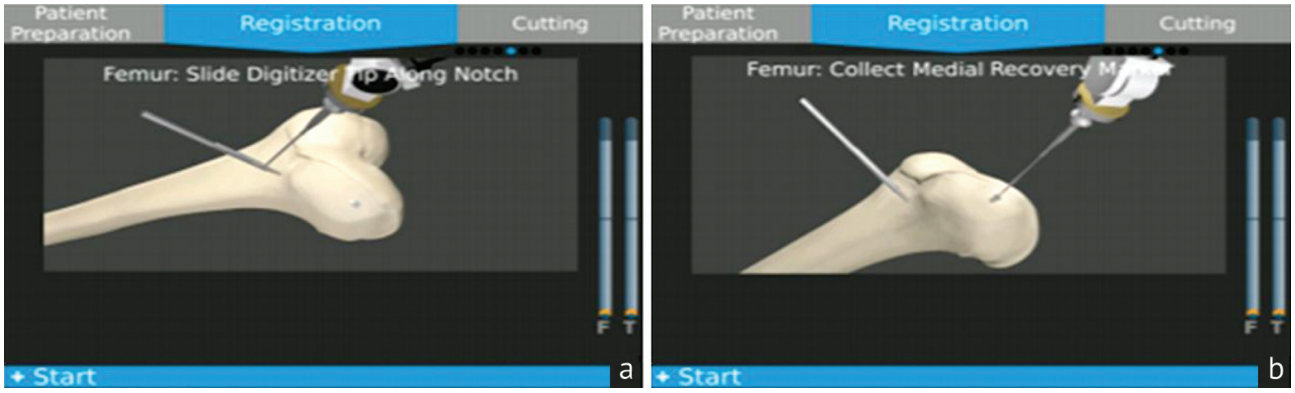

Fig. 5 Monitor screen by registration of the femur with the digitizer: a along the pin screw; b along pin button

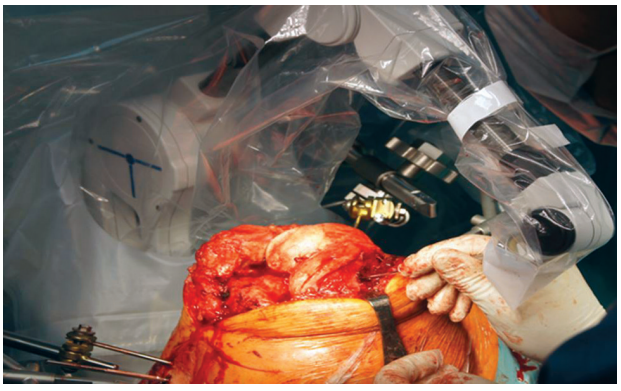

Fig 6 Registration of the femur point

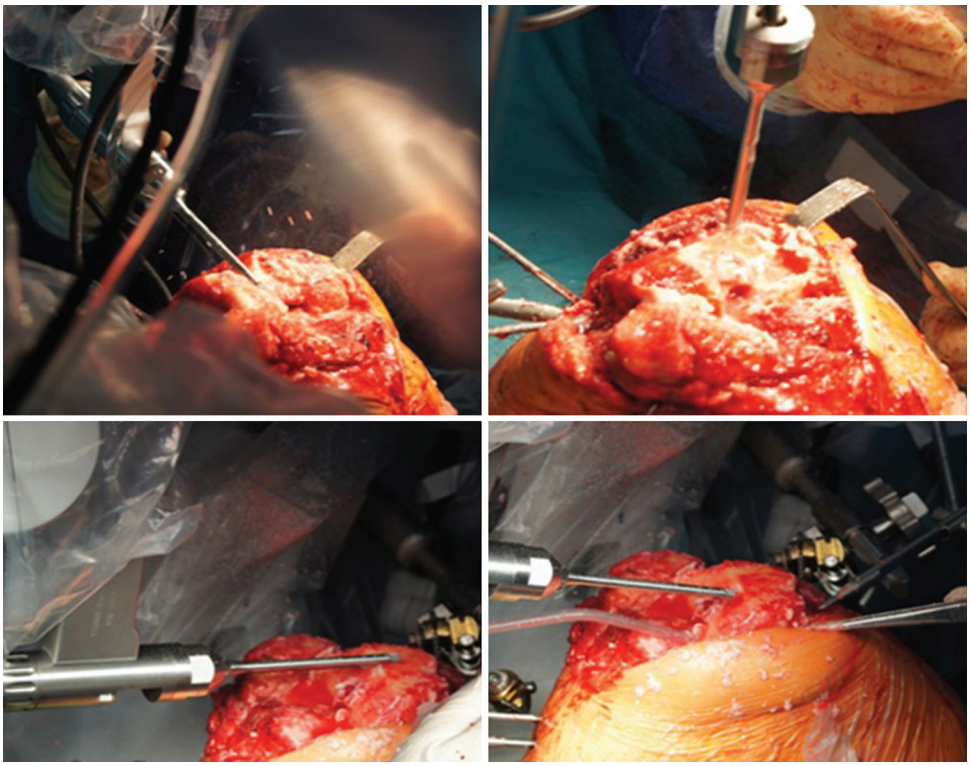

Fig. 7 The stage of bone resection

Thereby, the surgeon monitors the trajectory of the cutter and, in case of a threat to damage bone and soft tissues, has the opportunity to urgently stop the work of the robot, understand and eliminate the problem. If it is impossible to continue the robotic operation (bone shift, unrecoverable loss of landmarks, obstacle to the movement of the cutter and drive, or any other reason), the robot will stop, and then the surgeon will switch to the manual technique of the operation to ensure correct knee arthroplasty.

After the resection stage is completed, the robot is disconnected from the patient and pin buttons and pin screws are removed. The further course of the operation (fitting, balancing and fixation of the endoprosthesis in the bone) is carried out similarly to the traditional technique. Cemented implantation of components and wound closure are performed.

On the first day of the postoperative period, radiographic checking is performed on days 3-5: CT examination of the lower extremities under load (Fig. 8).

The postoperative rehabilitation program is similar to other arthroplasty methods.

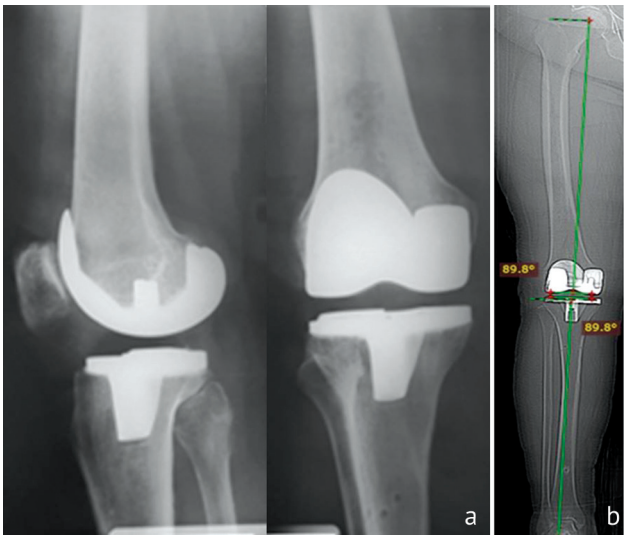

Fig 8 Postoperative knee joint radiographs in AP and lateral views (a) and full-length lower limb radiograph (b)

RESULTS

No complications, adverse events (damage to soft tissues, bones) were detected by performing RoTKA.

The average level of pain according to VAS before surgery was quite pronounced, 5.8 ± 1.5 points (95 % CI, p = 0.0248); it increased to 8.5 ± 1.4 on the first day after surgery (95 % CI), p = 0.0001). On the 3rd day there was a dynamic decrease to 5.9 ± 1.2 (CI 95 %, p = 0.0248), and on the 12th day the pain syndrome was significantly lower than before the operation, 2.9 ± 1.1 (95 % CI, p = 0.0248) (Fig. 9).

The range of motion in the knee joint on the first day after the operation (the ROM arch) was 99.5 ± 1.4°; three months after the operation, the range of motion increased to 115.1 ± 1.1°, after 6 months up

to 125.6 ± 1.5°. And one year after surgery, the mean ROM in the knee joint in 29 patients was 127.5 ± 1.6° ($p < 0.05$, two-tailed t-test) (Fig. 10).

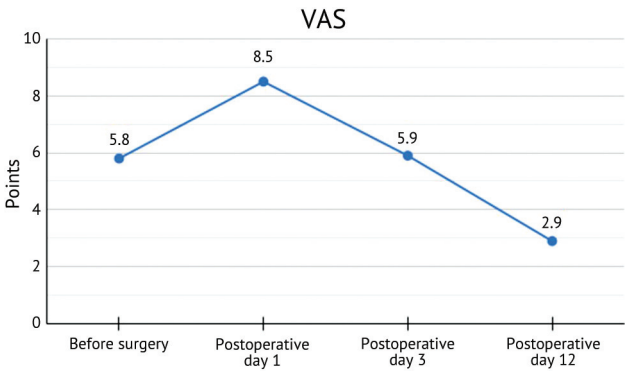

Fig. 9 VAS dynamics of pain

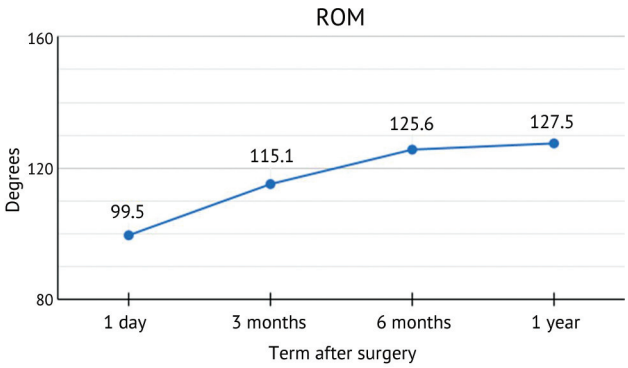

Fig. 10 Range of knee motion dynamics after the operation

Before the operation, the average WOMAC score was in the "satisfactory" range: 32.7 ± 3.3. After surgery, the mean score was 25.1 ± 2.1 points, three months after surgery 7.3 ± 1.3 points, 6 months after the operation 2.8 ± 0.2. 1 points, and a year after surgery the mean score for all 29 patients was 1.3 ± 0.5 points ($p = 0.0128$, two-tailed t-test) (Fig. 11).

Three months after RoTKA, the mean FJS-12 score was 68.2 ± 4.1. After 6 months, the average indicators increased to 80.3 ± 2.9. One year after surgery, all 29 patients had an average score of 94.0 ± 2.1 (Fig. 12).

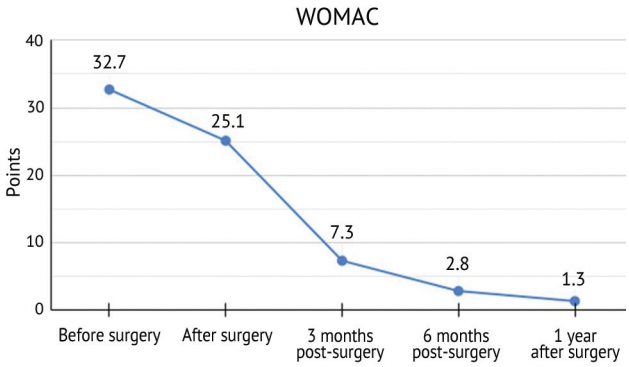

Fig. 11 Dynamics of WOMAC score (Points, Before surgery, After surgery, 3 months post-surgery, 6 months post-surgery, 1 year after surgery)

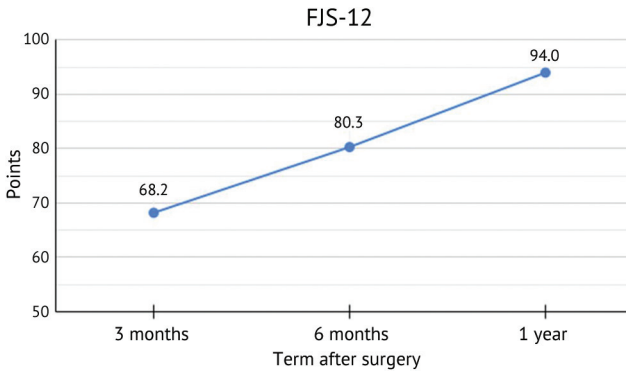

Fig 12 FJS-12 dynamics up to one year after RoTKA

The mechanical axis of the lower limb before surgery averaged 170.5 ± 1.8° of varus deformity, standard planning was 180°. After the operation, the mechanical axis was 179.6 ± 0.5°; a year after the operation, the axis was preserved at 179.7 ± 0.5°.

The analysis of postoperative full length radiographs showed that in 72 % (n = 21) of cases the deviation of the mechanical axis from the planned one was not found, in the remaining 28 % (n = 8) cases, deviation of the mechanical axis was up to 1° from the preoperative plan.

DISCUSSION

The study of the use of RoTKA in primary TKA showed its clinical effectiveness for treatment of gonarthrosis.

In the early postoperative period, according to the results of VAS, there was a positive tendency of pain relief after robotic arthroplasty. The same was shown by Kayani et^al. (2019), Batailler et al. (2021) and Wang et^al. (2022) that observed a reduction in the need for opiate analgesia compared to manual techniques. However, Hamilton et^al. (2021) found no significant difference in the intensity of pain syndrome by comparing the two methods [21, 22, 26-29].

ROM, WOMAC, and FJS-12 scores after surgery in our study were significantly improved compared to preoperative scores. It was also reflected in studies by other authors, but the degree of improvement requires comparison with manual technique and computer navigation [20, 21, 23, 25, 27, 30].

If patients have severe deformities of the lower extremities (varus/valgus > 15°), it is impossible to build axes on the TPLAN device, because in the technical condition (bone resection program), the head of the fibula limits the possibilities of resection, therefore deformities of more than 15° are a contraindication. A number of authors do not explain it in their studies,

but Chan et^al. (2020) and Stulberg et^al. (2021) included in their study patients with a deformity angle in the frontal plane of up to 20°. We could not confirm this by our study [11, 17-20].

Fixation of the lower limb is carried out in a special holder in the position of 90-100° knee flexion for correct operation of the robot. In extensor contracture, this stage cannot be performed, because the working area of the robot arm will not be in focus, which will be a contraindication [11, 17, 19, 21].

Features of preoperative planning and automatic functioning of the robot dictate a strict requirement: absence of metal or a hip joint endoprosthesis on the involved side, which can shield the bone during planning, making it impossible to mark anatomical landmarks, and interfere with the functioning of the robot during resection [11, 17-19].

Undesirable effects, specific complications inherent in RoTKA were not revealed during surgery and the examinations; and namely, damage to soft tissues and bones, what makes this technique safe for use. It was confirmed in the studies of other authors intra-operatively in patients and on cadaveric materials [16, 18, 22].

In our study series, there was no deviation of the mechanical axis from the preoperative plan by more than 1°. According to the literature, the alignment of the mechanical axis of the lower limb in TKA within ± 3° is acceptable. In the studies of Stulberg (2021) with RoTKA, deviations from the preoperative plan by more than ± 3° were detected only in 11.2 % of cases, in the study by Vaidya et^al. (2022) in 3.1 % of cases [11, 18, 20, 22-25].

Liow et^al. (2017) identified the following indications for RoTKA (ideal patient): patient age < 60 years; BMI < 25 kg/m^2; mild or moderate deformity in the frontal plane; intact neurovascular bundle of the affected limb. Relative contraindications included obesity with severe frontal deformity > 15°, fixed flexion contracture > 15°, inflammatory arthropathy, and ligament instability [17].

Chan et^al. (2020) conducted their study according to the following inclusion criteria: age from 21 years old, mature skeleton evidenced by closed growth zones. Exclusion criteria were previous open surgery on the affected knee joint; BMI > 40 kg/m^2; deformity in the frontal plane > 20°; flexion contracture > 15°; the need for a bilateral TKA; active systemic infection, infection in the knee joint area, previous infection of the knee joint; implants in the ipsilateral lower limb; insufficient bone stock; pathological condition of the bones [19].

In the study by Stulberg et^al. (2021), RoTKA was performed according to the following indications: no history of previous open surgeries on the affected knee joint; BMI ≤ 40 kg/m^2; deformity in the frontal plane < 20° or flexion contracture < 15° [11].

Unfortunately, the authors in their studies do not explain why RoTKA was performed according to these indications.

The authors understand the problems of the study presented above: single-center nature, small sample of patients, no long-term results, no studies with the constrained type without preserving the posterior cruciate ligament (Posterior Stabilized (PS)) and others. These problems require further investigation.

CONCLUSION

The study of RoTKA technology has demonstrated high clinical efficiency, accuracy of mechanical axis alignment and good early clinical results. The technology will speed up the return of patients to optimal motor activity and improve long-term clinical results.

Conflict of interests *The authors declare no conflict of interest.*

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Comparison of the strength characteristics of a carbon friction pair of a hip joint endoprosthesis, including components from monolithic or non-monolithic pyrolytic carbon

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Abstract

Introduction The problem a large number of revision operations due to aseptic loosening after primary hip arthroplasty necessitates the search for a new material for a friction pair. The pyrocarbon, which has high tribological characteristics, can be used both in a monolithic and in a prefabricated design; however, the manufacture of a monolithic pyrocarbon block complicates production. **Aim** Compare the strength characteristics of the stem head and liner designs with monolithic and non-monolithic pyrocarbon. **Materials and methods** To assess the reliability of the designs, a digital mathematical model of the head and liner implants with a monolithic and non-monolithic pyrocarbon component was built. After the manufacture of prototypes friction pairs, an assessment of the static load on bench tests was carried out. **Results** While analyzing the mathematical model, the construct of non-monolithic pyrocarbon broke in one of the experiments, while the strength of the construct of monolithic pyrocarbon was 4.5 times higher than the stresses arising under load. While studying the maximum static load, the friction pair from monolithic pyrocarbon exceeded the maximum possible load in the human hip joint by 5 times. **Discussion** The studies allow us to be confident about the reliability of the design in in vitro studies, which will create conditions for reducing the number of revision surgeries after hip arthroplasty. **Conclusion** Based on the data obtained, the design of the head and liner of the hip joint endoprosthesis with a friction pair made of carbon material will provide high reliability under conditions of functioning in the hip joint at maximum loads. It serves as a prerequisite for conducting a clinical study of the proposed friction pair.

Keywords: hip arthroplasty, friction pair, carbon

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INTRODUCTION

The incidence of hip arthrosis is more than 10 % in patients over 35 years of age and more than 35 % in patients over 85 years of age [1]. One of the most common and effective methods of surgical treatment of coxarthrosis is total hip replacement [2, 3].

The number of hip replacements in Russia has been growing annually, from 33 thousand per year in 2008 to 76 thousand in 2019 [4]. This tendency, according to the forecasts of a number of authors, will continue in the coming decades [5, 6].

Despite the successful results of hip replacement, the problems of osteolysis and aseptic loosening of implants caused by wear particles from friction pair materials remain unresolved [7-9]. According to a number of authors, the rate of revision interventions due to aseptic loosening ranges from 3 to 39.9 % [10-12]. The main cause of aseptic loosening of endoprosthetic components is periprosthetic osteolysis, the frequency of which reaches 66 % among all the causes of aseptic loosening [13-15]. Osteolysis most often occurs due to wear particles formed during the functioning of the friction surfaces of the friction pair materials [16]. Wear particles are absorbed by macrophages what leads to the formation of a large number of cytokines that activate osteoclasts and can cause osteolysis around the endoprosthesis resulting in loosening of its components [17, 18].

The level of wear of current materials used in hip replacement reaches 0.74 mm^3/million cycles for ceramic friction pairs, 1 mm^3/million cycles for metal-to-metal friction pairs and 30-100 mm^3/million cycles of a metal-polyethylene friction pair [19-22].

It is known that high-carbon metal alloys have an initial wear level of 0.21 mm^3/million – 0.24 mm^3/million cycles, while alloys with low carbon content have a significantly higher wear rate, 0.76 mm^3/million cycles [19].

Due to the high wear resistance of carbon, it was proposed to use the carbon material applied in cardiac surgery for prosthetic heart valves which is isotropic pyrolytic carbon. However, the functioning conditions of the material in the human heart and hip joint are very different. The loads on the components of the joint endoprosthesis are much higher, and the size of the carbon component must be larger. However, it is more difficult to obtain isotropic pyrolytic

carbon of the size needed to make a monolithic component than to create a prefabricated component from two parts of the material. Thus, assessing the reliability of such structures is a necessary stage of research for the manufacture of an optimal design of a friction pair for a hip joint endoprosthesis made of pyrolytic carbon.

Purpose To compare the strength characteristics of head and liner designs using monolithic and non-monolithic pyrolytic carbon.

MATERIALS AND METHODS

Two friction pair designs were studied. The head of the first design consisted of two parts of pyrolytic carbon, which were mounted on a titanium bushing; the liner was made of polyethylene and had a pyrolytic carbon insert, the diameter of the spherical surfaces was 28 mm (Fig. 1, 3).

The second design of the friction pair of the hip joint endoprosthesis consisted of a head having a monolithic pyrolytic carbon part, which was mounted on a titanium bushing. The pyrocarbon part of the liner was mounted directly into the titanium body. The diameter of the spherical surfaces was also 28 mm (Fig. 2; Fig. 4).

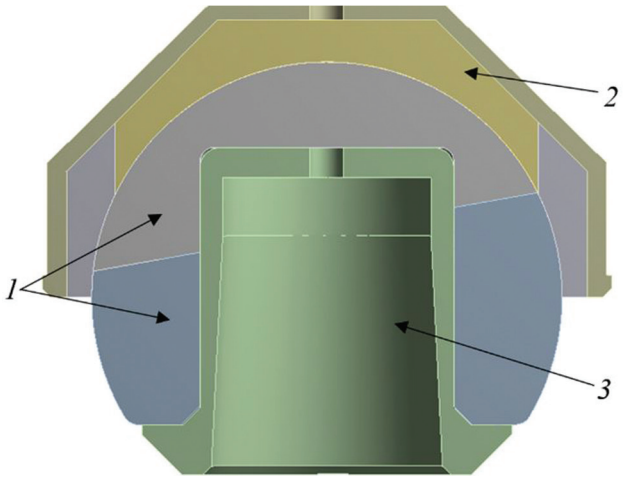

Fig. 1 The first design option for the motion unit of the hip joint endoprosthesis made of non-monolithic pyrolytic carbon: 1 – pyrolytic carbon part of the head, consisting of two parts; 2 – pyrocarbon part of the liner; 3 – titanium alloy bushing

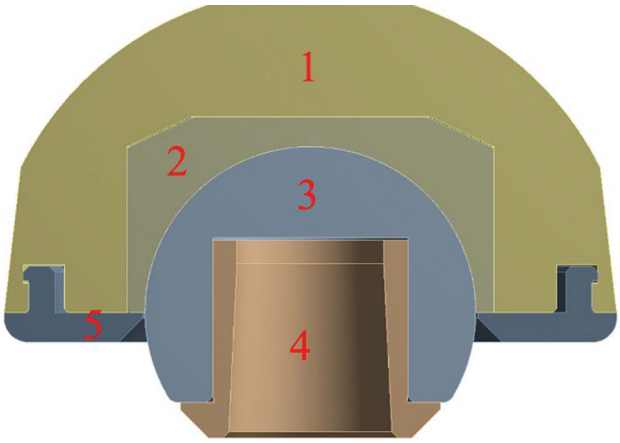

Fig. 2 The first design of the motion unit of the hip joint endoprosthesis made of pyrolytic carbon (diameter 28 mm): 1 – titanium liner; 2 – insert made of monolithic pyrocarbon; 3 – monolithic head made of pyrolytic carbon; 4 – bushing made of titanium alloy; 5 – polyethylene collar

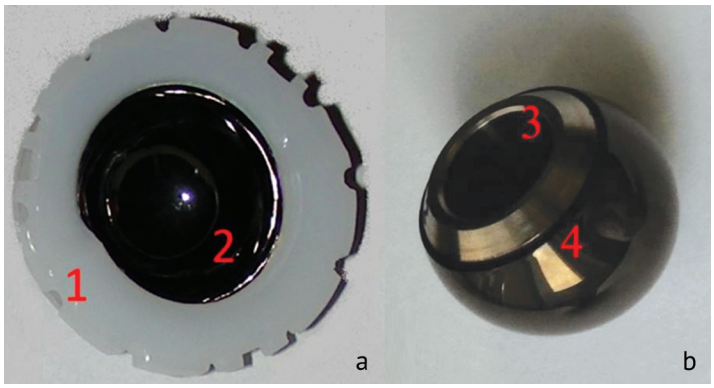

Fig. 3 Appearance of the liner (*a*) and head (*b*) with non-monolithic pyrocarbon: 1 – polyethylene liner, 2 – pyrocarbon insert, 3 – titanium bushing, 4 – pyrocarbon part of the head

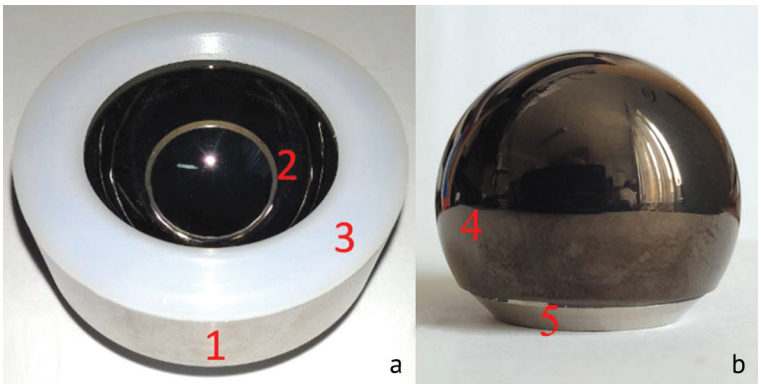

Fig. 4 Appearance of the liner (*a*) and head (*b*) with monolithic pyrocarbon: 1 – titanium body, 2 – pyrocarbon insert, 3 – polyethylene collar, 4 – pyrocarbon part of the head, 5 – titanium sleeve

The minimum gap between the block head and the liner was 0.15 mm, and the maximum gap was 0.35 mm.

The characteristics of the physical and mechanical properties of pyrolytic carbon indicate a significant difference in its resistance to fracture under tension and compression. The difference in the resistance of pyrolytic carbon to fracture during tension and compression requires consideration when assessing the strength of parts made from this material. To assess the strength of the parts of the motion unit of the hip joint endoprosthesis, the Balandin strength criterion was chosen. According to this criterion, the indicator of material destruction occurs when stress is reached in the structure of the unit.

The variable parameter was the angle of load application to the motion unit liner. Variation levels: 0° (vertical load application), 22.5° and 45°. The gap between the pyrocarbon parts of the head and the liner was 0.2 mm.

The angles of load application were selected to determine whether the stresses occurring in the structure depend on the direction of load application. The size of the gap varied within the technological tolerance of the product.

When calculating the stress-strain state of the motion unit of the hip joint endoprosthesis made of pyrolytic carbon, it is assumed that the head of the unit is fixed on the inner surface of the bushing, and the load is applied to the motion unit liner at an angle of 0° (vertical load application), 22.5° and 45°.

To conduct a study of the maximum static load on a friction pair, prototypes of the head and liner with monolithic and non-monolithic parts of pyrolytic carbon were manufactured. The design of the components corresponded to the schemes used in mathematical modeling (Fig. 3, 4).

The study was conducted on a specialized system TbcTester IR5145-500. The angle of stress application was 45°.

RESULTS

For both constructs, under all considered loading conditions, the maximum values of relative stresses arise in places of stress concentration, which are the edges or rounding on the inner surface of the head of the motion unit.

The second most important place for stress concentration is the contact patch between the spherical surfaces of the head and the liner of the motion unit.

A high level of relative stress occurs when the end surface of the titanium bushing contacts the inner surface of the head. Contact occurs when an axial load is applied and is accompanied by the occurrence of high stresses of a local nature.

When evaluating head designs with a non-monolithic pyrolytic carbon part, a peculiarity was that the load concentrations fell on the connection zones of the pyrolytic carbon parts. In one experiment, the stress exceeded the strength of the structure, which may cause the break of the structure. For a friction pair with monolithic pyrolytic carbon, the safety margin was 4.5 times higher than the stresses that arose during the modeling (Table 1).

Thus, the design of a friction pair with monolithic pyrolytic carbon provides a lower level of relative stresses in the entire considered range of angles of load application compared to the design in which non-monolithic pyrolytic carbon was used. The construct of a friction pair with non-monolithic pyrolytic carbon broke in an experiment with a load applied along the axis of the neck.

Table 1

Maximum values of relative stresses in the head and liner with monolithic and non-monolithic pyrocarbon

Construct variant	Angle of stress application		
	0°	22.5°	45°
Non-monolithic pirocarbon	1.628	0.580	0.390
Monolithic pirocarbon	0.149	0.222	0.202

According to the results of the static load study, the destruction of the friction pair with non-monolithic pyrolytic carbon was recorded at 1.5 tons. The destruction began with the deformation of the polyethylene adapter of the insert, which led to the destruction of the carbon liner.

The destruction of the friction pair with monolithic pyrocarbon occurred at a load of 3.5 tons. This value is 5 times higher than the maximum loads occurring in the hip joint.

Thus, the construct of a friction pair with monolithic pyrocarbon showed higher resistance to static loads than the design of a friction pair with non-monolithic pyrocarbon.

DISCUSSION

Advances in technology, improved materials and a better understanding of natural tissue responses will certainly lead to breakthroughs in implant selection. Due to the aging population, the number of joint replacement surgeries has increased in recent years [23]. Consequently, the number of revision surgeries is also increasing, since the life expectancy of patients is longer than that of endoprostheses [24-27].

Current trends in prosthetic design emphasize the importance of biocompatible materials that are durable enough to withstand the increasingly active lifestyles of many patients while generating minimal wear debris. Since the main problems affecting the survival of the prosthesis is wear and wear particles, extensive research has been currently carried out to improve such biomaterials and provide an "infinite life of the endoprosthesis".

Despite the currently available materials for friction pairs, such as ceramics, metals, and polyethylene [28], the use of carbon materials for friction pairs seems to us to be an extremely promising direction.

Despite the fact that the reliability of the structure after implantation has yet to be studied, we can confidently speak about the high mechanical strength of the design of the head and liner of the hip joint endoprosthesis with a friction pair made of carbon material. High tribological characteristics of materials containing carbon were described in the literature, and it is statedthat the improvement in wear resistance is directly proportional to the increase in the carbon content in the material [19].

Thus, the use of a material with the potential to multiply the surviva of the hip joint endoprosthesis will help to significantly improve the quality of life of such patients and will increase the age range for the use of this type of surgical care without the risk of early revision interventions [29, 30].

CONCLUSION

Technical result In all the experiments, only the friction pair structure with monolithic pyrolytic carbon withstood the specified loading conditions for structures in the mathematical model, with a safety margin of 4.5. The design of a friction pair with non-monolithic pyrocarbon collapsed in an experiment with a load applied along the axis of the neck. By comparing the maximum static load, the strength of the structure with monolithic pyrolytic carbon was 2.3 times higher than the strength of the structure with non-monolithic pyrolytic carbon.

Clinical relevance Due to the high strength characteristics of the friction pair construct with monolithic pyrocarbon and the insufficient strength of the structure with non-monolithic pyrocarbon, only the design with monolithic pyrocarbon might be used for clinical practice.

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Mitroshin A.N. – conceptualization; validation; writing – reviewing and editing; control; project management.
Ksenofontov M.A. – methodology; formal analysis; study; data processing; writing - the original version; visualization, writing – reviewing and editing.
Kosmynin D.A. – study; writing – the original version; data processing; visualization.

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Original article

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Prevention of postoperative pain after total hip arthroplasty in patients with proximal femur fractures

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Abstract

Introduction Proximal femur fractures can be associated with nailing and total hip arthroplasty (THA). Treatment of elderly inpatients necessitates adequate postoperative pain relief. Obese patients require specific inpatient and outpatient treatments. **The objective** was to evaluate the effectiveness of pain relief in obese patients at the stages of rehabilitation after primary THA performed for a proximal femur fracture. **Material and methods** VAS score was compared in two groups of 60 clinical cases to evaluate the effectiveness of postoperative multimodal pain relief using the author's method. **Results** Comparable results of an effective and stable pain relief were obtained in the two groups by the time the patient was discharged from the hospital 5-6 days after THA. Multimodal analgesia with a glucocorticosteroid injected in the projection of the sacroiliac joint provided an effect being greater by 29 % than with use of opioids after two postoperative days and by 11 % after five postoperative days. **Discussion** Old age, comorbidities are associated with optimal surgical strategy. THA in patients with extra-articular proximal femur fractures can improve the rehabilitation potential early after surgery and general clinical and functional results providing high quality of life in the late rehabilitation period. **Conclusion** THA demonstrated a stable positive effect of pain relief in the study group of patients with proximal femur fractures, regardless of the weight and the height. Positive dynamics in pain relief was seen in patients with elevated BMI of any gradation, including those with BMI ⩾ 40.

Keywords: proximal femur fracture, postoperative pain, obesity, total hip arthroplasty

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INTRODUCTION

Proximal femur fractures account for half of all femoral injuries and 3-4 % of all skeletal injuries [1, 2, 3]. The fractures are typical for elderly and associated with osteoporosis even with low-energy injuries [4]. Specifically designed population-based studies showed a high incidence of proximal femoral fractures (PFF) in patients aged 50 years and older in the Eurasian area: 176 cases per 100 thousand population in males and 279 cases per 100 thousand population in females [5]. PFF result in impaired support function, decreased quality of life and lead to life-threatening complications in severe cases [6]. The beginning of the century was marked by a rapid increase in elderly individuals and those suffering from excess weight that is characteristic of highly developed countries [7]. 1.5 billion people worldwide are obese and there is an association between body mass index and musculoskeletal disorders [8, 9].

Surgical treatment of PFF is considered the treatment of choice. Internal fixators commonly used for osteosynthesis include cannulated screws, dynamic femoral screw and locking intramedullary osteosynthesis with Gamma nail. Different fixation options are available for relatively stable PFF [10, 11], and unstable PFF can be repaired with IM nailing due to better biomechanical parameters and wide dispersion of stress [12]. Elderly patients suffer from severe osteoporosis and failed internal fixation [13] results in re-operation. The difficulties are associated with physical, psychological and financial burden on the patient and orthopaedic surgeons primarily use using total joint replacement to repair PFF in older people. According to Rosstat, the population of Russia number more than 140 million people, and the fastest growing segment of the population is people who are 60 or older [14, 15]. There are 1.66 times more older women than men, and 3.23 times more senile women [15]. Comparison of the figures with those of other regions indicated the average frequency of PFF fractures among Russian women, and a high rate among men [16]. This can be explained by longer life expectancy of the female population.

Total or unipolar hip arthroplasty (THA) is a well-established surgical procedure that allows for early weight-bearing, rehabilitation compared to other fixation options, which reduces the risk of postoperative complications [17, 18, 19]. The method is practical for ambulation, improves pain and reduces the length of hospital stay [20, 21]. THA can be used as a restorative surgical treatment option if internal fixation has failed. The proportion of obese patients

among those who have undergone THA constitutes 36-70 %, and the figure has been steadily growing in recent years [22, 23]. The objective was to evaluate the effectiveness of pain relief in obese patients who have undergone primary THA for a proximal femur fracture, at the stages of rehabilitation.

MATERIAL AND METHODS

The study included a prospective analysis of outcomes of 60 patients with proximal femur fractures repaired with cemented THA between 2016 and 2022 at the trauma center of the Republican Clinical Hospital of the Ministry of Health of the Republic of Tatarstan. The study was performed in accordance with ethical principles for medical research involving human subjects stated in the Declaration of Helsinki developed by the World Medical Association as amended in 2000, Order of the Ministry of Health of the RF dtd 19th June 2003 No. 266 on Clinical Practice Guidelines in the Russian Federation. Permission was obtained from the local ethical committee of The study received a favourable opinion from the relevant research ethics committee of the Ministry of Health of the Republic of Tatarstan at the Kazan State Medical University of the Ministry of Health of Russia.

Of the 60 patients, there were 23 male (38.3 %) and 37 female (61.7 %) patients. The average age of the patients was 82.69 ± 5.1 years. There were two groups identified: the treatment group included 30 patients (50 %) with an increased BMI (BMI of 25 kg/m^2 and over), a comparison subgroup of 30 patients with PFF (50 %) with normal weight (BMI of 18.5 to 24.99 kg/m^2). Four subgroups were identified in the treatment group including patients with different BMI measurements (Table 1).

The average age of patients was 83.2 ± 5.1 years in the treatment group and 81.8 ± 5.1 years in the comparison group. The inclusion criteria included the age of the patient (> 70 years) and surgical treatment method (THA) for PFF. The individual BMI was measured to determine the physical condition of patients. The BMI classification of weight status was produced according to the World Health Organization with the formula for BMI being weight in kilograms divided by height in meters squared:

• Normal weight – BMI greater than or equal to 18.5 to 24.9 kg/m^2.

• Overweight – BMI greater than or equal to 25 to 29.9 kg/m^2.

• Obesity class I – BMI 30 to 34.9 kg/m^2.

• Obesity class II – BMI 35 to 39.9 kg/m^2.

• Obesity class III (severe obesity) – BMI greater than or equal to 40 kg/m^2.

All patients underwent primary THA for a proximal femur fracture in the period from 1 to 5 days after the injury. Cemented implants with a Muller femoral component and a metal-polyethylene friction pair were used. The procedures were produced after a preliminary examination and preparation of patients in the intensive care unit with anesthetic risk not higher than ASA III. Almost all (n = 58) interventions were performed using neuraxial anesthesia.

The author's "Method for the prevention of postoperative pain syndrome" (RF Patent No. 2702759) [24] was used to optimize prevention of postoperative pain. Analgesia technique. The patient was positioned on his normal side and the area of the sacrum and sacroiliac joints was treated with antiseptic solutions after closing the postoperative wound and applying an aseptic dressing. Injections were performed at the sacroiliac joint on both sides (by palpation). A mixture of a long-acting glucocorticosteroid solution (Triamcinolone) 20 mg and 2 ml of 2 % Lidocaine (or other anesthetic in an appropriate dosage) was used for injection on each side. Then the patient was transferred to the department and was on bed rest until the next morning to be followed by verticalization and rehabilitation. The therapy administered for the patient included anticoagulant prophylaxis, and pain relief, if needed, was performed with an adjuvant combination of a nonsteroidal anti-inflammatory drug NSAID (Aceclofenac 100 mg twice a day) and a muscle relaxant (Mydocalm 150 mg three times a day) to continue reducing the intensity of the pain. The therapy was aimed at relieving the so-called. mixed pain, which is a combination of nociceptive and neuromuscular components.

Table 1

Distribution of patients by gender and BMI

Subgroups		Males		Females		Total	
Obesity class	BMI (kg/m^2)	abs.	%	abs.	%	abs.	%
Normal weight	18.5-24.9	11	18.3	19	31.7	30	50
Obesity class I	25-29.9	3	5	5	8.4	8	13.3
Obesity class II	30-34.9	4	6.6	4	6.6	8	13.3
Obesity class III	35-39.9	3	5	6	10	9	15
Obesity class IV	40 and over	2	3.3	3	5	5	8.4
Total		23	38.3	37	61.7	60	100

The author's technique [24] of postoperative pain relief was used after THA. The effectiveness of therapy was assessed in the form of a comparative survey using a continuous method among 30 (15 + 15 in each study group) patients who received postoperative analgesia using the author's method of multimodal pain relief (MPR) and 30 (15 + 15 in each study group) patients who had standard postoperative analgesia (SA) with opioids. Therefore, 15 patients from both study groups were included in the MPR subgroup and 15 patients from both groups were included in the SA subgroup. A standard horizontal VAS scale was employed to assess pain (in cm) on the day of surgery, daily after surgery and at ischarge. Patients were followed up at the outpatient stage during the rehabilitation. Control examinations were performed at 3, 6 and 12 months., The follow-up period was sufficient for recovery both in terms of functionality and quality of life [6]. The parameters were analyzed using tables, graphs and descriptive statistics. The results were saved in a database using Microsoft Excel 2019 for Windows®. For bivariate analyses, continuous variables were described using mean standard deviations. Binary variables were compared with percentages in cross-tabulations. Differences in BMI between the four groups were analyzed using the Kruskal-Wallis test for continuous variables (age, operating time, etc.) and the Chi-square test for dichotomous variables. The significance level was defined as $p < 0.05$. Statistical calculations were performed using SPSS (version 26, IBM SPSS Statistics for Windows, Armonk, New York, USA).

RESULTS

The difference in VAS scores between the subgroups of patients who received postoperative analgesia using the above methods was determined after two days. The pain index measured with the author's technique (MPR) was significantly lower, by 1.5 cm, i.e. by 29.9 %. The difference was 23.3 % after three days and decreased to 11.1 % at discharge (6 days on average) (Table 2).

Table 2

Comparison of pain on the VAS scale in inpatients using postoperative analgetic options

Timing	VAS score		p
	MPR subgroup (n = 30)	SA subgroup (n = 30)	
	(M ± m), cm	(M ± m), cm	
Day 1, surgery	9.04 ± 0.085	9.25 ± 0.14	
Day 2 post-op	3.74 ± 0.14	5.33 ± 0.09	0.001*
Day 3 post-op	3.32 ± 0.04	4.33 ± 0.09	0.02
Day 4 post-op	2.88 ± 0.04	3.74 ± 0.08	0.05
At discharge	2.10 ± 0.06	2.36 ± 0.19	0.03

Comparison with the previous stage of observation: *differences being statistically significant.

The data obtained demonstrate the presence of a statistically significant difference in the dynamics of pain after two postoperative days in both subgroups, followed a gradual leveling during the outpatient stage of treatment (Fig. 1).

The patients were monitored at the outpatient stage going through stages 1-3 of the rehabilitation process. An almost symmetrical decrease in VAS scores was an expected phenomenon with the difference being minimal at the end of the recovery period (12 months after surgery), (Table 3).

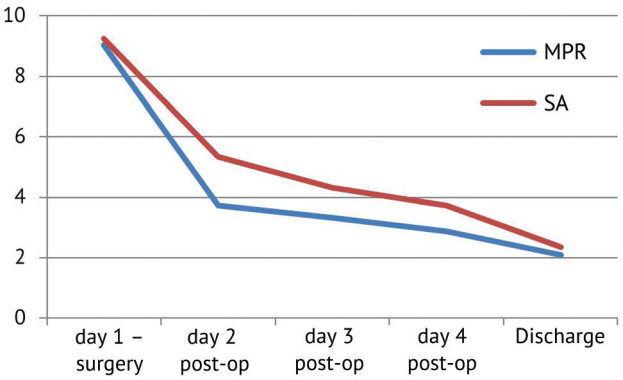

Fig. 1 Dynamics of pain measured with the VAS scale (in cm) using postoperative analgetic options by observation days

Table 3

Dynamics in pain measured with VAS scale in the THA group at the outpatient stage of treatment, depending on the methods used to prevent postoperative pain and the height and body weight characteristics

Timing	VAS score		P level
	MPR subgroup (n = 30)	SA subgroup (n = 30)	
At discharge	2.10 ± 0.06	2.36 ± 0.19	0.4019
At 3 months	1.86 ± 0.64	1.88 ± 1.07	0.7212
At 6 months	1.23 ± 0.53	1.40 ± 0.90	0.3340
At 12 months	0.48 ± 0.57	0.67 ± 0.71	0.1316

We were able to obtain the result of postoperative pain relief in each specific case of using MPR, and the effectiveness of the author's technique was evaluated in patients with normal and increased BMI.

The distribution of patients into the appropriate groups is presented above. The VAS score decreased in the "BMI Group" ("Normal BMI") by 72.1 % between the preoperative level to 3 postoperative months; by 79.3 %

between 3-month follow-up to 6-month follow-up period; by 90 % between 6-month follow-up to 12-month follow-up period. During the analyzed period of rehabilitation treatment in the category "Pain according to VAS", all indicators Positive statistically significant changes in pain were observed throughout the rehabilitation time points, at 12 months, in particular demonstrating the overall positive effect of arthroplasty (Table 4). It is important to note that the results had no correlation with the dynamics in changes in body weight, i.e. the analgesic effect was also present in patients with persisting obesity after injury.

Table 4

Analysis of the dynamics in VAS scores at different time points

Timing	VAS score	
	Normal BMI	Increased BMI
Pre-op, M ± S	6.74 ± 0.85	6.63 ± 0.69
At 3 months, M ± S (%)	1.88 ± 1.07 (-72.07)	1.86 ± 0.64 (-72.01)
At 6 months, M ± S (%)	1.40 ± 0.90 (-79.31)	1.23 ± 0.53 (-81.52)
At 12 months, M ± S (%)	0.67 ± 0.71 (-90.00)	0.48 ± 0.57 (-92.80)
P level	< 0.0001	< 0.0001

Table 5

VAS score measured in the group receiving multimodal pain management, depending on the BMI of patients

Timing	VAS score measured in patients with increased BMI				p level (df = 3)
	I (25-30)	II (30-35)	III (35-40)	IV (40 and over)	
VAS score					
At discharge	2.17 ± 0.75	2.4 ± 0.62	2.48 ± 0.71	2.64 ± 0.67	0.5112
At 3 months	2.00 ± 0.72	1.81 ± 0.63	1.68 ± 0.56	2.00 ± 0.63	0.2754
At 6 months	1.31 ± 0.59	1.19 ± 0.55	1.08 ± 0.40	1.45 ± 0.52	0.1466
At 12 months	0.53 ± 0.67	0.40 ± 0.54	0.48 ± 0.51	0.64 ± 0.50	0.5197

*p level (df = 3), degrees of freedom

DISCUSSION

Surgical treatment of proximal femoral fractures include internal fixation and THA. The use of a perticular method should suggest evaluation of characteristics of older patients, osteoporosis, comorbidities and obesity. THA provides good limb support and sufficient functionality reducing postoperative complications, improving the quality of life and creating conditions for early rehabilitation [25, 26]. A number of studies have shown [27] that obese patients are unable to perform a set of functional exercises due to postoperative pain, and other authors have found that the use of multimodal analgetic options can provide positive results in obese patients [28, 29, 30, 31]. These options include prolonged epidural blockade with limited use of oral anticoagulants for mandatory prevention of thromboembolic complications in the case. Intraoperative infiltration anesthesia of a wound with a various complex of drugs fails to provide the proper duration of postoperative pain relief [19, 32, 33]. Postoperative pain is one of the main factors restricting activity of patients after THA. Studies have shown that severe postoperative pain can directly lead to unfavorable short- and mid-term outcomes, and 1/3 of patients can develop chronic pain [34]. Routine clinical pain assessment and pain management regimens are non-recurring and may fail to reflect the pain status of patients performing functional activities. Severe pain reduces functional load during activities and does not facilitate restoration of joint function [35]. Single injections of a mixture of long-acting glucocorticosteroid solutions and anesthetic are performed in the projection of both sacroiliac joints immediately after the operation. Glucocorticosteroids are adaptive hormones that increase the body's resistance to stress. Surgery is a huge stress for the body with significantly increased production of endogenous cortisol (10 times or more) affecting the function of the endocrine system. The use of long-acting corticosteroids allows for termination of the body's stress response and potentiates the analgesic effect of anesthetics. The drug reduces the risk of developing reactive inflammation and swelling of the posterior portion of the pelvic ring and the hip joints [36].

The area of analgesic effect is limited to the area of the hip joint and the lateral surface of the femur, down to th knee joint. A mixture of corticosteroid and anesthetic solutions

ensures maximum concentration of drugs in plasma within 1.5 hours, and the biological half-life period is from 36 to 54 hours, which is sufficient for postoperative pain relief [37]. Glucocorticosteroids introduced at the site of the sacroiliac joints eliminates the risk of hematomas that can develop during epidural anesthesia using a catheter, which allows the use of thromboprophylactic agents early after surgery (4-6 hours) according to the instructions for the use of oral anticoagulants (Pradaxa, Xarelto, etc.). Injections at the site of both sacroiliac joints of the pelvis are necessary, to prevent pain irradiating from the lumbar spine to lower extremities [25].

With the perioperative management patterns being consistent in the two groups of our series, the results were mainly dependent on the use of analgesics. The goal of our development was to prevent postoperative complications after THA and reduce the dosage of opioids and a toxic effect on the body of elderly patients. The idea of the method for preventing postoperative pain was to conduct multimodal pain relief. Multimodal analgesia suggested simultaneous use of several drugs and/or techniques that had different mechanisms of action and allowed for achieving adequate pain relief with minimum side effects being inherent in the administration of large doses of one analgesic as monotherapy [32].

The results of the study demonstrated the effectiveness of the method at the inpatient stage of treatment. The advantage was especially evident on the second day after surgery with a decrease in the difference in the time the patients were discharged from the hospital. We can assume that the analgesic effect obtained was due to the use of multimodal anesthesia and further restorative treatment in both groups was performed without the use of our method. All patients were in equal conditions. This fact allowed us to specify the analgesic effect of surgical treatment in patients with different BMI at the stages of outpatient treatment. The VAS score was nearly identical at discharge and at 3 months in the two study groups at the outpatient stage which indicated effective operation, rehabilitation early post-op and equal potential of patients for improved quality of life. The patients across the groups developed pain relief with improved VAS score at the follow-up periods of 6 and 12 months. There was no statistical significance in VAS score for all parameters between the four categories of patients depending on BMI. Our findings showed no direct correlation between BMI and the pain severity. In addition to that, variations in the body weight were not reflected in the outcome, and the dynamics in pain relief measured with VAS scale demonstrated homogeneity in all patients.

CONCLUSION

A significant difference determined between the pain measured on the day of surgery and after two days post surgery indicated the efficiency of the method developed and implemented for postoperative pain relief in THA patients who underwent surgical treatment for a proximal femur fracture. THA dramatically reduces pain in patients with PFF. Positive dynamics in pain relief was noted in patients with increased BMI, including those with morbid obesity (BMI $\geq$ 40).

Conflict of interest *The authors declare no conflict of interest.*

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Ethical expertise *The authors confirm that the rights of people who took part in the study were respected, including obtaining informed consent in cases where it was necessary.*

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Comparative analysis of surgical techniques used to repair a closed sciatic nerve injury in patients undergoing total hip replacement

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Abstract

Introduction A variety of surgical techniques used to treat a closed sciatic nerve injury after total hip replacement (THR) require careful evaluation and comparison of short- and long-term outcomes of the complex management emphasizing a paucity of publications on the subject and a high social and economic role of the issue. **The aim of the study** was to compare outcomes of various surgical techniques used to treat closed sciatic nerve injuries after THR. **Material and methods** A total of 94 patients with closed sciatic nerves injuries associated with THR were divided into three groups. Microsurgical neurolysis of the sciatic nerve was produced for patients of Group I; patients of group II underwent microsurgical neurolysis of the sciatic nerve and electrical nerve stimulation; patients of group III had microsurgical neurolysis and electrical stimulation of the sciatic nerve with multichannel electrodes and segmental apparatus of the spinal cord at the conus and epiconus level. Clinical and neurological tests, dynamic electrophysiological monitoring were employed for clinical and functional evaluation. **Results** In In the postoperative period, positive dynamics in clinical and electrophysiological parameters with improved pain, lower limb functionality, increased amplitudes and decreased latency of M-response with most positive changes observed in Group III compared to Group I and Group II ($p < 0.05$). **Discussion** The function of the sciatic nerve restored in all patients with the most pronounced effect recorded in group III. The effect from the technique was associated with a simultaneous electrical stimulation of the trunk of the peripheral nerve and the segmental apparatus of the spinal cord causing synergetic effect on the structures. **Conclusion** The most effective method of surgical treatment was the use of Microsurgical neurolysis combined with two-level electrical stimulation was shown to be most effective and characterized by faster pain regression and positive dynamics in clinical and electrophysiological parameters in the affected lower limb of patients Group III.

Keywords: sciatic nerve, trauma, total hip replacement, electric stimulation, surgical management

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INTRODUCTION

A closed sciatic nerve injury (CSNI) following a total hip replacement (THR) is a challenging and devastating complication with the incidence between 0.17 and 8 % [1-3]. The condition can be transient in 50-70 % of cases and not accompanied by presenting signs [4, 5]. The increasing volume of THRs leads to greater prevalence of CSNI among patients of working age [6]. Risk factors are limb lengthening during surgery, female gender, re-operations, bone cement utilization, posterior approach to the hip joint correlate with a greater complication rate [7-10]. Sciatic nerve neuropathy (SN) following THR can cause pain, impaired contractile function of lower-limb muscles, atrophy and joint contractures negatively affecting treatment outcomes [11, 12].

Surgical management treatment of CSNI can be challenging due to the high level of damage to the nerve trunk at the level of the infrapiriform and greater sciatic foramen during THR, which can require a highly traumatic approach associated with massive dissection of soft tissue structures and lead to hip adhesions at the surgical site increasing the number of poor treatment results [13, 14]. Microsurgical neurolysis (MN) is performed as a standard treatment for the condition, and various methods of direct electrical stimulation (ES) of the SN can be offered [13, 15, 16]. However, the use of the techniques does not always provide recovery of lower-limb function and is accompanied by frequent recurrence of complex regional pain syndrome (CRPS) in the lower limb [17-19]. Combined stimulation of the peripheral nerve and the segmental apparatus of the spinal cord can be employed and improve outcomes at a short and long term [20]. With a variety of ES techniques, there is no consensus in the literature regarding indications, timing and regimens used, and most studies investigating its effect on the regenerative processes occurring in the myoneural complex were performed on experimental models [21-25]. The high incidence of CSNI following THR and the frequency of poor results determine the relevance of this study, aimed at search of the most effective method of surgical treatment. The objective of the study was to compare outcomes of various surgical techniques used to treat closed sciatic nerve injuries after THR.

MATERIAL AND METHODS

The study was longitudinal, open-label, prospective with a historical control group. Inclusion criteria were included working age, isolated nature of the SN injury after THR (grade 3 idiopathic coxarthrosis, body mass index from 18.5 to 24.99, use the anterolateral approach to the hip joint and cementless fixation of THR), Sunderland grades II, III, IV injury to the nerve trunks [26], CRPS in the affected limb, conservative treatment failed after 3 months of injury, voluntary informed consent signed by the patient participating in the study. The study included 94 patients with CSNI who were treated at the Research Institute of Trauma, Orthopaedics and Neurosurgery of Saratov State Medical University between 2005 and 2022. There were 41 (43.6 %) male and 53 (56.4 %) female patients. There were no gender differences between the study groups ($p = 0.785$). The study was conducted in three groups being homogeneous in severity of nerve damage. Microsurgical neurolysis of the sciatic nerve was produced for patients of Group I ($n = 29$); patients of group II ($n = 32$) underwent microsurgical neurolysis of the sciatic nerve and single-level electrical nerve stimulation; patients of group III ($n = 33$) had MN performed in combination with two-level ES (stimulating electrodes placed to the trunk of the SN and to the segmental apparatus of the SC). Outcome measures included visual analogue scale (VAS) [27], five-point muscle strength rating scale [28], five-point sensitivity rating scale [29], the Oswestry Disability Index (ODI) [30]. Dynamic electroneuromyography (ENMG) of the lower extremities was used as an objective research method. Statistical analysis of the results was performed using Statistica 13.0, Microsoft Office Excel 2019. The data did not follow the normal distribution and non-parametric statistical methods were used to calculate the median and interquartile range (Me (Q1; Q3)), the Wilcoxon test for related samples, the Kruskal-Wallis test. Differences between groups were considered statistically significant at $p < 0.05$.

RESULTS

Pain intensity was high in all patients ($n = 94$) and scored 7.0 (6.0; 8.0) points, motor impairment in the affected limb scored 1.0 (0; 2), sensitive disorders scored 1.0 (0; 2) and the groups were homogeneous with the parameters (Kruskal – Wallis test pVAS = 0.949, pmotor = 0.452, psens = 0.950). Functional deficiency measured preoperatively with the ODI scored 31.0 (25.0; 40.0) in group I, 27.0 (21.0; 36.0) in group II, and 29.5 (21.5; 41.0) in group III with no differences in the homogeneity of the three groups ($p = 0.579$). Preoperative ENMG indicated severe damage to the SN, with injury to both portions, as shown in Table 1.

As seen from Table 1, ENMG measurements of all patients ($n = 94$) showed a decreased amplitude and an increased latent period of the M-response, which indicated a severe axonal demyelinating damage to the SN. The patients demonstrated a decrease in the severity of pain with complete regression observed in patients of group III ($p < 0.05$) only (Fig. 1) at a six-month follow-up.

The dynamics in sensitivity and muscle strength in the groups were weakly expressed, and no statistically significant differences in the above parameters were detected throughout the observation period ($p > 0.05$). The postoperative dynamics in ODI score was less pronounced in patients of group I and group II compared to those in group III due to decreased severity of pain and led to an improvement in self-care routine. ODI scored 28.0 (20.0; 34.0) in group I, 16.5 (9.0; 21.5) in group II, 5.9 (4.3; 8.5) in group III, $p < 0.05$.

ENMG measurements indicated positive clinical and neurological dynamics in the parameters with restored peroneal and tibial nerve conduction through increased amplitude of the M-response and decreased latency. This indicated the improvement in sensory-motor regeneration of peripheral nerves of the lower limb. The median amplitudes of the M-response at the distal point of the stimulated peroneal nerve measured 1.2 (0.3; 2.6) in group I, 1.6 (1.2; 2.2) in group II, 1.7 (0.7; 2.4) in group III, ($p < 0.05$) (Fig. 2).

Table 1

Preoperative electroneuromyography parameters of the lower limb measured in patients with closed sciatic nerve injury following total hip arthroplasty

Nerve	Parameter	Group 1 Me (Q1; Q3)	Group 2 Me (Q1; Q3)	Group 3 Me (Q1; Q3)
Peroneal	M-response (mA)	0.7 (0.1; 1.5)	0.7 (0.0; 1.3)	1.0 (0.4; 1.3)
	LP (ms)	3.3 (3.1; 4.4)	3.3 (0.0; 4.4)	4.8 (4.2; 5.1)
Tibial	M-response (mA)	2.0 (1.0; 4.6)	1.3 (1.0; 2.2)	1.1 (0.6; 1.6)
	LP (ms)	4.3 (3.5; 5.5)	5.6 (4.6; 6.7)	5.3 (4.6; 6.5)

Note: Me, median (25^{th} and 75^{th} percentiles), $p > 0.05$.

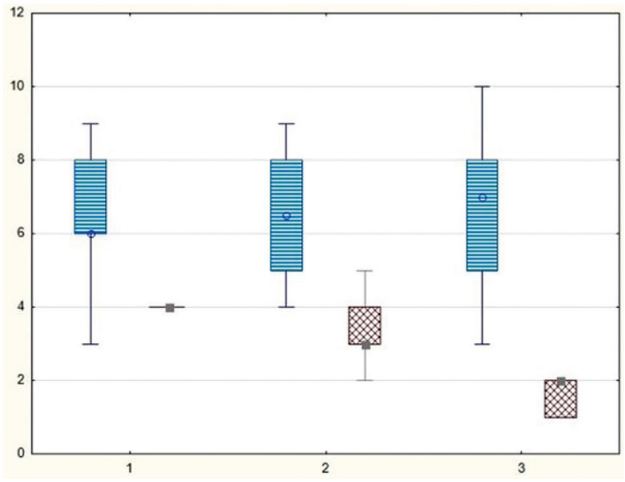

Fig. 1 Dynamics in pain intensity

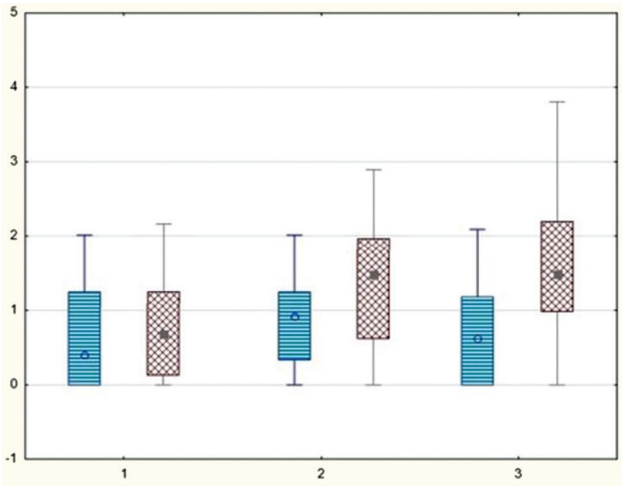

Fig. 2 Dynamics in M-response of the peroneal nerve

The amplitude of the M-response of the tibial nerve measured 2.1 (1.1; 2.9) in group I, 2.2 (1.4; 2.6) in group II, 3.2 (1.3; 5.60) in group III, ($p < 0.01$) postoperatively (Fig. 3).

Evident positive dynamics in clinical, neurological and electrophysiological parameters resulted in regression of pain, improved functionality of the lower limb, increased amplitude and decreased latency of the M-response registered in patients of group III, which indicated the advantage of combined MN and two-level ES in the treatment of patients with CSNI following THR.

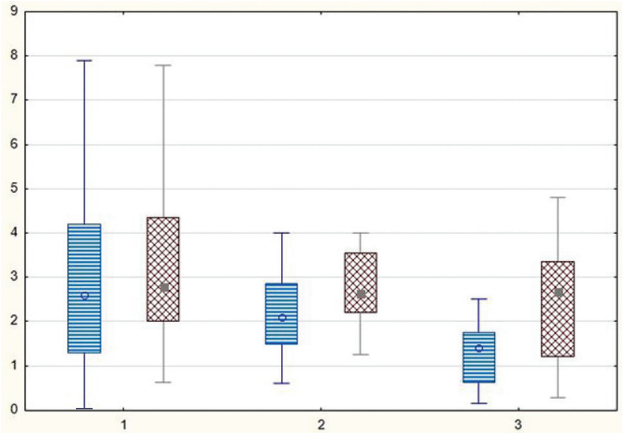

Fig. 3 Dynamics in M-response of the tibial nerve

DISCUSSION

The study was a continuation of work on exploring the results of treatment of patients with CSNI following THR [31]. The SN function recovered in all patients with the most evident effect seen in group III. Analysis of the literature data showed a small number of publications on the treatment of this pathology [32, 33], which complicated a significant comparison of the data obtained in the original study with data from Russian and foreign literature. The positive effect of the MN technique in combination with two-level ES was associated with the simultaneous electric-field pulses effect on the peripheral nerve trunk and the segmental apparatus of the spinal cord having had a mutually reinforcing effect on the peripheral nervous system. A similar technique was reported by I.A. Meshcheryagina. et al. in the complex treatment of patients with damage to peripheral nerves [20, 33] and the findings were in line with those of our series, despite some differences in placement of stimulating electrodes employed as minimally invasive technologies [34].

Clear criteria, indications and an optimal algorithm for a specific surgical treatment have not been identified for patients CSNI following THR. Although functional neurosurgery has undergone rapid growth over the last few years and clinical improvement being evident with different ES modalities the timing, duration and modes of electrical neuromodulation have not been fully elucidated [11, 35], which necessitates further research to determine the most effective method and establish a personalized approach to the treatment of patients with CSNI following THR.

CONCLUSION

A comparative analysis of different surgical treatments of patients with CSNI following THR demonstrated significant effectiveness of the SN technique in combination with ES of the SN trunks and the segmental apparatus of the spinal cord facilitating improved results of treatment with a faster pain relief in the affected lower limb and improved electrophysiological parameters.

Conflict of interest *The authors declared no potential conflicts of interest with respect to the authorship and/or publication of this article.*

Financing *The study was carried out as part of the research project of the Research Institute of Trauma, Orthopaedics and Neurosurgery of Saratov State Medical University SSMU "Development of a system for supporting medical decisions in the complex treatment of injuries of the peripheral nervous system using electrical neuromodulation methods", state registration number R&D 121032300173-9.*

Ethical expertise *The study was reviewed and approved by the local ethics committee of the Saratov State Medical University named after. IN AND. Razumovsky Ministry of Health of Russia (protocol No. 4, dated November 1, 2022).*

Written informed consent *for the participation in the research project was obtained from the patients.*

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Aitemirov Sh.M. – research, data processing.
Ostrovskii V.V. – control, project management.

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Hematological markers of periprosthetic joint infection after revision total hip arthroplasty

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Abstract

Analysis of clinical and laboratory tests is essential for monitoring the course of infectious complications after total hip arthroplasty (THA). **The objective** was to assess the reliability of differences in hematological parameters in patients with periprosthetic joint infection (PJI) for monitoring the infectious process. **Material and methods** Patients with acute (lasting 21.8 days on average) and chronic (lasting for 26.3 months on average) PJI were screened for hematological parameters on admission and during treatment in order to control the course of the purulent-inflammatory process. **Results** Preoperative parameters demonstrated mild anemia in patients with acute PJI, and the hemoglobin concentration was normal in patients with chronic PJI. Patients of both groups showed normal total leukocyte count. ESR and C-reactive protein levels were many times higher than the threshold values. The C-reactive protein level was more than 2 times higher in patients with acute PJI than that in patients with a chronic infection. The ratio of ESR / C-reactive protein was normally greater than 5 units, from 3 to 4.5 in chronic PJI and from 1.5 to 2.3 in acute PJI. Discussion Examination of pre- and postoperative clinically significant parameters is practical for identification of the criteria to assess the risk of chronic PJI. **Conclusion** Patients with acute PJI need no additional clinical and laboratory examination, integral laboratory parameters can be employed for accurate assessment of the extent of inflammation in a purulent wound.

Keywords: hip joint, revision total hip arthroplasty, blood, periprosthetic joint infection

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INTRODUCTION

Prosthetic joint infection (PJI) following total joint replacement surgery is a serious complication that negatively impacts patients' lives and is financially burdensome for healthcare providers. This is associated with high relapse rates and a significant risk of mortality among elderly patients [1, 2]. Lack of efficacy of the PJI treatment can be caused by limited data on the period of formation of an irreversible bacterial attachment to the endoprosthestic surface [3]. Effectiveness of treatment using different therapies remains low with failure of 24-75 % treated for PJI [4-6]. There is a wide range of infection diagnostic tools to mitigate the impact of disease. A clinical and laboratory diagnostic algorithm would facilitate the optimal treatment option for the patient and lower risk of recurrence [7-10].

New clinical and laboratory criteria for diagnosing PJI was discussed at the 2nd International Consensus Meeting on Musculoskeletal Infection (Philadelphia, 2018) [11-15]. Clinical recommendations of the Ministry of Health of the Russian Federation on "Prevention of infections in the area of surgical intervention" indicate the need for clinical (complaints, anamnesis, physical examination), hematological (leukocyte level, ESR, CRP), cytological (leukocyte level, neutrophils), microbiological and radiological (radiography, fistulography and CT, if needed) examinations [16]. Clinical and biochemical blood tests are performed for severity of the purulent process. Anemia, hypoproteinemia, thrombocytosis and hyperfibrinogenemia are the most characteristic signs of PJI [17]. Alterations in D-dimer, lipopolysaccharide-binding protein and presepsin (sCD14-ST) were noted in addition to the classic changes in acute phase proteins (interleukin-1, interleukin-6) [18-23].

The combination of ESR (> 30 mm/h) and CRP (> 10 mg/l) was the most sensitive diagnostic criterion indicating infection in 90-100 %, as reported earlier [24-26]. The diagnostic role of the parameters was not so high with low grade infection [27, 28]. We thought it was necessary to evaluate these data for different types of PJI (acute and chronic) with comparison of a large amount of literature data on the diagnosis of PJI including acute-phase hematological parameters. The objective was to assess the reliability of differences in hematological parameters of patients with PJI of the hip for monitoring the infectious process.

MATERIAL AND METHODS

Hematology blood tests of patients with PJI of the hip treated between 2005 and 2020 by one surgical team at the Federal State Budgetary Institution "National Medical Research Ilizarov Center for Trauma and Orthopaedics" Ministry of Health of the Russian Federation were analyzed. Exclusion criteria included inconsistency with the age group and incomplete data in the medical record, malignant and decompensated chronic diseases. Inclusion criteria included age, diagnosis, duration and severity of the disease. The disease was diagnosed based on physical examination and laboratory testing. Informed consent was given prior to inclusion in this study by all patients. The study received a favourable opinion from the relevant research ethics committee of the Federal State Budgetary Institution "Ilizarov National Medical Research Centre for Traumatology and Orthopaedics" Russian Ministry of Health.

The mean age of the patients was 54.7 ± 12.7 years (Me, 56; 95 % CI 52.7 to 56.8; IQR 46-65), with 36 % (n = 53) of patients aged 60 years and over, with males of 56 % (n = 82). On admission, 71 % (n = 105) of patients were diagnosed with a fistulous form of PJI, 9 % (n = 13) had open wounds and 20 % (n = 29) had swelling and hyperemia of the postoperative suture. Infection was observed in 78 % (n = 114) after primary joint replacement and in 22 % (n = 33) after revision surgery. Absolute signs of PJI were diagnosed in 114 (77.5 %) patients with the presence of a fistulous tract communicating with the joint cavity and/or with a pathogen strain with the same phenotype isolated from two biological samples. Relative signs were identified in 33 (22.5 %) patients with an average IMC score of 5.96 ± 2.70 (range, 2 to 14); Me, 6.0; 95 % CI 5.0 to 6.9; MQR 2.1-3.5, as mentioned in protocol of the 2nd International Consensus Meeting on Musculoskeletal Infection. Based on the nature of the infectious process, patients were divided into 2 groups. Group 1 (n = 28; 19 %) included patients with acute PJI (mean infectious period of 21.8 days; Me, 22; 95 % CI from 19.7 to 24.0; IQR 17-27.5). Group 2 included patients with chronic PJI (n = 119 or 81 %, respectively) (mean infectious period of 26.3 months, Me, 13; 95 % CI 20.5 to 32.3; IQR 8-35).

Data on isolated gram-positive (44 and 55 %) and gram-negative (7 and 10 %) bacteria are presented in Table 1 for comparison between the groups. Nearly every third (29 %) case of acute PJI was caused by methicillin-resistant strains of epidermal staphylococcus, and microbial associations (p = 0.04) and strains of methicillin-resistant staphylococci MRSE (p = 0.03) were common for acute cases as compared to chronic PJI.

The American Society of Anaesthesiologists physical status classification was used to assess a patient's overall health. Severe comorbidities were recorded in 56 % (n = 82) and 7 % of patients had no prior documented comorbidity. Hematological parameters of the patients were examined on admission and during treatment in order to monitor the dynamics of the disease. The equipment employed for the study included Hitachi/BM 902 automated analyzer (Japan, registration No. 2000/564 Ministry of Health of the Russian Federation); the Beckman automated Paragon protein chemistry analyzer (USA, registration no. 2005/282); Stat Fax spectrophotometer (registration no. 2004/1258). The reference intervals were referred to as normal ranges by clinical laboratories. Nonparametric statistical methods were used to process the data; significant differences were assessed in the groups using the Wilcoxon test. The samples were checked for normal distribution; differences were considered statistically significant at $p < 0.05$. Statistical processing was based on electronic database generated with Microsoft Excel integrated module AtteStat 1.0.

Table 1

Microbiological characteristics of patients with acute and chronic PJI of the hip joint

Evaluation criteria	Characteristics of patients with PJI (n = 147)		Statistical significance (p)
Type of PJI	Acute PJI (n = 28)	Chronic PJI (n = 119)	
Average manifestation of infection	21.8 (13-28) days	26.3 (1-204) months	–
Gram-positive bacteria	43 % (n = 12)	55 % (n = 66)	P = 0.23
Gram-negative bacteria	7 % (n = 2)	10 % (n = 12)	P = 0.64
Microbial associations	46 % (n = 13)	27 % (n = 32)	P = 0.04*
No growth detected	4 % (n = 1)	8 % (n = 9)	P = 0.46
MRSA	7 % (n = 2)	12 % (n = 14)	P = 0.48
MRSE	29 % (n = 8)	13 % (n = 15)	P = 0.03*
ESBL	7 % (n = 2)	3 % (n = 4)	P = 0.36
P. aeruginosa	11 % (n = 3)	10 % (n = 12)	P = 0.92

Note: statistically significant differences in the level of polymicrobial infection (p = 0.04) and MRSE strains (p = 0.03) were identified in the groups.

RESULTS

Clinically significant parameters of inflammation and postoperative blood loss were the most informative laboratory tests. Table 2 included hemoglobin and total leukocyte count, ESR and C-reactive protein; other hematological parameters were within the reference values and are not reported.

Preoperative measurements showed mild anemia in patients with acute PJI (hemoglobin Me 118 g/L, IQR 105-121) and normal hemoglobin values in patients with chronic PJI (hemoglobin Me 136.5 g/l, IQR 101-156). Patients of both groups had normal leukocyte count. ESR (average 61.5 ± 29.7 mm/h calculated using the Westergren method) and CRP (average 24.3 ± 23.5 mg/l) showed much higher values than the ESR and CRP threshold. C-reactive protein level was more than twice higher in patients with a short period of infection than in patients with a chronic infectious process.

Hemoglobin values were comparable in both groups and, as expected, below the preoperative level; they remained at the lower limit of normal at 7-10 postoperative days. Total leukocyte count was within the reference range in patients of both groups increasing insignificantly at 1-3 days of surgery. ESR and C-reactive protein levels were significantly higher than normal throughout the observation period and were statistically higher in patients with a chronic course of the inflammatory process than in patients with acute infection.

Table 2

Preoperative laboratory blood test performed in patients with PJI of the hip

Description	Acute PJI (n = 28)	Chronic PJI (n = 119)
Hb, g/L	Me 118 IQR (105-121)	Me 136.5 IQR (101-156)
WBC, 10^9/L	Me 6,3 IQR (6.2-7.2)	Me 7.7 IQR (6.2-8.8)
ESR, mm/h	**Me 52***# IQR (48-61)	Me 40.5* IQR (19.5-79.5)
CRP, mg/L	**Me 26***# IQR (10-64)	Me 11.5* IQR (6-18)
ESR /CRP, units	**Me 2.03***# IQR (1.5-2.3)	**Me 3.6*** IQR (3.0-4.5)

Note: *parameters having statistically significant differences with reference values at a significance level of $p < 0.05$; #, parameters having statistically significant differences between groups at a significance level of $p < 0.05$.

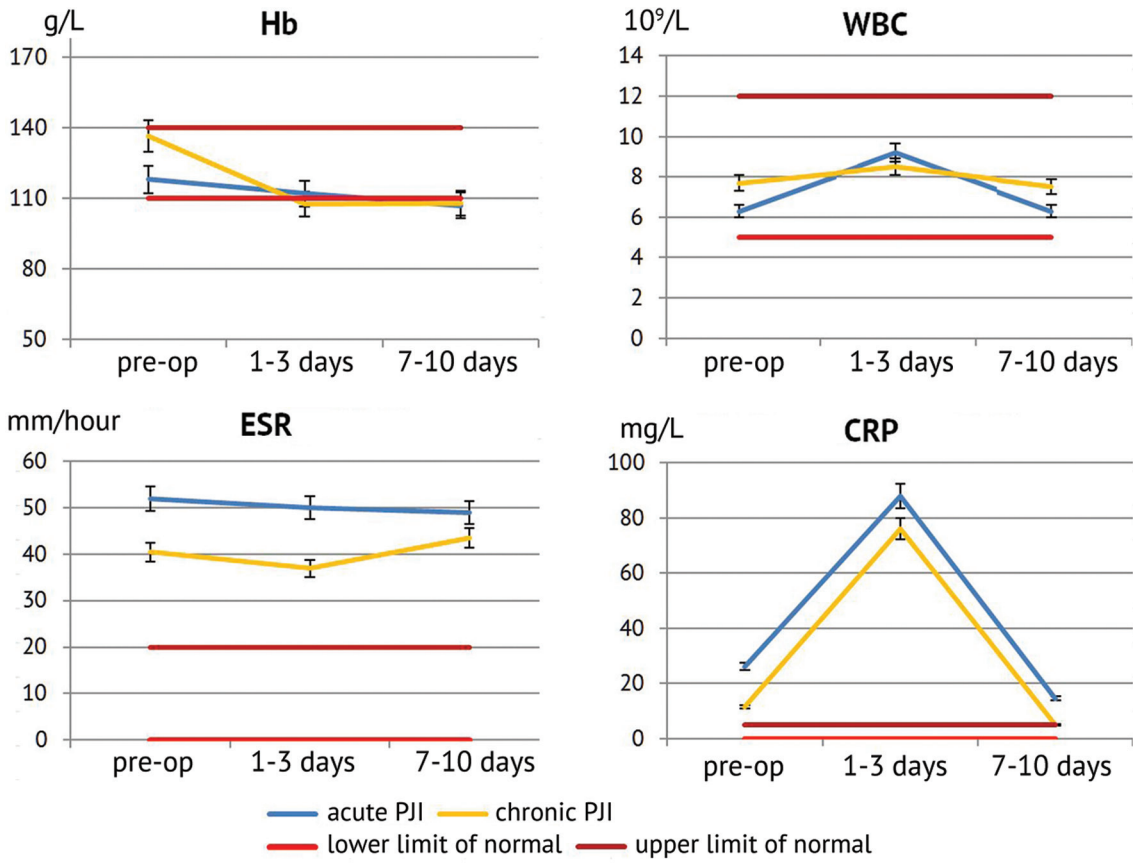

Fig. 1 Hematological parameters of patients of group 1 and group 2 measured preoperatively and at different time points: Hb, hemoglobin; WBC, white blood cells; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein

DISCUSSION

Complete resolution of the acute inflammatory process and total repair is the optimal way to address complications in the form of PJI after total hip replacement. Chronic PJI represents a huge challenge for physicians. Analysis of clinically significant pre- and postoperative parameters may help surgeons to make an appropriate choice of criteria for assessing the risk of chronic PJI. Preoperative and dynamic observations of major clinically significant hematological tests in patients with acute (mean infectious period of 21.8 days) and chronic (duration on average 26.3 months) PJI showed a high ESR level, one of the nonspecific markers of inflammation. The ESR values were several times higher than the reference range and amounted to 520 % in group 1 and 405 % in group 2. Similar findings were recorded for C-reactive protein, another nonspecific marker of the inflammatory response. C-reactive protein level was higher than the reference range in patients of both groups. However, the differences between the groups were more significant. The average values were 2.3 times higher in patients with acute inflammation than those in patients with chronic inflammation. A close relationship between hemoglobin and the activity level of the inflammatory process was reported [29, 30]. Although a decreased hemoglobin level is a most common cause of chronic inflammation, the patients showed some signs of anemia in the acute period. There might be no association between local clinical manifestations of purulent surgical disease and a WBC count [31]. The WBC count was within normal range preoperatively and increased early post-surgery and at 7-10 days in patients of both groups. It is known that leukocytes are the main line of defense against bacterial agents and one of the main criteria for assessing the degree of a purulent-inflammatory process, and the studied hematological parameters do not allow a differential assessment between acute and chronic inflammatory processes during revision hip arthroplasty. Leukocytes represent the body's initial line of defense against bacterial agents and one of the main criteria for assessing the degree of an inflammatory process. The hematological parameters explored do not allow a differential assessment between acute and chronic inflammation during revision THA. This opportunity is often provided by the use of integral laboratory indicators, and some researchers propose interesting mathematical models that make it possible to more accurately assess the degree of inflammation in a purulent wound [32, 33, 34]. The opportunity is often provided by integrated laboratory parameters, and some researchers report interesting mathematical models for more accurate assessment of the extent of inflammation in a purulent wound [32, 33, 34]. In our series, ESR/C-reactive protein ratio was used for the calculations. A normal ratio has been calculated as greater than 5 units, chronic PJI is characterized by a ratio ranging from 3 to 4.5 units and acute PJI has a range from 1.5 to 2.3. The use of the ESR/C-reactive protein ratio, leukocyte counts including the body resistance index, the leukocyte to ESR ratio index, the blood leukocyte shift index [5-7] requires no additional economic costs, giving advantages in predicting risks and potential indirect economic benefits.

CONCLUSION

The combination of clinical and laboratory parameters of PJI after primary THA has a high diagnostic value. However, the importance of clinical and laboratory methods is significantly reduced in the presence of low-virulent pathogens. Effectiveness of debridement prior to revision arthroplasty of large joints or timely detection of the latent phase of PJI remains an essential issue. Our findings have shown a unidirectional change in hematological parameters of patients with acute and chronic PJI during the first 10 days of revision arthroplasty. The dynamics in parameters was characterized the body's stereotypical reaction to surgery in both groups. Laboratory diagnostic methods of standard preoperative procedures allowed no prediction on the transition of the clinical form of acute PJI to the chronic stage. The strategy for improved outcomes of revision arthroplasty should focus on improved diagnostic algorithms for a comprehensive examination of patients prior to revision surgery to facilitate timely identification or elimination of latent PJI and adjustment of treatment plan if needed.

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Gasanova A.G., Spirkina E.S. – statistical processing.
Matveeva E.L., Luneva S.N. – writing text.
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Correlation between whole-blood serotonin level and flexible pes planovalgus deformity in children and adolescents

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Abstract

Introduction Timely diagnosis, etiopathogenesis, treatment and prevention of the progression of pediatric flexible pes planovalgus (FPPV) are essential to prevent irreversible complications. **The objective** was to determine a correlation between whole-blood serotonin level and flexible pes planovalgus in children and adolescents over a period of four years with progression of the condition. **Material and methods** The whole-blood serotonin level was measured in children and adolescents aged 5-15 years with FPPV and compared with data from photoplantograms, a pronation angle of the calcaneus and radiographs of the feet. Based on serotonin measurements and photoplantograms, two groups were identified according to the course of flexible pes planovalgus and measurements during the next four years. **Results** Normal serotonin levels were maintained in the non-progressive FPPV group throughout the study with a 9.2 % decrease in the pronation of the calcaneus at 4 years. Progressive FPPV patients showed higher serum serotonin at one year with a 38.3 % increase at 4 years, increased pronation of the calcaneus by 21.2% and radiologically decreased height of the arch by 18.7 %. A moderate correlation between whole-blood serotonin levels, pronation of the calcaneus and the height of the foot arch was radiologically revealed in patients with a different course of FPPV. Analysis of the diagnostic effectiveness of the whole-blood serotonin test in patients with FPPV showed high sensitivity and specificity in predicting the risk of progression of FPPV. **Discussion** Literature review showed a paucity of research on clinical and laboratory detection of the progression of FPPV and examination of neurotransmitter mechanisms in the foot pathology. Plantography, 3D scanning and radiography were the main methods for the diagnosis of the flat feet. **Conclusion** The correlation between whole-blood serotonin level and flexible pes planovalgus in children and adolescents was identified and suggested involvement of the serotoninergic system in the formation and progression of foot pathology.
Keywords: flexible flatfoot, serotonin, calcaneus pronation angle, progression, neuroreflex mechanisms

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INTRODUCTION

Pediatric flexible pes planovalgus (FPPV) is characterized by a decrease or absence of the medial longitudinal arch and hyperpronation of the hindfoot. The condition is common in the pediatric orthopaedic practice and encountered in 0.6-77.9 % [1-6]. A long held clinical opinion is that mature foot posture is reached between 10 and 11 years of age, and there is no standard assessment method for measuring foot posture in a clinical setting [7]. In most cases, FPPV in children do not cause symptoms, and, Asymptomatic FPPV therefore do not usually require conservative treatment. The growing child often develops an irreversible compensatory deformity of the foot which can lead to abnormal gait, plantar fasciitis, diseases of the patellar tendons increasing the risk of the knee and hip osteoarthritis, spodoloarthritis and seriously affecting the quality of life [8, 9]. Flat feet deteriorate foot function and quality of life with age and necessitate the use of special shoes and orthoses [10, 11].

General theories are based on structural bone deformities, muscular imbalance, and ligamentous laxity with the manifestations being influenced by a number of factors (foot overload, obesity, etc.). Although there is a paucity of studies exploring neuroreflex mechanisms of flexible flatfoot, an injury to the central nervous system or spondylomyelodysplasia were reported to be the leading mechanisms of the pathogenesis of FPPV [12]. I.G. Mikheeva reported the serum serotonin level in the newborns with hypoxic-ischemic injury to the central nervous system affecting the motor activity of the child in the form of depression or excitation of the nervous system and changes in muscle tone [13]. Serotonin effecting the ingrowth of serotonergic fibers into the hippocampus and cerebral cortex, synaptogenesis, microcirculation, smooth muscle tone, platelet aggregation was reported [13]. Our series showed that 50 % of children with FPPV suffered various orthopedic and neurological pathologies including scoliosis, hip dysplasia, spina bifida, cervical dorsopathy, muscle hypotonia, cephalgia, dyslalia and 36 % of them had a history of hypoxic-ischemic injury to the central nervous system at an early age detected with

neurosonography [14]. We sought to explore the effect of serotonin as neurotransmitter on the formation of FPPV. Methods for diagnosing FPPV include visual evaluation and foot mobility assessment, podometry and photoplantography with calculation of foot indices, computer pedobarography to examine the biomechanical function of the foot. Preoperative 3D CT imaging of the foot is performed to optimize the surgical plan and magnetic resonance imaging or ultrasound examination is produced to assess soft tissues (Achilles tendon, spring ligament, posterior tibial tendon, plantar fascia) [15-19]. Weight-bearing radiographs of the feet and ankle joints in two views measuring different parameters remain the "gold standard" for diagnosis of flatfoot to determine the severity of planovalgus deformity [20, 21].

With the variety of methods for diagnosis of flat feet, most of them require the use of special expensive equipment and have a radiological effect on the human body [22]. In addition to that, there are no scientific works reporting methods for predicting progression of foot deformities. Literature review showed ineffective conservative treatment of FPPV in 10-75 % of children with progression of the deformity due to failed stabilization of the osteoarticular structures and weak musculo-ligamentous apparatus and late treatment [12]. Neurotransmitter mechanisms of flatfoot are important to explore and find new non-invasive methods for diagnosing flatfoot and predicting progression of foot deformities during the child's growth for timely prevention and treatment of FPPV. The objective was to determine the correlation between whole-blood serotonin levels in children and adolescents with FPPV over a period of four years with the progression of the pathology.

MATERIAL AND METHODS

The study included 88 children and adolescents aged 5 to 15 years with FPPV. There were 50 male and 38 female patients. Written informed consent for the participation in the research project was obtained from the subject's parent/legally acceptable representative. The study was performed in accordance with ethical principles for medical research involving human subjects stated in the Declaration of Helsinki developed by the World Medical Association. Patients of the treatment group were divided by age: 5-8 years (n = 30; 34.1 %), 9-11 years (n = 33; 37.5 %), 12-15 years (n = 25; 28.4 %). The control group included 25 healthy children and adolescents aged 5-15 years with no signs of flat feet and plano-valgus deformation, including 11 females (44 %) and 14 males (56 %). The inclusion criteria were FPPV in children and adolescents in the absence of neurological diseases and other orthopaedic pathologies. Clinical, biochemical and radiological examination of children was performed with the informed consent signed by parents. Workup included orthopaedic examination, photoplantography measuring the subsummary index and pronation of the heel, determination of serum serotonin level measured with enzyme-linked immunosorbent assay using the ELISA Fast Track kit (reference values of serum serotonin 70-270 ng/ml), weight-bearing radiography of the feet in the lateral projection performed at 1, 2 and 4 years with parental consent. We explored the whole-blood serotonin level in children and adolescents aged 5 to 15 years old who suffered FPPV and compared that to the data from photoplantograms, pronation angle of the calcaneus and radiographs of the feet.

Statistical software package Statistica 12 and Microsoft Excel 2010 were used for statistical processing. The Pearson Chi-square test was used to determine a statistically significant difference in the gender distribution in groups according to the course of FPPV. Using the Kruskal – Wallis test, the type of distribution of patients by age was determined in the groups. Normality was assessed using the Shapiro – Wilk test. The results of the study are presented in tables in the form of a median (Me) with an interquartile range [Q1-Q3] within the standard range of 25-75 %. Serotonin levels measured in different years within the same group were compared using the Friedman test, and if it was significant, pairwise comparisons of results were performed between the years using the Wilcoxon W test; the level of significance was determined taking into account the Bonferroni correction. To study the relationship between two signs, correlation analysis was used using the nonparametric Spearman correlation coefficient rs with an assessment of the strength of the correlation relationship using the Chaddock scale. The threshold level of statistical significance was accepted at a criterion value of $p < 0.05$. The quality of the test for serum serotonin levels in groups of healthy children and patients with FPPV was assessed by sensitivity, specificity, accuracy, predictive value of positive and negative results.

RESULTS

In order to confirm the absence of FPPV children and adolescents of the control group underwent photoplantography was performed at the beginning and at the end of the study, a subsummary index calculated and the whole-blood serotonin measured at 1, 2, 4 years (Table 1).

Table 1

Whole-blood serotonin measurements and subsummary index of control patients

Group	Whole-blood serotonin, ng/ml				SI_1 (1)	SI_4 (2)	Wilcoxon test, p
	C_1 (1)	C_2 (2)	C_4 (3)	Wilcoxon test,			
	Me [Q1-Q3]	Me [Q1-Q3]	Me [Q1-Q3]	p	Me [Q1-Q3]	Me [Q1-Q3]	
Control (normal subjects)	120.0 [112.0-132.5]	125.0 [115.0-134.0]	142.0 [134.0-149.0]	$P^{1-2} = 0.282$ $p^{1-3} < 0.001$ $p^{2-3} = 0.001$	37.0 [36.0-38.5]	35.5 [35.0-36.5]	$p^{1-2} < 0.001$

Note: $C_{1,2,4}$ whole-blood serotonin measured at 1, 2, 4 years, ng/ml; $SI_{1,4}$ – subsummary index measured at 1 year, at 4 years; p^{1-2}, p^{1-3}, p^{2-3} – level of significant differences between groups at 1, 2, 4 years at $p < 0.017$.

The average serotonin levels in control patients measured 120.46 ± 18.92 ng/ml at 1 year, 140.92 ± 10.88 ng/ml at 4 years, which indicated slight changes in the serotonin levels over a four-year period with an increase of 14.5 %. The subsummary index was measured at 1 year and at 4 years to confirm the absence of FPPV in controls according to the photoplantogram with the mean values measuring 37.26 ± 1.64 and 35.84 ± 1.04, respectively. There was an increase in the subarch index of the foot by 3.8 % that indicated the physiological formation of the foot arch during the growth. The Wilcoxon test with Bonferroni correction was used to determine a statistically significant difference between whole-blood serotonin levels and the foot sub-summary index at the time points. The results of the analysis showed that there were significant differences in the serotonin level in controls between the results at 1 year and at 4 years; at 2 years and at 4 years, and between the subsummary index at 1 year and at 4 years. Photoplantography was performed for patients of the treatment group at the beginning of the study, the sub-summary index calculated, the pronation angle of the calcaneus and whole-blood serotonin measured to determine the extent of FPPV (Table 2).

Table 2 indicated that 65.9 % of patients in the treatment group had grade II FPPV and 29.5 % suffered grade I FPPV. Whole-blood serotonin levels were both within normal limits and above normal in all groups with grades I, II, III FPPV. An average positive correlation was revealed between the subsummary index, the angle of pronation of the calcaneus and the whole-blood serotonin level in patients with grades I, II FPPV, which allowed us to use one of the parameters for diagnosis of foot deformities. A correlation analysis of the variables was not performed for patients with grade III FPPV due to a small population.

Based on the whole-blood serotonin measured at the beginning of the study patients of the treatment group were divided into 2 subgroups according to the course of FPPV: non-progressive and progressive course (Table 3). The progressive FPPV group consisted of 43 patients with whole-blood serotonin measured over 270 ng/ml; the non-progressive FPPV group consisted of 45 patients with normal serotonin levels, with a predominance of males (62.2 %).

Table 2

Comparable indicators of plantography, calcaneal pronation angle and whole-blood serotonin level measured in patients of the treatment group at one

Grading of FPPV	Number		SI_1 (1)	PAC_1 (2)	C_1 (3)	Correlation coefficient, r
	abs.	%	Me [Q1-Q3]	Me [Q1-Q3]	Me [Q1-Q3]	
Grade I	26	29.5	52.25 [48.2-54.4]	8.0 [7.0-9.0]	143.0 [108.0-312.0]	$r^{1-2} = 0.632$; $r^{2-3} = 0.513$; $r^{1-3} = 0.295$
Grade II	58	65.9	66.4 [63.8-68.3]	13.0 [12.0-14.0]	255.0 [136.0-427.0]	$r^{1-2} = 0.759$; $r^{2-3} = 0.362$; $r^{1-3} = 0.358$
Grade III	4	4.6	81.15 [80.5-81.7]	18.5 [17.5-19.0]	546.0 [528.5-558.5]	–
Total	88	100				

Note: SI1, subsummary index measured at 1 year, PAC_1, pronation angle of the calcaneus measured at 1 year, degree; C_1, serotoninh measured at 1 year, ng/ml; r, Spearman correlation coefficient.

Table 3

Patients of the treatment group distributed by age and gender according to clinical and laboratory data

Course of FPPV	Number		Age, years	Kruskal – Wallis test	Gender				Pearson Chi-square test
					female		male		
	абс.	%	Me [Q1-Q3]	p	abs.	%	abs.	%	p
Non-progressive	45	51.1	9.0 [8,0-12.0]	0.420	17	37.8	28	43.2	0.296
Progressive	43	48.9	9.0 [7.0-12,0]	0.06	21	48.8	22	51.2	
Total	88	100			38	43.2	50	56.8	

The Pearson Chi-square test was used to determine a statistically significant difference in the gender distribution in the groups according to the course of FPPV. A homogeneous distribution by gender was revealed in the groups of non-progressive and progressive FPPV ($p = 0.296$). The type of the distribution by age was determined in the groups using the Kruskal – Wallis test, and the homogeneous distribution of patients by age in groups with non-progressive ($p = 0.420$) and progressive ($p = 0.06$) course of FPPV was demonstrated (Table 3).

Whole-blood serotonin and pronation angle of the calcaneus were measured in patients with non-progressive and progressive course of FPPV at 2, 3, 4 years; weight-bearing radiographs of the feet were produced at 2 and at 4 years (parents of children under 10 years of age refused the procedure due to radiation exposure) (Table 4). The assessment of whole-blood serotonin, calcaneal pronation angle, and arch height were performed for patients with different courses of FPPV and in controls using radiographs by comparing the median and quartile values of the variables (Table 4).

Table 4 showed that the average serotonin levels changed within normal limits in the group of non-progressive FPPV at 4 years. The average radiographic arch height measured 24.2 ± 4.59 mm at 2 years with a slight increase of 4.7 % measuring 25.4 ± 4.99 mm at 4 years. The pronation angle of the calcaneus was 11.6 ± 2.46 degrees at the beginning of the study with a decrease of 9.2 % and measured 10.53 ± 2.5 degrees at 4 years. The minor changes in the photoplantograms of patients with non-progressive FPPV could be explained by the fact that the study involved children aged 5-10 years who develop arches and musculo-ligamentous apparatus. X-rays and photoplantograms showed no signs of progression of foot deformity in patients with a non-progressive course of FPPV which was confirmed by whole-blood serotonin levels during 4 years.

Patients with progressive FPPV had higher whole-blood serotonin at 1 year, that increased by 38.3 % at 4 years measuring 656.02 ± 226.52 ng/ml. The mean calcaneal pronation angle was 12.22 ± 3.35° at baseline, with an increase of 21.2 % at 4 years. Weight-bearing radiographs of the feet showed the height of the arch decreased by 18.7 % over 4 years. The group with progressive FPPV, demonstrated a significant increase in medians and interquartile ranges of serotonin levels and a deteriorated parameters of the feet on photoplantography and radiography comparing measurements at baseline and over 4 years, which indicated a correlation between the whole-blood serotonin level and progression of FPPV.

The reliability of the results obtained in the control group and the groups with different courses of MPVDS was determined at time points using the Wilcoxon test. Table 4 showed insignificant differences in the whole-blood serotonin in controls and the group with non-progressive FPPV at 1 year, in the pronation angle of the calcaneus in patients with non-progressive and progressive FPPV at 1 year due to no difference in the parameters at the beginning of the study.

Table 4

Dynamics in absolute values of whole-blood serotonin, radiographs of the feet and the pronation angle of the calcaneus in patients with FPPV and in controls

Parameters	Groups of patients			Wilcoxon test, p
	controls (healthy) (1)	non-progressive FPPV (2)	progressive FPPV (3)	
	Me [Q1-Q3], n = 25	Me [Q1-Q3], n = 45	Me [Q1-Q3], n = 43	
C_1, ng/ml	120.0 [112.0-132.5]	127.0 [115.0-155.0]	424.0 [290.0-533.0]	$p^{1-2} = 0.216$; $p^{1-3} = 0.00001$; $p^{2-3} < 0.0001$
C_2, ng/ml	125.0 [115.0-134.0]	188.0 [172.0-211.0]	546.0 [358.0-694.0]	$P^{1-2} = 0.001$; $p^{1-3} = 0.00001$; $p^{2-3} < 0.0001$
C_4, ng/ml	142.0 [134.0-149.0]	227.0 [212.0-255.0]	687.5 [424.0-842.0]	$P^{1-2} < 0.0001$; $p^{1-3} = 0.00001$; $p^{2-3} < 0.0001$
AH_2, mm	–	23.0 [21.0-28.0]	22.0 [19.0-28.0]	$p^{2-3} = 0.379$
AH_4, mm	–	25.0 [22.0-30.0]	16.0 [15.0-23.0]	$p^{2-3} < 0.0001$
PAC_1, degree	4.0 [3.0-5.0]	12.0 [9.0-13.0]	13.0 [7.0-18.0]	$p^{1-2} < 0.0001$; $p^{1-3} < 0.0001$; $p^{2-3} = 0.328$
PAC_3, degree	4.0 [3.0-4.0]	12.0 [9.0-13.0]	14.0 [8.0-19.0]	$p^{1-2} < 0.0001$; $p^{1-3} < 0.0001$; $p^{2-3} = 0.0085$
PAC_4, degree	3.0 [2.0-3.0]	11.0 [8.0-12.0]	13.0 [10.0-21.0]	$p^{1-2} < 0.0001$; $p^{1-3} < 0.0001$; $p^{2-3} < 0.0001$

Note: $C_{1,2,4}$, serotonin measured at 1 year, at 2 and 4 years, ng/ml; $PAC_{1,3,4}$, pronation angle of the calcaneus measured at 1 year, at 3 and 4 years degree; $AH_{2,4}$, arch height measured on X-ray at 2 and at 4 years, mm; p, level of significant differences in groups of patients (Wilcoxon test); p^{1-2}, p^{1-3}, p^{2-3}, significant differences between groups at $p < 0.05$.

Correlation analysis revealed a statistically significant moderate positive and negative correlation between the whole-blood serotonin at 1 year, at 2, 3, 4 years, the pronation angle of the heel and the height of the arch on the radiograph in patients with different courses of FPPV throughout the study. There was a greater correlation at 4 years, and a more pronounced correlation (r = -0.633) was seen with the progressive course of FPPV (Table 5). That confirms the correlation between whole-blood serotonin and parameters of the foot pathology.

Sensitivity, specificity, diagnostic efficiency, predictive value of positive and negative results were calculated in groups with different courses of FPPV to assess the diagnostic effectiveness of the method for predicting progression of FPPV based on whole-blood serotonin levels. The sensitivity and specificity of the serum whole-blood serotonin test were 84 and 76 % for non-progressive FPPV and 79 and 76 % for progressive FPPV, respectively. A higher diagnostic accuracy was found for non-progressive FPPV amounting to 81 %, and to 77 % with progressive FPPV. The predictive value of positive results in patients of both FPPV groups was 86 and 85 %, which showed the highest probability of progression of FPPV with increased whole-blood serotonin levels. The AUC area under the ROC curve and threshold values were calculated in the FPPV groups to determine the quality of the diagnostic serotonin test. Excellent AUC values (0.967 and 0.942) with threshold values (0.355 and 0.453) were revealed in both FPPV groups, which indicated the good quality of the predictive test for measuring whole-blood serotonin.

The findings showed a significant moderate positive and negative correlation between the whole-blood serotonin and the pronation angle of the calcaneus and the height of the arch on radiographs. Serotonin measurements had high sensitivity and specificity in predicting progression of FPPV, which allowed the use of the method in the diagnosis of flexible flatfoot.

Table 5

Linear correlation between serotonin measured in patients with different courses of FPPV

Course of FPPV	Correlation coefficient, r			
	C_1-PAC_1	C_2-AH_2	C_3-PAC_3	C_4-AH_4
Non-progressive, n = 45	0.478 (p = 0.001)	-0.470 (p = 0.001)	0.539 (p = 0.0001)	-0.622 (p = 0.000)
Progressive, n = 43	0.562 (p = 0.0001)	-0.572 (0.0001)	0.606 (p = 0.000)	-0.633 (p = 0.000)

Note: $C_{1,2,3,4}$, serotonin measured at 1 year, at 2, 3 and 4 years, ng/ml; $PAC_{1,3}$, pronation angle of the calcaneus measured at 1 year, at 3 years, degree; $AH_{2,4}$, arch height measured on X-ray at 2 and at 4 years, mm

DISCUSSION

There are a variety of methods for diagnosis and assessment of a foot pathology. The most accessible and cheapest method is a visual examination to determine the shape and position of the foot. Pfeiffer et al. reported that visual examination showed 54 % of a flat foot in the group of 3-year-old children, whereas in the group of 6-year-old children only 24 % had a flat foot [1]. The Foot Posture Index-6 (FPI-6) is often used in clinical practice as a fast, simple, inexpensive, and multisegmental clinical quantification tool to assess static foot alignment in all three planes and to classify foot posture types using six individual criteria [23].

Plantography is used to calculate Staheli Plantar arch index, the Chippaux–Smirak index, Clarke's angle index to assess the medial longitudinal arch of the foot. Flat foot is diagnosed in 22-70 % of children aged 3-12 years. The incidence of flat foot varies depending on the foot indices calculated for the medial surface or plantar surface of the foot. Flat foot is 1.7-1.8 times as likely to be detected with assessment of the plantar surface [24]. Functional tests are practical for evaluation of the range of motion in the foot joints and the type of flatfoot (flexible, rigid).

Passive extension of the big toe (Jack's test) reveals changes in the talonavicular and naviculocuneiform joints; a tip toe standing test is applied to evaluate the strength of the calf and foot-stabilising muscles. The short muscles of the dorsum and plantar surface of the foot are assessed with active plantar flexion of the toes. Manual muscle test is performed for passive inversion and eversion of the foot and Achilles tendon shortening is determined by limited dorsiflexion in the ankle joint.

Foot flexibility tests have high specificity and sensitivity in the differential diagnosis of rigid planovalgus deformities [25]. Jiang et al. [19] proposed a new non-invasive method for diagnosing flat feet based on ultrasound. The authors defined the plantar fascia angle as the angle between the plantar fascia and the horizontal line being parallel to the probe and skin measured with a high-frequency linear transducer in B-mode. The study took the calcaneal pitch angle measured from X-radiographs of the lateral weight-bearing foot as the diagnostic standard. The value of the plantar fascia angle in diagnosing flatfoot was

evaluated by comparing it with the medial cuneiform height. The new method appeared to be portable and non-invasive, and could be a safe use for diagnosing flat feet in children and disabled patients [19]. Japanese scientists suggested important use of quantitative indices for 3D foot measurements which could not be revealed by footprint when evaluating the flattening of the foot[26].

The evaluation of X-radiographs of the weight-bearing foot and ankle is still the gold standard for the diagnosis of flatfoot in adults and children [15]. In addition to standard measurements of the angle and height of the foot arch, the coverage of the talar head, the talo-metatarsal angle, the calcaneal pitch, and the talo-calcaneal angle are measured to determine the relationships in the foot joints in three planes [27]. Children and their parents may experience anxiety and fear due to radiation exposure and assessment of radiation risk to the patient should be part of the decision for utilization of any specific imaging modality [28].

In addition to diagnostic methods for planovalgus foot deformity, we explored mechanisms of formation of the pathology. Although there are controversies on the etiology of the disease with the variety of theories on the occurrence of FPPV the factor that can cause muscle and ligament weakness include: excessive weight, low physical activity, prolonged standing, chronic overload of the feet, use of inappropriate footwear [29]. Pathological course of pregnancy and childbirth, structural features of the uterus, oligohydramnios, the use of medications must be also considered. In our series, the correlation between the whole-blood serotonin and the height of the foot arch, the pronation angle of the calcaneus include predisposing factors on the formation of FPPV. Some authors report PPV being associated with genetic and systemic skeletal diseases (arthrogrypposis, Marfan syndrome, neurofibromatosis) [29]. Other authors suggest that PPV develops in utero at 2-3 months under the influence of hereditary and external factors resulting from impaired development of the nervous system, which is manifested in the postnatal period during verticalization of the child [29]. Supporters of the tendon-ligament theory that PPV can be caused by disproportionate development of extensor muscles relative to normal flexors of the toes and the posterior tibial muscle [29]. Many authors support neurogenic theory of PPV. A group of foreign authors has identified a correlation between the severity of neuromuscular disorders and the severity of foot deformities. Russian scientists suggest that an injury to the spinal cord at the segmental level of lower limbs and suprasegmental injuries can lead to PPV [29]. Impaired innervation of the tibial muscles were revealed at the level of spinal motor neurons of the horns of the spinal cord in children with perinatal lesions of the cervical and lumbar spine indicating ischemia of the reticular formation of the spinal cord with electomyography. The genesis of PPV can be associated with congenital defects of the nervous system (myelodyslasia of the spinal cord, dysraphism) with impaired muscle balance and symmetry of reflexes [29]. Etiopathogenesis of PPV can also be associated with manifestations of congenital mesenchymal dysplasia: poor posture, scoliosis, spondylodysplasia of the lumbosacral spine, hip dysplasia, nocturnal enuresis, joint hypermobility, spondylolysis and spondylolisthesis, spina bifida, tibia valgus deformity, etc. [29].

Our study revealed an increased whole-blood serotonin with progressing PPV, which could be associated with impaired metabolism of the serotonin neurotransmitter, or with a genetic or traumatic defect in serotonin receptors located in the neurons of the brain and spinal cord, or with a deficiency of the transporter protein that ensures the serotonin transfer into the cell. Our findings supported the neurogenic theory on the formation of FPPV, and in addition to hypoxic-ischemic lesions of the central nervous system and the spinal cord, dysfunction of the serotonin neurotransmitter system was revealed in children with FPPV [29].

Literature review showed a paucity of research on the clinical and laboratory diagnosis of the progressing FPPV and of the neurotransmitter mechanism of foot pathology. Kadri et al. reported the flatfoot being related to lower serum calcium levels [30]. A pathological course of pregnancy and childbirth can cause an imbalance in the level of serotonin in the newborn, having a negative impact on the child's neurogenesis [13]. Long-term changes in serotonin concentration affect the transmission of nerve impulses, vascular tone and homeostasis [31] leading to impaired muscle tone and dysfunction of the lower limbs with progression of foot deformities. These data are consistent with our findings indicating the correlation between the whole-blood serotonin and progression of FPPV. A patent for invention No. 2773007 received on May 30, 2022 [32] had it that children and adolescents with FPPV having whole-blood serotonin of 270 ng/ml are characterized by a non-progressive course, and there is a greater risk of progression at values greater than 270 ng/ml. Therefore, measurement of the whole-blood serotonin in children and adolescents suggests the neurohumoral mechanism of the pathology and facilitates prediction of progressing foot deformity, which has the important clinical and social role.

CONCLUSION

Measurement of the whole-blood serotonin in children and adolescents showed a moderate correlation with the pronation angle of the calcaneus and the height of the arch on radiographs with excellent sensitivity and specificity in the diagnosis of FPPV. Changes in the whole-blood serotonin levels above the reference value can increase the risk of progression of FPPV in children indicating the involvement of the serotonergic system in the formation and progression of foot pathology and the test can be advocated for use in predicting the course of flexible pes planovalgus.

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Ethical expertise *The study was performed in accordance with ethical principles for medical research involving human subjects stated in the Declaration of Helsinki developed by the World Medical Association as revised in 2013 in compliance with the principles of research safety, awareness, voluntary involvement, and confidentiality.*

Informed consen *Written informed consent for the participation in the research project was obtained from the subject's parent/ legally acceptable representative.*

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Comparative evaluation of osseointegration of new percutaneous implants made of Ti Grade 4 ultrafine-grained alloy

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Abstract

Introduction It has been shown that titanium implants with a structured surface provide an increased rate of osseointegration what makes their application quite promising. **The purpose** of this work was to conduct a comparative evaluation of the efficiency of osseointegration of new percutaneous implants for prosthetics made of ultrafine-grained Ti Grade 4 alloy. **Materials and methods** The study was carried out on 12 male rabbits of the Soviet Chinchilla breed. Six rabbits of the control group had implants made of Ti6Al4V powder using selective laser sintering technology that were osseointegrated into the tibia, 6 rabbits of the experimental group had implants made of Ti Grade 4 by equal channel angular pressing. The formation of the "bone-implant" block was examined 26 weeks after the implantation. **Results** Histologically, after 26 weeks of the experiment, porous changes, enlargement of the Haversian canals, and pronounced osteoclastic resorption were not detected in the animals of the experimental group throughout the stump in the compact plate. Around the implant, a bony case repeating the bone shape was formed, represented by lamellar bone tissue. Using X-ray electron probe microanalysis, it was found that in the substrate formed on the surface of the implant in rabbits of the experimental group, there was significantly more calcium in all areas over the implant relative to the animals of the control group. In the control group, relative to the experimental group, an increased level of C-reactive protein in blood serum was retained longer. Complications and significant clinical and laboratory abnormalities were not found in both groups during the entire experiment. **Discussion** Our data are consistent with the results of other experimental studies, which unambiguously noted that titanium implants with a structured surface show increased osseointegration characteristics in comparative studies relative to implants without modification of the structure of the material of the threaded surface. The absence of complications and undesirable reactions of the animal organism also indicates the acceptable safety of the tested products. **Conclusion** Osseointegration of a percutaneous implant that has a mixed nanocrystalline and ultrafine-grained structure was more effective than the reference implant. This makes the use of such implant promising for solving clinical problems in prosthetics.

Keywords: prosthetics, osseointegration, titanium implant, nanocrystalline structure, selective laser fusion, experiment, rabbits, product safety

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INTRODUCTION

The use of titanium alloys in the nanostructured and ultrafine-grained (UFG) states along with their surface modification has been currently a universal strategy for improving the mechanical properties and biocompatibility of medical devices [1, 2]. For orthopaedic practice, studies of the osseointegration of percutaneous implants made of titanium alloys with different chemical composition, structure, and coating are relevant issues [3-6]. It has been shown that osseointegrated titanium implants made of materials with a structured surface provide an increased rate of osseointegration [7, 8]. To a greater extent, this issue has been studied for products used in dentistry and maxillofacial surgery [9-11]. Nevertheless, the studies are a promising direction to improve the survival characteristics of percutaneous implants that have been currently introduced to solve the problems of osteointegral prosthetics [12-14].

Purpose To conduct a comparative assessment of the osteointegration efficiency of new percutaneous implants for prosthetic application that are made from ultrafine-grained Ti Grade 4.

MATERIALS AND METHODS

The study was carried out on 12 male rabbits of the Soviet Chinchilla breed, age 6-10 months, average weight 3.2 ± 0.3 kg. Premedication for the operation was carried out by intramuscular administration of diphenhydramine 1 % 10 mg/kg, atropine 0.01 % 0.05 mg/kg, meditin 0.1 % 1 mg/kg,

zoletil 100 0.025 mg/kg; anesthesia was performed intravenously with propofol 1 % 10 mg/kg. All rabbits underwent osteotomy of the tibia at the border of the upper and middle thirds. Next, the medullary canal was reamed to 4.5 mm and an implant with a diameter of 5 mm (RF patent No. 152558) was screwed into the tibial stump. Animals of the experimental group (n = 6) received titanium implants made of the ultrafine-grained Ti Grade 4 alloy (Fig. 1 a), animals of the control group (n = 6) received titanium implants made of the standard Ti6Al4V alloy (Fig. 1 b). Installation of implants is shown in Figure 1 c. The shin stump was formed by the myoplastic method using one dermofascial flap.

Next, a compression device (RF patent 2631631) with a PTFE prosthesis was attached to the bone (Fig. 2). The bone was subjected to compression load of 3.5 N for 5 weeks after implantation. The choice of the compression value was substantiated by us in a previous study [15].

Implants of the control group were made from Ti6Al4V powder (Advanced Powders & Coatings Inc., Canada) with an average particle size of 23.5 μm and were produced by selective laser sintering (SLS) on an EOS EOSINT M 280 3D printer (Germany) at the Ural Federal University [16]. Implants for the experimental group were made from a bar of ultrafine-grained Ti Grade 4 with a diameter of 10 mm by equal-channel angular pressing at the Nanotech LLC enterprise (Ufa), and were produced on a MANURHIN K'MX 432 longitudinal lathe machine. Mechanical properties of the materials and the arithmetic mean deviation of the threaded surface microprofile of the implants are presented in Table 1. These data on the properties of the material of SLS-implants are consistent with the results of studies presented in the work of Kaplan et al. [17].

Additionally, to assess the structural changes that occur during the turning on lathe of an experimental implant, we studied the microstructure of the implant material after machining using a Zeiss CrossBeam AURIGA scanning electron microscope in the electron backscattered diffraction (EBSD) analysis mode. Figure 3 shows the microsections of the threaded part of the implant, the results of the EBSD analysis of scanning electron microscopy, and the histogram of the grain size distribution of the microstructure, built using the SIAMS 700 software package.

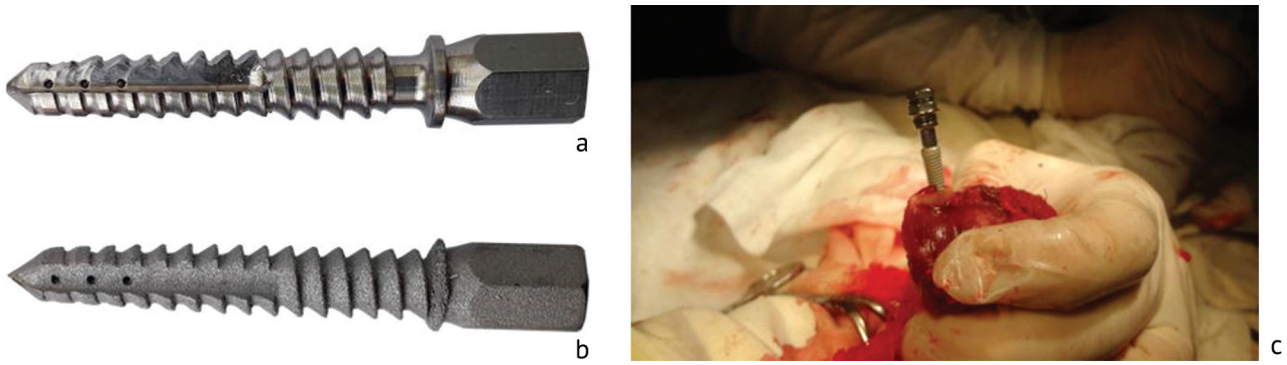

Fig. 1 Implants made of ultrafine-grained Ti Grade 4 alloy after mechanical processing (a) and Ti6Al4V alloy after selective laser sintering (b); installation of the implant in the rabbit tibia stump (c)

Fig. 2 X-ray of the rabbit tibia stump after surgery (a) and photo of the rabbit with the implant fixed in the external fixator featuring compression ability (b)

Table 1

Mechanical properties and mean arithmetic deviation of the threaded surface microprofile of the implants

Implant type	$\sigma_{0,2}$, MPa	σв, МПа	δ, %	Ra, mkm
SLS Ti6Al4V (control)	1045	1200	8	5.59
Mechanical treatment of UFG Ti Grade 4 alloy (experiment)	1071	1240	11	0.95

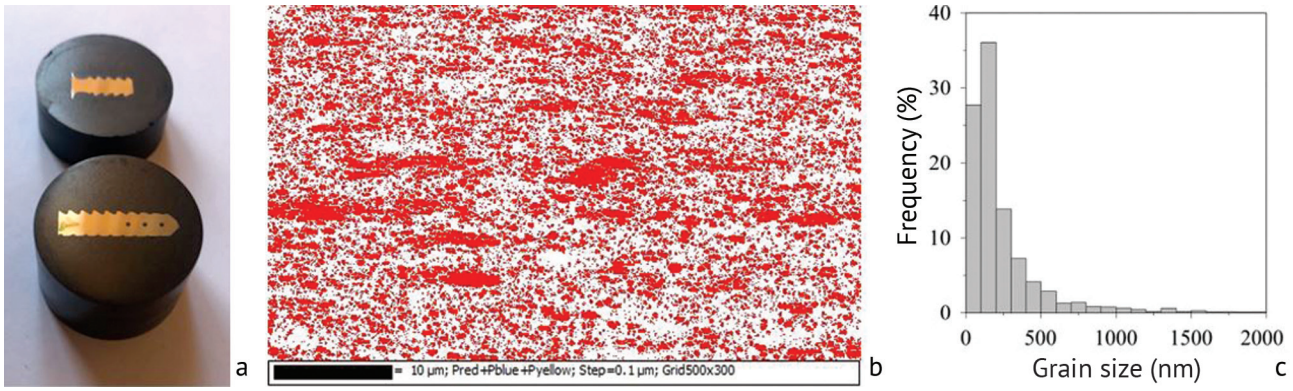

Fig. 3 Photo of microsections of the threaded part of the implant (a); phase-contrast EBSD image of the α-phase of the surface layer of the thread (b); grain size distribution histograms of the implant material after turning (c)

The result of the EBSD analysis showed that the microstructure under the study was a mixed ultrafine-grained and nanocrystalline with separate larger grains up to 2 µm in size. Grains sized from 100 to 300 nm prevailed; their number was about 28 %. There was also a large number of nanocrystallites of the sizes less than 100 nm, the content of which reached 32 %. The presence of such nanocrystallites in the material of the threaded surface of the implant suggests a significant increase in the efficiency of osseointegration.

Animal care In the course of the experiment, the animals were kept in cages, one animal in each, with containers for food and water. Wet cleaning of cells was carried out daily. Food was distributed to the animals once a day, clean drinking water was given without restrictions. Before entering the experiment, the animals were quarantined for 21 days. During the experiment, the animals were observed daily for general condition, respiration, function of the involved limb, as well as the condition of postoperative wounds. The duration of observation of all animals was 26 weeks after implantation. Euthanasia of animals was carried out by introducing lethal doses of barbiturates.

Radiographic study The radiographic complex Compact (Milan, Italy) was used for radiography. The current was 60 mA, the voltage was 57-69 kV, the exposure time was 0.4-0.6 sec. The specific parameters of the operation of the complex depended on the constitution of the animal. Radiography of the rabbit limb was performed in frontal and lateral views. Radiography was performed before and after surgery, on days 21, 42, 84, 105,180 after surgery.

Morphological study The tibia with the implant integrated into it was placed in a 10 % solution of neutral formalin. After 7 days of fixation, the bone was sawn in the longitudinal direction, leaving the implant in one of the halves of the cut, exposing only the surface of the implant; and fixation in formalin continued for another 3-5 days. Next, the half of the tibial stump with the implant in was dehydrated in ethyl alcohol (2 shifts of 70, 80, 96 and 100 degrees of strength), poured into 2.2-dimethyl-3-methylenebicyclo[2,2,1] heptane and dried in an open container until it had completely evaporated. The dried cuts were sprayed with a conductive layer of Pt and Pd and were examined by scanning microscopy using a Zeiss EVO MA18 electron microscope (Carl Zeiss Group, Germany). The distribution of Ca and P in tissues adhered to the surface of integrated implants was performed using a BRUKER QUANTAX 200 – XFlash 6/10 energy dispersive spectrometer (Bruker Nano GmbH, Germany). The work was carried out in the mode of constructing element maps, spectra and obtaining digital data on the content of each osteotropic element.

Fragments of the tibial stump without an implant were decalcified in a mixture of hydrochloric and formic acids, dehydrated, and embedded in paraffin-containing mixtures capable of hardening. Paraffin sections, 6 µm thick, were produced on a Reichard sledge-type microtome (Germany), and after deparaffinization, were stained with hematoxylin and eosin. Next, they were examined using an AxioScope A1 stereomicroscope (Carl Zeiss MicroImaging GmbH, Germany).

Laboratory tests In the dynamics of the experiment, blood samples were harvested before surgery, 3,

5, 12 and 26 weeks after implantation. A complex of biochemical and hematological studies was performed, including total protein, C-reactive protein (CRP), creatinine, urea, total calcium, inorganic phosphate, assessment of the activity of phosphatases (alkaline phosphatase – ALP; bone isoenzyme of acid phosphatase – TrAP) and transaminases (ALT, AST), determination of the content of leukocytes, erythrocytes and platelets.

Hematological studies were performed on a ProCyte Dx automatic analyzer (IDEXX Lab., Netherlands), biochemical studies were performed on a Hitachi/BM 902 automatic analyzer (F. Hoffmann-La Roche Ltd., Italy) using Vector-Best reagent kits (Russia).

Regulation standards The study was carried out in accordance with GOST ISO 10993-1-2021. Medical products. Evaluation of the biological effect of medical devices. Part 1. Evaluation and research in the risk management process; GOST ISO 10993-6-2021. Medical products. Evaluation of the biological effect of medical devices. Part 6. Studies of local response after implantation.

Ethical principles Prior to the start of the study, the approval of the local ethics committee was obtained, protocol No. 1(71) dated 28.04.2022. The study was conducted in compliance with the principles of humane treatment of laboratory animals in accordance with the requirements of the European Convention for the Protection of Vertebrate Animals used for experiments and other scientific purposes, and Directive 2010/63/EU of the European Parliament and the Council of the European Union of September 22, 2010 on the protection of animals used for scientific purposes.

Statistical methods The results in Tables 2 and Table 3 are presented as median, 1-3 quartiles (Me; Q1-Q3). The normality of the samples was determined using the Shapiro-Wilk test. The procedure for statistical assessment of the significance of differences between the parameters at the time of the experiment with preoperative values was performed using the Wilcoxon W-test. The significance of differences between groups was assessed using the Mann-Whitney T-test. The minimum significance level (p) was taken equal to 0.05.

RESULTS

In the post-implantation period, the general condition of the rabbits of both groups was satisfactory. The weight-bearing function of the limb was restored on the 4th to 5th day after the operation and was subsequently maintained in the animals of the experimental and control groups throughout the observation period. In all animals, inflammation and purulent processes of the skin at the site of the implant exit were not detected. Implant prolapse by the time of euthanasia (26 weeks) in animals of both groups was not observed. No serious adverse events were found during the follow-up; suppuration in the stump area and in the peri-implant space was not detected. The pathomorphological study of animals after euthanasia did not find any pathological changes in the internal organs.

In all animals of the experimental group, at 26 weeks after implantation, a complete organotypic restructuring of the bone was radiologically observed (Fig. 4 a). In the rabbits of the control group, there was no implant instability in all the cases; however, in two cases, slight resorption was detected at the "implant-bone" interface (Fig. 4 b).

Histologically, after 26 weeks of the experiment, no porous changes, enlargement of the Haversian canals, or pronounced osteoclastic resorption were detected in the animals of the experimental group throughout the entire length of the tibial stump in the compact plate (Fig. 5). In the proximal part of the stump, the metaphyseal bone was practically unchanged and was presented by large- and medium-cell spongy bone with adipose marrow in the intertrabecular spaces (Fig. 5 b, e). Around the implant, a bone envelope repeating its shape was formed by lamellar bone tissue (Fig. 5c). The bone tissue closely adjoined the implant structures, without gaps and without a connective tissue layer (Fig. 5 a). In the proximal part of the bone-implant block, a few resorption cavities were found in the newly formed bone on the surface of the implant (Fig. 5 d). The bone tissue growing into the inter-thread spaces of the implant was highly mineralized and vascularized (Fig. 5 f).

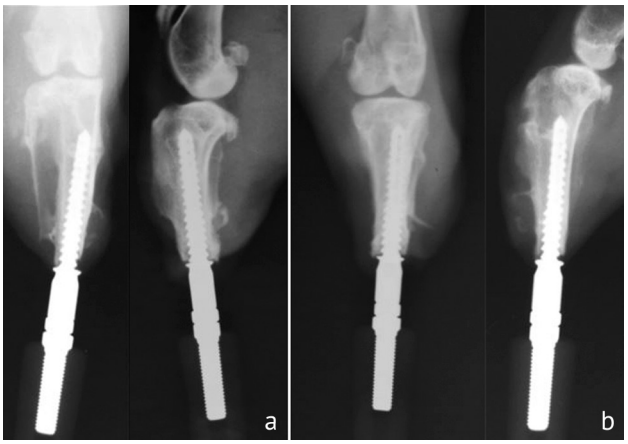

Fig. 4 X-rays of the tibiae 26 weeks after implantation: *a* experimental group; *b* control group

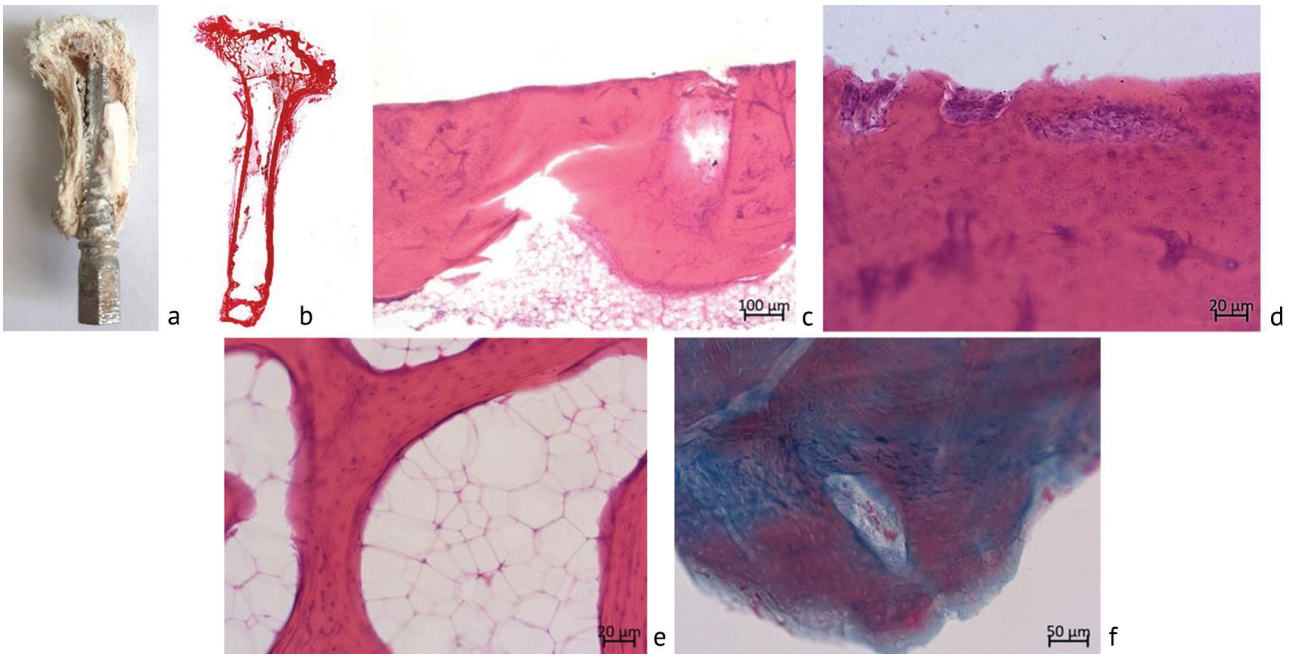

Fig. 5 Proximal area of the tibial stump of the animals of the experimental group: *a* fragment of the tibia of a rabbit with an implant installed; *b* histotopogram of the saw cut of the rabbit tibia after the removal of the implant. Mag. 1.5×; *c* formation of a bony envelope on the surface of the integrated implant. Mag. 50×; *d* resorption cavities on the surface of the bony sheath. Mag. 200×; *e* metaphyseal bone. Mag. 200×; *f* bone tissue in the inter-thread spaces. Mag. 200×. Staining: *b* Van Gieson; *c-e* hematoxylin and eosin; *f* according to Masson

Histologically, in the control group after 26 weeks of the experiment, close contact was observed between the surface of the SLS-implant and the bone tissue, which ensured a strong retention of the implant in the bone bed. By that period, a single bone-implant block had been formed. A continuous compact plate was preserved throughout the bone stump. Pronounced periosteal stratification was not found. In the distal and middle parts of the tibial stump, bone tissue ingrowth into the threaded spaces of the implant was noted (Fig. 6 a, b).

Studies with scanning electron microscopy showed complete integration of bone tissue into the structural surfaces of the implant (inter-thread spaces, holes in the implant structures) throughout the bone-implant contact in the animals of the experimental group (Fig. 7).

In the control group, tight contact of bone tissue and its integration into the surface structures of the implant was also confirmed by the data of energy dispersive analysis in the electronic maps of the distribution of osteotropic elements in the cut structures of the bone-implant block (Fig. 8).

Fig. 6 Formation of the "bone-implant" block in the animals of the control group after 26 weeks of the experiment: *a* cut of the tibia of a rabbit with an implant installed; *b* histotopogram of the saw cut of the rabbit tibia after the removal of the implant. Van Gieson staining; mag. 1.5×

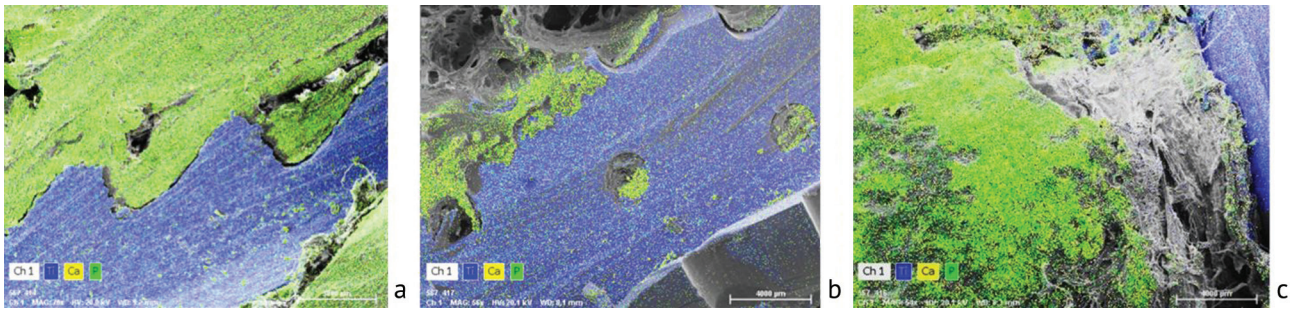

Fig. 7 Distribution maps of osteotropic elements in different parts of the bone-implant block after 26 weeks of the experiment, experimental group: *a* proximal area, *b* middle area, *c* distal area. X-ray electron probe microanalysis. Mag. 68×

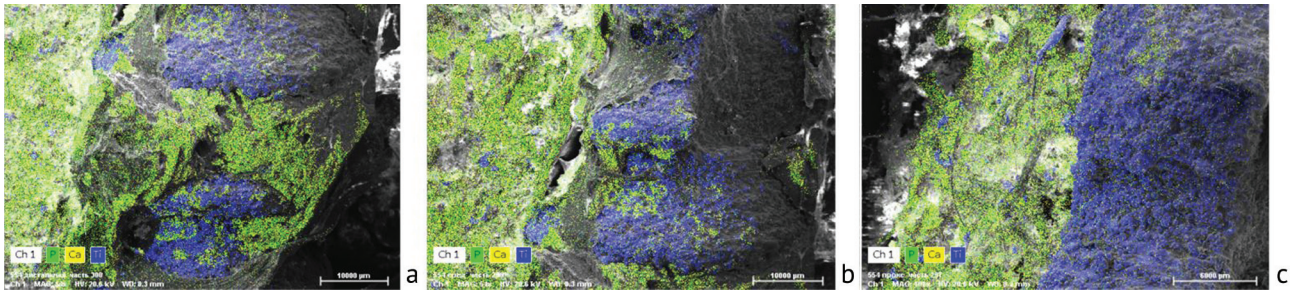

Fig. 8 Distribution maps of osteotropic elements in different parts of the bone-implant block after 26 weeks of the experiment, control group: *a* proximal area, *b* middle area, *c* distal area. X-ray electron probe microanalysis. Mag. 68×

X-ray electron probe microanalysis found that in the substrate formed on the surface of the implant in the rabbits of the experimental group, there was significantly more calcium in all areas of the implant relative to the animals of the control group (Table 2). The content of phosphorus on the surface of the implant in the animals of the experimental group was also significantly higher compared to the control in the proximal and middle regions of the implant.

Differences in the activity of phosphatases in the blood serum of the animals were noted in the dynamics of the experiment (Table 3). Thus, in the experimental group, there was an increase in the activity of alkaline phosphatase 12 weeks after implantation relative to preoperative values. In the control group, the activity of ALP, on the contrary, decreased at the 3rd week, and at the 3rd and 5th weeks the activity of the bone isoenzyme of acid phosphatase increased. Also, an increased level of CRP in blood serum was retained longer in the animals of the control group relative to the experimental group.

Table 2

Ca and P content (weight %) on the implant surface in the different areas of the tibial stump of the rabbits at 26 weeks of the experiment, Me (Q1-Q3)

Area	Calcium, weight %		Phosphorus, weight %	
	Experimental group	Control group	Experimental group	Control group
Proximal	13.6 (13.0-14.1)*	7.3 (6.9-7.6)	4.1 (3.9-4.3)*	3.6 (3.5-3.6)
Middle	15.8 (15.2-16.3)*	9.1 (8.9-9.4)	5.5 (5.1-5.8)*	4.6 (4.4-4.7)
Distal	12.2 (11.7-12.6)*	10.3 (10.0-10.5)	3.9 (3.7-4.2)	4.5 (4.2-4.8)

Notes: * – significant differences relative to the control group at $p < 0.05$

Table 3

Changes in some biochemical parameters of rabbits blood serum in experimental groups on observation time-points (weeks), Me (Q1-Q3)

Parameter	Group	0	3	5	12	26
ALP, u/l	E	51 (50-59)	45 (38-49)	59 (54-61)	67#(62-73)	60 (52-62)
	C	53 (48-63)	42#(38-46)	51 (49-56)	58 (45-66)	61 (56-66)
TrAP, u/l	E	28 (24-30)	30 (28-36)	33 (28-40)	25 (21-29)	19 (18-29)
	C	26 (22-26)	41#(35-42)	34#(29-38)	20 (16-28)	20 (16-29)
CRP, mg/ml	E	0 (0-1)	14#(4-30)	12 (2-20)	5 (0-7)	2 (0-2)
	C	0 (0-1)	13#(6-22)	10#(4-17)	2 (0-3)	4#(2-21)

Note: # – significant differences with preoperative values at $p < 0.05$. E – experimental group; C – control group

Other laboratory parameters (total protein, creatinine, urea, transaminases, total calcium, inorganic phosphate, leukocytes, erythrocytes, platelets) did not change significantly relative to preoperative values in both groups in the course of observation (data not presented). No significant deviations of laboratory parameters were noted in the analysis of individual dynamics for each animal.

DISCUSSION

Our data suggest that the process of osseointegration of a percutaneous implant that has a mixed ultrafine-grained and nanocrystalline structure was better relative to the reference product. This is confirmed by the data of quantitative indicators of X-ray electron probe microanalysis which showed higher calcium content in the newly formed bone tissue on the implant surface throughout the bone-implant block in the animals of the experimental group. The dynamics of alkaline phosphatase activity in rabbits of the experimental group also indicates the activation of osteogenesis in the implantation zone. Changes in laboratory parameters also suggest that the biocompatibility of an implant made of a material with an ultrafine-grained and nanocrystalline structure was higher relative to the SLS implant. First, in the animals of the control group, an osteolytic reaction was noted, as evidenced by an increase in the activity of TrCP and its radiological signs recorded in two animals. Second, the acute phase reaction to implantation in the animals of the control group, based on the dynamics of CRP, was longer than in animals of the experimental group. It should be noted that the absence of pronounced complications and significant clinical and laboratory abnormalities in animals of both groups during the entire experiment also indicates the acceptable safety of the tested products.

Our data are consistent with numerous results of other experimental studies, in which it is unequivocally noted that titanium implants with a structured surface show increased osseointegration characteristics in comparative studies relative to the implants without modification of the structure of the material of the threaded surface [18-24]. However, the experimental models used in those works differ significantly from our model. Thus, in a number of works [18, 21, 22], a dental implant was installed in the bone of the segments of the hind limbs of experimental animals. In other works, dental implants with a structured surface were implanted at the site of application, in the jaw [19, 23, 24]. Nan-Jue Cao et al. [19], using SMAT technology, were able to impart a gradient nanostructured surface (GNS Ti) to a titanium implant. It was established that, compared with coarse-grained titanium CG, the surface of GNS Ti stimulates cell adhesion, proliferation and differentiation and improves osteogenesis and osseointegration.

One of the works [20] reports the advantages of osseointegration of a titanium implant, the surface of which was modified by coating with osteogenic nanofibers, which composition included polycaprolactone, gelatin, hydroxyapatite, dexamethasone, beta-glycerophosphate, and ascorbic acid. In an experiment on rabbits, titanium implants with an osteogenic nanofiber coating showed better results than uncoated controls. Moreover, there were no pathological changes in the regenerated tissue around the implant.

It is worth highlighting the work of Jones et al., who showed the effectiveness of osseointegration of implants with a nanostructured surface both in cancellous bone and cortical bone [27].

We encountered a few works that focus on the advantages in terms of integration of percutaneous implants with a modified surface, and the authors of the works point to an improvement in the integration of these implants with soft tissues [25, 26].

In general, experimental research on the study of osseointegration of modified implants is ongoing. It has been shown, for example, that genetic mechanisms can be involved in the efficiency of biointegration of such implants [28]. It is noted that the introduction of surface modifications of biocompatible metals is the best solution for improving the corrosion resistance characteristics of such products [29]. A promising direction is the incorporation of individual metal ions into the modified surface [30, 31].

Despite numerous experimental studies, clinical experience with the use of titanium implants with spatial or surface ultrafine-grained nanostructures is scarce. The reason for this may be that some aspects of the use of these products in experimental studies are still poorly studied. In this regard, it is worth highlighting the work [32], which notes that the available studies do not cover the effect of modification of the structure of titanium implants, topographic and chemical changes in surfaces after osseointegration, complications of their use, and the survival of products in the long term, especially taking into account the conditions of constant load on the bone. Jayasree et al. point to the fact that the positive effects of osseointegration revealed in most experimental studies may be due to the fact that the implant in animals, as a rule, does not bear mechanical loads, therefore, *in vivo* studies on large animal models with mechanical loading are needed to overcome this gap in the long term [33].

Based on the current state of the topic in general, it can be noted that the advantage of our experiment is that titanium implants with a mixed ultrafine-grained

and nanocrystalline structure were studied on a model that is closer to the model of clinical use, with a fairly long observation period. This makes the use of such implants promising for solving clinical problems of prosthetics. Obviously, the limitations of this study relate to the sample sizes of the experimental animals.

CONCLUSION

Thus, the results of the study on a rabbit model have shown that the use of percutaneous implants made of a Ti Grade 4 alloy with a mixed nanocrystalline and ultrafine-grained structure by mechanical processing under compression loading of 3.5 N for 5 weeks improves the characteristics of osseointegration in comparison with SLS implants made of titanium alloy Ti6Al4V.

Conflict of interest *The authors declare no conflict of interest.*

Financing *The study was carried out within the framework of the topic "Controlled one-stage osseointegration of percutaneous implants with mechanobiological stimulation of bone formation under conditions of an external fixation system" of the state assignment for scientific research and development of the Federal State Budgetary Institution Ilizarov NMRC TO of the Ministry of Health of Russia, as well as with the financial support of the Ministry of Science and Higher Education of the Russian Federation as part of the Development Program of the Ural Federal University named after the first President of Russia B.N. Yeltsin in accordance with the program of strategic academic leadership "Priority-2030".*

Ethical expertise *Prior to the start of the study, the approval of the local ethics committee was obtained, protocol No. 1(71) dated 04/28/2022.*

Informed consen*t Not required.*

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In vivo effectiveness of polymer hydrogels impregnated with an antibacterial drug in chronic osteomyelitis

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Abstract

Introduction Polymethyl methacrylate (PMMA) is a common depot system in the treatment of chronic osteomyelitis. However, a lot of its shortcomings do not allow us to consider it ideal. **Purpose** of the work was to study *in vivo* the effectiveness of a polymer hydrogel containing an antibiotic for chronic osteomyelitis of the tibia in a rabbit model and compare it with PMMA **Materials and methods** The study was performed on the lower leg of 25 mature Chinchilla rabbits. A model of chronic osteomyelitis of the tibia was created. A methicillin-sensitive strain of *Staphylococcus aureus* (MSSA), highly active against cefazolin, was chosen as an infectious agent. Surgical debridement started 21 days after the clinical, laboratory, radiological and microbiological confirmation of the diagnosis, the technique for all animals was the same. The experimental group (n = 11) was treated by implantation of a polymer hydrogel, the comparison group (n = 11) with PMMA, and the control group (n = 3) had no implanted substance. In the postoperative period, monitoring of the local status, weight and body temperature of the animals, microbiological and radiological studies were carried out. Animals were taken out of the experiment by stages. Biopsies were sent for bacteriological and histomorphometric studies. Statistical comparison of the groups was performed using the Mann - Whitney, Kruskell - Wallis and Tukey criteria, descriptive statistics were used for the control group. **Results** In the experimental group, in all cases, postoperative wounds healed in a timely manner, the levels of WBC and CRP significantly ($p = 0.040$) decreased from 14 and 21 days, respectively. Microbiologically, the growth of microflora from the wound discharge and biopsy specimens was not detected; radiographic progression of chronic osteomyelitis was not observed; histomorphometry revealed a significant ($p = 0.002$) effective relief of the inflammatory process. In the comparison group, systemic antibiotic therapy was required from postoperative day 7. Levels of inflammatory markers decreased less effectively than in the experimental group. MSSA was verified from wound discharge and biopsy specimens at almost every follow-up time-point. X-rays and histomorphometry ($p = 0.001$), on average, detected exacerbation of osteomyelitis. In the control group, systemic therapy did not give positive dynamics. **Discussion** A comparative analysis showed that the hydrogel impregnated with an antibacterial agent, unlike PMMA, reliably arrests chronic osteomyelitis without auxiliary systemic antibiotic therapy and does not cause material-associated bone resorption. The clinical and laboratory picture is fully consistent with the data of microbiology, radiology and histomorphometry. **Conclusion** Hydrogel impregnated with an antibiotic reliably and effectively stops chronic osteomyelitis compared to PMMA.

Keywords: chronic osteomyelitis, polymer hydrogel, bone cement, polymethyl methacrylate, orthopedic infection, PMMA, *in vivo* study, experimental model

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INTRODUCTION

Chronic osteomyelitis is a challenging problem in modern traumatology and orthopaedics since it is considered one of the most severe infectious complications [1] and accounts for 3-25 % of all diseases of the musculoskeletal system [2]. As is known, chronic osteomyelitis triggers a whole cascade of successive reactions, resulting in inflammation, microbial biofilms, sequesters and destruction of bone tissue [1, 3].

The main method of combating microbial biofilms is the removal of an infected implant, if present, radical surgical debridement, and a combination of local and systemic antibiotic therapy. The combination of local and systemic therapy has shown better eradication of infection in animal models compared to the use of systemic antibiotics alone, since the bacterial biofilm hinders their penetration and ultimately contributes to a change in the metabolic state of microbial colonies and the acquisition of resistance to the drug used [4]. Depot systems are used as local therapy. The most common system in clinical practice for delivering antibiotics to the site of infection is bone cement based on polymethyl methacrylate (PMMA). However, despite the many ways to improve the methods of treatment and the structure of PMMA, recurrence of chronic osteomyelitis is observed in 20-30 % of cases, and in 16.75 % the treatment ends with amputation of the limb [1]. Moreover, such limitations as the elution of only 10 % of the impregnated drug, hydrophobicity and bioinertness of the material, requiring repeated surgical intervention to remove it [4] and contributing

to an increase in the duration of treatment and additional stress on the patient's body [1], as well as high temperature polymerization (up to 120 ºC), which causes bone tissue necrosis and limits the range of drugs used, does not allow us to consider the PMMA system as ideal. Therefore, a search for new local transport systems has been recently carried out that would be devoid of the shortcomings of bone cement. Preferences are mainly given to biodegradable depot matrices, one of which is hydrogel [5].

Purpose: to study *in vivo* the effectiveness of chronic tibial osteomyelitis on a rabbit model with an antibiotic-impregnated polymer hydrogel and compare it with PMMA.

MATERIALS AND METHODS

In vivo study was performed on 25 adult Chinchilla rabbits aged 5-6 months with an average weight of 2608 ± 112 g. All animals were males to exclude the effect of sex differences on the results of the study. Before inclusion in the study, the rabbits were subjected to examination by a veterinarian and were found to be healthy. The animals were allowed to acclimatize for 10 days prior to the start of the experiment. Feeding was carried out 3 times a day, water supply was constant. Sawdust was used as bedding. Much care was paid to a daily cleaning of the space and cages in order to prevent exogenous infection.

In all cases, the study segment was the lower leg. Modeling of chronic osteomyelitis was performed in the proximal tibia according to the previously described method [6]. The surgical technique was the same for all rabbits. Animals were anesthetized by intramuscular administration of Zoletil 100 and Meditin 0.1 % at a dosage of 30 mg/kg and 0.5 ml / 5 kg, respectively. Methicillin-susceptible *Staphylococcus aureus* (MSSA) [7, 8, 9], which is highly active against cefazolin and was isolated from intraoperative biopsies of patients treated by us, was used as an infectious agent as the leading etiological structure of orthopedic infections. After being infected, the rabbits developed chronic osteomyelitis for 21 days [6, 10]. Once the diagnosis was confirmed, they underwent surgical debridement of the focus of infection. Surgical debridement was performed according to the same technique. The distribution of rabbits into groups (experimental, comparison and control) was carried out randomly. After being infected and until the end of the study, all animals were kept in individual cages under vivarium conditions with 12-hour cycles of light and darkness at a temperature of 20 ± 1 °C and air humidity of 50-70 %.

In the postoperative period, like at the stage of infection and debridement, the wound area was treated with a 0.05 % chlorhexidine solution until it was completely healed. Monitoring of the local status, weight and body temperature of animals and blood parameters (hemoglobin (HB), leukocytes (WBC), C-reactive protein (CRP) and ESR) was performed on days 3, 7 and then with an interval of one week up to 21 days at the stage of infection and up to 42 days after the debridement. A microbiological study of wound discharge (if any) and of biopsy material taken at the stage of withdrawal of the animals from the experiment was conducted. Radiographic study was performed the next day after the operation, on the 21st day of the infection stage and on the 3rd, 15th, 30th and 45th days of the sanitation stage.

The duration of the sanitation phase was 45 days. The animals were taken out of the experiment on the 15th, 30th and 45th day. The rabbits were euthanized under anesthesia by air embolization through the ear vein. After harvesting bone and soft tissue biopsy material, including fragments of the compared depot systems, for microbiological examination, the bone was placed in a 10 % formalin solution and sent to the pathoanatomical laboratory for further histomorphometric examination. Micropreparations were examined with an AxioLab A1 light-optical microscope at a magnification from 100× to 400×.

Technique of surgical debridement of the infection focus In a fixed supine position under general anesthesia, having previously taken the discharge material if there was a fistula or wound, the hair was shaved and the surgical area was disinfected. After treating the surgical field three times with antiseptic solutions, a 3-cm long skin incision was made along the old postoperative scar of the tibia. Purulent streaks/ pockets were opened to evacuate the contents, if any. After excision of the altered soft tissues, the area of the defect was exposed and expanded with a utter to a size of 0.6 × 0.6 cm and a depth of 4 mm. Further, an additional hole was drilled somewhat distally from the defect to the same depth and size of 0.4 × 0.4 cm in order to take a bone biopsy for histological confirmation of infection. Next, the bone marrow canal was debrided with spoons for removal of pus, small sequesters and granulation tissue. Intra-operative biopsies were sent to the microbiological laboratory. The canal was abundantly washed with 20 ml of an antiseptic solution and hemostasis was performed.

After changing gloves, changing and additional processing of the surgical field, we proceeded to the stage of implantation of intra-operatively manufactured depot systems based on polymer hydrogel and PMMA, saturated with 300 mg of cefazolin, according to the previously described method [5]. The experimental group (n = 11) was injected with 2 ml of polymer hydrogel into the medullary canal using a syringe through a catheter. The comparison group (n = 11) received solitary bone cement prior to the start

of the polymerization reaction. In the control group (n = 3), no material was implanted. The operation was completed by layer-by-layer suturing of the wound.

The morphometric assessment of the infection process on histological preparations was carried out using the HOES scale (Histopathological Osteomyelitis Evaluation Score) [11], which is a graduated semi-quantitative and additive form for assessing the criteria for acute (A1-A3) and chronic (C1-C2) osteomyelitis. The following criteria were assessed: A1 – osteonecrosis, A2 – soft tissue necrosis, A3 – granulocyte infiltrate, C1 – bone neogenesis/fibrosis, and C2 – lymphocyte/macrophage infiltrate. Depending on the severity, determined by the number of formed elements per unit area of the infiltrate, each criterion was assigned a score from 0 to 3, where 0 is the absence of inflammation sign; 3 is severe inflammation. The sum of points A1-A3 $\geq$ 4 of the histopathological picture corresponded to acute osteomyelitis; A1-A3 and C1-C2 $\geq$ 6 to exacerbation of chronic osteomyelitis; C1-C2 $\geq$ 4 to chronic osteomyelitis; C1-C2 $\leq$ 4 points to subsidence of chronic osteomyelitis; C1-C2 $\leq$ 1 point to no signs of osteomyelitis. The area was measured using the MegaMorph12 morphometric program.

The obtained data were statistically processed using the IBM SPSS Statistics 22 and SigmaPlot 11.0 software package. The weight of animals and laboratory blood tests for the experimental and comparison groups of rabbits on the check days of the study are presented as the mean ± standard deviation (μ ± Sd). In order to identify intergroup significant differences, the Mann – Whitney test was used. Values were considered significant at $p < 0.05$. Descriptive statistics were used for the control group.

The significance of histomorphometric results was determined by the nonparametric Mann – Whitney test and the Kruskal – Wallis multiple comparison test. When intergroup differences were found, one-way analysis of variance with Tukey's post hoc comparisons was used. Values were considered significant at $p < 0.05$. Statistical data are presented as median and interquartile range (Me (25 %; 75 %)) as a range chart.

The experimental work was approved by the ethics committee of the scientific council of the Federal State Budgetary Institution Priorov National Medical Research Centre for TO of the Ministry of Health of the Russian Federation and was carried out in accordance with the ethical standards for the treatment of animals in compliance with the recommendations and requirements of the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes (Strasbourg, 2006). All manipulations on animals were carried out in accordance with the Declaration of Helsinki on the Humane Treatment of Animals (2000) and with the order of the Ministry of Health and Social Development of the Russian Federation No. 708n dated August 23, 2010 "On approval of the rules of laboratory practice". Animals were kept under the conditions specified in the "Guide for Care and Use of Laboratory Animals" (1996).

RESULTS

By the 21st day of the infection stage, the development of a fistula in the area of the postoperative scar was noted in 60 % of rabbits (n = 15), an abscess in 12 % (n = 3), wounds with thick purulent discharge in 16 % (n = 4), hyperemia and /or hyperthermia of the skin in 3 (12 %) cases. In 44 % of the animals (n = 11), the above symptoms were accompanied by an increase in body temperature, which averaged 41.7 ± 0.9 °C by the end of the infection stage.

All animals during the observation period had decreased appetite, were less active, more than half of the cases acquired a forced, limb-sparing position, which caused hypotrophy of the thigh and lower leg muscles. Lameness on the involved limb by walking was noted in 22 (88 %) rabbits. The body weight of the animals during the infection stage decreased on average by 564 ± 113 g. The levels of inflammatory markers in blood tests were higher than normal. The data of the results of laboratory blood parameters for each group are presented in Table 1.

By the 21st day after infection, there were radiographic signs of chronic osteomyelitis: heterogeneous structure of bone tissue with alternating foci of sclerosis and areas of enlightenment (Fig. 1 a), osteoporosis, periostitis of varying severity (Fig. 1 b, c), blurred contours of post-trepanation defect and bone sequestration detected in 7 (28 %) cases. Bacteriological study of the fistula discharge (n = 15) and intra-operative biopsies taken from all rabbits (n = 25) during surgical debridement verified the growth of MSSA.

Table 1

Laboratory blood tests versus the reference values on day 21 after infection of the rabbit's tibia

Tests	Reference values	Day 21 upon contamination (μ ± Sd)		
		Experimental group (n = 11)	Comparison group (n = 11)	Control group (n = 3)
Hb	110-136	104.6 ± 6.5	107.4 ± 8.8	108.3 ± 10.6
WBC	2.5-6.9	11.1 ± 1.8	10.5 ± 2.2	9.6 ± 1.9
ESR	1-4	8.8 ± 3.4	8.5 ± 3.1	6.3 ± 2.1
CRP	0-1	41 ± 15.5	43 ± 16.3	36 ± 22.6

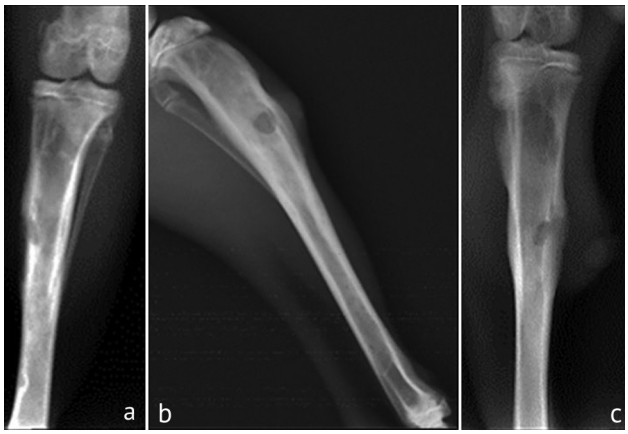

Fig. 1 Radiographs of the rabbit's tibia on the 21st day after infection: *a* heterogeneous structure of the bone tissue; *b* periosteal reaction and osteosclerosis; *c* fistula at the top of the abscess

Histological study showed that there were moderate and significant amounts of lipocytes in the reticular stroma of the bone marrow and the Haversian canals of the cortical plate (Fig. 2 a) and the septa between which were thickened and rich in fibroblast-like cells, gentle basophilic and oxyphilic fibers. Between the latter, cells of the lymphoplasmacytic series were detected in a moderate and significant amounts (Fig. 2 a). The fields of the lamellar bone in the proper bone marrow and some bars of the cancellous bone did not have osteocytes, and the lacunae were empty over large and small areas. Dilated Haversian canals showed signs of resorption and osteoreparative regeneration with layers of new bone substance with intact osteocytes and unusual bending in the lines of bone lamellar binding (Fig. 2 b). At the same time, the resorbable bone matrix at the border with the inflammatory infiltrate had a sharply oxyphilic edge, which indirectly indicated local acidification of the interstitial substance and, accordingly, the ongoing infectious inflammatory process.

In general, the results of clinical laboratory, radiological, microbiological and histological studies confirmed the development of chronic osteomyelitis of the tibia in rabbits by day 21 of the infection stage.

After surgical debridement of the infection focus in the experimental group (n = 11), wound healing proceeded without complications in all animals. The body temperature of the rabbits with the implanted hydrogel fluctuated within the normal range (N = 37-39.5 ºC). In the comparison group (n = 11), by the end of the first week, six (54.5 %) animals required systemic antibiotic therapy by intramuscular injection of cefazolin at a dosage of 30 mg/kg 3 times a day due to the absence of regression of clinical symptoms of chronic osteomyelitis. By week 3, the dosage of the drug was increased to 40 mg/kg in three (27.3 %) rabbits without positive dynamics. However, despite intensive therapy, we failed to achieve complete arrest of the infection in two (18.2 %) cases. In the control group, systemic antibiotic therapy turned out to be ineffective, since at each control period the animals retained certain signs of inflammation. Body temperature by the end of the study in that group was 40.7 ºC, which is above the upper limit of the norm.

Intergroup statistical data on the body weight of animals of the studied groups in dynamics are presented in Table 2.

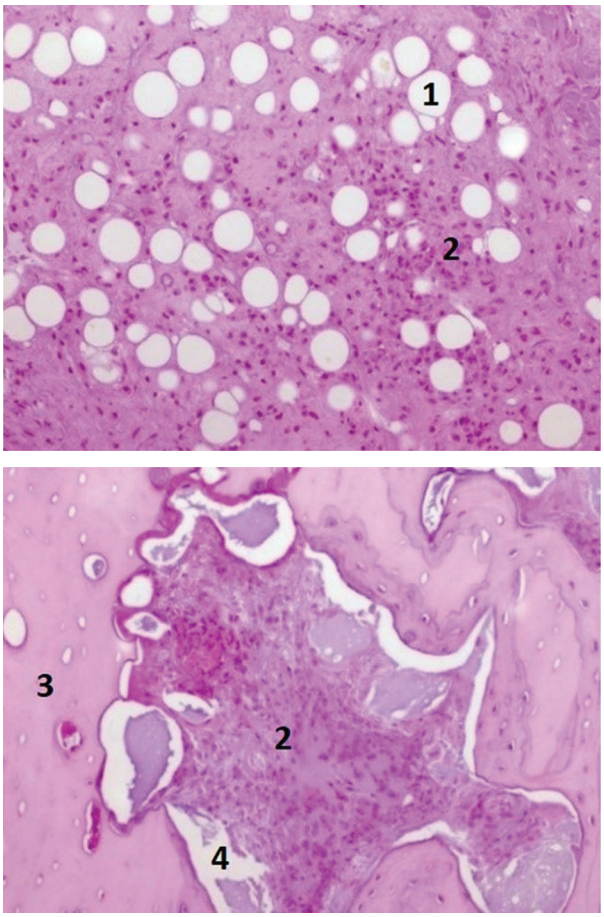

Fig. 2 *a* reticular stroma of the bone marrow with lipocytes (1), infiltration by lymphocytes and plasma cells (2); *b* bone matrix fields devoid of osteocytes (3). Bone resorption (4). Bone marrow infiltration of Haversian canals with lymphocytes and plasma cells (2). Stained with hematoxylin and eosin. ×200

Table 2

Weight of rabbits in each study group after surgical debridement on the control days of the study

Check day	Experimental group (μ ± d)	Comparison group (μ ± Sd)	Control group (μ)	p value (Mann – Whitney test)*
3	2418 ± 110.7	2435 ± 126.3	2294	p = 0.870
7	2989 ± 139.9	2909 ± 140.9	2764	p = 0.279
14	3639 ± 213.5	3512 ± 200.7	3323	p = 0.324
21	4223 ± 263.5	4012 ± 274.8	3945	p = 0.123
28	4901 ± 280.8	4544 ± 306.7	4751	p = 0.006
35	5578 ± 263.1	5175 ± 324.2	5393	p = 0.005
42	6308 ± 152.3	5948 ± 283.3	6116	p = 0.000

Note: * statistical difference for experimental and comparison groups

The dynamics of laboratory blood tests for the experimental and comparison groups presented as arithmetic mean values with a standard deviation, and for the control group as arithmetic mean values are given in Table 3. The statistical data of blood tests in the control periods of the study for the experimental and comparison groups are shown in Table 4.

Table 3

Dynamics of blood tests in the control study days in the experimental and comparison groups

Day	Blood tests			
	HB	WBC	ESR	CRP
	N = 110-136	N = 2,5-6,9	N = 1-4	N = 0-1
Experimental group (μ ± Sd)				
3	115.2 ± 9.7	9.4 ± 1.1	4.6 ± 2.1	35.1 ± 5.7
7	117.1 ± 7.3	8.6 ± 1	3.6 ± 1.6	23.5 ± 10.1
14	122.2 ± 6.2	7.4 ± 1.5	3.5 ± 2.7	15.1 ± 8.7
21	124.2 ± 8.2	6.9 ± 2.8	2.5 ± 0.7	12.5 ± 12.6
28	129.6 ± 7.4	5.4 ± 2.3	3 ± 2.5	8.2 ± 7.7
35	128 ± 5.8	5.2 ± 3.2	1.8 ± 1	4.7 ± 4.1
42	129.7 ± 4.5	3.9 ± 1.5	1.7 ± 1.1	2.7 ± 4.1
Comparison group (μ ± Sd)				
3	115 ± 12.1	10.1 ± 1.9	5 ± 1.8	42 ± 11.6
7	116.1 ± 5.9	9.6 ± 1.8	4.1 ± 1.7	29 ± 13.1
14	117.2 ± 11.7	8.7 ± 1.7	3.8 ± 1.8	19.8 ± 15.5
21	119. ± 12.6	8.8 ± 2.4	3.3 ± 1.5	18.3 ± 8.1
28	121.8 ± 17.9	8.1 ± 3.5	3.6 ± 2.1	14.3 ± 5.5
35	120 ± 19.1	8.1 ± 3.6	3.4 ± 1.9	14.7 ± 10.1
42	119 ± 14.3	7.7 ± 4.5	3.1 ± 2.4	11.8 ± 9.4
Control group (μ)				
3	121	9.03	4.7	37
7	116.3	8.6	4	20.7
14	121.7	8.1	4	17.7
21	118.5	8.2	2	11.5
28	126.5	9.2	2	11
35	132	6.8	2	19
42	128	7.9	4	24

Table 4

Statistical differences in inflammation markers in rabbits of the experimental and comparison groups (Mann – Whitney test)

Day	Blood tests			
	HB	WBC	ESR	CRP
3	0.478	0.478	0.748	0.116
7	0.478	0.151	0.652	0.519
14	0.606	**0.040***	0.332	0.562
21	0.297	**0.024**	0.340	**0.040**
28	0.436	**0.040**	0.258	*0.063*
35	0.209	*0.053*	*0.097*	**0.011**
42	*0.053***	**0.011**	0.383	**0.011**

Note: * statistically significant differences ($p < 0.05$) for polymer hydrogel are in bold; ** – statistical values, where $0.05 < p < 1$, are in italics

There were no obvious signs of progression of chronic osteomyelitis in the experimental group studied by X-rays; post-trepanation defects were replaced evenly, by the end of the study, the holes were almost completely closed (Fig. 3). In the comparison group, in all checking periods, on average, there were radiographic signs of ongoing infection of the tibia such as periostitis of varying severity, subperiosteal cystic cavities, heterogeneous structure of bone tissue, sequestration, and delayed osteoreparation (Fig. 4). In a number of cases, the spread of the osteosclerosis zone to the middle third of the bone diaphysis was observed. Resorption at the "bone-cement" border was traced on the images from the 15th day of the study. In the control group, the same situation was observed but the difference was in a pronounced degree of periosteal response and osteosclerosis of the entire thickness of the upper third of the tibia with spread to its lower parts (Fig. 5).

Microbiological analysis of wound discharge in the experimental group showed no growth of microflora. Negative results were also obtained in the bacteriological study of biopsy specimens of gradually withdrawn rabbits. The obtained single positive growth of MSSA from the soft tissue biopsy of the animal removed from the experiment on the 30th day after the implantation of the hydrogel was regarded by us as a contamination due to a violation of the material sampling technique and its transfer into a test tube. The strain was detected neither on the hydrogel itself, taken from the bone marrow canal and from the surface of this soft tissue biopsy, nor in the bone tissue and other parts of the soft tissue structures, nor in the smear from the area of the entire surgical intervention. In the comparison group, the growth of MSSA was verified at each checking point both from the wound discharge (up to45.5 %) and from the samples of animal materials harvested on the 15th day (9.1 %) and 45th day (27.3 %). It is worth noting that in one (9.1 %) of 2 cases by the end of the study, MSSA on bone cement was detected in a rabbit with a stable remission of the infection.

In the control group, the positive growth of the strain was detected in all rabbits while there was wound discharge, and from biopsy specimens of the animal withdrawn from the experiment on the 15th day of the study. In rabbits withdrawn on the 30th and 45th days, it was not possible to obtain a biopsy material from the medullary canal of the tibia due to the overlapping of the area of the holes with massive periosteal layers and pronounced osteosclerosis, and the inoculation of purulent detritus, taken by the end of the study from the area of the corresponding projection of the infiltrate, did not detect growth of microflora.

Histologically, the reticular stroma of the bone marrow was with weak signs of lymphocytic infiltration and with a large number of macrophage cells on the 15th day in the experimental group. Active osteoreparative signs were found such as an endosteal and periosteal reaction with the formation of reticulofibrous bone tissue featuring trabecularization on the cortical wall where the post-trepanation holes were located. The hydrogel itself occupied a vast area surrounded by giant cells of foreign bodies resorbing it (GCFB) (Fig. 6 a).

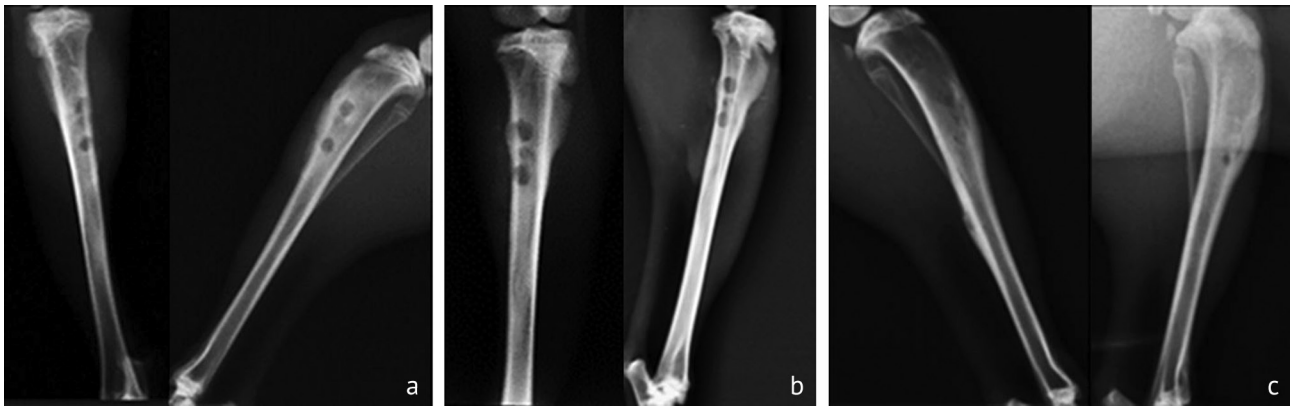

Fig. 3 X-ray images of the lower leg bones of the animals in the experimental group: *a* on the 15th day of withdrawal from the experiment; *b* on the 30th day of withdrawal from the experiment; *c* on the 45th day of withdrawal from the experiment

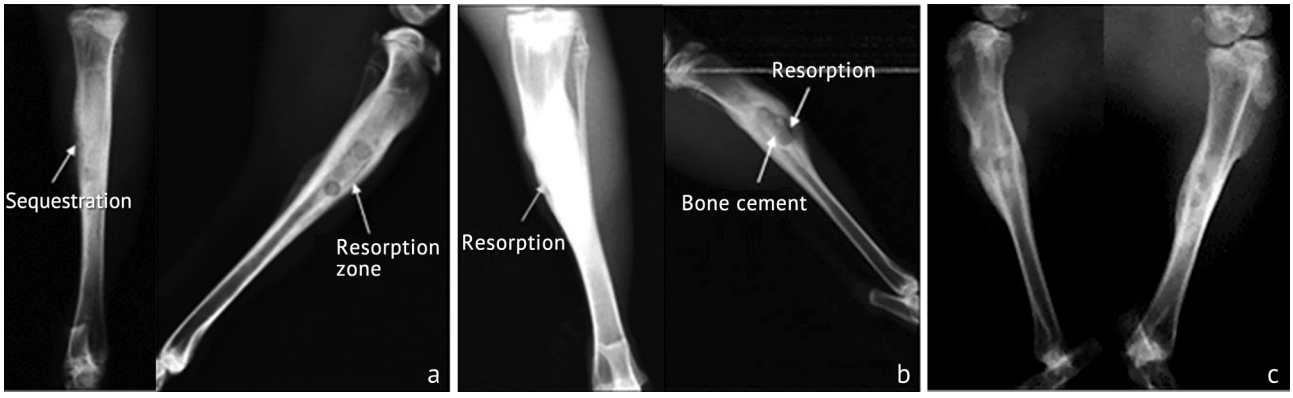

Fig. 4 X-ray images of the lower leg bones of the animals in the comparison group: *a* on the 15th day of withdrawal from the experiment; *b* on the 30th day of withdrawal from the experiment; *c* on the 45th day of withdrawal from the experiment

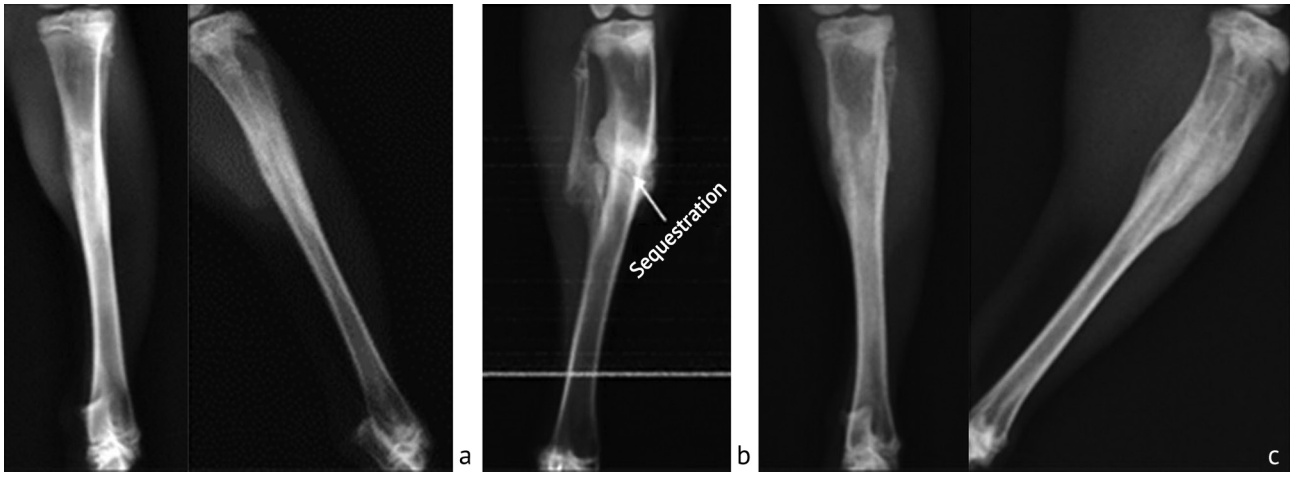

Fig. 5 X-ray images of the lower leg bones of the animals in the control group: *a* on the 15th day of withdrawal from the experiment; *b* on the 30th day of withdrawal from the experiment; *c* on the 45th day of withdrawal from the experiment

In the comparison group, the inflammatory infiltrate, represented by a significant number of lymphocytes and plasmocytes, occupied a large space, including between the exfoliated parts/granules of cement (Fig. 7 a). Proper reparative osteogenesis in the comparison group was less pronounced and contained a smaller volume of reticulofibrous bone tissue.

On the 30th day, a significant ($p = 0.002$) decrease in inflammation was noted in the experimental group. Cells of the lymphoplasmacytic series were determined in single quantities. The hydrogel volume decreased by that day, its fragments still continued resorption by GCFB (Fig. 6 b). No negative reaction such as material-associated bone resorption to the presence of the polymer hydrogel was found. At the same time, in the comparison group, despite the stable clinical and laboratory arrest of chronic osteomyelitis, histologically there was no positive dynamics in reducing the degree of inflammation (Fig. 7 b). Moreover, material-associated resorption of the newly formed bone tissue was traced at the "bone-cement" interface.

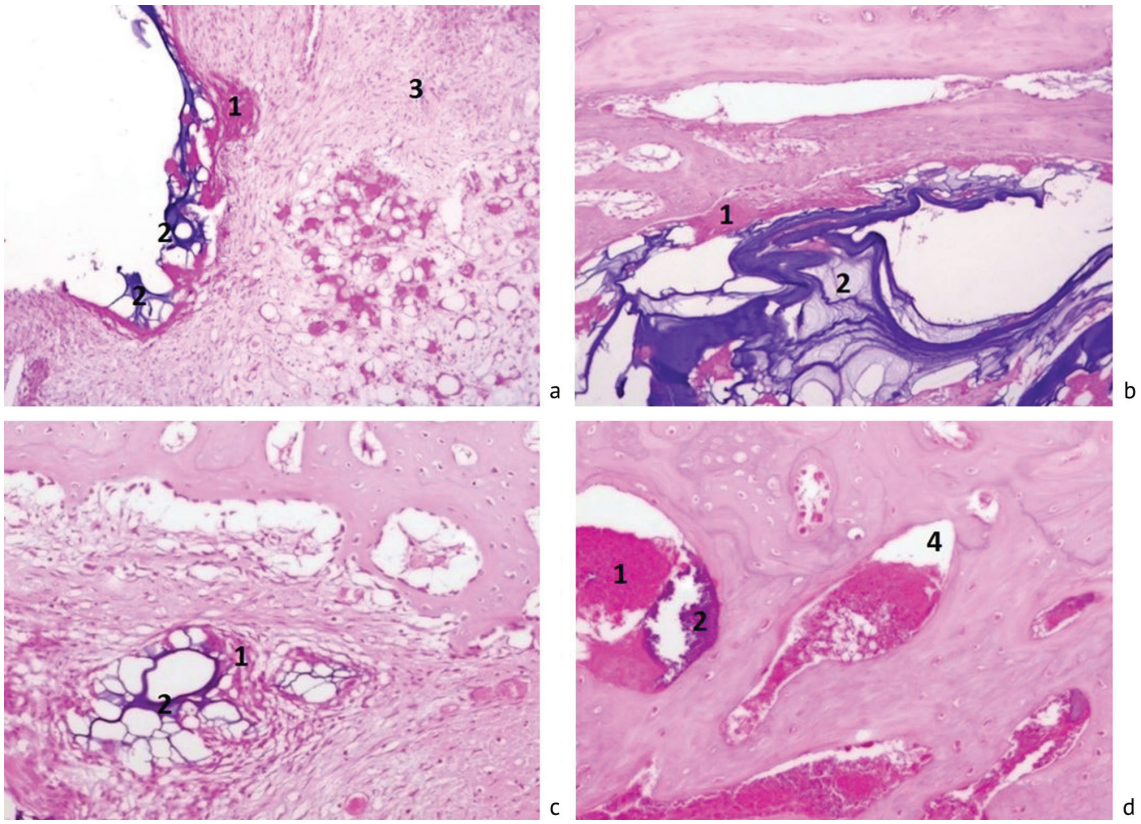

Fig. 6 Experimental group: *a, b* micropreparation on the 15th day after hydrogel implantation. GCFB (1) resorb the hydrogel (2). Weak infiltration by cells of the lymphocytic series (3) of the reticular stroma of the bone marrow. Stained with hematoxylin and eosin. ×200; *c* on the 30th day. GCFB (1) resorb hydrogel fragments (2); *d* on the 45th day. GCFB (1) resorb hydrogel residues (2) inside the lumen of the Haversian canals (4). Stained with hematoxylin and eosin. ×200

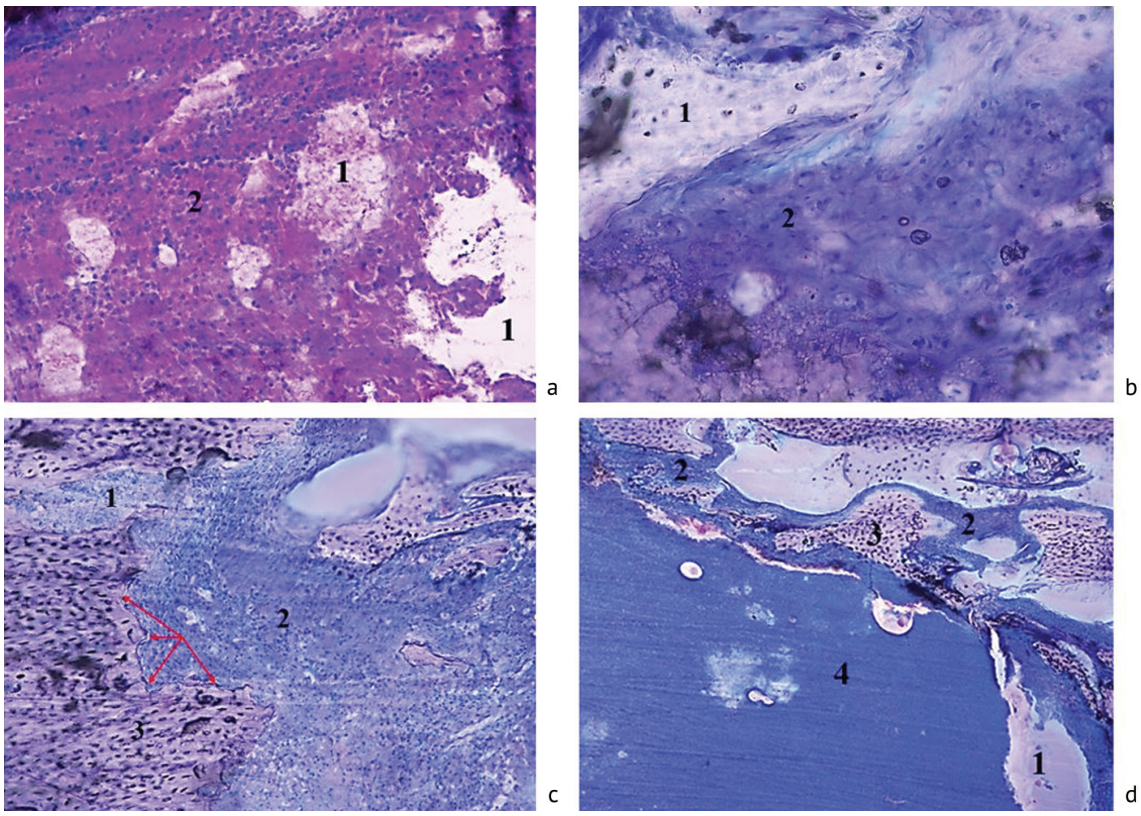

Fig. 7 Comparison group: *a* micropreparation on the 15th day after sanitation (inflammatory infiltrate of polymorphonuclear leukocytes (1) around PMMA granules (2), ×200); *b* on the 30th day (a granule of bone cement (1) of a stratified structure with signs of fragmentation surrounded by an inflammatory infiltrate (2); ×200); *c* on day 45 (resorption of bone substance (3) at the border with inflammatory infiltrate (2); ×200); *d* on the 45th day (fields of inflammatory infiltrate (2) in the bone marrow space; microabscess (4), ×50; staining – celestial trichrome)

By the end of the study, the inflammatory process almost completely subsided in the experimental group; only single plasma cells and cells of the macrophage series were found. The newly formed bone tissue in the area of post-trepanation holes was at the stage of remodeling, and the reticulofibrous bone tissue was at the stage of differentiation into adipose tissue of the yellow bone marrow. Residual hydrogel fragments, found in the lumens of the formed Haversian canals, were resorbed by GCFB (Fig. 6 c). Significant ($p = 0.001$) signs of exacerbation of hronic osteomyelitis were noted in the comparison group manifested by an aggravation of resorption of the newly formed bone tissue, more pronounced at the border with the inflammatory infiltrate (Fig. 7 c). In the area of post-trepanation holes, no bone tissue remodeling was observed. The area of the inflammatory infiltrate, represented by a significant number of polymorphonuclear neutrophils, increased significantly ($p = 0.001$) to such an extent that it occupied the space not only around and between the cement fields, but also the entire lumen of the medullary canal. More than half of the field of view of the histological preparation was occupied by the fields of microabscesses (Fig. 7 d)

In the control group, no histologically positive dynamics in arresting the infectious and inflammatory process was observed in any of the checking points (Fig. 8 a, b). The histological picture before the sanitation of the focus of infection and after it was the same. The difference was a high degree of compaction of the bone substance of the cortical wall and ongoing periosteal reaction (Fig. 8 c) and the detection of multiple foci of hemorrhage by the end of the study not only in the lumen of the narrowed medullary canal but also in the cortical plate (Fig. 8 d) .

The results of the morphometric study are presented as range diagrams in Figure 9.

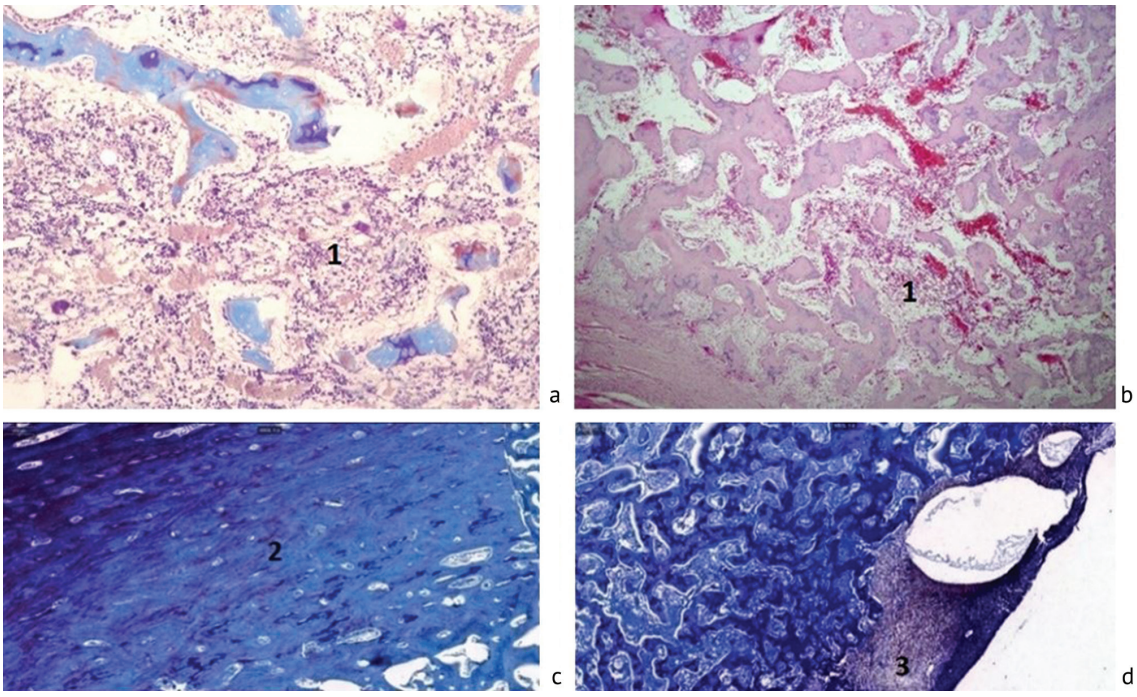

Fig. 8 Control group: *a* micropreparation of animal bone on the 15th day after sanitation (foci of lymphoplasmacytic infiltration (1) in the lumen of the medullary canal; staining with hematoxylin and eosin, ×100); *b* on the 30th day after sanitation (lymphoplasmacytic inflammatory infiltrate (1) in the reticular stroma of the bone marrow; staining with hematoxylin and eosin, ×50; *c,* d on the 45th day after sanitation; high degree of bone compaction (2) and focus of hemorrhage in the periosteal callus (3); Mallory stain)

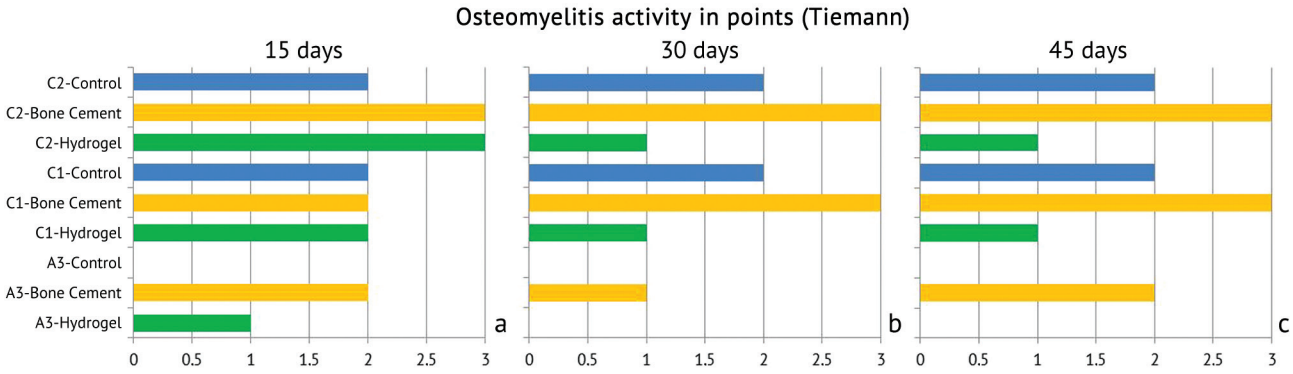

Fig. 9 Intergroup data on osteomyelitis activity following sanitation after: *a* 15 days; *b* 30 days; *c* 45 days

DISCUSSION

The analysis of the *in vivo* experiment showed that the local therapy provided by the polymer hydrogel in the experimental group contributed to the timely healing of the postoperative wound of the lower leg in all cases. In the comparison group, there was a need for auxiliary systemic antibiotic therapy in addition to local therapy from the 7th day until the end of the study due to the lack of regression of clinical symptoms of inflammation. However, despite enhanced systemic therapy, we failed to achieve remission of the infection in two cases. Treatment of chronic osteomyelitis with systemic antibiotic therapy alone is ineffective. Moreover, a significant ($p = 0.006$) increase in the body weight of animals from day 28 (Table 2) in the experimental group compared with the comparison group indirectly indicates a rapid postoperative recovery of their general condition.

Analysis of the inflammation markers showed a significant decrease in WBC ($p = 0.040$) and CRP ($p = 0.040$) in the experimental group from weeks 2 and 3 of the study, respectively (Table 4). In the control group, the blood test values obtained by the end of the study indicated a recurrence of the infection. For ESR and HB, there was no statistically significant difference between the groups (Tables 3 and 4). Despite the reliability we have established in WBC and CRP levels, it is not worth evaluating the effectiveness of treatment, focusing only on laboratory blood tests due to long-term fluctuations in their values without any definite dynamics. Foster et al. also observed that blood parameters in animals, and namely sheep, are not reliable criteria for the effectiveness of the infectious focus arrest [12]. Therefore, blood parameters in animals must be considered in conjunction with the data of clinical, microbiological, radiological and histological studies.

Despite a single positive case, which we regarded as contamination, no growth of microflora was found in the experimental group what we attribute to the high elution-antimicrobial and hydrophilic properties of the hydrogel [5]. In the comparison group, the MSSA strain was identified at almost every control period. The detection of growth of microflora on PMMA by the 45th day of observation in an animal with an arrested infection is associated with the hydrophobic surface of non-biodegradable PMMA predisposing to the adhesion of microorganisms, which subsequently contributes to the development of osteomyelitis recurrence and the acquisition of antibiotic resistance by microbes. The results obtained by us regarding bone cement, in general, do not contradict the conclusions of other authors. Ma et al. reported the presence of viable bacteria on the surface of spacers explanted from patients with managed periprosthetic infection (PPI). It was found that 30.8 % of cement samples had a high level of copies of bacterial 16S rRNA, which indicated the presence of viable microorganisms and was the cause of PJI recurrence in 10-20 % of the two-stage treatment [13]. Another study examined bacterial resistance before and after gentamicin spacer implantation in 33 patients with an infected hip joint. Before surgery, only 29 % of bacteria were resistant to gentamicin, and after treatment with bone cement, their proportion increased to 41 % [14]. George et al. compared the results of patients before and after implantation of PMMA saturated with vancomycin and found an increase in BMD in 36 % of cases [15]. Another *in vivo* experiment on rats showed a high percentage (78 %) of antibiotic-resistant *St. epidermidis* in the group where bone cement containing gentamicin was used as a prophylactic material [16].

As the analysis of the morphometric study showed (Fig. 9), there were significant differences in the histological picture of the groups. Thus, in the experimental group, as compared with the other groups, a significant ($p = 0.002$) effective arrest of the infectious and inflammatory process was observed. Thus, before the focus was sanated, the total result of C1 + C2 was 4 points, after implantation of the hydrogel, the amount significantly decreased to 2 points (Fig. 9 c). At the same time, only single cells of lymphocytes or plasmocytes were histologically noted, what may be due to a reaction to the presence of a foreign hydrogel material that was leveled after its complete resorption. The hydrogel itself did not affect the osteoreparative process and did not cause any toxic or negative reactions in the bone tissue. As seen in Figure 6 (a, d), the volume of the hydrogel matrix decreased with each control period. In contrast to the experimental group, implantation of PMMA causes a significant ($p = 0.001$) exacerbation of chronic osteomyelitis over time (A3 + C1 + C2 = 8 on the 45th day versus A3 + C1 + C2 = 4 before the sanation of the focus), and in the group without implantation depot system, but with systemic antibiotic therapy, there was no dynamics at all.

In general, the histomorphometric results obtained by us are consistent with the data of the radiographic study.

Comparison of our *in vivo* results with the experimental data of other studies on animal models is difficult, due to the long time passed on the scientific publications devoted to the study of PMMA, and many other circumstances (different conditions for performing the experiment, induction of chronic osteomyelitis, timing of observation, etc.). However, in general, the conclusions made by us regarding bone cement and the control group do not contradict the conclusions of other authors. Thus, Mendel et al. compared the *in vivo* results of the antimicrobial activity of PMMA and collagen and concluded that these matrices lead to a clear decrease in the number of bacteria, but are not capable of completely suppress

the infection [17]. Other authors compared the results of treatment of chronic osteomyelitis of the tibia in rabbits with spacer beads containing tazocin and surgical debridement without material implantation. Radiologically and histologically, the control group showed the worst result of treatment without the use of a local depot system. However, in the group of bone cement in 5 (41.7 %) out of 12 cases, a violation of reparative osteogenesis was found, of which in 25 % the onset of the reparative phase was noted by the 14th week after implantation, in 16.7 % there were no signs of reparative osteogenesis at all [18]. Tuzuner et al. showed that bone cement and calcium phosphate loaded with teicoplanin in the presence of MRSA were unable to prevent the development of femoral osteomyelitis in rats. Moreover, histological and radiological manifestations of osteomyelitis were significantly higher in the group of PMMA without antibiotic and PMMA with antibiotic without biodegradable material [19]. In another experiment on a rat model, no significant difference was found in the therapeutic effect of the treatment of chronic osteomyelitis upon implantation of a biodegradable matrix and PMMA impregnated with gentamicin [18]. Similar treatment results were obtained by Shirtliff et al. who compared the therapeutic effect of PMMA and hydroxyapatite impregnated with vancomycin [20].

The study revealed that PMMA implantation causes material-associated resorption over time. One of the reasons may be its bioinertness, which contributes to the formation of a fibrous layer at the "bone-cement" interface that prevents direct bone contact of the implant [21]. Another reason of loosening can be radiopaque agents added to the matrix (barium sulfate, zirconium dioxide), which initiate the release of pro-inflammatory cytokines and, consequently, the osteolytic reaction of tissues [22]. At the same time, barium sulfate has higher osteolytic properties compared to zirconium dioxide, characterized by more abrasive properties [23]. Implantation of the polymer hydrogel was not accompanied by such a reaction. It is one more merit of the many advantages compared to bone cement.

CONCLUSION

The results of the *in vivo* study have demonstrated the high efficacy of antibiotic-impregnated polymer hydrogel in the treatment of chronic osteomyelitis compared to PMMA. It was found that implantation of the hydrogel promotes timely healing of the postoperative wound of animals, significant ($p = 0.006$) rapid recovery of their general condition after surgery, does not cause progression of radiological signs of chronic osteomyelitis and significantly ($p = 0.002$) arrests the infectious and inflammatory process shown by histomorphometry without development any toxic effects in the bone tissue. And such properties of the material as hydrophilicity and biodegradability significantly reduce the risk of microbial adhesion and the formation of biofilms thus decreasing the likelihood of exacerbation of the infection.

Conflict of interests *Not declared.*

Funding *The authors did not have any grants for conducting the study.*

Ethical approval *The study was approved by the ethics board. The study was carried out in compliance with the principles of humane treatment of laboratory animals in accordance with the requirements of the European Convention for the Protection of Vertebrate Animals (Strasbourg, 2006) used for experiments and other scientific purposes and with the order of the Ministry of Health and Social Development of the Russian Federation No. 708n dated August 23, 2010 "On approval of the rules of laboratory practice".*

Informed consent *Not required.*

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Original article

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Revision total hip arthroplasty with custom-made hip implant for Paprosky type IV femoral bone loss

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Abstract

Introduction Replacement of extensive Paprosky type IIIB and type IV bone loss is a challenge in revision total hip arthroplasty (THA). **The purpose** was to demonstrate the possibility of femoral reconstruction in proximal femur bone loss using a custom-made implant for revision THA. **Material and methods** We report a case of a 72-year-old patient with an extensive Paprosky type IV femoral defect, which was replaced using a custom-made modular component. **Results** The femoral defect was successfully augmented with a custom-made modular component, and the hip function was restored. The locking mechanism of the constrained system failed at 6 months with the joint remained stable. The patient could ambulate with additional support. VAS, HHS and HOOS scores measured before and after 2 years showed positive dynamics. **Discussion** Paprosky type IIIB and type IV defects are a challenge for revision hip arthroplasty. There is a variety of surgical options with outcomes being ambiguous. Modular and monoblock tapered stems, the technique of impacted bone graft have been reported to have excellent results in revision THA with Paprosky type III and IV defects. A custom-made femoral component was developed based on the principle of modular stems. Joint stability is a concomitant problem with a severe bone defect that can be addressed with a double mobility or constrained system. Both methods are associated with a sufficient number of complications. **Conclusion** Replacement of a Paprosky type IV femoral defect with a custom-made modular component demonstrated satisfactory outcomes at a two-year follow-up. The patient had no complaints, could ambulate unassisted using an elbow crutch and positively evaluated the result of treatment.

Keywords: revision arthroplasty, hip joint, femoral defect, Paprosky type IV

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INTRODUCTION

The number of revision THAs is projected to grow at a higher rate [1]. Bone deficiency is often observed with repeated operations and removal of endoprosthetic components can lead to a greater bone defect [2]. Femoral bone loss can occur secondary to osteolysis, infection and periprosthetic fractures [3, 4], stress shielding, and iatrogenic damage during surgery. One commonly used classification is the Paprosky classification for femoral bone loss, which is a categorization based on bone loss location and degree of severity, and proposes a treatment algorithm for surgical reconstruction based on these measures [5]. Paprosky type IIIB and IV extensive femoral bone defects are very difficult to reconstruct [4, 6, 7]. Options for Reconstruction of defects is based on the remaining healthy bone [2]. The objective was to demonstrate the possibility of femoral reconstruction in proximal femur bone loss using a custom-made implant for revision THA.

MATERIAL AND METHODS

A 72-year-old patient underwent total replacement of the left hip joint in 2013, followed by revision surgery in 2015 due to loosening of the implant. She presented with pain and limited ROM in the left hip, inability to walk without without assistance or use of a walker and was seen at the Institute of Trauma and Orthopaedics of the University Clinic the Volga Research Medical University in January 2016. Radiological examination showed displaced construct and severe osteolysis and revision THA was recommended for the patient. The patient was seen again in the clinic in January 2019 and was diagnosed with a deep periprosthetic joint infection (PJI). The first stage of revision THA included removal of endoprosthetic components, debridement and placement of a spacer. The absence of the lateral cortical bone to the level of the lower third of the femur and partial absence of the cortical bone posteriorly and anteriorly to the level of the lower third of the femur were revealed intraoperatively. To treat periprosthetic infection and replace a bone defect, a spacer was manufactured using a femoral rod 380 mm long with a diameter of 12 mm to address PJI and the bone

defect. The femoral rod was fixed with bone cement and 2 cerclages placed at the border of the lower and middle third, middle and upper third of the femur (Fig. 1). A course of antibiotics was administered postoperatively, partial weight-bearing and isometric exercises recommended. Five months later, the patient was hospitalized for the second stage of revision THA. She could ambulate using a wheelchair due to lack of support and the lower limb length discrepancy of 5 cm. Laboratory tests indicated no infection. Subjective assessment of the functionality showed HHS of 39; HOOS of 24.4; VAS of 5. Standard components could not be used for Paprosky type IV extensive femoral bone defect of the femur and the absence of a "total hip" system required manufacturing and placement of a custom-made implant for the proximal femur. The patient was discharged from the hospital to allow time for manufacturing of a custom-made implant. The second stage of revision THA with placement of a custom-made implant was produced at the beginning of 2021. The patient's condition was consistent with that she had had during the previous hospitalization in 2019, without negative dynamics.

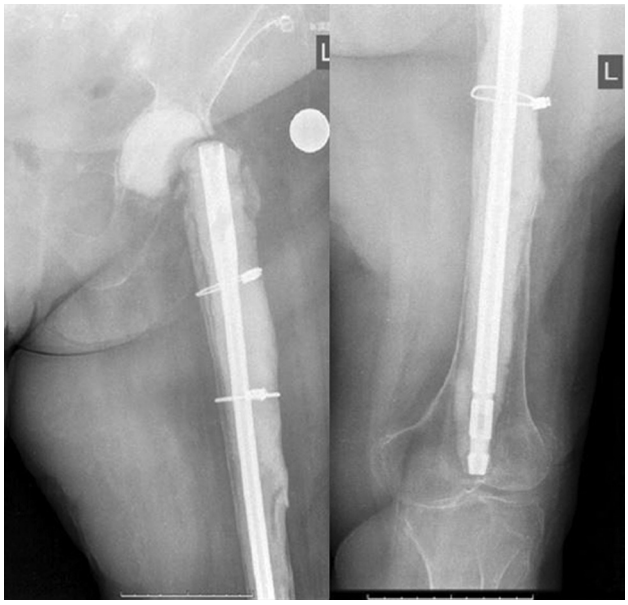

Fig. 1 AP and lateral views of the left femur with a spacer placed

Preoperative planning, implant manufacturing

Multislice computed tomography of the affected and contralateral femur was performed to create a three-dimensional digital model of the femur using Toshiba Aquilion 32 (Japan). On the created model of the affected joint, Metal constructs and cement were removed from 3D model to assess the length of the bone bed suitable for implant fixation. A model of the healthy femur was then mirrored to recreate the geometric parameters of the affected femur. A cylindrical component of the proximal femur with a neck was developed according to anatomical data. The custom-made femoral component consisted of a proximal and distal module. The proximal module of the cylindrical device with a neck was designed with the height being equal to the distance between the lesser trochanter to the great trochanter and the diameter being equal to the diameter of the healthy bone at the level of the lesser trochanter, and the neck ensured the adequate geometry (offset, neck-to-shaft angle, cervical length). The proximal module had a hole for the sleeve, and a comb with holes was formed on the side opposite the neck for suturing muscles and ligaments. A hirth coupling was designed to prevent rotation of the diaphyseal and proximal modules and to ensure fixation of the placement angle at the ends of the proximal and diaphyseal modules in the place where they were adjacent to each other. The distal module was made of two components: (1) a cylindrical diaphyseal component was equal to the diameter of the proximal module and had a hirth coupling in the proximal part, a sleeve recess and an axial fastening screw, the distal part of the diaphyseal component was represented by one of the parts of the Z-shaped connection; (2) the leg of the distal module in the proximal part had a geometry of the distal part of the diaphyseal component in inversed manner; it formed a Z-shaped connection with the diaphyseal component through intermediate fixing bushings and two transverse fastening screws. The rounded end of the custom-made stem was above the Blumenzaat line by at least 1 mm, the proximal end was designed in accordance with the level of immersion into the bone and the formation of a cement mantle of at least 2 mm with the stem placed. The length of the assembled custom-made femoral component ensured bone length equalization. With adjustment of the custom-made model of the implant, it was printed using a DMLS 3D printer. Heat treatment was carried out, step-by-step ultrasonic cleaning in distilled water, neutral, alkaline and acidic media and repeated washing in an ultrasonic bath with distilled water. The product underwent a standard disinfection and sterilization procedure by autoclaving.

Surgical technique

An extended Kocher-Langebeck approach was used for access to the joint with removal of the postoperative scar. The femoral component of the block spacer was removed en bloc and the acetabular cement was removed (Fig. 2).

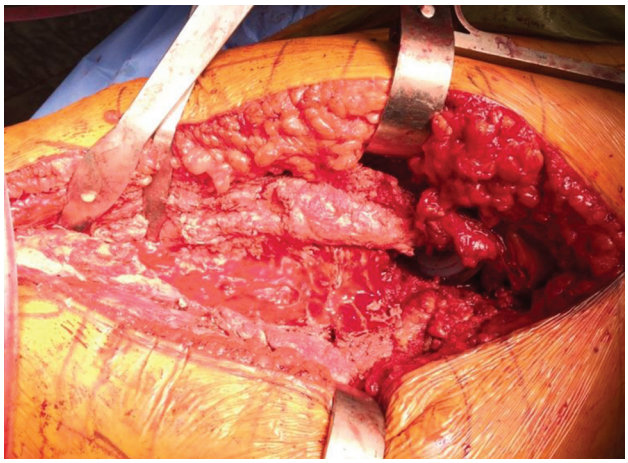

Fig. 2 Intraoperative appearance of the proximal femur defect

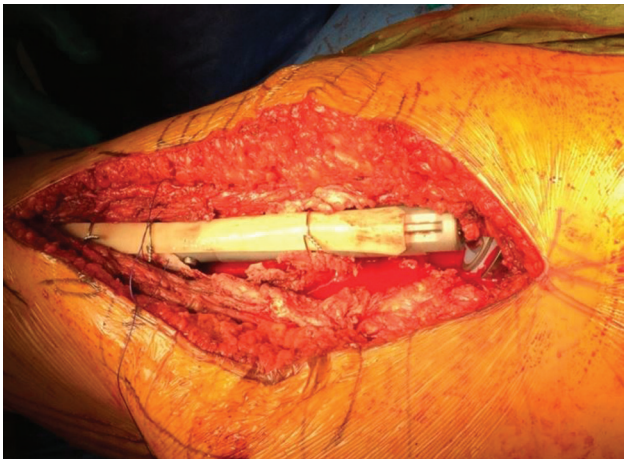

Fig. 3 Modular femoral component assembled

A Paprosky type IV femoral defect and a Paprosky IIA segmental and cavitary defect of the acetabulum were discovered after removal of the components, which conformed with the preoperative planning. Then curettage of the acetabulum and femoral canal was performed. Treatment of the acetabulum and implantation of a standard hemispheric acetabular component (Continuum, Zimmer, Warsaw, USA) fixed with five screws, was produced and an Longevity constrained liner (Zimmer, Warsaw, USA) placed. The custome-made implant was assembled and placed with bone cement into the treated bone canal (Fig. 3). A cortical tibial allograft of about 35 cm long was used to improve stability of the femoral component and fixed to the implant with cerclages extending onto the preserved lateral surface of the distal femur (Fig. 4).

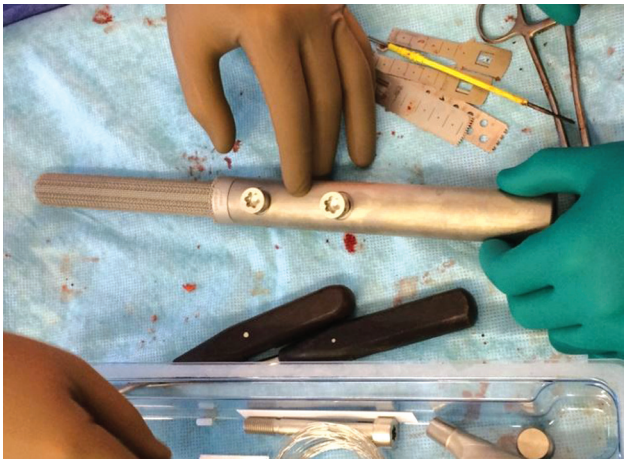

Fig. 4 Intraoperative appearance of the modular femoral component and constrained system placed

RESULTS

The postoperative period was uneventful. The patient was discharged from the hospital after 9 days of surgical treatment. The patient was recommended to walk using crutches for 31/2 months with the lower limb touching the floor and gradually increasing weight-bearing. Dabigatran etexilate was administered for 35 days and compression stockings recommended to prevent thrombosis added by non-steroidal anti-inflammatory drugs to relieve pain. The patient was seen at follow-up visits at 2 (Fig. 5) and 6 months. There were no negative dynamics early post surgery.

The constrained system failed by type III according to the classification developed by S.S. Cooke [8] with femoral head locking mechanism at 6 months with no signs of implant instability. Radiological examination showed signs of slight distal migration of the component, which did not progress throughout the observation period.

The patient could ambulate with the help of elbow crutches maintaining full weight on the operated limb at 12 months. She had no complaints of pain at the surgical site. ROM in the hip and knee joints was slightly limited. The patient could ambulate using an elbow crutch at two years sparing the operated limb (Fig. 7). The reported pain in the ipsilateral ankle joint and both knee joints. The subjective assessment of the function showed 48 HHS scores, 65.0 HOOS and 1VAS score.

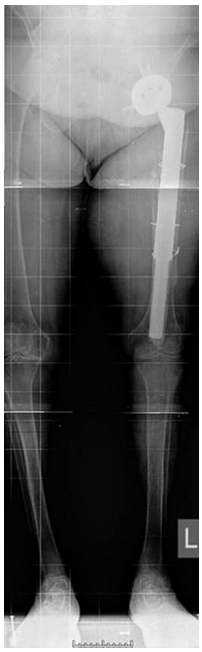

Fig. 5 A full-length standing AP radiograph of the patient's lower limbs at 2 months following revision THA with use of the custom-made femoral component

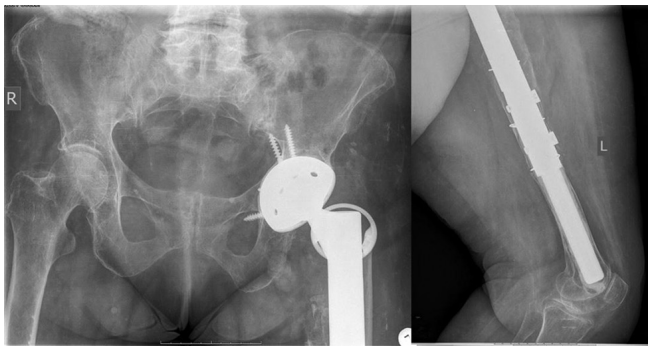

Fig. 6 AP view of the pelvis and lateral view of the shaft of the left femur at 6 months following implantation of a custom-made femoral component

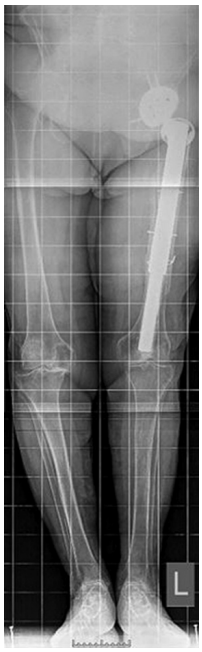

Fig. 7 A full-length standing AP radiograph of the patient's lower limbs at 2 years following revision THA with use of the custom-made femoral component

DISCUSSION

The case report is of particular interest, demonstrating reconstruction of the femur with a severe Paprosky type IV bone defect, which is rare in surgical practice, with joint stabilization achieved. It is difficult to achieve stable fixation of the femoral component with this type of defect. The techniques currently used include femoral impaction bone grafting using a cemented stem, proximally coated stems, fully porous-coated cylindrical stems, allograft prosthesis composite, proximal femoral replacement. Femoral impaction bone grafting using a cemented stem is the method of choice for the reconstruction of large bone defects of the femur. The available level of evidence is primarily derived from case series, which shows a mean survivorship of 90.4 %, with revision or re-operation as the end-point, with an average follow-up of 11 years [9]. The rate of femoral fracture requiring re-operation or revision of the component varies between several large case series, with an average of 5.4 % [9]. The disadvantages include the technical complexity and the need for a large volume of bone mass to repair a Paprosky type IV defect.

Cementless proximally coated stems were defined as poor because required sufficient metaphyseal fixation, which was impossible with extensive bone defects [10]. Despite good survival results, the use of fully covered revision stems was inappropriate for Paprosky type IV defect due to inability to achieve durable primary fixation because of the absent isthmus [11, 12]. However, cortical allografts could create additional conditions for better fixation of the stem and serve as the basis for restoration of the bone defect [13, 14, 15]. Kim et al. reported the results of revision arthroplasty in 120 patients with severe femoral bone defects treated with fully coated stems and cortical allografts with the survival rate of 91 % at a 16-year follow-up [15].

Other options include proximal femoral replacement or the use of a "megaprosthesis" for primary fixation in the setting of a severe femoral defect. These methods are associated with a risk of complications in the form of dislocations, aseptic loosening and bone loss [16]. I.D. Martino et al. conducted a retrospective study evaluating outcomes of 30 patients with Paprosky type IIIB and type IV defects, with a mean follow-up of 5 years [17]. The patients underwent proximal hip replacement. Nine patients required reoperation for aseptic loosening, periprosthetic fracture, etc. Modular and nonmodular tapered fluted titanium stems provide satisfactory midterm results in revision THA in Paprosky III-IV defects [18]. It is generally accepted that modular stems provide better functional results and allow more accurate restoration of limb length, offset and setting the anteversion of the component. However, there are doubts about the mechanical reliability of the constructs with modular stems [19, 20]. The use of allograft-endoprosthesis composite shows good outcomes of femoral reconstruction with long-term follow-up [21].

Prototyping and 3D printing technologies were used to produce a custom-made modular femoral component to obtain satisfactory primary stability and restore limb offset and length in our case. A cortical allograft was used to provide additional stability

to the stem. The choice of fixation method may seem controversial due to unpredictable long-term results. The size of the bone defect and the quality of the cortical bone of the distal portion of the affected femur were considered in preoperative planning. The lack of other options, insufficient amount of bone allograft for impaction bone grafting led to increase the contact area between the distal part of the implant and the cement mantle for a composite beam effect. In addition to reconstruction of the significant bone defect stabilization of the joint could be addressed with dual mobility or a constrained system.

V. Eecke et al. reported an evaluation of 5,617 cases of revision THA with higher survival rates (94.7 %) for dual mobility compared with the designs with constrained acetabular liners (81 %) [22]. The dislocation rates was lower with dual mobility (2.6 % vs. 11 %) and lower acetabular loosening rates (1.0 % vs. 2.0 %). No differences in functional outcomes were identified. Similar results were obtained in the study reported by N.N. Efimova et al. [23]. The dual mobility group showed less complications associated with component instability and periprosthetic joint infection. The difference in dislocation rates was statistically significant in the two groups. A greater risk of dislocation was found in the group of constrained acetabular liners with the system placed into the preserved acetabular component as compared with replacement, and with use of inserts for heads of smaller diameter. Some authors report a greater risk of dislocation with unconstrained acetabular liners in revision surgery and the presence of hip abductor deficiency. G.M. Alberton et al report a significantly greater risk of dislocation in patients with nonunion of the greater trochanter at revision surgery obsrved in 7 of 9 patients [26]. G. Zywiel et al. reported no association between abductor muscle quality and the incidence of failure using constrained systems in a group of 43 patients [25]. Survival of the constrained acetabular liners was 91 % at a mean follow-up of 51 months. Of the four hips that experienced failure of the acetabular liner/and or cup, there were two type I failures (at the cup/bone interface), one type II failure (at the liner/cup interface), and one type III failure (at the locking mechanism) as classified by S.S. Cooke. None of the four patients had abductor deficiency, which may indicate the ability of the systems to compensate for deficient hip stabilizers. There is a greater risk of dislocation with use of constrained systems in the presence of recurrent dislocations [26], inadequate placement of a constrained liner in a fixed cup [26, 27], and the inability to properly fix the cup with screws [28, 29].

A constrained system was used for our patient to stabilize the joint considering several factors: good fixation of the cup, both primary and with screws; total deficiency of the hip abductors and inability to perform a plastic surgery without additional injury to the soft tissues. The defect was classified as a type IV Paprosky femoral bone loss and treatment suggested avoidance of factors that could cause stress on the bone/cement/implant interfaces and recurrent dislocation. Type 3 constrained system (locking mechanism) failed, but the failure had no effect on the stability of the joint. The case report has limitations in presenting data for drawing unambiguous conclusions. Given the rarity of this type of femoral defect, demonstration of difficulties during treatment and the ways the issues were solved had a role.

CONCLUSION

Reconstruction of a Paprosky type IV femoral defect with a custom-made modular component demonstrated a satisfactory outcome over a two-year follow-up period. The patient presented no complaints, could ambulate unassisted using an elbow crutch and positively assessed the result of treatment.

Conflict of interest *The authors declared no potential conflicts of interest with respect to the authorship and/or publication of this article.*

Ethical review *Not required.*

Informed Consent *The patient gave voluntary written informed consent for the publication of the clinical observation.*

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Morozova E. A. – conducting research, writing the original text of the article.
Gerasimov E.A. – writing the original text of the article.
Gerasimov S.A. – control, reviewing and editing the text of the article.

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Original article

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Combination of flexible intramedullary nailing and Ilizarov frame for salvage of femur and humerus nonunion in a girl with osteogenesis imperfecta

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Abstract

Background Fixation of pathological long bones with telescopic intramedullary rods is well known to be a technically challenging procedure even in specialist centres, with a high complication rate due to rod migration, hardware failure, nonunion or malunion. However there is very little guidance in the literature regarding salvage treatment options when failure occurs. **Aim** We demonstrate a surgical technique that can be used for salvage treatment of both femoral and humeral complex nonunions following Fassier-Duval (FD) rodding in a child with osteogenesis imperfecta (OI). **Case description** A 13 year-old girl with OI type VIII presented sequentially with nonunion and deformity of the femur then the humerus following previous FD rods in those segments. The femur was also complicated with metallosis between the steel rod and an overlying titanium plate. Both segments were treated with pseudarthrosis debridement, removal of metalwork and stabilisation with hydroxyapatite (HA)-coated flexible intramedullary nails, with temporary Ilizarov frame to provide enough longitudinal and rotational stability to allow immediate weight-bearing. The femur Ilizarov frame was removed after 64 days, and the femur remained straight and fully healed at 2.5 years. The frame time for the humerus was 40 days, complete union was achieved and upper limb function restored and maintained at 9 months. **Discussion** The transphyseal telescopic rod is the traditional implant of choice in terms of treating fractures and stabilising osteotomies for deformity in OI. However, it does not provide enough torsional or longitudinal stability by itself to allow early weight-bearing which is detrimental to bone healing in this vulnerable patient group. The incidence of delayed union or nonunion at osteotomy site in telescopic rod application is not negligible: up to 14.5-51.5 %. Although the technique we have shown in this case may not be applied to all complex OI patients, we believe that the combination of flexible intramedullary nails and Ilizarov frame provides a favourable environment for bone healing in complex or revision cases. As a secondary learning point the initial revision surgery to the left femur demonstrated the perils of using a steel rod and a titanium plate in a biologically active environment which in this case lead to metallosis and lysis. **Conclusion** We found the technique of HA-coated flexible intramedullary nails combined with the Ilizarov frame effective in the salvage of failed telescopic rods in both femur and humerus and feel this technique can be used as a salvage option in similar cases worldwide. This case also demonstrates the perils of using different metals in combined internal fixation.

Keywords: osteogenesis imperfecta type VIII, flexible intramedullary nailing, external fixation, telescopic rodding

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BACKGROUND

Osteogenesis imperfecta (OI) is a phenotypically and genetically heterogeneous group of inherited bone dysplasias characterized by frequent fractures, bone deformities, low bone mineral density and osteopenia [1-4]. Although rare, each patient often requires multiple operations on several limbs throughout childhood and beyond, in order to maintain autonomy, self-care, physical activity and the ability to acquire and develop motor skills including independent ambulation.

The workhorse implant for the treating surgeon in cases of OI is the telescopic rod which strengthens and protects the full length of the long bones, where one component (male) slides inside the other (female) with growth. As well as allowing fractures and osteotomies to heal the rods prevent deformity and fracture recurrence [5, 6]. Models include the Fassier-Duval rod [7–9], the Sheffield rod [10], dual interlocking telescopic rod [11], and the titanium telescopic rod [12, 13].

Whatever the exact implant design telescopic rodding carries a steep learning curve, and even in the most experienced hands has a high complication rate, partly related to the lack of rotational and longitudinal stability of the implant [6, 11, 14, 15]. The technique is known to be even more difficult and prone to these complications in the humerus, including secondary displacement, malunion, nonunion, hardware failure and migration over time and bone growth [16-19]. This means that revision surgery in these cases is not at all unusual, and is even more challenging than primary cases requiring individual solutions as well as classic techniques [9, 18, 20-22].

Aim This article presents a case report of operative treatment of a 13-year-old girl affected with osteogenesis imperfecta type VIII, who was consecutively operated on with a combined technique with hydroxyapatite-coated flexible intramedullary nailing (HA-FIN) and reduced external frame for salvage of femoral pseudarthrosis complicated with metallosis and pseudarthrosis of humerus after Fassier-Duval (FD) rod failure in both segments.

CASE DESCRIPTION

The initial treatment of this child with regards to the right femur was described in a published report [18]. Two years later the patient represented to us with a symptomatic nonunion in the other (left) femur, having been treated with primary FD rod elsewhere in 2013, and then attempted revision with exchange FD rod followed by additional titanium plate 4 months before presentation.

On review, the girl was unable to walk or stand, on a background of short stature with rhizomelia, white sclerae, myopia and partial hearing loss. Pain was localized to the midshaft of the left femur and knee, in the area of the mobile nonunion site. There was a leg length discrepancy of 1.5 cm and 25 degree loss of extension in the left knee. There was no evidence of infection including on blood tests. Clinical alignment of the right lower limb remained excellent without any deformity rebound or implant migration, with satisfactory X-rays. Views of left femur showed a clear nonunion with a 4 mm gap, with FD rod in place as well as lysis around the supplementary plate and screws.

Left femur surgery

The existing FD rod was removed as well as open debridement of the pseudarthrosis and overlying plate and screws. Extensive metallosis was noted around the soft tissues and periosteum around the plate. The canal was reamed to remove any bone fragments from the screw tracts and the previous apex anterior deformity corrected. Two 2.5 mm HA-coated titanium flexible intramedullary nails (Orthopediatrics nails modified by Metis Ltd, Tomsk, Russia) were inserted in anterograde fashion. The Ilizarov apparatus (Experimental Plant at the Russian Ilizarov Scientific Center for Restorative Traumatology and Orthopaedics, Kurgan, Russia) consisted of a short proximal arch with three half-pins and a distal ring with three wires. This was a static construct which did not require any postoperative adjustment or correction.

Standing and progressive weight-bearing commenced on day 3 and the patient was discharged home on day 8 with a physical therapy programme including early knee movement. Postoperatively, no problems or obstacles were encountered such as pin-site infection or loosening. X-rays at 60 days showed union and the fixator was removed at day 64 under general anaesthetic. The lower limb was protected in a split cast for a period of two weeks and then weight-bearing was recommenced. Bisphosphonate therapy was resumed at 4 months. Independent standing and pain-free walking was restored and maintained at 2 years, with full union and alignment of the femur demonstrated on X-rays with remodelling and restitution of the intramedullary canal.

Right humerus presentation and surgery

Shortly after this episode there was a similar presentation of the right arm in the same child. The right humerus had been previously treated in another institution with FD rod. A painful and mobile non-union of the distal humerus was noted, with functional impairment. X-rays revealed an established nonunion as well as broken male component of the FD rod. There was no evidence of infection including on blood tests.

A proximal approach was used to remove both the female component of the FD rod as well as the proximal part of the broken male component. The nonunion site was debrided back to viable bone and the distal part of the male component removed. In similar principles to the femur surgery, the humerus was stabilised with two HA-coated flexible intramedullary nails and a reduced Ilizarov frame, consisting of 4 half-pins fixed over a short Ilizarov plate connected with threaded rods. This provided excellent bone contact, rotational stability and allowed free elbow movement. Neither casting nor bracing was required or any postoperative adjustments to the Ilizarov apparatus.

There were no problems or obstacles postoperatively. The humerus healed and the fixator was removed at 40 days, and the arm was left free to move. Bisphosphonate therapy was recommenced at 6 months. At 9 months there was pain-free restoration of upper limb function, as well as radiological union and remodelling of the canal.

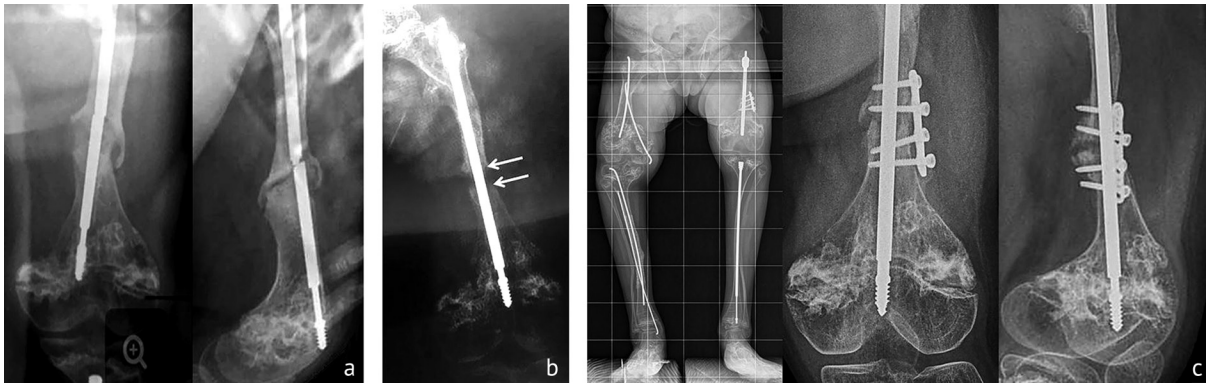

Fig. 1 Preoperative radiographs: a – pseudarthrosis of the left femur and hardware fracture; b – fractured rod has been replaced with another Fassier-Duval rod, note interfragmentary diastasis (fleshs) as result of longitudinal instability; c – standing radiograph of lower limbs, augmented radiographs demonstrate loosening of the plate and bicortical screws, nonunion

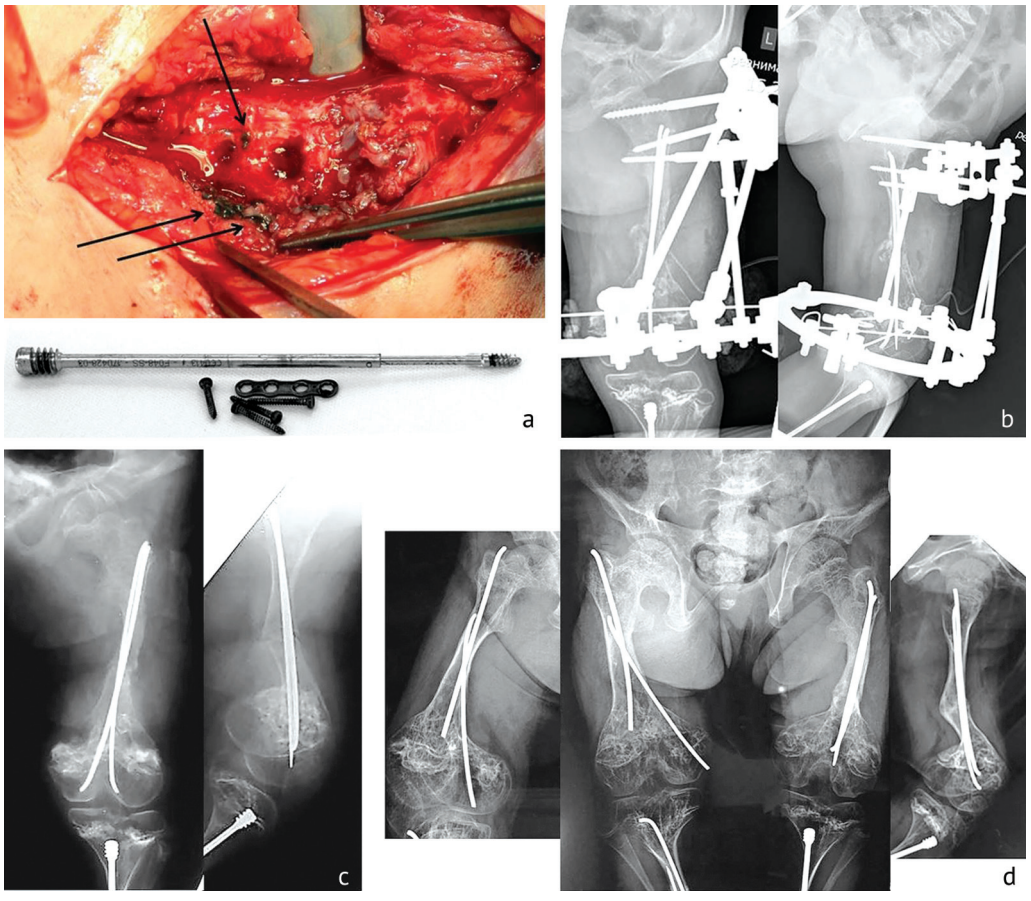

Fig. 2 Treatment of left femur pseudarthrosis: a – intraoperative view: nonunion site extensive metallosis of multiple charred appearance inclusions on the intraoperative view, removed hardware; b – postoperative X-rays; c – day 64 after surgery, radiographs at frame removal; d – 2 years after frame removal from left femur

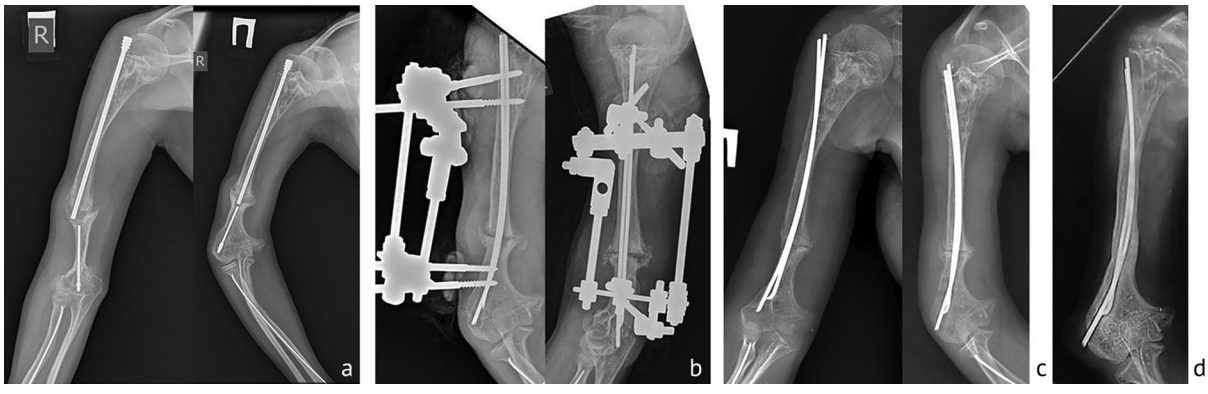

Fig. 3 Treatment of right humerus pseudarthrosis: a – preoperative radiographs, pseudarthrosis and broken Fassier-Duval rod; b – postoperative radiographs; c – bone union achieved, frame removed on day 40; d – 9 months after frame removal from right humerus

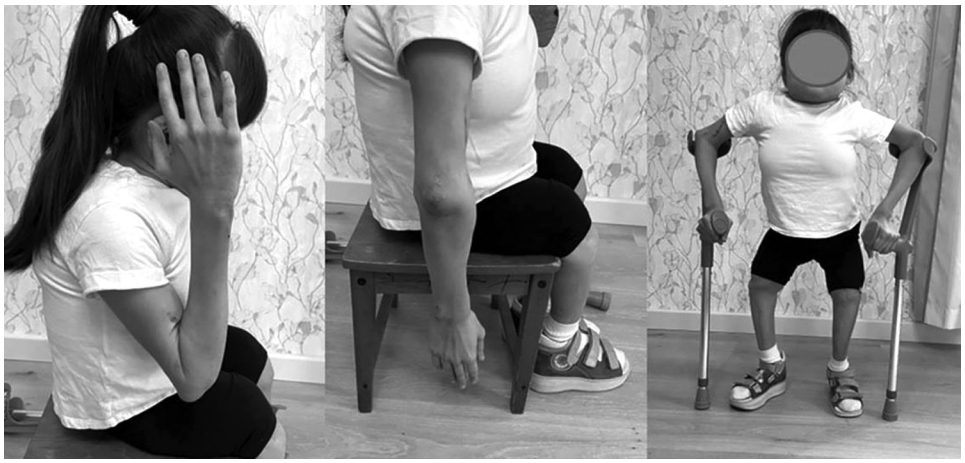

Fig. 4 Functional outcome

DISCUSSION

The transphyseal telescopic rod is the traditional implant of choice in terms of treating fractures and stabilising osteotomies for deformity in OI [5-8]. However, it does not provide enough torsional or longitudinal stability to allow early weight-bearing [6. 8, 10, 11, 16] which is detrimental to bone healing in this vulnerable patient group [23, 24] as well as the overall rehabilitation [22].

The incidence of delayed union or nonunion at osteotomy site in telescopic rod application is not negligible: up to 14.5 % [16]. Munns et al observed delayed bone union in 103 cases out of 200 (51.5 %) operated on with the Fassier-Duval rod [17]. Shin et al reported 5 cases of persisting cortical gap for a series of 59 rods [11]. The case presented in our article does not match to reported data. Nonunion and rod fracture occurred in two segments of three within period of 3 and 5 years. The peer-reviewed literature reports that for a five-year period, the telescopic rods did not required surgery in 63 % for the femur and 64 % for tibia according to Cox et al [25]. Shin et al used Dual Interlocking telescopic rod (D-ITR) and reported 75 % survival rate for 5.3 years follow-up, which is thebest result among all known telescopic rods [11]. On the other hand, the rate of revision surgery also depends on the severity of OI and it reaches 67.86 % in OI type III and 31.82 % in OI type IV [26]. We presume that there could be features of bone union in patients with type VIII of OI (recessive inheritance pattern). There is no relevant literature for OI type VIII specifically.

Even in "classic" OI the literature suggests that corrective osteotomy of the humerus with FD rod carries a high complication rate [19, 20]. Grossman et al reported revision rate of 34.3 % within 35 months including unscheduled surgery for nonunion and malunion in 8.6 % of cases [19].

Although the technique we have shown in this case may not be applied to all complex OI patients (such as the very young) we believe that the combination of HA-coated flexible intramedullary nails and Ilizarov frame provides a favourable environment for bone healing in complex or revision cases [28, 29]. There is an enhanced mechanical stability (both particularly rotational and longitudinal) compared to telescopic rods alone, as well as a favourable osteoconductive environment.

As a secondary learning point, the initial revision surgery to the left femur demonstrated the perils of using a steel rod and a titanium plate in a biologically active environment which in this case lead to metallosis and lysis [30, 31]. The technique of combined telescopic rodding and plate fixation per se is supported by the literature, but the metals used should be similar, also locking unicortical screws rather than plates with bicortical conventional screws [15, 27].

CONCLUSION

We found a high rate of nonunion and pseudarthrosis associated with hardware fracture in a patient with rare type VIII of osteogenesis imperfecta initially treated with FD rods in each segment. A combination of pseudarthrosis site resection, elastic intramedullary nailing with osteoinductive coating and external frame applied for a short period provides early function including full weight-bearing and enables bone union and further favorable bone remodeling in long-term follow-up. The surgeon should also be aware about the risks of use of dissimilar metals in combined osteosynthesis resulting in osteolysis and early loosening of implants.

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Popkov A.V. – Responsibility for managing and coordinating the planning and conduct of research activities
Foster P. – Preparation and writing of the initial draft (draft) of the work.
Popkov D.A. – Gathering data/evidence, Preparing and writing an initial draft of the paper, Applying formal methods to synthesize study data. Conducting surgical treatment.

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Original article

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Mycobacterium abscessus as a causative agent of periprosthetic infection

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Abstract

Introduction *Mycobacterium abscessus* species belongs to the group of non-tuberculosis mycobacteria responsible for chronic infections in people with weakened immunity. *M. abscessus* exist in various ecological niches and are able to colonize artificial surfaces, including medical and surgical instruments/devices. Due to the low incidence of *M. abscessus* as a causative agent of orthopedic infection, a rare clinical case of periprosthetic infection caused by *M. abscessus* would interest practitioners. **The aim** is to present a clinical case of periprosthetic infection caused by *M. abscessus*. **Materials and methods** From the medical records and discharge documents, it was known that female patient X. underwent total hip replacement at her residence hospital. Signs of acute infection of the postoperative wound appeared in the early postoperative period. **Results** Three months later, the patient was hospitalized in a specialized institution with a diagnosis of chronic deep periprosthetic infection. During the examination, the mycobacterial etiology of the process was established. During two hospitalizations, the patient underwent 4 consecutive revision surgeries (including muscle plastic surgery and installation of an antimicrobial spacer) and massive parenteral antibiotic therapy for 8 months, including at the outpatient stage, using at least 3 antibacterial agents. After 4 years, the patient does not complain of the infectious process. Postoperative scar is 45 cm. The residual shortening of the right lower limb of 3 cm was compensated by orthopedic shoes. **Discussion** Treatment of infection caused by M. abscessus is challenging due to the natural resistance of the pathogen to a wide range of antibacterial drugs. The literature describes separate cases of orthopedic infections caused by this pathogen. All authors agree that the key to successful treatment is a combination of radical surgical debridement and antibacterial therapy using at least three antimicrobial drugs. **Conclusion** A rare clinical case of periprosthetic infection caused by *Mycobacterium abscessus* after primary hip replacement is presented. This infectious agent is a rare pathogen, for which there is no proven therapeutic algorithm. Long-term aggressive antibiotic therapy in combination with stage-by-stage surgical treatment was successful.

Keywords: orthopedic infection, periprosthetic infection, non-tuberculosis mycobacteria, *Mycobacterium abscessus*, antibacterial therapy

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INTRODUCTION

The species *Mycobacterium abscessus* belongs to the group of non-tuberculous mycobacteria (NTMB) responsible for chronic infections in immunocompromised individuals or cystic fibrosis and includes 3 subspecies: *M. abscessus subsp. abscessus*, *M. abscessus subsp. bolletti* and *M. abscessus subsp. massiliense* [1]. Although *M. abscessus* has traditionally been regarded as an opportunistic pathogen, recent studies show the evolution of the pathogenic potential of *M. abscessus*. The ability of this species to cause the development of pathological processes is due to a significant set of virulence factors, including two groups of factors (mycobacterial and non-mycobacterial), which ensure the interaction of *M. abscessus* with the macroorganism [2].

M. abscessus exist in various ecological niches [1] and are able to colonize artificial surfaces, fomites, medical and surgical instruments/devices [3]. *M. abscessus* can affect the skin, soft tissues, bones, joints, lymph nodes, internal organs [4] and form characteristic granulomas, evading phagosomal defense mechanisms, inducing the production of inflammatory cytokines and recruiting B- and T-lymphocytes to the site of infection [5]. Tendon sheaths, joints, and bones can become infected as a result of various injuries, surgical interventions, invasive procedures, or deep skin puncture [3, 5]. In addition, risk factors for *M. abscessus* infection include prior surgery with implants, use of immunosuppressants, hematologic malignancies, and end-stage renal insufficiency [6].

Only a few confirmed cases of orthopaedic infection caused by *M. abscessus* have been published in the current scientific literature [3]. Due to the low incidence of *M. abscessus* as the causative agent of orthopaedic infection, a rare clinical case of periprosthetic infection caused by *M. abscessus* would be of undoubted interest to practicing physicians (orthopaedic surgeons, traumatologists, infectious disease specialists, therapists). The case to be presented further features complexity and long duration of antibiotic therapy aimed at arresting the infectious process.

Purpose: to present successful management of a clinical case of periprosthetic infection caused by *M. abscessus*.

MATERIALS AND METHODS

From the medical records and discharge documents, it was known that patient H., born in 1957, (180 cm, 68 kg) suffered bilateral idiopathic coxarthrosis in stage 3 and underwent hip replacement in June 2018 at her residence hospital: total cementless arthroplasty of the left hip joint (HJ). The postoperative period was uneventful. In October of the same year, the patient underwent total cementless arthroplasty of the right hip joint in the same hospital. Signs of acute infection of the postoperative wound were detected in the early postoperative period. Signs of inflammation were stopped with conservative measures; the patient was discharged for outpatient treatment.

Three weeks after total arthroplasty of the right hip joint, edema, redness of the area around the postoperative scars of the right thigh developed, and a fistula with abundant purulent hemorrhagic discharge opened. The patient was recommended hospitalization at a purulent surgical department with a diagnosis of phlegmon of the right thigh. In November 2018, debridement was performed, revision of the phlegmon of the right thigh. Bacteriological study of the contents did not reveal any pathogen. During hospitalization she received systemic antibiotic therapy: vancomycin, moxifloxacin, linezolid. At the time of discharge, there was an improvement in the condition, a decrease in the amount of discharge and a change of its nature in serous one. The patient was recommended to contact a specialized institution for further surgical treatment.

This work used clinical, laboratory, instrumental diagnostic methods. The patient signed an informed voluntary consent upon admission to use the results of treatment for educational and scientific purposes.

RESULTS

In mid-January 2019, the patient was hospitalized at the federal medical center. Diagnosis at admission: deep chronic periprosthetic infection of the right HJ, exacerbation, fistulous form (Fig. 1 a). Locally on admission: a granulating wound sized 2 × 3 cm in the upper third of the postoperative scar and two sinuses distal to the scar. The diagnosis was confirmed by fistulography (Fig. 1 b). Concomitant pathology: arterial hypertension in stage 2, risk of cardiovascular complications 3, chronic superficial gastroduodenitis, gastroesophageal reflux disease. She had a history of appendectomy, and three caesarean sections.

Laboratory tests revealed signs of an infectious process: WBC – 8.3 × 10^9/l (toxicogenic granularity of neutrophils ++), ESR – 120 mm/h, CRP – 81 mg/l, hypochromic anemia: Hgb – 74 g/l, RBC – 3.06 × 10^{12}/l, serum iron 3.7 μmol/l. In the dressing room, two tissue biopsies were taken through the fistulous tract from the depth of the wound. To prepare her for surgery, anemia and protein deficiency were corrected.

On January 16, 2019, radical debridement was performed with the installation of a block-shaped spacer (Fig. 2 a) impregnated with vancomycin (10 wt %). Signs of acute cellulitis, a 10 cm fascia defect, fasciitis, myositis, infection pockets posterior and anterior to the femur were revealed intra-operatively. During the removal of the femoral component, a femoral fracture occurred which required osteosynthesis with a cerclage wire. The wound was washed with antiseptic solutions in a volume of 6 liters. The operation was completed by draining the wound according to Redon.

From the day of the surgery, the patient received standard, accepted at the center, empirical antibiotic therapy with vancomycin and cefoperazone/sulbactam (Fig. 3). Having received the preliminary results of the microbiological study of the preoperative material on the 2nd day that detected the growth of *Fusobacterium varium*, the antibacterial drugs were changed to amikacin and levofloxacin. On the fifth day after the operation, the final results of the study were obtained: a pan-resistant strain of *M. abscessus* was isolated from the preoperative material (Table 1). Clarithromycin was added to antibiotic therapy. However, abundant wetting of the dressing with wound discharge was observed and remained significant by post-operative day 7.

The growth of *M. abscessus* was also detected in the intra-operative tissue biopsies and endoprosthesis components on the 12th day after the operation. Moreover, the growth of an unverified strain of *Staphylococcus* sp.

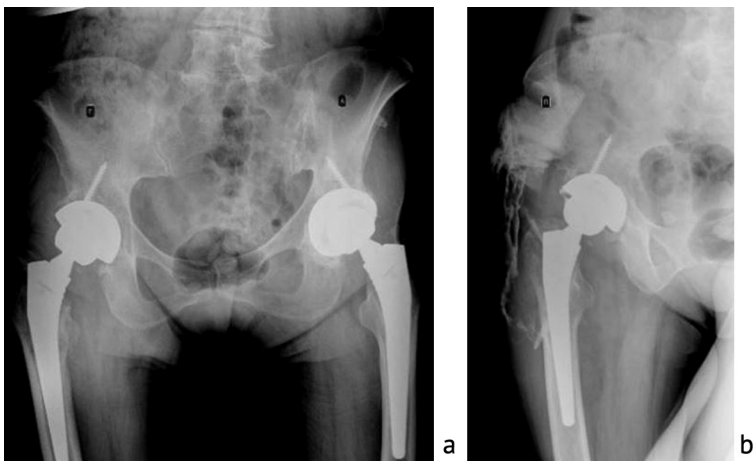

Fig. 1 X-rays of the pelvis upon admission to the federal medical center: *a* X-ray of the pelvis; *b* fistulography of the right hip joint, the spread of a contrast agent into the joint cavity

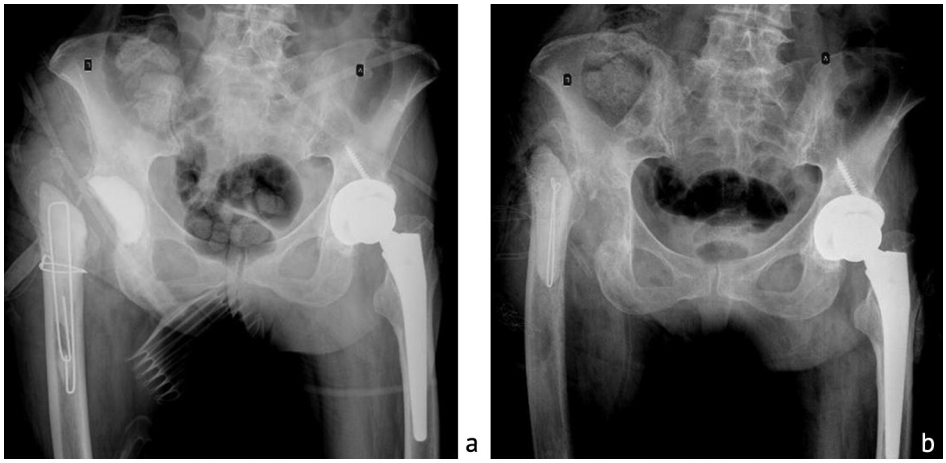

Fig. 2 X-rays of the pelvis after debridement with the installation of an antimicrobial spacer: *a* X-ray after installation of the first spacer into the right hip joint; *b* X-ray after installation of the second spacer into the right HJ

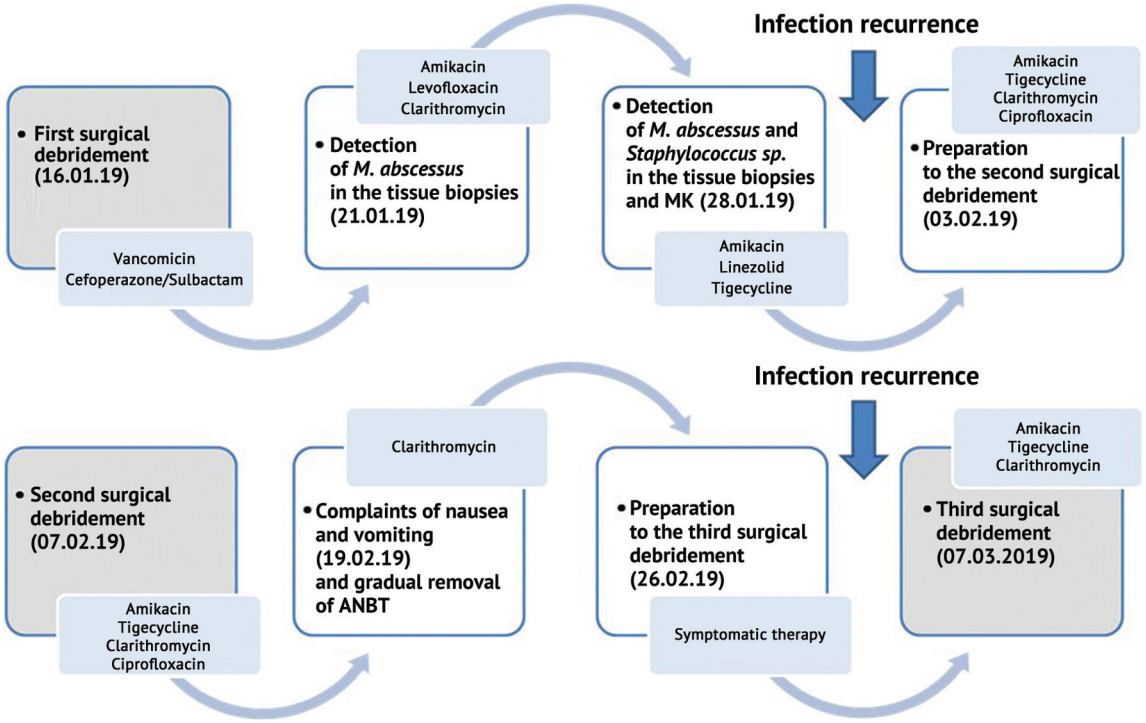

Fig. 3 Correction of the antibacterial therapy during the first hospitalization

Table 1

Sensitivity of the detected *M. abscessus* strain to antibacterial preparations

Mycobacterium abscessus		
Antibioticogram	Sensitivity	МПК
Amoxicillin/Clavulanic Acid	R	> 64/32
Doxycycline	R	> 16
Imipenem	R	> 64
Clarithromycin	R	> 64
Linezolid	R	> 64
Minocycline	R	> 8
Moxifloxacin	R	> 8
Tigecycline	–	4
Tobramycin	R	> 16
Trimethoprim/sulfamethoxazole	R	> 8/152
Cefepime	R	> 3
Cefoxitin	R	> 128
Ceftriaxone	R	> 64
Ciprofloxacin	R	> 16

MSC – minimal suppressive concentration, mg/l.

Due to negative clinical and laboratory dynamics, sutures were removed from the entire depth of the wound, and AB therapy was corrected for amikacin, linezolid, and tigecycline. On the 15th day after the first operation, it was decided to perform a second operation. Due to the final verification of the etiology of the infection caused by *M. abscessus*, the patient was examined by a tuberculosis surgeon. According to his conclusion, the patient was not epidemically dangerous and did not require isolation. It was recommended to continue massive combined antibiotic therapy after repeated sanitation (Fig. 4). On the 19th day after the operation, in order to prepare for surgery and considering the resistance of the isolated strain of *M. abscessus* to all tested antibiotics and the absence of growth of *Staphylococcus* sp., linezolid was discontinued but amikacin, tigecycline were continued, and clarithromycin and ciprofloxacin were additionally prescribed.

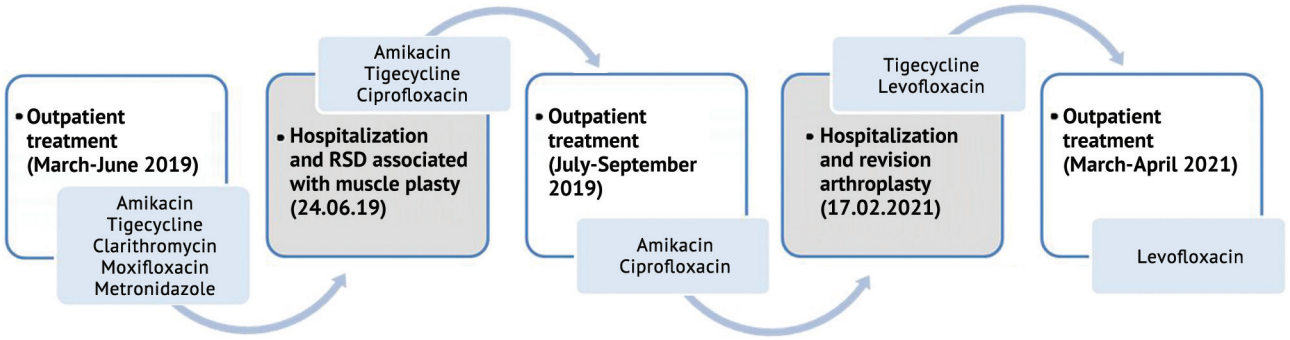

Fig. 4 Correction of antibacterial therapy in the second hospitalization

On February 7, 2019 (day 21 after the first operation), a repeated radical surgical debridement of the infection focus was performed with the reinstallation of a block-shaped antimicrobial spacer impregnated with amikacin (10 wt %) (Fig. 3 b). During the operation, an acute infectious process involving the fascia and muscles was revealed. Before installing a new spacer, the wound was treated with a pulsating stream of saline with the addition of amikacin (2.0 g per 500 ml) with a cavitation effect using the Sonoca 300 apparatus (Söring, Germany). Due to the acute course of the recurrent infectious process, sutures were placed on the fascia and skin.

In the postoperative period, in addition to antibacterial therapy a symptomatic therapy was prescribed: pain relief, correction of anemia and protein deficiency, and vitamin therapy. For the purpose of local ABT, a solution of 0.5 % dioxidine 20 ml was injected through the placed drains once for 5 days. The postoperative wound healed by secondary intention.

On the 12th day after the second operation, the patient began to experience nausea and vomiting associated with the administration of antibiotics. Therefore, antiemetics were prescribed and the number of antibiotics was reduced. First, amikacin and ciprofloxacin were canceled, however, complaints of nausea and vomiting persisted; after three days clarithromycin was canceled, and then tigecycline. The patient was no longer bothered by nausea and vomiting. However, due to the discontinuation of AB therapy, a second recurrence of infection developed and wound dehiscence. On February 26, 2019 (19th day after the second operation), a decision was made to perform a third sanitizing operation. Preparations for surgical intervention were: correction of anemia and protein deficiency. Taking into account previous complaints of AB therapy, amikacin, tigecycline, clarithromycin were prescribed from the day of surgical treatment.

On March 7, 2019, the third sanitizing operation was performed (Fig. 5 a) with repeated reinstallation of the block-shaped antimicrobial spacer, additionally impregnated with meropenem (10 wt %). The postoperative wound was sutured with the formation of a fistula. In the postoperative period, the wound healed throughout, except for the fistula in the lower corner. On March 21, 2019, the patient was discharged for outpatient treatment with a recommendation to continue systemic antibiotic therapy at an outpatient hospital at the place of her residence (Fig. 4).

In the period from March 26, 2019 to June 18, 2019, the patient was on conservative treatment at her residence hospital and received amikacin, tigecycline, moxifloxacin, clarithromycin, metronidazole. Throughout the course of ABT, laboratory monitoring was carried out in order to identify adverse drug reactions. From the moment of discharge and until admission to the federal medical center, she received moxifloxacin, metronidazole, clarithromycin.

On June 24, 2019, the patient was re-admitted to the department of purulent surgery for staged surgical treatment. Diagnosis at admission: chronic recurrent deep periprosthetic infection of the right hip joint, exacerbation, fistulous form; chronic osteomyelitis of the right femur and pelvis, 4 (B), l, exacerbation. Locally on examination: postoperative scar 20 cm in the area of the right hip joint, a functioning fistula in the lower corner with profuse serous purulent discharge.

The laboratory tests were: WBC – 5.4 × 10^9/l, ESR – 48 mm/hour, CRP – 5.1 mg/l, and hypochromic anemia was diagnosed: Hgb – 107 g/l, RBC – 3.42 × 10^{12}/l.

On June 26, 2019, a full-scale operation was performed: radical debridement, removal of the spacer, and replacement of the defect with a non-free muscle flap from the vastus lateralis muscle (LTM) (Fig. 5 b). From the day of surgery, the patient was transferred to parenteral ABT: amikacin, tigecycline, ciprofloxacin.

The wound healed by primary intention, the drains were removed on the 5th day after surgery. In the postoperative period, symptomatic therapy was performed. The growth of microorganisms from intra-operative tissue biopsies and the removed implant was not detected. Antibacterial therapy was continued 14 days post-surgery. On the 15th day after surgery, the patient was discharged for outpatient treatment with a recommendation to continue ABT for 8 weeks with the following drugs: amikacin, ciprofloxacin.

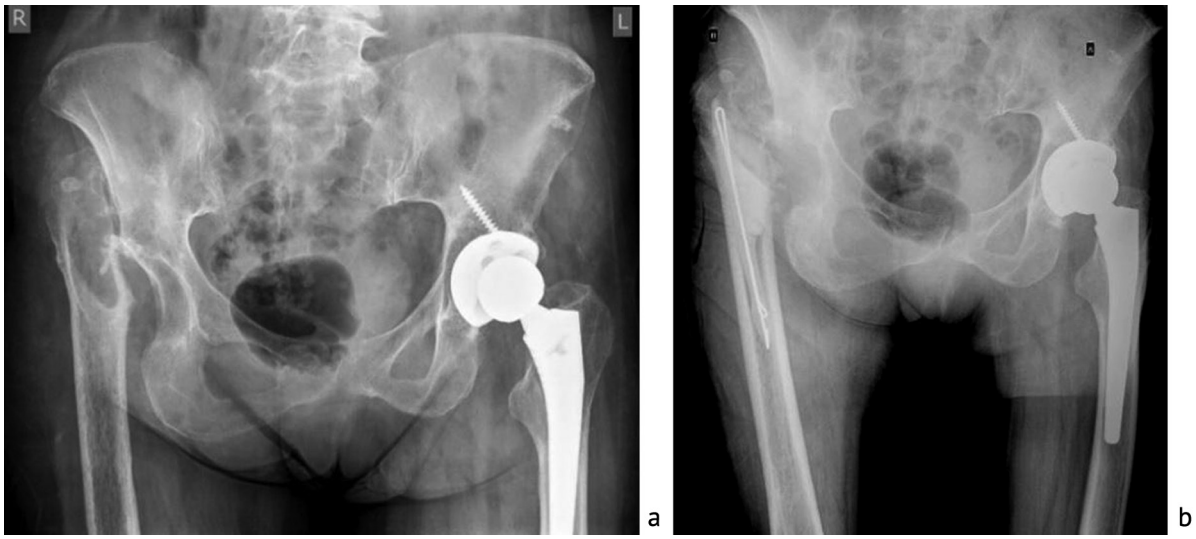

Fig. 5 X-ray of the pelvis after repeated sanitation: *a* X-ray of the pelvis after installation of the third spacer of the right hip joint; *b* X-ray of the pelvis after non-free muscle plasty with vastus lateralis muscle

A year later (17.02.2021), the patient was admitted for revision arthroplasty with a diagnosis of chronic recurrent deep periprosthetic infection of the right hip joint in remission; chronic osteomyelitis of the right femur and pelvic bone, 4 (B), l, remission. No microbial growth was detected in the aspirate from the right hip joint. Status localis: postoperative scar 45 cm in the area of the right thigh without signs of acute inflammation. Shortening of the right lower limb = 5 cm. There were no laboratory signs of exacerbation of the infectious process: WBC – 5.1 × 10^9/l, ESR – 11 mm/hour, CRP – 1.13 mg/l.

Revision arthroplasty of the right hip joint was performed using a cementless fixation of the implant (Zimmer Biomet, USA) (Fig. 6). The postoperative wound healed by primary intention. From the day of surgery, the patient received systemic antibiotics: tigecycline, levofloxacin. On the 7th day, the results of intra-operative cultures were obtained; growth of MSSE was detected in 1 of 5 biopsies. ABT continued 14 days after surgery. At the outpatient stage, the patient was recommended to continue taking levofloxacin 0.5 g twice a day for 1 month.

Being consulted distantly in February 2023, the patient did not complain of the infectious process. The postoperative scar was 45 cm and regular. The residual shortening of the right lower limb of 3 cm was compensated with orthopedic shoes. Laboratory parameters are within normal limits: WBC – 4.09 × 10^9/l, ESR – 15 mm/hour, CRP – 4.9 mg/l, as well as Hgb – 138 g/l, RBC – 4.20 × 1012/l. Checking radiographs show a stable implant components in the right hip joint (Fig. 7).

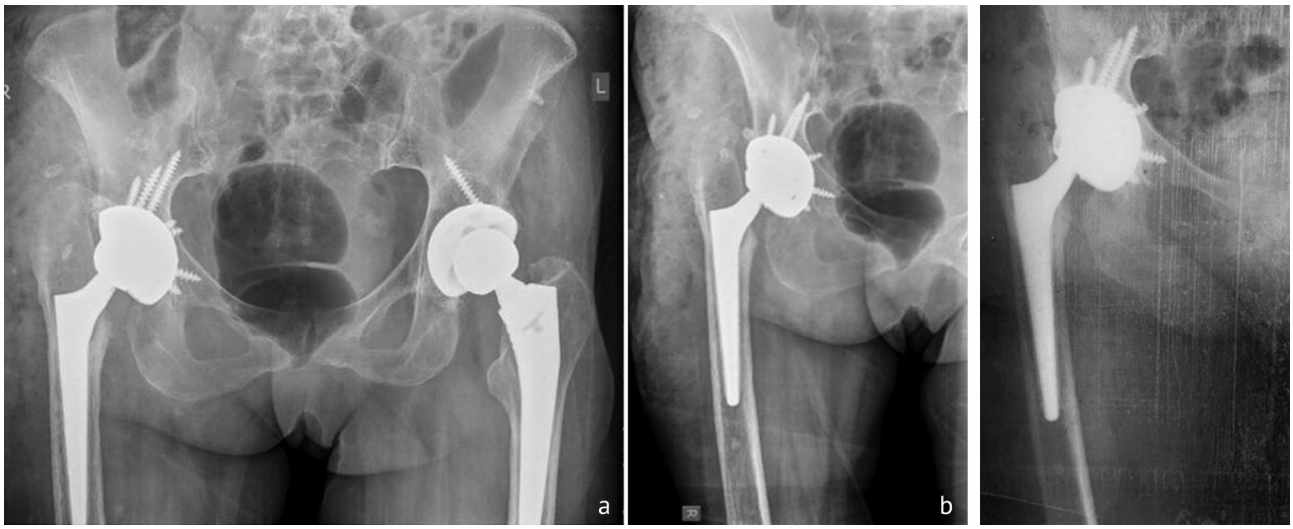

Fig. 6 X-ray of the pelvis after revision arthroplasty of the right hip joint: *a* plain X-ray of the pelvis; *b* X-ray of the right hip joint

Fig. 7 X-ray of the right hip joint at 2-year follow-up

DISCUSSION

Treatment of infection caused by *M. abscessus* is challenging due to the natural resistance of the pathogen to a wide range of antibacterial drugs. As a rule, it is necessary to prescribe at least three antibiotics active against the pathogen [7].

Cases of periprosthetic infection caused by *M. abscessus* are described in the world literature as case reports. One of them was an elderly 78-year old patient who developed an acute bilateral infection 5 weeks after bilateral knee arthroplasty [8]. A course of empirical anti-tuberculosis therapy (rifampicin, isoniazid, pyrazinamide and ethambutol), as well as joint debridement with replacement of modular components, did not lead to success. After the first relapse, bilateral installation of antimicrobial spacers was performed. To treat the second recurrence, arthrodesis of the right knee joint was performed using the Ilizarov apparatus and two-stage revision arthroplasty of the left knee joint using a combination of rifabutin, clarithromycin and amikacin. One-and-a half year treatment and 7 operations resulted in the arrest of the infectious process caused by *M. abscessus*.

There is a known case of multiorgan *M. abscessus* involvement in a patient with chronic back pain with a nodular lesion of the right leg, without fever, chills, rash, shortness of breath or cough. Laboratory data showed moderate leukocytosis. A computed tomography scan of the chest revealed bilateral cavitation nodules. Skin biopsies, sputum, and blood cultures revealed *M. abscessus*, and treatment with meropenem, tigecycline, and amikacin was prescribed. The patient was readmitted to the hospital due to worsened low back pain. Magnetic resonance imaging of the lumbar spine revealed destructive changes in L4 and L5 vertebral bodies and osteomyelitis. Blood culture and bone biopsy again detected *M. abscessus*. An echocardiogram was performed due to persistent bacteremia, which revealed large vegetations on the tricuspid valve and small vegetations on the mitral valve. Therapy was changed to a course of amikacin with cefoxitin for 8 weeks and imipenem for twelve months [9]. In addition, a nosocomial outbreak of septic arthritis caused by NTM following corticosteroid injections has been described [10]. The authors note that clinicians should be aware that mycobacterial infections, including *M. abscessus*, are one of the differential diagnoses in patients with subacute arthritis and soft tissue infection [6]. Despite long-term combined antibiotic therapy, treatment of infections caused by *M. abscessus* frequently fails, leading to progressive disease and ultimately death [7]. Fukui et al reported a fatal case of *M. abscessus* infection in a patient treated with corticosteroids for 17 years. X-ray of the right elbow showed osteolysis, and magnetic resonance imaging revealed fluid in the right elbow. The growth of *M. abscessus* was recorded from joint fluid and blood cultures. The patient received antimicrobial treatment with clarithromycin, amikacin, and imipenem/cilastatin in combination with debridement and, although blood and joint fluid cultures were negative after 1 week, the patient died 6 weeks after initiation of antimicrobial treatment [6]. In our case, the total duration of ABT was 8 months; the patient received, among other drugs, amikacin, tigecycline, ciprofloxacin, and clarithromycin.

Another clinical case was an 84-year-old patient who developed periprosthetic knee infection and sepsis 8 weeks after surgery [3]. Two consecutive revisions involving the replacement of modular components were unsuccessful. During the two-stage treatment, the infectious process was stopped. The antibacterial drugs used were vancomycin, azithromycin, amikacin, tigecycline, cefoxitin, ciprofloxacin and linezolid. The total treatment period was 84 weeks (more than 1.5 years), during which 4 operations on the knee joint were performed.

There are described cases of other locations of orthopedic infection caused by *M. abscessus*. Wong et al described two cases of foot infection following open fracture-dislocations. In one case, the patient was treated with clarithromycin and doxycycline, in the second with cefoxitin, clarithromycin and doxycycline. Ten months after debridement, the infection was arrested [11]. *M. abscessus* can also cause osteomyelitis of the thoracic spine [12-14], rupture of the flexor tendon of the hand [15], and post-injection septic arthritis [16].

In our case of chronic recurrent periprosthetic infection, five surgical interventions, long-term combined antibiotic therapy and two years of complex treatment were required to stop the infectious process caused by *M. abscessus*. Residual shortening of the right lower limb of 3 cm was the result of a long-term infectious process and many surgical interventions, which led to contraction of the thigh muscles with relative preservation of the bones that form the hip joint. Currently, the patient uses orthopedic shoes to compensate for length discrepancy and moves without additional support.

Pprescribing targeted therapy, doctors can only rely on the results of the antibiotic sensitivity of a particular *M. abscessus* isolate; however, due to the peculiarities of the bacteriological diagnosis of NTMB, correct results will be obtained no earlier than 5 days after harvesting the material (for slow-growing mycobacteria – from 7 days). In addition, this type of NTMB is characterized by an extreme antibiotic resistance profile. Within the framework of personalized medicine, it is also possible

to expand the therapeutic approaches of etiotropic therapy through genetically engineered bacteriophages or selected combinations of drugs in accordance with the determination of their senergid antimicrobial activity against a specific isolate. The effectiveness of new beta-lactamase inhibitors, including avibactam, against *M. abscessus* has been experimentally established [17]. Combinations of the antimicrobial agents, vancomycin/clarithromycin and dual beta-lactam therapy, have been shown to have a synergistic effect, suggesting their possible use in multidrug regimens [18, 19]. In addition, bacteriophage therapy has been effective in severe cases of disseminated *M. abscessus* infection [20]. Although many of those experimental therapeutic approaches demonstrate in vitro activity against *M. abscessus*, most do not currently have evidence of their effectiveness in clinical use for the treatment of infections caused by this pathogen.

CONCLUSION

Long-term aggressive antibiotic therapy in combination with staged surgical treatment yields success. This requires the coordinated work of bacteriologists, orthopedists, clinical pharmacologists and infectious disease specialists. Practitioners need to be aware of possible non-tuberculosis mycobacterial orthopedic infection and correctly perform differential diagnosis with other infectious diseases.

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Ethical review *Not required.*

Informed Consent *All patients sign an informed voluntary consent for the use of the results of their treatment for educational and scientific purposes.*

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Kochish A.A. – analysis and interpretation of the results, writing and editing the text of the article.
Gordina E.M. – preparation and writing of the initial draft of the work, literature search, and editing the text of the article.
Rukina A.N. – analysis and interpretation of the results.
Artyukh V.A. – control and management of planning and execution of research work, including mentoring.
Bozhkova S.A. – responsibility for managing and coordinating the planning and conduct of research activities.

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Review article

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Ceramic-related noise as an adverse outcome in total hip arthroplasty

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Abstract

Introduction Ceramic hip replacement bearings have shown to be low wearing and biocompatible. The last two generations of Biolox Forte and Biolox Delta ceramics have have established themselves as durable bearings. However, squeaking and noise from ceramic bearing THRs is well recognised in the 21st century. **The objective** was to explore the problem of noise in the ceramic bearing of THA based on the analysis of the foreign and Russian literature. **Material and methods** In presented the analysis of Foreign and Russian literature searches for the review were produced according to PRISMA recommendations using PubMed, Scopus, Google Scholar, eLibrary. MINOR was used to assess the methodological quality of articles. **Results and Discussion** Noise in ceramics is observed in 37.7 %. There are many theories on the origin and mechanism of noise including liner impingement and loading, film disruption, third body, microseparation and resonance. However, there is still no consensus on what is noise in the ceramic bearing and how to solve this problem. **Conclusion** Literature review of ceramic bearing indicated enough unanswered questions. The noise may play a role as a predictor of improper use of endoprosthesis with accumulated database resulting in better understanding of the phenomenon, methods of the correction and timely prevention of ceramic breakage.

Keywords: total hip arthroplasty, ceramic bearing, noise in ceramics, squeaking in ceramics

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INTRODUCTION

Total hip arthroplasty (THA) has been quoted as one of the most successful and cost-effective procedures in orthopaedics and can be used in patients aged 18-30 years [1]. A major long-term problem affecting THA survivorship is polyethylene wear and the resultant wear-induced osteolysis [2, 3]. Ceramic-on-ceramic hip bearings were first introduced by P. Boutin in 1971 with a first implantation of ceramic components from CeramTec in 1975 [4]. The first models of this pair were rejected by surgeons due to their fragility, and in 1993 the 3rd generation Biolox Forte was developed [5]. Although medium-term results of using theceramic were reported as good, the complication rate in the form of squeaking hips remained high [6]. Fourth generation ceramics made of alumina-zirconia composite followed by addition of 18 % zirconium dioxide, 1 % strontium oxide, 1 % chromium oxide was developed in 2003 [7]. The modern ceramics are described as a bioinert and wear-resistant material [8, 9]. The Biolox Delta generation showed excellent performance at a mid term [10, 11]. The fracture of ceramic heads decreased significantly [10, 12], and the fracture of the liner amounted to 0.03 % [13]. In percentage terms, the results may seem clinically insignificant, but the consequences of ceramic breakage are catastrophic [9, 11] because destroyed ceramic components are not recommended to be replaced with less fragile materials due to the fact that ceramic debris and the third body remaining in the surrounding soft tissues as a result of a fracture can penetrate into the friction surface and destroy it if it is softer than ceramics [11, 14, 15]. Before 2005, squeaking was not recognized as a clinically important complication of ceramic bearings [6]. Patient demands have increased with intention for an artificial joint feeling much more like the patient's natural hip [16]. Many factors have been described that provoke noise in a ceramic pair, but the complication can develop with well aligned prosthetic components [17, 18] that is associated with the quality of life of patients [18]. Owen D.H. et al. reported the incidence of revision for squeaking of 0.2 % [19]. Therefore, squeaking has become an unanticipated clinical outcome and an adverse event of the 21st century in THA [6].

The objective was to assess the problem of squeaking in the ceramic friction pair of THA based on an analysis of foreign and Russian literature.

MATERIAL AND METHODS

This review was conducted in accordance with PRISMA guidelines [20]. The search was performed using open electronic databases of PubMed, Scopus, Google Scholar, eLibrary and keywords and phrases: ceramic bearing[Title/Abstract] or ceramic on ceramic [Title/Abstract] or ceramic squeaking [Title/Abstract]) and hip[Title/Abstract] in English databases and ceramics, squeaking, endoprosthetics in the Russian-language database. The literature was reviewed by two independent reviewers: the first stage included screening by title and abstract. The search depth was 20 years until 2002. Inclusion criteria: literature of any level of evidence, full text in Russian and English freely available, focused on squeaking of the ceramic friction pair of THA. Exclusion criteria included reviews, expert opinions, book chapters, conference abstracts, case reports and studies in Russian and English. Studies with follow-up of less than 5 years. The second stage included an analysis of the full texts of the relevant studies. The methodological quality of articles was assessed using MINOR (Methodological Index for Nonrandomized Studies) [21].

RESULTS AND DISCUSSION

The results of a literature analysis showed that squeaking in ceramics can occur in 36 % [22-26]. The frequency of squeaking in 3rd generation ceramics was 2.4 % [27]. Squeaking statistics averaged 3 % in a recent meta-analysis of 4th generation ceramics [28]. Many causes for squeaking have been reported and the complication appeared to be a multifactorial problem [6, 29]. The factors were classified into three categories: surgical, patient-related, and implant-related [6].

Surgical factors

Incorrect positioning of components. Patients who complain squeaking in THA have excessive or insufficient anteversion or inclination of components over 45 degrees [22, 25, 28, 30-32]. In contrast, other studies have not found a similar relationship with acetabular component orientation [27, 33-36]. Medialization or lateralization of the center of rotation of the acetabulum, according to F. Castagnini and S. Sexton, also contributes to the genesis of squeaking, disrupting the contact patch [29, 31, 37].

A *loosely fitted liner* has not only a high risk of squeaking in the prosthetic joint, but also the risk of early destruction due to micromobility between the surfaces of the liner and the acetabular component, resulting in the formation of a second friction pair between the liner and the cup [6, 35]. The reason for the early failure of ceramics in the form of chips after THA may be a situation that was demonstrated in laboratory conditions, with loosely fitted liners being more susceptible to squeaking than tightly fitted liners [38].

Screws. The acetabular screws may come into contact with the rear surface of the liner with extrusion and cause either noise or microcracks in the liner [39-41].

Patient-related factors

Age. Young, tall, and active patients are more susceptible to squeaking [29]. Siddhard M.S. et al. reported a statistically significant difference in age between patients with and without squeaking in a prospective cohort study [22]. The authors suggested the correlation between greater activity and physical performance in young people.

BMI. Walter W.L. suggested that demographic data indicated to squeaking being more likely in patients with greater weight and height [6, 27]. Patients weighing more than 91 kg were 4.76 times more likely to have ceramic fractures than patients weighing less [42, 43].

Gender. Choi I.Y. et al. reported gender as a factor influencing the occurrence of squeaking. The study suggested that men were more susceptible to squeaking due to greater physical activity [36, 44].

Concomitant pathologies of the lower extremities. Limb length discrepancy can be assessed with complications such as muscle imbalance, impingement, dislocation and displacement of the contact patch. McDonnell S.M. et al. suggested that squeaking was more common in patients with excessive range of motion, which was associated with muscle imbalance [23]. Excessive motion can lead to microseparation or rim loading being the underlying mechanism for squeaking [23, 45]. McDonnell S.M. reported that muscle atrophy and a wide range of motion significantly increased the risk of squeaking [23]. Rheumatoid arthritis can be a risk factor for squeaking, although the association was difficult to explain [46].

Consequences of fractures of ceramic components. A major problem includes the spread of small sharp ceramic particles into soft tissues as a result of fracture, that cannot be removed during revision [47, 48]. The consequences of fractured ceramic components

would also affect subsequent implantation of prostheses in the form of a third body effect [49, 50]. In contrast to the above studies, Keurentjes J.C. and Restrepo C. reported no correlation between squeaking and the above factors [34, 35].

Implant-related factors

Component size. Component size in a ceramic friction pair do not increase wear [51]. Many authors have recommended the use of larger heads to reduce the risk of dislocation by increasing the vault distance. Recent studies have shown a higher risk of squeaking with larger sizes of friction pair components [18, 44] which can increase the risk of cleavage. The first five-year results of the Australian registry showed that the revision rate of THA with larger heads was not less than the of revision rate with 32-size heads [52]. Thomas et al. reported the squeaking rate of 13.5 % with 36 mm heads and 5.9 % with 28 mm heads in a comparative prospective study, and suggested that head size was the only predictor had no effect on outcome, but only in combination with several other factors (predictors) [53]. Larger heads can increase the rim pressure on the liner when the cup is placed more vertically, creating the potential for squeaking. The dimensions of the components can increase the mass of the implant reducing the natural frequency of component vibrations, increasing the amplitude and enhancing the initial vibration leading to squeaking [18].

Differences between technological manufacturing assembly and manual intraoperative assembly. The incidence of squeaking in the group of the factory-assembled Delta Motion cup was significantly higher compared to the ceramic friction pairs assembled intraoperatively [28]. The use of Pressfit Delta Motion cups increased the frequency of squeaking. This could happen due to the fact that the pelvic component could not be fixed with screws causing loosening of the pelvic component and changing the components position. Parvizi J. suggested that cups with a high rim were more susceptible to squeaking when the rim of the ceramic liner was higher than the rim of the cup [54]. Stanat S.J. reported no association between squeaking and higher rim of ceramic liners in the meta-analysis [27].

Design features of the femoral component (offset and neck thickness). Swanson T.V. and Wu G.L. reported Stryker Accolades being more susceptible to squeaking due to the short neck and offset of the femoral component [46, 55, 56]. Thick necks were more susceptible to impingement on the rim of the liner, with a 28 mm femoral head, in particular. Kim H.S. et al. reported the collision statistics of 10 %, which was extremely high for ceramics. No liner fractures were reported in the impingement group at 10 year follow-up, with 21 out of 27 "squeaking" prostheses having a 28 mm head and a thick neck of the femoral component [57]. A study was also conducted to determine the relationship between squeaking and implant models and manufacturers. "Stryker Accolade" and "De puy Summit" were the most 'squeaking' endoprostheses due to tapered proximal portion "Müller" and the philosophy of proximal fixation [27, 28, 46]. Several studies reported that the squeaking could be associated with low-profile femoral components and a thin neck [17, 33, 34]. Fan N. et al. conducted an *in vitro* study and demonstrated that stiffer and shorter femoral components had a higher critical coefficient of friction, which correlated with clinical data [58]. Lee T.H. reported the meta-analysis which included 132 studies on squeaking with the only significant factor being the angle of inclination of the acetabular component [59].

Component materials. Loosening of the femoral component can produce an abrasive and impair lubrication properties of the friction pair causing squeaking [54, 60]. The authors reported that the Stryker Accolade had a more flexible structure, that resulted in better pain relief [56]. The implant had greater potential for resonance due to the flexibility [28, 56]. Restrepo C. et al. suggested that the metal alloy of the endoprosthesis could affect squeaking due to differences in vibration conductivity [56].

Pathogenesis of squeaking in ceramics

Theories about the mechanism of noise vary. Some studies indicate that the noise is a consequence of abnormal friction. Others hypothesize resonance of components during normal friction [61, 62].

Impingement and stress on the rim of the liner. The noise may be a product of the neck of the femoral component impinging on the ceramic rim of the liner. Third bodies can also cause impingement if the metal rim of the cup does not overlap the ceramic edge of the liner [63]. The studies demonstrated traces of regular impact along the medial rim in the acetabular components removed. An impact at the moment of movement could shift the head from the center to the rim, which increased the pressure between the friction pair, shifting the contact patch and the force vector [8, 28]. In this case, the thin liquid film was destroyed leading to the effect of dry friction.

The hallmark of the rim loading is the presence of wear bands in components [32]. The distance from the contact patch to the rim of the liner (CPR) is essential since a direct correlation is reported between the presence of noise and a decrease in CPR [32]. Other studies indicate that impingement may have occurred in patients only when rising from a chair or climbing stairs. The pressure in the friction surface increases significantly with such movements, when an individual is on one supporting limb [64]. The wear rate does not increase even in malalignment [65]. This situation is a predictor of the risk of noise and explosive destruction of ceramics. Walter W.L. et al. explored 12 ceramic components removed during revision in patients with noise complaints, and all components showed signs of the rim wear. The wear thickness was 94 μm, compared to 72 μm in patients without noise. This difference was not significant. However, Walter W.L. et al. reported the liner tending to tilt out of the acetabular shell opposite the applied load with separation of the surfaces measuring 40 μm in the experiment. This separation could allow the acetabular shell to emit a squeaking sound [6]. The study demonstrated that the load on the anterior rim of the liner could be associated with excessive anteversion and inclination of the acetabular component with the load on the posterior rim of the liner being reduced [64]. This mechanism is considered one of the reasons for the dissociated liner and the acetabular component [66]. Posterosuperior marginal load occurs 4 times greater than anterosuperior load [23].

Recent studies have reported the functional orientation of the acetabular component, and it was found that the components required individual selection of anteversion and inclination angles when using a ceramic friction pair in accordance with the philosophy of kinematic arthroplasty [67, 68].

Film damage. The destruction of the synovial film in a tribological pair can be affected by excess pressure in the contact patch, that can occur with high BMI and inadequate placement correct of the components [69]. Insufficient substance to reduce surface friction with use of large diameters can increase the risk of vibration and cause noise [70]. A liquid film acting as a lubricant requires a fine balance of a number of factors, which include sliding speed (1), viscosity of the lubricating fluid (2), surface roughness (3), gap (4), contact pressure – patch (5) [71]. Impaired lubrication by a liquid film can occur as a result of rim loading (reduction of contact area) and the appearance of third bodies (ceramic fragments) in the tribological couple [49].

Third body. Wear streaks were observed in the ceramic components removed from patients with noise complaints. Toni A. et al. reported a high level of ceramic particles found in the aspirates of the artificial joint in patients with complaints of noise. This may indicate the presence of a third body [49, 72]. Lucchini S et al. hypothesized a multi-stage crack growth mechanism to occur following damage at the head-neck taper interface [12].

Microseparation is another theory for the appearance of wear bands [45]. The use of large heads has become popular in recent years. However, this may be the cause of microseparation between the head and the cup due to a small opening angle, which can lead to constant microcollisions in the pair and cause noise [73].

Resonance. The rotational force exceeds the static force in the friction pair at the movement, which leads to the acceleration of one articular surface relative to the other. This causes vibration of ceramic components [6]. Recent studies have shown that the acetabular and femoral components play the role of vibration oscillator [6]. Resonance does not occur if the frequency of vibration does not match the frequency of the component. Fan N. et al. reported the noise frequency of ceramics of 400-7500 Hz [6, 58]. Modal analysis was performed to understand the resonance of the components, which showed that the ceramic liner and cup alone could not resonate, but the ceramic head with the femoral component showed resonance in several modes and planes [6]. The metal composition and design of the implant can influence noise. And this indicates that the vibration frequency of endoprosthetic components is at the same level with noise in this range [62]. Metal components are vibration amplifiers [74].

Features of noise

Noise is described as knocking, clicking, grinding, creaking. The audible sounds are interpreted as creaking which is the most common of the noises described [22, 27]. The authors reported a revision rate of 0.2 % due to squeaking [19]. Creaking has been described as a high-frequency and highly audible sound that is unique to ceramics [28]. It is often painless but affects quality of life. Moreover, noises can be indicators of inadequate placement of endoprosthetic components [28]. Noise in friction pairs was first described in 2008 [73]. Glaser D. et al. were the first to describe characteristics of noise and the classification.

Knocking (*clicking*) is defined as a sign of stress, representing temporary impulses of short duration

and high amplitude (like a high-pitched note) [73]. This sound can be identified in patients when the head is separated from the socket, which can occur in the presence of a slot [73]. Schroder D. et al. reported a clicking noise as the most common noise instead of a creaking noise [75]. A similar observation was reported in other studies [17, 33].

Grinding is defined as a high-frequency audible sound resulting from forced vibration generated by a driving force, resulting in a dynamic response [6]. It is observed with intense, sliding movement between the head and the acetabulum in full contact [73]. Shah M.S. et al. reported squeaking as the most common type of noise, accounting for half of the noise (7.7 out of 14.7 %) [22].

Crunching indicates cracking of ceramic components [49]. The mechanism consists in the formation of a small and hard abrasive that also rubs between the ceramic components. This indicates the appearance of abrasive noise, which can be compared to the sound of sand rubbing against glass. This noise must be identified urgently to prevent the spread of particles into the surrounding soft tissue resulting from the patient's motor activity [76].

The nature of noise can be classified into two types. The authors of a recent experimental study on the occurrence of noise in three different conditions (dry friction, water and blood plasma) found that high-frequency noise occurred only with dry friction with a standard tilt of the acetabular component according to ISO 14242-1 which indicated the adhesive noise. Audible sounds appeared everywhere with the same specified conditions with a change in the edge slope corresponding to ISO 14242-4.

Dry test conditions are inappropriate when assessing ceramic squeaking, as noise will be generated at any angle. It has been demonstrated that noise occurs when edge pressure is applied to the liner with any lubrication condition [77]. It can be assumed that the integrity of the lubricating film is disrupted with edge pressure, movement and impact leading to dry contact and generating noise. Squeaking may indicate an impaired liquid film due to a high coefficient of friction [71]. Another experimental study aimed to detect component wear using acoustic emission showed differences in the sounds of adhesive and abrasive wear [78]. Adhesive wear can be considered dry friction in the case of a ceramic friction pair, and abrasive wear can be considered in the presence of a third body. Both experiments demonstrated the noise being high-frequency and instantaneous with the film being intact and the frequencies decreased and their duration increased with dry friction or with the integrity of the surface being impaired. The noise frequency mainly fluctuated in the range perceived by humans [79, 80].

An analysis of the literature to interpret the types of noise in a ceramic friction pair reflected questions to which the answers are ambiguous, since there is no single consensus on the classification and type of noise [25]. There are a large number of laboratory studies on friction pairs for wear resistance and noise production exploring the noise phenomenon [81]. However, not all the models can reproduce a human joint. First, the tribological couple must have good wettability for the suction effect and have a lubricating fluid like synovial fluid. Secondly, we must understand that noise is mainly produced in the friction pair of the endoprosthesis at a high pressure and can be obtained with statics of the lower limb and dynamics of the pelvis. The acetabular component must move relative to the axis of the femoral head of the hip endoprosthesis and not otherwise.

Clinical management of patients with hip noise

Patients undergoing THA with a ceramic friction pair should be aware of the risks of noise in the joint and should contact the operating surgeon if noise occurs. The femoral component must be carefully selected to prevent noise considering spinopelvic relationship according to the principle of kinematic arthroplasty [81]. Navigation is practical for implanting endoprostheses with a ceramic friction pair that can reduce the risk of ceramic splitting by 2.7 times and promote optimal spatial orientation of the endoprosthetic components [22]. When a patient complains of noise in the joint the orthopaedic surgeon must rule out a fracture of ceramic components using computed tomography [6]. The majority of patients with fractured ceramic components have no history of trauma, and the events leading to the noise are trivial [14, 48, 82, 83]. Noise with a ceramic friction pair can become a predictor of the risk of endoprosthetic destruction [83]. A recent study demonstrated that fracture of ceramic components is rather to continuous exposure to certain forces than as a result of one-time trauma [12]. Levêque R. et al. reported no delayed ceramic implant breakage in THA at a median 3 years follow-up [84]. CT is used to measure the position and spatial orientation of components. Having ruled out splitting, the specialist must determine whether the noise is acceptable or unacceptable. Acceptable noise is typically the result of posterior edge loading and

probably occur with edge loading when the hip is flexed, such as with rising from a chair or with climbing a high step [64]. This type of noise is usually associated with some kind of excessive movement, which can be avoided by using an orthotic regimen and limiting the provoking movements. Disenabling noise occurs during a normal movement cycle and can be accompanied by pain and disturbs the patient [64]. This type of noise is believed to be associated with loading on the anterior edge of the liner. Walter W.L. et al. recommended revision surgery for noises that are accompanied by pain, or for incorrect orientation of components [6]. If the noise affects the patient's lifestyle and if there are indications the specialist should perform revision surgery. Examination of synovial fluid aspirate can be an addition to diagnosis [72]. The presence of particles of 2-5 microns in the aspirate may indicate an early stage of fractured ceramic components. Fragments exceeding 5 μm indicate macroscopic destruction in ceramics [49].

Traina F. et al. reported 81 % of cases with the noise being associated with the fracture of the ceramic friction pair in patients with audible noise at the site of the prosthetic joint based on the synovial fluid analysis. In the group of patients, only there were Signs of ceramic destruction were seen in 6.1 % of cases with a silent course of the noise, which makes us treat ceramic friction pairs with some caution [85]. Moreover, it has been repeatedly reported that a fractured ceramic component was detected in patients who previously had noise complaints [31]. Stripe wear and metal transfer to ceramic components were reported in 100 % of cases of noise [31, 35]. Inagaki K. et al. described a 2-stage prospective screening of patients with a ceramic friction pair with the number of patients with complaints increasing with each screening, and patients who had noise complaints in previous screenings had them in subsequent screenings demonstrating an accumulation effect of patients with noise complaints [25]. One patient who complained of squeaking was subsequently revised for a fractured ceramic liner.

Kim M.W. et al. reported changes in the frequency and pitch of noise in patients in a multi-stage control observation [86]. Due to the versatility of noise in a ceramic friction pair, it is not entirely clear whether noise production is the cause of ceramic splitting or microdestruction in a ceramic friction pair with subsequent complete separation of the component. The splitting of the ceramic components of a friction pair results in repeated revisions despite its statistical insignificance. The Australian registry demonstrated that the rate of second revision of 29.6 % over 3.5 years after fracture of ceramic components [11].

A ceramic pair is recommended for young and active patients due to high survival rates and excellent laboratory results for wear [87]. However, the ceramics paradigm needs to change due to recent research. Use of ceramics for a young patient suggests a lifetime choice of a ceramic friction pair. Subsequent revisions can be associated with a friction pair other than a ceramic one. A "ceramics-polyethylene" friction pair can be a method of choice for young and active patients with a "ceramics-ceramics" pair offered for a subsequent revision. Fang Y. et al. reported an insignificant difference in the wear of friction pairs and an insignificant statistical difference in complications in a meta-analysis of comparative randomized controlled studies of ceramic-ceramic and ceramic-polyethylene friction pairs [88]. Jack C.M. et al. reported the results of revisions at 8.3 years with a metal or ceramic head with a polyethylene liner being replaced with a ceramic-ceramic friction pair. Patients reported no noise at the site of the prosthesis [89].

CONCLUSION

Literature review on the problem of ceramic friction pairs demonstrated a lot of unresolved issues regarding functioning of ceramic friction pairs in THA, which force us to be cautious about the choice of the ceramic pair. The use of ceramic pairs suggest measures to be taken to ensure optimal functioning of the pair through ideal implantation of prosthetic components using robotic technologies and subsequent medical examination of patients. The assessment of noise in a functioning endoprosthesis is considered an unreliable and very expensive method with the size of the components and the design causing different sound frequencies. Patient related factors can affect the frequency of the sound with the amplitude, duration and nature of the sound to be assessed [6, 73]. The accumulated database can help formulate a new hypothesis for the genesis of noise, methods for their correction and prediction of splitting ceramics. The ceramic friction pair is not as good as it is advertised, which, admittedly, is a good job of marketers, despite the fact that the ceramic friction pair can play the role of an "iceberg" for any Titanic.

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