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Features of surgical treatment for primary injury to the flexor tendons of the three-phalangeal fingers in the second zone: a retrospective cohort study

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Abstract

Introduction Three-phalanx finger flexor tendon injuries in the fibrous-osseous canals of the fingers represent a complex orthopedic problem requiring multifaceted treatment. The functional outcome of flexor tendon reconstruction depends on the surgical strategy, timely provision of necessary rehabilitation support, and patient compliance. Failure to adopt a comprehensive approach to treating patients with this injury often leads to poor clinical and functional outcomes.

The **purpose** was to determine key surgical and rehabilitation factors that have impact on the outcomes of primary reconstruction of the flexor tendons of the three-phalangeal fingers in the second zone.

Materials and Methods We analyzed the postoperative results of 100 patients who underwent primary reconstruction of the deep flexor tendon of one three-phalangeal finger after damage to both flexor tendons in zone 2 according to the Verdan classification. These included finger function using the Strickland criteria and the Boyes – Lister scale, and clinical and functional assessment of the limb using the validated DASH and MHQ scales. The impact of patient morphological characteristics, anatomical topography of the injury, surgical strategy, and rehabilitation protocol on postoperative outcome was assessed.

Results A statistically significant improvement in function was found according to the Strickland criterion with a surgical incision size not exceeding 1.5 phalanx lengths ($p < 0.05$). Functional results with the use of a four-thread 3/0 intrasegmental suture and a six-thread 3/0 suture according to the Strickland criterion and the Boyes Lister scale were statistically significantly better ($p < 0.05$). Poor results according to the Strickland criterion were observed statistically significantly more often in the absence of rehabilitation than with any type of rehabilitation ($p < 0.05$). Suture ruptured more frequently without rehabilitation ($p < 0.001$) than if rehabilitation with a hand therapist was provided.

Discussion The obtained results both differ from the published ones in the literature and confirm some parameters. The use of four- or six-thread 3/0 tendon suture configurations and a rehabilitation protocol with a specialist improves functional outcomes in the treatment of flexor tendon injuries of the triphalangeal fingers and reduces the risk of suture rupture. Combined flexor tendon and digital nerve injuries do not show functionally significant differences compared to isolated tendon injuries.

Conclusion A retrospective cohort analysis identified key surgical and rehabilitation factors that influence the outcomes of primary zone 2 flexor tendon reconstruction of the three-phalangeal fingers: the configuration and caliber of the intra-articular suture, the size of the surgical incision, and the availability and type of rehabilitation provided. These factors significantly had a significant impact on the clinical and functional outcomes of treatment.

Keywords: flexor tendons, tendon suture, tendon treatment

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INTRODUCTION

Primary reconstruction of the flexor tendons of the fingers following their injury in the area of fibrous-osseous canals remains a pressing orthopedic problem due to the high incidence of poor functional outcomes in the postoperative period [1, 2]. To achieve good function after tendon suture is possible with comprehensive treatment, which includes an appropriate surgical strategy, early rehabilitation support from a specialist (a hand rehabilitation physical therapist), and high patient compliance [3, 4].

One of the challenges in tendon reconstructive surgery remains the high incidence of suture failure in the early postoperative period, often due to the use of double-thread axial configurations [5]. According to current data, to prevent ruptures, the number of intrasegmental threads used in suture should be at least four [6]. Minimal invasiveness and the choice of surgical approach are among the significant surgical factors determining the success of rehabilitation and functional outcome. Extensive approaches, as well as the lack of precision technique for exposure of flexor tendons from the osteofibrous canal, contribute to the formation of extensive adhesions and scars. This complicates the recovery process and increases the risk of tendon suture failure [7–9].

Early active rehabilitation should be performed by a specialized therapist in hand rehabilitation. Without a rehabilitation protocol, poor results occur in 100 % of cases [10]. Currently, various rehabilitation protocols exist for treating patients with flexor tendon injuries, which are selected individually for each clinical case [11–13].

A significant challenge in achieving good functional outcomes in the management of flexor tendon injuries is low patient compliance. Failure to comply with postoperative recommendations and rehabilitation protocols is associated with long-term disability, as well as a high portion of patients with low socioeconomic status in the structure of injuries to this anatomical region [14, 15]. Analysis of factors that affect rehabilitation outcomes reveals a paradoxical relationship: patient adherence to treatment increases proportionally to the severity of the injury. However, even when only one finger is injured, low compliance often undermines the surgeon's efforts, necessitating the search for new approaches to managing this group of patients [16]. In addition to the above factors, patient compliance is also affected by different insurance status, race, and bad habits [17–19].

The functional outcome of reconstruction in injuries of finger flexor tendon zone 2 depends on a large number of factors that arise at each stage of the treatment process. This clinical study was conducted to analyze surgical outcomes, identify key risk factors critical to the treatment of this patient cohort that influence long-term functional outcomes, and highlight the most significant aspects of flexor tendon treatment.

The **purpose** was to determine key surgical and rehabilitation factors that have impact on the outcomes of primary reconstruction of the flexor tendons of the three-phalangeal fingers in the second zone.

MATERIALS AND METHODS

Study design A single-center retrospective cohort study conducted according STROBE recommendations.

Ethical approval The study was approved by the ethics committee of the Vreden National Medical Research Center of Traumatology and Orthopedics (Protocol No. 4, September 20, 2024). Informed consent for the processing of personal data and inclusion in the study was obtained from all patients.

Conditions and terms The study included data from a retrospective analysis of medical case records, clinical examinations, and instrumental studies of 100 patients after primary suture of the deep flexor tendon of one triphalangeal finger. All patients underwent urgent surgical care at the Vreden National Medical Research Center of Traumatology and Orthopedics between 2022 and 2023.

Inclusion criteria: patients with injury to the superficial and deep flexor tendons of one triphalangeal finger in zone 2 according to the Verdan classification who underwent primary reconstruction of the deep flexor tendon.

Exclusion criteria: injury to both neurovascular bundles of the finger; injury more than 24 hours old; patients with congenital malformations of the hand, a history of severe hand injuries (mine-explosive, gunshot, etc.), systemic diseases, including autoimmune diseases.

Methods of data collection and analysis

To evaluate long-term results of surgical treatment, patients were clinically and instrumentally examined in an outpatient setting, and interviewed using standard questionnaires. Finger function was assessed by measuring the range of motion in the proximal and distal interphalangeal joints of the finger using the Boyes-Lister scale and Strickland criteria, as well as the validated Disability of the Arm, Shoulder, and Hand (DASH) and Michigan Hand Outcomes Questionnaire (MHQ). The length of the surgical incision was measured using an orthopedic ruler along the axis of the finger being examined. The length of half a phalanx was equal to 0.5 units of measurement, while the length of one phalanx was equal to 1 unit of measurement. Grip strength was measured using an electronic dynamometer.

Description of medical intervention

All surgical procedures were performed by surgeons experienced in treating patients with digital flexor tendon injuries. The procedure was performed in the operating room, with the patient in the supine position and the injured upper limb supported on a side table. The procedure was performed under conduction anesthesia in the brachial plexus area or local infiltration anesthesia. After placing a tourniquet in the middle third of the arm, the primary wound was extended proximally and distally using a Bruner Z-shaped approach or a mid-lateral approach. The proximal and distal ends of the deep flexor tendon were brought into the wound, and the tendon was sutured using monofilament or polyfilament suture material with a thread of 3/0 or 4/0 with various intrasegmental suture configurations (two-, four-, or six-thread). An adapting suture was then applied. In cases of injury to the proper digital nerve, epineural suturing was performed using 8/0 or 9/0 monofilament sutures under optical magnification. Repair of the latter was performed individually at the surgeon's discretion. Skin suturing was performed using 3/0 or 4/0 monofilament sutures. After applying an aseptic dressing, the upper limb was immobilized in a plaster cast in physiological flexion of 30° at the wristand flexion at the metacarpophalangeal joints at 30–45° along the dorsal surface from the distal phalanges of the second through fifth fingers to the middle third of the forearm.

Statistical processing of the findings

The database was created using the Excel spreadsheet program of the Microsoft Office suite (Microsoft, USA). Statistical processing of the data was performed using SPSS Statistics (IBM, USA).

The distribution type of the quantitative variable values was tested using the Shapiro–Wilk test. The test results revealed that none of the quantitative variables followed the normal distribution law. For this reason, and given the small number of observations in the samples formed for the comparative and exploratory analysis, nonparametric statistical methods were used. The quantitative variables were described using the median (Me), interquartile range (Q1; Q3), and extreme sample values (min–max). These descriptive statistics are presented as Me [Q1; Q3] (min–max). For qualitative variables, absolute frequency values and proportions expressed as a percentage are presented.

Comparative analysis of quantitative variables was performed using the Mann-Whitney test when comparing two independent groups, and the Kruskal-Wallis test when comparing three or more independent groups. In the latter case, when statistically significant differences between groups

were identified, a Dunn post-hoc test with a Bonferroni correction for multiple comparisons was performed on the p-value. Correlation analysis with the calculation of the Spearman correlation coefficient (ρ) was used to assess the presence of a relationship between two quantitative variables.

A comparative analysis of qualitative variables was performed by constructing contingency tables and then calculating the Pearson χ^2 test. If the applicability conditions of the Pearson χ^2 test were violated (the presence of zero values of empirical frequencies in cells, the presence of cells with expected frequencies less than 5), the exact tests were applied: Fisher's (for four-field contingency tables) or Fisher-Freeman-Halton's (for multi-field contingency tables). If statistically significant differences between event frequencies were detected in the case of multi-field contingency tables, post-hoc tests were performed, consisting of pairwise comparisons of proportions using the Z-test. A Bonferroni correction for multiple comparisons was also applied to the obtained p-values.

To assess the influence of significant predictors identified during the preliminary analysis on the Strickland and Boyes tests, ordinal regression was used. The applicability of this model was tested using a parallel lines test. Model validity was confirmed at a p value > 0.05. To estimate the proportion of variance in the dependent variable explained by the model, Nigelkirk's pseudo R2 was calculated. This indicator can take values from 0 to 1, where higher values correspond to better model quality. The results of ordinal regression are presented as coefficient estimates, *p* values, and odds ratios (ORs) with corresponding 95 % confidence intervals (95 % CI).

The study of the joint relationship of thread thickness and axial suture type with the Strickland, Boyes-Lister, DASH and MHQ indices was performed using a two-way nonparametric rank analysis of variance (ART-ANOVA) with post-hoc testing using Student's t-test on equalized ranks with Bonferroni correction.

The critical level of significance for this study was chosen to be $\alpha = 0.05$, that is, at $p < 0.05$ the null hypothesis was rejected.

Patients

The baseline clinical and demographic characteristics of 100 patients included in the study are presented in Table 1.

Table 1

Clinical characteristics of patients

Parameter	Number of patients (*n* = 100)	
	n	%
Gender: males	68	68
Non-dominant hand injury	56	56
Finger V injury	56	56
Mechanism of injury: knife	64	64
A cut wound with smooth edges	68	68
Associated nerve injury	18	18
Location of the wound in the PIP joint area	46	46

Note: PIP — proximal interphalengeal joint

RESULTS

In most cases, interventions were performed under local infiltration anesthesia (82 %) using the Bruner Z-shaped approach (79 %). The most commonly used configuration was a four-thread axial suture (59 %) and a 3/0 suture thread (70 %). Monofilament suture material was used in 65 % of cases. Ligament injuries occurred in 20 patients (20 %). The average incision size was two units, or the length of two phalanges. Immobilization lasted an average of four weeks.

Fifty-six patients (56 %) consulted a hand rehabilitation therapist, while 21 patients (21 %) did not undergo rehabilitation. The average total range of motion of the interphalangeal joints of the injured finger was 110°, which is considered satisfactory according to the Strickland criteria. Poor results were more common according to the Boyes-Lister Scale and the Strickland criteria. However, the average DASH (20) and MHQ (75) questionnaire scores showed good results. Suture rupture occurred in 16 % of cases. The most common contractures were in the proximal interphalangeal joint (30 %). Handgrip strength averaged 26 kg on the injured upper limb side and 27 kg on the uninjured one.

The comparison of patient characteristics such as gender, age, hand dominance, and the number of the injured finger with the results of the Strickland criteria and the Boyes-Lister scale found no statistically significant differences ($p > 0.1$).

The comparison of surgical factors such as nerve injury, traumatic agent, type of surgical approach with the results of the Strickland criteria and the Boyes-Lister scale found no significant statistical differences ($p > 0.1$).

The comparison of the category of surgical approach size with the obtained results of the Strickland criteria found statistically significant differences (Table 2).

Table 2

Comparison of the size of surgical approach by the number of phalanges with the Strickland criterion

Approach size by number of phalanges		Критерий Strickland				Total
		Poor	Fair	Good	Excellent	
1.5	*n*	7	1	8	7	23
	%	18.9	4.3	28.6	58.3	23.0
2.0	*n*	20	15	14	4	53
	%	54.1	65.2	50.0	33.3	53.0
2.5	*n*	10	7	6	1	24
	%	27.0	30.4	21.4	8.3	24.0
Total	*n*	37	23	28	12	100
	%	100.0	100.0	100.0	100.0	100.0

Pearson's χ^2 criterion: 14.060; $p = 0.029$.

Excellent results according to the Strickland criterion were statistically significantly more frequent with approach of 1.5 phalanx ($p = 0.002$) than with 2.0 ($p = 0.028$*) and 2.5 ($p = 0.050$*) phalanges. For the remaining compared pairs of proportions, statistically significant differences were not revealed ($p > 0.05$*).

[1]The comparison of the type of axial suture in combination with the thread thickness with the obtained functional results of the Strickland criterion and the Boyes-Lister scale, there was a statistically significant difference between the configurations of a two-thread 3/0 suture and a four-thread 4/0 suture ($p = 0.0203$ — Strickland; $p = 0.0469$ — Boyes-Lister), as well as a two-thread 3/0 suture and a six-thread 3/0 suture ($p = 0.0094$ — Strickland; $p = 0.0440$ — Boyes-Lister). The functional results with a four-thread 4/0 suture and a six-thread 3/0 suture were statistically significantly better than the use of a two-thread 3/0 suture.

The comparison of the type of rehabilitation protocol with the functional results of the Strickland criterion and the Boyes-Lister scale, statistically significant differences were obtained.

Poor results according to the Strickland criterion were statistically significantly more common if rehabilitation was not performed than with any type of rehabilitation (rehabilitation in a clinic — $p = 0.036$*; hand rehabilitation specialist — $p < 0.001$*; independently on one' own — $p = 0.005$*).

* *p* values are given taking into account the Bonferroni correction for multiple comparisons.

Also, poor results according to the Strickland criterion were statistically significantly more common if patients performed rehabilitation independently than with a hand rehabilitation specialist ($p = 0.005$*).

Good results according to the Strickland criterion were statistically significantly more frequent if rehabilitation was with a hand rehabilitation specialist ($p = 0.010$*) than if done on one's own.

Excellent results were achieved only if rehabilitation was done with a hand rehabilitation specialist (Table 3).

Table 3

Comparison of the type of rehabilitation protocol in relation to the functional outcome according to the Strickland criterion

Rehabilitation type		Strickland criterion				Total
		Poor	Fair	Good	Excellent	
No rehabilitation	*n*	20	1	0	0	21
	%	54.1	4.3	0.0	0.0	21.0
At the clinic	*n*	3	3	0	0	6
	%	8.1	13.0	0.0	0.0	6.0
With a rehabilitation specialist	*n*	6	12	26	12	56
	%	16.2	52.2	92.9	100.0	56.0
On one's own	*n*	8	7	2	0	17
	%	21.6	30.4	7.1	0.0	17.0
Total	*n*	37	23	28	12	100
	%	100.0	100.0	100.0	100.0	100.0

In the absence of rehabilitation, poor results according to the Boyes criterion were statistically significantly more frequent ($p = 0.003$*) than fair ones.

If rehabilitation was done with a hand rehabilitation specialist, good results according to the Boyes criterion were statistically significantly more frequent than poor ($p < 0.001$*) and fair ($p = 0.001$*) results.

Poor results according to the Boyes criterion were statistically significantly more frequent if rehabilitation was not performed ($p < 0.001$*) or was performed independently ($p = 0.005$) than if rehabilitation was done with a rehabilitation specialist.

Excellent results were achieved only if rehabilitation was performed under supervision of a hand rehabilitation specialist (Table 4).

Table 4

Comparison of the type of rehabilitation in relation to the functional outcome according to the Boyes–Lister scale

Rehabilitation type		Strickland criterion				Total
		Poor	Fair	Good	Excellent	
No rehabilitation	*n*	18	3	0	0	21
	%	51.4	13.0	0.0	0.0	21.0
At the consultation clinic	*n*	3	3	0	0	6
	%	8.6	13.0	0.0	0.0	6.0
With rehabilitation therapist	*n*	6	10	22	18	56
	%	17.1	43.5	91.7	100.0	56.0
On one' own	*n*	8	7	2	0	17
	%	22.9	30.4	8.3	0.0	17.0
Total	*n*	35	23	24	18	100
		100.0	100.0	100.0	100.0	100.0

* *p* values are given taking into account the Bonferroni correction for multiple comparisons.

No statistically significant differences were found for comparison of the type of rehabilitation and the development of interphalangeal joint contractures ($p = 0.216$). However, statistically significant differences were found comparing the type of rehabilitation and the rate of tendon suture rupture (Table 5). Tendon suture rupture occurred more frequently in the absence of rehabilitation ($p < 0.001$*) than in rehabilitation with a hand therapist.

Table 5

Comparison of the type of rehabilitation protocol in relation to tendon suture rupture incidence

Type of rehabilitation		Suture rupture		Total
		no	yes	
No rehabilitation	*n*	12	9	21
	%	14.3	56.3	21.0
At the consultation clinic	n	5	1	6
	%	6.0	6.3	6.0
Physical therapist	n	53	3	56
	%	63.1	18.8	56.0
On one's own	n	14	3	17
	%	16.7	18.8	17.0
Total	n	84	16	100
	%	100.0	100.0	100.0

DISCUSSION

This retrospective study conducted a multivariate analysis of outcomes after primary surgical reconstruction of the flexor tendons of the three-phalangeal fingers. Factors that did not affect the clinical and functional results were interpreted. Injury to the proper digital nerves in combination with injuries to the flexor tendons on one finger and their simultaneous restoration did not correlate with a reduced range of motion, thus, it can be accomplished by performing an epineural suture without the use of nerve grafting, which is confirmed by data from foreign sources [20, 21]. Gender and age of patients were not statistically significant factors. This suggests that patients of both sexes, young and elderly, have similar levels of compliance and potential for functional recovery. Hand dominance and the number of the injured finger also had no relationship with the functional results obtained. High-quality data on the effect of hand dominance on postoperative outcome in adult patients are practically not presented in the literature. However, a group of authors reports functionally better results in pediatric patients if injury to the flexor tendons was on the dominant hand [22].

Our study identified the main predictors associated with poor functional outcomes. These include the use of a double-thread suture configuration, regardless of the thread size, and the absence of rehabilitation. If present, these predictors increased the risk of poor results and tendon suture ruptures. The absence of rehabilitation or its implementation in an outpatient setting, although not statistically significantly different from rehabilitation by a specialized specialist, tended to increase the extension deficit in the interphalangeal joints. The obtained results regarding the intrasegmental suture configuration are inconsistent with previously published studies [23, 24]. Regarding the use of a specialized rehabilitation protocol performed by a hand rehabilitation therapist, there are scientific studies confirming the obtained results [10, 25].

Due to its anatomical and technical complexity, as well as the need for early rehabilitation supervised by a specialist, surgical treatment of digital flexor tendons in the second zone should follow the well-known "one-shot surgery" concept: a technically reliable, minimally invasive final surgical

* *p* values are given taking into account the Bonferroni correction for multiple comparisons.

intervention. Key surgical and rehabilitation factors identified in this study are recommended for achieving high functional outcomes.

Study limitations The retrospective design of the study restricts the ability to establish cause-and-effect relationships. Some data on intraoperative details and the rehabilitation protocol were obtained from medical records which carries a risk of incomplete data. The single-center nature of the sample may not allow the generalization of the results to other institutions. The relatively small sample size (n = 100) reduces statistical power for analyzing rare outcomes. These limitations should be considered when interpreting the results.

CONCLUSION

The statistical analysis of this retrospective group of patients has revealed significant functional differences in the category of intrasegmental suture configuration and suture material size, as well as a correlation between functional outcomes and rehabilitation interventions. Patient's gender, age, hand dominance, surgical approach type, and combined tendon and proper digital nerve injury did not significantly differ in the postoperative period.

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

Funding source *The study was conducted without additional funding.*

Ethical approval *The study was approved by the institutional ethics committee of the Vreden National Medical Research Center of Traumatology and Orthopedics (protocol no. 4, dated September 20, 2024).*

Informed consent *Informed voluntary consent to participate in the study and process personal data was obtained from all patients.*

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Microcirculation measured in patients with limb fractures during stimulation of reparative regeneration

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Abstract

Introduction With advances in the study of bone reparative regeneration there are no methods for early detection of impaired consolidation. Methods for stimulating consolidation processes remain an unresolved question. The development of accessible criteria for assessing impaired fracture consolidation and medications for skeletal muscle tissue repair are challenges of orthopedic trauma care.

The **objective** was to measure microcirculation in patients with uncomplicated fractures to the long bones of the lower limb, impaired consolidation processes, and stimulation of reparative regeneration.

Material and methods The study included 100 young patients with long bone fractures: group 1 (n = 40) with uncomplicated fractures; group 2 (n = 40) with delayed consolidation; group 3 (n = 20) with established delayed consolidation treated with a bioregulator (peptides from the cerebral cortex). The control group (n = 40) consisted of healthy individuals matched for gender and age. Diagnosis, treatment and rehabilitation were produced according to clinical guidelines. Microcirculation index (MI), shunt index (SI), neurogenic (NT) and myogenic (MT) vascular tone, the amplitude of the endothelial, neurogenic, myogenic and respiratory oscillation ranges were measured using laser Doppler flowmetry on the first, second, fifth, tenth and 90th days after the injury. Statistical processing of the findings was performed using the IBM SPSS Statistics Version 25.0 software package.

Results Patients with normal consolidation showed a progressive increase in PM and active oscillation amplitudes in both limbs, a decrease in NT and MT after two days. Patients with delayed consolidation demonstrated a consistently low perfusion index and increased NT and MT in the injured limb ($p < 0.05$). Patients treated with the neuropeptide drug showed significantly decreased NT and MT in the injured limb, reaching levels comparable to those in normal consolidation ($p < 0.05$) after 90 days.

Discussion Long-term hypoperfusion, elevated NT and MT in the injured limb, precapillary spasm, and less efficient blood flow redistribution in patients with impaired consolidation were associated with persistent sympathetic activation, which led to persistent vasoconstriction and perfusion restriction, creating unfavorable conditions for angiogenesis and migration of progenitor cells to the area of regenerative bone formation. The mechanism of action of the peptide bioregulator could be explained by activated neuropeptides and neurotrophic factors, optimization of the balance of excitatory and inhibitory amino acids, and GABAergic effects, which ultimately led to the creation of more favorable local conditions for the completion of osteogenesis.

Conclusion Microcirculation in patients with normal bone reparative processes demonstrated early activation of all regulatory mechanisms, decreased HT and MT as early as the fifth day on the injured side, and rapid restoration of perfusion in the healthy limb. Normalized microcirculation was recorded after ten days of surgery. Prolonged hypoperfusion, prolonged precapillary spasm, and less effective blood flow redistribution, high HT and MT were observed in patients with impaired fracture consolidation. Neuropeptide bioregulator had a significant effect on the regulation of microcirculation at the fracture site through reduced HT, MT, and PSH and could be recommended for stimulating reparative regeneration in patients with impaired fracture healing.

Keywords: fractures, microcirculation, impaired consolidation, reparative regeneration, stimulation

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INTRODUCTION

Impaired reparative regeneration in long bone fractures remains a pressing issue, accounting for 30 % of musculoskeletal injuries [1, 2, 3]. The range of therapeutic options for conservative methods to stimulate regeneration is limited due to an adverse event detected in a delayed manner. Early diagnostic modalities include genetic polymorphism prediction methods, photoacoustic imaging, magnetic resonance imaging (MRI), dynamic contrast MRI, and contrast ultrasonography [4, 5, 6]. With their effectiveness, the methods are not widely used in practice due to cost, difficulty in data verification, or lack of necessary equipment [7].

The multifactorial nature of reparation and a variety of causes for impaired consolidation dictate the search for fundamental links in this process, such as changes in regional blood flow at the site of injury, which determine the conditions for tissue oxygenation, progenitor cell migration, and growth factors. With a deficient blood supply, bone reparative processes are impaired. However, established data, such as the There is a phenomenon of "vascularization paradox" in the formation of hypertrophic pseudoarthrosis, and circulatory parameters are to be comprehensively analyzed [8, 9].

Neuropeptide-based drugs stimulate bone repair in fractures; however, the mechanism by which they influence osteogenesis has been poorly explored. Given the drug's effect on stimulating angiogenesis, recording microcirculation parameters will help expand our understanding of the drug's stimulating effect [10]. Examination of dynamic microcirculation parameters in patients with bone fractures to identify early prognostic criteria and new application areas for therapeutic methods to stimulate reparative regeneration is an important task from theoretical and practical aspects.

The **objective** was to measure microcirculation in patients with uncomplicated fractures to the long bones of the lower limb, impaired consolidation processes, and stimulation of reparative regeneration.

MATERIAL AND METHODS

The study was approved by the local ethics committee of the Chelyabinsk State Medical Academy (registration number NIR - RK 034 (03) No. AAAA-A16-116063010015-6) and complied with the ethical principles enshrined in the Helsinki Declaration of the World Medical Association (1964, as amended in 2024) [11]. A comprehensive clinical examination of 100 patients of both genders aged 18 to 45 years with uncomplicated and complicated closed fractures of the tibia was conducted:

— Group 1 (n = 40): patients with an uncomplicated postoperative period;

— Group 2 (n = 40): patients with impaired consolidation processes (delayed consolidation);

— Group 3 (n = 20): patients with delayed fracture consolidation who underwent stimulation of reparative processes after 60 days of injury;

— Control group (n = 40): healthy individuals, matched for gender and age.

The RUST (Radiological Union Scale for Tibia) scale [12, 13, 14] and radiographic criteria were used to assess the signs of consolidation. Complete fracture union according to the RUST was recorded when the total score was 10 or greater. Analysis of radiographic data was associated with characteristic signs including a weakly expressed periosteal bone callus, partially covering the fracture line with poor prognosis for complete union indicated delayed consolidation (Clinical guidelines "Fractures of the femur (except for the proximal femur)", 2024; "Fractures of the tibia shaft", 2024). Patients were comparable in age, gender, and fracture type. All patients underwent open bone reduction upon admission, followed by functional metal osteosynthesis (FMO) with pins or plates (Table 1). Subsequently, traditional conservative therapy was used (according to clinical recommendations).

The study did not include patients with acute and/or chronic concomitant diseases, other pathological conditions/injuries, insufficiently "anatomical" bone alignment during reduction, diabetes mellitus, concomitant arterial and venous diseases, repeated surgeries, and patients receiving antiresorptive

therapy. A course of local therapy with a peptide bioregulator (LP-No.-(000636)-(RG-RU) was administered for patients in Group 3 to improve regenerative processes through neuromotor homeostasis. A solution of neuropeptide (10 mg) was obtained by diluting 1.0–2.0 ml in a 0.5 % novocaine solution. The drug was administered by paraosseous injection into the fracture site under aseptic conditions and ultrasound guidance [10].

Table 1

Distribution of study groups by gender, age, nature of injury and type of osteosynthesis

Description		Controls (n = 40)		Group 1 (n = 40)		Group 2 (n = 40)		Group 3 (n = 20)	
		abs.	%	abs.	%	abs.	%	abs.	%
Gender	Male	25	62.5	24	60	23	57.5	12	60
	Female	15	37.5	16	40	17	42.5	8	40
AO/ASIF tibia fracture	42A1	–	–	12	30	14	35	7	35
	42A2	–	–	11	27.5	13	32.5	7	35
	42A3	–	–	14	35	10	25	4	20
	42B1	–	–	3	7.5	3	7.5	2	10
Type of fixation	Pin	–	–	20	50	18	45	11	55
	Plate	–	–	20	50	22	55	9	45
Age, years Me [Q_1;Q_3]		43 [41;45]		42 [41;45]		42 [41;45]		43 [41;45]	

Microcirculatory parameters were examined using the noninvasive method of laser Doppler flowmetry (LDF) and the LAKK-02 device (NPP Lazma, Russia). LDF-grams were recorded for 7–10 minutes. The sensor was placed on the anterior surface of the proximal part of the first intermetatarsal space of the affected limb. The microcirculation index (MI) was measured. Regulation components of vascular tone was calculated using a computer program supplied by the equipment manufacturer. Wavelet transform of blood flow oscillations yielded shunting (S), neurogenic (NT), and myogenic (MT) vascular tone indices, maximum amplitudes of the endothelial (Ae), neurogenic (An), myogenic (Am), and respiratory (Ar) oscillation ranges. LDF was performed at the same time and at the same room temperature (21 °C). No eating, drinking or smoking was allowed before examination. The studies were conducted on the first day after the injury, and subsequently after two, five, ten and 90 days of surgery.

Statistical processing of the findings was performed using the IBM SPSS Statistics Version 25.0 software package (license no. Z125-3301-14, IBM, USA). The statistical analysis was produced in accordance with the principles of the International Committee of Medical Journal Editors (ICMJE) and guidelines of the Statistical Analysis and Methods in Published Literature (SAMPL). Considering the number in the study groups, the normality of the distribution was assessed using the Shapiro – Wilk W-test. Given the non-normal distribution of variables, interval data were presented as the median, first and third quartiles (Me [Q1; Q3]). The statistical significance of differences in indicators between thegroups was assessed using the Mann – Whitney U-test. The Holm correction was additionally used for multiple comparisons, [15].

RESULTS

The first stage of the work included a dynamic study of microcirculation and vascular tone parameters in patients with an uncomplicated postoperative period (group 1), delayed consolidation (group 2), and the controls (Table 2). The average perfusion values (PV) were 3.89 on the intact limb in patients with uncomplicated fractures on the first day after surgery, which was lower in comparison with controls (4.93, U_{0-1a} = 444, p = 0.017) and group 2 with delayed consolidation (4.06, U_{1a-2a} = 497, p = 0.047). No significant differences were found on the involved side between the groups, but the values were lower in both groups in comparison with the controls.

Starting from the second day, the prevalence of PV in the group with normal consolidation was recorded on both limbs: 4.4 versus 3.96 ($p < 0.001$) on the healthy side, 2.52 to 1.63 ($p = 0.024$) on the involved side after two days; there were no changes after five and ten days ($p < 0.001$). MI on the healthy limb in group 1 increased to the level of the control group, starting from the second day (day two, $U_{0-1a} = 546$ ($p = 0.209$); after five days: $U_{0-1a} = 564$ ($p = 0.291$); after ten days, $U_{0-1a} = 610$ ($p = 0.582$)). With delayed consolidation after two and five days, perfusion was significantly lower than that in controls (($U_{0-2a} = 313$, $p = 0.028$) and ($U_{0-2a} = 342$, $p = 0.076$)), and the difference ceased to be significant after ten days ($U_{0-2a} = 355$, $p = 0.113$) (Table 2).

The Ae on the healthy limb did not differ significantly between the groups throughout the study period. Differences were established on the involved side in patients with normal consolidation after ten days (0.19 vs. 0.13, $p < 0.001$); no differences were registered during the rest of the study period. An, Am, and Ad fluctuations did not show statistically significant differences either between the groups with normal and delayed consolidation, or with the controls ($p > 0.05$) throughout the observation period. The NT on the first day was higher on the healthy limb in patients with normal consolidation (3.07 vs. 2.69, $p < 0.001$) and did not differ from the control values ($p = 0.083$). The NT in the group with delayed union did not differ from the control. The situation changed after ten days: the NT with normal consolidation became lower in both limbs (healthy: 2.65 to 2.89, $p = 0.006$; involved: 2.21 to 3.47, $p = 0.005$). The difference disappeared on the healthy limb after ten days, and the NT remained lower with normal fusion (2.23 versus 3.81, $p < 0.001$) on the involved side. Compared with the control group, the NT had no significant differences on the healthy limb in both groups on all studied dates (Table 2).

Table 2

Parameters of microcirculation of the skin of the foot in patients with uncomplicated fractures, delayed consolidation and healthy individuals, Me[Q1;Q3]

Description	Day	Controls ($n = 40$)	Group 1 Uncomplicated cases ($n = 40$)		Group 2 Delayed consolidation ($n = 40$)		Mann – Whitney test (U)
		HL	HL	IL	HL	IL	
MI (pf. unit)	1	4.93 [2.03;7.75]	3.89 [3.13;4.29]	1.89 [0.73;6.8]	4.06 [3.19;4.41]	1.96 [0.13;4.58]	$U_{0-1a} = 444$, $p = 0.017$ $U_{0-2a} = 336$, $p = 0.063$ $U_{1a-2a} = 497$, $p = 0.047$ $U_{1b-2b} = 680$, $p = 0.0978$
	2	4.93 [2.03;7.75]	4.4 [3.46;4.9]	2.52 [0.7;3.69]	3.96 [2.92;4.37]	1.63 [0.41;4.0]	$U_{0-1a} = 546$, $p = 0.209$ $U_{0-2a} = 313$, $p = 0.028$ $U_{1a-2a} = 174$, $p < 0.001$* $U_{1b-2b} = 472$, $p = 0.024$
	5	4.93 [2.03;7.75]	4.51 [3.72;4.93]	3.76 [1.27;6.73]	4.16 [3.12;4;57]	1.88 [0.31;5.1]	$U_{0-1a} = 564$, $p = 0.291$ $U_{0-2a} = 342$, $p = 0.076$ $U_{1a-2a} = 211$, $p < 0.001$* $U_{1b-2b} = 288$, $p < 0.001$*
	10	4.93 [2.03;7.75]	4.71 [3.74;5.23]	3.8 [0.27;8.34]	4.19 [3.32;4.54]	1.79 [1.0;7.13]	$U_{0-1a} = 610$, $p = 0.582$ $U_{0-2a} = 355$, $p = 0.113$ $U_{1a-2a} = 124$, $p < 0.001$* $U_{1b-2b} = 270$, $p < 0.001$*
Ae (pf. unit.)	1	0.32 [0.11;0.7]	0.29 [0.14;0.36]	0.03 [0.01;0.5]	0.28 [0.19;0.31]	0.03 [0.01;0.35]	$U_{0-1a} = 543$, $p = 0.197$ $U_{0-2a} = 338$, $p = 0.067$ $U_{1a-2a} = 490$, $p = 0.039$ $U_{1b-2b} = 680$, $p = 0.983$
	2	0.32 [0.11;0.7]	0.3 [0.18;0.37]	0.1 [0.02;0.22]	0.29 [0.02;0.35]	0.05 [0.02;0.35]	$U_{0-1a} = 583$, $p = 0.396$ $U_{0-2a} = 400$, $p = 0.348$ $U_{1a-2a} = 594$, $p = 0.343$ $U_{1b-2b} = 493$, $p = 0.042$
	5	0.32 [0.11;0.7]	0.31 [0.19;0.38]	0.12 [0.02;0.98]	0.34 [0.25;0.37]	0.09 [0.03;0.52]	$U_{0-1a} = 611.5$, $p = 0.593$ $U_{0-2a} = 453$, $p = 0.863$ $U1_{1a-2a} = 467$, $p = 0.021$ $U_{1b-2b} = 508$, $p = 0.061$
	10	0.32 [0.11;0.7]	0.33 [0.18;0.41]	0.19 [0.11;0.98]	0.36 [0.30;0.38]	0.13 [0.09;0.47]	$U_{0-1a} = 639$, $p = 0.817$ $U_{0-2a} = 392$, $p = 0.292$ $U_{1a-2a} = 475$, $p = 0.026$ $U_{1b-2b} = 205$, $p < 0.001$*

Table 2 (continued)

Parameters of microcirculation of the skin of the foot in patients with uncomplicated fractures, delayed consolidation and healthy individuals, Me[Q1;Q3]

Description	Day	Controls (n = 40)	Group 1 Uncomplicated cases (n = 40)		Group 2 Delayed consolidation (n = 40)		Mann – Whitney test (U)
		HL	HL	IL	HL	IL	
An (pf. unit.)	1	0.14 [0.05;1.25]	0.29 [0.04;0.4 1]	0.04 [0.01; 0.23]	0.29 [0.24;0.32]	0.04 [0.01;0.46]	U_{0-1a} = 509, p = 0.096 U_{0-2a} = 365, p = 0.149 U_{1a-2a} = 648, p = 0.714 U_{1b-2b} = 676, p = 0.948
	2	0.14 [0.05;1.25]	0.3 [0.09;0.42]	0.08 [0.01;0.27]	0.33 [0.27;0.35]	0.08 [0.02;0.31]	U_{0-1a} = 475, p = 0.041 U_{0-2a} = 278, p = 0.007* U_{1a-2a} = 549, p = 0.152 U_{1b-2b} = 668.5, p = 0.884
	5	0.14 [0.05;1.25]	0.32 [0.14;0.42]	0.15 [0.03;0.47]	0.31 [0.19;0.35]	0.1 [0.01;0.68]	U_{0-1a} = 442, p = 0.016* U_{0-2a} = 338, p = 0.067 U_{1a-2a} = 511, p = 0.066 U_{1b-2b} = 404, p = 0.003*
	10	0.14 [0.05;1.25]	0.35 [0.1;0.47]	0.19 [0.05;1.12]	0.32 [0.23;0.35]	0.27 [0.07;0.51]	U_{0-1a} = 425, p = 0.01* U_{0-2a} = 316, p = 0.031 U_{1a-2a} = 482, p = 0.031 U_{1b-2b} = 538, p = 0.121
Am (pf. unit.)	1	0.13 [0.04;1.13]	0.17 [0.06;0.27]	0.05 [0.01;0.29]	0.15 [0.06;0.18]	0.02 [0.01;0.4]	U_{0-1a} = 502, p = 0.081 U_{0-2a} = 461, p = 0.954 U_{1a-2a} = 421, p = 0.005* U_{1b-2b} = 479, p = 0.029
	2	0.13 [0.04;1.13]	0.19 [0.07;0.26]	0.07 [0.02;0.29]	0.14 [0.3;0.19]	0.06 [0.02;0.36]	U_{0-1a} = 405, p = 0.005* U_{0-2a} = 439, p = 0.707 U_{1a-2a} = 235, p < 0.001* U_{1b-2b} = 628,5, p = 0.565
	5	0.13 [0.04;1.13]	0.2 [0.05;0.28]	0.12 [0.01;0.3]	0.19 [0.08;0.24]	0.1 [0.02;0.47]	U_{0-1a} = 385.5, p = 0,002* U_{0-2a} = 281, p = 0,008* U_{1a-2a} = 569, p = 0,224 U_{1b-2b} = 535,5, p = 0,115
	10	0.13 [0.04;1.13]	0.23 [0.11;0.4]	0.15 [0.09;1.62]	0.21 [0.1; 0.26]	0.14 [0.05;0.31]	U_{0-1a} = 306.5, p < 0.001* U_{0-2a} = 223, p < 0.001* U_{1a-2a} = 546, p = 0.143 U_{1b-2b} = 628, p = 0.561
Ar (pf. unit.)	1	0.1 [0.03;0.68]	0.12 [0.06;0.15]	0.05 [0.01;0.3]	0.1 [–0.01;0.15]	0.06 [0.02;0.3]	U_{0-1a} = 566, p = 0.298 U_{0-2a} = 411, p = 0.436 U_{1a-2a} = 445, p = 0.011* U_{1b-2b} = 581, p = 0.276
	2	0.1 [0.03;0.68]	0.13 [0.1;0.15]	0.05 [0.01;0.32]	0.11 [0;0.16]	0.05 [0.02;0.29]	U_{0-1a} = 467.5, p = 0.044 U_{0-2a} = 464, p = 0.988 U_{1a-2a} = 404, p = 0.004* U_{1b-2b} = 680, p = 0.983
	5	0.1 [0.03;0.68]	0.13 [0.01;0.2]	0.1 [0.02;0.32]	0.13 [0.11;0.15]	0.09 [0.01;0.48]	U_{0-1a} = 500, p = 0.077 U_{0-2a} = 300, p = 0.017 U_{1a-2a} = 632, p = 0.590 U_{1b-2b} = 578, p = 0.263
	10	0.1 [0.03;0.68]	0.15 [0.03;0.22]	0.1 [0.02;0.38]	0.14 [0.12;0.16]	0.09 [0.02;0.47]	U_{0-1a} = 363.5, p = 0.001* U_{0-2a} = 229, p = 0.001* U_{1a-2a} = 621, p = 0.511 U_{1b-2b} = 558, p = 0.181
NT (rel. unit)	1	2.61 [0.26;5.0]	3.07 [2.22;3.52]	2.73 [1.27;8.8]	2.69 [1.71;3.09]	3.68 [1.19;7.9]	U_{0-1a} = 502.5, p = 0.083 U_{0-2a} = 450, p = 0.829 U_{1a-2a} = 203, p < 0.001* U_{1b-2b} = 615, p = 0.471
	2	2.61 [0.26;5.0]	2.75 [1.93;3.18]	3.83 [1.3;7.0]	2.76 [1.76;3.17]	3.32 [1.47;6.32]	U_{0-1a} = 611, p = 0.590 U_{0-2a} = 440, p = 0.718 U_{1a-2a} = 651, p = 0.739 U_{1b-2b} = 609.5, p = 0.435
	5	2.61 [0.26;5.0]	2.65 [2.02;2.99]	2.21 [1.15;7.63]	2.89 [1.74;3.36]	3.47 [1.56;6.0]	U_{0-1a} = 636, p = 0.792 U_{0-2a} = 407, p = 0.403 U_{1a-2a} = 424, p = 0.006* U_{1b-2b} = 418.5, p = 0.005*
	10	2.61 [0.26;5.0]	2.6 [1.9;2.97]	2.23 [0.7;5.8]	2.71 [1.56;3.18]	3.81 [2.05;5.9]	U_{0-1a} = 652, p = 0.930 U_{0-2a} = 453, p = 0.863 U_{1a-2a} = 585, p = 0.297 U_{1b-2b} = 301, p < 0.001*

Table 2 (continued)

Parameters of microcirculation of the skin of the foot in patients with uncomplicated fractures, delayed consolidation and healthy individuals, Me[Q1;Q3]

Description	Day	Controls (n = 40)	Group 1 Uncomplicated cases (n = 40)		Group 2 Delayed consolidation (n = 40)		Mann – Whitney test (U)
		HL	HL	IL	HL	IL	
MT (rel. unit)	1	3.57 [2.23;5.44]	3.23 [2.2;3.78]	5.24 [0.97;8.59]	3.12 [2.4;341]	4.83 [1.98;6.95]	U_{0-1a} = 434.5, p = 0.013* U_{0-2a} = 251, p = 0.002* U_{1a-2a} = 494, p = 0.043 U_{1b-2b} = 662, p = 0.830
	2	3.57 [2.23;5.44]	3.41 [2.68;3.79]	4.91 [2.02;7.8]	3.16 [2.44;3.45]	4.38 [1.91;6.46]	U_{0-1a} = 560, p = 0.271 U_{0-2a} = 264, p = 0.004* U_{1a-2a} = 274, p < 0.001* U_{1b-2b} = 587, p = 0.307
	5	3.57 [2.23;5.44]	3.52 [2.67;3.97]	2.94 [1.14;6.1]	3.24 [2.52;3.53]	5.0 [2.26;6.40]	U_{0-1a} = 639, p = 0.817 U_{0-2a} = 299, p = 0.017* U_{1a-2a} = 267, p < 0.001* U_{1b-2b} = 369, p = 0.001*
	10	3.57 [2.23;5.44]	3.59 [2.99;3.92]	3.47 [1.45;6.0]	3.28 [2.56;3.57]	4.98 [2.37;6.22]	U_{0-1a} = 621, p = 0.668 U_{0-2a} = 309, p = 0.024* U_{1a-2a} = 159, p < 0.001* U_{1b-2b} = 347.5, p < 0.001*
SI (rel. unit.)	1	1.09 [0.04;3.61]	1.4 [0.80;1.73]	0.6 [0.2;3.0]	1.3 [0.58;1.59]	0.86 [0.36;3.0]	U_{0-1a} = 523.5, p = 0.133 U_{0-2a} = 433, p = 0.644 U_{1a-2a} = 450, p = 0.013 U_{1b-2b} = 557.5, p = 0.180
	2	1.09 [0.04;3.61]	1.43 [0.91;1.71]	0.9 [0.3;2.7]	1.37 [0.65;1.66]	0.97 [0.45;2.73]	U_{0-1a} = 504, p = 0.086 U_{0-2a} = 411, p = 0.436 U_{1a-2a} = 515, p = 0.072 U_{1b-2b} = 595, p = 0.349
	5	1.09 [0.04;3.61]	1.48 [0.89;1.78]	1.15 [0.2;3.6]	1.27 [0.55;1.56]	0.98 [0.14;3.20]	U_{0-1a} = 498, p = 0.074 U_{0-2a} = 443, p = 0.751 U_{1a-2a} = 285, p < 0.001* U_{1b-2b} = 572, p = 0.236
	10	1.09 [0.04;3.61]	1.46 [0.97;1.72]	1.0 [0.5;3.7]	1.36 [0.64;1.65]	1.02 [0.21;2.65]	U_{0-1a} = 496.5, p = 0.072 U_{0-2a} = 414, p = 0.462 U_{1a-2a} = 431, p = 0.007* U_{1b-2b} = 628, p = 0.561

Note: HL, healthy limb, IL, injured limb; U_{0-1a}, the difference from the corresponding indicator of the control group with group 1 on the healthy limb is reliable at $p < 0.05$; U_{0-1b}, the difference from the corresponding indicator of the control group with group 2 on the healthy limb is reliable at $p < 0.05$; U_{1a-2a}, the difference of group 1 from the corresponding indicator of group 2 on the healthy limb is reliable at $p < 0.05$; U_{1b-2b}, the difference of group 1 from the corresponding indicator of group 2 on the injured limb is reliable at $p < 0.05$; * the presence of statistical significance after applying the Holm correction

The MT on the intact limb did not reveal any significant differences at any time during the observation period. There were no intergroup differences on the injured limb on the first to second days, but the MT became significantly lower with normal consolidation after five to ten days (2.94 versus 5.0 after five days; 3.47 versus 4.98 after ten days; all values, $p < 0.001$) (Table 2). SI on the healthy limb was higher with normal consolidation on the first, fifth, and tenth days ($p < 0.005$). The differences did not reach statistical significance after two days. No reliable intergroup differences were found on the injured side at any of the studied time points. Compared with the control group, SI demonstrated a higher level on the healthy side in Group 1 at all times (first day, $p = 0.133$; second day, $p = 0.086$; fifth day, $p = 0.074$; tenth day, $p = 0.072$). In the delayed consolidation group, SI remained at the level of the control group (all $p > 0.05$) (Table 2).

Changes in microcirculation and vascular tone parameters were identified in patients with delayed consolidation during neurotrophin stimulation in the second stage (group 3). The data were compared with the data of patients receiving standard therapy (groups 1 and 2) and healthy individuals (control group) after 90 days of surgery (Table 3).

Most microcirculation parameters in the limbs did not have statistically significant differences from those in patients with normal (group 1, $n = 40$) and delayed (group 2, $n = 40$) consolidation after 90 days of surgery and after 30 days of treatment with the peptide bioregulator (group 3,

n = 20). Changes in the amplitude of myogenic oscillations, neurogenic and myogenic tone, in the bypass index were detected. Am was higher on the injured limb of patients in group 1 than that in group 4 (0.16 to 0.12, $p = 0.011$). NT with delayed consolidation in group 2 exceeded the values of group 3 on the injured limb (3.18 versus 2.20, $p < 0.001$) with no differences on the healthy limb. MT on the involved side was also significantly higher in group 2 than in group 3 (4.06 versus 2.90, $p = 0.002$) with no differences recorded on the healthy limb. PS on the involved limb in group 1 significantly exceeded that in group 4 (1.96 [1.62; 2.22] versus 1.22 [0.75; 1.80], $p < 0.001$) and PS did not differ in other comparisons. PM, Ae, An, Ad did not demonstrate significant intergroup differences in any of the comparison options (Table 3).

Comparison with the control group showed that PV on the healthy limb remained significantly lower in all patients, regardless of the nature of consolidation and the fact of treatment, (group 1: $U_{0-1a} = 222$, $p < 0.001$; group 2: $U_{0-2a} = 231$, $p < 0.001$; group 3: $U_{0-3a} = 58$, $p < 0.001$). Ae on the intact side was also lower than the control in all groups (all values: $p < 0.005$). An did not differ from the control in any of the groups ($p < 0.005$). MT on the healthy side was also comparable with the norm, although a tendency towards its increase was noted in group 3 (4.10 vs. 3.57, $p = 0.052$). SI on the intact limb corresponded to the control level in all groups (all: $p > 0.05$). Am, Ad, NT and SI in all groups at this time did not differ from the indicators in the control group ($p > 0.05$) (Table 3).

Table 3

Parameters of microcirculation of the skin of the foot in patients with uncomplicated fractures, delayed consolidation and stimulation of reparative regeneration at 90 days of injury

Description	Group 0 (*n* = 40)	Group 1 (*n* = 40)		Group 2 (*n* = 40)		Group 3 (*n* = 20)		Mann – Whitney test (U)
		HL	IL	HL	IL	HL	IL	
PV (pf. unit.)	4.93 [2.03;7.75]	2.05 [0.85;7.82]	1.75 [0.10;8.01]	1.69 [0.80;6.79]	1.11 [0.36;6.85]	1.65 [0.80;7.30]	1.52 [0.80;6.20]	$U_{0-1a} = 222$, $p < 0.001$* $U_{0-2a} = 231$, $p < 0.001$* $U_{0-3a} = 58$, $p < 0.001$* $U_{1a-2a} = 659$, $p = 0.800$ $U_{1a-3a} = 349$, $p = 0.185$ $U_{2a-3a} = 273$, $p = 0.475$ $U_{1b-2b} = 646$, $p = 0.698$ $U_{1b-3b} = 407$, $p = 0.633$ $U_{2b-3b} = 288$, $p = 0.664$
Ae (pf. unit.)	0.32 [0.11;0.7]	0.10 [0.01.0.78]	0.17 [0.02;1.04]	0.08 [0.01;0.72]	0.09 [0.02.0.50]	0.07 [0.01;0.75]	0.09 [0.04;0.48]	$U_{0-1a} = 320$. $p < 0.001$* $U_{0-2a} = 198$, $p < 0.001$* $U_{0-3a} = 145$, $p = 0.002$* $U_{1a-2a} = 613$, $p = 0.454$ $U_{1a-3a} = 385$, $p = 0.421$ $U_{2a-3a} = 310$. $p = 0.862$ $U_{1b-2b} = 440$. $p = 0.009$ $U_{1b-3b} = 310$. $p = 0.060$ $U_{2b-3b} = 275$, $p = 0.493$
An (pf. unit.)	0.14 [0.05;1.25]	0.10 [0.01;0.98]	0.12 [0.01;1.34]	0.09 [0.02;0.73]	0.09 [0.02;0.61]	0.08 [0.01;0.85]	0.07 [0.02;0.50]	$U_{0-1a} = 506$, $p = 0.090$ $U_{0-2a} = 319$, $p = 0.035$ $U_{0-3a} = 178$, $p = 0.015$ $U_{1a-2a} = 639$, $p = 0.639$ $U_{1a-3a} = 371$, $p = 0.314$ $U_{2a-3a} = 271$, $p = 0.445$ $U_{1b-2b} = 508$, $p = 0.060$ $U_{1b-3b} = 336$, $p = 0.130$ $U_{2b-3b} = 305$, $p = 0.923$
Am (pf. unit.)	0.13 [0.04;1.13]	0.17 [0.02;0.92]	0.16 [0.07;2.51]	0.11 [0.02;0.60]	0.12 [0.04;0.48]	0.11 [0.02;0.80]	0.12 [0.05;0.45]	$U_{0-1a} = 610$. $p = 0.581$ $U_{0-2a} = 376$, $p = 0.199$ $U_{0-3a} = 267$, $p = 0.512$ $U_{1a-2a} = 505$, $p = 0.056$ $U_{1a-3a} = 363$, $p = 0.264$ $U_{2a-3a} = 279$, $p = 0.549$ $U_{1b-2b} = 412$, $p = 0.004$* $U_{1b-3b} = 265$, $p = 0.011$ $U_{2b-3b} = 297$, $p = 0.802$

Table 3 (continued)

Parameters of microcirculation of the skin of the foot in patients with uncomplicated fractures, delayed consolidation and stimulation of reparative regeneration at 90 days of injury

Description	Group 0 (n = 40)	Group 1 (n = 40)		Group 2 (n = 40)		Group 3 (n = 20)		Mann – Whitney test (U)
		HL	IL	HL	IL	HL	IL	
Ad (pf. unit.)	0.1 [0.03;0.68]	0.15 [0.01;078]	0.09 [0.01;0.36]	0.09 [0.01;057]	0.07 [0.01;0.45]	0.07 [0.01;0.65]	0.07 [0.02.0.04]	U_{0-1a} = 565, p = 0.295 U_{0-2a} = 342, p = 0.075 U_{0-3a} = 212, p = 0.081 U_{1a-2a} = 480. p = 0.029 U_{1a-3a} = 322, p = 0.086 U_{2a-3a} = 307, p = 0.954 U_{1b-2b} = 540. p = 0.125 U_{1b-3b} = 353, p = 0.204 U_{2b-3b} = 304, p = 0.900
NT (rel. unit.)	2.61 [0.26;5.0]	2.26 [1.40;5.23]	1.80 [0.61;5.87]	3.0 [1.15;5.60]	3.18 [1.78;5.97]	1.9 [1.30;5.40]	2.20 [1.60;5.20]	U_{0-1a} = 654, p = 0.947 U_{0-2a} = 397, p = 0.327 U_{0-3a} = 253, p = 0.352 U_{1a-2a} = 544, p = 0.138 U_{1a-3a} = 353, p = 0.205 U_{2a-3a} = 184, p = 0.015 U_{1b-2b} = 368, p < 0.001* U_{1b-3b} = 371, p = 0.314 U_{2b-3b} = 112, p < 0.001*
MT (rel. unit.)	3.57 [2.23;5.44]	3.01 [2.06;6.04]	3.20 [1.38;5.69]	3.9 [1.76;5.50]	4.06 [2.25;5.90]	4.10 [1.90;5.80]	2.90 [2.30;5.40]	U_{0-1a} = 586, p = 0.412 U_{0-2a} = 385, p = 0.248 U_{0-3a} = 202, p = 0.052 U_{1a-2a} = 584, p = 0.292 U_{1a-3a} = 373, p = 0.328 U_{2a-3a} = 206, p = 0.045 U_{1b-2b} = 530. p = 0.101 U_{1b-3b} = 411, p = 0.674 U_{2b-3b} = 151, p = 0.002*
SI (rel. unit.)	1.09 [0.04;3.61]	1.21 [0.82;1.48]	1.96 [1.62;2.22]	1.14 [0.54.1.42]	1.07 [0.68;1.59]	1.12 [0.70.1.48]	1.22 [0.75;1.80]	U_{0-1a} = 654, p = 0.943 U_{0-2a} = 448, p = 0.806 U_{0-3a} = 286, p = 0.774 U_{1a-2a} = 590. p = 0.319 U_{1a-3a} = 411, p = 0.669 U_{2a-3a} = 295, p = 0.772 U_{1b-2b} = 000. p < 0.001* U_{1b-3b} = 41, p < 0.001* U_{2b-3b} = 213, p = 0.06

Note: HL, healthy limb, IL, injured limb; U_{0-1a}, the difference from the corresponding indicator of the control group with group 1 on the healthy limb is reliable at $p < 0.05$; U_{0-2a}, the difference from the corresponding indicator of the control group with group 2 on the healthy limb is reliable at $p < 0.05$; U_{0-3a}, the difference from the corresponding indicator of the control group with group 3 on the healthy limb is significant at $p < 0.05$; U_{1a-2a}, the difference between group 1 and the corresponding indicator of group 2 on the healthy limb is significant at $p < 0.05$; U_{1a-3a}, the difference between group 1 and the corresponding indicator of group 3 on the healthy limb is significant at $p < 0.05$; U_{2a-3a}, the difference between group 2 and the corresponding indicator of group 3 on the healthy limb is significant at $p < 0.05$; U_{1b-2b}, the difference between group 1 and the corresponding indicator of group 2 on the injured limb is significant at $p < 0.05$; U_{1b-3b}, group 1 from the corresponding indicator of group 3 on the healthy limb is reliable at $p < 0.05$; U_{2b-3b}, the difference between group 2 and the corresponding indicator of group 3 on the healthy limb is significant at $p < 0.05$; *, presence of statistical significance after applying the Holm correction.

DISCUSSION

The study demonstrates the divergent dynamics of microcirculatory parameters in patients with normal and delayed consolidation of tibial fractures in the postoperative period. The relationship between angiogenesis and osteogenesis is a fundamental principle of bone regeneration, allowing microcirculation parameters to be considered as objective criteria for the progress of the reparative process. The LDF method enables noninvasive, real-time recording of tissue perfusion levels and the state of the mechanisms that actively modulate vascular tone (endothelial, neurogenic, and myogenic), which distinguishes it from routine imaging techniques. In the first postoperative day, patients in both clinical groups showed a significant decrease in perfusion in the healthy

and involved limbs compared to controls. These results are consistent with the concept of a systemic response of the microcirculatory bed to injury, mediated by the activation of the sympathoadrenal system and the release of vasoconstrictor mediators [16, 17].

At this stage, the PV in the intact limb was lower in patients with normal consolidation than in the delayed group, which may reflect a more pronounced redistribution of blood flow from the peripheral bloodstream in favor of the injury zone. A progressive increase in PV was recorded in both limbs in patients with uncomplicated progression, whereas with impaired consolidation, perfusion remained consistently low between the second and the tenth day. Comparison with the control group confirmed this pattern. Therefore, with normal fusion, the perfusion level on the healthy side was restored to normal within two days with normal consolidation level, and a significant decrease relative to healthy individuals persisted with impaired consolidation within five days, which may indicate prolonged hypoperfusion and insufficiency of compensatory hemodynamic mechanisms [16, 17].

Significant differences in vascular tone modulation were detected between the groups. Unlike the amplitude parameters (Ae, An, Am, Ar), which showed no difference between the normal and delayed consolidation groups (except for Ae in the involved limb on day 10), the tone parameters (HT and MT) demonstrated clear dynamics. Higher amplitudes of endothelial, myogenic, and respiratory oscillations were recorded on the healthy limb with normal consolidationon on days 1–2, reflecting a sufficient response from the active mechanisms regulating microhemodynamics — endothelium-dependent vasodilation. Patients with normal consolidation had NT elevated on the healthy limb on day 1 compared to the delayed consolidation group, which can be considered a compensatory response aimed at mobilizing blood flow from tissue pools. However, these patients showed the decrease in both limbs after five days, and NT remained high in the group with delayed consolidation. Persistent sympathetic activation, manifested by increased neurogenic tone, led to persistent vasoconstriction and limited perfusion, which created poor conditions for angiogenesis and the migration of progenitor cells to the area of regenerative tissue formation. Myogenic tone in the healthy limb showed no differences between groups. In contrast, MT in the involved limb was significantly lower with normal consolidation after five to ten days ($p < 0.001$) and remained high with delayed consolidation. A persistent increase in myogenic tone in patients with impaired consolidation suggested spasm of the precapillary sphincters and limited nutrient blood flow. This phenomenon, previously described as a component of the "vascularization paradox" in the formation of hypertrophic pseudoarthroses, is characterized by excessive vascularization of the fracture site and a simultaneous deficiency of the nutritional fraction of microcirculation [8, 18, 19], which was also recorded in this study.

The shunting index, which characterizes the ratio of the nutritive and shunting components of microcirculation, was significantly higher in the healthy limb with normal consolidation, indicating a more efficient redistribution of blood flow in favor of metabolically active tissues. This did not occur with delayed consolidation. The PV in the normal consolidation group demonstrated a tendency to exceed the values of the control group throughout the early observation period, and remained at the level of healthy individuals with impaired fusion, suggesting the absence of compensatory hemodynamic shifts required during this period. The combination of changes we identified (low PV, suppression of the amplitudes of active oscillations, high precapillary tone, and the absence of an adequate increase in shunting) represented a complex of manifestations of microcirculatory dysfunction, which was associated with a poor course of reparative osteogenesis and could be used as an early prognostic criterion after five to tens days of surgery [16].

A comparison with the control group revealed that all patients, regardless of consolidation type, retained reduced basal blood flow and suppressed amplitudes of endothelial and neurogenic oscillations after 90 days. This indicates a long-term change in microhemodynamics after a fracture, extending beyond the acute phase and not fully normalizing even with a favorable clinical course. Moreover, the amplitude of neurogenic oscillations in the healthy limb showed no differences with the control, indicating restoration of neurogenic regulation in the long-term period. With local therapy, neurogenic and myogenic tone values in the group with initially delayed consolidation significantly decreased only in the involved limb, reaching a level comparable to those of normal consolidation. No significant effect of the drug was observed in the healthy limb, suggesting a local effect without a significant systemic effect.

The mechanism of action of the peptide bioregulator was associated with the activation of neuropeptides and neurotrophic factors, optimization of the balance of excitatory and inhibitory amino acids, and GABAergic effects. It can be assumed that the normalization of neurogenic tone could be caused by a decrease in pathological sympathetic hyperactivation at the level of suprasegmental and peripheral mechanisms of vascular tone regulation [20]. The shunting index in the involved limb in patients receiving the neuropeptide drug was lower than with normal consolidation, which could indicate a decrease in arteriovenous shunting in favor of nutritive blood flow and creation of more favorable local conditions for the completion of osteogenesis. The findings are consistent with the concept of neuroosteogenic interactions, with neurotransmitters and neurotrophic factors playing a significant role in the regulation of both angiogenesis and osteogenesis [10].

CONCLUSION

Microcirculation parameters in patients with normal bone regeneration demonstrated early activation of perfusion regulation processes, a decrease in neurogenic and myogenic tone on the involved side, and rapid restoration of perfusion in the healthy limb after five days. Normalization of microcirculation parameters in the healthy limb was recorded after ten days of surgery. Patients with impaired fracture consolidation experienced prolonged hypoperfusion, increased neurogenic and myogenic tone in the involved limb, precapillary spasm, and less efficient blood flow redistribution. The neuropeptide bioregulator had a significant effect on regulation of microcirculation at the fracture site by reducing neurogenic and myogenic tone and the shunting index. It can be used to stimulate reparative regeneration in patients with fracture healing disorders. Therefore, laser Doppler flowmetry can provide quantitative, objective, and reproducible microcirculation parameters that would correlate with the nature of the healing process and can be used for early prediction of fracture healing disorders.

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Effect of a preparation of branched-chain amino acids on the regeneration of the anterior tibial muscle after compression injury

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Abstract

Introduction Histological data on the effect of intramuscular administration of branched-chain amino acids (BCAA) on muscle recovery are lacking.

The **purpose** of the work was a histomorphometric assessment of the effect of intramuscular administration of BCAA in a dosage for injections on the regeneration of the anterior tibial muscle (ATM) after its closed partial crushing in rats.

Materials and methods Compression of the ATM was performed for one minute in 48 male Wistar rats. After 24 hours, animals of series 1 received a single injection of saline into the ATM, while animals of series 2 received BCAA. Euthanasia was performed after 7, 14, 28, and 42 days. In paraffin section images, the volumetric densities of muscle fibers (MF) (V_{Vm}), microvessels (V_{Vmv}), and endomysium (V_{Ve}) were determined; MF diameters were measured, the numerical densities of MF (Na_m), microvessels (Na_{mv}), and intramuscular nuclei (Na_n) were determined, and the vascularization (kv as Na_{mv}/Na_m) and nucleation (kn as Na_n/ Na_m) coefficients were calculated. Ten intact rats were a control group.

Results After seven days, VVm in both series decreased by 36–37 %; in the rest of the periods, the indicator was significantly higher in series 2, but remained below normal in both groups. Within 28 days, the MF diameter was higher in series 2. After seven, 14 and 28 days, the indicator exceeded the values of series 1 by 17 % ($p = 0.026$), 11 % ($p = 0.012$) and 5 % ($p = 0.048$); after 28 days in series 1 and 2 it was 79 % and 84 % of the norm. The kn indicator in series 2 was lower than normal only after seven days of experiment, and in series 1 after seven, 14 and 42 days by 24 % ($p = 0.002$), 24 % ($p = 0.004$) and 10 % ($p = 0.034$), that indicates less active myogenesis. The kv indicator after 14 and 28 days was higher in series 2 by 10 % ($p = 0.045$) and 32 % ($p = 0.014$). On the 42nd day in series 2, the MF diameter decreased against the increase in their Nam and was 47 % lower than the norm ($p = 0.0006$) and 30 % lower than in series 1 ($p = 0.0023$).

Discussion The findings obtained suggest that a BCAA injection has a positive effect on the MF regeneration and microvessels, and was more active than in series 1.

Conclusion A single BCAA injection has a myogenic stimulating effect. Further studies on side effects and long-term outcomes are needed.

Keywords: rat, crush injury, lower leg, tibialis anterior, histomorphometry, branched-chain amino acids

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INTRODUCTION

Treatment of musculoskeletal injuries remains a complex medical problem [1–3]. Skeletal muscle injuries account for approximately 30 % [4], and modern treatment methods in most cases are aimed at relieving pain and inflammation using nonsteroidal anti-inflammatory drugs, immobilization, and external physical stimulation [5, 6]. Severe injuries result in rhabdomyolysis (destruction of skeletal muscles), characterized by damage to muscle cells with the release of myoglobin and sarcoplasmic proteins into the extracellular fluid [7, 8]. The most common causes of rhabdomyolysis include compression injuries [9], in which ischemic necrosis is observed in skeletal muscle tissue, followed by the development of granulation tissue and the formation of muscle-connective tissue regenerate [10]. Despite the ability of skeletal muscles to regenerate thanks to the stem cell population [11, 12], the available reserve of myosatellite cells in such severe injuries usually does not ensure complete histo- and organotypic regeneration [13, 14], which leads to the loss of contractile tissue, its replacement with adipose and fibrous scar tissue, causing a long-term deficit in muscle structure and strength [5]. Thus, proper regeneration of skeletal muscles plays a key role in the restoration of their function after injury [15].

The available treatment methods remain insufficiently effective [16], which determines the demand for fundamental research on the development of new methods for inducing reparative rhabdomyogenesis and reducing fibrosis in clinical practice [5, 13, 14]. Numerous recent studies have focused on the investigation of the molecular mechanisms underlying muscle regeneration [17], on the search for activators of myogenesis of muscle progenitor cells and angiogenesis of endothelial cells [18, 19]. It is known that essential branched chain amino acids (BCAA), leucine, isoleucine and valine, posess such properties. They are potent regulators of protein synthesis in healthy skeletal muscles and in muscle atrophy; and leucine is used as a "pharmaceutical nutrient" to prevent atrophy and restore muscle in the elderly [20]. As dietary supplements, BCAAs have found wide application in repairing muscle damage and alleviating exercise-induced delayed-onset muscle soreness [21]. Intraperitoneal administration of leucine to mice has shown to reduce muscle atrophy and promote muscle mass maintenance during sepsis [22]. Orthopedic surgery and associated events (immobilization or prolonged muscle inactivity) result in significant muscle loss and long-term functional decline [23, 24]. Oral BCAA supplementation in such patients has improved muscle quality and mass compared to placebo [25, 26]. There is some positive experience with perioperative intravenous amino acid administration to patients undergoing elective total hip arthroplasty to compensate for surgically induced skeletal muscle protein loss [27, 28]. Data on preclinical studies of the effectiveness of intramuscular administration of BCAA in the area of damage are rare [29], and histological data on its effect on muscle regeneration are absent in the relevant literature, which determined the purpose of this work.

The **purpose** of the work was a histomorphometric assessment of the effect of intramuscular administration of BCAA in a dosage for injections on the regeneration of the anterior tibial muscle (ATM) after its closed partial crushing in rats.

MATERIALS AND METHODS

Study design

The study is interventional (experimental), single-center, prospective, selective, controlled, randomized.

Description of the experiment

Closed partial crushing of the anterior tibial muscle (ATM) using surgical forceps was performed on 48 Wistar rats (male, eight months old, weighing 462 (454; 477) g). The animals were divided into two groups: animals in series 1 (n = 24) received a single injection of saline into the ATM, while animals in series 2 (n = 24) were injected a preparation of branched chain amino acids.

To standardize the experimental model, the forceps were positioned perpendicular to the longitudinal axis of the tibia so that their jaws, when closed, exerted pressure on the tissue in the middle ATM belly. The forceps rings were directed cranially, and the clamp-lock was snapped into place in the same position for one minute in all cases. The experimental model is fully reproducible [30].

The procedure was performed in the operating room under general anesthesia using Rometar 2 % (Bioveta, Czech Republic) and Zoletil 100 (Virbac Sante Animale, France). After 24 hours, the animals in series 1 were injected with 0.02 ml of saline into the injured muscle area, while animals in series 2 were injected with 0.02 ml of solution of amino acids in saline (L-valine: L-isoleucine: L-leucine in equal weight ratios, 0.04 g of each amino acid in 10 ml of saline). In both series, injections were single.

The rats were then kept in cages, two in each cage, and were withdrawn from the experiment 7, 14, 28 and 42 days after the injury (n = 6 in each series at all time-points of the experiment).

Methods: ATM fragments, excised from the area of compression injury, were fixed in 10 % neutral formalin and embedded in paraffin. Transverse paraffin sections (5 μm thick) were prepared on a Thermo Scientific HM 450 microtome (USA) and stained with Masson's three-color method, hematoxylin, and eosin. After aldehyde-osmium fixation, a portion of the material was embedded in Araldite. Semithin sections (1 μm) were prepared on a Nova LKB ultramicrotome (Sweden) and stained with methylene blue, azure II, and basic fuchsin.

Full-color digital images were obtained using an AxioScope.A1 microscope and an AxioCam digital camera (Carl Zeiss MicroImaging GmbH, Germany). Using the electronic version of the original equidistant point test grid [31] in PhotoFiltre 7.0 software, stereological parameters were calculated on the 14th, 28th, and 42nd days after injury: volumetric densities of muscle fibers (V_{Vm}), microvessels(V_{Vmv}) and endomesium (V_{Ve}). The VideoTesT Master-Morphology 4.0 software (Russia) was used to measure the average diameter of muscle fibers (up to 400 for each animal), determined the numerical density of muscle fibers (Na_m), microvessels (V_{Vmv}), and intramuscular nuclei (Na_m) per 1 mm^2 of area, and calculated the vascularization coefficients (kv as Na_{mv} / Na_m) and nucleation coefficients (kn as Na_n / Na_m). The proportion (%) of reactive-destructive altered myelinated nerve fibers in the total sample volume of intramuscular nerve trunks was determined. Ten intact male rats, 8–9 months old, were a control group.

During the experiment, the rats' motor activity was assessed in the open field test. At one and the same time (11:00 AM), the animals were placed in a circular arena 120 cm in diameter, the floor of which was marked with 12-cm squares. After the animals adapted (one minute after placement), video recording was performed for one minute, recording the total number of square crossings.

Ethical statement

The study was approved by the institutional ethics committee (protocol dated November 29, 2024 No. 1(76)), conducted in compliance 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 analysis

The sample size was calculated based on the minimum number necessary to obtain reliable results. Statistical data processing was performed using the AtteStat version 9.3.1 software program (developed by I.P. Gaidyshev, Rospatent registration certificate No. 2002611109, Russia). The Kolmogorov test was used to check the normality of the sample distribution. The Mann – Whitney test was used for pairwise comparisons of animal groups. Differences were considered significant at $p < 0.05$.

RESULTS

The motor activity indices according to the open field test in the rats of series 1 by the end of the observation period (day 42) were significantly lower than the initial values and amounted to 13.0 (12.0–14.0) square intersections versus the initial 19.5 (16.8–24.3), $p = 0.007$. In series 2, on the 28th day after the injury, statistically significant differences with the initial indices were absent: 15.5 (12.3–18.0) square intersections versus the initial 18.5 (15.8–26.0), $p > 0.05$.

Seven days after the injury, a similar morphological picture was revealed in the ATM of both series: destructively altered muscle fibers (MF), regenerating MF and areas of granulation tissue were found in the surface layer and the area of adjacent muscle to the tibia. In cross sections, disorganization of part of the fascicles, swelling of the endomysium, its hypervascularization, and increased cellularity with a predominance of fibroblasts, fibrocytes and macrophages are visible. MFs had a smaller diameter and rounded contours (Fig. 1 a, b). Intramuscular nuclei were located both on the periphery, solely, sometimes in chains or conglomerates, and in the central part of the fibers; some of the regenerating fibers were at the myotube stage (Fig. 1 c). After seven days of the experiment, myelinated nerve fibers of intramuscular nerve trunks changed destructively in both series (Fig. 1 e). In longitudinal sections at this stage of the experiment, MFs without transverse striations were found, there were areas with wavy, crimped MFs of uneven thickness, some of them with impaired integrity and areas of necrobiosis, thin regenerating MFs with chains or agglomerated nuclei, fibers in the myotube stage (Fig. 1 d) and rare MFs expanded at the ends with clusters intramuscular nuclei ("muscle buds") (Fig. 1 f).

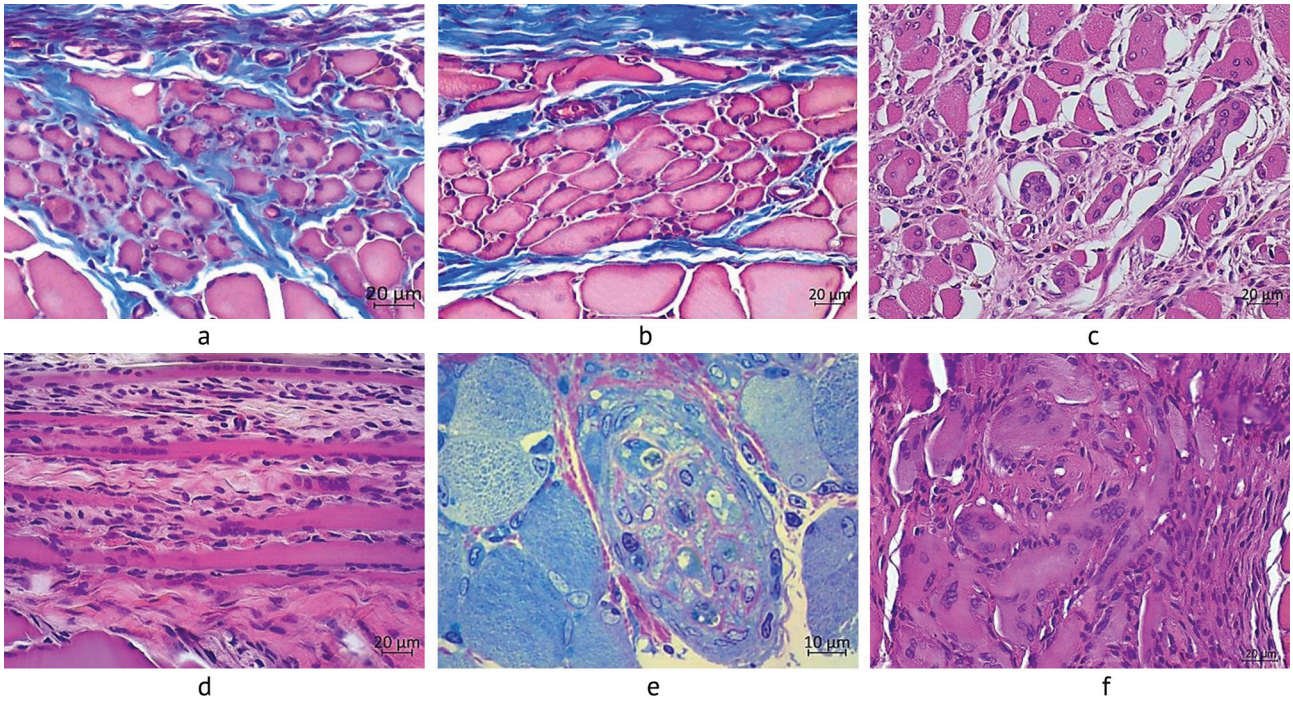

Fig. 1 Anterior tibial muscles of rats after seven days (a — series 1; b–e — series 2) and 14 days (f — series 2) after compression injury. Transverse paraffin sections, stained with hematoxylin and eosin (c, d, f) and Masson's three-color method (a, b), magnification 400×. Transverse semithin section (e), stained with methylene blue, azure II, and basic fuchsin, magnification 1000×

After 14 and 21 days of the experiment, regenerative processes predominated in the superficial and deep zones of both series. The MFs were predominantly rounded in shape with peripheral or central nuclei (Fig. 2 a, b); myotubes continued to be present, and in longitudinal sections, corrugated fibers were observed, club-shaped at the ends of the MFs with clusters of nuclei ("muscle buds") (Fig. 1 e). The interstitial spaces remained dilated with an increased content of fibroblasts and fibrocytes.

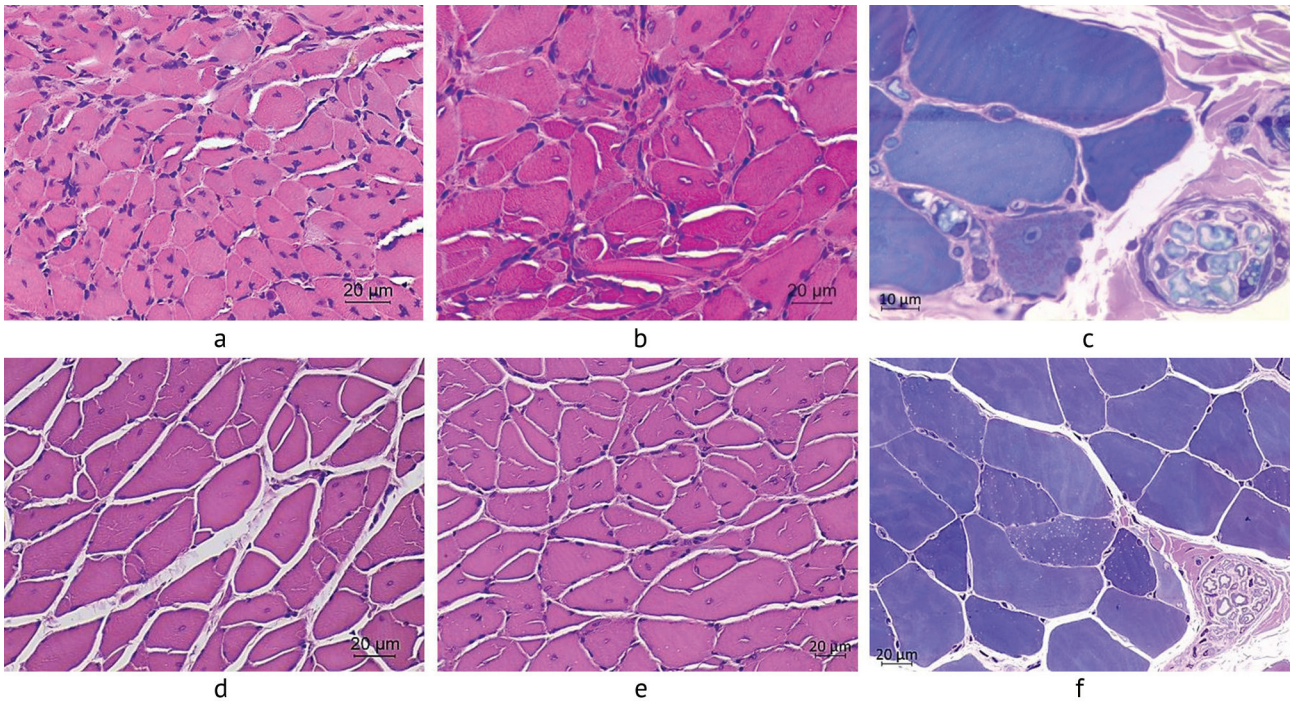

Fig. 2 Anterior tibial muscles of rats after 21 days (a — series 1; b, c — series 2) and on the 42nd day (d — series 1; e, f — series 2) after compression injury. Transverse paraffin sections, stained with hematoxylin and eosin (a, b, d, e), magnification 400×. Transverse semi-thin sections (c, f), stained with methylene blue, azure II and basic fuchsin, magnification 1000× (c), 400× (f)

On the 42nd day after injury, the MFs were polymorphic in the superficial and deep zones; there were small regenerating fibers with rounded contours, and some of the MFs acquired a polygonal shape. The nuclei occupied both peripheral and central locations, interstitial spaces remained expanded (Fig. 2 d, e) in both series.

In the intramuscular nerve trunks, after 14 days, destructively altered nerve fibers predominated, and after 21 days and at the end of the experiment, nerve fibers of normal structure predominated (Fig. 2 c, f).

In the layer of the anterior tibial muscle between the superficial and deep zones, the fascicular structure was preserved in both series at all stages of the experiment, but the endomysial layers were thickened. Some of the MFs had a normal structure and a polygonal shape, while others had rounded or deflated contours shifted to the center of the nucleus, uneven staining, and vacuolization. Dystrophic changes became less pronounced toward the end of the experiment.

Histomorphometric study of the size and numerical characteristics of the MFs showed that after seven days in series 1 and 2 their median diameter was reduced (Fig. 3 a) by 50 % ($p = 0.0001$) and 39 % ($p = 0.003$), and their numerical densities exceeded the norm by 2.8 ($p = 0.00002$) and 1.7 ($p = 0.0005$) times, respectively (Fig. 3 b). After 14 days of the experiment, the MF diameter in series 1 and 2 increased relative to the previous period and amounted to 59 % ($p = 0.001$) and 67 % ($p = 0.0013$) of the norm, respectively (Fig. 3 a). The numerical density of MFs in series 2 increased, and in both series it exceeded the norm ($p = 0.0002$) by 2.6 times (Fig. 3 b).

A stereological study showed that in series 1 and 2, V_{Vm} was reduced ($p < 0.001$) relative to the parameters of the intact muscle by 37.6 % and 36.5 %; V_{Ve} was increased by 34.7 % and 34.2 %; V_{Vmv} was increased by 2.5 and 2.2 times, respectively (Table 1). Comparison of series 1 and 2 did not reveal significant differences in these parameters.

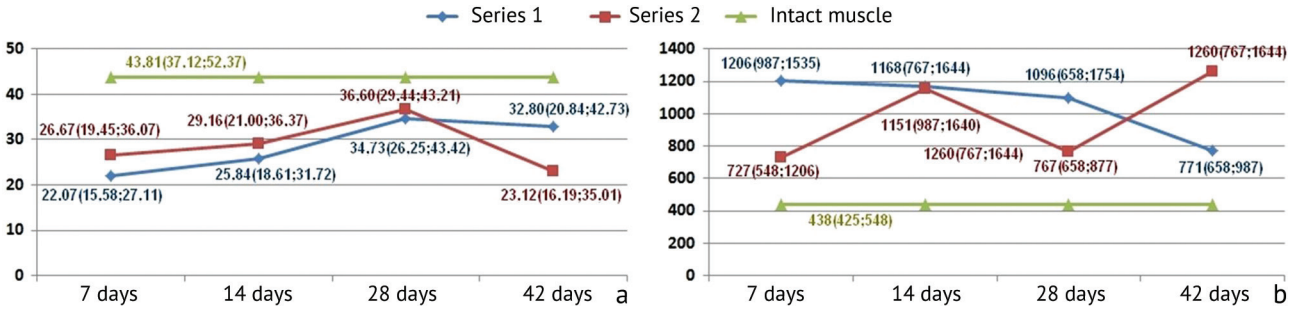

Fig. 3 Diagram of changes in the diameter (μm) of muscle fibers (a) and the numerical density (in 1 mm^2 of section area) of muscle fibers (b) of the anterior tibial muscles of series 1 and 2 at the stages of the experiment (Me (Q1; Q3))

After 28 days, the diameter of the MFs in series 1 and 2 increased and was 79 % (p = 0.007) and 84 % (p = 0.004) of the norm (Fig. 3 a), and the numerical density of MFs decreased relative to the previous period, but exceeded the norm by 2.5 (p < 0.001) and 1.8 (p = 0.006) times, respectively (Fig. 3 b).

Stereological analysis showed that V_{Vm} increased in series 1 and 2 by 6.8 % and 11.3 %, but remained low (p < 0.001), and V_{Ve} and V_{Vm} remained elevated (p < 0.001) relative to intact values (Table 1). A comparison of the experimental series showed that in series 2 V_{Vm} was 5.6 % higher, and V_{Ve} was 5.5 % lower (p < 0.001) than the values of series 1 (Table 1), but there were no significant differences in V_{Vmv} (Table 1).

At the end of the experiment (42nd day), the diameter of the MFs in series 1 was not restored and was 75 % (p = 0.0005) of the norm (Fig. 3 a), and the numerical density of Mfs was increased (p = 0.006) by 1.8 times (Fig. 3 b). In series 2, the numerical density of MFs increased, and the diameter decreased relative to the previous period, amounting to 53 % (p = 0.0006) of the norm (Fig. 3 a, b). The ratio of the proportions of tissue components in both experimental series did not restore to normal values: V_{Vm} remained reduced (p < 0.001), but in series 2, as after 28 days, the value of V_{Vm} was higher than in series 1 by 5.7 % (p < 0.001), and V_{Ve} was lower (p < 0.001) by 5.6 % (Table 1). There were no significant differences in the V_{Vmv} parameter between series 1 and 2.

Table 1

Volumetric densities of tissue components (%) of the intact anterior tibial muscle in experimental series ones at the stages of the experiment (M ± σ)

Term	Series	Volumetric density		
		Muscle fibers	Microvessels	Endomysium
14 days	Series 1	54.9 ± 3.2; $p^n = 4{\cdot}10^{-8}$*; $p^{1-2} = 0.184$	5.0 ± 1.4; $p^n = 9{\cdot}10^{-7}$*; $p^{1-2} = 0.069$	40.2 ± 3.4; $p^n = 4{\cdot}10^{-8}$*; $p^{1-2} = 0.273$
	Series 2	56.0 ± 13.1; $p^n = 4{\cdot}10^{-8}$*	4.4 ± 0.8; $p^n = 1{\cdot}10^{-7}$*	39.7 ± 12.9; $p^n = 4{\cdot}10^{-8}$*
28 days	Series 1	61.7 ± 6.4; $p^n = 4{\cdot}10^{-8}$*; $p^{1-2} = 0.001$*	4.8 ± 1.3; $p^n = 4{\cdot}10^{-7}$*; $p^{1-2} = 0.882$	33.5 ± 6.7; $p^n = 4{\cdot}10^{-8}$*; $p^{1-2} = 0.002$*
	Series 2	67.3 ± 5.3; $p^n = 4{\cdot}10^{-8}$*	4.8 ± 0.9; $p^n = 9{\cdot}10^{-8}$*	28.0 ± 5.4; $p^n = 4{\cdot}10^{-8}$*
42 days	Series 1	60.4 ± 5.0; $p^n = 4{\cdot}10^{-8}$*; $p^{1-2} = 0.002$*	4.4 ± 0.7; $p^n = 8{\cdot}10^{-8}$*; $p^{1-2} = 0.694$	35.3 ± 4.8; $p^n = 4{\cdot}10^{-8}$*; $p^{1-2} = 0.001$*
	Series 2	66.1 ± 4.6; $p^n = 4{\cdot}10^{-8}$*	4.3 ± 0.7; $p^n = 4{\cdot}10^{-8}$*	29.7 ± 4.6; $p^n = 4{\cdot}10^{-8}$*
Intact muscle		92.5 ± 1.6	2.0 ± 0.7	5.5 ± 1.4

* — differences between the experimental series and the norm (p^n), series 1 and 2 (p^{1-2}) were considered statistically significant according to the Mann – Whitney test at p < 0.05

The analysis of the distribution of MFs by diameters showed that in both series at all stages of the experiment the histograms retained a unimodal character, but their bases shifted to the left relative to the norm (Fig. 4). After seven days in series 1 (Fig. 4 a), the proportion of small regenerating and atrophied muscle fibers D < 30 μm was 84 % (normally — single, 1 %), by the 42nd day it decreased to 44 %, and large fibers D > 50 at all stages (Fig. 4) account for 1–2 % (normally — 62 %). In Series 2,

after seven days (Fig. 4 a), the proportion of small fibers D < 30 μm is 60 %, decreases after 28 days to 29 %, but increases again by the 42nd day of the experiment to 67 %, and large muscle fibers D > 50 at all stages account for 3-5 % (Fig. 4). At the end of the experiment in series 2, the mode shifts to the left (Fig. 4 d) into the range of smaller values of 11–20 μm (series 1, 31–40 μm).

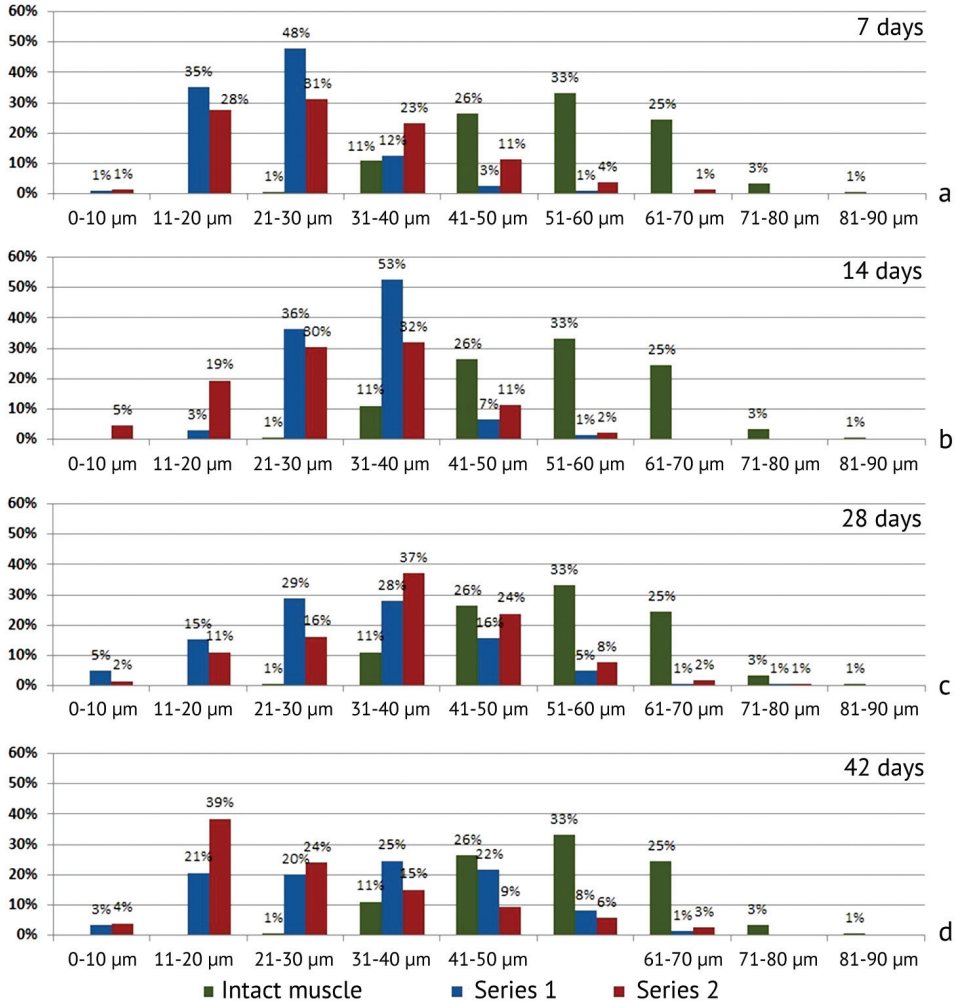

Fig. 4 Histograms of the distribution of muscle fibers of the anterior tibial muscle by diameter in rats of the intact group, series 1 and series 2 after seven (a), 14 (b), 28 (c) and 42 (d) days of the experiment. The X-axis is the fiber diameters (μm), the Y-axis is the percentage of fibers in the sample

The Na_{mv} and Na_n parameters of 1 mm^2 exceed the norm in both series at all periods of the experiment (Table 2), but this *kv* in Series 1 remains reduced after seven, 14, and 28 days by 1.6, 1.6 and 1.3 times, respectively, and exceeds the norm by 1.3 times only on the 42nd day (Table 2). In series 2, after 7 and 14 days *kv* was reduced by 1.6 and 1.4 times, after 28 it exceeded the norm by 1.1 times, but on day 42 it was reduced by 1.9 times (Table 2). It should be noted that after seven days there were no significant differences in this parameter between the series; after 14 and 28 days, the vascularization coefficient was significantly increased in series 2, but by the end of the experiment its value becomes 2.3 times lower than in series 1 (Table 2).

The nucleation coefficient in Series 1 was reduced by 1.3 times within 14 days, increased by 28 days and exceeded the norm by 1.2 times, and decreased by 1.1 times on the 42nd day (Table 2). In Series 2, this indicator was reduced by 1.2 times only after seven days of the experiment, after 14 days it exceeded the norm by 1.1 times, and at the remaining time points it had normal values (Table 2). The nucleation coefficient in Series 2 exceeded the values of Series 1 after 14 days by 1.4 times, and became lower by 1.3 times on the 28th day; at the end of the experiment, there were no reliable differences between the series (Table 2).

Table 2

Quantitative indices of vascularization and nucleation of the intact anterior tibial muscle and the experimental one at the stages of the experiment: Me (Q1; Q3)

Term	Series	Na_{mv}	Na_n	*kv*	*kn*
7 days	Series 1	1315 (981; 1526) p^n = 0.0001* *p* = 0.02*	1370 (877; 1755) p^n = 0.0015* *p* = 0.002*	1.11 (0.89; 1.19) p^n = 0.0031* *p* = 0.09	1.18 (0.87; 1.38) p^n = 0.002* *p* = 0.049
7 days	Series 2	1041 (658; 1315) p^n = 0.002*	877 (658; 1863) p^n = 0.004*	1.12 (0.91; 1.73) p^n = 0.003*	1.29 (1.00; 1.62) p^n = 0.0035*
14 days	Series 1	1261 (987; 1535) p^n = 0.0002* *p* = 0.04*	1370 (1206; 1754) p^n = 0.00002* *p* = 0.032*	1.08 (0.89; 1.29) p^n = 0.002* *p* = 0.045*	1.18 (1.00; 1.33) p^n = 0.004* *p* = 0.033*
14 days	Series 2	1480 (1315; 1644) p^n = 0 .00002*	1863 (1644; 2083) p^n = 0.00033*	1.20 (0.83; 1.70) p^n = 0.0026*	1.63 (1.31; 1.88) p^n = 0.052
28 days	Series 1	1425 (987; 2192) p^n = 0.0013* *p* = 0.056	1809 (1315; 2631) p^n = 0.00005* *p* = 0.029*	1.31 (1.00; 1.60) p^n = 0.020* *p* = 0.014*	1.88 (1.36; 2.20) p^n = 0.036* *p* = 0.03*
28 days	Series 2	1535 (1096; 1644) p^n = 0.0002*	1096 (877; 1315) p^n = 0.003*	1.93 (1.25; 2.14) p^n = 0.03*	1.50 (1.29; 1.55) p^n = 0.131
42 days	Series 1	1754 (1206; 1836) p^n = 0.008* *p* = 0.028*	1096 (767; 1206) p^n = 0.010* *p* = 0.003*	2.20 (1.43; 2.60) p^n = 0.01* *p* = 0.006*	1.41 (1.00; 1.70) p^n = 0.034* *p* = 0.044*
42 days	Series 2	987 (767; 1535) p^n = 0.04*	1762 (1425; 2521) p^n = 0.005*	0.94 (0.64; 1.31) p^n = 0.008*	1.53 (0.94; 2.60) p^n = 0.371
Intact group		767 (658; 1096)	655 (532; 877)	1.75 (1.33; 2.33)	1.56 (1.20; 2.00)

Note: Na_{mv} is the numerical density of muscle fibers; Na_{mv} is the numerical density of microvessels; Nan is the numerical density of intramuscular nuclei (Nan) in 1 mm^2 of cross-sectional area; *kv* is the vascularization coefficient (Na_{mv} / Na_m), *kn* is the nucleation coefficient (Na_{mv}/ Na_m). * — differences between the experimental series and the norm (p^n), series 1 and 2 (*p*) were considered statistically significant according to the Mann – Whitney test at $p < 0.05$.

Morphometric study of intramuscular nerve trunks showed that after seven days of the experiment the proportion (%) of destructively altered myelinated nerve fibers in series 1 and 2 was (91.8 ± 4.5) % and (94.4 ± 6.1) %, after 14 days — (88.2 ± 5.3) % and (80.0 ± 7.2) %, after 21 days — (27.3 ± 2.8) % and (33.4 ± 6.4) %, and at the end of the experiment (42nd day) — (8.9 ± 3.1) % and (9.5 ± 2.2) %, respectively.

DISCUSSION

Our study assessed the effects of a single intramuscular injection of a BCAA preparation developed by the authors in an injectable dosage into the closed partial crush ATM zone in rats on regenerative processes. Previously, a single administration at the studied concentration demonstrated its safety in rats, and lower serum creatine phosphokinase activity (a marker of muscle damage) was observed in animals injected with this preparation compared to controls [29].

It is known that the compression injury of skeletal muscles due to mechanical pressure and ischemia-reperfusion injures not only muscle fibers but also blood vessels and nerves [30, 32], extensive degradation of which is observed during the degenerative and inflammatory phases [33, 34]. Activation of myogenesis of muscle progenitor cells and angiogenesis of endothelial cells is crucial for muscle regeneration after injury [35]. There is evidence that essential branched chai amino acids (leucine, isoleucine and valine (BCAA)) are activators of reparative rhabdomyogenesis and angiogenesis [20].

Our stereological study of changes in the ratio of ATM tissue components in rats regenerating after compression injury revealed an equivalent decrease in the proportion of muscle fibers (by 36–37 %) and an increase in the proportion of endomysium in both series after seven days. At other time-points, the volume fraction of muscle fibers was significantly higher in the series with BCAA injection, but at the end of the experiment remained below normal in both groups. The obtained data are consistent with the results of stereological studies by Shchudlo et al. [30], who, using

the same experimental model of closed partial crushing of the rat ATM, but with a shorter duration of compression (20 s), did not reveal a complete restoration of the volume fraction of muscle fibers even 90 days after the injury.

To assess the effectiveness of muscle regeneration after traumatic and denervation injuries, the indicator "average or median diameter of muscle fibers" is most often used [30, 36–38]. Our quantitative analysis of the population of muscle fibers regenerating after closed partial crushing showed that during 28 experimental days their median diameter was significantly higher in the series with the BCAA injection. Moreover, in that series, the nucleation index (the number of nuclei in the cross-sectional profile of one muscle fiber) was significantly reduced relative to the norm only after seven days of the experiment, and in the series without the injection after seven, 14 and 42 days. Lower values of this indicator in the series with natural regeneration may indicate less active myogenesis, since, according to the literature, it is the activation of myosatellite cells that is one of the main factors determining the ability of skeletal muscle to regenerate [39]. At the end of the experiment (day 42), the diameter of muscle fibers in both series did not reach normal values and even decreased, but was significant only in the series with BCAA injection, in which the proportion of small fibers with a diameter of 10–30 μm increases simultaneously with an increase in the numerical density and higher values of the volumetric density of muscle fibers than in series 1. Such dynamics may be associated with persistent atrophy of some muscle fibers, a hyperplastic regenerative response in the form of myon splitting and their dystrophic changes [30], associated with impaired blood supply and innervation. Thus, in our study, within 28 days, the muscle fiber vascularization index (the number of vessels supplying one muscle fiber) was significantly higher in the series with BCAA, but by the 42nd day after the injury it was lower than the values of series 1 and the norm. It is known that the rate of muscle regeneration and the completeness of muscle tissue restoration directly depend on angiogenesis and restoration of the microvascular network [40]. Dense vasculature may be more important for rapid repair of muscle damage than abundance of satellite cells, and lower capillary density may impair regeneration [41].

Our study showed that the innervation of the skeletal ATM in the projection of the compression groove was impaired in both series to the same extent due to the destruction of the myelinated nerve fibers of the intramuscular nerve trunks and was not restored by the end of the experiment, which is also one of the causes of muscle fiber atrophy [42], which persisted until the end of the experiment. Denervated skeletal muscles lose their contractile function, which leads to decreased blood perfusion and a state of muscle hypoxia, excessive production of reactive oxygen species, and muscle fiber damage due to oxidative stress [43].

Thus, the results of our morphological, stereological, and morphometric studies of the ATM after compression injury suggest that a single BCAA injection has a positive effect on muscle fiber and microvascular regeneration. It is more effective than spontaneous regeneration.

Further research is needed on the effect of injectable BCAA on muscle regeneration, with adjustments to dosage, schedule, number of injections, study of adaptive responses, potential side effects, and long-term results to confirm its effectiveness.

CONCLUSION

A single BCAA intramuscular injection of the original preparation based on branched chain amino acids (BCAA) in the medical injection dosage into the area of a partial crush injury of the anterior tibial muscle has a myogenic stimulating effect.

Conflict of interest *The authors declare that they have no competing interests related to the study and its publication.*

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Comparative analysis of clinical and instrumental study of the results of using standard and modified stromal-vascular fractions in the treatment of patients with chondromalacia patellae

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Abstract

Introduction Chondromalacia patellae is a leading cause of anterior knee pain and is considered an early form of degenerative patellofemoral cartilage disease. The limited regenerative potential of the hyaline cartilage and the variable effectiveness of conservative treatments motivate the search for biological technologies capable of providing structure-modifying effects. A promising approach is the use of autologous stromal vascular fraction (SVF) of adipose tissue that has anti-inflammatory and regenerative potential.

The **purpose** of the work is to conduct a comparative assessment of clinical and instrumental studies of the results of standard and modified SVF therapy technologies in the treatment of patients with chondromalacia patella.

Materials and Methods A non-randomized, retrospective, multicenter cohort study was performed. It included 41 patients with Outerbridge grades I–III chondromalacia patellae. Patients were divided into two groups according to treatment protocol provided: standard SVF (n = 20) and modified SVF (n = 21). Assessments were performed before treatment and after one, six, and 12 months. VAS, KOOS-PS, and quantitative parameters of cartilage defect based on MRI data (linear dimensions, area, volume) were analyzed. Differences were considered statistically significant at $p < 0.05$.

Results In both groups, a significant reduction in pain and improvement in function were noted after 12 months ($p < 0.001$). In the standard SVF group, the defect area decreased by 27.4 % and volume by 44.6 %; in the modified SVF group, by 40.2 % and 53.8 %, respectively ($p < 0.001$). Intergroup comparison revealed a more pronounced decrease in defect width with the modified technique ($p = 0.007$). One month after treatment, the modified SVF group showed a more pronounced reduction in pain and improvement in function ($p < 0.01$), while the differences leveled out at six and 12 months.

Discussion The modified SVF therapy technique resulted in earlier pain reduction and improved function compared to the standard technique. These differences leveled over the long term, confirming the high efficacy of SVF therapy regardless of the protocol variant. Comparable morphological results based on MRI data indicate that the structural effect was maintained with the modified technique. Limitations of the study include the non-randomized design and a moderate sample size.

Conclusion SVF therapy demonstrates significant clinical and structural benefits in chondromalacia patellae. The modified technology provides a more rapid onset of clinical effect with comparable long-term morphological changes based on MRI data, suggesting it as a promising option for optimizing cell therapy.

Keywords: stromal-vascular fraction, chondromalacia, adipose tissue, mesenchymal stromal cells

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INTRODUCTION

Chondromalacia patellae is traditionally considered an early form of degenerative articular cartilage disease of the patellofemoral joint and one of the leading causes of pain in the anterior knee joint [1, 2]. Modern concepts have evolved from an isolated mechanical concept to an understanding of the multifactorial nature of the disease, including biomechanical disturbances, changes in the intra-articular environment, and molecular mechanisms of matrix degradation [3–5]. Impaired patellar tracking, imbalances in muscle control, and changes in lower limb kinematics lead to increased contact stresses in the patellofemoral joint and the progression of cartilaginous damage [6, 7]. At the molecular level, chronic overload initiates a cascade of inflammatory-degenerative reactions accompanied by the activation of proinflammatory cytokines (IL-1, TNF-α), disruption of TGF-β/BMP signaling pathways and the formation of a phenotype of hypertrophied and senescent chondrocytes [8–9]. Low-intensity chronic inflammation is considered a key mediator of the progression of degenerative changes in the cartilage [10, 11]. Given the limited regenerative potential of hyaline cartilage [12], traditional conservative approaches, including exercise therapy and load modification, demonstrate variable effectiveness and do not have a proven structure-modifying effect [13, 14].

Surgical methods of cartilage restoration (microfracture, autologous chondrocyte implantation, osteochondral grafting) can provide clinical improvement; however, they are characterized by invasiveness, limited indications, and variability in long-term results [15–19]. The limitations of both conservative and surgical treatment methods have led to an active search for biological approaches aimed not only at relieving symptoms but also at modifying the intra-articular microenvironment and stimulating reparative processes. In recent years, the use of cell technologies, in particular mesenchymal stromal cells (MSCs) and stromal vascular fraction (SVF) of adipose tissue, has attracted considerable interest. Adipose tissue is considered an available and rich source of regenerative cells [20, 21]. SVF contains mesenchymal stromal cells, pericytes, endothelial and immunomodulatory elements, which provide a pronounced paracrine and immunoregulatory effect [22, 23]. Experimental data indicate the ability of these cells to reduce inflammatory activity and stimulate cartilage tissue remodeling processes [24].

Clinical studies demonstrate pain reduction and improved function following intra-articular administration of autologous adipose-derived cell products [25–27]. Reviews and analyses of clinical trials confirm the potential of SVF and adipose-derived mesenchymal cells in knee osteoarthritis; however, they point to significant heterogeneity in study designs, cell product production methods, and administration regimens, highlighting the need for protocol standardization [28–30].

Despite growing data on the use of SVF for degenerative cartilage lesions, comparative studies of its effectiveness in chondromalacia patellae remain limited. The impact of cell product preparation on the clinical effect and severity of post-injection synovial reactions has also been insufficiently studied. Therefore, a comparative evaluation of the results of standard and modified SVF therapy is relevant.

The **purpose** of the work is to conduct a comparative assessment of clinical and instrumental studies of the results of standard and modified SVF therapy technologies in the treatment of patients with chondromalacia patella.

MATERIALS AND METHODS

A non-randomized, retrospective, multicenter cohort study was conducted. It included 41 patients with chondromalacia patellae who underwent treatment in 2021–2024 at Medsi Group of Companies (Moscow) and the Ilizarov National Medical Research Center of Traumatology and Orthopedics (Kurgan). The study

was conducted in accordance with the ethical principles set forth in the World Medical Association's Declaration of Helsinki (2013 edition and subsequent amendments) and with the requirements of Good Clinical Practice (GCP) and the Rules of Clinical Practice in the Russian Federation, approved by Order of the Ministry of Health of Russia dated April 1, 2016, No. 200n. All study participants signed informed consent to participate and publish anonymized findings obtained during the study.

The sample was selected based on predefined inclusion and exclusion criteria. The study included patients aged 25 to 80 years with clinically significant anterior knee pain lasting more than three months and its severity greater than 40 mm on the visual analog scale (VAS), along with chondromalacia patellae grades I–III according to the Outerbridge classification, confirmed by magnetic resonance imaging. A mandatory inclusion condition was the absence of a clinically significant effect from previous conservative therapy lasting at least three months, including kinesitherapy, nonsteroidal anti-inflammatory drugs, chondroprotectors, and/or intra-articular hyaluronic acid injections.

The study did not include patients with grade IV chondromalacia, clinically significant axial deformities of the lower limb (varus, valgus, patella alta), active systemic inflammatory diseases (rheumatoid arthritis, seronegative spondyloarthropathies, systemic connective tissue diseases), a history of infectious lesions of the knee joint, severe somatic pathology (decompensated diabetes mellitus, chronic heart failure of functional class III-IV, oncological diseases), as well as with clinically significant abnormalities of laboratory parameters. Also excluded were patients who received intra-articular injections of biological preparations (PRP, SVF, BMAC) or hyaluronic acid less than six months before the study, individuals with hemostatic disorders, history of anticoagulant therapy, a body mass index of more than 35 kg/m², women during pregnancy and lactation. Occasional use of NSAIDs was allowed before enrollment in the study in the absence of systematic anti-inflammatory therapy. This minimized the impact of systemic diseases and concomitant medications on clinical outcomes.

All patients were divided into two groups based on the orthobiological treatment method used. Group I (n = 20) included patients who underwent a single intra-articular injection of SVF obtained mechanically using the standard ACT technology recommended by the manufacturer SOLOPHARM. Group II (n = 21) included patients treated using a modified protocol for mechanical SVF production [31]. Hyaluronic acid preparations were not used for 12 months after the procedure in any group.

The patients' average age was 45.4 ± 11.7 years, ranging from 27 to 73 years. The distribution of gender, age, body mass index (BMI), and chondromalacia severity did not differ significantly between the groups, allowing the study cohorts to be considered comparable and allowing for valid intergroup comparative analysis. Detailed patient characteristics are presented in Table 1.

Table 1

Patients' data

Parameter		SVF standard (n = 20)		SVF modified (n = 21)	
		n	%	n	%
Age, years	(M ± SD)	47,2 ± 11,3		43,8 ± 11,8	
	18–44	10	50,0	11	52,4
	45–59	7	35,0	8	38,1
	60–74	3	15,0	2	9,5
Gender	Males	14	70,0	12	57,1
	Females	6	30,0	9	42,9
BMI, kg/m²	Norm (18.5–24.9)	7	35,0	5	23,8
	High (25.0–29.9)	9	45,0	12	57,1
	Obesity grade I (30.0–34.9)	4	20,0	4	19,0
Chondromalacia severity (Outerbridge)	Grade I	1	5,0	3	14,3
	Grade II	10	50,0	11	52,4
	Grade III	9	45,0	7	33,3

Clinical effect assessments were conducted before treatment and after one, six, and 12 months of follow-up. Pain was assessed using a visual analogue scale (VAS). Knee joint function was analyzed using the KOOS-PS score. Patients completed all questionnaires independently under physician supervision.

The instrumental evaluation included magnetic resonance imaging of the knee joint, performed before treatment and 12 months after the intervention using systems with a magnetic field strength of 1.5 T and 3.0 T. In every patient, the initial and follow-up examinations were performed with the same system using an identical scanning protocol, which ensured comparability of the obtained data. The thickness of the articular cartilage in the areas of interest, defect location (medial facet, lateral facet, interfacet groove), linear dimensions of the lesion (width, height, depth) as well as the area (mm^2) and volume (mm^3) of the defect were analyzed. MRI signs of synovial reaction were additionally taken into account. For the intergroup analysis, the magnitude of the change in the indicator (Δ) was calculated, defined as the difference between the values after treatment and the baseline data.

Statistical data processing was performed using the R software environment (version 3.2.4). Statistical analysis was performed using standard methods of variation statistics. The normality of the distribution of quantitative indicators was preliminarily assessed using the appropriate criteria. If normal distribution was confirmed, the intragroup dynamics of quantitative parameters were analyzed using the paired Student's t-test for dependent samples. To assess the intragroup dynamics of indicators obtained from clinical scales (VAS, KOOS), the Friedman criterion was used. Intergroup comparison of independent samples was performed using the Mann-Whitney U-test. Differences were considered statistically significant at $p < 0.05$. The results are presented as the mean and standard deviation (M ± SD) or the median and interquartile range (Me [Q1–Q3]).

RESULTS

In the standard SVF therapy group, a statistically significant reduction in chondral defect size ($p < 0.001$) was recorded after 12 months of follow-up. The lesion area decreased by an average of 27.4 %, and its volume by 44.6 % compared to baseline. The changes reflect moderate structural reorganization of the damaged area and the development of reparative processes in the cartilage tissue. These results demonstrate the structurally beneficial effect of standard SVF therapy, manifested in a significant reduction in defect size and stabilization of the degenerative process (Table 2).

Table 2

MRI dynamics of cartilage defect parameters according to MRI data

Parameter	SVF srandard (*n* = 20)					SVF modified (*n* = 21)				
	Before therapy	After therapy	Δ (after-before)	t	Before therapy	After therapy	Δ (after-before)	Δ (after-before)	t	*p*
Defect width, mm	6,78 ± 2,61	5,84 ± 2,52	−0,95 ± 0,52	8,14	< 0,001	6,85 ± 3,31	5,19 ± 2,48	−1,65 ± 1,10	6,86	< 0,001
Defect height, mm	7,03 ± 2,17	5,81 ± 2,11	−1,22 ± 0,76	7,22	< 0,001	6,97 ± 4,18	5,54 ± 3,30	−1,43 ± 0,95	6,87	< 0,001
Defect depth, mm	1,96 ± 0,52	1,46 ± 0,40	−0,50 ± 0,29	7,56	< 0,001	2,66 ± 0,94	2,05 ± 0,88	−0,61 ± 0,46	6,06	< 0,001
Defect area, mm^2	50,32 ± 30,52	36,53 ± 25,39	−13,79 ± 8,62	7,15	< 0,001	50,11 ± 37,73	29,97 ± 20,59	−20,14 ± 17,84	5,17	< 0,001
Defect volume, mm^3	105,28 ± 91,90	58,36 ± 56,02	−46,92 ± 41,82	5,02	< 0,001	123,65 ± 96,03	57,16 ± 52,15	−66,48 ± 51,49	5,92	< 0,001

Analysis of the linear and volumetric parameters of the patellar chondral defect in the modified SVF therapy group demonstrated a statistically significant reduction in all studied parameters 12 months after the procedure ($p < 0.001$) (Table 2). The defect area decreased by 40.2 % on average and its volume by 53.8 % from the baseline values. These results indicate significant structural reorganization of the damaged area and the development of beneficial morphological dynamics in the patellofemoral joint.

In the standard SVF therapy group, pain relief was progressive and sustained. The most pronounced change according to VAS was noted by the sixth month of observation, with the achieved level being maintained by the 12th month. The obtained data indicate the formation of a stable analgesic effect, increasing over time and reaching its maximum expression in the late period. Statistical analysis confirmed the reliability of changes over time (Friedman criterion: $\chi^2(3) = 58.13$; $p < 0.001$) (Table 3). The dynamics of functional indicators according to the KOOS-PS scale corresponded to the reduction in pain: the most pronounced improvement was noted by the sixth month, with the achieved level being maintained by the 12th month of observation. Statistical analysis confirmed the reliability of changes over time (Friedman criterion: $\chi^2(3) = 59.71$; $p < 0.001$) (Table 3). The findings indicate a persistent functional improvement after SVF therapy, which is consistent with the positive MRI dynamics of morphological changes.

In the modified SVF therapy group, pain relief was noted as early as one month after the intervention. The VAS score showed early and significant improvement, with further reduction by the sixth month and maintenance of the achieved level by the 12th month of follow-up. Statistical analysis confirmed the significance of changes over time (Friedman criterion: $\chi^2(3) = 57.75$; $p < 0.001$) (Table 3). The obtained data indicate a rapid analgesic effect, followed by stabilization and long-term maintenance of the clinical result. The dynamics of functional indicators according to the KOOS-PS scale were also early: improvement was recorded as early as one month and by the sixth month reached a level comparable to the results of the standard SVF therapy group, with the achieved values maintained by the 12th month of follow-up. Statistical analysis confirmed the significance of changes over time (Friedman criterion: $\chi^2(3) = 61.32$; $p < 0.001$) (Table 3). The obtained data indicate the rapid formation and stable maintenance of functional improvement, which corresponds to the positive MRI dynamics of morphological changes.

Table 3

Dynamics of questionnaire findings

Term	Шкала ВАШ						Шкала KOOS-PS					
	SVF standard (n = 20)			SVF modified (n = 21)			SVF standard (n = 20)			SVF modified (n = 21)		
	median	Q1–Q3	min–max	median	Q1–Q3	min–max	median	Q1–Q3	min–max	median	Q1–Q3	min–max
Baseline	6,0	4,5–7,5	3–9	6,0	5,0–7,0	2–9	11,0	7,0–15,3	3–26	11,0	4,0–15,0	3–26
1 month	5,0	4,0–6,5	2–8	3,0	2,0–5,0	1–6	9,5	5,0–13,3	3–24	5,0	2,0–11,0	1–16
6 months	3,0	1,0–4,5	1–6	2,0	1,0–3,0	1–5	3,5	2,0–9,0	1–15	2,0	1,0–7,0	0–12
12 months	1,0	1,0–1,0	1–2	1,0	1,0–2,0	1–2	1,0	0–2,0	0–10	1,0	1,0–2,0	0–10

Intergroup comparison

In an intergroup comparison of the dynamics of the linear and volumetric parameters of the defect, a significant advantage of the modified technique over the standard technique was revealed in terms of decreasing the defect width ($p < 0.05$). No statistically significant differences were found for other parameters ($p > 0.05$) (Table 4).

Table 4

Comparative dynamics of chondral defect MRI parameters

Parameter	SVF standard Δ	SVF modified Δ	*p*
	Me (Q1–Q3)		
Defect width, mm	0.98 (0.46–1.29)	1.42 (1.18–1.66)	0.007
Defect height, mm	1.14 (0.54–1.91)	1.14 (0.92–1.54)	0.629
Defect depth, mm	0.44 (0.25–0.72)	0.36 (0.30–0.92)	0.705
Defect area, mm^2	12.54 (7.10–16.41)	15.99 (5.78–16.90)	0.540
Defect volume, mm^3	33.49 (24.43–61.15)	37.22 (19.33–114.69)	0.382

An intergroup analysis of pain dynamics using the VAS scale revealed differences in the time to clinical effect depending on the technique used. The modified SVF therapy group demonstrated a more pronounced reduction in pain one month after the procedure compared to standard SVF therapy ($p < 0.01$). At longer follow-up periods (six and 12 months), no statistically significant differences were found between the groups ($p > 0.05$) (Fig. 1).

Intergroup analysis of the KOOS-PS score demonstrated a similar pattern: the use of modified SVF therapy was associated with earlier functional improvement compared with standard SVF therapy. Statistically significant differences in the dynamics of KOOS-PS indicators were detected one month after treatment ($p < 0.01$). At six and 12 months, the differences between the groups did not reach the level of statistical significance ($p > 0.05$) (Fig. 2).

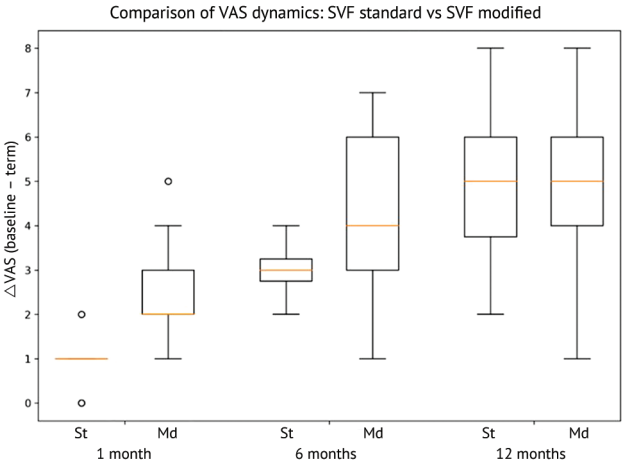

Fig. 1 Intergroup comparison of VAS score

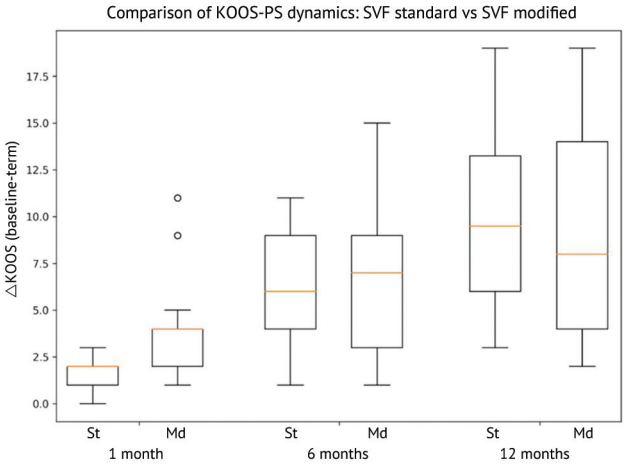

Fig. 2 Intergroup comparison of KOOS-PS

DISCUSSION

The analysis revealed that the use of modified SVF therapy provides a faster onset of clinical effect compared to the standard technique. Already during the first month of observation, we noted a significantly more pronounced relief of pain and an earlier improvement in functional indicators. This dynamics has important clinical significance, as it allows patients to quickly return to physical activity, including targeted programs to strengthen the muscles of the lower extremities, which helps to stabilize the achieved result. In addition, faster pain relief and a milder course of the early post-injection period increase the tolerability of the procedure and create a higher level of confidence in the therapy.

Despite the identified early benefit of the modified technique, pain scores on the VAS and KOOS-PS functional scales were comparable in both groups in the long-term period (6–12 months), confirming the overall high efficacy of SVF therapy regardless of the cell substrate treatment method. The absence of significant intergroup differences in the morphological parameters of the defect,

as measured by MRI, also indicates the preservation of regenerative potential with the modified technique. These data suggest that the protocol modification is primarily aimed at optimizing cell composition and procedure tolerability, without reducing cell viability or diminishing the structure-modifying effect of the therapy.

The results of the present study are consistent with the data of a number of clinical studies devoted to the use of stromal-vascular fraction and micro-fragmented adipose tissue in degenerative lesions of the knee joint. Thus, in the study of Yokota et al., the reduction in pain syndrome according to the VAS scale after six months in the SVF group was 44.0 % [32], whereas in our study, by this time, pain relieved more than 50 % with a further increase in the effect with a longer follow-up. A similar trend in dynamics was shown by Bisicchia et al., where the use of micro-fragmented SVF in combination with microfragmentation led to a decrease in VAS to (2.6 ± 1.8) points after 12 months [33]. In our study, at 12 month, the median VAS score decreased from 6 to 1 point in both SVF groups and reflected a pronounced analgesic effect of cell therapy. Similar results were obtained by Hudetz et al.: pain relief by movement was approximately 56–57 %, and at rest up to 85 % by the 12th month [34], which is comparable with the 80–85 % pain reduction in our study. In the work of Onoi et al., after a single administration of ADRCs, a 75–80 % pain reduction by the sixth month and an improvement in KOOS scores were also noted [35]. The findings of Michalek et al. confirm the sustainability of the effect of SVF therapy: pain reduction reached 65–70 % by the 12th month and was maintained up to 36 months of observation [36]. Finally, Russo et al. demonstrated a median pain reduction of 40–50 % and an improvement in KOOS of 30–35 % after 12 months [37], which also confirms the pronounced clinical and functional effectiveness of adipose cell therapy.

Taken together, these data indicate the reproducibility of the analgesic and functional effects of SVF therapy, with pain reduction rates obtained in our study being in a range comparable to or greater than the results published.

Limitations of the study include the non-randomized nature of patient allocation and the moderate sample size. However, the standardized treatment protocol and comparability of the groups minimize the influence of potential systematic factors.

CONCLUSION

The study demonstrated the high clinical and structural efficacy of SVF therapy in the treatment of chondromalacia patellae. Both groups showed a significant relief in pain, significant functional improvement, and a statistically significant reduction in the linear and volumetric parameters of the chondral defect, as measured by quantitative MRI analysis, confirming the structurally beneficial effect of cell therapy.

The modified SVF technology provided a more rapid onset of clinical effect with comparable structural changes according to MRI data in the long-term period, which indicates the preservation of the regenerative potential of the cell substrate with the optimization of its preparation protocol.

The obtained data allow us to consider SVF therapy as an effective biological method for correcting degenerative changes in the patellofemoral joint, and the modified technology as an option that ensures accelerated formation of a clinical response while maintaining structural effectiveness.

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Effects of Glucosamine-Chondroitin, Chitosan, and Phytoestrogen on Knee Osteoarthritis Inflammatory and Cartilage Degeneration Biomarkers and Clinical Symptoms in Postmenopausal Women

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Abstract

Introduction Knee osteoarthritis (OA) is a progressive disease causing pain and dysfunction in postmenopausal women.

Purpose This study aimed to evaluate the therapeutic efficacy of a combination of glucosamine-chondroitin, chitosan, and phytoestrogen with paracetamol compared to paracetamol alone in postmenopausal women with knee osteoarthritis.

Materials and Methods A double-blind randomized controlled trial was conducted on 60 postmenopausal women with Kellgren – Lawrence grade II–III knee osteoarthritis. A total of 60 patients were included in this study and divided into treatment and control groups with a 1:1 ratio. The mean age of patients was 59.77 years (± 2.99) while the control group had a mean age of 60.4 years (± 3.21), there was no significant difference ($p = 0.43$). Patients were randomly assigned into two groups: the treatment group ($n = 30$), which received glucosamine-chondroitin, chitosan, and phytoestrogen in combination with paracetamol, and the control group ($n = 30$), which received paracetamol alone. The levels of soluble interleukin-6 receptor (sIL-6R), interleukin-10 (IL-10), cartilage oligomeric matrix protein (COMP), as well as Visual Analog Scale (VAS) and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores were measured at baseline and after two weeks of treatment.

Results After the pharmacological intervention, the treatment group showed significant reductions in WOMAC score, COMP, and sIL-6R compared to the control group ($p < 0.01$). Both groups had increased IL-10 levels following treatment, but the increase was greater in the control group.

Discussion The combination therapy demonstrated improvement in joint function and a reduction in inflammatory and cartilage degeneration markers. These findings support the anti-inflammatory and chondroprotective potential of natural compounds in the management of knee osteoarthritis.

Conclusion The combination of glucosamine-chondroitin, chitosan, phytoestrogen, and paracetamol demonstrated superior short-term effects in reducing inflammatory and cartilage degeneration biomarkers and improving clinical symptoms in postmenopausal women with grade II-III knee osteoarthritis compared with paracetamol alone.

Keywords: knee osteoarthritis, postmenopausa, glucosamine-chondroitin, chitosan, phytoestrogen

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INTRODUCTION

Knee osteoarthritis (OA) is a progressive degenerative disease with an inflammatory condition of the knee joint that contributes quite a lot to the disruption of daily activities. In 2019, approximately 528 million people worldwide suffered from OA, an increase of 113 % since 1990 [1]. The progression of OA causes chronic severe pain. At some point, it may reduce the knee function, limiting the activity of 80 % of OA patients. Moreover, 25 % of patients may have a severe disability that affects their quality of life [2].

Osteoarthritis is largely driven by an imbalance between pro- and anti-inflammatory cytokines, with menopause women being more vulnerable due to estrogen depletion affecting chondrocyte metabolism. While NSAIDs are commonly used to relieve symptoms, they do not halt disease progression. This may be due to the involvement of signaling pathways like NF-κB and MAPKs, which contribute to OA progression through mechanisms that NSAIDs do not target [3].

The goals of managing OA are to reduce pain, decrease disability, improve functional outcomes and quality of life. Knee OA treatment typically starts with conservative approaches and advances to surgery if needed. While medications may slow disease progression, no disease-modifying treatment has been proven effective. Anti-inflammatory drugs remain the primary therapy, though they carry risks of gastrointestinal side effects [4, 5]. NSAIDs can cause ulceration in the patient's stomach or intestines, especially if the patient takes them for a long time or in large doses. In addition, paracetamol can also be used for OA treatment and has fewer side effects, but its effectiveness is still lower than of other NSAIDs [6].

Glucosamine-chondroitin, chitosan, and phytoestrogens are commonly used as alternative treatments for osteoarthritis due to their anti-inflammatory and potential chondroprotective properties. While they help support cartilage health and have minimal toxicity, their direct effectiveness in treating osteoarthritis remains uncertain and requires further research [7–10]. Glucosamine-chondroitin, chitosan, and phytoestrogens are used as alternative treatments to avoid NSAID side effects. While glucosamine-chondroitin support cartilage health and are considered safe, their direct effect on osteoarthritis remains unclear and needs further research [4]. Therefore, the researchers aimed to prove the effect of glucosamine-chondroitin sulfate, chitosan, and phytoestrogen on identifiable markers in knee OA. Currently, there are few studies that discuss directly the effect of glucosamine-chondroitin, chitosan, and phytoestrogen combined with paracetamol on OA markers in joint fluid, including soluble interleukin-6 receptors (sIL-6R), interleukin-10 (IL-10) and Cartilage Oligomeric Matrix Protein (COMP) as well as visual analog scale (VAS) values and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores as a standard of pain measurement in post-menopausal patients with knee OA.

Purpose This study specifically aimed to evaluate the therapeutic efficacy of a combination therapy consisting of glucosamine-chondroitin, chitosan, and phytoestrogen with paracetamol and compare it to paracetamol alone, in reducing inflammatory biomarkers (sIL-6R, IL-10, and COMP levels) and clinical symptoms severity (VAS and WOMAC scores) in postmenopausal women with knee osteoarthritis.

MATERIALS AND METHODS

Type of study and study design

This study was a double-blind randomized controlled trial. The study subjects were randomly allocated into 2 groups using the block randomization method by pharmacist as an independent third party. The same number of participants in each group was ensured. The treatment group received a combination of glucosamine 31.5 mg, chondroitin 135 mg, chitosan 29.8 mg, and phytoestrogen 1.5 mg once daily for two weeks in addition to paracetamol intake 500 mg three times daily for two weeks. The control group received paracetamol 500 mg three times daily for two weeks with placebo supplementation. The levels of sIL-6R, IL-10, and COMP in synovial fluid, as well as VAS scores and WOMAC scores, were examined before pharmacological intervention and after 2 weeks of pharmacological intervention. After the randomization process, participants were assigned to either the treatment or control group by the pharmacist, while both the researchers and participants remained blinded to the group allocation throughout the study period. All data

were collected at Karya Darma Husada General Hospital (RSU), Buleleng, Bali. The research was conducted in the laboratory of FK UNDIKSHA, Bali, in October-December 2024.

Patients and criteria

The sample inclusion criteria in this study are as follows: 1) Post-menopausal women, diagnosed with grade II or III knee OA with effusion; 2) no deformity; 3) body mass index < 30 kg/m^2; 4) who have not received anti-inflammatory pharmacological therapy in the last 2 weeks and 5) had never received operative therapy. The exclusion criteria are: 1) patients with a history of knee trauma; 2) history of knee infection; 3) history of hysterectomy. The sample size was calculated using the Charan & Biswas formula [11]:

$$n = \frac{2SD^2(Z_{\alpha/2} + Z_{\beta})^2}{d^2}.$$

The standard deviation (SD) was set at 20, reflecting the variability within the population. A significance level of 5 % ($\alpha = 0.05$) was adopted, corresponding to a Z-value of 1.96 for a two-tailed test. To achieve a statistical power of 80 %, the β error probability was set at 0.20, corresponding to a Z_β of 0.84. The effect size (d) was determined to be 15. Standard deviation and effect size were included from the previous study by A.M.T. Lubis et al. [12]. These parameters ensure an adequately powered study. The minimum sample size for our study is 28 samples per group:

$$n = \frac{2.20^2(1.96 + 0.84)^2}{15^2}; \; n = \; 27.87.$$

Data collection and study variables

The levels of sIL-6R, IL-10, and COMP were measured from the synovial fluid of a single predefined index knee per patient using the enzyme-linked immunosorbent assay (ELISA) method by the laboratory technician. According to the manufacturer's protocol, the sIL-6R levels were measured using the Biotinylated Human sIL-6R antibody ELISA Kit (BT LAB, Zhejiang, China, E0090Hu). The IL-10 levels were measured using the Biotinylated Human IL-10 antibody ELISA Kit (BT LAB, Zhejiang, China, E0102Hu). The COMP levels were measured using the Biotinylated Human COMP antibody ELISA Kit (BT LAB, Zhejiang, China, E1486Hu). Synovial fluid samples were obtained by aspirating 1 ml of synovial fluid from a single predefined index knee per patient at baseline and after 2 weeks of intervention. Synovial fluid sampling is done with an aseptic technique. Data collection for VAS scores and WOMAC scores was carried out by interviewing patients directly before and after 2 weeks of pharmacological intervention.

Study outcomes

The outcome of this study was the significance of glucosamine-chondroitin, chitosan, and phytoestrogen with paracetamol in improving sIL-6R, IL-10, COMP levels, VAS, and WOMAC scores compared to the paracetamol group. There were no changes to the primary or secondary outcomes after the trial commenced in the study.

Statistical analysis

Laboratory variables such as sIL-6R, IL-10, and COMP were presented in ratios, while clinical variables such as VAS and WOMAC scores were presented in intervals. Each variable was analyzed for mean, median, mode, and standard deviation. Normality and homogeneity tests were performed using the Shapiro-Wilk test and Levene test. The difference between post-therapy and baseline value of sIL-6R, IL-10, and COMP was analyzed with a dependent t-test. The difference between the control and experimental groups following the therapy was analyzed with an independent t-test. Path analysis was performed to explore the association and interaction between sIL-6R, IL-10, and COMP levels after normality test, heteroscedasticity, and autocorrelation between variables had been excluded. Heteroscedasticity between variables was explored with the Breusch-Pagan test while autocorrelation was analyzed with the Durbin-Watson test. Significance level was set at 5 %. Data analysis was performed using SPSS by an independent statistician, who were blinded to the group assignments.

Ethical principles

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments. The study was approved by the Research Ethics Committee of the Faculty of Medicine, Universitas Udayana (0340/UN14.2.2.VII.14/LT/2025), and informed consent was obtained from all study participants.

RESULTS

A total of 93 participants were assessed for eligibility in this study. Of those, 33 were excluded, 29 participants did not meet the inclusion criteria and 4 declined to participate. The remaining 60 participants were randomized equally into two groups. In the treatment group, all 30 participants received the allocated pharmacological intervention consisting of glucosamine-chondroitin, chitosan, phytoestrogen, and paracetamol according to the study protocol, and none discontinued treatment or were lost to follow-up. All participants in this group were included in the primary outcome analysis. In the control group, all 30 participants received paracetamol therapy with placebo supplementation according to the study protocol. However, there were no discontinuations or losses to follow-up in that group either, and all 30 participants were also included in the primary outcome analysis. In total, there was a 100 % follow-up and analysis rate for both groups. Participants were recruited between October and December 2024, with follow-ups conducted throughout the same period.

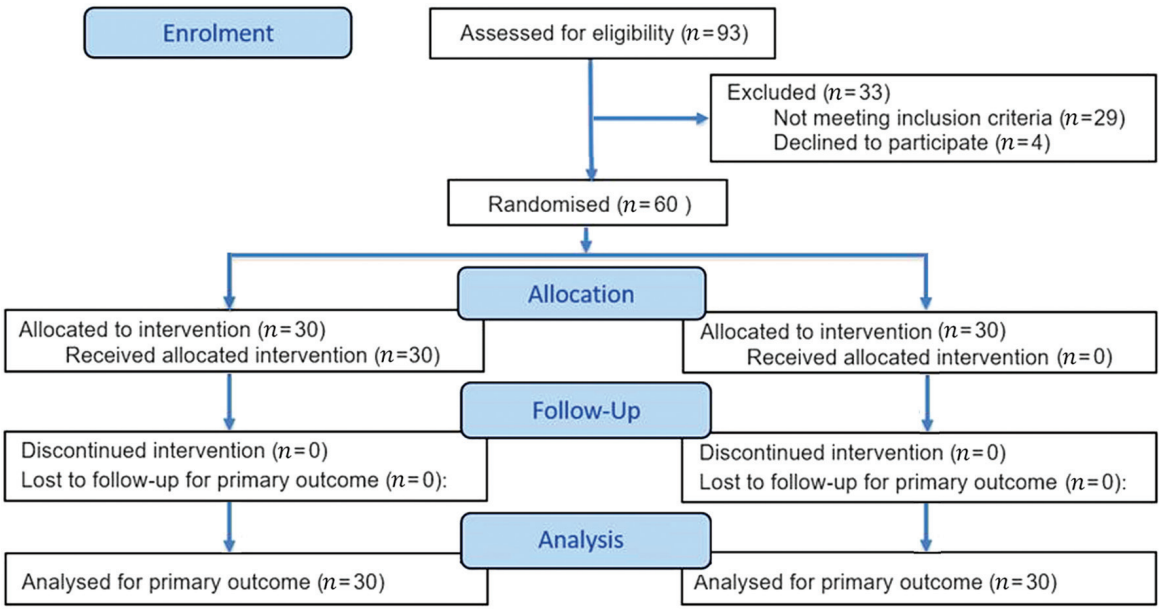

Fig. 1 CONSORT trial diagram

All participants who were randomized, met the eligibility criteria, provided informed consents, and completed the pharmacological intervention and a follow-up as scheduled, resulting in 100 % retention. The trial was completed as planned without early termination. Both treatment and control groups continued receiving standard non-pharmacological management for knee osteoarthritis throughout the study period, and no additional pharmacological treatments were permitted. Concomitant care was monitored for consistency, and no adverse events or harms were reported. Both treatments were administered by pharmacists with high adherence, and no deviations from the study protocol occurred, ensuring high fidelity in the pharmacological intervention delivery.

Baseline characteristics

After screening the patients who met the study criteria, a total of 60 patients were divided into treatment and control groups with a 1:1 ratio. Data distribution with the Shapiro-Wilk test found that age, BMI, VAS, and WOMAC data were distributed according to the Gaussian graph while COMP, sIL-6R, and IL-10 showed non-parametric distribution. The significance value of each variable can be seen in Table 1.

Table 1

Data distribution test

Variables		Shaphiro – Wilk Test (*p*-value)		Levene Test (*p*-value)
		Treatment Group	Control Group	
Age (years)		0.315	0.064	0.471
BMI (kg/m^2)		0.688	0.912	0.622
VAS	Before pharmacological intervention	0.212	0.289	0.289
	After pharmacological intervention	0.54	0.174	0.174
WOMAC	Before pharmacological intervention	0.311	0.41	0.122
	After pharmacological intervention	0.562	0.355	0.931
COMP (ng/mL)	Before pharmacological intervention	0.09	< 0.01	0.228
	After pharmacological intervention	0.809	< 0.01	0.014
sIL-6R (ng/mL)	Before pharmacological intervention	< 0.01	< 0.01	0.492
	After pharmacological intervention	< 0.01	< 0.01	0.037
IL-10 (ng/mL)	Before pharmacological intervention	< 0.01	< 0.01	0.852
	After pharmacological intervention	< 0.01	< 0.01	0.107
	Age (years)	0.315	0.064	0.471
	BMI (kg/m^2)	0.688	0.912	0.622

The baseline data of the 60 patients after being divided into treatment and control groups can be seen in Table 2. In the treatment group, the mean age of patients was 59.77 years (± 2.99) while the control group had a mean age of 60.4 years (± 3.21). Although the age in the control group was older, there was no significant difference ($p = 0.43$). The BMI in the treatment and control groups were 20.53 kg/m^2 (± 2.25) and 20.69 kg/m^2 (± 2.33), respectively. There was no significant difference in the statistical test ($p = 0.78$). There was also no difference in VAS scores before pharmacological intervention between the two groups (treatment 6.65 ± 0.69 vs. control 6.69 ± 0.56; $p = 0.79$). WOMAC score was higher in the control group (58.17 ± 5.59) compared to the treatment group (56.07 ± 3.43) and was tested on statistical tests ($p = 0.047$). The sIL-6R value between groups had a significant difference ($p < 0.01$). COMP and IL-10 between groups showed no difference.

Table 2

Baseline data of patient characteristics before pharmacological intervention

Variables	Treatment Group	Control Group	*p*-value
Age, mean ± SD (years)	59.767 ± 2.991	60.4 ± 3.212	0.43[a]
BMI, mean ± SD (kg/m^2)	20.53 ± 2.249	20.689 ± 2.328	0.78[a]
VAS, mean ± SD	6.647 ± 0.694	6.69 ± 0.56	0.791[a]
WOMAC, mean ± SD	56.07 ± 3.433	58.17 ± 5.592	0.047[a]
COMP, median (IQR) (ng/mL)	108.6 (74.6–177.1)	95.6 (53.1–122.6)	0.096[b]
sIL-6R, median (IQR) (ng/mL)	66.33 (35.5–107.167)	68 (33–129.67)	< 0.01[b]
IL-10, median (IQR) (ng/mL)	20.4 (9.4–56.4)	26.4 (17.4–77.9)	0.28[b]

Note: [a] — independent T-test, [b] — Mann – Whitney test

Changes in VAS values and WOMAC scores

The results show that no statistically significant VAS scores in the treatment group compared to the control group (MD (–0.27); 95 % CI (–0.58 – 0.03), ($p = 0.78$)). The WOMAC scores were statistically significant lower in the treatment group than those in the control group (MD (–4.87); 95 % CI (–7.56) – (–2.08); $p = 0.01$) (Table 3).

Table 3

Changes in VAS scores and WOMAC, COMP, sIL-6R, and IL-10 after pharmacological intervention

Variables	Treatment Group	Control Group	Mean difference (95 % CI)	*p*-value
VAS, mean ± SD	6.3 ± 0.6558	6.653 ± 0.514	–0.273 (–0.578; 0.031)	0.78[a]
WOMAC, mean ± SD	52.17 ± 2.991	60.4 ± 5.592	–4.867 (–7.565; –2.077)	0.01[a]
COMP, median (IQR) (ng/mL)	85.6 (62.6–106.6)	173.6 (132.6–246.1)	N/A*	< 0.01[b]
sIL-6R, median (IQR) (ng/mL)	46.33 (28.83–103.83)	149.67 (68.83–313.83)	N/A*	< 0.01[b]
IL-10, median (IQR) (ng/mL)	34.4 (18.4–65.9)	133.4 (59.9–271.9)	N/A*	< 0.01[b]

Note: [a] — independent T-test, [b] — Mann – Whitney test

Changes in sIL6-R, IL-10. and COMP

The level of sIL-6R, IL-10, and COMP in the treatment group were lower than the control group and statistically significant between the group ($p < 0.01, p < 0.01, p < 0.01$). The results of the analysis of COMP, sIL-6R, and IL-10 values can be seen in Table 3.

Pathway analysis of sIL-6R, IL-10, and COMP

Path analysis was obtained after data cleaning by minimizing outliers. Two pathways were obtained where IL-10 affected COMP by modulating sIL-6R and IL-10 directly modulated COMP (Fig. 2). However, the IL-10 receptor pathway with COMP showed no significance (Table 4). In the sIL-6R-mediated pathway, Sobel test results showed no significance (p-value = 0.14).

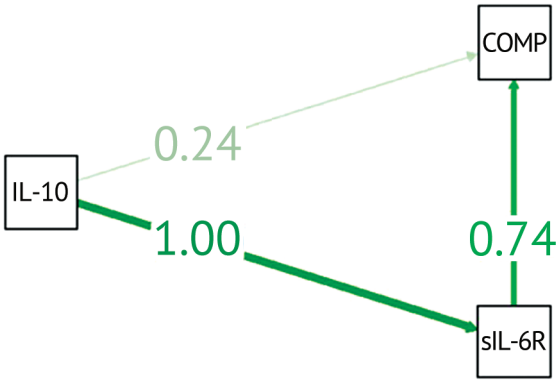

Fig. 2 Pathway analysis of sIL-6R, IL-10, and COMP

Table 4

Changes in VAS scores and WOMAC, COMP, sIL-6R, and IL-10 after pharmacological intervention

	Estimation Coefficient	Standardized Coefficient	Standard Error	p-value
Direct IL-10 and COMP pathway analysis				
Intercept	−9.57984	NA	4.1409	0,026
IL-10	1.35689	0.99672	0.01812	< 0,01
Pathway analysis of IL-10 with sIL-6R-mediated COMP				
Intercept	41.4338	NA	9.9816	<0,01
IL-10	0.3174	0.2434	0.5042	0,533
sIL-6R	0.7083	0.7394	0.3704	0,064

DISCUSSION

This study demonstrated that the combination of glucosamine-chondroitin, chitosan, and phytoestrogen combined with paracetamol improved clinical symptoms, reduced inflammatory and cartilage degradation markers in postmenopausal women with knee osteoarthritis. The reductions in WOMAC scores, COMP, and sIL-6R levels in the treatment group indicate potential chondroprotective and anti-inflammatory effects. Although IL-10 levels increased in both groups, the greater rise in the control group may reflect a compensatory response to inflammation rather than a direct treatment effect.

The combined pharmacological intervention decreased sIL-6R levels by a significant amount, which indicated an anti-inflammatory effect via NF-κB pathway inhibition. Chitosan, the primary constituent of shrimp shell extracts, has also been reported to inhibit pro-inflammatory cytokines TNF-α, IL-6, and IL-1β, inhibiting inflammation and cartilage degradation [13–15]. Similarly, phytoestrogens inhibit inflammatory activity by inhibiting mainly JAK/STAT3 activation, which helps in inhibiting inflammatory responses [16–18]. This highlights the therapeutic potential of natural molecules in regulating OA pathogenesis and inhibiting disease progression.

The anti-inflammatory cytokine IL-10 was elevated in the control group compared with the treatment group. In previous studies, the cytokine IL-10 is shown to be a very common anti-inflammatory marker [19]. Glucosamine-chondroitin compounds inhibit the activation of NF-κB, a transcription factor involved in inflammatory response, which in turn may increase the expression of IL-10 [20]. The chitosan and phytoestrogen compounds contained may also increase IL-10 expression through inhibition of the NF-κB pathway [21,22]. This could be a compensatory response to inflammation, a phenomenon seen before in aging subjects. In older subjects, increased IL-10 could be secondary to a response against increased inflammatory activity and not because of the treatment [23–26]. This has been seen in other inflammatory conditions and suggests that the role of IL-10 in OA pathophysiology is complex and further studies must be done in order to be able to categorically state its role in disease progression and symptom relief.

This research also demonstrated that the treatment group experienced decreased cartilage oligomeric matrix protein (COMP) levels, a cartilage degradation marker. This concurs with the current body of evidence indicating that chitosan and estrogen analogs are chondroprotective in enhancing type II collagen synthesis and inhibition of matrix metalloproteinase (MMP) activity [27]. Chitosan also enhances extracellular matrix stability and inhibits excessive activation of cartilage tissue degradation [10]. Additionally, estrogen enhances cartilage homeostasis via the ERK-mTOR pathway and could inhibit chondrocyte apoptosis and joint function [28–30]. The inhibition of COMP in the treatment group suggests the therapeutic value of these compounds to slow the progression of OA and preserve cartilage integrity in the long term.

In this study, pain severity assessed with VAS did not show a statistically significant difference between the two groups. This results in line with previous meta-analyses showing modest efficacy of glucosamine-chondroitin and phytoestrogens for pain relief [31–34]. OA pain sensation is regulated by various parameters like inflammatory mediators, joint damage of structure, and patients' tolerance to pain. The variability of the pain effect could be due to the nature of pain, including OA with mechanical and biochemical factors [35]. Further studies could explore other formulations or combination regimens to maximize the analgesic effect of these drugs.

Clinical symptoms were assessed using WOMAC scores, which showed significant improvement in the treatment group. This is consonant with earlier studies highlighting the superiority of glucosamine, chitosan, and phytoestrogens for functional benefit [36–38]. Reduction in WOMAC scores demonstrates that these molecules also hold potential in promoting mobility and activities of daily living in patients with OA. Rehabilitation of joint function is also directly associated with maximizing the quality of life in postmenopausal females, who are also predisposed to disability secondary to OA by virtue of hormonal changes and aging cartilaginous degeneration.

Glucosamine-chondroitin, chitosan, and phytoestrogen possess anti-inflammatory and chondroprotective properties and are useful to joint function in postmenopausal women with knee OA. This study employs a new panel of markers, sIL-6R, IL-10, and COMP. Pathway analysis was also conducted to explain the interventional effects and interaction between these markers. A double-blind randomized controlled trial (RCT) design is additionally used for further minimizing bias and hence reinforcing the reliability and solidity of the findings.

Paracetamol was included as standard symptomatic therapy because previous meta-analyses demonstrated its efficacy in mild to moderate knee OA pain and its favorable safety profile compared with long-term NSAID use [39]. Meanwhile, glucosamine-chondroitin, chitosan, and phytoestrogens were selected based on their potential anti-inflammatory and chondroprotective properties [7–10]. To our knowledge, studies evaluating the combined use of these agents remain limited. Therefore, this study provides preliminary evidence that the combination therapy may contribute to short-term reduction of inflammatory activity and clinical symptom severity, although no conclusions regarding disease-modifying effects can yet be made.

This study had several limitations, including the relatively small sample size and short follow-up duration, which may limit generalizability and prevent evaluation of long-term outcomes. In addition,the study relied primarily on clinical scores and biomarker analysis without radiographic or MRI assessment to evaluate structural cartilage changes in knee osteoarthritis.

CONCLUSION

Glucosamine-chondroitin, chitosan, and phytoestrogen combined with paracetamol can reduce the inflammatory process, as seen from sIL-6R; reduce the process of joint cartilage destruction, as seen from COMP; and improve joint functionality studied at short-term, as seen from significantly lower WOMAC scores compared to the control group. However, the VAS score had comparable outcomes between two groups. On the other hand, the treatment group showed a decrease in anti-inflammatory activity through a significant increase in IL-10, but lower than the control group. In contrast to the control group, the treatment group experienced chronically high IL-10 levels accompanied by substantially lower levels of IL-6, which suggests that glucosamine-chondroitin,

chitosan, and phytoestrogen play a role in assisting in anti-inflammatory functions through IL-10 pathways. Thus, there is a need for more studies on the anti-inflammatory pathway of glucosamine-chondroitin, chitosan, and phytoestrogen.

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

Funding *This study did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.*

Ethical Principles *The study was approved by the Research Ethics Committee of the Faculty of Medicine, Universitas Udayana (0340/UN14.2.2.VII.14/LT/2025), and informed consent was obtained from all participants.*

Informed Consent *Statement Informed consent was obtained from all participants.*

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Evaluation of quality of life in children and adolescents during treatment with Rigo – Cheneau type braces using the Russian version of the Brace Questionnaire

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Abstract

Introduction Special questionnaires recommended by SOSORT are used to study the quality of life (QoL) of children and adolescents undergoing brace treatment for scoliosis. One of them is the Brace Questionnaire (BrQ) which has undergone the stage of linguistic and cultural adaptation and validation in the Russian language.

Aim To reveal groups of patients with scoliosis requiring special attention during brace treatment using the BrQ which was validated in Russia.

Methods 405 patients that wore braces were surveyed with the automated BrQ. Changes in the domains and the overall quality of life score were statistically analyzed based on gender, age, duration of brace wear, and daily brace wear time. In 325 individuals, changes were tracked based on the magnitude of the main scoliotic curve.

Results Boys showed statistically significantly higher scores in the "Vitality" ($p = 0.05$) and "Bodily Pain" ($p = 0.03$) domains. A main trend was identified: a decrease in domain scores and the overall QoL score with increasing age, duration of brace wear, and magnitude of the main curve. Statistically significant differences in various domains were found between the study groups for these parameters. The dependence of scores on the daily brace wear time was their growth.

Discussion The identified trends in changes of domain scores and the overall QoL score in regard to increase in age, duration of brace wear, daily wear time, and the magnitude of the main curve are consistent with scientific literature data.

Conclusion Determination of the significance of differences revealed groups of patients requiring special attention during brace treatment for scoliosis. These are girls who have a lower QoL level in the "Emotional Functioning" and "Social Functioning" domains; middle and senior school-age children who show a decrease in the "General Health Perception", "Bodily Pain", "Self-Esteem and Esthetics", and "Social Functioning" domains. These are patients who wore a brace for 4 years or more: the "General Health Perception", "Emotional Functioning", and "Self-Esteem and Esthetics" domains decrease; and for the "Bodily Pain" domain, pain increased already after 2–3 years of brace use. A special group of patients are those who at the initial stage of brace wear had the lowest Quality of Life (QoL) scores. High grades of scoliosis significantly reduce the scores in the domains such as "General Health Perception", "Vitality", and "School Activity", while the "Social Activity" domain score is reduced with a curve more than 50°.

Keywords: spine, idiopathic scoliosis, quality of life, brace

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INTRODUCTION

Idiopathic scoliosis (IS) is a progressive disease associated with psychosocial consequences. Quality of life (QoL) in children and adolescents with IS can be affected by both scoliosis itself and therapeutic interventions, such as brace therapy. However, the impact of brace use on health-related QoL parameters in individuals with IS remains controversial. Some studies suggest that brace fixation does not have adverse effects on health-related QoL parameters in individuals with IS [1–4]. Other authors report that wearing a brace may result in various psychological reactions, such as negative thoughts, stress and anxiety, emotional instability, and impaired self-perception and self-esteem [5–8].

To effectively improve the quality of life of the individuals who wear a brace for a long time, it is necessary to use appropriate questionnaires to identify the factors that most significantly influence it. In 2006, Greek researchers developed a specialized questionnaire to study the quality of life of children and adolescents with scoliosis who are prescribed brace treatment: the Brace Questionnaire (BrQ) [9], which underwent linguistic and cultural adaptation and validation in Russian [10].

The **purpose** of the study was to use the BrQ questionnaire, validated in Russia, to identify groups of patients with scoliosis that require special attention during treatment with Rigaud – Cheneau braces.

MATERIALS AND METHODS

The study included school-age patients with idiopathic scoliosis ($n = 405$) who came for an outpatient appointment as they used Rigaud-Cheneau braces, modeled in the Rodin 4D software environment and manufactured using CAD/CAM technology from thermoplastics in the conditions of the prosthetic and orthopedic center "Scoliologic.ru" and the North-West Scientific and Practical Center for Rehabilitation and Prosthetics "Ortetika".

Their examination survey used the automated Russian-language BrQ questionnaire, integrated into the website of the prosthetic and orthopedic center "Scoliologic.ru". In addition to 34 questions from the BrQ questionnaire, the questionnaire included information on gender, age, total duration of brace use, and duration of daily bracing. Patients completed the questionnaire independently using a tablet in the waiting room before their appointment with an orthopedic specialist.

Patient groups by age were formed on the basis of pedagogical practice grouping [11]:

— Junior school age (6–10 years old);
— Middle school age (10–15 years old) that was divided into 2 subgroups: 10–13 year-old and 13–15year-old children;
— Senior school age (15–18 year old).

Groups by duration of bracing:

— one year,
— two–three years,
— four years and more.

Groups by daily period of bracing:

— Fewer than 8 hours,
— 8–14 hours,
— More than 15 hours.

Additionally, a random sample of 325 persons was selected, in whom changes in domain scores and overall QoL scores were monitored based on the grade of the main scoliosis curve. The scoliosis grade based on the main curve was determined in accordance with national clinical guidelines.

Groups of scoliosis grades:

— Grade II: 11–25°;

— Grade III: 26–40°;

— Grade IV: ⩾ 41° which was divided into 2 subgroups (< 50° and > 50°).

The BrQ contains 34 Likert scale items and covers eight domains to measure QoL in patients with adolescent IS who are on brace treatment:

1. General perception of health (questions 1, 2);

2. Physical functioning (questions 3–9);

3. Emotional functioning (questions 10–14);

4. Self-esteem and esthetics (questions 15, 16);

5. Vitality (questions 17, 18);

6. School activity (questions 19–21);

7. Bodily pain (questions 22–27);

8. Social functioning (oquestions 28–34).

Evaluation BrQ for questions 4, 5, 6, 12, 14, 15, 16 and 17:

— always: 5 points;

— most of the time: 4 points;

— sometimes: 3 points;

— almost never: 2 points;

— never: 1 point.

Evalution BrQ for questions 1. 2. 3. 7. 8. 9. 10. 11. 13. 18. 19. 20. 21. 22. 23. 24. 25. 26. 27. 28. 29. 30. 31. 32. 33 and 34:

— always: 1 point;

— most of the time: 2 points;

— sometimes: 3 points;

— almost never: 4 points;

— never: 5 points.

Calculation techniques: Each score is multiplied by 20, and the total score is divided by 34. Theoretically, the minimum score is 20 and the maximum is 100. A higher score indicates a better quality of life.

A subscale score can be calculated for each of the eight domains by dividing the total score of each domain by the number of items it comprises [9. 10].

The material was statistically processed to determine the significance of differences between the indicators of the groups.

Publication of the study was approved by the Ethics Committee of the Prosthetic and Orthopedic Center "Scoliologic.ru", based on the principles of the World Medical Declaration of Helsinki (Protocol No. 6 of August 25,, 2025). It presents the results of studies without identifying the patients which do not contradict the ethical standards of the World Medical Association Declaration of Helsinki "Ethical Principles for Scientific Research Involving Human Subjects" with the amendments of 2000 and the "Rules of Clinical Practice in the Russian Federation", approved by Order of the Ministry of Health of the Russian Federation dated June 19, 2003; No. 266. Study participants and their legal representatives are informed of the goals, methods, expected benefits of the study, and the risks and inconveniences associated with participation in the study.

RESULTS

The survey yielded data on 405 individuals, including 58 boys (14.3 %) and 347 girls (85.7 %). The subjects were 14.2 ± 1.7 years old, with the main group being middle school age (65.4 %). Spinal bracing started at the age of 11.98 ± 1.90 years for 2.47 ± 1.37 years with a daily brace fixation time of 15.00 ± 3.78 hours.

The domain scores and overall QoL scores by gender are presented in Table 1.

Table 1

Domain scores and overall QoL scores according to the BrQ questionnaire by gender and the significance of the differences

Domains	QoL score. points			*p* between M and F
	Gender		Means	
	M (*n* = 58)	F (*n* = 347)		
General health perception	3.56 ± 0.64	3.54 ± 0.68	3.54 ± 0.68	0.87
Physical functioning	4.00 ± 0.49	4.00 ± 0.49	4.00 ± 0.49	0.99
Emotional functioning	3.76 ± 0.63	3.64 ± 0.61	3.65 ± 0.62	0.30
Self-Esteem and Esthetics	3.53 ± 0.76	3.55 ± 0.75	3.55 ± 0.75	0.92
Vitality	3.67 ± 0.53	3.47 ± 0.71	3.50 ± 0.68	0.05
School activity	4.19 ± 0.59	4.21 ± 0.70	4.2 ± 0.69	0.86
Bodily pain	4.42 ± 0.43	4.24 ± 0.53	4.27 ± 0.52	0.03
Social functioning	3.88 ± 0.47	3.81 ± 0.61	3.82 ± 0.59	0.46
Total score, QoL	79.15 ± 6.55	77.71 ± 8.86	77.91 ± 8.53	0.26

Scores for the domains "General Health Perception", "Physical Functioning", "Self-Esteem and Esthetics", and "School Activity" were similar for boys and girls. Boys showed a slight predominance of scores for the domains "Emotional Functioning" and "Social Functioning". Boys also had statistically significantly higher scores for the domains "Vitality" ($p = 0.05$) and "Bodily Pain" ($p = 0.03$). These domain scores contributed to a higher overall QoL score in boys than in girls.

The domain scores and the overall QoL score according to the BrQ questionnaire were studied in regard to age (Table 2).

Table 2

Domain scores and overall QOL scores according to the BrQ questionnaire by age and the significance of the differences

Domains	QoL score, points				*p* between columns			
	Junior school age	Middle school age		Senior school age				
	6–10 years old (*n* = 16)	10–13 years old (*n* = 117)	13–15 years old (*n* = 148)	15–18 years old (*n* = 124)				
	1	2	3	4	1 & 2	1 & 4	2 & 3	3 & 4
General health perception	3.88 ± 0.59	3.71 ± 0.65	3.52 ± 0.65	3.38 ± 0.73	0.42	**0.03**	0.07	0.22
Physical functioning	3.71 ± 0.59	3.92 ± 0.50	4.09 ± 0.45	4.00 ± 0.49	0.29	0.15	**0.02**	0.24
Emotional functioning	3.85 ± 0.54	3.65 ± 0.61	3.64 ± 0.59	3.64 ± 0.66	0.29	0.26	0.91	0.95
Self-Esteem and Esthetics	4.03 ± 0.60	3.53 ± 0.78	3.68 ± 0.69	3.34 ± 0.80	0.02	**0.001**	0.21	**0.001**
Vitality	3.75 ± 0.56	3.42 ± 0.74	3.60 ± 0.71	3.42 ± 0.63	0.10	0.09	0.11	0.08
School activity	4.23 ± 0.73	4.20 ± 0.72	4.25 ± 0.59	4.15 ± 0.75	0.89	0.74	0.57	0.32
Bodily pain	4.65 ± 0.28	4.28 ± 0.55	4.31 ± 0.48	4.16 ± 0.53	**0.001**	**0.001**	0.72	0.07
Social functioning	4.23 ± 0.56	3.78 ± 0.58	3.83 ± 0.56	3.81 ± 0.62	**0.03**	**0.04**	0.56	0.85
Total score, QoL	81.62 ± 7.24	77.51 ± 8.51	78.75 ± 8.06	76.82 ± 8.89	0.11	0.07	0.36	0.18

The following patterns of change in domain scores depending on age were identified.

Scores for the "General Perception of Health" and "Vitality" domains decrease with increasing age. Scores for the "Physical Functioning" domain increase. It is noteworthy that a statistically significant decrease was observed for the "General Perception of Health" domain between junior and senior school-aged children ($p = 0.03$). An increase was observed for the "Physical Functioning" domain between the "10 to 13 Years Old" and "13 to 15 Years Old" groups of middle school-age children $p = 0.02$).

The "Emotional Functioning" domain scores slightly decrease, indicating an increase in potential experiences and anxieties associated with the brace. More significantly, statistically significantly, the "Bodily Pain" domain scores were observed in the junior and middle school age groups ($p = 0.001$), as well as in the junior and senior school age groups ($p = 0.001$). This should be interpreted as an increase in pain perceptions in IS patients with age.

Similar trends were revealed in the changes in the "Self-esteem and Esthetics" domain scores. A statistically proven decline in scores was observed between children of junior and middle school age ($p = 0.001$), as well as between children of middle and senior school age ($p = 0.001$).

The scores in the "Social Functioning" domain also declined. A significant difference was found between children of junior and middle school age ($p = 0.03$) and junior and senior school age ($p = 0.04$).

The scores of "School Activity" domain remain unchanged.

The highest overall QoL score is observed in junior school age children — (81.62 ± 7.24). In the group of children aged 10 to 13 years, the QoL level declines to (77.51 ± 8.51) points and in senior school age children it is (76.82 ± 8.89) points.

The domains and the overall QoL score were analyzed in regard to the overall duration of brace use (Table 3).

Table 3

Domain scores and overall QOL scores according to the BrQ questionnaire by duration of brace wear and the significance of the differences

Domains	QoL scores, points			*p* between columns		
	1 year ($n = 159$)	2–3 years ($n = 162$)	⩾ years ($n = 84$)			
	1	2	3	1 & 2	1 & 3	2 & 3
General health perception	3.75 ± 0.63	3.44 ± 0.70	3.36 ± 0.73	**0.001**	**0.001**	0.51
Physical functioning	4.03 ± 0.49	4.01 ± 0.49	3.94 ± 0.50	0.79	0.29	0.41
Emotional functioning	3.79 ± 0.51	3.62 ± 0.68	3.45 ± 0.64	0.06	**0.001**	0.12
Self-Esteem and Esthetics	3.70 ± 0.77	3.55 ± 0.75	3.23 ± 0.68	0.16	**0.001**	**0.01**
Vitality	3.54 ± 0.69	3.51 ± 0.69	3.40 ± 0.65	0.80	0.24	0.36
School activity	4.24 ± 0.66	4.13 ± 0.72	4.27 ± 0.65	0.27	0.76	0.22
Bodily pain	4.34 ± 0.47	4.17 ± 0.58	4.31 ± 0.47	**0.03**	0.68	0.12
Social functioning	3.88 ± 0.54	3.77 ± 0.64	3.81 ± 0.57	0.21	0.51	0.69
Total score, QoL	79.45 ± 7.67	77.08 ± 9.46	76.60 ± 7.97	0.06	**0.04**	0.75

The scores for the "General Health Perception", "Emotional Functioning", and "Self-Esteem and Aesthetics" domains decrease with longer duration of bracing. It is noteworthy that a highly significant difference in scores for the "General Health Perception" domain was observed between the "one year" and "more than four years" bracet use groups ($p = 0.001$), as well as between the "one year" and "two to three years" groups ($p = 0.001$).

Similar significance of differences was revealed in the parameter "Emotional functioning" domain between the "one year" and "more than four years" groups ($p = 0.001$).

In the domain "Self-Esteem and Aesthetics", a high level of significance of differences was found between the "one year" and "more than four years" groups ($p = 0.001$) and a less significant difference between the "one year" and "two to three years" groups ($p = 0.01$)

No significant differences were found in the domain scores for "Physical Functioning", "Vitality", "Social Functioning", and "School Activity" based on the duration of brace use.

The scores of the "Bodily pain" domain significantly show that patients who used a brace for two to three years give more affirmative answers about feeling pain than patients who wore a brace for one year ($p = 0.03$). And the QoL scores of patients who used a brace for four years or more are practically comparable with the patients who wore braces for one year. The highest overall QoL score (79.45 ± 7.67) is observed in use period of one year. If the period of use was two to three years the score decreased by two units or more (77.08 ± 9.46). The lowest QoL score (76.60 ± 7.97) was noted in the period of four years or more. Moreover, significant differences were found between the "one year" and "four years or more" groups ($p = 0.04$).

The domain scores and the overall QoL score according to the BrQ questionnaire based on the daily time of brace fixation and the significance of differences are presented in Table 4.

Table 4

Domain scores and the overall QoL score according to the BrQ questionnaire based on the daily time of brace fixation and the significance of differences

Domains	Qol scores, points			*p* between columns		
	< 8 hours per day (*n* = 14)	8–14 hours per day (*n* = 122)	⩾15 hours per day (*n* = 269)			
	1	2	3	1 & 2	1 & 3	2 & 3
General health perception	3.61 ± 0.54	3.48 ± 0.63	3.57 ± 0.71	0.58	0.86	0.36
Physical functioning	3.72 ± 0.48	3.98 ± 0.49	4.03 ± 0.49	0.13	0.07	0.44
Emotional functioning	3.31 ± 0.56	3.65 ± 0.61	3.67 ± 0.62	0.11	0.08	0.78
Self-Esteem and Esthetics	3.11 ± 0.77	3.32 ± 0.81	3.67 ± 0.72	0.46	**0.05**	**0.001**
Vitality	3.21 ± 0.53	3.50 ± 0.57	3.52 ± 0.73	0.16	0.13	0.82
School activity	3.90 ± 0.82	4.26 ± 0.70	4.20 ± 0.67	0.24	0.32	0.52
Bodily pain	3.95 ± 0.70	4.26 ± 0.44	4.29 ± 0.54	0.22	0.18	0.70
Social functioning	3.65 ± 0.75	3.85 ± 0.60	3.82 ± 0.57	0.44	0.52	0.67
Total score, QoL	72.65 ± 9.58	77.65 ± 8.18	78.31 ± 8.53	0.15	0.10	0.59

The lowest scores in the domains "Physical Functioning", "Emotional Functioning", "Self-Esteem and Esthetics", "Vitality", and "School Activity" were observed with a daily bracing period of less than eight hours. This group primarily includes patients who adapt to brace wear. With longer corset use, these scores grow. Significant differences were found between the "less than eight hours" and "more than 15 hours" groups ($p = 0.03$) and between the "8–14 hours" and "more than 15 hours" groups ($p = 0.001$).

The scores for the General Health Perception and Social Functioning domains remain almost unchanged.

The "Bodily Pain" domain score increased slightly, indicating a decrease in pain as the patient adapts to the brace.

The lowest overall QoL score is observed with a daily bracing period of less than eight hours (72.65 ± 9.58). During other periods, the QoL score increases. The highest score (78.31 ± 8.53) is noted with a brace fixation duration of 15 hours or more per day.

The results of a survey of 325 children and adolescents were compared with data from a medical database on the magnitude of the Cobb angle of the main deformity curve (Table 5).

Table 5

Domain scores and the overall QoL score according to the BrQ questionnaire based on scoliosis grade and the significance of differences

Domains	QoL scores, points				*p* between columns				
	Grade II Main curve 11–25° (*n* = 89)	Grade III Main curve 26–40° (*n* = 121)	Grade IV Main curve 41° and more						
			< 50° (*n* = 46)	> 50° (*n* = 69)					
	1	2	3	4	1 & 2	1 & 4	2 & 3	2 & 4	3 & 4
General health perception	3.78 ± 0.57	3.55 ± 0.75	3.61 ± 0.70	3.30 ± 0.61	**0.05**	**0.001**	0.69	0.07	0.06
Physical functioning	4.09 ± 0.39	4.07 ± 0.49	3.97 ± 0.51	3.97 ± 0.52	0.76	0.20	0.35	0.30	0.99
Emotional functioning	3.80 ± 0.57	3.68 ± 0.61	3.52 ± 0.64	3.66 ± 0.56	0.22	0.23	0.25	0.87	0.36
Self-Esteem and Esthetics	3.61 ± 0.75	3.50 ± 0.76	3.59 ± 0.75	3.51 ± 0.71	0.44	0.53	0.63	0.94	0.69
Vitality	3.66 ± 0.57	3.42 ± 0.74	3.40 ± 0.67	3.59 ± 0.67	**0.04**	0.55	0.90	0.22	0.26
School activity	4.40 ± 0.56	4.14 ± 0.73	4.17 ± 0.74	4.22 ± 0.64	**0.02**	0.12	0.83	0.53	0.80
Bodily pain	4.37 ± 0.43	4.26 ± 0.52	4.25 ± 0.55	4.22 ± 0.54	0.22	0.15	0.94	0.68	0.80
Social functioning	3.92 ± 0.52	3.82 ± 0.59	3.61 ± 0.68	3.95 ± 0.58	0.32	0.79	0.15	0.26	**0.03**
Total score, QoL	80.36 ± 6.91	77.97 ± 8.82	76.41 ± 9.32	77.94 ± 8.35	0.10	0.15	0.47	0.98	0.51

No statistically significant changes were found in the domains "Physical Functioning", "Emotional Functioning", and "Self-Esteem and Esthetics".

In the "General Health Perception" domain, a significant reduction in scores was observed between the groups with grades II and III scoliosis ($p = 0.05$). The most significant reduction was between the groups with grade II and grade IV scoliosis with an angle greater than 50° ($p = 0.001$).

The scores of "Viability" and "School Activity" domains also reduced with increasing curve magnitude, with a significant decrease between the groups with grades II and III scoliosis ($p = 0.04$ and $p = 0.02$, respectively).

A similar tendency was identified for "Social Activity" domain; significant differences were found between the scores of the "less than 50°" and "more than 50°" degree scoliosis subgroups IV ($p = 0.03$).

The "Bodily Pain" domain scores decrease with increasing curve, indicating an increase in pain as the severity of the deformity increases. However, this was not statistically confirmed.

The overall quality of life score also decreased statistically insignificantly.

Thus, the main trend is a decrease in domain scores and the overall QoL score as age, duration of brace use, and the main curve grow.

An increase in the domain score and the overall quality of life score was revealed as the duration of daily brace fixation grew.

DISCUSSION

International scientific societies that study scoliosis (SOSORT, SRS) place considerable emphasis on patient-subjective assessment of QoL conducted with various questionnaires. The most informative of these, in terms of brace treatment, are the specific Greek BrQ questionnaire, validated in Russia, and the Italian ISYQOL questionnaire, which has not yet undergone language adaptation and validation in Russia.

Our findings on higher QoL in boys with IS are confirmed by a study of Italian scientists [12]. Moradi et al. noted that for girls with IS undergoing brace treatment, body appearance and shape are of great importance and may affect their social relationships [13]. Our data indicate that boys show a slight predominance of scores in the domains of "Emotional Functioning" and "Social Functioning". However, statistically significantly higher scores in boys are found in the domains of "Viability" ($p = 0.05$) and "Bodily Pain" ($p = 0.03$).

The data on the domain scores and the overall QoL score based on age were confirmed by the study by Korovessis et al. [6], who showed that compliance with bracing is higher in junior school-age children than in senior school-age adolescents. Indeed, the scores of the domains "General Perception of Health", "Emotional Functioning", "Vitality", "Self-Esteem and Esthetics", and "Social Functioning" decrease as age increases. However, the significance of differences in the indicators of the "Physical Functioning" domain increases between the groups of middle school-age children: from 10 to 13 years old and from 13 to 15 years old ($p = 0.02$). It should be noted that with age, a reduction in the scores of the "Bodily Pain" domain is observed. This is especially significant in the groups of junior and middle school age ($p = 0.001$). as well as junior and senior school age ($p = 0.001$) which indicates an increase in pain sensations with age. The highest overall quality of life indicator is observed in junior school age — (81.62 ± 7.24).

According to Moradi et al., the scores of school activity and social functioning according to the BrQ questionnaire were better in the participants aged 13 years than in the participants over 13 years old [13]. Our data on the "School Activity" domain do not support this statement. The scores of the "Social Functioning" domain significantly decrease in the groups of children of junior and middle school age ($p = 0.03$) and junior and senior school age ($p = 0.04$) what confirms the data obtained earlier.

The study by Babaee et al. on the effect of the brace fixation duration on QOL showed that at the early stage of wearing a brace, adolescents with IS may experience emotional stress and psychological reactions that affect their self-esteem [5]. However, after the initial shock caused by its use, children adapt to it, and the problems cease. In support of these data, we found that the scores in the "Bodily Pain" domain significantly show that patients who used a brace for two to three years give more affirmative answers about feeling pain than patients who wore a brace for one year ($p = 0.03$). And the group of patients who used a brace for four years or more is practically comparable in scores with the group who used it for one year. However, we found that the scores in the "General Perception of Health", "Emotional Functioning", and "Self-Esteem and Aesthetics" domains decrease as brace fixation duration increases. The highest overall QoL score (79.45 ± 7.67) was found in a period of one year use. If the fixation period was two to three years, the score lowers by two units or more: (77.08 ± 9.46). The lowest QoL scorer (76.60 ± 7.97) was found if the brace use period was four years or more. Moreover, significant differences were found between the "one year" and "four years or more" groups ($p = 0.04$).

Moradi et al. noted that there is a significant relationship between the BrQ domain "Emotional Functioning" and compliance with the brace treatment regimen [13]. Patients with a higher compliance with the brace fixation regimen had worse emotional functioning scores. The present study did not confirm these findings. On the contrary, the lowest scores of the domains "Physical Functioning", "Emotional Functioning", "Self-esteem and Esthetics", "Vitality", "School Activity" and the overall QoL scores (72.65 ± 9.58) were noted with a duration of daily brace fixation of less than eight hours. This group mainly includes patients who are at the stage of adapting to the brace. This is consistent with the data of MacLean et al. [14], who described the initial period of wearing braces as stressful in 84 % of patients, and with the data of Chan et al. who showed that the overall QoL score on the BrQ scale in the group with daily brace fixation for 0–8 hours was 16.28 lower than in the group with daily fixation for 17–23 hours [15]. The scores for the "General Perception of Health" and "Social Functioning" domains remained unchanged while the "Bodily Pain" score increased slightly, indicating a relief in pain as patients got used to the brace.

We have determined that as the main curve increases, the overall QoL score decreases. However, the statistical significance of these changes could not be proven. This result is confirmed by the study of Aulisa et al., in which QoL indicators correlate with the severity of curvature [12]. In their works, Kaya et al. and Asher et al. also show that the severity of scoliosis affects the QoL of IS patients [16, 17]. In the present study, it was found that the most pronounced changes are in the parameters of the "Viability" and "School Activity" domains. As the magnitude of the curve increases, they decrease. Moreover, the difference is significant between the groups with scoliosis

grades II and III ($p = 0.04$ and $p = 0.02$, respectively). A similar trend was revealed for the "Social Activity" domain. Moreover, significant differences were found between the subgroups of grade IV scoliosis (less than 50° and more than 50°, $p = 0.03$).

We compared the number of affirmative responses to several BrQ questions in the Spanish language in the sample published by Piantoni et al. [18] with our own data. Table 6 presents questions with significant differences in the number of affirmative responses.

Table 6

The number of affirmative answers of respondents to BrQ questions in the Argentinean and Russian samples

N of question	Questions	Affirmative answers, %	
		Piantoni et al. [18]	Our data
Emotional functioning			
12.	You felt happy?	24	64.7
14.	You believed that brace treatment was beneficial?	39	87.4
15.	You felt proud of yourself?	18	52.1
16.	You were satisfied with you body?	27	53.4
Physical functioning			
5.	You managed the brace without any help?	50	86.4
6.	You managed to take off the brace without any help?	50	94.4
Social functioning			
31.	You ad problems with your family?	42	26.2
32.	You believed that your relationship with your family or your friends would be better if you were not on brace?	50	30.4
33.	You stayed at home because yiu were ashamed?	42	25.7
Bodily pain			
23.	You had pain during the night?	55	20.8
24.	You had pain when walking?	47	27.4
25.	You had pain when sitting?	58	38.5
26.	You had pain when climbing stairs?	43	16.3
School activity			
19.	You had difficulties with your lessons?	48	27.4
20.	You were absent from schoool?	35	16.3
21.	You found it hard to pay attention in the classroom?	36	27.4

The table shows that Russian children and adolescents undergoing conservative treatment with braces feel more confident in emotional functioning. It is noteworthy that 87.4 % of the children we surveyed responded affirmatively to the question, "Did you think that brace treatment helped you?", which can be considered a success of teamwork. The survey on the "Physical Functioning" domain showed that fewer affirmative answers were given in the Russian population to the questions, "Did you feel tired while walking?" and "Were you unable to eat or breathe well?" To questions related to problems of putting on and taking off a brace, the patients of the prosthetic and orthopedic centers "Skoliologic.ru" and "Ortetika" also overwhelmingly responded that they did not experience such problems.

Training in brace putting on and taking off is a priority for our specialists. In the "Social Functioning" domain, responses from Russian children and adolescents indicate that they feel more confident in social settings. However, the questions "Did you feel different from your peers?" and "Did you wear bulky clothing that concealed your brace?" yielded identical responses in both studies. A lower percentage of affirmative responses was also given by Russian children and adolescents to the questions related to the "Bodily Pain" domain. However, the responses to the question "Did you feel tingling in your arms and legs?" were identical. Regarding questions related to the "School Activity" domain, the trend persists. Our own data demonstrate a lower number of affirmative responses. Thus, the overall QoL score in the present study is 77.9 points, compared to 63.7 points in the Argentinean study.

Figure 1 presents our own data on the average values of domain scores in comparison with data from the scientific literature presented in the works of Aulisa et al. [19], Deceuninck et al. [20], Kinel et al. [21] and Peeters et al. [22]. The diagram shows that: that the values do not differ significantly from each other. The same can be said about the overall quality of life: Russia — 77.9 points; Poland — 77.1 b.; Italy — 78.8 b.; France — 76.0 b.; Denmark — 75.9 b.

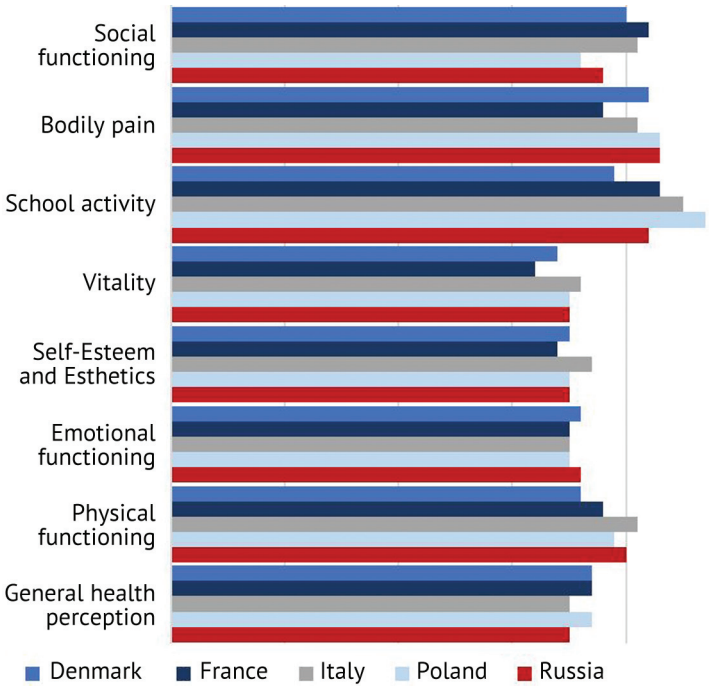

Fig. 1 Comparison of our own data (Russia) on average values of domain indicators with data from scientific literature

CONCLUSION

The results of our study show that children and adolescents rate their quality of life at 77.9 points out of a possible 100 when they are treated with bracing for idiopathic scoliosis.

The following trend was identified: at the beginning of brace treatment, as the duration of daily brace use increases, QoL scores grow as the patient becomes accustomed to the brace, suggesting a reduction in initial stress at the initial stage of treatment. However, after prolonged treatment over many years, QoL scores decrease due to psychological fatigue from the treatment.

The study showed that girls require special attention from the specialist team during brace treatment, as their quality of life declines more significantly, particularly in the "Emotional Functioning" and "Social Functioning" domains.

More attention should be paid to middle school age and senior school age children, who show significantly lower scores in the domains "General Perception of Health", "Bodily Pain", "Self-Esteem and Esthetics", and "Social Functioning".

Patients who wear a brace for four years or more should be the focus of specialists' attention due to significantly declining scores in the domains "General Health Perception", "Emotional Functioning", and "Self-Esteem and Esthetics". In the "Bodily Pain" domain, pain sensations are increased after two to three years of brace use.

Patients at the initial stage of brace corset use should be specially cared as they have the lowest QoL scores.

High grades of scoliosis significantly reduce scores in the "General Perception of Health", "Vitality", and "School Activity" domains. Scoliosis scores in the "Social Activity" domain decrease significantly at curves greater than 50°.

Conflict of interest *The authors declare no potential conflicts of interest related to the this study.*

Source of funding *The study was conducted without additional funding.*

Ethical approval *Publication of the study was approved by the Ethics Committee of the Prosthetic and Orthopedic Center "Scoliologic.ru" (Protocol No. 6 dated August 25, 2025). The study results are presented without identifying the patients. Study participants and/or their legal representatives signed informed consent for publication of the results.*

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Evaluation of the condition of adolescent patients with spastic types of cerebral palsy admitted for orthopedic surgery: a cross-sectional study

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Abstract

Introduction Cerebral palsy (CP) is the most common neurological disorder in children, associated with movement disorders. The maximum age for reconstructive surgery is twelve years, but the optimal age for maintaining the results of multi-level orthopedic interventions is considered to be the second half of the adolescence period. Analysis of established orthopedic impairments and their impact on gait, as well as their characteristics depending on previous interventions, is of interest for determining the optimal conditions for reconstructive surgery on the lower extremities in adolescents.

The **purpose** of this study was to evaluate the kinematic and kinetic gait parameters of adolescents with cerebral palsy (GMFCS I–III) before orthopedic surgery using a cross-sectional comparative analysis. The null hypothesis was the absence of differences in gait parameters between patients with previous orthopedic surgery and those who did not undergo it.

Materials and methods This retrospective study included 102 adolescents aged 13–17 years with cerebral palsy, divided into two groups: Group A (GMFCS I–II, $n = 63$) and Group B (GMFCS III, $n = 39$). Three subgroups were identified in each group based on surgical history. All patients underwent computer video gait analysis. The gait analysis presents the parameters as medians with a percentile distribution level of 25 %–75 %. The unpaired Wilcoxon test ($p \leqslant 0.05$) was used for comparison. The relationship between the parameters was assessed using Spearman's rank correlation. The chi-square test for binary samples was used to compare the incidence of the crouch gait pattern.

Results Gait characteristics revealed a predominance of horizontal movement disorders (due to torsional deformities) in previously unoperated GMFCS I–II patients, while the prevalence of crouch gait increased in the remaining subgroups. An increase in decompensated crouch gait patterns was observed in the subgroups of patients who underwent early triceps surae interventions. A significant difference was found between groups 1A and 2A in the incidence of decompensated crouch gait (chi-square test, $p = 0.002$). No significant differences were found between the other subgroups.

Discussion The systemic nature of motor impairments in children with cerebral palsy and the resulting orthopedic disorders, necessitate not only the assessment and monitoring of individual orthopedic impairments of the lower extremity locomotor chains but also the consideration of integrated movement indices (GPS), as well as kinematic and kinetic data in their interrelationships.

Conclusion In patients with GMFCS levels I–II and no previous orthopedic interventions, indications for surgical treatment are determined by joint contractures and torsional deformities of the lower extremity segments. In patients with GMFCS level III, the crouch gait pattern, which remains compensated, predominates in adolescence. In the group of patients with triceps surae lengthening performed at an early age, the development of compensated and decompensated types of crouch gait with high-energy movements was observed. This should be taken into account both when choosing a surgical treatment strategy and during subsequent rehabilitation measures and orthotics. In adolescents with previous multilevel interventions, torsional deformities, recurrent contractures, and the development of knee flexion remained indications for surgical treatment. However, the spatiotemporal and strength characteristics of movements remained relatively high.

Keywords: spastic diplegia, cross-sectional study, crouch gait, adolescents

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INTRODUCTION

Cerebral palsy (CP) is the most common neurological disorder in children, characterized by motor impairment [1]. There is significant heterogeneity in CP manifestations, such as issues of etiology, clinical manifestations, movement and postural impairments, functional severity, and the evolution of impairments, including the development of orthopedic complications [2, 3]. This heterogeneity complicates monitoring of patient condition, particularly in terms of the evolution of impairments over a long period of time.

On average, 50–80 % of children with cerebral palsy develop walking ability [4]. However, they exhibit a wide range of deviations in both kinematic and kinetic parameters. Computerized gait analysis is recognized as a comprehensive objective test for gait assessment, allowing for the reliable monitoring of movement evolution throughout the observation period [1, 5].

A factor leading to reduction in the motor abilities of children with cerebral palsy, even to the loss of independent mobility, is the development of secondary orthopedic complications [6]. The method of multilevel surgical interventions is currently recognized and remains the most effective method for correcting these secondary orthopedic problems [7, 8].

Graham et al., summarized their clinical experience and distinguished two periods coinciding in age (4–12 years), when the place of orthopedic surgery becomes justified: the period of contractures and the period of bone deformities [9]. During these periods, the nature of orthopedic surgery is reconstructive, and palliative elements of operations (arthrodesis, reorienting osteotomies) have not yet found their indications. The publications of Shore et al. [10], Thomason et al. [11], Gough et al. [12] emphasized that the maximum age for reconstructive orthopedic interventions on the lower extremities is an age period of no older than 12 years. On the other hand, the optimal age for performing multilevel interventions is recognized as the period of the second half of pubertal growth acceleration (13-16 years), when the risk of recurrence of orthopedic problems decreases [13, 14]. Putz et al. [15] indicate a significant decrease in the effect of multilevel interventions when performed in childhood. Other authors show the stability of the positive effect of multilevel interventions, but only after a two-year interval [16]. Thus, there is a dissonance: the maximum age for reconstructive interventions is twelve years but the optimal age for maintaining the results of multilevel orthopedic interventions is the second half of adolescence.

Furthermore, there is a large cohort of patients in whom indications for surgery are identified quite late, in adolescence [17, 18]. The initial stage in determining the optimal conditions for performing reconstructive surgery on the lower extremities in adolescents is an analysis of developed orthopedic disorders and their impact on gait, as well as their characteristics based on previous interventions.

The **purpose** of this study was to evaluate the kinematic and kinetic gait parameters of adolescents with cerebral palsy (GMFCS I–III) before orthopedic surgery using a cross-sectional comparative analysis. The null hypothesis was the absence of differences in gait parameters between patients with previous orthopedic surgery and those who did not undergo it.

MATERIALS AND METHODS

This retrospective study included 102 patients with spastic cerebral palsy who underwent bilateral multilevel orthopedic intervention.

Inclusion criteria:

— Age of the second half of adolescence from 13 years until 18 years;

— Possibility to evaluate the results of computer gait analysis for levels of global motor function impairment I, II, III GMFCS;

— Interval of at least six months after a session of botulinum therapy;

— No history of selective dorsal rhizotomy;

— Interval of at least three years after the last orthopedic surgery on the lower extremities.

Exclusion criteria: more severe levels of global motor impairment; insufficient or absent instrumental gait analysis; age at the time of multilevel intervention under 13 years and older than 18 years.

According to the level of impairment of global motor functions, patients were divided into two groups: group A (GMFCS I–II, $n = 63$) and group B (GMFCS III, $n = 39$).

Within each group, based on surgical history, patients were divided into three subgroups:

— 1A and 1B — patients who did not have previous surgical interventions on the muscular system of the lower extremities;

— 2A and 2B — patients who underwent interventions on the triceps of the lower legs (lengthening of the Achilles tendon or percutaneous "minimally invasive" fibromyotenotomy) at an early age;

— 3A and 3B — patients who underwent multilevel orthopedic interventions.

In addition to the clinical and radiological examination, the patients underwent computer gait analysis, during which they walked barefoot independently or held a parent's hand on a seven-meter path at their usual walking speed. Kinematic data was recorded using Qualisys 7+ optical cameras with passive marker video capture technology; synchronized with six KISTLER dynamometer platforms (Switzerland). The IOR model was used for setting markers. Analysis of kinematics and kinetics was carried out with the QTM (Qualisys) and Visual3D (C-Motion) featuring automated calculation of values. The results of a previously conducted gait analysis in a cohort of children without motor disorders were used as the norm for the corresponding age-related parameters [19].

The AtteStat 12.0.5 program (© 2002–2025 Igor Gaydyshev) was used for statistical processing. Population indicators are presented as mean values with standard deviation. The study of the hypothesis of compliance of quantitative gait parameters with a normal distribution using the Kolmogorov criterion at a significance level of $\leqslant 0.05$ showed that the normality hypothesis is rejected. For this reason, in sample populations (identified subgroups), gait analysis indicators are presented as a median with a percentile distribution level of 25 % ÷ 75 %. The statistical significance of differences was determined using the unpaired Wilcoxon test with a significance level of $p \leqslant 0.05$. The relationship between parameters was assessed using Spearman's rank correlation. To compare the incidence of the "crouch gait pattern", the chi-square test for binary samples was used.

The study received approval from the Ethics Board of the Ilizarov National Medical Research Center of Traumatology and Orthopedics. The study was conducted in accordance with the ethical standards of the World Medical Association's Declaration of Helsinki, "Ethical Principles for Medical Research Involving Human Subjects", as amended in 2000, and the "Rules for Clinical Practice in the Russian Federation", approved by Order No. 266 of the Russian Ministry of Health dated June 19, 2003. The parents of the children participating in the study provided informed consent for publication of the results and were present during the gait analysis test.

RESULTS

The distribution of demographic characteristics and gait types of patients by subgroups is presented in Table 1.

The data in Table 1 show no differences in age, gender, or body mass index (BMI) between the patient subgroups. Regarding gait characteristics, we note a predominance of horizontal movement disorders (due to torsional deformities) in previously unoperated GMFCS level I–II patients, while the proportion of crouch gait patterns increased in the remaining subgroups. An evident increase in the proportion of decompensated crouch gait patterns was observed in the subgroups of patients

following early triceps surae interventions. A significant difference was found between subgroups 1A and 2A in the incidence of decompensated crouch gait (chi-square test, $p = 0.002$). There were no significant differences in this criterion between the other subgroups.

Table 1

Patients' characteristics

Parameter	GMFCS I–II			GMFCS III		
	1A	2A	3A	1B	2B	3B
Number of patients	29	21	13	12	15	12
Age, years	14.9 ± 1.2	15.2 ± 1.3	15.4 ± 1.98	14.6 ± 1.3	14.9 ± 1.5	15.1 ± 2.4
Sex F/M	13/16	9/12	5/8	5/7	9/6	7/5
BMI	17.9 ± 3.9	19.4 ± 2.8	18.4 ± 3.22	19.3 ± 4.2	20.2 ± 3.7	19.6 ± 2.8
Type of gait						
Equinus gait with rotational disorders	4	1	3	–	–	–
Jump gait with rotational disorders	10	3	1	2	2	–
Apparent equinus	2	1	–	1	–	–
Crouch gait compensated	12	7	3	7	5	5
Crouch gait decompensated	1	4	1	2	4	1
Crouch gait+stiff knee gait	–	5	–	–	2	1
Rotational disorders, isolated	–	–	4	–	1	–
Calcaneal gait and rotational deviations	–	–	1	–	–	–
Rotational deviations and stiff knee gait	–	–	–	–	1	2
Flexed knee and rotational deviations	–	–	–	–	–	3

The comparison of the spatiotemporal characteristics of gait (Table 2) between the subgroups of patients of GMFCS level I–IIb revealed that the worst parameter values were observed in subgroup 2A (early isolated lengthening of the triceps surae): gait speed and swing period length are significantly lower, swing width and duration of the double-support phase were increased, which reflects instability of body position.

Table 2

Gait index, spatio-temporal characteristics of gait

Parameter	GMFCS I–II			GMFCS III		
	1A	2A	3A	1B	2B	3B
Gait index (GPS — gait profile score), °	12 (10.7÷15.6)	14.9 (13.68÷17.43)*	12.1 (11.4÷13.7)	20.2 (16.0÷23.9)	16.1 (15.0÷18.9)	14.5 (14.3÷15.9)*[1]
Speed, m/sec	0.93 (0.67÷1.05)	0.65 (0.53÷0.84)*	0.84 (0.66÷1.0)[1]	0.71 (0.58÷0.78)	0.65 (0.44÷0.76)	0.42 (0.38÷0.49)*[1]
Swing length, m	1.03 (0.85÷1.12)	0.84 (0.68÷0.95)*	0.95 (0.86÷1.07)[1]	0.8 (0.76÷0.91)	0.78 (0.56÷0.93)	0.74 (0.57÷0.79)
Step width, m	0.13 (0.1÷0.18)	0.17 (0.14÷0.19)*	0.17 (0.14÷0.23)*[1]	0.14 (0.135÷0.16)	0.15 (0.14÷0.18)	0.19 (0.17÷0.20)*[1]
Number of gait cycles/min	53.5 (48.4÷59)	51.5 (47.85÷55.45)	53.5 (51.65÷56.38)	51.4 (42.4÷55.6)	47.6 (41.6÷54.2)	39.8 (29.2÷46.3)*[1]
Duration of stance from the gait cycle duration, %	62.8 (61.85÷66.55)	65.7 (64.15÷72.35)*	64.1 (62.7÷67.45)[1]	64.1 (62.1÷68.9)	69.0 (66.3÷72.9)*	72.1 (68.0÷76.8)*
Duration of swing from the gait cycle duration, %	36.9 (33.13÷38.28)	33.9 (27.65÷35.48)*	35.9 (32.8÷37.6)[1]	35.4 (30.9÷38.3)	31.1 (27.4÷33.9)*	27.8 (22.4÷31.9)*
Duration of double support phase from the gait cycle duration, %	25.9 (24.85÷31.23)	32.3 (28.18÷44.98)*	29.7 (26.7÷32.8)*[1]	29.8 (26.2÷35.9)	36.7 (30.4÷46)*	39.1 (36.4÷45.2)*

Note: * — significant differences with subgroup 1A at the same GMFCS level; [1] — significant differences between groups 2 and 3 at the same GMFCS level

The parameters in subgroup 2A (GMFCS III) reflect a regular degradation of walking parameters, correlating with the development of the crouch gait pattern: a significant increase in the movement disorder index (GPS), step width and duration of the double-support period while maintaining a relatively high walking speed.

In regard of comparing gait speed and GPS, the combination of low GPS values and comparatively slow gait speed in patients with previous multilevel interventions (subgroup 3B) is interesting. While they walk more slowly, their lower limb joint movements (amplitude and distribution) are closer to normal.

Kinematic data (Table 3) in Group 1 (GMFCS I–II) characterize the development of the crouch gait pattern predominantly in patients after isolated triceps lengthening in the early period: a contineous position of the foot in dorsiflexion, excessive flexion of the knee joint both at the moment of initial contact and in the support phase (with a maximum average flexion of 35.6° at point G1), which is accompanied by a significant decrease in the range of motion in the joint throughout the entire gait cycle compared to subgroups 1A and 3A. Also noteworthy is the decrease in the range of plantar flexion at the moment of push-off in subgroup 3A and its absence in subgroup 2A. The placement of the foot in the plantar flexion position at the initial contact and the significantly increased range of rotational movements in subgroup 1A compared to subgroups 2A and 3A indicate the predominance of the features of the jump gait and equinus gait patterns in patients who have not previously undergone surgery.

Table 3

Several kinematic parameters

Parameter	GMFCS I–II			GMFCS III		
	1A	2A	3A	1B	2B	3B
Foot position at initial contact (Г0), °	−2.5 (−9.1÷4.4)	6.4 (1.7÷10.8)*	5.7 (0.3÷7.1)*	5.1 (−2.8÷9.75)	7.9 (2.6÷10.5)	−1.1 (−7.5÷3.1)[1]
Maximum dorsal flexion in support phase (Г2), °	13.1 (7.3÷15.9)	17.9 (13.7÷24.4)*	15.3 (10.7÷19.6)	19 (9.9÷24.14)	24.5 (14.9÷29.8)	11.7 (8.8÷13.98)[1]
Maximum plantar flexion in propulsion (Г3), °	−7.4 (−17.7÷−0.6)	4.8 (−0.95÷9.95)*	0.3 (−6.9÷6.5)*	−5.3 (−11.2÷7.58)	1.8 (−4.4÷9.05)*	−3.1 (−7.4÷2.95)
Foot position in swing phase (Г4), °	5.9 (−3.5÷13.9)	14.6 (9.7÷19)*	11.8 (6.2÷14.5)	11.4 (1.98÷15.95)	13.2 (7.7÷18.4)	3.3 (−0.6÷12.3)[1]
Knee position at initial contact (K0), °	21.7 (14÷30)	33 (28.3÷40.2)*	22.2 (16.6÷26.7)[1]	46.9 (29.85÷55.3)	45.9 (29.2÷48.7)	28.7 (25.1÷35.2)*[1]
Maximum knee flexion in support phase (K1), °	28.6 (22.7÷33.2)	35.6 (31.9÷43.4)*	28.3 (19.2÷31.5)[1]	52.3 (30.8÷56.9)	47.9 (26.7÷52.0)	31.4 (29.2÷35.1)*[1]
Maximum knee extension in support phase (K2), °	9.5 (5.4÷15.4)	22.7 (14.8÷31.3)*	5.4 (1.6÷10.7)[1]	35.9 (22.8÷45.4)	33.7 (10.4÷41.7)	9.6 (1.38÷21.6)*[1]

In Group 2 (GMFCS III), excessive knee flexion at initial contact was observed in all subgroups, but was least pronounced in subgroup 3B. Sufficient plantar flexion of the foot during propulsion was present only in subgroups 1B and 3B, indicating preserved plantar flexor function, unlike in subgroup 2B. Maximum knee extension during the support phase can be considered sufficient only in subgroup 3B and reflects the effectiveness of previously performed multilevel interventions to correct sagittal plane movement disorders. However, a significant increase in pelvic and femoral rotational movements in this same subgroup indicates persistent torsional deformities of the lower extremity segments and the presence of indications for their correction. Non-operated patients and patients after early interventions on the triceps muscles of the lower legs show significant elements of the crouch gait pattern (excessive flexion in the knee joint in the support phase) or completed formation of this pattern.

Kinetic data (Table 4) show the maintenance of a sufficient level of plantar flexor strength after multilevel interventions in subgroup 3A, which does not require a compensatory increase in knee joint movement power, unlike in subgroups 1A and 2A. In groups with more severe global motor function impairments (GMFCS III), high values of generated power for gait are noted in subgroup 2B, reflecting the increased energy intensity of walking itself. Significantly low knee extension forces and sufficient extension range during the stance phase in the multilevel intervention subgroup indicate the comparatively good movements in the sagittal plane after multilevel interventions. High values of hip extension moment and generated hip movement power reflect the increased contribution of the pelvic girdle muscles to gait in all subgroups. Finally, in subgroup 2B, the need to output movement power in the knee and ankle joints again indicates increased energy intensity of walking after early isolated interventions on the triceps of the lower leg.

Table 4

Several kinetic parameters

Parameter	GMFCS I–II			GMFCS III		
	1A	2A	3A	1Б	2Б	3Б
Hip extension torque, Nm/kg	0.9 (0.66÷1.07)	0.9 (0.76÷1.34)	0.8 (0.66÷0.98)	1.11 (0.79÷1.17)	0.94 (0.63÷1.18)	0.83 (0.49÷0.97)
Knee extension torque, Nm/kg	0.6 (0.38÷0.81)	0.7 (0.49÷0.96)*	0.7 (0.48÷0.84)	1.0 (0.61÷1.18)	0.89 (0.63÷1.15)	0.53 (0.33÷0.87)*[1]
Plantar flexion torque, Nm/kg	1.04 (0.89÷1.2)	0.99 (0.71÷1.21)	1.12 (1.03÷1.29)[1]	0.81 (0.55÷0.88)	0.9 (0.74÷0.99)*	0.87 (0.85÷0.93)*
Useful power output at the hip, W/kg	0.34 (0.06÷0.86)	0.48 (0.23÷0.86)	0.29 (0.04÷0.64)	0.47 (0.36÷0.85)	0.55 (0.4÷0.83)	0.27 (0.04÷0.57)[1]
Useful power output at the knee, W/kg	–0.45 (–0.74÷–0.09)	–0.24 (–0.69÷0.01)	–0.01 (–0.58÷0.02)[1]	–0.21 (–0.61÷0.01)	–0.34 (–0.71÷–0.03)	–0.02 (–0.23÷0.0)[1]
Useful power output at the ankle, W/kg	0.17 (–0.01÷1.12)	0.2 (–0.06÷0.42)	0.17 (0.03÷0.63)	0.15 (–0.01÷0.38)	0.29 (0.01÷0.45)	0.01 (–0.06÷0.07)[1]

Some moderate and strong correlations were found between the kinematic, spatiotemporal, and kinetic parameters in all subgroups except subgroup 1A. The negative BMI-gait speed correlation (–0.521) in subgroup 2A reflects the critical value of body mass for slowing down movement in surgical weakening of the plantar flexion function after early operations, even in patients with moderate neurological impairment. In many subgroups, plantar flexion strength had a positive significant correlation with gait speed: subgroups 2A (0.631), 1B (0.738), 2B (0.797), 3B (0.673). Moreover, walking speed decreases with increasing ankle joint range of motion, as a consequence of the development of pathological excessive dorsiflexion of the foot in patients with GMFCS level III. The correlation becomes negative for subgroups 1B (–0.761) and 3B (–0.689). The importance of plantar flexion strength is also shown by the negative correlation of this parameter with GPS (–0.522) in subgroup 3A. The positive correlation between knee extension range of motion (K1–K2) during the stance phase and the efficiency of generated power during knee joint movements in subgroup 2A reflects sufficient compensatory potential even with early weakening of the plantar flexors.

However, at a more severe level of global motor function impairment (GMFCS III), a significant positive correlation is observed between GPS and kinematic or kinetic parameters in subgroup 3B. This reflects the development of functional decompensation due to orthopedic impairments: with the hip extension power (0.522), with the knee extension power (0.533), with the total power of movements in the knee (0.739) and ankle (0.565) joints. Moreover, for this subgroup, a positive correlation was found between BMI and the knee extension power (0.630) and plantar flexion of the foot (0.649). thus, a positive correlation was found between BMI values and the total generated power of movements in the ankle joint (0.543), which reflects the preservation of the adaptive capacity of plantar flexors in patients

after multilevel interventions. Finally, we note the importance of the identified significant negative correlation "GPS-range of motion in the sagittal plane in the hip joint" (–0.619) in subgroup 1B, probably reflecting the capability of compensating for the decrease in the motor abilities of the knee and ankle joints by increasing the motor activity of the pelvic girdle muscles.

DISCUSSION

A critical element in the pathogenesis of motor disorders and secondary orthopedic complications is the progressive reduction in the range of passive movements during child's growth [20]. The development of muscle length deficit, initially caused by spasticity, evolves towards retraction [21]. The morphological changes observed in muscles are accompanied by an increase in sarcomere length, a decrease in the number of satellite cells, and an increase in collagen structures, which causes a decrease in contractile force, a decrease in regenerative potential, and an increase in muscle stiffness observed due to other orthopedic complications of cerebral palsy [22, 23].

In clinical practice, multilevel interventions are usually performed at the age of 11–15 years; they are accompanied by the stability of the surgical result without regression, especially if the intervention is performed after the pubertal growth acceleration [24, 25]. At the age of over 12 years, full anatomical restoration of the structures and relationships between the limb segments and muscle proportions is often no longer possible, and the only solution is palliative orthopedic surgery for crouch gait [9, 26]. This is why Graham et al. [9] distinguish the age period of 4–12 years (the period of contractures and bone deformities), when orthopedic surgery becomes justified. During this period, the nature of orthopedic surgery is reconstructive, and palliative interventions do not have indications yet.

Adolescence, after the peak of growth acceleration in the lower extremities has passed, still belongs to the period of childhood and is termed as senior school age [27, 28]. At this age, there is still a large cohort of patients with indications for surgical correction of cerebral palsy complications [17, 18]. A specific feature of operations and their result prognosis is the lack of remodeling potential in the process of residual growth and the onset of early arthrotic changes [9, 15]. That is why in adolescence, when the pubertal growth acceleration slows down and the child's BMI gradually increases, surgical treatment is often aimed at correcting the crouch gait pattern [9]. Moreover, the results of correction, due to the cessation of active longitudinal growth of the long bones of the lower extremities, remain relatively stable in the late period [7, 15].

Various factors may explain the relatively late orthopedic interventions, often of a palliative nature. A number of authors attribute this situation to drawbacks of healthcare system organization. The lack of a consistent and comprehensive approach to treating children with cerebral palsy is low availability of medical care, inadequate awareness among physicians of evidence-based treatment methods, late diagnosis of the disease, and inadequate parental awareness of the nature of the disease and the effectiveness of various treatment methods, as well as the lack of national registries [29, 30, 31].

An unfavorable factor that combines age and surgical aspects is the performance of so-called fibromyotenotomies, fibrotomies, and Achilles tendon lengthening at an early age. Groundless orthopedic interventions on spastic muscles, even the ones that increase passive range of motion in the joints, lead to their excessive weakening, which manifests itself in early functional decompensation and the development of iatrogenic disorders and orthopedic complications in adolescence, resulting in the formation of the iatrogenic crouch gait pattern [5, 32, 33].

It should be noted that there is a certain group of patients in whom the correction of orthopedic complications of cerebral palsy was not fully achieved even with multi-level interventions; in particular, correction of torsion deformities was not performed [34, 35, 36]. In some cases,

recurrence of contractures is possible, which may also require repeated interventions, the frequency of which (excluding the removal of osteosynthesis material) in the late period after primary multilevel operations reaches 39 %. Thus, Terjesen et al. [25] indicate the development of mild foot equinus after three to four years of follow-up with normal kinematic parameters in the support phase, which is accompanied by a progressive decrease in the range of dorsiflexion during subsequent growth at an average rate of 4° per year. Finally, planning the volume of multilevel interventions without the use of computer gait analysis increases the risk of inadequacy, insufficiency or inaccuracy in the amount of surgical correction, which requires repeat interventions in the future [37, 38].

In our study, gait parameters varied significantly between the subgroups. In patients with mild global motor impairment (GMFCS I-II) and no previous orthopedic interventions, rotational movement disorders and contractures of the knee and ankle joints remained the dominant gait disorders. However, kinetic movement characteristics remained relatively intact. Therefore, surgical interventions indicated in this situation are strictly reconstructive in nature, as there is no decompensation of movements in the sagittal plane. In the group of patients with similarly mild motor impairments (GMFCS I-II), but who had undergone isolated triceps lengthening surgery at an early age, decompensation of motor impairments with the development of an iatrogenic crouch gait pattern was observed in most cases. This pattern was accompanied by both deterioration in the spatiotemporal characteristics of gait and an increase in its energy consumption. In the subgroup of multilevel interventions in GMFCS I–II patients, indications for surgical treatment were due to individual unresolved orthopedic problems, such as rotation or recurrent contractures.

We believe that in the GMFCS III subgroup without previous surgical interventions, movement disorders naturally reflected the final stage of the typical crouch gait pattern, characterized by a full deterioration in spatiotemporal parameters and an increase in movement energy consumption, but with a predominance of compensated forms. In the subgroup of adolescents with global movement disorders of the same level (GMFCS III), but after isolated interventions on the triceps surae, decompensated forms of crouch gait predominated. In the subgroup after previous multilevel interventions, GMFCS III patients demonstrated impairments characterized by rotational deviations, knee flexion without excessive dorsiflexion of the foot, and a compensated crouch gait pattern. However, the adaptive capacity of the plantar flexors is preserved in the patients after multilevel interventions, and the integral GPS index has the lowest values for GMFCS III level patients.

Overall, it can be noted that the best values for spatiotemporal gait parameters and the absence of crouch gait are observed in the patients who maintain sufficient plantar flexion strength and lack excessive dorsiflexion of the foot during the stance phase. This is confirmed by the significant negative correlation in subgroup 2B between BMI and gait speed, as well as the negative correlation between the total range of motion in the ankle joint and gait speed.

It is known that there is a natural evolution of movement disorders towards the crouch gait pattern that develops in adolescence in patients with spastic diplegia, caused, among other things, by torsion deformities of the femurs, foot deformities and high position of the patella [9, 25, 35, 39]. However, a predictor of this unfavorable evolution, clearly shown in the studies of Pilloni et al. [32], is surgical weakening of the plantar flexors, which leads to an increase in the minimum flexion of the knee joint in the stance phase. The study of Bernthal et al. [40] noted that decompensation of the extension function of the lower limb initially manifested itself as a tendency to excessive dorsiflexion of the foot in the stance phase. In our study, the obvious adverse walking parameters in adolescents with a history of isolated triceps lengthening confirms the negative effect of percutaneous fibromyotenotomies and Achilles tendon lengthening, which manifests itself in late childhood and adolescence.

The limitations of our study include the cross-sectional nature of the study and the lack of a retrospective analysis of kinematic and kinetic gait parameters in this group of patients. Another limitation is the relatively small number of patients in the compared groups. A significant limitation is the comparison of groups divided by the level of global motor impairment, but without an in-depth neurological analysis. Furthermore, the study did not include patients who had previously undergone multilevel interventions but who did not have indications for repeat surgery in the long-term period. To obtain a comprehensive conclusion on the motor status of the studied patient groups, we plan to compare data with gait parameters using the FMS scale in future studies and assess patients' quality of life, which will provide a more complete picture of the condition of adolescent cerebral palsy patients admitted for orthopedic surgery. Finally, we note that the purpose of the study was not to compare patient groups, but to identify characteristic features of motor impairments that allow us to describe and individualize categories of gait disorders in adolescent patients admitted for surgery.

CONCLUSION

In patients with spastic diplegia admitted for surgery in adolescence, indications for orthopedic intervention are determined by the level of global motor impairment, as well as by the type and extent of previous surgeries. In patients with GMFCS levels I–II who have no previous surgeries, indications are determined by the presence of joint contractures and torsion deformities of the lower extremity segments. In contrast, in patients with GMFCS level III, a compensated crouch gait pattern predominates in adolescence. We observed the development of compensated and decompensated forms of crouch gait with high energy consumption movements in a group of patients who underwent triceps surae lengthening at an early age. This should be considered when choosing a surgical approach, subsequent rehabilitation measures, and fitting orthotics. After multilevel interventions performed in the earlier period, indications for surgical treatment in adolescents remained torsion deformities, recurrent contractures, and the development of flexion position of the knee joint; however, the spatio-temporal and strength characteristics of movements remained at a relatively high level.

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Complications of total elbow arthroplasty: experience with 622 cases and implant developments

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Abstract

Introduction Total elbow arthroplasty (TEA) is increasingly used for the treatment of advanced elbow conditions with the rate of adverse events after surgery being high.

The **objective** was to analyze the spectrum and causes of complications following TEA depending on the biomechanical implant design and evaluate the effect of humeral trochlear resection on hand grip strength.

Material and methods A retrospective non-randomized cohort study of 622 primary and revision TEA procedures was performed between 2002 and 2025. Depending on the biomechanical principle of implant fixation, patients were stratified into two groups to include constrained implants (ESI, $n = 404$) and semi-constrained implants (Zimmer Coonrad – Morrey, Conmet, Treza, Logeeks, $n = 218$). Clinical and radiological data, intraoperative findings during revisions, and instrumented dynamometry results ($n = 80$) were analyzed preoperatively and at 6 weeks of surgery. Statistical analysis was performed using non-parametric tests (Mann – Whitney U, Wilcoxon, Chi-square).

Results The overall complication rate was 7.0 % (44/622). Aseptic loosening of TEA was more common for constrained implants (4.5 %, 18/404) due to stress concentration at the bone-cement interface. Mechanical failure of the hinge joint/polyethylene wear (3.2 %, 7/218) was the leading cause of revision in the semi-constrained group. Resection of the humeral trochlea had no clinically significant effect on hand and pinch grip strength ($p > 0.05$).

Discussion Existing TEA constructs exhibit a predictable complication profile directly related to their biomechanical design. Optimizing outcomes is associated with advanced surgical techniques and a transition to new-generation implants considering the complex three-dimensional kinematics of the joint and providing balanced load transfer with a reinforced, wear-resistant hinge system.

Conclusion The complication profile after TEA was implant dependent. Constrained systems could predispose to aseptic loosening, and semi-constrained systems can be associated with fatigue wear of the hinge. Trochlear resection did not compromise the hand strength. Future implant developments should focus on optimization of controlled varus-valgus laxity (5–7°), reinforcing the hinge coupling mechanism, considering the anatomical torsion of the distal humerus.

Keywords: elbow joint, total elbow arthroplasty, complications, revision arthroplasty, biomechanics, implant design

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INTRODUCTION

Total elbow arthroplasty (TEA) is the surgery of choice for patients with severe rheumatoid arthritis, posttraumatic arthrosis, and distal humeral fractures unsuitable for reconstruction, allowing for pain relief and restoration of limb function [1, 2, 3]. Severe rheumatoid arthritis with persistent loss of joint function and pain was traditionally the main indication for TEA. Over time, TEA has become a treatment option for severe comminuted distal humeral fractures in the elderly thanks to improvements in prosthetic designs and surgical techniques. Kholinne et al. reported in the meta-analysis that 71.7 % of TEA patients were over 70 years of age [4, 5, 6]. The functional and clinical results of TEA, the survival rate of implants in post-traumatic patients are statistically significantly better than in patients who underwent this type of surgical intervention for rheumatoid arthritis [5, 7, 8]. With more than a half-century of development, the frequency of complications and revision interventions after TEA, according to the world literature, reaches 20-40 %, which is significantly higher than similar indicators for hip and knee arthroplasty [9, 10, 11, 12, 13, 14].

TEA implant designs have evolved from unconstrained to constrained and semi-constrained systems. Constrained implants, primarily providing maximum stability, are unable to withstand torsional and bending force changes, leading to stress concentration at the bone-cement-prosthesis interface and, consequently, to aseptic loosening. Semi-constrained constructs, offering some mobility at the hinge, are designed to reduce the loads; however, the insufficient mechanical strength of the joint is the vulnerable point [15, 16, 17]. Humeral trochlea is commonly resected in cases of severe post-traumatic or rheumatoid defects of the distal humerus, in correction of persistent flexion contractures to achieve sufficient range of motion and proper component placement. This manipulation inevitably alters the attachment points of the collateral ligaments and stabilizer muscles, which can potentially impact the biomechanics of the hand grip. There are conflicting data in the literature regarding the impact of trochlear resection on functional outcome. Some authors report a decrease in grip strength post-op [18], which can critically limit patients' daily activities. Maintaining intact tendon-muscle complexes objective evidence of clinically significant impairment of hand strength remains insufficient, and assessment methodology varies between studies.

With the clinical significance of a strong grip for patients' quality of life, its relationship with the extent of bone resection and the type of implanted device has been insufficiently studied. Therefore, an analysis of the complication rate depending on implant design, an objective assessment of the impact of humeral trochlea resection on hand strength, are relevant issues in modern orthopedics [19, 20, 21, 22, 23].

The **objective** was to analyze the spectrum and causes of complications following TEA depending on the biomechanical implant design and evaluate the effect of humeral trochlear resection on hand grip strength.

MATERIAL AND METHODS

A retrospective, non-randomized cohort study was conducted at the Tsivyan Novosibirsk Research Institute of Traumatology and Orthopedics. Outcomes of 622 primary and revision TEA surgeries performed between 2002 and 2025 were reviewed. Patients were divided into two groups based on the biomechanical fixation principle of the implanted constructs:

— group of constrained systems (n = 404): ESI endoprosthesis (Russia), Fig. 1 a;

— a group of semi-constrained systems (n = 218): combined cohort, including:

- Zimmer Coonrad – Morrey endoprostheses (Zimmer Biomet, USA), Fig. 1 b;
- Conmet (Russia), Fig. 1 c;
- Treza (Russia) and Logeeks (Russia), Fig. 1 d.

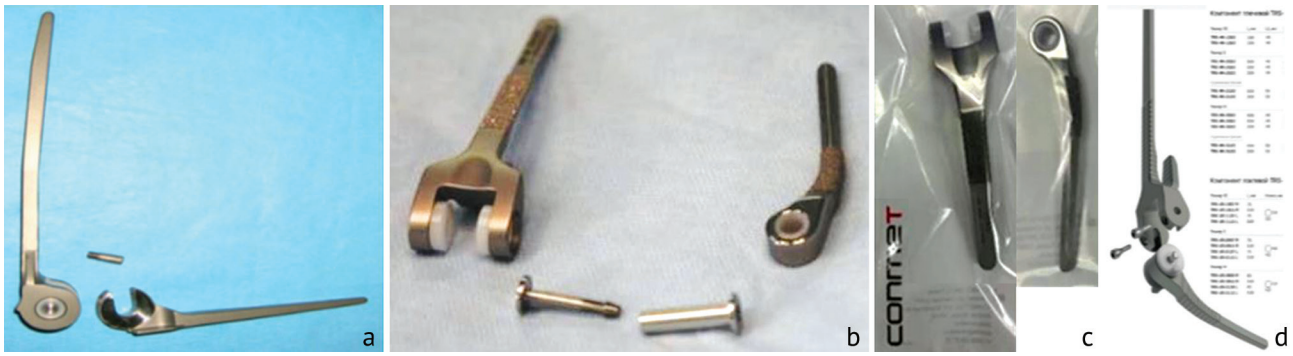

Fig. 1 Elbow joint implants: ESI (a); Zimmer Coonrad – Morrey Total Elbow (b); Conmet (c); Logeeks (d)

Russian analogues (Conmet, Treza, Logeeks) combined into a single subgroup are characterized by identical design principle (the presence of varus-valgus play in the hinge joint of 5–7°) and insufficient sample power for pairwise statistical comparison of each model ($n < 30$ for Conmet, Treza, and Logeeks separately).

The clinical and demographic characteristics of the patients are presented in Table 1. Statistical analysis suggested the comparability of the groups by gender, age, observation period, and nosological structure ($p > 0.05$), which minimizes the influence of covariates on the assessment of the frequency and nature of complications.

Table 1

Clinical and demographic characteristics of patients

Description		All patients (n = 622)		Constrained systems (n = 404)		Semi-constrained systems (n = 218)		p
Age, years, Me [Q1; Q3]		61.0 [52; 71]		61.5 [53; 72]		59.0 [50; 69]		0.312
Observation period, years, Me [Q1; Q3]		7.2 [4.1;11.5]		9.5 [5.8; 14.2]		4.8 [2.3; 7.9]		0.184
		abs.	%	abs.	%	abs.	%	
Gender	Male	199	32,0	106	26.2	93	42.7	0.415
	Female	423	68,0	298	73.8	125	57.3	
Nosology	Post-traumatic arthrosis	280	45.0	179	44.3	101	46.3	0.682
	Rheumatoid arthritis	236	38.0	123	30.4	113	51.8	
	Acute comminuted fractures of the distal humerus	75	12.1	71	17.6	4	1.8	
	Other conditions	31	4.9	31	7.7	0	0.0	

Note: Me is the median, [Q1; Q3] is the interquartile range; p is the level of statistical significance (Mann–Whitney test for quantitative variables, Pearson χ^2 or Fisher's exact test for qualitative variables).

Surgical technique and intraoperative protocol

Surgical procedures were performed through a standard posterior approach with preservation or re-fixation of the triceps tendon [24, 25]. Constrained ESI was implanted through the triceps tendon and the preserved attachment to the olecranon process provided sufficient visualization for the installation and assembly of components in the wound to allow for early function without additional re-fixation.

Semi-constrained systems were implanted through expanded access creating additional medial and lateral "windows" for visual control of the collet installation and the hinge mechanism axis. The triceps tendon was temporarily dissected in some Logeeks cases to be followed by transosseous re-fixation and adherence to a gentle orthopedic regimen early post-op.

Ulnar nerve management was based on the initial clinical status. In primary TEA, the ulnar nerve was not isolated to preserve the vascularity and anatomical relationship with surrounding tissues. Revision procedures involved decompression performed by opening the aponeurotic membrane without complete mobilization. Total ulnar nerve isolation using traction devices was used exclusively for newly diagnosed neuropathy.

Methods of diagnosis and verification of complications

Verification of postoperative complications was based on a comprehensive analysis of the clinical manifestations, standard radiography with two views, and multislice computed tomography (MSCT). The radiographic criteria for aseptic loosening included:

— progressive areas of radiolucency > 2 mm at the bone-cement-implant interface involving the entire fixation zone of the component;

— migration, subsidence, or change in the inclination angle of components;

— fracture or avulsion of the cement mantle;

— periprosthetic osteolysis: localized areas of bone resorption associated with a reaction to wear particles;

— periprosthetic fractures, which are a cause or consequence of instability;

— mechanical failure of the structure (liner wear, axle breakage, hinge dissociation).

Intraoperative assessments during revision interventions included:

— the degree of wear of the polyethylene liner;

— the integrity of the hinge locking mechanism;

— the stability of the stem fixation;

— the condition of the cement mantle;

— the nature of the bone bed.

Evaluation of functional results (dynamometry)

Instrumentation dynamometry was performed in a subset of patients (n = 80) to objectively assess the impact of humeral trochlea resection on hand function. Wrist grip strength (wrist dynamometer) and pinch grip strength (pinch dynamometer) were measured on the dominant and non-dominant limbs. The study was performed preoperatively and at six weeks to allow primary soft tissue healing to be completed, a stable scar to be formed, and safe functional loading to be performed.

Ethical Standards

The study was approved by the Local Ethics Committee of the Ya.L. Tsivyan Novosibirsk Research Institute of Traumatology and Orthopedics of the Russian Ministry of Health (extract No. 014/25 from protocol No. 006/25 dated September 5, 2025). All patients signed informed voluntary consent to participate in the study and process their personal data.

Statistical analysis

Data processing was performed using the SPSS v.26 / R v.4.2 software. The normality of distribution of quantitative variables was assessed using the Shapiro – Wilk test. Due to the absence of a normal distribution, comparison of independent samples was performed using the nonparametric Mann – Whitney test, and the Wilcoxon test was employed for paired measurements (dynamics before/after surgery). Qualitative variables were compared using Fisher's exact test or Pearson's χ^2 test. The results are presented as median and interquartile range [Q1; Q3], absolute (n) and relative (%) frequencies. Differences were considered statistically significant at a significance level of $p < 0.05$.

RESULTS

In a cohort of 622 TEA procedures performed, 44 cases of various complications were identified in the late postoperative period, accounting for 7.0 % of the total number of procedures. Analysis of adverse outcomes demonstrated a direct correlation between the nature and frequency of complications and the biomechanical principle of the implanted device.

The nature of complications in the group of constrained systems (Fig. 2)

Revision interventions were required in 29 cases (7.2 %) who underwent ESI implantation (*n* = 404). Poor results were caused by aseptic loosening of the components, recorded in 18 patients (4.5 %), mainly at the site of the humeral component. Biomechanically, this is due to the complete coupling of the system with the physiological torsional and varus-valgus loads being transferred directly to the bone-cement interface, initiating periprosthetic osteolysis and loss of fixation stability (malignant osteolysis). Other adverse events in this group included fatigue fracture of the metal hinge axis (*n* = 3; 0.7 %); deep tissue periprosthetic infection (*n* = 3; 0.7 %); ulnar nerve neuropathy (*n* = 3; 0.7 %); Periprosthetic fracture (*n* = 1; 0.2 %). No cases of dislocation or dissociation of the hinge were recorded, suggesting the high primary stability of the constrained construct; however, this was associated with an increased risk of aseptic instability.

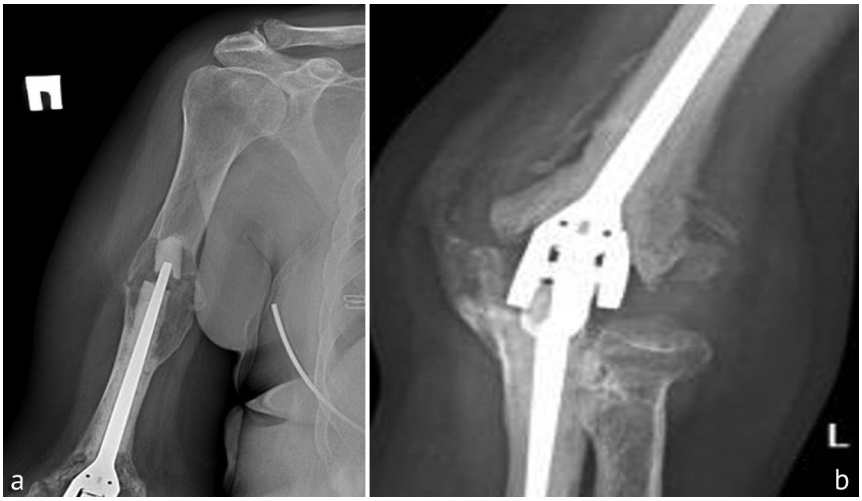

Fig. 2 Radiographs of the elbow joint, complications of ESI implant: (a) malignant osteolysis; (b) destruction of the hinge joint

Complications in the group of semi-constrained systems (Fig. 3)

Patients with semi-constrained implants(ZimmerCoonrad – Morrey, Conmet, Treza, Logeeks; *n* = 218) developed 15 adverse events (6.9 %). Revisions (*n* = 7; 3.2 %) were caused by mechanical failure of the articulation unit including critical wear of the polyethylene liner or fatigue fracture of the locking mechanism leading to dissociation of the hinge. Aseptic loosening of the components was detected in five patients (2.3 %). Other complications included periprosthetic joint infection (*n* = 1;

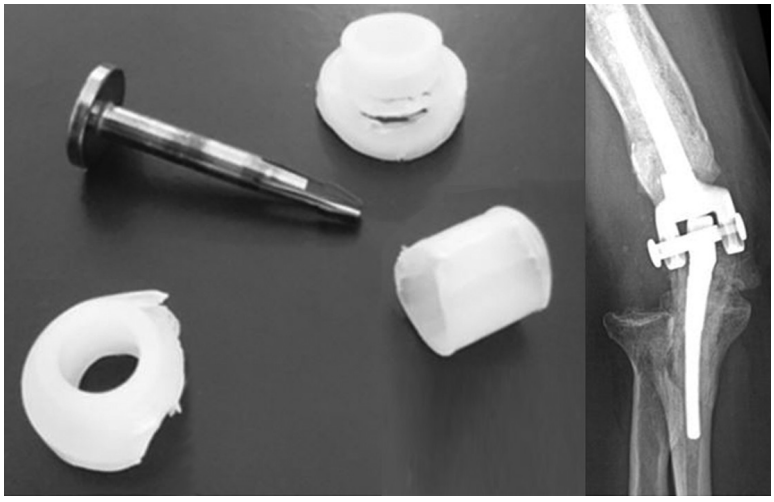

Fig. 3 Broken hinge of the Zimmer Coonrad – Morrey implant

0.5 %), periprosthetic fracture (n = 1; 0.5 %), and ulnar nerve injury (n = 1; 0.5 %). Due to insufficient sample power for each individual model of domestic semi-constrained implants (Conmet, Treza, Logeeks; n < 10), statistical analysis was performed for the combined subgroup. One case of aseptic loosening and two cases of hinge mechanism failure were recorded in the cohort.

The complication rate in the Zimmer Coonrad – Morrey group was consistent with global rates for this design. The exact absolute and relative values for each type of complication are presented in Table 2.

Table 2

Complications in the Zimmer Coonrad – Morrey group

Type of complication	ESI		Coonrad – Morrey		Conmet / Trez / Logeeksa		Total	
	abs.	%	abs.	%	abs.	%	abs.	%
Aseptic loosening	18	4.5	4	1.8	1	0.4	23	3.7
Destruction/wear of the lock	3	0.7	5	2.3	2	0.8	10	1.6
PJI	3	0.7	0	0.4	0	0.0	3	0.5
Periprosthetic fracture	3	0.7	1	0.4	0	0.0	4	0.6
Ulnar neuropathy	1	0.3	1	0.4	0	0.0	2	0.3
Triceps tendon reinsertion	1	0.3	0	0.0	1	0.4	2	0.3

Note: The data are presented in the n (% of the group) format. The combination of domestic systems was performed due to the identical design principle and low sample power for pairwise analysis.

Structural and biomechanical features of the late period

An analysis of the long-term results in the semi-constrained group revealed changes in the mechanical axis of the limb. Some patients developed a static varus deformity of the elbow joint, a "gunstock deformity", due to the peculiarities of ligamentous apparatus balance and the structural geometry of the humeral component (Fig. 4). The design of the semi-constrained lock creates a sensation of "dropping" of the forearm due to play in the hinge joint. The problem of heterotopic ossification (HO) is essential. In a subgroup of 10 patients who underwent implantation of the constrained ESI with preserved humeral epicondyles, heterotopic ossifications in the projection of the hinge mechanism developed in all cases (100 %) post-op. Radiological and clinical monitoring confirmed that ectopic bone formation led to a significantly limited range of motion in the elbow joint, requiring surgical correction in some cases (Fig. 5).

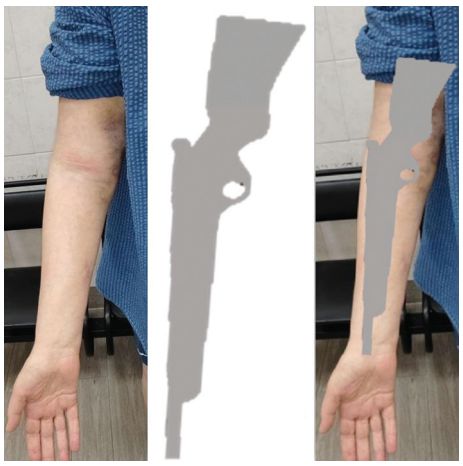

Fig. 4 Varus deformity of the elbow joint: photograph of the patient after TEA

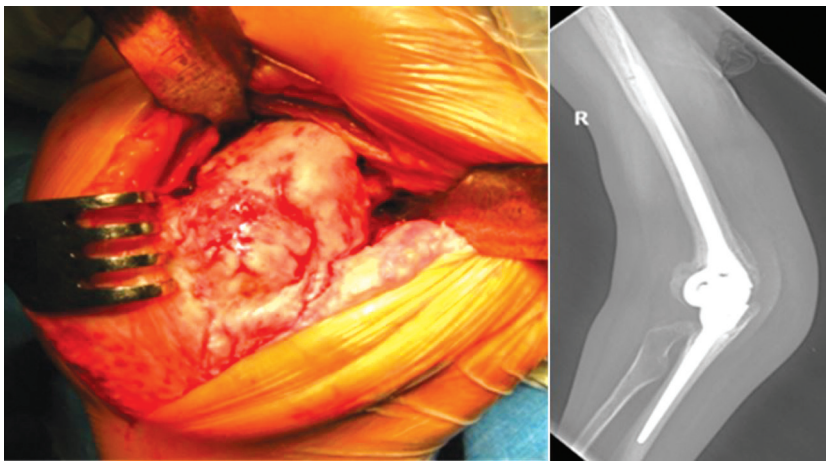

Fig. 5 Heterotopic ossification around the ESI lock

Assessment of the functional condition of the hand (dynamometry)

Instrumentation dynamometric examination was conducted for a subgroup of 80 patients (primary and revision TEA with confirmed trochlea defect) to objectively assess the impact of distal humeral trochlea resection on upper limb function. The results are presented in Table 3.

Table 3

Results of dynamometry and pinch grip tests

Description	Pre-op	At 6 weeks	Effect	Wilcoxon test, *p*-level
	MED [Q1; Q3]		PSEUDO MED [95 % ДИ]	
Dynamometry of the right hand (*n* = 80, 100 %)	38.5 [25; 50]	38.5 [25; 52.5]	−1 [−1; −0.5]	0.152
Pinch grip on the right (*n* = 79, 99 %)	9 [7.25; 10.75]	10 [7; 11.75]	−0.25 [−0.25; −0.25]	0.009*
Dynamometry of the left hand (*n* = 78, 98 %)	39.5 [20.5; 53.75]	40 [24.25; 53]	−0.5 [−0,5; −0.5]	0.187
Pinch grip on the left (*n* = 77, 96 %)	9 [7; 11]	9 [7.4; 11]	0 [0; 0]	0.290

* $p < 0.05$.

A dynamic analysis of the dynamometry performed (comparing preoperative and six-week postoperative measurements) revealed maintenance of dynamometry in both the right and left hands, and the pinch grip on the left. Postoperative pinch grip measurements on the right showed statistically significant differences compared to preoperative values.

DISCUSSION

The findings of this study suggested that the incidence and nature of complications after TEA were directly related to the biomechanical design of the implant. The overall revision rate in our cohort was 7.0 %, which is at the lower end of the ranges reported in the current literature (10–25 %) [7, 10, 26, 27]. This figure may be due to strict adherence to the surgical protocol, centralization of operations in a specialized center, and patient selection characteristics. However, analysis of the failure pattern revealed a fundamental biomechanical trade-off between primary stability and long-term durability of the implant [9, 15, 22, 23, 28].

Constrained systems and aseptic loosening. Aseptic loosening of the humeral component was the most common complication (4.5 %) in the ESI group. The biomechanical mechanism of this phenomenon is well described in the literature: full coupling of the hinge compensates for pathological instability but blocks physiological varus-valgus and torsional mobility. As a result, peak loads are not absorbed by the soft tissue complex but are transmitted directly to the bone-cement interface. This initiates a body response to wear microparticles (metal, polyethylene, cement), the formation of a thick fibrous membrane, and the progression of periprosthetic osteolysis, which we objectively verified during revision surgeries. Our data are fully consistent with the results of studies reporting that constrained constructs demonstrate earlier radiographic instability despite the absence of hinge dissociation [1, 30, 31]. In this case, the fatigue fracture of the metal axis (0.7 %) suggests extreme cyclic loads exceeding the ultimate strength of the material under conditions of blocked kinematics [26, 29, 32, 33].

Semi-constrained systems and mechanical failure of the articular joint. Revisions in semi-constrained (3.1 %) were caused by fatigue failure of the locking mechanism or critical wear of the polyethylene liner followed by dissociation of the hinge. The engineering solution incorporated into the Coonrad Morrey design and its analogs involved the presence of an inherent varus-valgus play (5–7°). This allowed for the redirection of some angular and torsional loads from the bone bed to the articular joint, significantly reducing the risk of early aseptic loosening. However, the hinge module became a new "weak link", subject to cyclic shear and compressive loads. The frequency of joint failure in our sample corresponded to global rates for this type of design [9, 29, 32].

It is noteworthy that, unlike constrained systems, we rarely observed total osteolysis of the bone bed during revision of semi-constrained implants. Instability was commonly localized, with massive debris in the projection of the hinge joint [1, 30].

The influence of the surgical approach and heterotopic ossification. Preservation of the humeral epicondyles is essential. A subgroup of 10 patients with preserved epicondyles who underwent implantation of a constrained systems developed heterotopic ossification around the hinge in all cases. This confirms the literature data that the preservation of bony prominences creates areas of increased soft tissue friction and local ischemia, triggering a cascade of ectopic bone formation [25, 34]. We believe that resection of the epicondyles at the level of the cubital fossa is practical to prevent heterotopic ossification in TEA. The design of the hinge joint should be developed taking into account delicate handling of soft tissues, excluding or minimizing a technically more complex approach with the formation of additional medial and lateral "windows" [35, 36, 37, 38].

Functional outcome: dynamometry and humeral trochlea resection. The absence of a clinically significant decrease in the strength of the hand and pinch grip after resection of the distal humeral trochlea was an important practical observation. The statistically significant improvement in the pinch grip on the right ($p = 0.009$) by 1.0 kg did not exceed the minimal clinically important difference (MCID) and probably reflected pain relief and postoperative rehabilitation, rather than biomechanical changes. Our results refute claims about a critical weakening of the grip after trochlea resection [19, 20, 22]. This could be explained by the fact that the main traction of the flexor and extensor muscles of the fingers was intact, and the collateral ligaments attached to the epicondyles retained their function with proper balancing. This observation has a clinical role: the surgeon can perform the necessary resection for adequate placement of the components without the risk of functional disability of the hand.

Prospects for biomechanical design. Analysis of our own data and the results of revision procedures allows us to formulate a development vector for next-generation implants. First, the concept of "controlled axial rotation" in the elbow component is essential, as the implant is an artificial hinge placed in pathologically altered tissue and cannot replicate the native elbow joint. Priority should be given to optimizing the hinge's varus-valgus mobility within 5–7°, with reinforcement of the coupling unit capable of withstanding cyclic shear loads. Second, the humeral component should accommodate the natural anteversion and torsion of the distal metaphysis to minimize asymmetric contact of the cement mantle. Thirdly, further development should be aimed at creating modular systems with wear-resistant friction pairs and improved stem geometry, which will reduce stress concentration at the implant-cement-bone interface and ensure balanced load redirection [1, 17, 38, 39, 40].

The existing TEA designs exhibit a predictable complication profile directly related to the biomechanical design. Optimizing outcomes requires an improved surgical technique and transition to new-generation implants that would consider the complex three-dimensional kinematics of the joint, ensure balanced load transfer providing a reinforced, wear-resistant hinge system.

CONCLUSION

The overall complication rate after total elbow arthroplasty in the cohort of patients was 7.0 %. The nature and frequency of adverse outcomes were associated with the biomechanical principle of implant fixation.

Aseptic loosening of components was the common mechanism of failure for constrained caused by the transfer of peak varus-valgus and torsional loads to the systems bone-cement interface without physiological cushioning.

Revision surgery with the semi-constrained systems was caused by mechanical failure of the hinge and critical wear of the polyethylene liner, being associated with cyclic shearing effects on the coupling mechanism. Implantation of these systems was associated with the development of static varus deformity of the limb.

Instrumentation dynamometry suggested that the distal humeral trochlea resection required for proper component placement had no clinically significant effect on hand and pinch grip strength. The statistically significant improvement in right-sided pinch grip strength did not exceed the minimum clinically significant difference and was associated with postoperative rehabilitation rather than biomechanical change.

The development of next-generation implants should be based on the principles of balanced load transfer including optimization of varus-valgus joint mobility within 5–7°, engineering reinforcement of the coupling unit and locking mechanisms, and consideration of the natural anatomical torsion and the distal metaphysis of the humerus.

Conflict of interest *None of the authors has any potential conflict of interest.*

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Ethical review *The study was approved by the Local Ethics Committee of the Ya.L. Tsivyan Novosibirsk Research Institute of Traumatology and Orthopedics of the Ministry of Health of the Russian Federation (extract No. 014/25 from protocol No. 006/25 dated September 5, 2025).*

Informed consent *The patients gave informed consent for publication of the findings without identification.*

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Surgical correction of pes planovalgus deformity in ankle osteoarthritis: clinical and functional outcomes

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Abstract

Introduction Pes planovalgus is a progressive, collapsing deformity of the foot, stage IV (subtype IV B according to the Myerson classification), associated with ankle joint involvement. This pathology remains one of the most complex and disabling in foot and ankle surgery. Surgical correction of the hindfoot associated with ankle osteoarthritis suggests careful planning and may include isolated arthrodesis procedures and strategies to be followed by total ankle arthroplasty.

The **objective** was to evaluate the clinical and functional results of surgical correction of pes planovalgus deformity in patients with concomitant ankle osteoarthritis.

Material and methods This retrospective, single-center study included data from 13 surgically treated patients with stage IVB flatfoot deformity and concomitant ankle osteoarthritis. All patients underwent surgery to correct the hindfoot deformity, using various arthrodesis procedures depending on the clinical situation. Clinical and functional outcomes were assessed using the visual analog scale (VAS), the AOFAS scale, and the FAOS questionnaire before and after surgery. The minimum follow-up period was 12 months. Statistical analysis was performed using the Wilcoxon signed-rank test with exact two-tailed *p* values calculated.

Results Postoperatively the median VAS score decreased from 8 [7; 8] to 2 [2; 3.5] scores ($p = 0.000244$). The median FAOS score increased from 22 [16.5; 42] to 86 [69; 89.5] ($p = 0.001709$). The median AOFAS score improved from 40 [32.5; 42.5] to 88 [80; 90] ($p = 0.000977$).

Discussion The findings are consistent with those reported in international literature and demonstrate the high efficacy of hindfoot arthrodesis in this condition. Significant improvement in the functional parameters suggests the appropriateness of the surgical approach. In some cases, hindfoot arthrodesis can be considered as the first step prior to the total ankle arthroplasty.

Conclusion Surgical correction of pes planovalgus deformity through hindfoot arthrodesis provides a statistically significant reduction in pain and improved functional status in patients with concomitant ankle osteoarthritis.

Keywords: pes planovalgus, ankle osteoarthritis, subtalar arthrodesis, total ankle replacement, AOFAS, clinical outcomes

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INTRODUCTION

Flat-valgus foot deformity in adults is a progressive and potentially disabling musculoskeletal disorder characterized by collapse of the medial longitudinal arch of the foot with valgus deviation of the hindfoot and abducted forefoot, combined with pronation of the midfoot. In modern international literature, the term "progressive collapsing foot deformity" (PCFD) is used to denote this condition. This term was proposed by a consensus group of experts headed by Myerson in 2020 as the one that most fully reflects the three-dimensional and progressive nature of the pathological process [1]. The Johnson – Strom classification (1989), supplemented by Myerson in 1997, is more common in Russian clinical practice. It grades four stages of deformity with stage IV as the most severely involved ankle joint [2, 3].

There are primary degenerative, post-traumatic, and inflammatory forms of involvement among degenerative diseases of the lower limb joints with each requiring an independent diagnostic and treatment algorithm [4]. Ankle osteoarthritis (OA) differs in the etiology from lesions of the knee and hip joints. According to modern research, 70 % to 80 % of cases of ankle OA are post-traumatic, with the deformity being idiopathic in the remaining cases (primary degenerative) [5]. Hallux valgus is associated with abnormal biomechanics, increasing the load on the medial ankle joint with progressive cartilage destruction, and deltoid ligament insufficiency is often a key factor in the development of talus valgus, as confirmed by clinical observations of surgical correction of hindfoot valgus [6, 7]. This relationship explains the high incidence of combined pathology (flat-valgus foot deformity and ankle OA) in patients aged 50 and over; degenerative lesions of the foot joints in this age group are often polysegmental [8].

Surgical treatment of patients with Myerson stage IVB PCFD accompanied by ankle OA remains technically challenging with a limited evidence base. Current recommendations suggest ankle arthrodesis or total ankle arthroplasty (TAA) in combination with correction of foot deformity. A staged strategy can be employed in some cases: arthrodesis of the hindfoot is performed at the first stage to eliminate deformity and normalize biomechanics, and TAA is performed at the second stage [9, 10]. The importance of correcting the deformity before TAA is confirmed by data on long-term implant survival: Burkov et al. reported the 10-year survival rate of TAA of 77–87.5 % in a systematic review, and the authors suggested unrepaired axial deformities as a factor in reducing implant survival [11]. The PCFD Consensus Group emphasizes that priority is given to preserving joint mobility where possible with the strategy, however, arthrodesis is the method of choice in cases of rigid posterior deformity and the presence of subtalar joint OA [12].

Good functional outcomes of subtalar and double subtalar arthrodesis are reported for various indications, including hindfoot deformities. Dutra et al. reported in a systematic review the average AOFAS scored 44 and 79 before and after arthrodesis, respectively ($p < 0.001$) [13]. However, there is a paucity of clinical and functional outcomes reported in the Russian literature regarding a cohort of patients with concomitant ankle OA including deformative and degenerative components of the pathology.

The **objective** was to evaluate the clinical and functional results of surgical correction of pes planovalgus deformity in patients with concomitant ankle OA.

MATERIAL AND METHODS

This was a retrospective, single-center study. The analysis included data from 13 patients (13 feet) with flatfoot and associated ankle involvement surgically treated at the Orthopedics Department of City Clinical Hospital No. 31 named after Academician G.M. Savelyeva, which is the clinical site of the Department of Traumatology and Orthopedics of the RUDN University Institute of Medicine. The minimum postoperative follow-up period was 12 months.

Inclusion criteria. The study included patients aged 18 and over with clinically and instrumentally confirmed adult acquired flatfoot deformity (Myerson AAFD Stage IV B) accompanied by signs of ankle OA. Inclusion criteria included surgical correction of the hindfoot deformity and a complete clinical and functional examination before and after surgery.

Non-inclusion criteria. The study did not include patients with rheumatoid arthritis, neuroarthropathy (Charcot foot), severe vascular pathology of the lower extremities, idiopathic flatfoot without signs of PCFD graded by Myerson, and cases without complete clinical observation in the postoperative period.

The study cohort included 13 clinical cases (13 feet). The median age was 62 [55; 69.5] years. By etiology, post-traumatic deformity was predominant (Table 1).

Table 1

Age, gender and clinical characteristics of patients (n = 13)

Description		Value	
Age, years	(Me [Q1; Q3])	62 [55; 69.5]	
	(M ± SD)	63,0 ± 7,8	
		абс.	%
Gender	Female	9	69.2
	Male	4	30.8
Side of involvement	Left	8	61.5
	Right	5	38.5
Etiology of the deformity	Post-traumatic	9	69.2
	Degenerative	4	30.8

Note: Me is the median; Q1, Q3 are the lower and upper quartiles; M is the mean; SD is the standard deviation. Quantitative data are presented as Me [Q1; Q3] and M ± SD.

Hindfoot deformity was surgically corrected in the patients. Depending on the clinical situation, arthrodesis procedures performed included subtalar arthrodesis and double arthrodesis (talocalcaneal and talonavicular joints). Ankle arthrodesis (tibiotalar arthrodesis) was produced in two cases. Total ankle arthroplasty was performed in one patient during the second stage of treatment, 3 years after subtalar arthrodesis (see clinical case). The extent of surgical intervention was determined individually based on the clinical presentation and radiographic data. Joint fixation was performed with cannulated compression screws.

Clinical and functional outcomes were assessed preoperatively and at postoperative follow-up. Pain intensity was assessed using the visual analogue scale (VAS, 0–10 scores). Foot and ankle function were assessed using the American Orthopaedic Foot and Ankle Society Ankle–Hindfoot Score (AOFAS, 0–100 scores) and Foot and Ankle Outcome Score (FAOS, 0–100 scores).

Statistical data processing was performed using standard methods of variation statistics in IBM SPSS Statistics version 27.0 (IBM Corp., Armonk, NY, USA). Quantitative indicators are presented as median and interquartile range, Me [Q1; Q3], as well as mean and standard deviation, M ± SD. The exact Wilcoxon signed-rank test for related samples was used to compare indicators before and after surgical treatment. Differences were considered statistically significant at a significance level of $p < 0.05$.

The study was conducted in accordance with the ethical principles of the Declaration of Helsinki. Informed consent was obtained from all patients for the publication of information and images in a scientific article.

RESULTS

The median VAS scored 8 [7; 8] at baseline, indicating severe pain. Postoperatively, the VAS score decreased significantly compared to the preoperative level: median 2 [2; 3.5] scores (Wilcoxon test, T = 0; p = 0.000244). The relative reduction in median pain was 75 %.

The FAOS score was 22 [16.5; 42] at baseline, indicating severe functional deficit. Post-treatment, the FAOS score increased significantly compared to baseline: median 86 [69; 89.5] scores (T = 4; p = 0.001709). The median FAOS score increased by 64.

The pre-op AOFAS scored 40 [32.5; 42.5], which corresponded to a poor functional condition. A statistically significant improvement in the AOFAS score after treatment was revealed: a median of 88 [80; 90] scores (T = 1; p = 0.000977). Thus, the increase in the AOFAS scored 48 by median points with the majority of patients having good and excellent results. A comparative assessment of the clinical and functional indicators before and after surgical treatment is presented in Table 2.

Table 2

Comparative assessment of clinical and functional scores before and after surgical treatment

Description	Pre-op, Me [Q1; Q3]	Post-op, Me [Q1; Q3]	T (Wilcoxon)	p
VAS, score	8 [7; 8]	2 [2; 3.5]	0	0.000244
FAOS, score	22 [16.5; 42]	86 [69; 89.5]	4	0.001709
AOFAS, score	40 [32.5; 42.5]	88 [80; 90]	1	0.000977

Note: Me is the median; Q1, Q3 are the lower and upper quartiles; T is the exact statistic of the Wilcoxon signed-rank test (sum of the ranks of the smaller group, W– or W+); VAS — Visual Analogue Scale; FAOS — Foot and Ankle Outcome Score; AOFAS — American Orthopaedic Foot and Ankle Society Ankle–Hindfoot Score.

Clinical case

A 54-year-old female patient with bilateral involvement was diagnosed with stage IVB flat-valgus foot deformity, post-traumatic osteoarthrosis of the subtalar and ankle joints. The injury occurred eight years ago. The first stage of treatment included subtalar arthrodesis of the left foot (2020) performed as a staged intervention to correct the deformity and normalize biomechanics in the context of progressive osteoarthrosis of the ankle joint. Scores at baseline included VAS of 8, AOFAS of 45. Preoperative radiometry measurements included MDTA = 98°, TTA = 93°, Tilt = 5° at baseline and MDTA = 90°, TTA = 90°, Tilt = 0° after completion of both stages of surgical treatment.

With a stable bone fusion achieved and the deformity stabilized three years later (in 2023), total ankle arthroplasty (stage two) was performed. This case illustrates the validity of a two-stage approach for severe concomitant ankle osteoarthritis in patients with planovalgus deformity (Fig. 1).

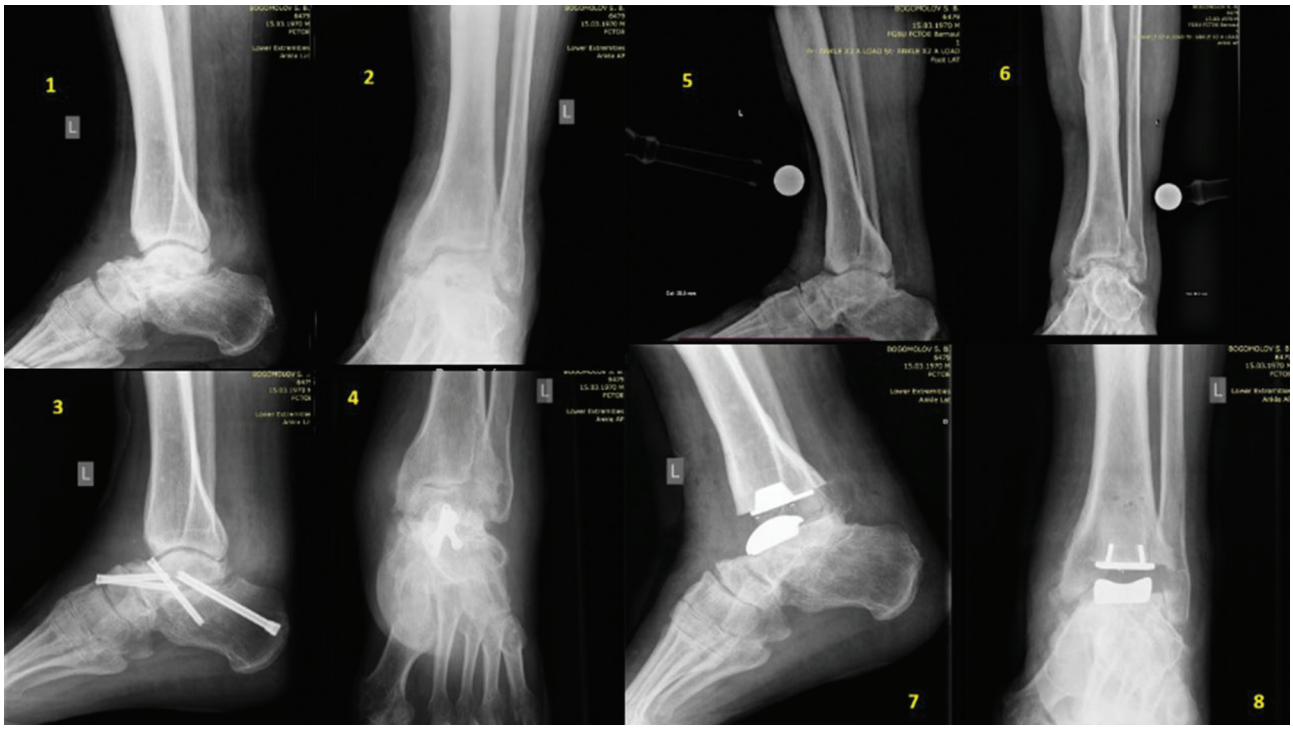

Fig. 1 Radiographs of the patient's feet at stages of surgical treatment of planovalgus deformity and osteoarthrosis of the ankle joint: (1) pre-op, lateral view; (2) pre-op, AP view; (3) post-op, lateral view; (4) post-op, AP view; (5) after the first stage of surgical treatment, lateral view; (6) after the first stage of surgical treatment, AP view; (7) after the second stage of surgical treatment, lateral view; (8) after the second stage of surgical treatment, AP view

DISCUSSION

The results obtained in this study demonstrate statistically significant and clinically relevant improvements in the three assessment scores (VAS, FAOS, and AOFAS) after surgical correction of planovalgus deformity in patients with ankle osteoarthritis. The increase in AOFAS from a median of 40 to 88 scores, and in FAOS from 22 to 86 scores suggests transition of most patients from the poor to good and excellent functional status, which is consistent with the results of international cohort studies.

Dutra et al. performed a systematic review and reported the mean AOFAS increasing from 44 to 79 scores ($p < 0.001$) after subtalar arthrodesis in 180 patients with a mean follow-up period of 18 months [13]. In our series, the median AOFAS scored 88 post-op, which is slightly higher than the values described in the literature. This may be due to differences in patient selection, timing of follow-up examinations, and the surgical techniques used. Some authors suggest limitations of the AOFAS scale as an unvalidated instrument and recommend its use in combination with validated PROMS, such as FAOS. In Russian practice, the AOFAS scale is used as part of comprehensive postoperative rehabilitation protocols [14].

A significant reduction in pain measured with the VAS (from a median of 8 to 2 scores) is consistent with the results reported by Bernasconi et al. on subtalar arthrodesis for subtalar joint degeneration: a significant improvement in functional and anatomical parameters was observed in 33 patients with a median age of 62 years [15]. Interestingly, the age and demographic profile of our cohort (median age 62 years, predominance of females) is almost identical to that in this study, which increases the comparability of the results.

The high proportion of post-traumatic etiology in our cohort (69.2 %) is consistent with epidemiological data: Valderrabano et al. and Rungprai et al. reported 70 to 80 % of ankle osteoarthritis being caused by previous trauma in the general population [5]. In the remaining cases, the deformity is idiopathic (primary degenerative), which was also observed in our cohort: four out of 13 patients (30.8 %) had a degenerative etiology of planovalgus deformity without indications of previous trauma. Post-traumatic deformities are normally characterized by more severe degenerative damage to the articular surfaces and require more extensive arthrodesis. This is precisely what determined the use of double subtalar arthrodesis in a significant proportion of patients in the study group.

In the presented clinical example, the patient with post-traumatic osteoarthrosis of the ankle joint was treated with subtalar arthrodesis as the first stage in order to correct the deformity and optimize biomechanical conditions for subsequent total ankle arthroplasty. The strategy is gaining increasing recognition. It is emphasized that the foot deformity should be corrected first in the presence of severe foot deformity and osteoarthrosis of the ankle joint since uncorrected deformity can lead to eccentric loading on the prosthetic components and early aseptic loosening [3, 12, 16]. According to Burkova et al. reported a systematic review of 13,859 primary ankle arthroplasties with non-repaired axial deformities as one of the main reasons for revision interventions, the frequency of which averaged 12.9 % over 19 years of observation [11].

TAA and ankle arthrodesis in end-stage osteoarthritis was compared in the multicentre randomised controlled trial TARVA (2023) demonstrated comparable improvements in quality of life, however neither group included patients with non-corrected foot deformity [17], supporting the need for a stepwise approach.

Limitations of the study

First, the retrospective design and small sample size (n = 13) preclude generalizability; the results should be interpreted with caution given the potential for patient selection bias. Second, the lack of a control group precludes comparison with alternative treatments. Third, a 12-month follow-up period is the minimum for assessing long-term outcomes and the progression of associated osteoarthritis.

The ***advantages of the study*** include the use of validated (FAOS) and widely used (AOFAS, VAS) assessment tools; their reliability and reproducibility have been confirmed in specialized psychometric studies [18, 19]. The AOFAS scale is used as the main tool for the quantitative assessment of the clinical and functional results of reconstructive interventions on the foot [20]. An analysis of the results of the clinical subgroup of stage IVB PCFD with ankle osteoarthritis was conducted; the treatment of this nosology is insufficiently covered in the Russian literature. The findings can be compared with data on earlier stages of PCFD [21] and form the basis for planning prospective multicenter studies with a longer follow-up period.

Clarification of diagnostic staging criteria within the PCFD classification, including verification of the deformative and degenerative components, remains a priority to improve the homogeneity of the compared cohorts [22]. Preoperative planning, including radiographic assessment of deformity parameters and articular cartilage condition, is of fundamental importance for choosing the optimal scope of intervention during foot reconstruction [23]. The role of hindfoot instability in the progression of degenerative changes in the ankle joint is confirmed by data from Russian

studies. Thus, optimization of the lateral calcaneal extension osteotomy technique based on CT scan results in the Russian population demonstrates the importance of precise positioning of bone structures for restoring normal load distribution in the tibiotalar joint [24].

The use of custom-made implants allows for expanded indications for TAA in complex multi-stage reconstructions in cases of severe talar bone deficiency [25]. Systematization of historical and contemporary approaches to treating patients with planovalgus deformity suggests that conservative and surgical methods continue to evolve with more personalized and functionally oriented strategies [26]. Diagnostic imaging methods, including MRI and CT, play a key role in determining the extent of degenerative lesions of the ankle joint and adjacent structures of the hindfoot which would be associated with the choice of surgical strategy [27]. Comparison of long-term results of isolated subtalar arthrodesis shows that, when the indications and technical conditions of the surgery are followed, a lasting satisfactory result can be achieved in the majority of patients [28]. Russian experience with an individualized approach to the level of osteotomy of the calcaneus in flat-valgus deformity, based on 3D modeling, demonstrates an improvement in the AOFAS scores and radiographic parameters after 12 months of observation [29], which correlates with the results of our study.

A comparison of double subtalar arthrodesis combined with talonavicular arthrodesis and calcaneal displacement osteotomy showed comparable functional outcomes with similar complication profiles, suggesting that both approaches are equivalent in the appropriate clinical situations [30]. Double versus triple arthrodesis would be controversial in more severe lesions involving the talocalcaneal, talonavicular, and calcaneocuboid joints. A prospective comparative study by Fadle et al. found no significant differences in functional outcomes [31]. Subtalar arthrodesis demonstrates satisfactory functional results in patients with posttraumatic subtalar joint osteoarthritis following calcaneal fractures with the underlying fracture pattern having a significant impact on outcome [32].

An algorithm for postoperative patient care after ankle arthroplasty, including rehabilitation protocols and complication monitoring, has been developed and verified using Russian clinical data [33]. It should be emphasized that the accumulated experience of reconstructive interventions for foot deformities in pediatric patients cannot be extrapolated to adult patients due to fundamental differences in pathogenesis and surgical approaches [34].

CONCLUSION

Surgical correction of flatfoot deformity through arthrodesis of the hindfoot (subtalar arthrodesis, double arthrodesis) provides statistically significant improvement in clinical and functional parameters in patients with concomitant ankle osteoarthritis. The findings demonstrate the effectiveness of the surgical approach. A staged approach can be recommended in cases of severe ankle osteoarthritis: the first stage involves correction of the hindfoot deformity to be followed by total ankle arthroplasty (if necessary) and rehabilitation with a strict postoperative management protocol.

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Original article
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Osseointegration of new percutaneous Press-fit implants coated with zinc-containing calcium phosphate in the limb stump: experimental study

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Abstract

Introduction The use of transcutaneous implants for the attachment of limb prostheses is a rapidly developing modern technology for restoring function of lost limbs, particularly relevant for lower limb prosthesis applications. The primary challenge in developing this technology is the need to significantly improve implant survival, which depends on its design and the presence of biocoatings.

The **purpose** of the work is to experimentally evaluate the survival rate of original Press-Fit-type percutaneous implants produced without coating the surface of the osseointegrated part and with an applied zinc-containing calcium phosphate coating during one-stage osseointegration.

Materials and Methods The study was performed on 10 mongrel male dogs aged 1.5 to 2 years and weighing 19.2 ± 1.3 kg. Animals in Group 1 (n = 5) received an uncoated implant, while animals in Group 2 (n = 5) received an implant coated with a zinc-containing calcium phosphate. Osseointegration was assessed using a combination of clinical, radiographic, and laboratory studies. Quantitative analysis of the results was performed using statistical methods.

Results Twenty-six weeks after implantation, all animals had implant stability. A single bone-implantation unit with a continuous and sufficiently dense compact plate was formed. Animals in Group 1 demonstrated organotypic bone remodeling and compaction of periosteal layers. By that time, animals in Group 2 featured completion of organotypic remodeling around the implant that indicated signs of more pronounced osteogenesis in the implant-bone system. The zinc-containing calcium phosphate coating promoted the formation of denser and more mineralized structures on the implant surface and prevented calcium efflux from the compact plate of the bone stump.

Discussion The studies conducted and clinical observations demonstrated the absence of significant local or systemic disorders in the experimental animals during the implant osseointegration period, indicating good tolerability. The zinc-containing calcium phosphate coating provided excellent biocompatibility and stimulated osteogenesis. The obtained results are consistent with data presented in the domestic and international scientific literature and expand the evidence base of the effectiveness of Press-Fit titanium SLM implants with zinc-containing calcium phosphate coating for osseointegration prosthetics.

Conclusion The data obtained during the experiment show fairly good results of osseointegration of Press-Fit implants without coating the surface of the osseointegrated part and with an applied zinc-containing calcium phosphate coating. They did not show pronounced restrictions on their use. However, from the point of view of minimizing the the risks, preference should be given to product with a zinc-containing calcium phosphate coating of the osseointegrated part.

Keywords: osseointegration, prosthetics, titanium implant, Press-Fit, calcium phosphate coating

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INTRODUCTION

The use of transcutaneous implants for the attachment of limb prostheses is a rapidly developing modern technology for restoring the functions of lost limbs [1–6], and is particularly relevant in the case of lower limb bone prosthetics [7, 8]. The main problem in the development of this technology is the need to significantly improve the implant survival characteristics, which depend on its design and biocoatings [9–13]. In terms of acceptable design of osseointegrated implants for long bone prosthetics, preference is increasingly being given to Press-Fit systems [14–19]. Additional factors that contribute to improving the quality of osseointegration of titanium Press-Fit implants include options for additional fixation and compression loading on the bone [20], as well as the application of bioactive and antibacterial coatings, in particular zinc-containing calcium phosphate coatings, to the osseointegrated part [21–22].

The **purpose** of the work is to experimentally evaluate the survival rate of original Press-Fit-type transcutaneous implants produced without coating the surface of the osseointegrated part and with an applied zinc-containing calcium phosphate coating during one-stage osseointegration.

MATERIALS AND METHODS

The study was performed on 10 mongrel male dogs aged 1.5 to 2 years and weighing 19.2 ± 1.3 kg. Animals in Group 1 (n = 5) received an uncoated implant, while animals in Group 2 (n = 5) received an implant coated with a zinc-containing calcium phosphate.

The experimental animals were kept in the vivarium of the Ilizarov National Medical Research Center of Traumatology and Orthopedics. The dogs were housed in individual cages with equipped food and water containers, and hay was used as bedding. The cages and boxes were wet-cleaned daily. The animals were fed once daily and had access to clean drinking water ad libitum. The animals were quarantined for 30 days before the experiment. To assess the efficacy and safety of the experimental devices, the observation period after implantation was 26 weeks.

Prior to the study, approval was obtained from the institutional ethics committee (protocol dated 29.11.2024, No. 1(76)). 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 Experimental and other Scientific Purposes and Directive 2010/63/EU of the European Parliament and of the Council of 22.09.2010 on the protection of animals used for scientific purposes.

Study design

The implants were manufactured using SLM printing on a DMP Flex 350 3D printer (USA) using Russian-produced PTN-8 titanium powder with a particle size of 15–45 μm. The design is described in Russian patents for utility models No. 194912 and 207637 [23, 24]. Photos of the implants are shown in Figure 1.

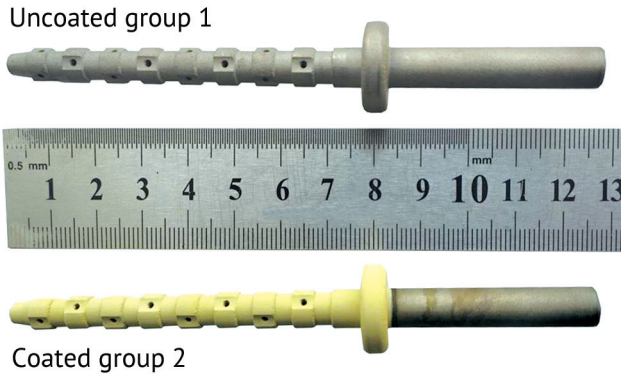

Fig. 1 External appearance of Press-Fit implants (uncoated group 1 and coated group 2)

To ensure implantation in the tubular bone of the limb stump, the implant's insertion section is designed as a truncated cone with teeth on the stepped entry and calibration sections. The teeth on the entry section gradually decrease in diameter toward the implant tip by a value of $D_i - D_{i-1} = 0.1$ mm (Fig. 2 a).

The step-type entry section has teeth with cutting edges and grooves for the sheared bone chips, which act as autologous material (Fig. 2 b, c). The cutting teeth of the entry section contain openings connected to a through-channel inside the implant for drug delivery. The through-channel is closed with a plug.

The cutting edges on the teeth of the entry and calibration sections are inclined at an angle of 5° (Fig. 2 c). The arrangement of the edges around the teeth is shown in Fig. 2 d. Flat areas on the teeth ensure the delivery of medications in the bone-implant system.

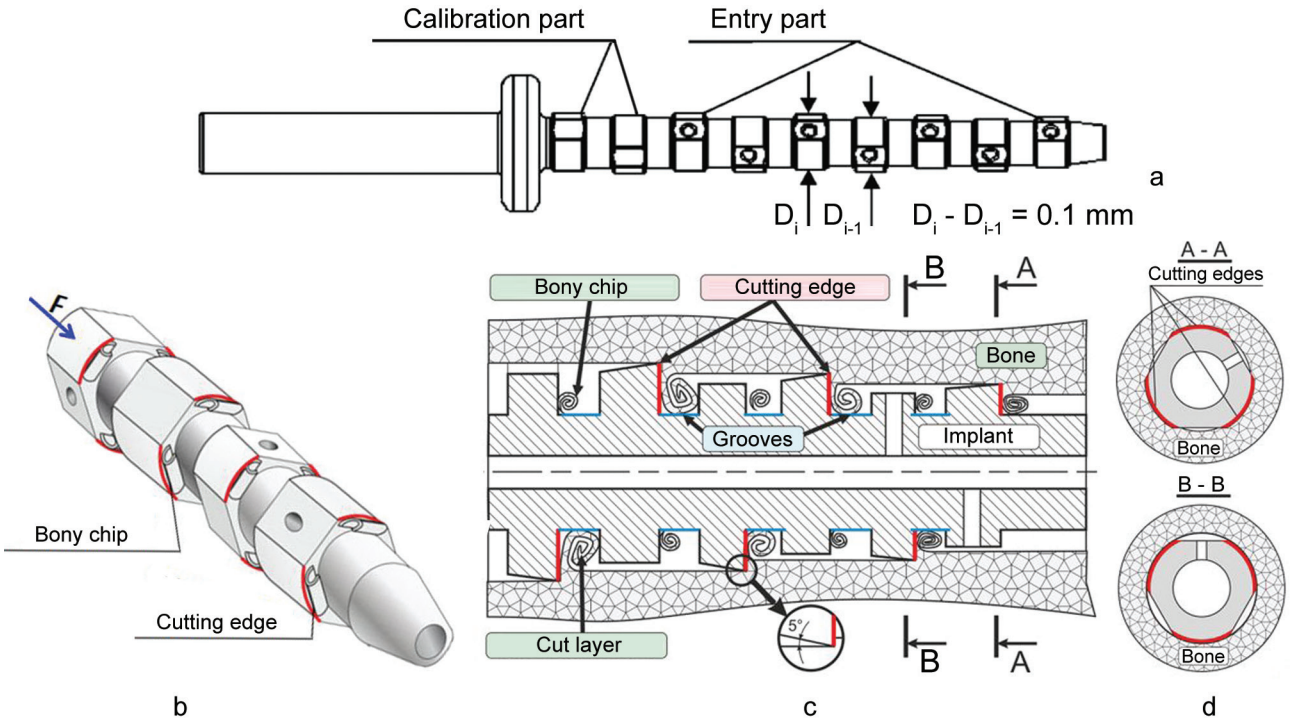

Fig. 2 Press-Fit implant for prosthetics of tubular bone stumps: (a) schematic representation; (b) three-dimensional image of the entry part; (c) longitudinal section of the entry part; (d) cross-sections of the entry part

Coating application

To obtain group 2 implants, the surface of the osseointegrated part of the products was modified by applying a zinc-containing calcium phosphate coating. The coatings were applied using microarc oxidation (MAO), which allows for the deposition of a homogeneous coating on the surface of samples of complex geometric shapes of any size. The semi-industrial Micro-Arc 3.0 MAO unit (IPMS SB RAS, Tomsk) includes a high-voltage pulsed current source, an electrolytic water-cooled titanium bath (cathode), titanium sample holders (anode), and a computer for controlling the MAO process [21, 25, 26]. The suspension composition and electrophysical parameters of coating application are presented in the work of Stogov et al. [21]. Zinc-substituted hydroxyapatite included in the suspension was obtained by mechanochemical synthesis [27]. The coating on the implants had a thickness of 30–35 μm and a surface roughness of Ra = 2.0 – 2.5 μm. In our previous studies [28, 29], the microstructure, phase and chemical compositions, physicochemical, and mechanical properties of the coatings were described in detail. The duration of sterilization treatment in a dry-heat oven was 60 min at a temperature of 180 °C.

Insertion of the implant into limb stump

A study of osseointegration characteristics, as well as an assessment of the safety profile and determination of limitations associated with the product on a post-amputated limb, was conducted experimentally on two groups of mongrel dogs. The surgeries were performed in two stages under sterile conditions under intravenous anesthesia with propofol 10 mg/ml and preliminary premedication.

The first stage involved shaping a limb stump. A skin incision was made in the middle third of the tibia on the medial surface. The soft tissues were dissected, and an osteotomy was performed on the tibia using an oscillating saw at the junction of the upper and middle thirds. After the stump was formed, the soft tissues were sutured layer by layer.

The second stage of the experiment was conducted 10 weeks later. During the second operation, a skin flap was created in the stump area, adapted to the bone edges. The medullary canal was then drilled to accommodate the implant diameter, in our case up to 7 mm. The implant was driven into the hole with precisely aimed short hammer blows (Fig. 3).

Fig. 3 Photo of the procedure for installing a Press-Fit implant into a tubular bone

To expose the external portion of the implant, an opening was created in the skin flap, after which the stump was modeled and the soft tissues were sutured layer by layer. To prevent loosening and to apply a compressive load of 20 N to the prosthetic bone, the implant was secured with a special device for the first five weeks after surgery (Fig. 4 b) [30].

Assessment of osteointegration

To assess the effectiveness (survival) and safety of the implants, a series of clinical, radiological, histological and laboratory studies were performed.

Clinical examination of animals (physical examination, local status, condition of soft tissues and postoperative wounds) was carried out throughout the entire experiment term.

A Compact X-ray system (Milan, Italy) was used for radiography. The current was 60 mA, the voltage was 57–69 kV, and the exposure time was 0.4–0.6 s. Specific operating parameters depended on the animal's constitution.

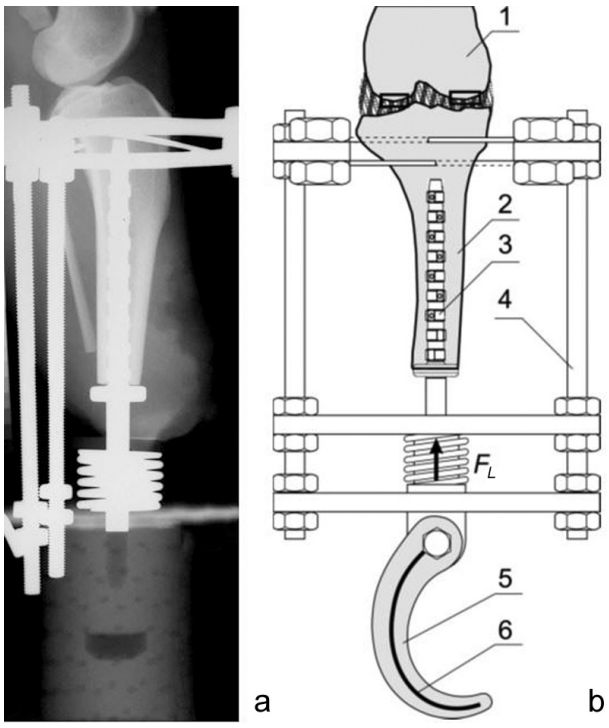

Fig. 4 Radiograph of the dog's lower leg after implant placement (a) and the fixation and compression loading device (b): 1 — femur; 2 — tibia; 3 — implant; 4 — assembled fixation and compression loading device; 5 — silicone prosthesis; 6 — stiffness spring, F_L — compression load

Radiographs of the limb were taken in the frontal and lateral views. Radiographs were taken before and after surgery, every seven day for the first five weeks after surgery, and then once every 14 days of the experiment.

Histological study

The weight fraction of Ca and P (in wt.%) in different areas of the tibial stump with an integrated implant was determined using a Zeiss EVO MA18 scanning electron microscope (Carl Zeiss Group, Germany) and a BRUKER QUANTAX 200 - XFlash 6/10 energy-dispersive spectrometer (Bruker Nano GmbH, Germany) mounted on the microscope base. The operating accelerating voltage was 20 kV. Data collection and analysis were performed using ESPRIT software (Bruker Nano GmbH, Germany).

Biochemical study

Levels of total protein, urea, creatinine, total calcium, inorganic phosphate, C-reactive protein (CRP), as well as the activity of alkaline (ALP) and tartrate-resistant (bone) isoenzyme of acid (TrAP) phosphatase, transaminases (AST, ALT) in the blood serum of experimental animals was determined on an automatic biochemical analyzer Hitachi/BM 902 (F. Hoffmann-La Roche Ltd., Italy) using reagent kits from Vital Diagnostics and BioSystems (Russia).

Statistical methods

The results in the tables are presented as the median and quartiles 1–3 (Me, Q1–Q3), the median and minimum and maximum values (Me, min–max), and the arithmetic mean and standard deviation (X ± SD). The statistical evaluation of the significance of differences in quantitative indicators at the experiment time points compared to preoperative values was performed using the Wilcoxon signed-rank test for related samples. The significance of intergroup differences was assessed using the Mann – Whitney t-test. The Barnard test was used for frequency indicators; differences were considered significant at $p < 0.05$.

RESULTS

The clinical condition of all animals after implantation was satisfactory; the implants remained stable. A week after surgery, despite intermittent lameness, all dogs began using the operated limb. By the fourth week of the experiment, dogs in both groups showed only slight residual lameness, which completely resolved by the sixth week of the study.

One animal in Group 1 experienced inflammation in the area of the compression device pins in the early postoperative period. The inflammation resolved within a week treated with an antiseptic solution and anti-inflammatory ointment. It should be noted that all animals in that group experienced hyperemia in the area of skin-implant contact in the early postoperative period, which also resolved within seven days with the use of a heparin-based decongestant ointment.

In Group 2, one dog had a suture rupture, but the wound healed by primary intention. No inflammatory changes were observed in the early postoperative period in animals in this group.

Six weeks after implant placement, the compression device was removed. The implant was stable in animals from both experimental groups; however, dogs in Group 1 showed some signs of bone resorption and minor periosteal stratification in the distal bone (Fig. 5 a). In contrast, in Group 2, stratification appeared near the "stop ring", indicating active endosteal bone formation in the implantation area (Fig. 5 b).

Twenty-six weeks after the implantation, implants were stable in all animals. In animals of group 1, organotypic bone restructuring and compaction of periosteal layers were noted (Fig. 6 a). In animals of group 2, the organotypic reorganization of the bone around the implant was already completed (Fig. 6 b).

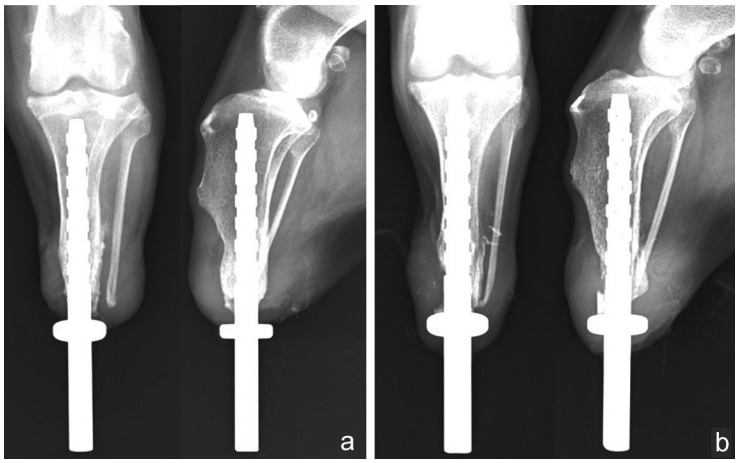

Fig. 5 Fragments of radiographs of the lower leg of dogs from group 1 (a) and group 2 (b) 42 days after surgery

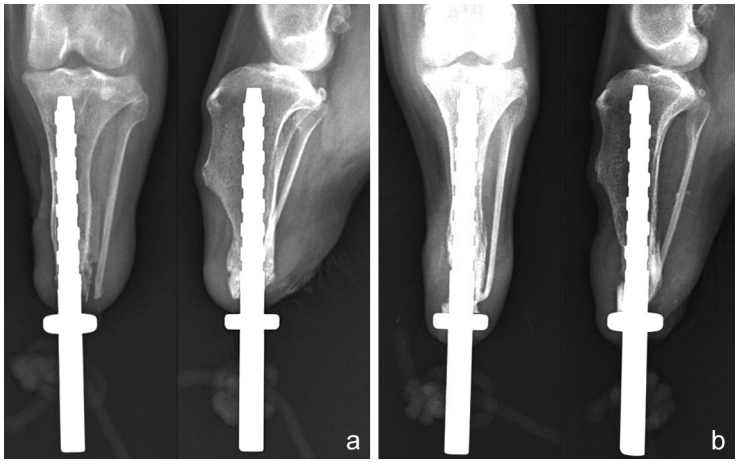

Fig. 6 Fragments of radiographs of the lower leg of dogs from group 1 (a) and group 2 (b) 180 days after surgery

The radiographic images indicate that signs of more pronounced osteogenesis in the "implant-bone" system were observed in the animals of group 2.

By the end of the experiment (26 weeks), a single bone-implant block was formed in both groups (Fig. 7), with the implant fully integrated into the bone tissue. Cancellous bone tissue, predominantly fine-meshed and, in some areas, medium-meshed, was formed along the entire perimeter of the implant surface in both groups. Throughout the entire bone-implant block, the compact plate was continuous and sufficiently dense.

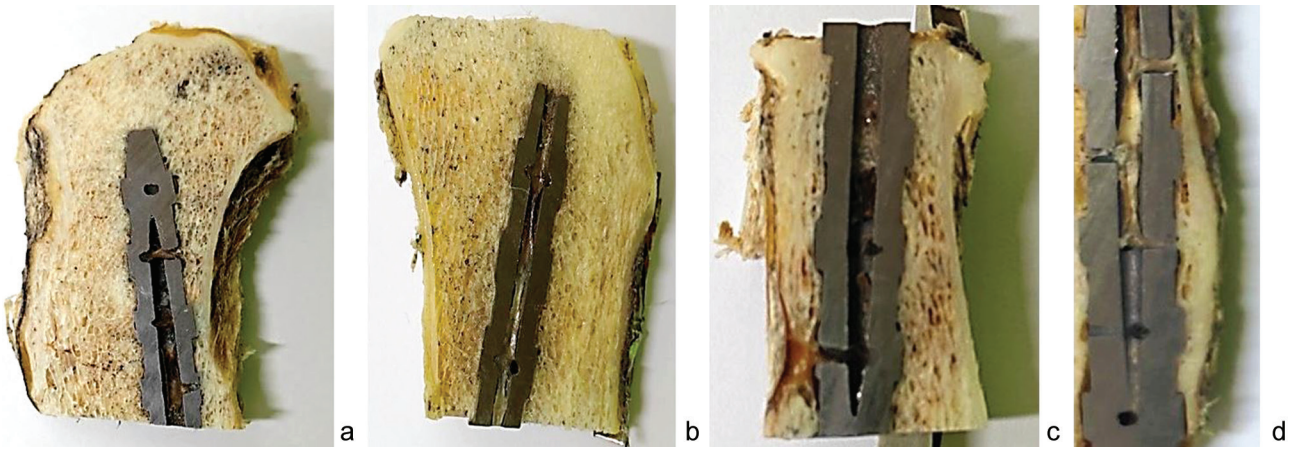

Fig. 7 Photos demonstrate the formation of the bone-implant block 26 weeks after implantation: (a) saw cut through the proximal part of the tibia of a dog from group 1 (without coating); (b) saw cut through the proximal part of the tibia of a dog from group 2 (with coating); (c) saw cut through the diaphysis of the tibial stump of a dog from group 1 (without coating); (d) saw cut through the diaphysis of the tibia of a dog from group 2 (with coating). Magnification: 1.5×

Energy-dispersive analysis revealed that the bone tissue calcium content in all areas of the bone-implant blocks of animals in Group 1 was significantly lower than in Group 2 (Table 1), and the phosphorus content in Group 1 was significantly higher than in Group 2. The exceptions were the areas of the compact plate in the distal part and the cancellous bone formed around the implant in the middle part of the tibial stump, where the phosphorus content in both groups was identical and did not differ significantly. In both groups, in the compact plate zone, the concentration of the determined elements was slightly higher in the distal part. A lower content of osteotropic elements was noted in the proximal part of the bone stump. Endosteally formed bone tissue that was localized around the implant in both groups contained lower amounts of calcium and phosphorus compared to the compact plate in each of the analyzed zones of both groups.

Table 1

Content of Ca and P in different parts of bone-implant block 26 weeks after implantation

Group	Element	Content of Ca and P (wt.%), X ± SD					
		Distal part		Middle part		Proximal part	
		Compact plate	Round the implant	Compact plate	Round the implant	Compact plate	Round the implant
1	Ca	18.4 ± 0.14	8.37 ± 0.23	16.16 ± 0.97	8.99 ± 0.71	14.12 ± 0.43	6.16 ± 0.13
	P	9.90 ± 0.31	4.98 ± 0.42	9.02 ± 0.23	4.87 ± 0.04	6.98 ± 0.25	3.04 ± 0.04
2	Ca	19.9 ± 0.84*	9.60 ± 0.17*	18.1 ± 0.67*	9.98 ± 0.91	16.97 ± 0.83*	8.61 ± 0.11*
	P	9.10 ± 0.85	3.99 ± 0.12*	8.89 ± 0.09*	4.78 ± 0.07	6.36 ± 0.17*	3.63 ± 0.07*

Note: * significance of difference at $p < 0.05$ compared to group1

The dynamics of changes in ALP activity revealed an increase relative to preoperative values in the animals of group 1 at the third and sixth weeks after implantation, and in group 2 at the sixth and 12th weeks (Table 2). Moreover, at the sixth and 12th weeks, ALP activity in the animals of group 2 was higher relative to the animals of group 1. TrAP activity in group 1 was higher than the preoperative level at the sixth and 26th weeks after implantation, while in group 2 it was reduced at the third week and increased at the 26th weeks, while the values were significantly higher relative to the values of group 1 at those time points. A single decrease in the level of total calcium in the blood serum of group 1 dogs was noted at the third week after implantation. Such changes indicate a more significant activation of osteogenesis in the animals of group 2 relative to group 1.

Table 2

Changes in phosphatase activity and concentrations of total calcium and inorganic phosphate in the blood serum of dogs after implantation

Week	Group	Activity and concentrations, Me (Q1–Q3)			
		ALP, units/l	TrAP, units/l	Calcium, mmol/l	Phosphate, mmol/L
0	1	36 (29–42)	4.85 (4.78–4.93)	2.60 (2.57–2.63)	1.20 (1.09–1.30)
	2	37 (33–41)	4.40 (4.22–4.95)	2.58 (2.44–2.61)	1.25 (1.12–1.42)
3	1	62* (59–65)	4.50 (3.90–5.10)	2.50* (2.46–2.54)	1.30 (1.23–1.37)
	2	38 (33–60)	**3.40*(2.03–3.60)**	2.58 (2.44–2.62)	1.45 (1.23–1.47)
6	1	54*(50–58)	5.85*(5.73–5.98)	2.64 (2.62–2.67)	1.29 (1.22–1.36)
	2	**64*(60–76)**	3.70 (2.23–5.08)	2.59 (2.54–2.64)	1.13 (1.09–1.27)
12	1	38 (30–45)	4.50 (4.12–5.12)	2.61 (2.50–2.64)	1.28 (1.21–1.38)
	2	**67*(58–93)**	3.85(3.45–4.43)	2.60 (2.56–2.65)	1.24 (1.24–1.29)
26	1	43 (36–61)	8.30*(7.05–9.55)	2.68 (2.53–2.70)	1.43 (1.32–1.55)
	2	39 (26–53)	**5.90*(5.15–6.10)**	2.54 (2.52–2.58)	1.24 (1.17–1.31)

Notes: * — differences with preoperative (period 0) values at $p < 0.05$; **bold** — differences in the indicator with group 1 at $p < 0.05$.

No differences were observed in the dynamics of changes in total protein, urea, creatinine, or transaminase (ALT, AST) levels between the animals in the studied groups (data not shown). However, in the animals in Group 1, CRP levels were significantly elevated relative to preoperative values at three weeks post-implantation, which was not observed in any animals in Group 2.

Thus, based on the histological study, it can be concluded that both uncoated and zinc-containing calcium phosphate-coated Press-Fit threaded implants exhibited acceptable osseointegration characteristics. The coated Press-Fit implant exhibited greater osseointegration, as confirmed by quantitative characteristics obtained during the histological study. The formation of denser, more mineralized structures on the surface of the bioactive-coated implant prevented calcium efflux from the compact plate of the bone stump. Furthermore, the zinc-containing calcium phosphate coating promoted the formation of a denser bone envelope around the implant in the distal portion of the stump, which is beneficial for implant stabilization in the bone at the implant-abutment junction.

The laboratory findings show the absence of any significant pathological changes in parameters characterizing the body's systemic response to implantation (including the response of visceral organs, such as the liver and kidneys). The individual changes noted, such as an increase in CRP, can be attributed to expected changes associated with the body's response to implantation, moreover those changes were transient.

In general, a complex of histological and laboratory studies, as well as clinical examination, allow us to note the absence of significant local and systemic disorders in the animals of both groups during the period of implant osseointegration, which indicates their good tolerability. At the same time, zinc-containing calcium phosphate coated products have a more beneficial safety profile compared to uncoated products.

DISCUSSION

Currently, there are opinions about the advantages of using percutaneous implants, such as Press-Fit, for solving prosthetic problems, in particular, the implementation of a one-stage integration which reduces the rate of complications] and increases the survival rate of the implant [32]. Literature data [33] and the findings of our study show the absence of any pronounced adverse effects during implantation, including reactions of visceral organs (liver, kidneys, etc.) after Press-Fit type implant application.

The improvement of this type of implants for prosthetics is being pursued in several directions: improvement of the design of the product and materials it is made of [34, 35], including an attempt to personalize the implant [36]; modification of the surface of the integrated part, including the application of additional coatings that facilitate integration [37–39]; control of the load on the implant [40, 41]. These principles were also implemented by us in the study, demonstrating the advantages of using a zinc-containing calcium phosphate coating under the conditions of compressive load on the implant due to an increase in the efficiency of osseointegration and the safety profile, what is consistent with the literature data [42].

Thus, the results of the study are confirmed by the data reported in the domestic and foreign scientific literature and expand the evidence base for the effectiveness of the use of titanium SLM Press-Fit implants with a zinc-containing calcium phosphate coating in osseointegration prosthetics.

Study limitations Osseointegration of the implants in this study was tested on a small number of animals. The lack of long-term results necessitates additional comparative studies of the long-term stability of implant integration with this type of coating. Furthermore, growing experience with the use of osseointegration technology for prosthetic applications demonstrates the need to develop specialized instrumentation for implant removal (infection, reinstallation, wear) [43].

CONCLUSION

The data obtained in this study demonstrate that both products are able to sufficiently integrate into the bone stump and have no significant limitations for their intended use. Given the approach that requires minimizing the risks associated with the use of implantable medical devices, the zinc-containing calcium phosphate coated product may be preferred as it offers certain advantages in terms of osseointegration efficiency and safety.

Conflict of interests *Not declared*

Funding source *This work was conducted as part of the state assignment to the Ilizarov National Medical Research Center of Traumatology and Orthopedics "Development of new Press-Fit implants that ensure the formation and activation of bone matrix particles to improve the survival rate and reliability of prosthetics". The production of coatings on medical devices and the study of their characteristics were carried out within the framework of the state assignment of the Institute of Strength Physics and Materials Science SB RAS (project No FWRW-2026-0004).*

Ethical statement *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 Experimental and other Scientific Purposes and Directive 2010/63/EU of the European Parliament and of the Council of 22 September 2010 on the protection of animals used for scientific purposes. Approval for the study was obtained from the institutional ethics committee (protocol dated 29.11.2024 No. 1(176)).*

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Evaluation of bone substitute material based on polyurethane polymers for treatment of chronic osteomyelitis (experimental morphological study)

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Abstract

Introduction Treatment of patients with post-osteomyelitic defects is one of the most challenging areas in traumatology and orthopedics.

Purpose To substantiate, on an experimental model, the potential of a partially bioresorbable material *Rekost* used to compensate for osteomyelitic cavities in combination with an antibiotic.

Materials and methods The study was performed on nine male Soviet Chinchilla rabbits (16–18 months old, 4.3–4.5 kg of weight), in which osteomyelitis was modeled in the proximal metaphysis of the tibia by producing a trepanation hole and installing an Osteolite™ containing a *Staphylococcus aureus* culture. The animals were divided into three groups. Animals in group 1 were withdrawn from the experiment after 21 days of osteomyelitis modeling. In groups 2 and 3, the second stage included sequestronecrectomy and substitution of the bone defect thus formed with *Rekost* material (OOO AikonLabGmbh, Nizhny Novgorod, RZN 2014/1646 dated 03.07.2014, for indefinite) impregnated with an antibiotic in group 3. After 21 days of implantation, the animals were withdrawn from the experiment. Clinical, radiological, biochemical and histological methods were used.

Results In Group 1, signs of osteomyelitis were recorded: necrotic fragments of bone trabeculae, inflammatory infiltrate, osteoclastic resorption and osteogenesis, bone marrow fibrosis, and pronounced CD15 expression. In groups 2 and 3, three weeks after implantation, a network of newly formed bone trabeculae at the bone-material interface was noted, and bone trabeculae were observed in the implant cavities. In the epiphysis of group 2, a HOES score of ⩾ 6 points corresponded to active chronic osteomyelitis. In group 3, a median HOES score of 2 points indicated a remission of chronic osteomyelitis, and CD15 marker expression was less pronounced than in group 2. C-reactive protein levels continued to increase in Group 2 and significantly decreased in Group 3.

Discussion Bioresorbable implants, impregnated with antibiotics, provide gradual replacement of the material with bone tissue, eliminate the need for repeated surgeries, reduce the risk of chronic infection, and are biocompatible.

Conclusion In an in vivo experimental model, minimal degradation of the *Rekost* material was observed three weeks after implantation, manifested by highly frequent foreign-body-type giant multinucleated cells. Early data on the osteoplastic properties of the Rekost material and its ability to suppress infection and inflammation in combination with an antibiotic suggest the potential for further experimental studies of this product to be used in the treatment of patients with chronic osteomyelitis.

Keywords: coronary osteomyelitis, bone defects, Recost bone-substituting material, antibiotics, histology

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INTRODUCTION

High incidence of chronic osteomyelitis that ranges from 3 to 25 % of all musculoskeletal diseases, its recurrence rates of up to 30–40 %, secondary amputations and functional limb disability in 10.3–57 % of cases required the search for new ways to improve the outcomes of its surgical treatment [1, 2, 3]. Regardless of pathophysiology, the majority of osteomyelitis cases are caused by the gram-positive bacterium *Staphylococcus aureus* [4, 5], which can persist in the Haversian canals, in the interlamellar spaces of osteons and trabeculae, and intracellularly in macrophages. This fact plays a major role in chronic bone infection, characterized by persistent inflammation, destruction of bone tissue, and impaired regeneration [6, 7]. Osteomyelitis triggers pathological bone remodeling, which isolates foci of infection from the effectors of innate immunity [5]. Current approaches to treating patients with chronic osteomyelitis include antibiotic therapy, surgical resection of infected areas, and compensation of bone defects. Bone compensation is a key step, as insufficient bone tissue lead to recurrent infections and musculoskeletal dysfunction [8].

Surgical intervention in the management of osteomyelitis allows for the targeted delivery of high-dose antibiotics to the site of inflammation, reduces the toxic and side effects of drugs through the use of various types of implants and materials for substitution in bone cavities, which is an important component of the therapy [9, 10, 11]. Particular efforts are directed at the development of new antimicrobial biomaterials that not only eliminate infection but also promote the subsequent process of bone tissue restoration [2, 9]. The use of local drug carriers based on polymethyl methacrylate [12, 13], carbon, ceramics [14, 15] and biopolymers [16, 17, 18] enables arrest of infection, compensation of defects, support of soft tissue tension and stimulation of bone tissue regeneration, which has been confirmed by a number of studies [19, 20, 21, 22]. However, non-biodegradable materials do not provide prolonged release of antibiotics [23, 24]; their main disadvantages are incompatibility with many antimicrobial drugs [25] and the need for repeated surgery to remove such a spacer [5, 26].

The use of a partially bioresorbable material impregnated with an antibiotic is a promising option for treating infection and restoring bone in a single surgical procedure, thus reducing costs and shortening the length of hospital stay [27, 28, 29].

The advance in surgical treatment methods for patients with chronic osteomyelitis requires experimental studies aimed at modeling the chronic process, developing effective technologies, and identifying materials that combine antibacterial and osteoinductive properties [30, 31, 32].

Purpose To substantiate, on an experimental model, the potential of a partially bioresorbable material *Rekost* used to compensate for osteomyelitic cavities in combination with an antibiotic.

MATERIAL AND METHODS

Study design

The study was conducted on nine male laboratory rabbits of the Soviet Chinchilla breed, aged 16–18 months, weighing 4.3–4.5 kg, which were randomly divided into three groups of three animals each.

Inclusion criteria: Clinically healthy rabbits of Soviet Chinchilla breed, free from musculoskeletal diseases.

Exclusion criteria: Animals with somatic diseases and pathologies of the musculoskeletal system.

At the first stage, chronic osteomyelitis of the proximal metaphysis of the right tibia through infection of the bone marrow cavity with a culture of *Staphylococcus aureus* (MSSA, reference strain, 1×10^6 CFU). A block of bone matrix *Osteolite*® measuring 4 × 4 mm was used as a carrier

of the infectious agent (RZN 2023/19470 Lyophilized bone bioimplants, sterile for traumatology and orthopedics *Osteolite*®, Russia). Before the operation, the bone matrix block *Osteolite*® was placed for 5–7 minutes in an aqueous suspension of a 24-hour culture of *Staphylococcus aureus* for soaking. The volume of absorbed culture was 0.05 ml (0.0386 g).

A surgical approach to the bone surface was performed on the medial surface of the proximal tibial metaphysis. A bone burr was used to create a hole in the cortex corresponding to the size of the infectious agent carrier. A bone matrix block soaked in the infectious agent culture was placed in the metaphysis cavity so that its outer surface was within the burr hole but did not protrude above its surface. The burr hole was then hermetically sealed with Knochenwachs bone wax (AESCULAP AG, Germany). The surgical wound was sutured with single-layer interrupted PDS 4/0 sutures (Ethicon, Johnson & Johnson, USA). The waiting time for osteomyelitic process to develop was 21 days. At that point, animals from Group 1 were withdrawn from the experiment for morphological confirmation of osteomyelitic process.

In the second stage, animals in Group 2 and Group 3 underwent sequester necrectomy and bone defect filling with *Rekost* polymer bone substitute material (OOO AikonLabGmbh, Nizhny Novgorod, RZN 2014/1646 dated July 3, 2014, indefinite). Fistula tract tissue was excised, and exostoses on the cortical surface around the trepanation hole were removed. Using spherical bone burrs (Ø 1 and 4 mm), the osteomyelitic lesion was opened, removal of sequestra followed along with granulation tissue and purulent exudate, with cleaning of the endosteal surface of the metaphysis down to the blood-supplied areas of the bone. Next, according to the instructions, the components of the *Rekost* bone substitution polymer material were mixed and animals in Group 3 received Vancomycin antibiotic powder at a ratio of 1 g of active ingredient per 10 ml of bone cement. The resulting mixture was drawn into a 1 ml syringe with a cut-off needle cone and evenly filled into the bone defect cavity, avoiding air pockets. After partial polymerization, the excessive material was trimmed with scissors to the level of the cortex. The surgical wound was closed with single-layer interrupted sutures using PDS 4/0 (Ethicon, Johnson & Johnson, USA) on the skin. In Groups 2 and Group 3, the study continued 21 days after defect repair, after which the animals were withdrawn from the study.

Surgical interventions were performed under general anesthesia. For premedication, a solution of diphenhydramine 1 % (0.02 mg/kg), atropine sulfate 0.1 % (0.02 mg/kg) and meditin 1 % (0.35 mg/kg) was used. For anesthesia, a propofol emulsion 1 % (4 mg/kg/min) was used. Thirty minutes before the start of the operation, a solution of ethamsylate 12.5 % (10–12 mg/kg) was administered to prevent bleeding and a solution of ketoprofen 10 % (2 mg/kg) as an analgesic and anti-inflammatory agent. Antibiotic therapy was not used. Euthanasia was performed by intravenous administration of high doses of anesthetics under general anesthesia.

Ethical approval

The study was carried out in accordance with the rules of the European Convention (ETS No. 123) for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes and interstate standards (GOST 33044-2014), and was approved by the local ethics board (protocol dated 11/29/2024 No. 1 (76)).

Clinical and laboratory methods

The general condition of the animals, the condition of the skin, the color of the mucous membranes, food and water consumption, the condition of the implantation area (local changes in soft tissues, healing of the postoperative wound) were assessed. The general body temperature was measured

rectally for 1 minute using a DT-623 thermometer Vega Technologies Inc (China). Animals were weighed on a Shtrikh-MIB 15–2.5 desktop electronic scales (Russia). Radiography of the implantation site was performed in frontal and lateral views at the stages of surgical intervention and on the 21st day after defect filling using a Toshiba (Rotanode) Model E7239 system; N: 10G749 (Japan). The current was 2.5–3.2 mA, the voltage was 43-44 kV, the focal length was 90 cm: the shutter speed was set automatically.

Biochemical method

C-reactive protein (CRP) levels were determined in the serum of the experimental animals. The studies were performed on a Hitachi/BM 902 automated biochemical analyzer (F. Hoffmann-La Roche Ltd., Italy) using Vital Diagnostics reagent kits (Russia).

Histological method

The object of the study was the proximal metaepiphysis of the tibia.

The material harvested was fixed in 10 % neutral formalin, decalcified, and subjected to standard histological processing using a HISTOSAFE™ INFILTRA™ tissue vacuum processing apparatus (ErgoProduction LLC, Russia). Paraffin sections (5–7 μm) were prepared on a Thermo Scientific HM 450 microtome (USA) and stained with hematoxylin and eosin and Masson's three-color staining. An AxioScope.A1 microscope with an AxioCam ICc 5 camera and Zenblue software (Carl Zeiss Micro Imaging GmbH, Germany) was used to obtain digital images of the specimens.

To assess the infectious and inflammatory process, the semi-quantitative HOES score developed by A. Tiemann et al. was used, including an analysis of the severity of soft tissue necrosis, osteonecrosis, bone neogenesis and fibrosis, and inflammatory infiltrate in points (0 — no changes, 1 — mild, 2 — moderate, 3 — severe) [33]. Five to 10 fields of view were analyzed in each animal at a magnification of ×100.

Granulocytes were detected by immunohistochemistry using mouse polyclonal antibodies to CD15 (ab233869) (Abcam, UK) and a peroxidase detection system with diaminobenzidine and micropolymer (ab236469, Rabbit-specific HRP/DAB Detection IHC Detection Kit-Micropolymer, Abcam, UK). All steps were performed according to the protocol recommended by the antibody manufacturer. Sections were counterstained with hematoxylin.

Statistical methods

The study was conducted on small samples (three animals per group). Table 1 presents the primary data. Table 2 presents the data as medians and quartiles (Me ($p25$;$p75$)). Statistical processing was performed in Microsoft Excel spreadsheets using the Attestat program (version 9.3.1, author I.P. Gaidyshev, Rospatent Certificate No. 2002611109). For comparative analysis, the nonparametric Mann – Whitney test was used, which allows for the detection of differences between small samples at a significance level of $p < 0.05$.

RESULTS

In Group 1 animals, slight edema, moderate hyperemia, and scant to moderate purulent exudate were observed at the site of inoculation of the infectious agent. The general condition was characterized by a poorer appetite and a decrease in body weight by an average of 13.5 %. The general body temperature remained within the physiological norm throughout the entire stage of osteomyelitis modeling. In animals of Group 2, soft tissue edema, diffuse hyperemia, moderate to profuse purulent discharge were observed at the surgical site after defect filling, and focal dermatitis and phlegmon

were observed in the perioperative area. The body weight decreased relative to the preoperative values by 25.8 % on average. The general body temperature was above normal physiological values. In Group 3, after defect filling, the general condition was assessed as good in two cases, and the healing of the surgical wound was uneventful. The body weight decreased relative to preoperative values by an average of 17.8 %. The general body temperature was within normal physiological reference limits. In one case, the general condition and local symptoms corresponded to the clinical picture of osteomyelitis.

In the radiographs taken after the procedure of the infectious agent insertion into the proximal metaphysis of the tibia, the edges of the trepanation hole and the *Osteolite*® bone matrix block were clearly visible (Fig. 1 a). Twenty-one days after infection, multiple rounded areas of bone tissue lysis were observed in the intervention area. The edges of the trepanation hole were indistinct, the bone tissue was partially sclerotic and surrounded by a lysis zone, and the boundary between the bone matrix block and the bone was smoothed. Dense periosteal exostoses were noted on the cortical plate (Fig. 1 b). During sequester necrectomy, the pathologically altered tissue was removed, and the bone defect cavity was filled with *Rekost* bone substitute material, which was non-radiopaque in radiographs, including after the addition of vancomycin (Fig. 1 c).

In Group 2, by day 21 after sequesternecrectomy and defect repair, radiographs showed signs of total inflammatory destruction of the metaphyseal bone tissue. The central metaphysis had low optical density, and the boundaries of the trepanation hole and bone defect were blurred. The defect cavity projection showed randomly distributed structures of medium and low intensity, varying in size and with an unclear outline. The cortex had a blurred outline and a heterogeneous structure. Weak, thin, cloud-like periosteal deposits were noted on its lateral surface (Fig. 1 d).

In Group 3, the proximal tibial metaphysis had smooth contours and a homogeneous bone structure. The radiographic density of bone tissue in the defect area was identical to that of the parent bone. The boundaries of the bone defect cavity were undetectable. No foci of bone destruction or lysis were observed. Periosteal layers were dense, organized, and located around the trepanation hole. The metaphyseal cortex had a clear contour, uniform structure, and average radiographic density (Fig. 1 e). In one animal with purulent exudate discharge from the surgical wound in the postimplantation period, radiographs showed signs of chronic osteomyelitis manifested by focal bone destruction in the epiphyseal and distal parts of the metaphysis and weak periosteal layers around the trepanation hole (Fig. 1 f).

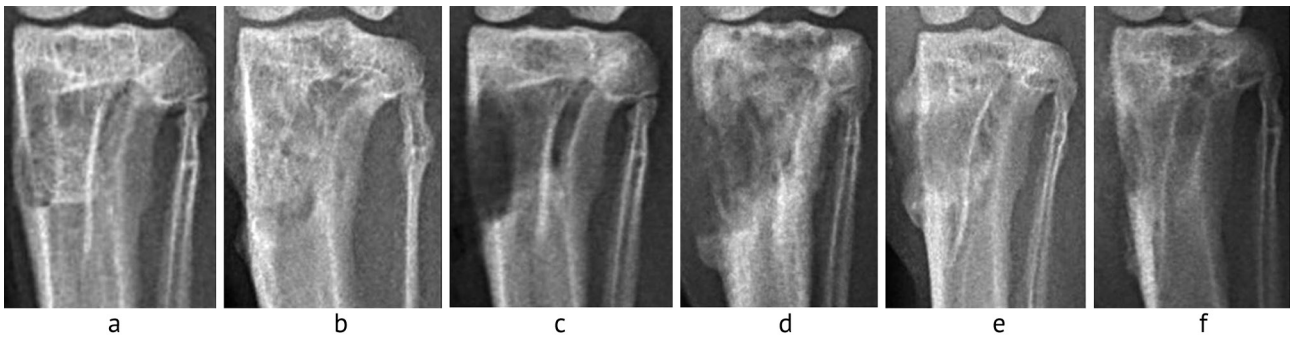

Fig. 1 Radiographs of the proximal metaphysis of the tibia of rabbits (anteroposterior view) at the stages of the study: (a) introduction of an infectious agent, the day of surgery; (b) 21 days after introduction of infection; (c) sequester necrectomy and filling of the bone defect, the day of surgery; (d) Group 2, 21 days after defect filling; (e) Group 3, 21 days after defect filling, fair result; (f) Group 3, 21 days after defect filling, poor result

The CRP level in the blood serum of all animals in all groups increased significantly on the 21st day after infection agent introduction (Table 1).

Table 1

Concentration of C-reactive protein in the blood serum of the animals in the experimental groups

Groups / animals		Концентрация СРБ (мкг/л)		
		0 days	21 days	42 days
Group 1	1	0	11.8	–
	2	0	15.2	
	3	1.8	30.7	
Group 2	1	0	12.7	25.3
	2	0	18.0	50.4
	3	0	25.3	31.6
Group 3	1	0	10.0	0
	2	0	18.3	7.6
	3	0	23,4	20.5; $p^{2-3} = 0.0495$

Note: p — level of significance of differences after comparing Groups 2 and 3 using the Mann – Whitney test $p < 0,05$.

In Group 2, CRP levels increased in all animals 21 days after implantation of the material (day 42 of the experiment), indicating further development of the infectious process. In Group 3, CRP levels decreased significantly in two animals 21 days after implantation of the antibiotic-impregnated material, and less significantly in one.

Light-optical investigation of histological group preparations revealed extensive fields of granulation and connective tissue in the proximal metaphysis of the tibia (Fig. 2 a), bone trabeculae with signs of necrosis (Fig. 2 b), bone microsequesters (Fig. 2 c), inflammatory infiltrate of focal and diffuse types of distribution (Fig. 2 c, d) containing neutrophils, plasma cells, macrophages, and single giant multinucleated cells of the foreign body type (Fig. 2 e). Signs of osteoclastic resorption (Fig. 2 e) and reparative osteogenesis (Fig. 2 b, f) were recorded. The median score on the HOES scale [33] of 6 points corresponded to the active inflammatory phase of chronic osteomyelitis (Table 2).

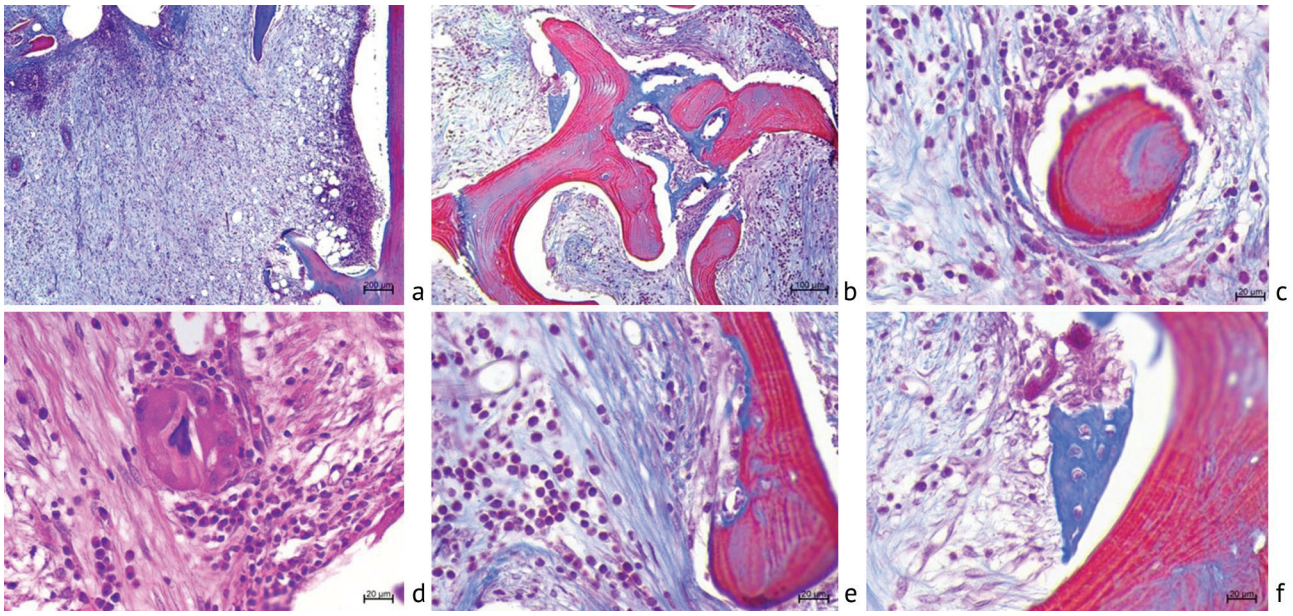

Fig. 2 Fragments of images of the proximal metaphysis of the tibia of Group 1: (a) extensive fields of granulation and connective tissue in the metaphysis; (b) trabeculae with empty osteocyte lacunae and newly formed bone trabeculae; (c) bone microsequestrum; (d) giant multinucleated cell, inflammatory infiltrate; (e) thinning of the bone trabecula, "corrugated edge" resulting from of osteoclastic resorption; (f) in the center, a newly formed area of bone tissue (the matrix is stained blue). Paraffin sections, stained with Masson's three-color method (a, b, c, e, f), hematoxylin and eosin (d). Magnification ×40 (a), ×100 (b), ×400 (c, d, e, f)

Table 2

Semiquantitative assessment of chronic osteomyelitis using the HOES scale

Groups	HOES score, points, Me ($p25$;$p75$)	Chronic osteomyelitis stage
Group 1	6 (5;6)	CAO
Group 2	7 (6;7); $p^{1-2} = 0.0165$	CAO
Group 3	2 (1;3); $p^{1-3} = 0.0001$; $p^{2-3} = 0.0001$	COR

Notes: COR — chronic osteomyelitis remission; CAO — chronic osteomyelitis active; p — level of significance by comparing Groups 1, 2 and 3 Mann – Whitney test at $p < 0.05$

In Group 2, histological signs of chronic osteomyelitis were noted in the epiphysis, including replacement of bone marrow with connective tissue (Fig. 3 a), intense signs of bone trabeculae remodeling, osteoclastic resorption (numerous osteoclasts resorbing the ground substance, trabeculae with ulcerated surfaces, with interstitial osteonecrosis), reparative osteogenesis (numerous osteoblasts lining the bone trabeculae) (Fig. 3 c, d), and lymphohistiocytic infiltrate containing neutrophils of focal and diffuse distribution (Fig. 3 e). The median semiquantitative HOES score [33] of 7 points corresponded to the active inflammatory phase of chronic osteomyelitis (Table 2).

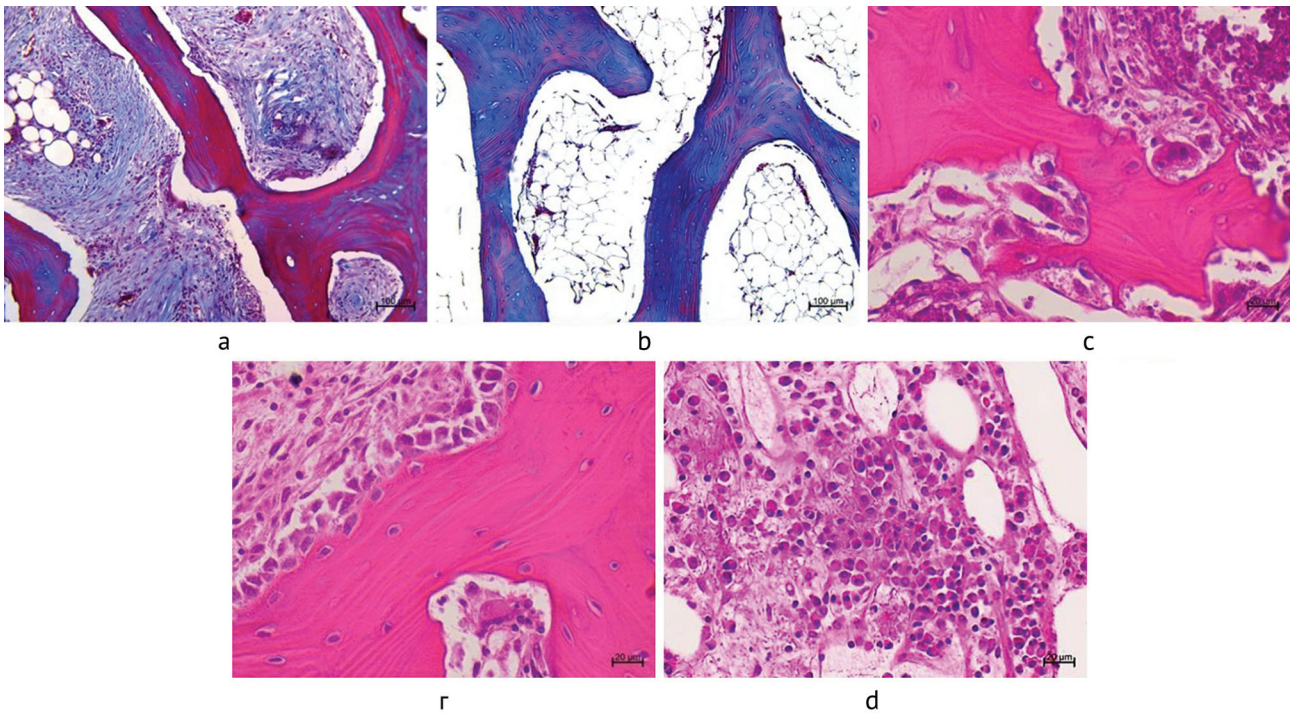

Fig. 3 Fragments of images of the proximal tibial epiphysis: (a) Group 2, replacement of bone marrow with connective tissue; (b) Group 3, fatty bone marrow in the intertrabecular spaces; (c) Group 2, numerous osteoclasts; (d) Group 2, osteoblasts on the surface of the trabecula, osteoclasts below; (e) Group 2, lymphohistiocytic infiltrate of diffuse distribution. Paraffin sections, stained with Masson's three-color method (a, b), hematoxylin and eosin (c, d, e). Magnification ×100 (a, b), ×400 (c, d, e)

In Group 3, histological signs of chronic osteomyelitis were not detected in the epiphysis of two animals; the intertrabecular spaces were filled with fatty bone marrow (Fig. 3 b). The median HOES score [33] of 2 points indicated remission of chronic osteomyelitis (Table 2). Focal bone marrow fibrosis was seen in one animal; rare arrangement of bone trabeculae, disruption of their architecture, and a lymphohistiocytic infiltrate with solitary neutrophils of diffuse distribution were observed in the intertrabecular spaces.

Immunohistochemical study showed that the intensity of CD15 expression was highest in Group 2 and lowest in Group 3 (Fig. 4).

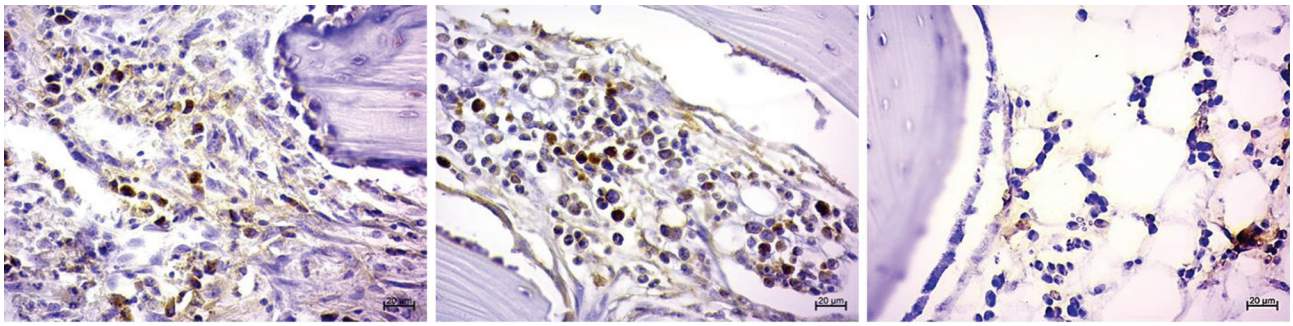

Fig. 4 Fragments of images of the proximal tibial epiphysis, CD15 expression: (a) Group 1; (b) Group 2; (c) Group 3. Paraffin sections. Magnification ×400

Filling the defect between the epiphysis and the implant in Group 2 featured extensive fields of loose connective tissue (Fig. 5 a); in Group 3 there was predominantly fatty bone marrow (Fig. 6 a). At the border with the implant, the formation of a network of newly formed bone trabeculae was noted in all cases. In the partially bioresorbable implant in Group 2, part of the polymer cavities was filled with blood cells and primary matrix, loose connective tissue, newly formed bone trabeculae (Fig. 5 b) with numerous active osteoblasts (Fig. 5 c); giant multinucleated cells of the foreign body type (Fig. 5 d), dense, diffusely distributed lymphohistiocytic infiltrate with single neutrophils (Fig. 5, c, d) were noted.

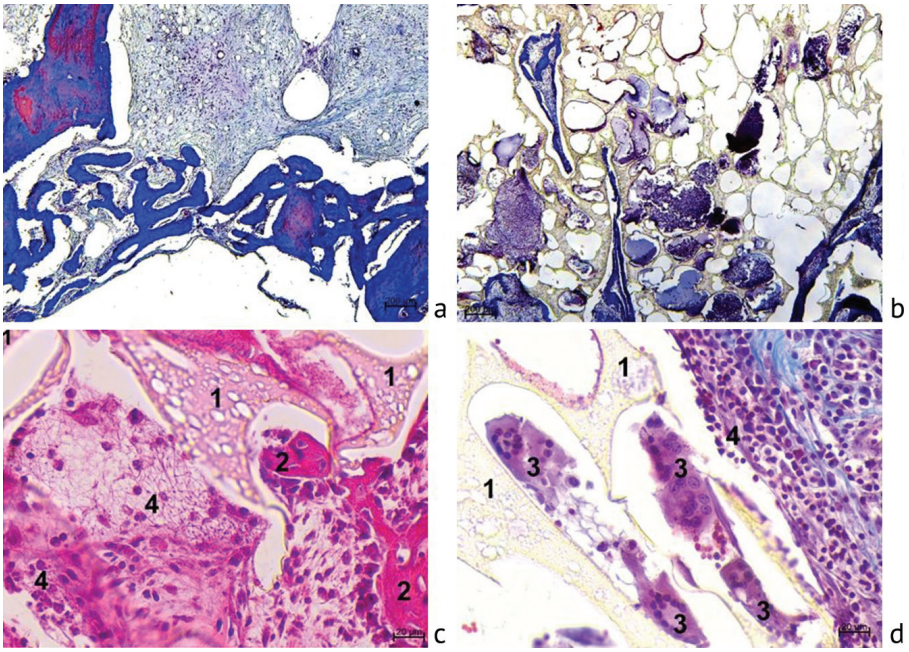

Fig. 5 Fragments of images of the proximal metaphysis in Group 2: (a) at the border with the implant there is a network of newly formed bone trabeculae; (b) implant cavities are empty and filled with newly formed tissues; (c) osteoblasts on the surface of trabeculae, diffuse lymphohistiocytic infiltrate; (d) giant multinucleated cells of the foreign body type, inflammatory infiltrate. Designations: 1 — polymer, 2 — bone tissue, 3 — giant multinucleated cells of the foreign body type, 4 — inflammatory infiltrate. Paraffin sections, stained with the three-color method according to Masson (a, b, d), hematoxylin and eosin (c). Magnification ×40 (a), ×100 (b), ×400 (c, d)

In Group 3, most of the polymer cavities were filled with erythrocytes, granulation and connective tissue, and newly formed bone trabeculae (Fig. 6 b). Masson's three-color staining revealed fuchsinophilic areas of the bone matrix (Fig. 6 c). Highly frequent foreign-body-type giant multinucleated cells (Fig. 6 d) and focal and diffuse lymphohistiocytic infiltrate were observed (Fig. 6 c).

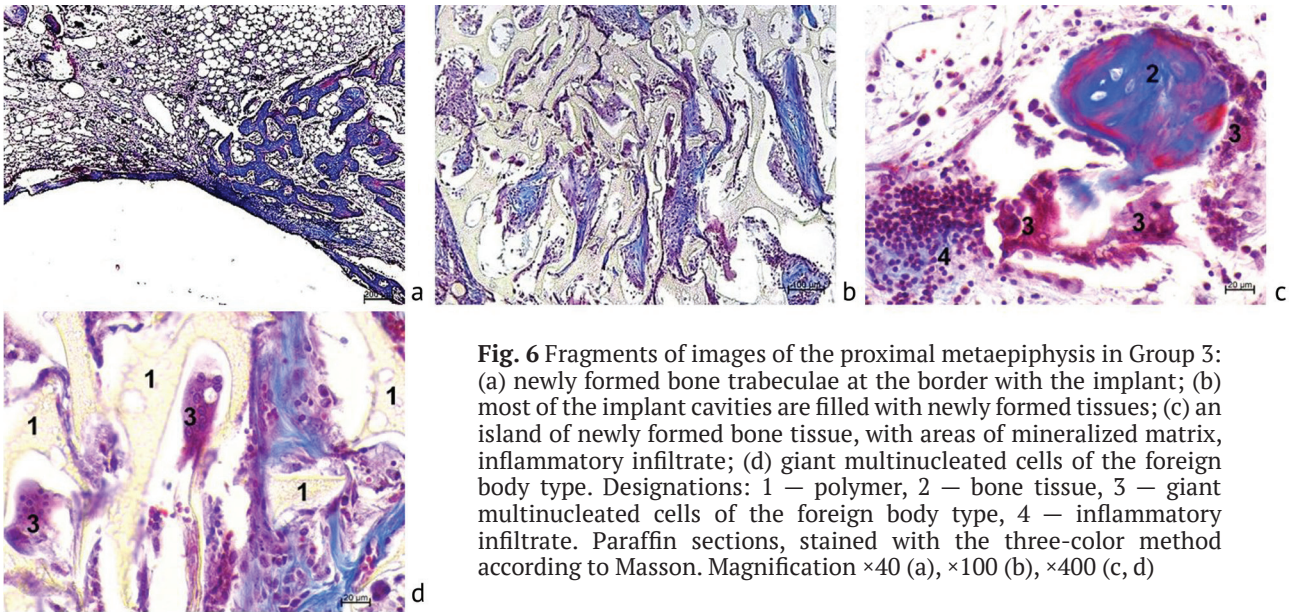

Fig. 6 Fragments of images of the proximal metaepiphysis in Group 3: (a) newly formed bone trabeculae at the border with the implant; (b) most of the implant cavities are filled with newly formed tissues; (c) an island of newly formed bone tissue, with areas of mineralized matrix, inflammatory infiltrate; (d) giant multinucleated cells of the foreign body type. Designations: 1 — polymer, 2 — bone tissue, 3 — giant multinucleated cells of the foreign body type, 4 — inflammatory infiltrate. Paraffin sections, stained with the three-color method according to Masson. Magnification ×40 (a), ×100 (b), ×400 (c, d)

DISCUSSION

Treatment of patients with chronic osteomyelitis is based on surgical debridement of infected necrotic bone (radical sequestrectomy) and antibacterial therapy. Local antibiotic delivery systems are frequently used. Systemic antibacterial therapy, in the absence of adequate blood supply to the sites of bone infection, fails to deliver and maintain effective concentrations of antibacterial drugs, leading to poor treatment outcomes. Local antibiotic delivery aims to achieve therapeutically effective drug concentrations at the site of infection while minimizing side effects [11, 34, 35].

One-stage technology for treating patients with osteomyelitic cavities is a more effective method compared to traditional methods due to a reduction in the number of surgical interventions, in rehabilitation periods, early functional recovery of patients and a reduction in the frequency of relapses of the purulent process [36, 37, 38].

The development and experimental testing of antibiotic-impregnated bioresorbable materials for the treatment of patients with osteomyelitis is a promising area. Bioresorbable implants, saturated with antibiotics, provide gradual replacement of the material with bone tissue, eliminate the need for repeated surgeries, reduce the risk of chronic infection, promote bone regeneration, are biocompatible, and allow for local administration of antibiotics [11, 35].

In 2014, a domestic partially bioresorbable bone substitute material *Rekost* (ZN 2014/1646, state registration date 03.07.2014, unlimited), was developed. It is a mixture of components: a polyurethane polymer prepolymer, calcium orthophosphate powder, and a polyol hardener [39]. *In vitro* studies have shown that *Rekost*, compared to polymethyl methacrylate, has advantages in terms of the duration of antibiotic release at therapeutic doses [40].

This in vivo study demonstrated that *Rekost* is a partially biodegradable material with osteoplastic properties. Our results are consistent with other experimental and clinical studies on the *Rekost* application in paranasal sinus wall reconstruction, as well as in the treatment of patients with bone defects after oncological diseases [41, 42].

The presented method of experimental modeling of osteomyelitis allows us to obtain a chronic inflammatory process in bone tissue 21 days after infection. In experiments on modeling the purulent-necrotic process in bone (Group 1), the main histological signs of osteomyelitis were seen: necrotic fragments of bone trabeculae surrounded by connective tissue and inflammatory infiltrate, active processes of osteoclastic resorption and reparative osteogenesis, bone marrow

fibrosis, and intensive CD15 expression. Neutrophilic granulocytes, as well as plasma cell aggregates, along with lymphohistiocytic infiltration against the background of fibrosis, and the presence of bone microsequesters are diagnostic signs of chronic osteomyelitis [43].

In Groups 2 and 3, three weeks after implantation, the presence of a network of newly formed bone trabeculae at the bone-material interface demonstrated the osteoconductive properties of this polymer. In both groups, bone trabeculae were observed in the implant cavities, along with red blood cells and provisional matrix, granulation tissue, and connective tissue, confirming the osteoplastic properties of the polymer.

In the epiphysis of Group 2, histological signs of chronic osteomyelitis (bone marrow fibrosis, trabeculae with interstitial osteonecrosis) were observed; a HOES score of ⩾ 6 points corresponded to an active course of chronic osteomyelitis. In Group 3, a median HOES score of 2 points indicated a remission of chronic osteomyelitis; expression of the CD15 marker was less pronounced compared to Group 2. The CRP level in Group 2 continued to increase in all animals three weeks after implantation, indicating further development of the infectious process. Persistence of inflammation for more than three weeks usually indicates the development of an infectious process [44].

In Group 3, the CRP level in two animals decreased significantly, and in one less intensively, which, however, allows us to speak about signs of infectious process arrest in this group.

The results of this study showed that the use of *Rekost* material to fill post-osteomyelitic cavities without the addition of an antibiotic in Group 2 led to further development of the infection and bone tissue destruction. The impregnation of the *Rekost* bone substitute with antibiotic vancomycin in Group 3 stopped the infection in two out of three animals (one case had active chronic osteomyelitis) and facilitated favorable organotypic bone tissue remodeling aimed at restoring bone structure.

According to literature data and our experience, the partially bioresorbable material *Rekost* allows for modeling of complex anatomical contour and, over time, is gradually replaced by bone tissue, while simultaneously acting as a local carrier of antibiotics, which meets modern requirements for bioresorbable implants in the correction of post-osteomyelitic defects [37, 41, 42].

It should be noted that the treatment outcome is influenced not only by the composition of the bone substitute material, but also by the quality of bone preparation during sequester necrectomy. Incomplete removal of necrotic and/or infected bone tissue after sequester necrectomy is the main cause of recurrence of chronic osteomyelitis [45].

In all observations, high frequent giant multinucleated cells of the foreign body type may be considered as a morphological manifestation of the polymer biodegradation process (the giant cell reaction is one of the markers of tissue reactions to the implant) and as a pathomorphological component of persistent inflammation in the conditions of chronic osteomyelitis [44].

Limitations

The design of this study has limitations. It was conducted on a small sample of animals at early stages of the experiment. The duration of implanted degradable/resorbable sample tests depends on the time and rate of their degradation. We plan to conduct further studies on a larger sample for a longer experiment term.

CONCLUSION

An experimental in vivo model showed minimal degradation of the *Rekost* material at three weeks after the implantation, manifested by highly frequent foreign-body-type giant multinucleated cells. Early data on the osteoplastic properties of the *Rekost* material and its ability to suppress infection and inflammation in combination with an antibiotic suggest the potential for further experimental studies of this product for the treatment of patients with chronic osteomyelitis.

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

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Ethical statement *The study was conducted in accordance with the European Convention (ETS No. 123) for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes and interstate standards (GOST 33044-2014) and was approved by the institutional ethics committee (protocol dated November 29, 2024, No. 1(76)).*

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Optimization of the first stage of hip revision in 2-stage surgery to replace infected artificial hips using a new molding spacer tool

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Abstract

Introduction The first stage of two-step surgery to replace infected hip suggests the intraoperative fabrication of an articulating cement spacer. A critical step is manual holding the metal reinforcement in the mold for 8–12 minutes while the bone cement cures, which increasing the overall surgical time. Optimizing this stage is essential.

The **objective** was to evaluate the effectiveness of the first stage of hip revision in 2-stage surgery optimized with a new device for fixing reinforcement in the manufacture of a cemented spacer for the hip joint.

Material and methods A new device (RU Patent No. 232924 U1), made of medical-grade AISI304 stainless steel, which is reusable and sterilizable, allows for the fixation of reinforcement used to manufacture hip articulating spacers in a clamp and their positioning over the center of a mold cell sized to fit the acetabulum (diameters 46–62 mm in 2 mm increments). With the cell filled with cement, the reinforcement was inserted to the specified depth and secured with the device. After 8–12 minutes, to allow polymerization completed, the construct was removed for cementation of the femoral component. A retrospective analysis of 85 patients with infectious coxitis surgically treated between 2023 and 2026 was conducted: the spacer was made by manual retention of reinforcement in the control group ($n = 51$) and the spacer was made using a new fixation device in the study group ($n = 34$). Total operative time (min), the frequency of spacer revisions, and early complications were assessed. The groups were comparable for key parameters.

Results Operating time was reduced by 13.7 minutes in the study group ((84.5 ± 8.9) min versus (98.2 ± 12.5) min, $p = 0.008$). The frequency of intraoperative spacer adjustments decreased fivefold (6 % versus 29 %, $p = 0.012$). No dislocations were recorded early post-op in either group. No significant differences in the accuracy of radiographic parameters (offset, neck-to-shaft angle) were found.

Discussion There are no publications reporting similar devices for the fabrication of the acetabular component of the hip articulating spacers. Patients with an underlying infectious process (tuberculous or purulent coxitis) and frequent comorbidities (HIV, hepatitis) may benefit with even a relatively small reduction in surgical time improving the prognosis. The lack of need for spacer modification preserves the integrity of the femoral head surface and ensures a more uniform distribution of the antibiotic in the cement.

Conclusion The device offered can be recommended for clinical implementation reducing surgical time by an average of 14 minutes and the frequency of spacer modifications.

Keywords: two-stage hip replacement, hip spacer, infectious coxitis, optimization, operative time, fixation device

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INTRODUCTION

Two-stage hip replacement remains the main method of treating septic coxitis [1–9]. The first stage includes resection of the femoral head, debridement of the lesion, and placement of an articulating antimicrobial cement spacer to facilitate temporary weight-bearing capacity of the limb and local deposition of antibiotics [10, 11]. The use of a custom-made antibacterial spacer, manufactured intraoperatively manually, is practical in septic coxitis. The key advantages of such bone cement spacers over factory-made analogs include the ability to adapt the shape to the individual anatomy of the defect, optimization of the dosage and combination of antibiotics considering the resistance of the pathogen, a significant reduction in mechanical conflict with surrounding tissues due to re-modeling of the articular head in the wound [3, 4, 12, 13, 14]. However, as our clinical experience shows, intraoperative mold of the spacer head remains a technically complex stage requiring optimization. The surgeon must manually hold the metal stem reinforcement in the mold cavity until the bone cement has fully cured (8–12 minutes). This stage involves static muscle tension, increases the overall surgical time, distracts the surgeon from other important procedures (debridement, hemostasis), and, if fatigued (with less surgical experience), can lead to displacement of the reinforcement, requiring subsequent correction of the spacer shape [15, 16].

In mechanical engineering, coordinate posts and stands are used for similar tasks [17]. In medicine, attempts to adapt such designs are known [18, 19], however, they are not designed to fix reinforcement with complex cross-sections (round, oval, with a keel). We have developed a new device for fixing reinforcement of the femoral component of a spacer during polymerization [20].

The **objective** was to evaluate the effectiveness of the first stage of hip revision in 2-stage surgery optimized with a new device for fixing reinforcement in the manufacture of a cemented spacer for the hip joint.

MATERIAL AND METHODS

Description of the device (Patent RF № 232924 U1) [20]

The device (Fig. 1, 2) is made of medical stainless steel AISI304, which allows multiple sterilization. The design includes a rectangular frame (80 × 75 mm) — base (1), a vertical threaded rod (Ø 8 mm, L = 120 mm) (2) with a nut (3) for moving the carriage; guide post (Ø 10 mm, L = 120 mm) for stability (4), movable carriage (70 × 30 mm) with a vertical travel range of 50–100 mm (5), rotation unit (lever 50 × 17 mm) with tilt angle lock of 0–90° (6), angle lock nut (7), clamping device with a clamp and lateral movement of 0–10 mm for fixing reinforcement of different sections (8), low knurled nut (9), height lock screw (10).

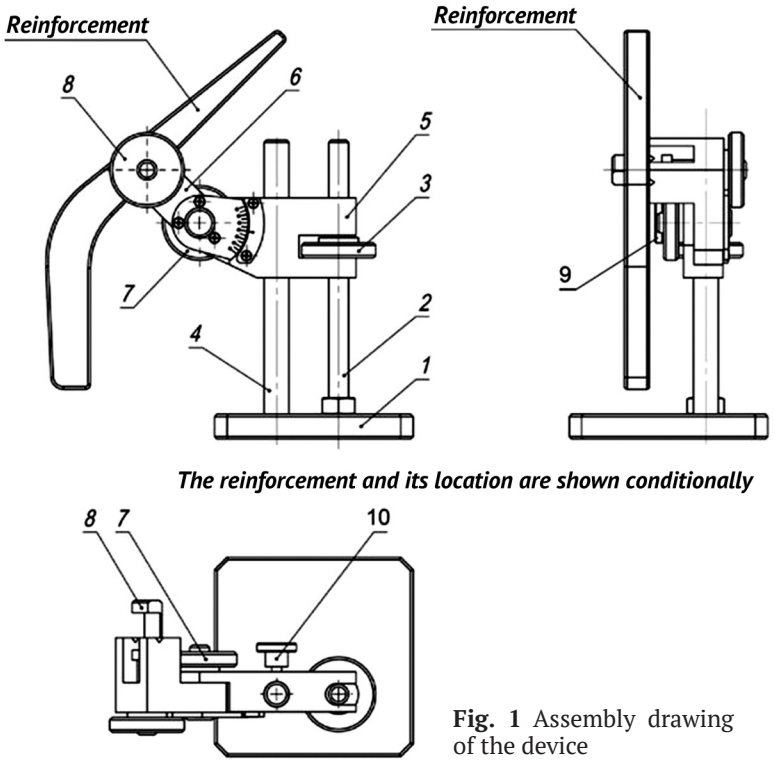

Fig. 1 Assembly drawing of the device

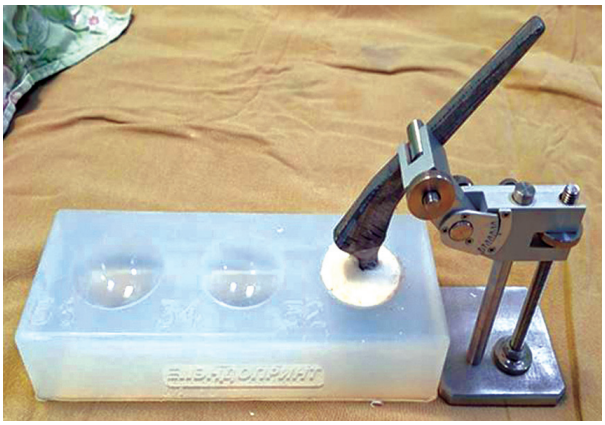

Fig. 2 Device for holding spacer fittings

Method of application

The device is placed on a separate table. The reinforcement is secured in a clamp and positioned over a mold cavity sized to fit the acetabulum (diameters 46–62 mm). An antibacterial agent is added to the bone cement powder, taking into account the individual sensitivity of the pathogen. Vancomycin, gentamicin, lincomycin, and amikacin are preferred for nonspecific infections, while amikacin, rifampicin, and isoniazid are used for tuberculous coxitis. The components are thoroughly mixed. With the cavity filled with cement, the reinforcement is inserted to the specified depth and secured using the device. Once polymerization is complete after 8–12 minutes, the device is removed for subsequent cementation of the femoral component.

Study design

The study was a single-center retrospective cohort.

Inclusion criteria:

— patients with infectious coxitis (of tuberculous and non-specific etiology);

— the first stage of a two-stage hip replacement with the installation of an articulating cement spacer being completed;

— availability of complete medical documentation (operation protocol, anesthesia chart, postoperative radiographs).

Non-inclusion criteria: lack of data on the time of surgery; radiographs unavailable for analysis.

The study was conducted at the Department for Patients with Extrapulmonary Tuberculosis of the National Medical Research Center for Phthisiopulmonology and Infectious Diseases between 01.01.2023 and 29.02.2026.

Characterization of the groups

The study included 85 patients who met the selection criteria. Distribution into groups depended on the availability of the device at the time of surgery:

— treatment group (n = 34): spacer made with the device developed to fix the reinforcement during polymerization.

— control group (n = 51): spacer made using the traditional manual method (the surgeon held the reinforcement in the mold until the cement was completely polymerized).

The groups were comparable in terms of gender, age, etiology of the process and initial radiographic parameters (Table 1).

Table 1

Comparative characteristics of groups

Description		Treatment (n = 34)		Control (n = 51)		p
Age, years		46.1 ± 13.2		47.5 ± 12.0		0.61
Acetabulum size, mm		50.8 ± 3.9		50.3 ± 4.0		0.57
		abs.	%	abs.	%	
Gender	Male	22	64.7	33	64.7	0.94
	Female	12	35.3	18	35.3	
Tuberculous coxitis		22	64.7	32	62.7	0.85

The total operating time (min) was defined as the interval between incision and dressing applied, as specified in the surgical protocols and anesthesia records. The frequency of intraoperative spacer adjustments was determined based on the presence of protocol entries. Postoperative radiographs were used to measure the offset (distance from the center of the femoral head to the femoral axis, mm); the femoral neck-shaft angle (°); and deviation from the preoperative plan. Early postoperative complications included dislocations and spacer instability within three months.

Statistical analysis

Statistical analysis was performed using Statistica 10.0 software (StatSoft, USA). Quantitative data are presented as M ± σ. Groups were compared using the Student's t-test for independent samples (for normal distribution) and the Mann–Whitney U-test (for non-normal distribution). Categorical variables were compared using the χ^2 test with Yates' correction. Differences were considered statistically significant at $p < 0.05$.

RESULTS

A significant reduction in total operative time by 13.7 minutes was observed in the treatment group. The frequency of intraoperative spacer adjustments in the treatment group was five times lower (Table 2). No significant differences in the accuracy of reinforcement positioning were found between the groups. The deviation of the offset and the neck-to-shaft angle from the planned values was comparable (Table 3). Postoperative complications (dislocations and spacer instability) early post-op (up to three months) were not recorded in either group.

Table 2

Intraoperative parameters

Description	Treatment (n = 34)	Control (n = 51)	Difference	p
Operating time, min	84.5 ± 8.9	98.2 ± 12.5	–13.7	0.008
Spacer to be adjusted	2 (6 %)	15 (29 %)	–23 %	0.012

Table 3

Radiological parameters

Description	Treatment (n = 34)	Control (n = 51)	p
Offset deviation from plan, mm	3.2 ± 1.1	3.3 ± 1.2	0.69
Deviation of the neck-to-shaft angle from the plan, °	4.0 ± 1.6	4.1 ± 1.8	0.79

Clinical case

A 35-year-old patient was admitted to the NMIC FPI clinic with complaints of pain in the right hip joint and forced ambulation with crutches.

Anamnesis He experienced pain in the right hip joint for 18 months after a fall from a height. He developed fistula along the outer surface of the joint repeatedly. An abscessotomy was performed at the central district hospital at the place of residence. His concomitant disease included HIV

infection (stage 4B, progression phase with antiretroviral therapy (ART)), recurrent bacterial infections. The patient continuously took ART drugs for two years according to the following regimen: raltegravir 400 mg twice daily, etravirine 200 mg twice daily, lamivudine 150 mg twice daily. On admission: CD4+ = 360 cells/μL, HIV RNA < 20 copies/ml.

Objective status upon admission Functionality of the right hip joint demosntrated 33 HHS, 74 WOMAC and 7 VAS scores. Computed tomography of the right hip joint revealed destruction of the proximal femur and lysis of the head (Fig. 3).

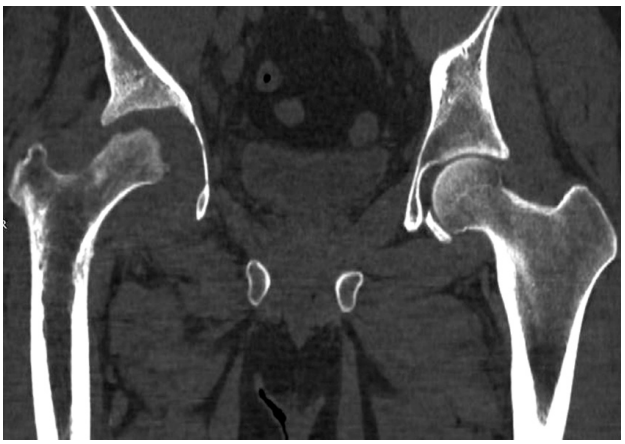

Fig. 3 Computed tomography of the patient's right hip joint

Laboratory and instrumentation studies Immunological examination: CD4+ = 350 cells/μL, viral load < 20 copies/ml. Complete blood count: ESR, 61 mm/h. A trephine biopsy from the site of bone destruction of the femoral head was performed under radiation guidance. Microbiological examination of the biopsy yielded cultures of Acinetobacter baumannii (susceptible to amikacin) and Staphylococcus aureus (sensitive to all antibiotics tested). Pathohistological conclusion: signs of chronic nonspecific coxitis.
Diagnosis Based on clinical, radiological, microbiological and histological data, the patient was finally diagnosed with right-sided infectious coxitis (M00) of non-specific etiology associated with HIV infection.

Surgical intervention included resection of the proximal end of the right femur at the first stage of hip replacement. An antibacterial spacer was made on a separate table. The head of the spacer was formed using the device (Fig. 2). Powdered amikacin was added to the powdered polymer of bone cement at a rate of 2 g of the drug per 40 g of cement with the components mechanically mixed. The femoral component of the spacer was immersed in a mold filled with a cement-antimicrobial composition until hardening (10 minutes after mixing), after which the sample was removed from the plastic mold. The neck area of the spacer was additionally covered with a cement mantle.

The fabricated spacer was inserted into the femoral medullary canal, and the spacer head repositioned into the acetabulum (Fig. 4). The patient was verticalized on the second postoperative day. The postoperative wound healed by primary intention, with no signs of purulent-inflammatory complications. Pain relieved with nonsteroidal anti-inflammatory drugs. The patient was discharged after 10 days in satisfactory condition to be supervised by an infectious disease specialist and a traumatologist-orthopedist at his place of residence. He was recommended to continue ART, antibacterial therapy, and could receive the second stage of hip replacement at the National Medical Research Center of the Federal Pedagogical Institute after confirmation of joint debridement (normalized ESR, negative cultures, absence of clinical signs of infection for three months).

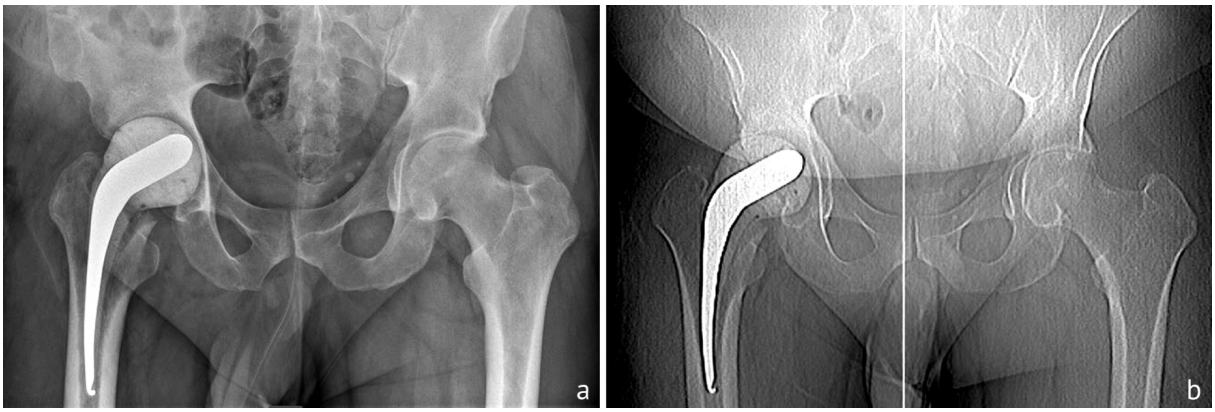

Fig. 4 Radiographs of the patient's right hip joint: (a) the first day after surgery with the articulating cement spacer placed; (b) at three months of surgery

DISCUSSION

We were unable to find any information in the literature on similar devices for the fabrication of the acetabular component of the hip articulating spacer. A significant reduction in the duration of the first stage of two-stage arthroplasty using the fixation device developed was the major result of our study. The difference of 13.7 minutes ($p < 0.01$) is clinically significant for a number of reasons.

Firstly, an increased length of surgery increases the risk of infectious complications [21–23]. A relatively small reduction in surgical time can improve the prognosis in patients with an underlying infectious process (tuberculous or purulent coxitis) and frequent comorbidities (HIV, hepatitis) [24, 25].

Secondly, a fivefold reduction in the frequency of intraoperative spacer adjustments (from 29 % to 6 %, $p < 0.05$) indirectly indicates a higher quality of primary positioning. Although we did not identify any obvious differences in radiographic parameters (offset, neck-o-shaft angle), the lack of need for spacer adjustments maintains the integrity of the head surface and ensures a more uniform antibiotic distribution in the cement, which is also confirmed by other authors [26, 27].

There was no evidence of the device being advantegous in terms of the precision of spacer positioning in the resected joint. We attribute this to the high level of surgical technique at the clinic: the surgeries were performed by experienced surgeons (with over 10 years of experience), which allowed us to achieve anatomical parameters even with the manual method. However, the stabilizing effect of the device may be more pronounced for less experienced surgeons or in high-speed surgical settings [23, 27, 28].

The absence of dislocations in both groups (0 out of 85) also indicates a high level of surgical technique and is not a limitation of the study. This means that the device does not worsen clinical outcomes, but does reduce surgical time and improve ergonomics. We believe the functional advantages of the device are also important.

Manually holding the reinforcement for 8–12 minutes is assoiated with certain static muscular effort, leading to fatigue, and can be accompanied by tremors. The surgeon can be relieved with the device and perform other stages of the procedure (debridement, hemostasis, drainage).

Limitations of the study:

— retrospective design (possible unaccounted systematic errors);

— lack of a formal assessment of ergonomics (for example, using a visual analogue scale of surgeon fatigue).

Prospects

A prospective, randomized study involving multiple centers and surgeons of varying levels of training would be practical. This would allow for the evaluation of the device's contribution to positioning accuracy and dislocation rates in a less selective population.

CONCLUSION

The use of a new device for fixing reinforcement during the intraoperative fabrication of a cemented hip spacer optimizes the first stage of two-stage hip arthroplasty reducing the overall operating time by an average of 13.7 minutes ($p < 0.01$), and decreasing the frequency of intraoperative spacer adjustments by five times ($p < 0.05$). The device is comparable to the traditional manual method in clinical outcomes (dislocation rate, positioning accuracy) and is superior in ergonomics and standardization of the polymerization stage. The findings substantiate the feasibility of clinical implementation of the device for optimizing the first stage of two-stage hip arthroplasty for infectious coxitis.

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

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Ethical expertise *The study was conducted in accordance with ethical standards and applicable Russian legislation. The study was approved by the local ethics committee of the National Medical Research Center for Pediatrics and Pedagogical Research of the Russian Ministry of Health (Protocol No. 3, dated January 31, 2023).*

Informed consent *The patients gave informed consent for publication of the findings without identification.*

Information on the use of artificial intelligence *The authors declare that they used the DeepSeek language model to improve the readability of the manuscript after writing the first draft. The authors are solely responsible for the content of the article.*

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