16+

ISSN 1028-4427 (Print)
ISSN 2542-131X (Online)

Гений Ортопедии
Orthopaedic Genius

Том 31
№ 2
2025

Научно-теоретический и практический журнал
Основан в память академика Г.А. Илизарова

Курган

Учредитель и издатель журнала:

федеральное государственное бюджетное учреждение «Национальный медицинский исследовательский центр травматологии и ортопедии имени академика Г.А. Илизарова» Министерства здравоохранения Российской Федерации

Издание журнала осуществляется при поддержке Ассоциации по изучению и применению метода Илизарова России (A.S.A.M.I. Россия)

Журнал включен в перечень научных специализированных изданий ВАК, в которых могут публиковаться основные результаты диссертационных работ на соискание ученой степени кандидата наук, ученой степени доктора наук (3.1.8 – травматология и ортопедия)

Журнал включен в Реферативный журнал и Базы данных ВИНИТИ

Сведения о журнале ежегодно публикуются в международной справочной системе по периодическим и продолжающимся изданиям «Ulrich's Periodicals Directory»

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Оригинал-макет изготовлен ОИАиВР ФГБУ «НМИЦ ТО имени академика Г.А. Илизарова» Минздрава России

Журнал зарегистрирован Федеральной службой по надзору в сфере связи, информационных технологий и массовых коммуникаций ПИ № ФС77-68207 от 30 декабря 2016 года

Территория распространения: Российская Федерация, зарубежные страны

Язык: русский, английский

Издается 6 раз в год

Цена свободная

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Обзоры литературы

Некролог

Original article
https://doi.org/10.18019/1028-4427-2025-31-2-143-152

Definitive fixation of open tibial fractures using the Ilizarov ring fixator: an analysis of functional outcomes

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Abstract

Introduction Open tibial fractures are generally managed by wound debridement and temporary stabilisation with AO external fixators followed by delayed internal fixation provided the soft tissue cover is adequate and there is no infection.

This study **aims** at analysing the factors influencing the outcome of treatment of open tibial fractures using external fixation with Ilizarov ring fixators as definitive method.

Materials and methods Twenty eight patients of both sexes aged more than 18 years who presented with open tibial fractures were included as our study subjects. The open fractures were classified according to Gustilo-Anderson classification of open fractures. Skeletal stabilisation was done either with Ilizarov ring fixators primarily or with AO external fixators in whom within 5 days since the injury the Ilizarov ring fixators were applied after thorough debridement of wounds. Patients were followed up first 4 weeks after the definitive procedure, then after 6 weeks, 3 months, 6 months and 1 year. The results were analysed using Tuckers criteria.

Results We achieved union in 25 patients without infection. Three patients were lost for follow-up. In majority of patients (48 %) union occurred in 24 weeks. In 10 patients we had pin site infections. The functional outcome was studied using Tucker's Criteria according to which 5 patients (20 %) had excellent outcomes, 9 patients (33 %) had good outcomes, 8 patients (29 %) had fair outcomes and 3 (16 %) had poor outcomes.

Discussion Limitation of the present study is the absence of a comparison group, though it was possible because of the nature of the injuries that these patients had while arriving at the trauma care facility. Another limitation is the follow-up period. We followed the patients for one year but if we followed the patents for longer periods we could have assessed the long-term prognosis.

Conclusion The definitive treatment of open tibial fractures especially Type 3B fractures with the Ilizarov Ring Fixator system is found be optimal and cost-effective.

Keywords: open tibial fractures, Ilizarov method, definitive fixation

For citation: Radhakrishnan E, Duraisamy E. Definitive fixation of open tibial fractures using the Ilizarov ring fixator: an analysis of functional outcomes. *Genij Ortopedii*. 2025;31(2):143-152. doi: 10.18019/1028-4427-2025-31-2-143-152.

INTRODUCTION

With the increase in the number of automobiles and national highways, India ranks number two in the list of road traffic accidents among 207 countries as per World Road Statistics 2020 published by the International Road Federation in Geneva. In 2021, India recorded a mammoth 412,432 road traffic accidents. Tamilnadu, a state in the southern India where our hospital is located, recorded the highest number of road accidents in 2021 (55,680) among all the Indian states. This resulted in a greater number of open tibial fractures presented to the Emergency Department of hospitals across the state of Tamilnadu as tibia is the most common long bone fractured in humans and the least soft tissue coverage makes open fractures common in tibia. Hence it is needed to have an optimal and a cost-effective protocol to address these injuries. Though closed tibial fractures are commonly managed by internal fixation methods, there are no clear cut standard guidelines regarding management of open tibial fractures especially Type 3 injuries.

These fractures are generally managed by wound debridement and temporary stabilisation with AO external fixators followed by delayed internal fixation provided the soft tissue cover is adequate and there is no infection. The deep infection rate might be as high as 17 %, delayed union rate 14 % and the need for secondary bone grafting 17 % even if this protocol was followed [1]. Pin-site infection would preclude the use of intramedullary nail in tibial fractures following the use of AO external fixators [2]. There is a need to devise an optimal management protocol in the management of open tibial fractures so that the morbidity they cause decreases and the cost-effectiveness increases. This is more relevant in countries like ours where much of the healthcare costs are borne by the state and the chance of patients having adequate insurance cover is low. Hence this study aims at analysing the factors influencing the outcome of treatment of open tibial fractures using external fixation with Ilizarov ring fixators as definitive method using Tucker's criteria [3].

METHODOLOGY

This prospective study was conducted in the Fracture Clinic of the Department Of Orthopaedic Surgery, Govt Royapettah Medical College & Hospital, Chennai for a period of two years. The study was started after getting approval from the Institutional ethics committee. Informed consent was obtained from all the participants. A non-random purposive sampling technique was followed to select the study subjects. Patients aged more than 18 years of age of both sexes who presented with open tibial fractures were included as our study subjects. Paediatric patients aged under 18 years and patients with pre-existing malignancies and metabolic bone disorders were excluded from the study. Also patients with fractures older than seven days were excluded from our study.

A total of 28 patients reported to the Emergency Department with open tibial fractures satisfying our inclusion criteria during the above mentioned study period. Three patients were lost for follow-up and so finally 25 patients were studied. ATLS protocol was followed in managing these patients. Open fractures were classified according to Gustilo-Anderson classification of open fractures [4]. Once the patients were hemodynamically stabilised and all the life threatening injuries were addressed radiological examination was carried out and skeletal stabilisation was done either with Ilizarov ring fixators primarily or with AO external fixators after thorough debridement of wounds. In those patients where AO external fixators were used initially, the fractures were revisited within five days and the Ilizarov ring fixator was applied. We followed accepted standards in applying Ilizarov ring fixators. We used a leg holder which we were able to construct using Italian arches, rings and threaded rods to keep the leg off the operation table which made the wires to be easily drilled though the bones and soft tissues (Fig. 1).

After the fractures were stabilised with Ilizarov Ring Fixators, the patients were encouraged knee and ankle range of motion the next day of surgery. Patients were followed up first at 4 weeks after the definitive procedure, then at 6 weeks, 3 months, 6 months and at 1 year. Pin sites were cared and any pin-site infection was noted and classified according Checketts-Otterburn Classification [5] (Table 1). Partial weight-bearing was allowed once the wounds settled and progressed to full weight-bearing which depended on presence or absence of associated injuries and condition of the patient (Fig. 2). We considered removal of the fixator once the patient satisfied the clinical

criteria of absence of pain at the fracture site at rest as well as on bearing weight with dynamization and radiological criteria of union evidenced by presence of bridging callus in at least three planes at the fracture site.

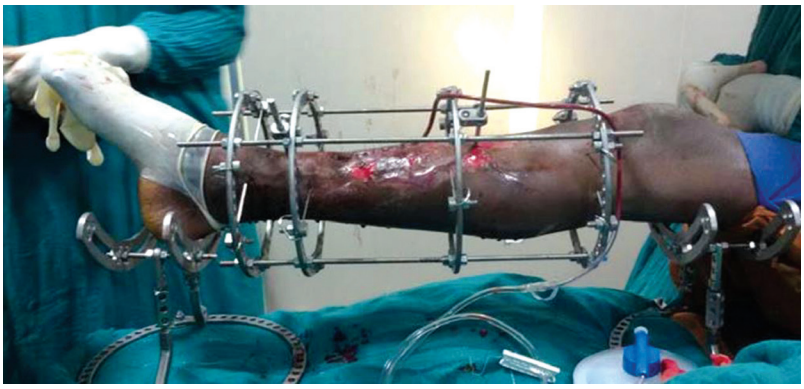

Fig. 1 Leg stand

Table 1

Checketts-Otterburn classification of pin-site infections

Grades	Characteristics of Infection	Management
Grade I*	Slight discharge ,Redness around the pins (problem rather than infection)	Improved pin-site care
Grade II*	Redness of the surrounding skin, pus at the pin site, pain and tenderness in the soft tissue	Oral antibiotics, Improved pin-site care
Grade III*	Similar To Grade-II but fail to settle with oral antibiotics and improved pin site care	The affected pin or pins are re-sited and external fixation can be continued
Grade IV#	Severe soft tissue infection involving several pins, sometimes with associated loosening of the pins	External fixation should be abandoned
Grade V#	In addition to the soft tissue infection, in Grade V infections there is involvement of the bone. Radiographs will show areas of osteolysis and possibly sequestrum formation	External fixation should be abandoned
Grade VI#	These infections occur after fixator removal. The pin track heals initially, but will subsequently break down and discharge at intervals. Radiographs shows new bone formation and sometimes sequestra	Curettage of pin track

* — minor infections; # — major infections.

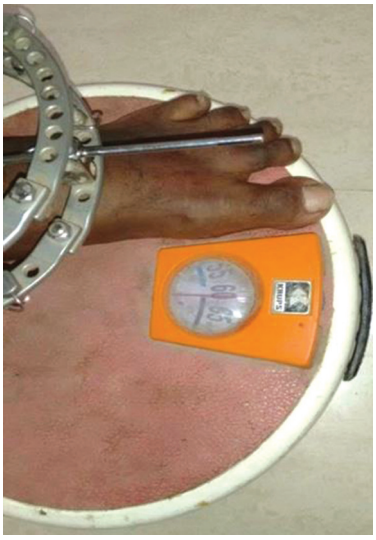

Fig. 2 Weight-bearing measure

RESULTS

Twenty-five patients that fulfilled the inclusion criteria were included in our study, of which 22 patients (88 %) were males and only 3 patients (12 %) were females. Most of the patients were in their fourth decade of their age (48 %). The commonest mode of injury was road traffic accidents involving motorcycles (52 %) because most of the working class population in this part of the world generally use motorcycles for their daily commuting. In 72 % of the patients, the right leg was injured and in 22 patients (88 %) both tibia and fibula were fractured and only in 3 patients (12 %) we encountered an isolated tibia fracture. According to Gustilo-Anderson classification we had 13 Type 3A injuries (52 %), 5 Type 3B injuries (20 %), 6 Type 2 injuries (24 %) and only one Type 1 injury (4 %). We didn't encounter Type 3C injuries in our study. Of these 25 patients, only two had intra-articular fractures (8 %). In our study 18 patients (72 %) had communited fractures and others were simple fractures. By AO classification of fractures, a majority fell under 42 C 1 (15 %), 42 C 2 (11 %) and 42 C 3 (11 %). Of these 25 patients, in 19 patients the fractures were stabilized temporarily with AO external fixators. This was to achieve hemodynamic stability, to address other injuries in the same patient and to plan for definitive management. In remaining 6 patients, Ilizarov ring fixators were used primarily. Of the 19 patients where AO external fixators had been used initially, the ring fixator was applied in 12 patients on the third day since injury and in 7 patients on the fourth day since injury. Thus, in all the 25 patients the ring fixator was applied within 5 days after injury. In 10 patients we had pin-site infections (Fig. 3, Table 2) which were managed appropriately and during the course of management pin removal and insertion at a different position was needed in 52 % of the fractures for want of flap cover. All patients were able to flex the knee up to 90 degrees as beyond that point the proximal most rings hindered any further movement (Fig. 4). One patient (4 %) had equinus contracture at the ankle which was corrected with physical therapy. At 8 weeks, 18 patients were able to bear full weight on the injured limb. We noticed that with proper education and motivation patients tolerate the fixator and were willing to carry on their routine activities with the fixator (Fig. 5).

Table 2

Pin-Site Infections Managed

Grade	I	II	III	IV	V	VI
Number of Pin-Site Infected	2	5	3	Nil	Nil	Nil

Fig. 3 Pin-site infection

Fig. 4 90° flexion with fixator on

Fig. 5 Patient feels comfortable with fixator

We achieved union in all the 25 patients without infection (Table 3). In majority of patients (48 %), union occurred after 24 weeks. The signs of clinical union appeared 4 weeks earlier than radiological union. We considered the probability of delayed union when no signs of union were noted radiologically even after 24 weeks since injury. This situation happened in 5 patients, and in 2 patients where diaphyseal fracture site non-union occurred, we did bone grafting following the standard procedure. Two patients needed bone marrow injection alone in metaphyseal fracture non-union. In one patient, we did excision of the non-union and carried out bone transport after corticotomy at the proximal tibia (Fig. 6). All these 5 fractures united after 48 weeks. We had no non-union or residual/deep infection at the end of 1 year follow-up period but two cases of limb shortening, one had 2.0-cm shortening and the other had 1.5-cm shortening. These were managed with shoe-rise alone and no additional procedure was required. We considered fixator removal once the fracture showed signs of union clinically and radiologically. We removed the fixator at the end of 24 weeks in 12 patients (48 %), 32 weeks in 8 patients (32 %) and 48 weeks in 5 patients (20 %) (Fig. 7–9).

Table 3

Period of Bony Union

S.No.	Period For Union	Noof Fractures	Percentage
1	< 4 weeks	0	0 %
2	4 weeks – 6 weeks	1	4 %
3	6 weeks – 3 months	7	28 %
4	3 months – 6 months	12	48 %
5	6 months – 1 year	5	20 %

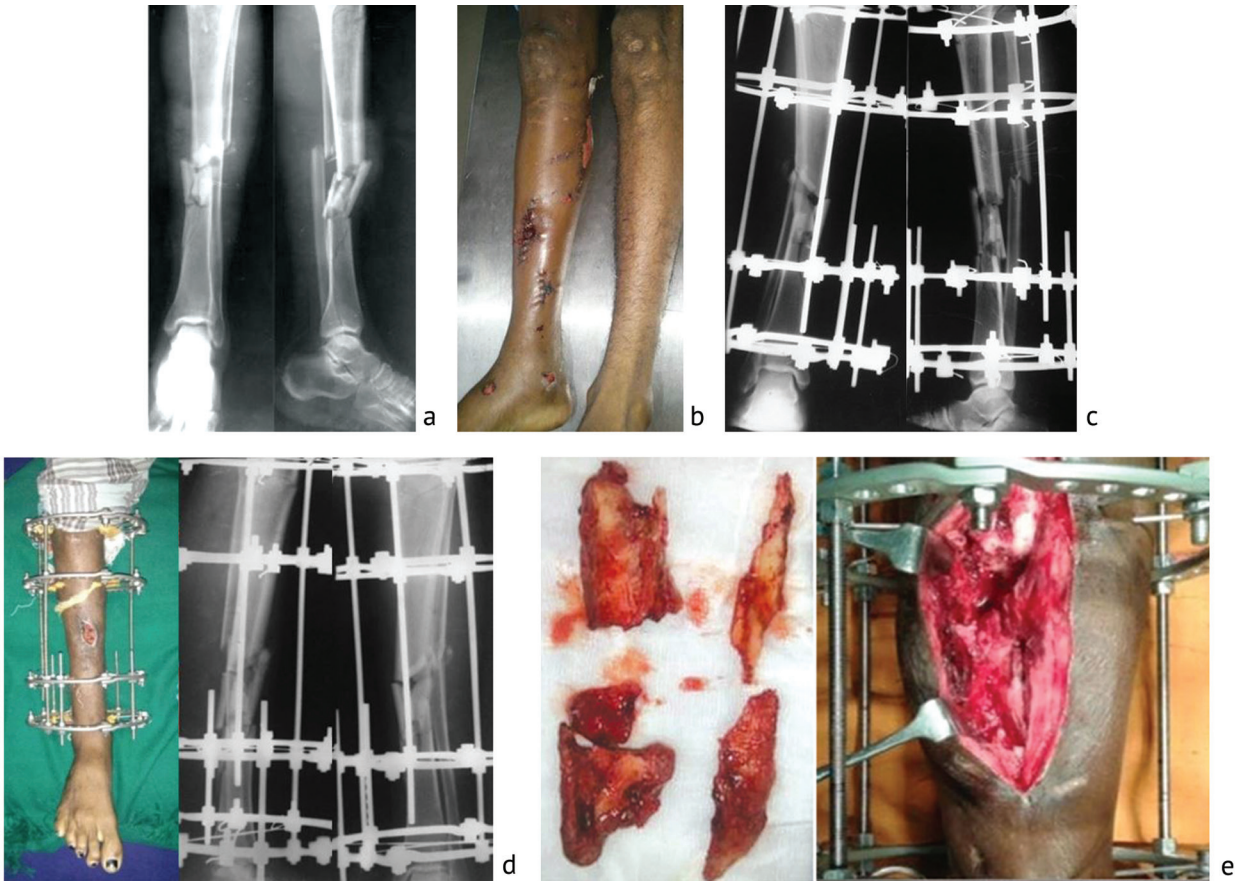

Fig. 6 Patient 1: *a* segmental communited fracture, day 1; *b* condition of the skin at presentation; *c* definitive Ilizarov fixation of the fracture; *d* patient at 10 weeks — wound open, no signs of union; *e* resection of non-union segment

Fig. 6 (continued) Patient 1: *f* corticotomy, distraction, consolidation; *g* X-rays AP and lateral views post-fixator removal (well united and consolidated); *h* clinical outcome — patient is comfortable in sitting cross-legged and squatting

Fig. 7 Patient 2 with communited proximal left tibia fracture: *a* X ray AP and lateral views; *b* post-operative X rays (from left to right — 1st month AP view;1st month lateral view; 3rd month AP view; 3rd month lateral view; 6th month AP view; 6th month lateral view); *c* X ray and photo of the patient after 8 months (patient could squat and sit cross-legged)

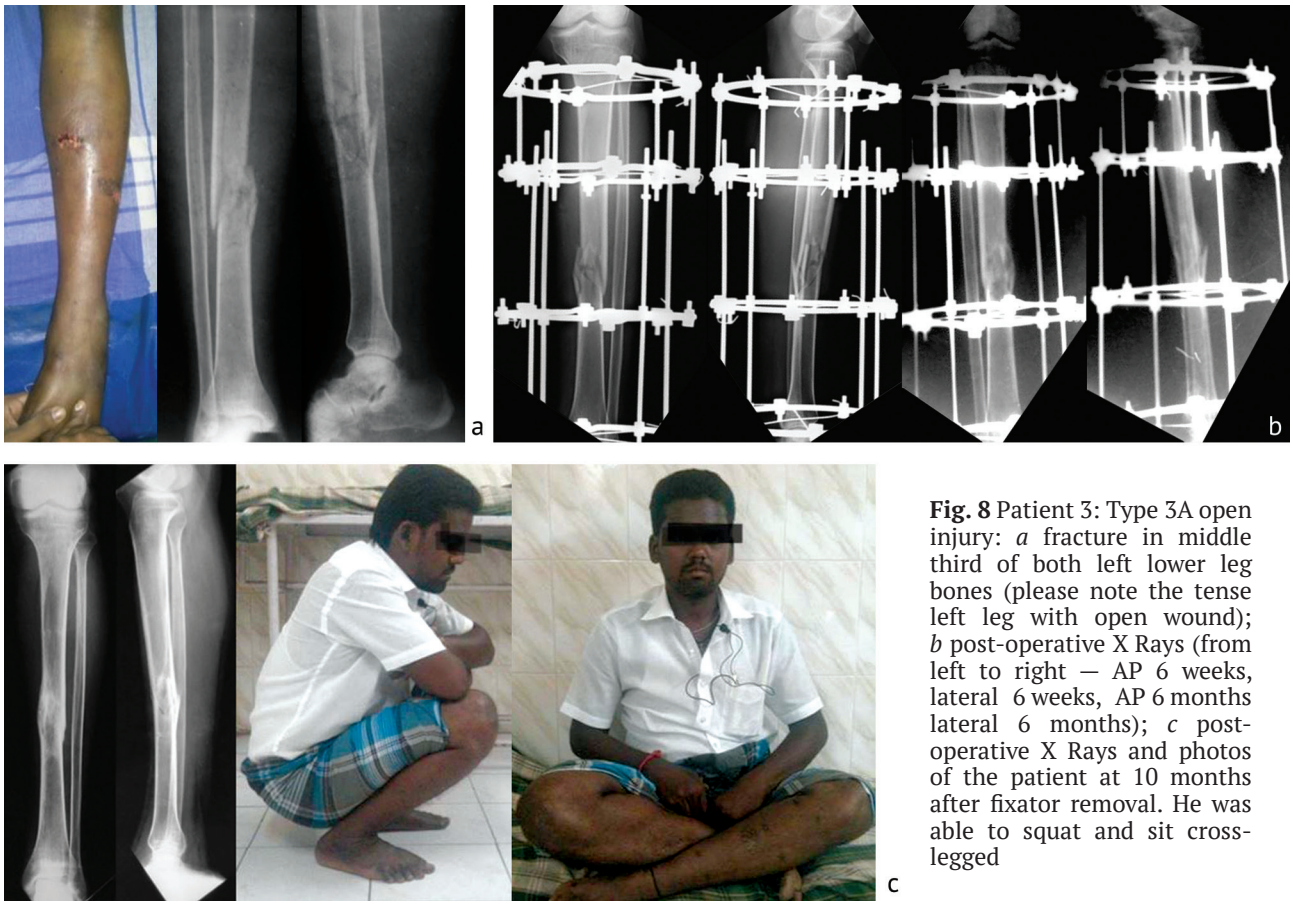

Fig. 8 Patient 3: Type 3A open injury: *a* fracture in middle third of both left lower leg bones (please note the tense left leg with open wound); *b* post-operative X Rays (from left to right — AP 6 weeks, lateral 6 weeks, AP 6 months lateral 6 months); *c* post-operative X Rays and photos of the patient at 10 months after fixator removal. He was able to squat and sit cross-legged

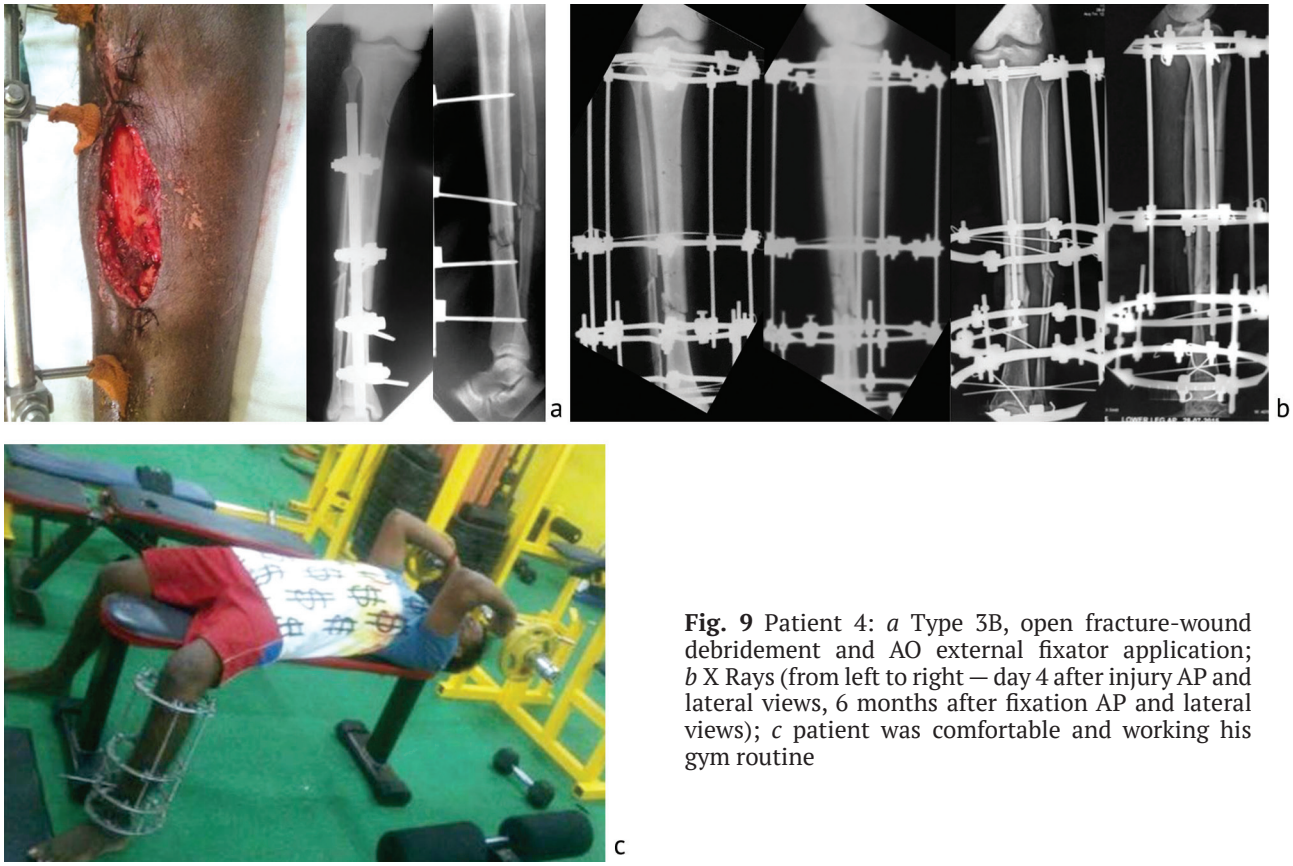

Fig. 9 Patient 4: *a* Type 3B, open fracture-wound debridement and AO external fixator application; *b* X Rays (from left to right — day 4 after injury AP and lateral views, 6 months after fixation AP and lateral views); *c* patient was comfortable and working his gym routine

The functional outcome was studied using Tucker's Criteria (Box 1) according to which 5 patients (20 %) had excellent outcome, 9 patients (33 %) had good outcome, 8 patients (29 %) had fair outcome and 3 (16 %) had poor outcome (Table 4).

Box 1

Tucker's Criteria

Excellent: Fracture union plus full knee extension with 125° knee flexion and 75 % of ankle motion when compared to normal side(if both sides are involved ankle motion above neutral with 30° flexion, no limb length discrepancy greater than 1 cm, angulation not greater than 7° in any plane, rotation not greater than 15° and no infection.

Good: Fracture union with one criteria missing

Fair: Fracture union with two criteria missing

Poor: Fracture union with three criteria missing

Table 4

Functional Outcome using Tucker's Criteria

S. No	Outcome	No of cases	Percentage
1	Excellent	5	20.52 %
2	Good	9	33.33 %
3	Fair	8	29.63 %
4	Poor	3	16.52 %

DISCUSSION

The development of highways along with availability of high performance motor vehicles and rapidly increasing number of motor cycle users with general lack of awareness about road rules result in high velocity injuries in fast developing nations like India. Most of the available literature on open tibial fractures reveals a male preponderance in the age group of 30–40 years similar to our study [6, 7, 8, 9]. In general, the mainstay of management of open fractures is thorough debridement the principles of which were laid by Desault and Larry [10, 11] which are still relevant today. We did thorough debridement of all the wounds before stabilising the fractures regardless of whether we used AO or ring fixators primarily. A general protocol that is followed across many centres in management of open tibial fractures is thorough debridement, early antibiotics (within 1–3 hours since injury), hemodynamic stabilisation, primary internal fixation with intramedullary nails or temporary stabilisation with AO external fixators followed by secondary internal fixation with intramedullary nailing [12, 13, 14]. Complications like deep infection, delayed union and need for bone grafting is high even if this regimen is followed strictly [1]. Plate fixation in open tibial fractures did not yield favourable results in the past [15]. Limb Reconstruction System (LRS) was studied in open tibial fractures. Patil et al. studied 54 patients with Type 3A and Type 3B open tibial fractures who were managed with LRS and stated that LRS was a simple and easy system which could be used for all open tibial fractures but cautioned that their study was limited as it did not have a control group [16]. In our view the LRS, though offers stability and provision of bone transport, is costly and not versatile as it would be difficult with LRS to achieve compression of fracture fragments in comminuted fractures. These would be possible with the Ilizarov ring fixator using drop wires and posts. The Ilizarov ring fixator shows optimal biomechanical properties such as low axial stiffness on axial loading and high axial stiffness to bending loading which promote bone healing [17]. It has axial elasticity and is inherently dynamic. Conventional large pin fixators and LRS could be dynamized but jamming of telescopic rods is often a problem since they are not inherently dynamic. Not many studies are

there regarding the use of Ilizarov ring fixators in definitive management of open tibial fractures. Wani et al. in their study of 60 patients with Type 2, Type 3A and Type 3B open fractures of the tibia concluded that the Ilizarov external fixator could be recommended as primary modality of fixation in open tibial fractures despite technical difficulties and possible of pin-site infection [18]. The most common complication in their study was pin site-infection (32 patients). We had pin site-infection in 10 patients that were managed appropriately.

The principle of distraction histogenesis could be used to treat soft tissue defects simultaneously while addressing the bone problem. In their series of 34 patients with open tibial fractures treated primarily and definitively with the Ilizarov ring fixator, Hosny and Fadel used soft tissue distraction system successfully in four patients [19]. In open tibial fractures without bone loss or infection its advantages are less tissue trauma and minimal or no surgical bleeding unlike with the use of internal fixation methods. The Ilizarov method allows the surgeon to treat bone loss and infection simultaneously [20]. In the presence of diaphyseal bone defect with infection the Ilizarov method offers good results [21]. Fortunately, in our study we did not have infected diaphyseal bone defects. Bone defects might be treated with alternative methods like vascularised fibular grafts, free fibular transfers or Papineau technique [22, 23] but these methods need prolonged pre- and post-procedure antibiotic therapy, no mechanism to correct deformities and do not allow the patient to bear weight during treatment. Even though bony union might be achieved by alternative methods, the bone that is formed needs years of remodelling to get the biomechanical structure and radiological appearance as that one formed by bone transport using Ilizarov distraction histogenesis. In our series we had one patient who needed a corticotomy and bone transport to achieve bone union. The mean time of bone union ranged from 21 weeks to 34 weeks in most of the series [18, 19, 20, 21] which is comparable to the present study.

Limitation of the present study is the absence of a comparison group, though it was possible because of the nature of the injuries that the patients had while arriving at the trauma care facility. Another limitation is the follow-up period, we followed the patients for one year but if we followed the patents for longer periods we could have assessed the long-term prognosis.

CONCLUSION

The definitive treatment of open tibial fractures especially Type 3B fractures with the Ilizarov Ring Fixator system is found be optimal and cost-effective. The Ilizarov Ring Fixator is a versatile tool which allows the orthopaedic surgeon to treat fracture, infection and bone loss simultaneously. Since it is inherently dynamic, weight-bearing is possible even during the treatment period. It yields excellent and good results in the conditions where internal fixation methods would be counterproductive.

Conflicts of Interest *None.*

Funding *None.*

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The article was submitted 04.04.2023; approved after reviewing 11.09.2023; accepted for publication 21.02.2024.

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Original article
https://doi.org/10.18019/1028-4427-2025-31-2-153-164

Treatment of children with pelvic polytrauma with minimally invasive and combined osteosynthesis techniques

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Abstract

Introduction Pelvic fractures in children are rare but extremely severe injuries associated with a significant threat to life. The search for new rational tactics of their surgical treatment based on a combination of various minimally invasive osteosynthesis techniques and instruments for its implementation remains relevant.

The **aim** of the work was to evaluate the results of staged treatment and a combination of minimally invasive osteosynthesis techniques at different periods of traumatic disease in children with combined and multiple pelvic injuries.

Materials and methods An analysis of 48 cases of treating pelvic ring fractures in children who sustained combined and multiple injuries within the period of 2000 to 2023 was carried out. The study group included 23 children treated at the pediatric polytrauma center of the Amur Regional Children's Clinical Hospital, in whom the author's methods and instruments were used for anti-shock and final osteosynthesis of the pelvic ring. The comparison group included 25 patients treated at the Republican Scientific Center for Emergency Medical Care (Tashkent). The comparison group was divided into three subgroups based on the treatment method: conservative treatment, osteosynthesis with pins, osteosynthesis with an external fixation device (EFD). Pelvic fractures were classified according to AO/ASIF; the severity of polytrauma was assessed according to the ISS scale. Anatomical and functional treatment results were evaluated using the methods of I.L. Shlykov and S.A. Majeed.

Results In patients of the main study group, residual displacement was observed by 57.6 % less frequently than in the subgroup with conservative treatment, by 32.6 % than in the subgroup with wire osteosynthesis and by 15.9 % than in the subgroup with osteosynthesis with an external fixation device (EFD). The functional treatment result of patients in the main study group was significantly better than in the subgroups of conservative treatment and wire osteosynthesis of the comparison group, with no significant difference when compared with the subgroup of EFD osteosynthesis.

Discussion Staged combined treatment using developed techniques and metal structures for osteosynthesis allows better reduction and stabilization of pelvic ring fractures and achieves good functional results. Not all problems of pelvic surgery can be solved with EFD; a number of injuries require the use of internal osteosynthesis for more accurate reduction. Disintegrating pelvic injuries accompanied by complete bilateral instability should be operated using temporary transpedicular fixation, since there is no alternative to this method.

Conclusion The combination of external fixation with internal osteosynthesis provides accurate reduction and reliable stabilization of pelvic ring fragments. Staged specialized care including internal bleeding arrest and fixation with an anti-shock device at the first stage and final stabilization of pelvic ring fragments at the second stage is the most rational tactical approach to polytrauma in children. External fixation can be used not only as a reliable and simple anti-shock fixation, but also as a method of final osteosynthesis.

Keywords: pelvic ring fractures, paediatric trauma, multiple and combined trauma, damage control orthopaedics, external fixation device

For citation: Borozda IV, Nikolaev RV, Karimov MYu, Salakhiddinov FB, Mashsripov FA. Treatment of children with pelvic polytrauma with minimally invasive and combined osteosynthesis techniques. *Genij Ortopedii*. 2025;31(2):153-164. doi: 10.18019/1028-4427-2025-31-2-153-164.

INTRODUCTION

Pelvic fractures in children are rare but extremely severe injuries associated with a significant threat to life and the need for surgical interventions [1]. The anatomically immature skeleton of a growing child features increased flexibility with a greater range of motion of the sacroiliac joints and pubic symphysis. Factors contributing to the overall elasticity of the child's pelvis include an abundance of cartilaginous tissue, which provides excellent shock absorption, and an increased remodeling potential [2, 3, 4]. Therefore, a pelvic fracture in children is an indicator of a severe devastating injury, which leads to damage to other body systems and, accordingly, an increase in mortality.

As shown by current studies, pelvic trauma in children occurs in 1.6–2 % of cases, with the most common cause of pelvic trauma being road traffic accidents [5]. Having analyzed 163 hospitalization cases, Michelle et al [6] found that the most common concomitant trauma in children with pelvic ring fractures is fractures of other segments of the musculoskeletal system (60 %), damage to parenchymatous organs of the abdominal cavity (55 %) and organs of the chest (48 %), with the majority of children (61 %) sustaining injuries to several organs. Unstable pelvic fractures are associated with damage to the chest (70 % versus 40 %), heart (15 % versus 2 %) and spleen (40 % versus 18 %), $p < 0.05$. Concomitant injuries often cause such late sequelae as chronic pain, scoliosis, sexual dysfunction, leg length discrepancy, and even growth retardation, which are observed in up to 30 % of pelvic fracture cases in children [7]. In a retrospective study of 29 acetabular fractures in children aged 2 to 16 years with an average follow-up of 14 years, Heeg et al. showed that patients with central hip dislocations had a relatively poor outcome, with only one out of four patients who underwent surgical treatment achieving congruence [7]. The researchers note that the most common complications recorded after pelvic fractures are pelvic asymmetry (9.2 %), lameness (6.0 %), and leg length discrepancy (5.0 %) [8]. Although pelvic fractures occur in a relatively small number of children with injuries, the mortality rate after them reaches 25 %, which is mainly due to concomitant injuries to other organs and systems. Moreover, mortality among boys is 13 % higher than among girls (18 % versus 5 %) [1, 9–14].

Most contemporary authors agree that classifications and treatment strategies used for adults are not applicable to children due to differences in the physiology and mechanisms of pelvic injury [1, 15–17]. Publications on this topic have small sample sizes, limited analysis, or are simply outdated, which is noted by a number of researchers. Most articles are based only on the analysis of the nature and location of fractures and do not contain data on concomitant injuries, their treatment, and outcomes [2, 3, 16–21]. All this leads to the lack of clear recommendations for the management and treatment of pediatric patients with pelvic injuries [5, 11]. The search for a new rational tactic of surgical treatment based on a combination of various minimally invasive osteosynthesis techniques and instruments for its implementation remains relevant.

Purpose To evaluate the results of staged treatment and a combination of minimally invasive osteosynthesis techniques at different periods of traumatic disease in children with combined and multiple pelvic injuries.

MATERIALS AND METHODS

We analyzed the treatment results of 48 children who sustained combined and multiple pelvic ring injuries in the period from 2000 to 2023.

Inclusion criteria were patients under 17 years of age, pelvic ring fractures with impaired stability, relatively stable and unstable according to the AO/ASIF classification [22] in combination with damage to other bones of the skeleton and internal organs (multiple and combined injuries).

Based on the conducted retrospective analysis, two clinical groups were formed: the main group of the study (n = 23) and the comparison group (n = 25).

The main group of the clinical study included children aged 3 to 17 years who were treated at the pediatric polytrauma center (Level I TC) in the Amur Regional Children's Clinical Hospital (ARCH, Blagoveshchensk). The author's methods and tools were used in the treatment of patients.

The comparison group was formed from patients aged 5 to 17 years who received treatment at the Republican Scientific Center for Emergency Medical Care (RSCEMC, Tashkent, Republic of Uzbekistan), and was divided into three subgroups depending on the treatment method: conservative treatment (n = 8), osteosynthesis with pins (n = 9), osteosynthesis with external fixation devices (n = 8).

The study began in 2000, when transosseous osteosynthesis with external fixation devices (EFD) started to be used for the first time in the above-mentioned medical institutions. These institutions are regional (republican) centers for the provision of specialized care for children, which ensured the random nature of the study groups, since all patients who sustained severe pelvic injuries in the region were transferred to these institutions.

The main group and the comparison group were homogeneous in gender and age, and the groups did not have significant differences. The average age of the groups was 13.5 years in the main group, and 14.4 years in the comparison group ($p > 0.05$) (Table 1).

In the overwhelming majority of cases, the cause of the injuries was road traffic accidents (Table 2).

Table 1

Distribution of patients according to gender and age

Groups		Gender		Age					
		Boys	Girls	0–3	4–7	8–11	12–15	16–17	Mean value
Основная группа (n = 23)	абс.	14	9	1	2	2	7	11	13,5
	%	60,9	39,1	4,3	8,7	8,7	30,4	47,8	
Группа сравнения (n = 25)	абс.	14	11	–	1	1	8	15	14,4
	%	56	44		4	4	32	60	

Table 2

Distribution of patients based on trauma mechanism

Mechanism	Main study group (n = 23)		Comparison group (n = 25)	
	No	%	No	%
Road traffic accident	19	82,6	22	88
Fall from height	3	13,1	2	8
Compression	1	4,3	1	4

All patients in the main study group were diagnosed with closed pelvic ring fractures of AO/ASIF types B and C and acetabular fractures accompanied by traumatic shock. The children sustained pelvic injuries as a result of high-energy injuries, mainly road traffic and catatrauma; all these injuries were combined and multiple (Table 3). The severity of the injuries according to the ISS scale ranged from 15 to 50 points.

All patients in the comparison group were also diagnosed with closed pelvic ring fractures of AO/ASIF types B and C and acetabular fractures accompanied by traumatic shock (Table 3).

Table 3

Distribution of patients based on associated pathology

Complications and associated injuries	Pelvic injury type											
	Relatively stable				Unstable				Acetabular fracture			
	Main study group (*n* = 23)		Comparison group (*n* = 25)		Main study group (*n* = 23)		Comparison group (*n* = 25)		Main study group (*n* = 23)		Comparison group (*n* = 25)	
	No	%	No	%	No	%	No	%	No	%	No	%
Traumatic shock	15	65.2	19	76	8	34.8	6	24	12	52.2	12	48
Fractures of other segnebts	1	4.3	3	12	2	8.7	2	8	–		2	8
Celebro-cranial injury	1	4.3	6	24	3	13.1	4	16	4	17.4	2	8
Trauma of abdominal organs	2	8.7	7	28	7	30.4	7	28	3	13.1	1	4

Five patients of the main study group (mostly residents of the region central city) were referred to the ARCCH within the first three hours after the injury, 18 patients were transported to the clinic within a period of one day to two weeks from level II trauma centers. The treatment tactics was based on the principles of staged medical care in full compliance with damage control orthopaedics. All patients in the level II trauma center were treated according to the ATLS protocol by the on-duty team or the mobile team of the level I trauma center and injuries were fixed with anti-shock devices with an anterior frame. Then, after complete stabilization of the general condition, on the sixth to eighth day, final reduction and stabilization of the pelvic ring fragments were performed using one of the selected methods, according to the developed algorithm (rationalization proposal No. 1837 dated 20.03.2012).

The following author's techniques and instruments were used for anti-shock and final osteosynthesis of the pelvic ring: devices for repduction and fixation of pelvic fractures [23, 24]; a method of combined osteosynthesis for unstable pelvic injury with rupture of the sacroiliac joint [25], a method of transosseous osteosynthesis for unstable pelvic injury associated with a vertical fracture of the sacrum [26], a method of transosseous osteosynthesis for unstable pelvic injury [27], and a transosseous module for reduction and fixation of the posterior sections of the pelvis [28]. Osteosynthesis of the sacroiliac joint with a screw and fixation with a half-pin apparatus with an anterior module was used in four patients. Three patients underwent final reduction and fixation with a device with a posterior external module in addition to the anti-shock apparatus with an anterior frame. Osteosynthesis of the acetabulum fracture with screws, as a final osteosynthesis after conversion of the anti-shock apparatus with an anterior external frame, was performed in two patients.

During the first three hours after the injury, 12 patients of the comparison group were delivered to the RRCEM, and 13 were transported there from district medical institutions within a period of one day to two weeks. All patients sustained high-energy trauma (road traffic accidents and catatrauma). The ISS severity of the injuries ranged from 15 to 50 points, similar to the main group patients. Eight injured children (32 %) received intensive anti-shock treatment, arrest of intracavitary bleeding and stabilization of pelvic ring fragments with skeletal traction until fracture consolidation (conservative treatment). Damage control tactics and the ATLS protocol were used in 17 patients (68 %). Pelvic osteosynthesis with an external fixation device with an anterior frame was performed in eight patients (32 %), internal pelvic osteosynthesis with Kirschner wires (36 %) in nine patients.

Anatomical and functional treatment results were assessed using the methods of IL Shlykov [29] and SA Majeed [30]. The residual deformation (anatomical result) was assessed using the method of IL Shlykov, and the functional treatment result (except for sexual dysfunction, since not all patients were adults at the time of assessment) was assessed using the method of SA Majeed. Thus, combining these scales allowed us to obtain an integrated indicator (overall result), which we reported in our earlier studies [31]. The studies were approved by the Ethics Committee. The patients' parents gave informed consent for the treatment.

Statistical analysis was performed using the Statistica v 12.0 software packages. The reliability of differences in mean values was assessed using the nonparametric Student's t-test (for independent samples). To assess the sample indicators, the arithmetic mean (*M*) and the error of the mean (*m*) were calculated. Differences were considered significant at $p < 0.05$.

RESULTS

Treatment results were followed from one to 14 years after the injury (Table 4). To assess the anatomical treatment result, an analysis of the presence and magnitude of residual displacement was used [29]. In patients of the main study group, residual displacement was detected in four (17 %) cases. Its mean value was (5.0 ± 0.3) mm.

Table 4

Treatment results

Результат лечения	Main study group		Comparison group (n = 25)					
			Conservative treatment		Osteosynthesis with pins		EFD osteosynthesis	
	No	%	No	%	No	%	No	%
Number of patients	23	100	8	32	9	36	8	32
Anatomical result								
Number of residual displacement	4	17,4	6	75	6	66,6	4	50
Magnitude of residual displacement, M ± m, mm	5.0 ± 0.3		9.5 ± 1.1		6.0 ± 0.33		6.0 ± 0.38	
	$p_{1,2} < 0.001$				**$p_{1,3} < 0.05$**		**$p_{1,4} < 0.05$**	
Functional outcome according to Majeed (1989)								
Excellent (85–96 points)	12	52.2	2	25.0	1	11.1	4	50.0
Good (70–84 points)	6	26.1	–	–	3	33.3	2	25.0
Fair (55–69 points)	5	21.7	2	25.0	1	11.1	2	25.0
Poor (< 55 points)	–	–	4	50.0	4	44.5	–	–
Mean, M ± m, points	77.0 ± 2.5		69.0 ± 1.09		70.0 ± 1.33		79.0 ± 2.82	
	$p_{1,2} < 0.01$				**$p_{1,3} < 0.05$**		**$p_{1,4} > 0.05$**	
Total result								
Good	19	82.6	2	25.0	4	44.5	6	75.0
Fair	4	17.4	2	25.0	3	33.3	2	25.0
Poor	–	–	4	50.0	2	22.2	–	–

Note: $p_{1,x}$ — significance of the criterion of reliability of the difference between the indicators in the main study group and the comparison groups

Thus, the functional treatment outcome of (77.0 ± 2.5) points in patients of the main study group was significantly better than in the subgroups of conservative treatment, (69.0 ± 1.09) points ($p_{1,2} < 0.01$), and osteosynthesis with pins in the comparison group (70.0 ± 1.33) points ($p_{1,3} < 0.05$), with no significant difference in comparison with the subgroup of osteosynthesis with EFD (79.0 ± 2.82)

points ($p_{1,4} > 0.05$). Consequently, the use of osteosynthesis with EFD in the treatment of children with combined pelvic injuries provides better functional results compared to conservative treatment and osteosynthesis with pins.

However, residual deformity at the end of treatment was detected in 16 (64 %) patients of the comparison group. The values of this indicator were as follows: 6 (75 %) patients in the conservative treatment subgroup — (9.5 ± 1.1) mm ($p_{1,2} < 0.001$); 6 (66.6 %) patients in the subgroup of osteosynthesis with pins H_{mean} = (6.0 ± 0.33) mm ($p_{1,3} < 0.05$); in the subgroup of osteosynthesis with an external fixation device (EFD) in 4 patients (50 %) — with H_{mean} = (6.0 ± 0.38) mm ($p_{1,4} < 0.05$).

Thus, in patients of the study main group compared with the subgroup of conservative treatment, residual displacement was observed less frequently by 57.6 %, with the subgroup of osteosynthesis with pins by 32.6 %, with the subgroup of osteosynthesis with external fixation devices by 15.9 %. The average value of residual displacement in patients of the main study group was significantly lower than in patients of the comparison group in all compared subgroups. Consequently, the use of the developed methods and metal structures for osteosynthesis in the patients of the main group provides more accurate reduction and reliable fixation of pelvic fractures than with the use of conservative treatment and traditional methods of osteosynthesis.

The evaluation of the overall treatment outcome in patients of the main study group found that the number of good results was 57.6 % higher than in the patients treated conservatively, 38.1 % higher than in patients with osteosynthesis using pins, and 7.6 % better than in the subgroup of traditional EFD osteosynthesis. The number of satisfactory results was lower than in the subgroups of the comparison group, and there were no poor results in patients of the main study group and in the comparison subgroup of EFD osteosynthesis.

The long-term treatment outcome was assessed as fair in two patients of the main study group who sustained severe high-energy pelvic trauma due to fall from a five-story building (a 15-year-old boy) and being hit by a tractor (a 9-year-old girl) despite the complete restoration of the musculoskeletal system, since in the first case there remained a neurological deficit due to rupture of the sacral plexus roots, and in the second case, there were long-term consequences of damage to the urinary tract.

Case report 1 *(main group patient)*

Patient Z., 14 years old, sustained a road traffic injury while driving a motobike, he collided with a car. First aid was provided by an ambulance team. He was transported to the central district hospital at his place of residence (level II trauma center), where his examination revealed damage to the pelvic ring, closed craniocerebral injury, forearm fracture, blunt abdominal trauma, and traumatic I–II degree shock. Anti-shock therapy was administered.

Clinical diagnosis: severe combined road traffic injury; closed fracture of the pelvic bones (fracture of the upper branch of the left pubic and ischium without displacement of fragments, rupture of the pubic symphysis with displacement, rupture of the sacroiliac joint on the right with diastasis in the upper part up to 2 cm and bone fragments (AO type C 1.2); closed fracture of the L5 transverse process on the right with displacement of fragments; closed fracture of the middle third of the right radius with displacement; blunt abdominal trauma; closed craniocerebral injury; concussion; multiple abrasions and bruises of the upper and lower extremities, on the head and body; traumatic shock stage II. ISS = 21.

CT of the pelvis revealed a rupture of the pubic and right sacroiliac joints with vertical displacement of the right half of the pelvis, a fracture of the pubic and ischial bones on the left without displacement, and a fracture of L5 right transverse process with displacement of fragments (Fig. 1 a).

In an emergency, two hours after admission, osteosynthesis was performed with an anti-shock half-pin based EFD with an anterior frame. After stabilization of the general condition, two days later, the child was delivered by air ambulance to the level I pediatric polytrauma center of the Regional Children's Clinical Hospital, where he was treated for three days in the intensive care and anesthesiology department, then transferred to the department.

A repeated operation was 10 days after the injury, osteosynthesis was performed with an additional posterior module using our own technique for the purpose of final reduction of the pelvic fragments (Fig. 1 b). A course of restorative treatment was carried out from the second day after the operation (Fig. 2 a).

The EFD was dismantled after eight weeks. Partial weight-bearing on the right leg was allowed one month after the operation, full weight-bearing after two months. The patient's treatment period was three months. The long-term result was assessed one year after the injury (Fig. 2 b). The overall treatment result is good. There is no residual displacement; the functional result is 90 points on the Majeed scale.

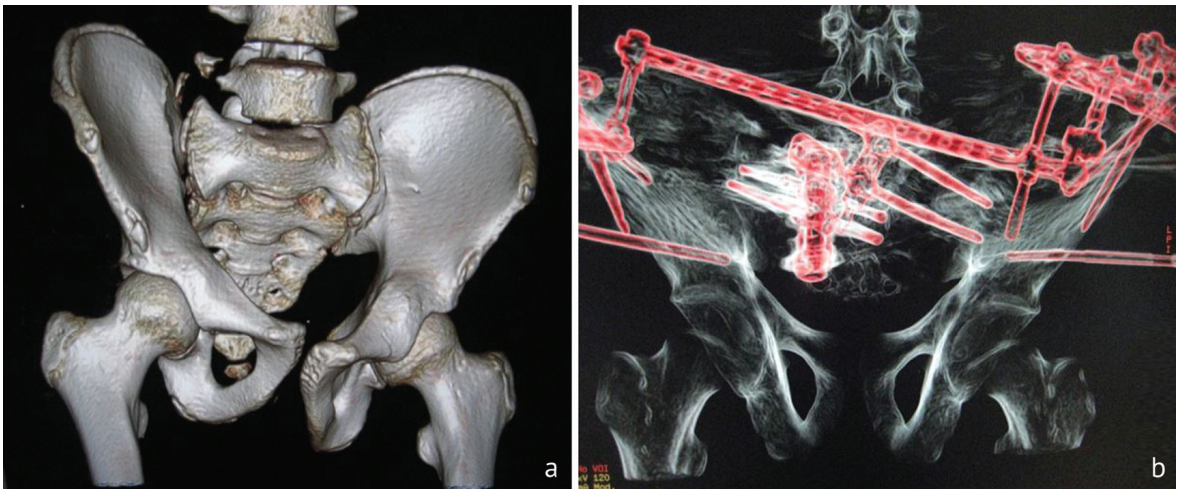

Fig. 1 CT scan of the pelvis with 3D reconstruction: *a* rupture of the pubic and right sacroiliac joint, fracture of the pubic bone and ischium on the left, fracture of L5 right transverse process of with displacement of fragments; *b* condition after final osteosynthesis with a half-pin based external fixator with two modules

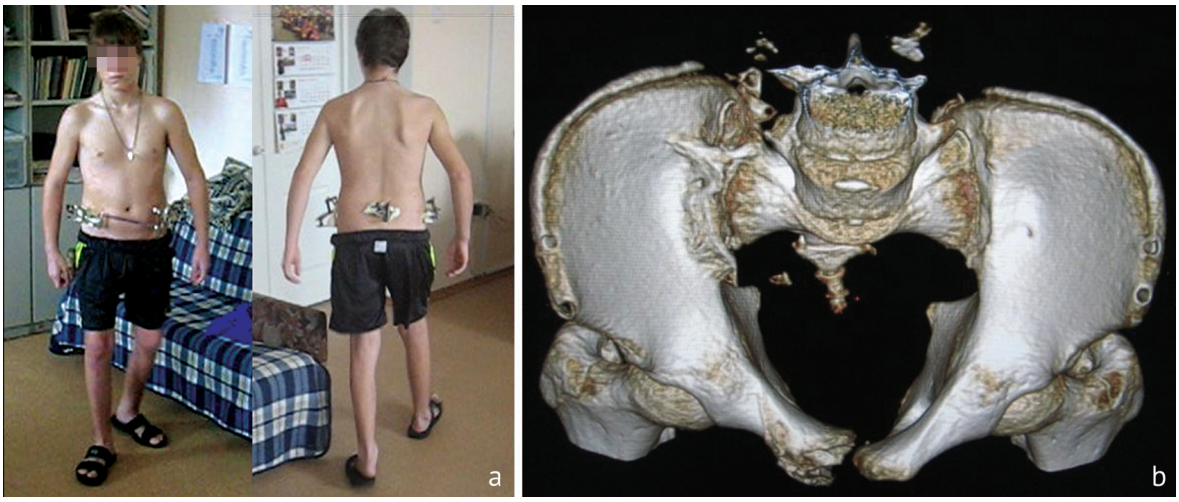

Fig. 2 The result of treatment of the patient of the main group: *a* photo during treatment, exercise therapy; *b* CT of the pelvis with 3D reconstruction one year after the injury

Case report 2 *(main group patient)*

Patient S., 5 years old, was struck with a falling heavy metal object (a vise) on her pelvic area. She was taken by an ambulance team to the Central District Hospital (Level II Trauma Center) 30 minutes after the injury.

Diagnosis upon admission: severe combined injury; open unstable multi-fragmentary fracture of the pubic and ischial bones, with a rupture of the pubic and sacroiliac joints (AO type B 1) (Fig. 3 a); urethra and vaginal injury, rupture of the bladder; traumatic shock stage III. ISS = 33.

In the course of anti-shock therapy, urgent suturing of the bladder wound, primary surgical treatment of the vaginal wound, and epicystostomy were performed. Fixation with skeletal traction was performed. Two days after stabilization of the condition, the patient was transferred to a level I trauma center (Amur Regional Children's Clinical Hospital). The operation was performed as planned, on the third day after the injury, pelvic osteosynthesis with an external fixation device and urethral reconstruction were performed (Fig. 3 b). Stabilization with the external fixation device continued for four weeks (Fig. 4).

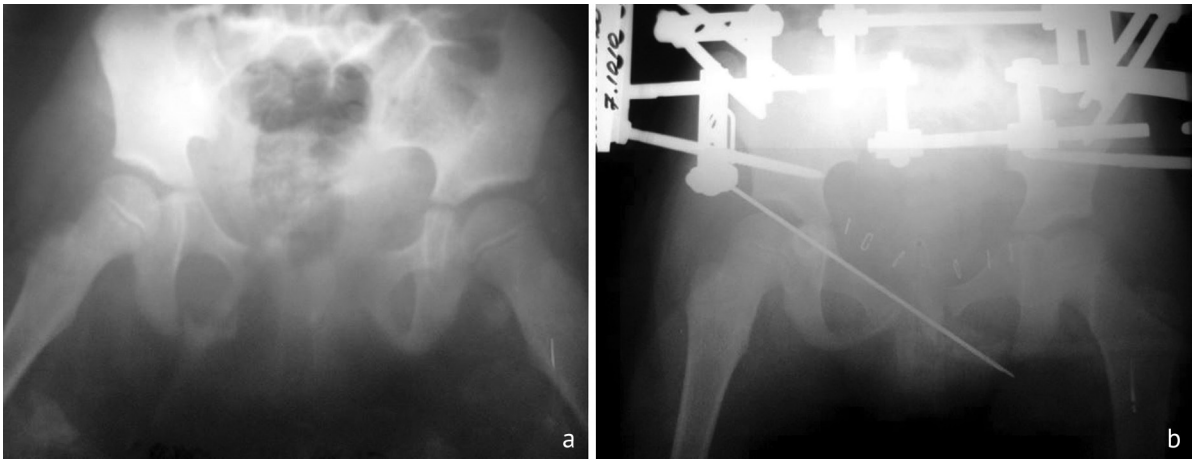

Fig. 3 Radiographs of the pelvis: *a* upon admission (direct view, fracture of the pubic and ischial bones with rupture of the pubic and sacroiliac joints); *b* condition after the intervention (urethral reconstruction, pelvic osteosynthesis with a wire-and-half-pin EFD)

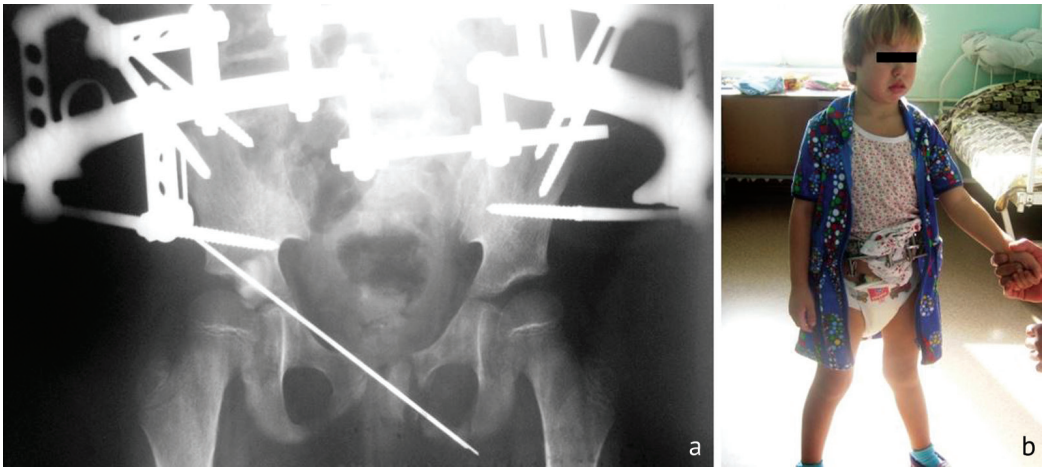

Fig. 4 The patient 4 weeks after the operation before dismantling the external fixation device: *a* X-ray of the pelvis; *b* photo during treatment

The device was dismantled four weeks later and a course of rehabilitation treatment started. The function of voluntary urination was restored three months after the operation. The treatment period was four months. The long-term result was assessed after three years (Fig. 5 a) and 10 years after the injury (Fig. 5 b). The overall treatment result was rated good. There was no residual displacement; the functional outcome was 90 points on the Majeed scale.

Fig. 5 Long-term follow-up result: *a* photo of the patient 3 years after the injury; *b* CT scan of the pelvis with 3D reconstruction 10 years after the injury

Case report 3 *(comparison group patient)*

Patient G., 16 years old, was injured by a stack of wooden boards that fell on the pelvic area. Forty minutes later, an ambulance team delivered him to the Margilan City Medical Association. After examination, the following clinical diagnosis was made: combined injury; multiple fractures of the pelvic bones; closed fracture of the pubic and ischial bones on both sides with displacement of bone fragments with transition to the bottom of the acetabulum; rupture of the symphysis; fracture of the lateral mass of the sacrum on the right with transition to the bodies S1,2 (AO Type C 1.3); complete rupture of the membranous part of the urethra; traumatic shock I–II stage. ISS = 25 points.

The radiograph of the pelvic bones showed a fracture of the pubic and ischial bones on both sides with displacement of bone fragments with transition to the bottom of the acetabulum on both sides, rupture of the symphysis, a fracture of the lateral mass of the sacrum on the right with transition to the bodies S1,2 (Fig. 6 a). On cystography (with a bladder filled with contrast), the bladder is completely filled, has a rounded shape, the contrast leak is noted in the projection of the membranous part of the urethra (Fig. 6 b).

According to emergency indications, laparotomy, abdominal cavity revision, epicystostomy, tamponade and drainage of the small pelvis were performed. The pelvic fragments were fixed with skeletal traction and a "hammock". After stabilization of the general condition, the patient was transported to the RSCfor EMC the next day.

On the 13th day after the injury, under endotracheal anesthesia, anterior stabilization of the pelvic bones was performed with a halfpin-based EFD, and the symphysis rupture was eliminated. A control X-ray of the pelvic bones revealed that the position of the bone fragments was satisfactory, the symphysis rupture was eliminated (Fig. 7 a).

Diagnostic urethroscopy was also performed intraoperatively: a 19 CH urethrocystoscope tube was freely passed through the urethra. The revision showed that the mucosa of the hanging section and bulbous part of the urethra was normal. At the level of the membranous section of the urethra, swelling of the mucosa and a sharp narrowing of the urethral lumen were observed, followed by complete obliteration, due to which it was not possible to pass the cystoscope tube. It was decided to stop the diagnostic intervention and the cystoscope tube was removed. There were no complications. The course of restorative treatment was started on the second day after the operation (Fig. 7 b).

The EFD was dismantled after eight weeks. Partial weight-bearing on the right leg was allowed one month after the operation and after two months full weight-bearing was initiated. The patient's treatment period was three months. The long-term result was assessed one year after the injury (Fig. 8). The overall treatment result was good, there was no residual displacement and the functional result was 90 points on the Majeed scale.

Fig. 6 X-ray of the pelvis: *a* fracture of the pubic and ischial bones on both sides with displacement of bone fragments with transition to the bottom of the acetabulum on both sides, rupture of the symphysis, fracture of the lateral mass of the sacrum on the right with transition to the bodies of S1 and S2; *b* leakage of thecontrast in the projection of the membranous part of the urethra

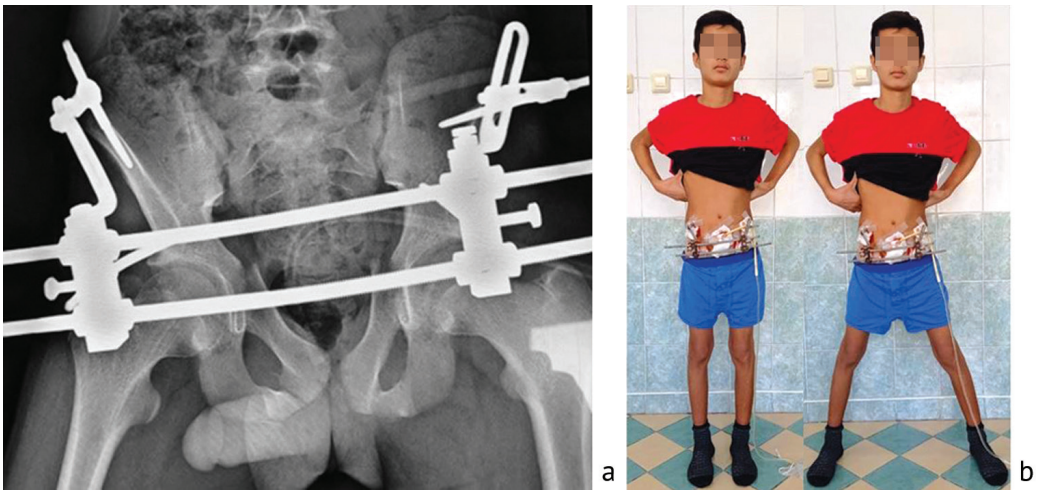

Fig. 7 The period of rehabilitation treatment: a X-ray of the pelvis with EFD fixation; b photo during treatment, exercise therapy

Fig. 8 X-ray of the pelvis one year after the injury

DISCUSSION

The use of staged combined treatment with the developed methods and metal structures for osteosynthesis allows improving the reduction and stabilization of pelvic ring fractures and achieves good functional treatment results. Therefore, staged transosseous osteosynthesis

in the treatment of children with pelvic fractures and polytrauma can be positioned as a method of choice in the fight against shock in the first period of traumatic disease, and can also be successfully used for final reduction and stable fixation of pelvic fragments.

Transosseous osteosynthesis has a number of advantages that are especially important in the treatment of multiple injuries. First of all, it is low invasiveness of transosseous elements, the ability to control fragments "in time" and combine the method with internal treatment technologies.

Back in 2004, the authors from the Ural Research Institute of Traumatology and Orthopedics demonstrated a series of technological solutions for treating patients with chronic pelvic injuries, allowing for full or partial correction of the deformation and stabilization of the pelvic ring [29]. If the most severe spatial deformations of the pelvic ring can be successfully corrected with halfpin-based external fixation devices, then the use of the same devices for the final reduction and retention of bone fragments allows for guaranteed good anatomical and functional treatment results.

However, not all problems in pelvic surgery can be solved with the help of external fixation devices; a number of injuries require internal osteosynthesis for more precise reduction, primarily acetabular fractures and sacral fractures with compression of the lumbar plexus roots. Heeg et al [7] and Michelle et al [6] indicate that these fractures are the cause of such long-term consequences as chronic pain, scoliosis, sexual dysfunction, leg length discrepancy and even growth retardation, which are observed in 30 % of pelvic fractures in children. However, transosseous osteosynthesis can also be used in this case as anti-shock fixation, after which it is possible to convert to open reduction with internal fixation.

The technical solutions we propose allow us to eliminate deformity and reliably fix the fragments until complete consolidation in case of unilateral vertical instability of the pelvic ring, as in the presented case 1. However, patients with disintegrating pelvic injuries accompanied by complete bilateral instability should be operated on using temporary transpedicular fixation, since there is no alternative to this method. In case of sacral fractures with compression of nerve roots, their early decompression is necessary in a specialized hospital with the mandatory participation of a neurosurgeon.

In case of damage to the urinary and genital tracts, it is necessary to strive to carefully restore the anatomy of the pelvic ring. A team approach is also necessary with the participation of a urologist and, if necessary, a gynecologist, which will allow to avoid severe post-traumatic complications not only from the musculoskeletal system, but also from the internal organs of the pelvis in the future, as in clinical case 2.

CONCLUSION

Optimization of the tactics of staged treatment of children with combined and multiple pelvic injuries using rational diagnostics and minimally invasive osteosynthesis with original designs provided a greater number of good and satisfactory results in the main study group compared to the treatment with traditional surgical methods in the comparison group. The severity of injury in children with pelvic fractures equal to 15 points of the ISS scale requires to use the damage control tactics. External fixation can be used not only as a reliable and simple anti-shock fixation, but also as a method of final osteosynthesis. The combination of external fixation with internal osteosynthesis can achieve accurate reduction and reliable stabilization of pelvic ring fragments. Staged provision of specialized care to stop internal bleeding and fixation with an anti-shock device at the first stage and final stabilization of pelvic ring fragments at the second stage is the most rational tactical approach to polytrauma with pelvic injuries in children.

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The article was submitted 18.06.2024; approved after reviewing 26.11.2024; accepted for publication 05.02.2025.

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Original article
https://doi.org/10.18019/1028-4427-2025-31-2-165-174

Clinical and statistical stump characteristics for identifying contraindications to prosthesis

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Abstract

Introduction Limb amputation impacts physical activity and quality of life. Complications of limb amputation and prosthesis are essential for individuals who are losing limbs from vascular diseases and in military casualties.

The **objective** was to identify contraindications to prosthesis based on clinical and statistical stump characteristics.

Material and methods Medical records of 253 lower limb amputees aged 18 to 85 years including 15 individuals with bilateral amputations and 238 with unilateral amputations caused by mine blast injuries, vascular diseases and infections, peacetime injuries, congenital anomalies, osteomyelitis, osteosarcoma. Assessment of the amputee was produced by multidisciplinary teams at the prosthetic orthopedic company, military hospitals, medical and preventive healthcare institutions in 2023. The patients' stumps were examined radiologically and with ultrasound. A total 228 prostheses were manufactured including 120 for tibia and 108 femur amputees. Stabilometric platform and a rehabilitation complex were used for suitable alignment of lower limb prostheses.

Results The stump defects that complicated prosthesis included osteophytes, the fibula cut located distally to the tibia cut, the bone cut protruding to under the skin or a scar, foreign bodies of soft tissues, stiff scars, high location of truncated muscles. Prosthesis was complicated in 59 cases (23.3 %), of which 33 patients (56 %) had absolute contraindications.

Discussion The findings indicated the importance of timely assessment and preparation of stumps for effective prosthesis. Modern technologies and rehabilitation methods help improve quality of life of amputees. Pain and psychological difficulties were the main problems associated with primary permanent prosthesis. The multidisciplinary approach appeared to be practical for successful prosthesis and rehabilitation of patients. Limb amputation caused by combat injuries and other reasons is associated with physical challenges affecting the patient's quality of life.

Conclusion A failure to maintain proper prosthetic socket fit is an absolute contraindication to prosthesis preventing the patient from prosthetic use after amputation. Inadequately cut tibia, club-shaped or excessively conical stump, a stump being too short or too long, osteomyelitis, impaired wound healing or ulcer, ligature fistulas are relative contraindications.

Keywords: amputation, stump, prosthesis, rehabilitation, multidisciplinary approach, digital technologies, clinical analysis, digital twins, soft tissue visualization, digital rehabilitation

For citation: Pepeliaev AV, Skoblin AA. Clinical and statistical stump characteristics for identifying contraindications to prosthesis. *Genij Ortopedii*. 2025;31(2):165-174. doi: 10.18019/1028-4427-2025-31-2-165-174.

INTRODUCTION

Limb amputation impacts physical activity and quality of life. According to WHO, there are about 40 million people living with limb stumps due to amputation or congenital anomaly [1]. Complications of limb amputation and prosthesis are essential for individuals who are losing limbs from vascular diseases and in military casualties.

The most common causes leading to lower limb amputation are obliterating endarteritis, diabetes mellitus including diabetic foot syndrome, oncopathology, trauma including industrial injuries, those resulting from road accidents and natural disasters, and combat injuries [2]. Lower limb amputations can be caused by venous and arterial thrombosis of the lower limbs with the development of acute thromboembolism of major vessels, untimely treatment, inadequate patient monitoring, or a lack of understanding of the pathogenesis of the pathogen at the initial stage of the COVID-19 pandemic [3]. Chronic ischemia can induce bleeding disorder in the compromised limbs and lead to a multiple increase in proximal thromboses and high amputations [4].

Quite often, amputation of a limb segment can be performed significantly more proximal than the level of the affected area,which is caused by the surgeon's need to complete the treatment quickly and at once, neglecting the topographic and anatomical levels of injury and functional changes in the remaining tissues. High amputations can interfere in the prosthesis adaptation process, causing greater difficulty for young disabled individuals [5]. When a lower limb amputation is considered, preservation of the knee which plays an important role in the biomechanics of the musculoskeletal system and proprioceptive innervation [6] allows for optimal functional recovery [7].

The absence of a limb joint, coupled with painful sensations in the stump, leads to the fact that amputees can develop self-stigmatization, feelings of self pity, distorted body image, cognitive rejection of what happened and low motivation for prosthetic use [8]. On the other hand, maintaining stumps that are too short without disarticulation in the overlying joint can also lead to complications during prosthetics, increasing or declining recovery and adaptation periods, due to the need for more careful adjustment of the prosthetic socket [9]. However, high amputations are still performed today, and rehabilitation of the patients is to be arranged by selecting optimal prosthetic designs. Characteristics of the affected area with tissue deficiency and specificity of the transplanted skin are essential as supporting areas upon completion of free autoplasty in the postoperative period and, in some cases, can result in defects and diseases of the formed stumps. Higher amputation and reduced loading on the grafted skin can be practical in the scenario [10].

The **objective** was to identify contraindications to prosthesis based on clinical and statistical stump characteristics.

MATERIAL AND METHODS

The study was conducted in 2023 at the prosthetic and orthopedic enterprise JSC CITO, military hospitals and medical and preventive healthcare institutions. Medical records of 253 lower limb amputees aged 18 to 85 years including 15 (5.93 %) individuals with bilateral amputations and 238 (94.07 %) with unilateral amputations. In our series, 209 cases (78 %) were classified as functional stumps, 26 cases (10 %) as low-functional, and 33 cases (12 %) as non-functional.

Type of study: clinical observational.

Study design: retrospective analysis of medical data and observations.

Inclusion criteria: patients who have undergone lower limb amputation and are at the stage of rehabilitation and prosthesis, who have expressed consent to participate in the study.

Exclusion criteria: patients with upper limb amputations, patients with exacerbation of concomitant diseases that could interfere with prosthetics, or patients who fail to obtain a complete set of medical records.

The patients' readiness for prosthetics was assessed based on the presence or absence of defects and diseases of the stumps [11].

Measurement technique The stump condition was assessed by a multidisciplinary team including trauma and orthopedic surgeons, prosthetic technicians and rehabilitation specialists. Medical documentation data (discharge summaries, inpatient cards, medical histories, prosthesis manufacturing order forms, questionnaires) and the results of 135 instrumentation examinations submitted by patients were used. The stumps were examined radiologically and using ultrasound. However, not all patients could be included in the process of taking a plaster cast and producing a trial socket, which was due to factors that prevented the patient from adapting to the prosthesis. During the study, patients were supplied with 228 prostheses including 120 for the tibia and 108 for the femur. Patients were referred for prosthesis 2–13 months after amputation, depending on objective and subjective factors.

Ethical principles All patients were informed about the conditions of the study and gave written consent to participate. The study was conducted in accordance with the Declaration of Helsinki.

Data processing The data were analyzed to assess the prevalence of stump defects and diseases, their impact on the process of prosthesis and rehabilitation.

Defects and diseases affecting the prosthetic limb significantly reduce the functionality of the stump, complicate the prosthetic process and increase the time required for rehabilitation and preparation of the truncated area for prosthesis. Such cases are classified as complicated. The functionality of the stump is determined by its condition, readiness for prosthesis and ability to accept mechanical impact from the prosthesis. The functionality of stumps is divided into three categories: functional, low-functional, and non-functional, to assess whether the stump is ready for prosthesis and develop rehabilitation strategies [12].

The level of prosthesis acquirability was determined using the COBS stabilometric platform with biofeedback and Motek C-Mill virtual reality treadmill. The exercise therapy instructor assessed the distance covered by the patient in the prosthesis, the ability to maintain balance on the platform and cope with tests on an innovative sensor treadmill. Spatiotemporal parameters including the length and width of the step were measured taking into account the difference between the left and the right (in meters), as well as dynamic parameters - walking on marks, Butterfly, Aggregated force, weight distribution supported one leg, step frequency.

The treatment goal is to improve the symmetry between the left and right steps, improve characteristics of the reaction force to the support during walking on the platform. The downloaded information serves as an important indicator of the detection and correction of pathological gait. The information obtained is important for accurate monitoring of the progress of the prosthesis acquirability and the formation of the correct motor stereotype of walking.

RESULTS

Medical records indicated wound healing of the stump by primary intention in 194 patients with sutures removed on time (Table 1). Stump diseases caused by an accompanying infection were identified as a long-term granulating wound or ulcer, wound healing by secondary intention, a fistula, osteomyelitis. Defects of the stump that complicate prosthetics were identified as osteophytes,

location of the fibula cut distal to the tibia cut, protrusion of the bone cut under the skin or scar, foreign bodies in soft tissues, stiff scars, high location of truncated muscles.

Table 1

Clinical data of patients obtained during the assessment of stump condition

Description	Number of cases	
	abs.	%
Wound healing by primary intention	194	76.6
Stump disorder (infection)	24	9.5
Defects of stumps	20	7.9
Painful neuromas	10	4.0
Unspecified pain in stump	4	1.6
Neuritis of the peroneal nerve	1	0.4
Total	253	100

Lower limb amputations were caused by mine-blast wounds, peacetime injuries, osteomyelitis, osteosarcoma (Fig. 1). In two cases, the limbs were unsuitable for prosthesis due to a congenitally underdeveloped limb being nonsupporting, and amputations were performed to form a stump. Diabetes and atherosclerosis diagnosed in 76 cases (30 %) led to gangrene followed by amputation. Progressive thromboangiitis, obliterating endarteritis, embolism and thrombosis of major arteries followed by critical limb ischemia were detected in 12 cases (4.7 %). These data confirm high significance of problems associated with military injuries and chronic vascular diseases in the context of limb amputation and rehabilitation potential.

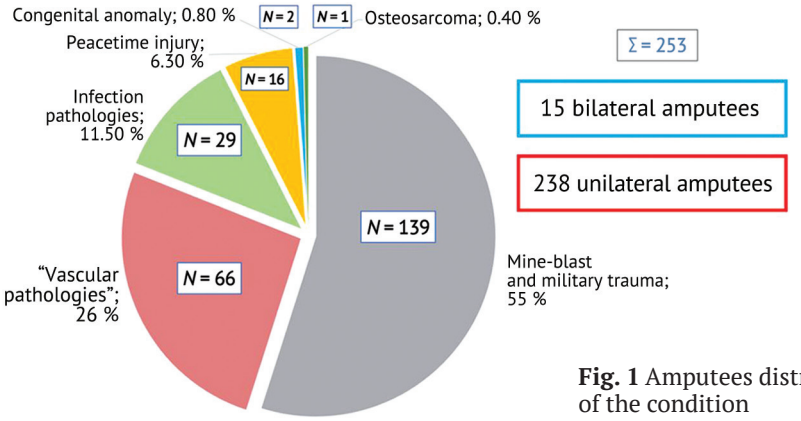

Fig. 1 Amputees distributed by a cause of the condition

Prosthetic fitting was complicated in 59 cases (23.3 %) including 33 patients (56 %) having absolute contraindications, such as stump defects or infectious complications requiring additional treatment prior to prosthesis (Fig. 2).

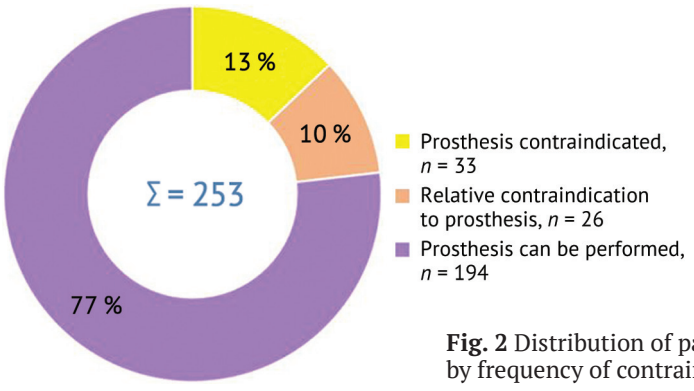

Fig. 2 Distribution of patients by frequency of contraindications

Relative contraindications included stump defects including those developed after repeated amputation, which was an absolute contraindication to prosthetics at the time of examination and required additional diagnosis and treatment procedures including reamputation. Radiographs and ultrasound facilitated verification of stump defects and justify the need for reamputation. Reamputation was performed once in 42 cases (16 %) prior to prosthetic reference, and repeated surgical interventions on the lower limb stumps had to be performed for five patients (2 %). Osteophytes were detected in three cases (1 %) after reamputation and required surgical treatment.

Absolute contraindications to prosthesis may include cases when specialists are unable to make a socket in such a way that the patient can bear weight on the stump and use the prosthesis. Stump diseases include neuromas of nerve stumps, painful osteophytes of bone sawing in places of limb truncation. Stump defects include protrusion of the bone-saw under the skin or scar, a more distal location of the fibula relative to the tibia, a bone stump protruding without a muscular sheath with a deficiency of soft tissue coverage at the site of the postoperative scar of the stump, and severe pain at the postoperative wound of unknown origin. Relative contraindications include inadequate bone-saw of the tibia, club-shaped or excessively conical stump, excessively short or too long stump and diseases such as osteomyelitis, long-term granulating wound or ulcer, ligature fistulas. The latter may prevent from product delivery and delayed prosthetic use. Treatment and recovery procedures including rehabilitation and exercise therapy can help eliminate the complicating factor or reduce its impact.

DISCUSSION

Conservative and surgical methods can be used to prepare patients for primary prosthesis. Experienced orthopedic surgeons can decide on the need for reamputation during the initial examination at the prosthetic enterprise. Conservative treatment, including therapeutic exercise, massage and physical methods can be offered prior to surgical intervention [13]. Medical and technical reports were issued on the need for surgical treatment of 59 patients who were examined for defective stumps and needed surgical preparation for prosthesis. The operation was performed for 17 patients (29 %). At the time of the study, not all patients gave voluntary consent to surgical treatment. Referring to the sources of the Second World War, to the classification offered by P.A. Kupriyanov and N.N. Burdenko, we grade amputations into types, systematized and confirmed by modern scientific works dividing amputations by time into primary, secondary, late and repeated amputations (reamputations) for studying clinical outcomes. This classification is relevant today, when the need for a multidisciplinary approach and timely diagnosis remains crucial to reduce complications [14].

The main idea of the work is supported by other modern authors who report the importance of adequate formation of the stump during primary amputation to minimize the risk of reamputation and improve rehabilitation prospects [15, 16].

Mine blast injuries resulted in amputation in 55 % of patients. Specific approaches to the treatment and rehabilitation are essential for the patients and those with combat injury. It is important to note that 30 % of amputations are caused by diabetes and atherosclerosis indicating the role of prevention and timely treatment of chronic diseases [17]. In modern injuries, the skin of the extremities can be compromised over a large area, which emphasizes the importance of preserving the maximum length of damaged areas with the help of early skin grafting, as discussed in classical guidelines [18] and remains relevant, especially in the modern conditions of mine-explosive wounds described in later sources [19]. The principles of surgical treatment for mine-blast wounds suggest removal of non-viable tissues of the affected lower limb in a field hospital to avoid threat risk. Further processing and formation of the stump occurs in a specialized hospital [5].

The level of amputation and proper stump formation determine how quickly the patient can initiate rehabilitation. The surgical technique of amputation is determined by the level of limb truncation and the anatomy of the segment. The level of amputation is the cornerstone of discussions between surgeons and specialists involved in prosthesis of lost limbs. The resection level selected preoperatively does not always coincide with the demarcation line of viable tissues identified intraoperatively [2, 5, 6], which can also affect the likelihood of developing defects and diseases of the stumps.

Delayed primary amputation is reported to allow minimize tissue damage and facilitate rehabilitation. Excessive resection of healthy tissue should be avoided with amputation at the level of non-viable tissue. Although some involved tissues may regain their viability after appropriate therapy, the possibility of secondary necrosis cannot be ruled out postoperatively due to local hypoxia and edema [14]. Abrasions, cracks and irritation of the skin may result from the pressure of the prosthesis on the stump. This is a rare case with a prosthesis used without a silicone cover to prevent formation of skin folds and infection. The formation of infiltrates and nodes at the prosthetic loading zones can be associated with excess skin on the stump. The resulting nodes can contribute to the formation of postoperative scars. N.N. Priorov recommended resorting to skin plastic surgery in exceptional cases to avoid wide and long flaps strengthening the transplanted skin through gymnastics and self-massage [20]. Today, these recommendations remain relevant [21].

Requirements for the stump are formulated in prosthetics manuals [10, 19] as follows: the truncated limb should be as long as possible, covered with intact skin without ulcers, bruises, abrasions, phlyctenas, and should not be excessively conical or club-shaped. The postoperative scar should be mobile, smooth, located outside the supporting zones of the receiving sleeve, the muscles should be developed. There should be no neuromas, and the bone saw should be horizontal, smooth, and joint movements are not limited [22, 23]. An additional requirement is imposed on the tibial stumps: sawing of the tibial crest should be performed at an angle of 45° to the longitudinal axis.

The shape of the stumps changes from club-shaped to moderately conical, the tension of tissues and skin changes, resulting in increased pain in the areas of terminal neuromas and post-amputation skin diseases. Softening inserts, silicone liners with damping properties and lodgements are used in these cases to relieve the trigger painful points of contact of the stump and the socket. Preliminary use of silicone covers during primary prosthetics was recommended to patients for an average of two weeks.

The results of this study show that the condition of the stumps is a critical factor in the success of prosthesis. Wounds healed by primary intention in most cases (76.6 %) indicating the effectiveness of surgical treatment. However, almost a quarter of patients (23.3 %) encountered problems (infections, stump defects, and painful neuromas) that complicated prosthesis. Our findings are consistent with the literature data on the importance of correct surgical technique and preparation of the stump for successful prosthesis [24]. Stump defects such as osteophytes and inadequately positioned bone cuts complicating prosthesis were detected in 7.9 % of cases. This is consistent with the data of other authors, who indicate the need for more thorough preparation and constant monitoring of the condition of the stump [25].

Failure to comply with the stages of surgical treatment, surgical principles of amputation, insufficient diagnosis and observation in the postoperative period can cause diseases and defects of the stumps, contractures of the remaining joints. This can be due to the consequences of surgical treatment and inadequate prosthesis [15, 26].

The study emphasizes the importance of stump preparation for prosthesis, which is confirmed by other studies [14, 26, 27]. Anthropometric and statodynamic characteristics of patients should be considered prior to prosthesis. Measures for preliminary formation and preparation of the stump included elastic bandaging, use of compression hosiery, polymer covers, massage, physiotherapy and exercise therapy.

Neglect of preparation for prosthesis can induce formation of problematic stumps. Strict adherence to the surgical technique and postoperative care, involvement of specialists at all stages of treatment can reduce cases of non-functional or low-functional stumps and improve the quality of prosthesis [15]. It should be borne in mind that a relatively stable stump is formed approximately 10-12 months after amputation. The stump is formed depending on the timing of the beginning of the use of the prosthesis and the activity of its use. Bandaging the limbs is essential to avoid club-shaped stumps of the femur and tibia. Stump dimensions in patients who follow recommendations for preliminary stump formation differ significantly from those in patients who do not follow the instructions.

Tissue reorganization and adaptation to new anatomical and physiological post-amputation scenario: muscle truncation, deprivation of tendon attachment zones in the distal parts, exposure of the medullary canal and trophic changes. Matching volumetric dimensions of the sleeve and the stump are important for the patient to begin use the prosthesis. Accurate dimensions of the stump and the receiving socket are difficult to arrange at the stage of manufacturing and delivery of a trial receiving socket due to the dynamic change in the volume of soft tissues of the stump of the truncated limb caused by muscle atrophy and redistribution of the load on the supporting areas. There is often a need to correct or replace the trial socket and search for an alternative silicone liner no smaller in size. With repeated corrections of the socket and changes in the fastening system, complications may develop at the contact between the socket and the stump,leading to repeated surgical interventions, repair/replacement of the receiving socket or complete prosthetic replacement [19]. Trophic disorders, trauma to soft tissues upon contact with the receiving socket slow down the rehabilitation and socialization of amputee [28].

Manufacturing the ideal socket is a complex process that involve many factors to provide long-term use, comfortable use and overall functionality of the prosthesis [29]. A personalized approach in the production of prostheses for amputees is key to the widespread adoption of technology, which should be accessible and meet the needs of the disabled person [30].

In this context, digital technologies, including the concept of digital twins, are of particular importance. The creation of personalized digital models of stumps allows us to predict the interaction of tissues with the prosthesis, adapt the socket design and increase the overall effectiveness of rehabilitation. Modern methods are used in clinical practice: from quantitative MRI (T2 mapping) to 3D modeling and biomechanical simulations. A. Gentili et al. [31] demonstrate the economic feasibility of these solutions. In conditions of limited healthcare budgets, it is important to take into account the cost of technologies and their contribution to the restoration of patients' ability to work, using cost-effectiveness assessment models (CEA, BIA, CBA).

Our study also addresses infectious and other purulent complications, which prevents successful prosthesis. This is consistent with the data presented in studies describing the increased risks of thrombosis and amputation in infections including COVID-19 indicating the importance of careful postoperative monitoring [3, 4]. Post-amputation stump diseases refer to absolute contraindications to prosthesis. Disregarding preventive immobilization, therapeutic exercise and elastic bandaging in the postoperative period are major reasons for their formation. Discussion of the presented data

indicates the importance of adhering to surgical and rehabilitation principles in the treatment of amputees, implementing new technologies in the prosthetic process. Clinical data indicate the importance of careful stump preparation and proper prosthesis selection, which is consistent with international studies.

Despite the development of prosthetics over the past decades, patients may fail to use prosthetic and orthopedic products due to discomfort caused by mismatch between the receiving socket and the current dimensions and characteristics of the stump of the amputated limb [3, 16].

A limitation of this study is the lack of opportunity to observe patients before admission to the prosthetic and orthotic institution, a long-term follow-up which would provide a better picture of the long-term effectiveness of prosthesis. Nevertheless, the findings indicate the importance of a multidisciplinary approach and personalized stump preparation for successful prosthesis.

It is necessary to emphasize the importance of interdisciplinary cooperation between professionals involved in primary specialized medical care and the prosthetic experts. The correlation of amputation goals and the possibility of prosthesis is achieved by increasing competencies in these areas of knowledge, continuous training and professional communication. The scientific focus today is shifting towards progressive technologies, leaving in the shadow the need for proper consideration of current problems in the application of traditional methods. High-tech biomechanical analysis and accurate imaging are used for stump assessment to prevent complications. Innovative methods such as 3D printing, CAD/CAM, robotic prostheses and biomechanical assessment can improve patient adaptation to prostheses and rehabilitation of amputees [32].

As the number of amputees continues to grow, the approaches used to prosthetic limbs are to be improved. Growing experience in interacting with amputees entails the need to improve existing methods in the military field and in cases of providing assistance to the civilian population with truncated limbs. It is also important to consider the economic feasibility of implementing new technologies, assessing how they can achieve the maximum health benefit for people within the budget. Despite the growing interest in investing in digital health interventions, the evidence regarding cost and effectiveness of digital tools in health is scarce and limited [31]. Further studies based on a standardized approach are needed to systematically analyze incremental cost-effectiveness ratios, health and diagnostic costs and benefits, as the high cost of these technologies may be a barrier to the widespread implementation [30].

The development of quantitative criteria and standardized diagnostic methods is a priority for clinicians, which indicates the need to introduce objective scales to improve the assessment of the stump and prosthesis and reduce possible errors with use of modern technologies [23].

In our series, repeated reamputations due to pain were performed in five cases (2 %). Sometimes specialists are forced to recommend repeated amputation without pronounced pain but for the presence of radiographic osteophytes which may lead to difficulties in using the prosthetic and orthopedic device including a complete refusal to use the latter. Not all of the subjects agreed to invasive treatment, which may be dictated by the emergence of psychological barriers when realizing the prospect of re-experiencing a similar experience.

Despite identified obstacles to further prosthesis in patients, it is necessary to do everything possible to ensure that the manufactured prostheses including atypical prosthesis are convenient to use facilitating adaptation to new circumstances, return to normal life and socially useful work. The study makes an important contribution to the understanding of the problems of rehabilitation and prosthesis of amputees and confirms the need for further study in this area. The results

of this analysis confirm the conclusions of a number of international sources on the importance of the correct choice of socket and careful preparation of the stump.

CONCLUSION

The majority of patients in our sample included cases caused by mine-explosive injuries. The second most common are amputation stumps in patients with vascular pathologies. The study showed that defects and post-amputation diseases complicated further prosthesis in 23 % of cases.

The impossibility of producing a socket that would allow the patient to bear weight on the stump and fully use the prosthesis is an absolute contraindication to prosthesis. Inadequate saw cut of the tibia, a club-shaped or excessively conical stump, a stump that is too short or too long, osteomyelitis, long-term granulating wound or ulcer, ligature fistulas are relative contraindications.

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

Funding *The study was funded by the institution's internal resources. No external funding was received.*

Ethical Approval *A. The study received a favourable opinion from the relevant research ethics committee. The conclusion on the compliance of the study with ethical standards was obtained before its commencement.*

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

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The article was submitted 18.06.2024; approved after reviewing 06.11.2024; accepted for publication 05.02.2025.

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Original article
https://doi.org/10.18019/1028-4427-2025-31-2-175-182

Comparative analysis of surgical outcomes of arthrodesis and suspension arthroplasty of the saddle joint

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Abstract

Introduction Trapeziometacarpal osteoarthritis is a very common condition that leads to progressive loss of functionality of the first finger that can be surgically treated with arthrodesis of the saddle joint and suspension arthroplasty of the first metacarpal bone. There is a controversy over the surgical technique to choose without consensus in the literature.

The **objective** was to compare surgical outcomes of patients with trapeziometacarpal osteoarthritis treated with arthrodesis and suspension arthroplasty of the saddle joint.

Material and methods The use of both surgical options resulted in significantly reduced pain measured with the VAS ($p < 0.001$) and improved upper limb function evaluated with the Quick DASH scale. The treatments differed in the median duration of plaster immobilization. The duration of postoperative immobilization in arthrodesis patients was statistically higher ($p = 0.004$) than that in suspension arthroplasty group. No statistically significant differences were found between the two groups of heavy and light manual laborers (Pearson coefficient = 0.311).

Discussion The findings of the series indicated parameters being different from those published in the literature. The dependence between functional results and the type of working activity of patients treated with both surgical methods was not confirmed. The choice between trapezio-metacarpal arthrodesis and suspension arthroplasty of the first metacarpal bone based on the criterion of severity of work was not always correct. Increased periods of plaster immobilization in the saddle arthrodesis group are reported in the literature and associated with complications of the treatment option.

Conclusion No significant differences were found between the outcomes of saddle arthrodesis and suspension arthroplasty of the first metacarpal bone.

Keywords: osteoarthritis, trapezio-metacarpal joint, suspension arthroplasty, arthrodesis

For citation: Afanasyev AO, Chizhov AE, Abdiba NV, Rodomanova LA. Comparative analysis of surgical outcomes of arthrodesis and suspension arthroplasty of the saddle joint. *Genij Ortopedii*. 2025;31(2):175-182. doi: 10.18019/1028-4427-2025-31-2-175-182.

INTRODUCTION

Trapeziometacarpal (saddle joint, first carpometacarpal) joint (TMJ) osteoarthritis is a very common condition, it is the second most common location for degenerative arthritis in the hand after the distal interphalangeal joint [1, 2]. Trapeziometacarpal osteoarthritis affects 20 % of the adult population over 55 years old affecting postmenopausal women in 36 % of cases [3–5]. Saddle joint arthritis is accompanied by progressive loss of function of the thumb with common symptoms of pain and loss of pinch/grip strength which is characterized by pain, impaired pinch grip and gradually increasing deformity of the bone and ligament structures [6, 7]. The Eaton-Littler radiological classification is used to assess arthrotic changes and determine the treatment strategy. It includes four stages and describes criteria for the severity of the pathology: narrowing of the joint space, subchondral osteosclerosis, the presence of osteophytes [8]. The first line of treatment of TMJ osteoarthritis is non-surgical but in most cases, patients seek medical help in the late stages of degenerative changes in the joint with severe deformity of the first ray, requiring surgical correction [9, 10].

Arthrodesis and suspension arthroplasty of the first metacarpal bone are the main surgical methods for treating TMJ osteoarthritis , but there is no consensus in the Russian and foreign literature on which surgical treatment is optimal [11–13].

Some authors consider suspension arthroplasty to be the “gold standard” in the treatment of arthrosis of the first carpometacarpal joint, while others are inclined to choose trapeziocarpal arthrodesis, which, despite the reduced range of motion of the first ray, maintains greater pinch grip strength compared to suspension arthroplasty [14–17]. Barakat et al. established the normal ranges of movements for the thumb joints and identified that a reduction in certain thumb joint movements appeared to be compensated for by an increased movement range in the other joints somewhat leveling out the functional volume reduced as a result of arthrodesis [18].

The ongoing debate about the choice of surgical treatment for arthritis of the first carpometacarpal joint in the presence of conflicting literature data led to a comparative analysis of the outcomes of surgical treatment of patients after arthrodesis and suspension arthroplasty of the saddle joint.

The **objective** was to compare surgical outcomes of patients with trapeziometacarpal osteoarthritis treated with arthrodesis and suspension arthroplasty of the saddle joint.

MATERIAL AND METHODS

Design of the study A single-center, cohort, retrospective study conducted in accordance with the STROBE guidelines.

Terms and conditions The data of a retrospective analysis of medical records and radiological examination of 60 patients divided into two groups were included in the study. Patients of group 1 were treated with arthrodesis of the first trapezio-metacarpal joint (n = 29) and patients of group 2 treated with suspension arthroplasty of the first metacarpal bone (n = 31). All patients received elective surgical treatment at the R.R. Vreden National Medical Research Center for Trauma and Orthopedics between 2020 and 2023.

Eligibility Criteria: patients with Eaton-Littler stage III arthritis of the first carpometacarpal joint treated with arthrodesis or suspension arthroplasty.

Non-inclusion criteria: patients with congenital malformations of the hand, a history of severe hand injuries (mine blasts, burns, etc.), neuropathy of the upper extremities, systemic diseases including autoimmune conditions (SLE, scleroderma, seropositive rheumatoid arthritis).

Methods of data collection and analysis Long-term results of surgical treatment were assessed through communication with patients with remote examination and use of standard questionnaires. Hand function and pain were evaluated based on subjective criteria using the Quick DASH (Disability of the Arm, Shoulder and Hand) and VAS (Visual Analogue Scale). The volume of opposition of the first finger was measured using the Kapandji Thumb Opposition Scores test. Informed consent for data processing and inclusion in the study was obtained from all patients.

Description of medical intervention All surgical interventions were performed by one surgeon-researcher in the operating room, with the patient in the supine position with the upper limb placed on a side table. Conduction anesthesia in the brachial plexus and intravenous sedation were employed for monitoring patient's vital functions. The first carpometacarpal joint was approached with the tourniquet placed in the upper third of the forearm. A longitudinal incision of 5 cm was made in the trapeziocarpal joint area along the dorsal radial side performing suspension arthroplasty. The trapezium bone and visible osteophytes were removed after capsulotomy. A figured approach was performed at the site of the first bone-fibrous canal of the extensor tendons and the tendon of the long abductor muscle of the first finger could be visualized. A split was taken from the radial side of the tendon of the long abductor muscle to its distal attachment. The split was produced under the tendons of the long abductor muscle and the short extensor of the first finger. A 1 cm dissection of the tendon of the long radial extensor of the carpi radialis was performed along the midline. The split was passed through the formed opening, and the optimal tension of the tendon was determined. Then the split was wound around the tendons of the long abductor muscle of the first finger and the short extensor of the first finger and stitched with the tendon of the long extensor of the carpi radialis with a 3/0 Prolene thread. A tendon ball (tenoball) was formed from the remaining tendon split, then placed and sutured to the residual cavity after removal of the trapezium bone. The joint capsule was sutured and the wound closed. A longitudinal access was made in the joint area up to 5 cm performing arthrodesis of the first carpometacarpal joint. Resection of the articular surfaces of the base of the first metacarpal bone and the trapezium bone to the subchondral bone was performed after capsulotomy. Preliminary fixation of the first finger was performed in the functional position of 30° adduction and 15° radial deviation using two Kirschner wires. The final fixation was performed with a 1.0 mm T-plate with its wide base facing the trapezium bone and its narrow base facing the metacarpal bone, fixed with 2.0 mm screws. After that, the joint capsule was sutured and the wound closed.

Statistical data processing. Statistical analysis was performed using IBM SPSS Statistics 26. The normality of the distribution of the original data was checked using the Shapiro-Wilk test (arthrodesis group $n = 29$; suspension plasty $n = 31$) with the distribution considered normal at $p > 0.05$ and different from normal at $p < 0.05$. Comparison of nominal binary indicators (gender, dominant limb, presence of complaints, bad habits, postoperative rehabilitation) was performed in the study groups using four-field tables with calculation of the Fisher criterion. Comparison of two independent groups according to qDASH indicators before surgery and qDASH after surgery was performed using the Student's t-test and considering the normal distribution of data, VAS before surgery and VAS after surgery, Kapandji score using the Mann-Whitney test for distribution different from normal. Dependent groups for qDASH scores before and after surgery were analyzed using the paired Student's t-test and the Wilcoxon test used for VAS scores before and after surgery. Comparative analysis of groups depending on patient activity (heavy physical labor/light physical labor) was performed by constructing four-field tables and calculating according to the Pearson criterion with visual display in normalized histograms with accumulation.

The study was approved by the institutional ethics committee and was conducted in accordance with the ethical standards set out in the Declaration of Helsinki.

RESULTS

Surgical treatment was normally performed on the dominant hand (68.9 %, group 1; 80.6 %, group 2). Most patients complained of pain at the time of treatment (72.4 %, group 1; 80.6 %, group 2). No injuries to the operated hand were observed in the patients. Most patients did not have bad habits or chronic diseases. The majority of patients in both groups did not undergo rehabilitation with a hand therapist (72.4 %, Group 1; 64.5 %, Group 2). Heavy physical activity was common for 51.7 % patients of Group 1 and for 38.7 % of Group 2 (Table 1).

Table 1

General characteristics of the patients

Description			Group 1 (n = 29)	Group 2 (n = 31)	Level of statistical significance (p)
Gender	male	abs.	12	7	0.166
		%	41.4	22.6	
	female	abs.	17	24	
		%	58.6	77.4	
Age, full years	M ± SD		59.79 ± 14.044	57.97 ± 12.674	0.6
	(95 % SI)		(54.45–65.14)	(53.32–62.62)	
Limb	dominant	abs.	20	25	0.376
		%	68.9	80.6	
	non-dominant	abs.	9	6	
		%	31	19.3	
Complaints at the time of hospitalization	pain	abs.	21	25	0.451
		%	72.4	80.6	
	pain + limitred function	abs.	8	6	
		%	27.6	19.4	
Injuries to the operated hand			0	0	
Bad habits	none	abs.	25	22	0.213
		%	86.3	70.9	
	smoking	abs.	4	9	
		%	13.7	29.1	
Chronic diseases	none	abs.	25	27	0.561
		%	86.3	87.1	
	DM	abs.	4	3	
		%	13.7	9.7	
	CKD	abs.	0	1	
		%	0	3.2	
Duration of plaster immobilization, weeks, Me (Q1–Q3)			6 (6–8)	6 (6–6)	0.004*
Hand rehabilitation specialist	none	abs.	21	20	0.585
		%	72.4	64.5	
	yes	abs.	8	11	
		%	27.5	35.4	
Postoperative infection			0	0	
Relationship between work and loads	none	abs.	14	19	0.311
		%	48.3	61.3	
	yes	abs.	15	12	
		%	51.7	38.7	

* — the differences in the indicators are statistically significant.

The statistical analysis showed no significant differences in the Quick DASH questionnaire, the VAS visual analog pain scale and in the Kapsandji Score in arthrodesis and suspension arthroplasty groups (Table 2).

Both surgical options resulted in a statistically significant reduction in pain intensity measured with the VAS scale ($p < 0.001$) and an improved upper limb function measured with the Quick DASH scale (Table 3). The effectiveness of the treatment options differed only in the median duration of plaster immobilization.

Table 2

Comparative analysis of the treatment methods evaluated with the Quick DASH, VAS pain scale and Kapandji score

Description	Group 1 (n = 29)	Group 2 (n = 31)	Level of statistical significance (p)
Satisfaction with the results, %	100	100	
Pre-op qDASH, M ± SD (95 % CI)	75.06 ± 6.27 (72.67–77.44)	75.22±6.17 (72.96–77.48)	0.92
Post-op qDASH , M ± SD (95 % CI)	33.14 ± 5.12 (31.19–35.09)	34.65±7.86 (31.77–37.53)	0.38
Pre-op VAS, Me (Q1–Q3)	8 (7–8)	8 (7.5–8)	0.462
Posyt-op VAS, Me (Q1–Q3)	2 (1–2)	2 (1–2.5)	0.562
Kapandji score, Me (Q1–Q3)	6 (6–6)	6 (5–6)	0.448

* — the differences in the indicators are statistically significant.

Table 3

Comparative analysis of the preoperative and postoperative functional results of the treatment methods

Surgical technique	Functional results		P
	pre-op	post-op	
Arthrodesis (calculated with qDASH)	75.06 ± 6.27 (72.67–77.44)	33.14 ± 5.12 (31.19–35.09)	< 0.001*
Suspension arthroplasty (calculated with qDASH)	75.22 ± 6.17 (72.96–77.48)	34.65 ± 7.86 (31.77–37.53)	< 0.001*
Arthrodesis (calculated with VAS)	8 (7–8)	2 (1–2)	< 0.001*
Suspension arthroplasty (calculated with VAS)	8 (7.5–8)	2 (1–2.5)	< 0.001*

* — the differences in the indicators are statistically significant.

The duration of postoperative immobilization in the group of patients who underwent arthrodesis was significantly higher ($p = 0.004$) than that in patients with suspension arthroplasty (Fig. 1). There were no statistically significant differences between the two groups of patients with heavy and light manual labor (Pearson coefficient = 0.311). Correlations identified with the Chaddock scale was not informative. The results are displayed in normalized stacked histograms (Fig. 2).

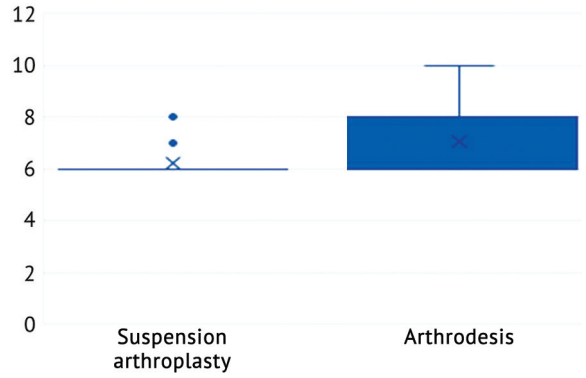

Fig. 1 Duration of immobilization in two comparison groups represented as a box plot, weeks.

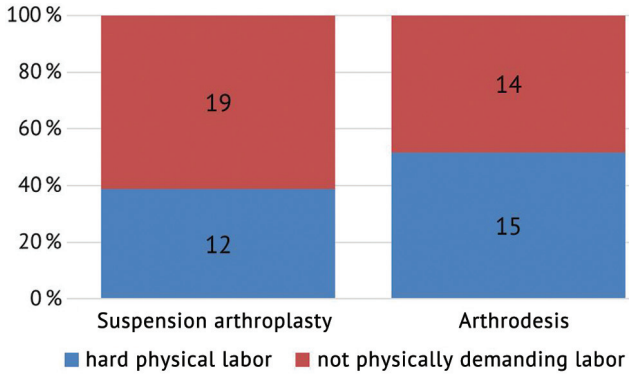

Fig. 2 Correlation of the treatment method depending on the type of physical work

DISCUSSION

The objective of the study was to compare surgical outcomes of patients with thumb saddle joint arthrosis after trapeziometacarpal arthrodesis and suspension arthroplasty of the first metacarpal bone. The postoperative functional efficiency findings contradict the results reported in the literature.

Various fixation methods for trapeziocarpal arthrodesis include Kirschner wires, cerclage wire, metal staples, compression screws and locking plates [17, 19]. Save et al. described a neutralizing plate used in combination with compression screws placed in the saddle joint of 10 patients with resultant fusion observed in 100 % [20]. A T-shaped locking plate without compression screws was employed in our series for trapezio-metacarpal joint fixation, because the combination of the implants may fail in case of a deformity of the trapezium bone and the basal part of the first metacarpal and loss of bone mass due to osteoporotic changes. Smeraglia et al. reported non-union as a major complication of saddle joint arthrodesis, and no statistical differences found in most of the clinical outcomes between the patients who obtained bone union in the trapezio-metacarpal joint and those who did not [17, 21]. Forseth et al. 26 reviewed 26 trapeziometacarpal arthrodeses that used plate and screw fixation with nonunions observed in 8 % and delayed fusion seen in 11 % [22]. Given the conflicting opinions about the effect of fusion on the functional outcome of saddle joint arthrodesis, this criterion was neglected with hand function being evaluated.

Suspension arthroplasty is the method of choice in most cases to treat saddle joint arthritis, despite the reduction in grip strength [23]. In our series, suspension arthroplasty suggested trapeziectomy and suspension of the first metacarpal bone using a split of the abductor longus tendon of the first finger and interposing the residual cavity with a tendon graft (tenoball). No statistically significant benefit between different types of suspension arthroplasty with or without tendon graft interposition or with ligament reconstruction was reported in a systematic review performed in 2022 [24]. Esenwein et al. showed that suspension of the first metacarpal bone using a strip of the abductor pollicis longus tendon is a less technically demanding technique, but is not inferior to the suspension option using a strip of the flexor carpi radialis tendon [25]. The comparative analysis did not reveal any statistically significant difference between the two methods of surgical treatment of trapeziocarpal joint arthritis as evidenced by the functional scales. Postoperative immobilization was longer in the group of patients who underwent trapeziocarpal arthrodesis, which suggested complications associated with the treatment method described in the literature.

Arthrodesis is indicated for young manual workers who tolerate some limitations of mobility [26] and is accompanied by a high degree of patient satisfaction, but considering the previously listed

complications, the surgical method in question cannot be the “gold standard” in the treatment of saddle joint arthritis. In our series, the ratio of hard and light physical laborers in the arthrodesis group was 51.7 % and 48.3 %, the age ranged between 54.45 and 65.14 years.

Suspension arthroplasty is recommended for patients with high functional demands on the hand and who are hard physical laborers in everyday life [27, 28], the ratio of hard and light physical laborers in the suspension arthroplasty group was 38.7 % to 61.3 %, the age ranged from 53.3 to 62.6 years.

Statistical analysis showed no significant differences in the Quick DASH questionnaire, visual analog pain scale VAS and Kapsandji Score measured in independent groups (arthrodesis and suspension arthroplasty). Patients were satisfied with the treatment results in both groups indicating the comparability of the methods regardless of the nature of the patient's activity.

A statistically significant improvement in the parameters was revealed with two types of surgical treatment, comparable with previously published research results [24, 29, 30].

CONCLUSION

A comparative analysis of the surgical outcomes of patients with arthritis of the first carpometacarpal joint after arthrodesis and suspension arthroplasty of the saddle joint showed no significant advantage with any of the methods. The statement that arthrodesis should be performed for hard physical laborers, and suspension arthroplasty would be beneficial for those patients who aims at a greater range of motion, was not confirmed by our study. We suggest that the choice of the optimal method of treatment of the condition requires individual consideration for each clinical case.

Conflict of interest *Not declared.*

Funding *Not declared.*

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The article was submitted 27.12.2024; approved after reviewing 15.01.2025; accepted for publication 05.02.2025.

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Original article
https://doi.org/10.18019/1028-4427-2025-31-2-183-193

Risk factors for hardware failure after total spondylectomy in patients with spinal tumors

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Abstract

Introduction Total spondylectomy for spinal tumors provides optimal local control and is associated with a high risk of implant instability.

The **objective** was to determine risk factors for implant instability after spondylectomy in patients with neoplastic lesions of the spine.

Material and methods A retrospective cohort study included patients with spinal tumors treated with tumor resection between 2007 and 2023. Inclusion criteria were spondylectomy and vertebral body replacement, thoracic or lumbar spine localization, follow-up period ⩾ 12 months. LASSO regression and Random Forest methods and multivariate analysis were used to identify instability predictors.

Results Implant instability was observed in 16 patients (18.4 %). Risk factors included the use of bone cement instead of allograft (OR = 0.125, $p = 0.014$), contact surface mismatch > 10° (OR = 0.214, $p = 0.026$), prosthesis subsidence > 2 mm at 3 months (OR = 4.497, $p = 0.023$).

Discussion The risk factors identified had a great clinical role for the prevention of implant instability. The use of bone graft instead of cement, precise matching of contact surfaces and control of early prosthetic subsidence can significantly reduce the risk of metal construct failure. Careful preoperative planning and regular postoperative monitoring are essential for the outcome.

Conclusion Three independent risk factors for implant instability after spondylectomy identified in patients with spinal tumor lesions included the use of bone cement instead of allograft, a discrepancy between the contact prosthetic surfaces of more than 10°, and an implant subsidence of more than 2 mm after 3 months. These factors are important for planning of the surgical intervention and postoperative monitoring to prevent metal construct instability.

Keywords: spinal tumors, spondylectomy, implant instability, risk factor, vertebral body replacement

For citation: Zaborovskii NS, Masevnin SV, Murakhovsky VS, Mukhiddinov RA, Smekalyonkov OA, Ptashnikov DA. Risk factors for hardware failure after total spondylectomy in patients with spinal tumors. *Genij Ortopedii*. 2025;31(2):183-193. doi: 10.18019/1028-4427-2025-31-2-183-193.

INTRODUCTION

According to oncological concepts, total en bloc spondylectomy (TES) for spinal tumors provides adequate local control [1–4]. The influence of TES on spinal stability is substantial, necessitating careful planning of the reconstructive stage of the intervention [5–7].

Modern principles of reconstruction after TES are based on the concept of circular stabilization of the spine [8]. The vertebral body replacement is essential for the reconstruction of the anterior column, providing adequate anatomical height of the interbody space and distribution of axial load [9]. Posterior instrumentation can ensure the fixation strength that would prevent excessive mobility in the operated segment [10].

Despite advancements in implant technology and surgical techniques, implant failure remains a significant concern [11]. Most serious complications include instability of the metal construct, migration of the vertebral body replacement implant and formation of pseudoarthrosis [12, 13]. The complications can lead to the need for repeated operations, deterioration in quality of life and lower cancer treatment effectiveness[14, 15].

Understanding the factors that influence the development of implant instability is critical for optimizing surgical strategy and improving long-term treatment outcomes.

The **objective** was to determine risk factors for implant instability after spondylectomy in patients with neoplastic lesions of the spine.

MATERIAL AND METHODS

The retrospective cohort study included patients with spinal tumors who underwent tumor resection between 2007 and 2023. The study was approved by the local ethics committee.

The inclusion criteria included (1) previous spondylectomy, (2) vertebral body replaced with mesh cage, (3) thoracic or lumbar location; (4) complete information on the hardware status; (5) follow-up period ⩾12 months.

Exclusion criteria included (1) patients with more than 20 % missing values in the dataset; (2) non-aggressive benign tumors; (3) pathological vertebral fractures unrelated to tumors.

The study included 87 patients who underwent surgical treatment between 2007 and 2023. Incomplete data (no more than 20 % missing values) were identified in 8 cases (9.2 %) without instability which was adjusted using the multiple imputation method. The majority of the patients were males (60 %). The median age was 56 (48.5; 62) years. Most patients (63 %) were able to ambulate unassisted prior to surgery, 17 % used additional support devices, and 20 % could not ambulate. Sixty-seven per cent of patients scored 1–2 points on the ECOG scale. The median time from diagnosis of the pathology to surgery was 4 (2; 6) months (Table 1).

Total en bloc spondylectomy was produced for tumor resection. Wide en bloc resection was performed in cases where it was technically possible without compromising significant structures. Meningiolysis, vessel isolation, elective marginal or intrafocal en bloc spondylectomy with maximum possible tumor removal (intentional transgression) were performed in case of epidural spread of the tumor or involvement of major vessels. After spondylectomy, the post-resection defect was replaced with a mesh of the vertebral body and a transpedicular fixation system was used for reconstruction of the spine. The prosthesis was filled with bone cement or allogeneic bone graft. The posterior approach was employed for the thoracic spine surgery; a combined approach was used in some cases to mobilize massive tumors. The lumbar spine was approached in two stages using the posterior and anterior aspects. Post surgery, patients were referred to an oncologist to decide on adjuvant therapy.

Table 1

General characteristics of patients

Description		Indicators		
		The median	abs.	%
Number of patients			87	100
Females			35	40.2
Males			52	59.8
Age, years		56 (48.5; 62.0)		
Body mass index		23.9 (21.9; 26.5)		
Comorbidity index, score		7 (2.0; 8.5)		
Ambulation prior to surgery	Unable to walk		17	19.5
	Walking using additional support		15	17.2
	Walking unassisted		55	63.3
ECOG status	0		3	3.4
	1		27	31.0
	2		31	35.6
	3		16	18.4
	4		10	11.6
Sacropene index		0.7 (0.7; 0.8)		
Time before surgery, months		4 (2; 6)		

The data contained both quantitative and qualitative variables including age, gender, spinal lesion level, tumor characteristics, preoperative neurological function, surgical parameters, blood loss volume, intraoperative and postoperative complications and outcomes such as ambulatory status and presence of mechanical instability of the construct. A total of 42 variables were analyzed.

The sacropeneia index was assessed as the ratio of the transverse area of the iliopsoas muscle to the area of the L4 vertebral body [16], tumor invasion evaluated with the Tomita score [17], bone density measured in Hounsfield units (HU) at the L1 level [18], surgical invasiveness assessed with a scoring system reported by Kumar et al. [19], radiological parameters measured in the midsagittal projection in the operated segment (affected level and adjacent vertebrae) using CT scan. The local angle was considered as the Cobb angle between the upper endplate of the cranial vertebra adjacent to the prosthesis and the lower endplate of the caudal vertebra adjacent to the prosthesis [20]. The segment height (the average height of the segment with the prosthesis) was calculated as the arithmetic mean of two values. The anterior distance was defined as the distance from the upper anterior edge of the adjacent cranial vertebra to the lower edge of the caudal vertebra, the posterior distance was defined as the distance from the upper posterior edge of the adjacent cranial vertebra to the lower edge of the caudal vertebra (Fig. 1). Prosthesis subsidence was considered as a decrease in segment height compared to postoperative values, and contact surface mismatch was considered as an angle greater than 10° between the contact surface of the prosthesis and the endplate (Fig. 2) [21]. Complications were assessed using the SAVES 2 system [22]. Overall survival was calculated as the time from spinal surgery to death or the end of follow-up; survival without local recurrence was calculated as the time from surgery to diagnosis of recurrence based on instrumental research methods. Late postoperative complications and the functional outcome of the patient's ability to ambulate unassisted (the degree of recovery of the neurological status) were also monitored.

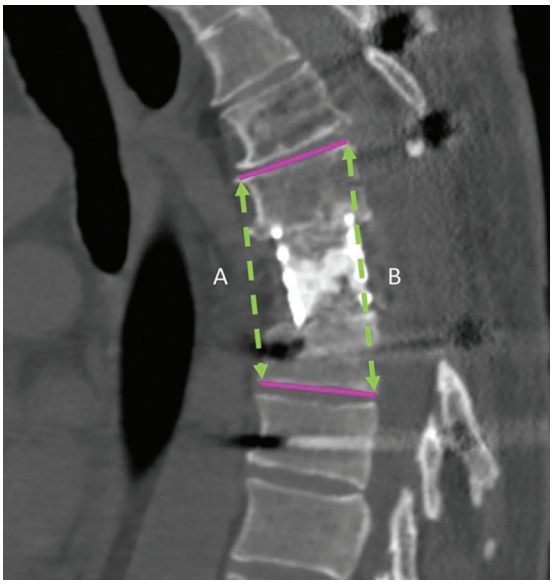

Fig. 1 CT scan of the thoracic spine, midsagittal section showing condition after resection of chondrosarcoma of Th7 vertebra: (A) anterior distance of the segment, (B) posterior distance of the segment with vertebral body prosthesis

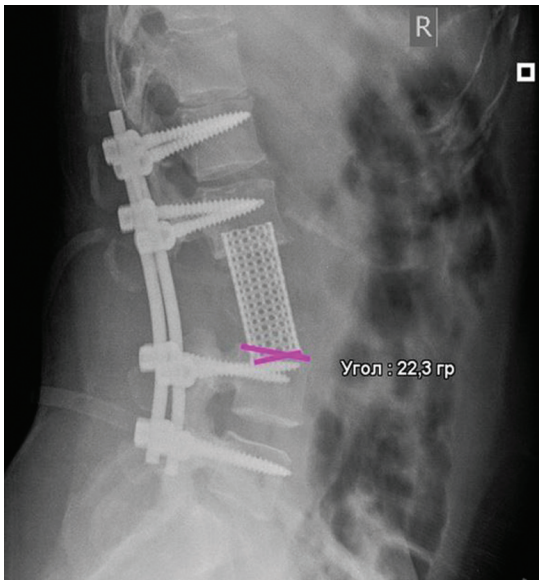

Fig. 2 Lateral radiograph of the lumbar spine showing condition after resection of hemangioendothelioma of the L3 vertebra; angle of 22° discrepancy between the contact surfaces of the prosthesis and the endplate of the L3 vertebra

The R language version 4.3.3 and the R. Studio development environment were used for data analysis [23]. Missing values in the data were processed using the multiple imputation method and the PMM (Predictive Mean Matching) algorithm from the mice package for R. Five imputations were performed for each missing variable to consider the uncertainty associated with missing data [24]. The mean values were presented as the median, the interval estimate the interquartile range (25 %; 75 %).

Regularized logistic regression was employed using the LASSO (Least Absolute Shrinkage and Selection Operator) method to reduce the dimensionality of the data and select significant predictors. This method allows for reducing the number of variables and eliminating multicollinearity issues [25]. LASSO regression was performed using the **cv.glmnet** function from the **glmnet** package in the R environment. The optimal value of the regularization parameter λ was selected based on cross-validation. Variables with non-zero coefficients selected using LASSO were employed to build the final model.

Additionally, the Random Forest method was employed using the **ranger** package to validate the LASSO results and identify potential nonlinear interactions between variables. This method allowed us to estimate the importance of variables taking into account their mutual influence and nonlinear relationships [26]. The results of Random Forest were used to confirm the choice of predictors obtained by the LASSO method.

Firth logistic regression was used to simulate risk factors for metal construct instability to eliminate the problem of bias in small samples and rare outcomes [27]. The regression was performed using the **logistf** package in R. The quantitative assessment of risk factors was presented as an odds ratio.

RESULTS

The majority of patients (67 %) had solitary metastatic lesions of the spine. The thoracic spine was affected in 68 %, the lumbar involvement observed in 28 %. The localization classified with SINS was distributed between the transitional (39 %), semi-rigid (37 %) and mobile (24 %) regions. The majority

of patients (86.2 %) had lesions of one segment. Mechanical pain was diagnosed in 83 % of patients. The lytic type of bone lesion was predominant (61 %). The spine axis was normally aligned in 67 % of patients. Tomita type 4 lesion with epidural compression was seen in 56 % (Table 2).

Table 2

Characterization of the tumor

Description		Parameters (n = 87)		
		The median	abs.	%
WHO tumor type	metastasis		58	66.7
	primary malignant		22	25.3
	primary benign (aggressive)		7	8.0
Spine section	thoracic (Th3–10)		59	67.8
	thoracic-lumbar (Th11–L1)		4	4.6
	lumbar (L2–L5)		24	27.6
Localization classified with SINS	transitional		34	39.1
	mobile		21	24.1
	semi-rigid		32	36.8
Number of segments	more than 1 segment		12	13.8
	1 segment		75	86.2
Mechanical pain	pain free		12	13.8
	there is		72	82.8
	none		3	3.4
Type of bone involvement	lytic		53	60.9
	mixed		34	39.1
Presence of deformity	De novo kyphosis or scoliosis		19	21.8
	normal alignment		58	66.7
	subluxated or translated		10	11.4
Tumor invasion evaluated with the Tomita score	3		7	8.1
	4		49	56.3
	5		12	13.8
	6		19	21.8
HU in L1		103 (83.5; 122.5)		
Preoperative radiation therapy			7	8.1

A combined surgical approach was used in 66 % of cases. The median operation time was 270 (227.5–360.0) min, the median blood loss was 1700 (1000–2500) mL. Spinal fixation was performed 2 levels above and 2 levels below the affected segment in 55 %. Titanium rods with a diameter of 5.5 mm were used in 82 %. Spinopelvic fixation was required for one patient. Bone graft was used as a common filling material for the bone contact area (62 %) and bone cement was employed in 38 %. The median prosthesis height was 40 (29–54) mm, the median support surface area measured 420 (280–450) mm². A discrepancy of more than 10° between the contact surface of the prosthesis and the adjacent endplate was observed in 46 % of cases. A change in the local angle (median 3 (0–6.5)°) and the height of the operated segment (median 0.0 (–1.0–1.5) mm) was observed after the operation (Table 3).

Table 3

Surgical treatment and implant parameters

Description		Parameters (n = 87)		
		The median	abs.	%
Surgical approach	posterior		30	34.5
	combined		57	65.5
Blood loss, mL		1700 (1000; 2500)		
Operating time, min		270 (227.5; 360.0)		
Surgical invasiveness index		17 (16; 20)		
Length of fixation, segments	3		8	9.2
	4		2	2.3
	5		48	55.3
	6		9	10.3
	7		15	17.2
	8		3	3.4
	9		2	2.3
Type of rods	5.5 mm		71	81.6
	6 mm		13	14.9
	additional rods		3	3.4
Prosthesis filling material	cement		33	37.9
	bone graft		54	62.1
Height of prosthesis, mm		40 (29; 54)		
Mismatch of contact surfaces > 10°			40	46.0
Changing local angle, °		3 (0; 6.5)		
Change in segment height, mm		0.0 (–1.0; 1.5)		

The treatment results indicated the median prosthesis subsidence of about 1 (0; 2) mm after 3 months and about 2 (1; 3) mm at the last observation. The majority of patients (76 %) experienced no complications evaluated with Spinal Adverse Events Severity System, version 2 (SAVES-V2). Postoperatively, 20 % of patients received bisphosphonate therapy and 14 % received radiation therapy. Improved motor function was noted three months after surgery and 77 % of patients were able to ambulate unassisted. Local tumor recurrence developed in 23 (26 %) patients. The median overall survival was 28 (16; 55.5) months.

Table 4

Treatment outcomes and survival rates

Description		Parameters (n = 87)		
		The median	abs.	%
Subsidence of the prosthesis after 3 months.	> 2 mm		29	33.3
	⩽ 2 mm		58	66.7
	prosthesis subsidence at last follow-up, mm	2 (1; 3)		
Severity of complications SAVES v.2, degree	1 (complications)		66	75.9
	2		6	6.9
	3		10	11.5
	4		1	1.1
	5		4	4.6
Postoperative bisphosphonates			17	19.5
Postoperative radiation therapy			12	13.8
Ambulation at 3 months	no ambulation		7	8.0
	walking using additional support		13	14.9
	walking unassisted		67	77.1
Local recurrence			23	26.4
Overall survival, months		28 (16.0; 55.5)		

Implant instability requiring revision surgery developed in 16 patients (18.4 %). Instability was caused by broken rod (n = 6; 36.5 %), screw loosening and development of transitional kyphosis (n = 8; 50 %) and vertebral body prosthesis migration (n = 2; 12.5 %). Cases of broken rod and screw loosening were accompanied by prosthesis subsidence of greater than 4 mm into the bodies of adjacent vertebrae. Pseudoarthrosis was noted in 75 % of cases in patients with implant instability.

The results of LASSO regression (λ = 0.036) indicated most significant associations with the risk of implant instability out of 42 initial predictors:

—prosthesis filling material (β = –0.984);

—mismatch of contact surfaces more than 10° (β = 0.448);

—prosthesis subsidence of more than 2 mm after 3 months (β = 0.188);

—length of fixation (β = –0.114);

—number of operated segments (β = –0.104);

—difference in segment height before and after surgery (β = 0.116);

—functional status after 3 months (β = 0.113);

—prosthesis subsidence observed at the last follow-up (β = 0.081);

—age (β = 0.010);

—overall survival (β = 0.006);

—time before surgery (β = –0.004);

—duration of operation (β = –0.004).

Additional analysis was conducted using the Random Forest method to confirm the choice of predictors and assess the importance of variables taking into account the nonlinear interactions.

From the 42 characteristics, the following parameters appeared to be most important:

— prosthesis subsidence observed at the last follow-up (importance score = 0.031);

— prosthesis filling material (0.008);

— difference in segment height before and after surgery (0.007);

— overall survival (0.007).

Prosthesis subsidence of more than 2 mm after 3 months (0.007) and contact surface mismatch (0.005) were among the most significant factors that are partially consistent with the results of LASSO regression.

Three predictors with the highest LASSO regression coefficients were selected for multivariate analysis using Firth regression. Limiting the number of predictors to three allowed us to avoid overfitting the model, given the size of the sample [28]. The factors selected were of great clinical significance characterizing major biomechanical parameters of the design. Multivariate analysis using Firth regression revealed the following independent risk factors for implant instability (Fig. 3):

— the use of bone graft instead of cement reduced the odds of instability by 8 times (OR = 0.125, 95 % CI: 0.026–0.475, p = 0.014);

— absence of contact surface mismatch was associated with a lower risk (4.7 times lower odds) of instability (OR = 0.214, 95 % CI: 0.047–0.815, p = 0.026);

—Prosthesis subsidence of more than 2 mm after 3 months increased the likelihood of instability by 4.5 times (OR = 4.497, 95 % CI: 1.224–18.41, p = 0.023).

The model demonstrated statistically significant predictive value (LR χ^2 = 24.74, df = 3, p < 0.001).

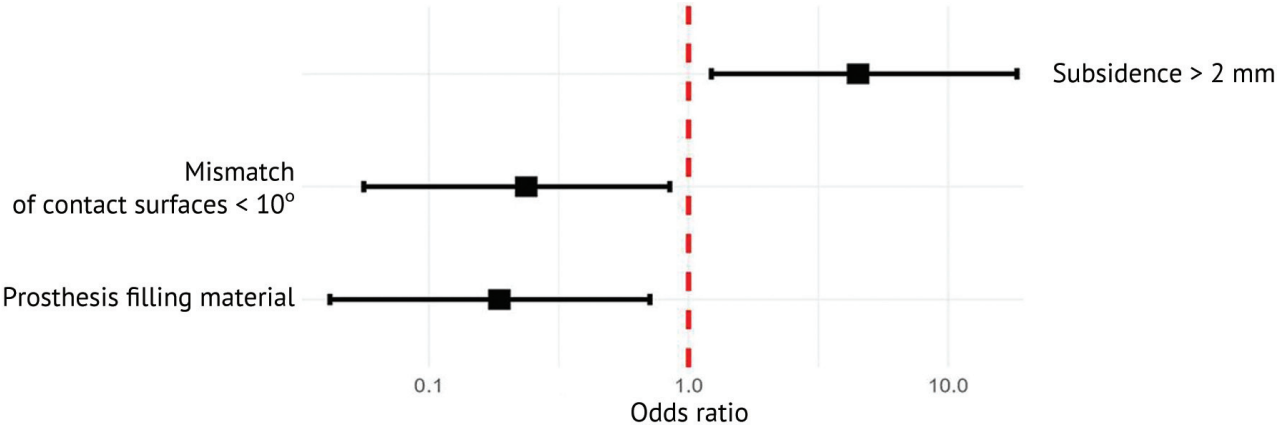

Fig. 3 Firth regression results

DISCUSSION

Risk factors for implant instability in patients with spinal tumors after spondylectomy were reviewed in the series. The instability rate was 18.4 %, which is Yoshioka et al. reported significant differences in the frequency of instability depending on the level of intervention with instrumentation failure occurred in 5.9 % after thoracic multilevel TES to 42.9 % after lumbar multilevel TES [30]. Hardware failures were associated with broken rods (36.5 %), screw loosening and junctional kyphosis (50 %), and cage migration (12.5 %). These data are consistent with those reported in the systematic review by Li et al. with hardware failure of 12.1 % as one of the most frequent complications [31].

Multivariate analysis revealed three independent predictors of implant instability. The choice of filling material for the prosthesis was most significant factor with the bone graft reducing the risk of instability by eight times compared to cement. This is consistent with the concept offered by Akamaru et al. who reported better bone integration with bone graft in cases of benign or primary malignant tumors [32]. Melcher and Harms reported the use of bone cement as an acceptable option for anterior reconstruction in cases of metastatic lesions or severe osteoporosis [33]. The strategy is practical for patients with limited life expectancy. However, modern advances in the treatment of cancer patients have led to a significant increase in survival, including patients with metastatic lesions of the spine [34]. In our series, the overall median survival was 28 months creating preconditions for the development of late complications. With use of cement, patients can survive to the development of pseudoarthrosis and hardware failure, which is confirmed by the high frequency of pseudoarthrosis (75 %) in patients with implant instability.

A discrepancy between the contact surfaces of the prosthesis and adjacent endplates of more than 10° increased the risk of instability by 4.7 times. Mohammad-Shahi et al. reported the critical importance of this factor, demonstrating the risk of hardware failure at angular mismatch from 0° to 10° [35]. This factor is very important in multilevel resections [36], and Yoshioka et al. reported higher risk of instability with increasing length of reconstruction [30]. This may be explained by the fact that the increase in the number of contact points during multi-level reconstruction creates a more complex biomechanical system in which small deviations in the positioning of the prosthesis at each level can add up and lead to a significant redistribution of loads on the entire construct. In this case, uneven

distribution of forces on the contact surfaces can create zones of local overstress accelerating wear of the rods.

Subsidence of the prosthesis by more than 2 mm 3 months after surgery increased the likelihood of instability by 4.5 times. Shimizu et al. identified early subsidence (⩾ 2 mm after 1 month) as an independent risk factor for instrumentation failure [29]. Vaccaro et al. suggested early subsidence could be influenced by several factors including bone quality, the area of contact between the implant and the vertebral body, the extent of intraoperative distraction, the technique of preparation of the endplates and the correspondence of the mechanical properties of the implant and bone (modulus of elasticity) [37]. Interestingly, all these factors are interrelated and can enhance each other's influence. For example, with reduced bone mineral density, increasing contact area of the implant with the vertebral body is essential for better load distribution [38]. Excessive intraoperative distraction can lead to injury to the endplates, which, in combination with the mismatch between the elastic modulus of the implant and the bone, can create preconditions for early subsidence even with initially correct positioning of the prosthesis.

The findings and literature analysis allowed us to formulate practical recommendations to reduce the risk of implant instability:

— bone graft is to be considered as a method of choice in the absence of contraindications, taking into account its ability for biological integration and remodeling;

— preoperative planning suggests careful consideration of the fixation points, contact zones of the prosthesis; imaging is practical for assessment of the bone quality and preoperative modeling of implant placement;

— the most accurate fit of the contact surfaces is to be ensured intraoperatively avoiding excessive distraction and minimizing damage to the endplates when preparing the prosthetic bed;

— careful radiological monitoring and control of osseointegration are important postoperative steps;

— rods of greater diameter, lengthening of the fixation zone and additional rods can be used in the presence of risk factors (osteoporosis, multi-level lesions, localization in transitional areas);

— individual vertebral body prostheses manufactured with 3D printing can be used to prevent instability, optimize load distribution due to precise conformity with the patient's anatomy, creating additional fixation points in the implant construct and using materials with an elastic modulus close to bone tissue (PEEK composites).

Individualization of surgical treatment with the above recommendations can help reduce the incidence of implant instability and improve long-term treatment outcomes in patients with spinal tumors.

The study has several limitations. The retrospective nature of the study prevents control of the quality of the data collected and increases the risk of systematic errors. The single-center design may reduce the external validity of the results. The relatively small sample size (87 patients) limits the statistical power of the study, given the heterogeneity of the population by tumor types (metastatic, primary malignant and aggressive benign tumors). The long period of material recruitment (2007–2023) could be accompanied by changes in surgical technique and perioperative patient management. Despite the use of modern statistical processing methods missing data (9.2 % of cases) could have affected the results of the analysis. Although justified by the sample size limiting the number of predictors to three variables in the final model could have led to the loss of potentially significant risk factors. In addition to that, the potential influence of competing risks (e.g., death) limits the assessment of the incidence of instability at a long term.

CONCLUSION

Three independent risk factors for implant instability after spondylectomy identified in patients with spinal tumor lesions included the use of bone cement instead of allograft to fill in the vertebral body prosthesis, mismatch of the contact surfaces of the prosthesis with the adjacent endplates by greater than 10°, and an implant subsidence of more than 2 mm 3 months post surgery. These factors are important for planning of the surgical intervention and postoperative monitoring to prevent metal construct instability.

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

Funding *The study was performed without additional funding.*

Ethical review *All patients signed informed consent for the use of information for educational and scientific purposes.*

Informed consent *The study was approved by the local ethics committee and conducted in accordance with the principles of the Declaration of Helsinki.*

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The article was submitted 15.01.2025; approved after reviewing 21.01.2025; accepted for publication 05.02.2025.

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Original article
https://doi.org/10.18019/1028-4427-2025-31-2-194-201

Kinematic and kinetic features of an unaffected limb during walking in children with spastic hemiplegia

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Abstract

Introduction The study of the functional characteristics of the unaffected side of the musculoskeletal system in patients with spastic hemiparesis contributes to the development of various aspects of medical rehabilitation.

Objective To determine the features of compensatory and adaptive behavior of the limb not involved in the pathogenesis in children with hemiplegia during walking and their dependence on age and previous surgical interventions on the triceps surae.

Materials and methods Locomotor characteristics of 78 children under 16 years of age with spastic hemiplegia and motor disorders corresponding to levels I–II GMFCS (Gross Motor Function Classification System) were compared with 77 healthy peers. Based on age and the triceps surae lengthening surgery, all children were divided into 6 groups. Kinematic data were recorded using Qualisys 7+ optical cameras and KISTLER dynamometric platforms. The video material was analyzed using QTM and Visual3D programs, and statistical data processing was performed using Microsoft EXCEL-2013 and AtteStat 12.0.5.

Results In the unaffected limb of children with spastic hemiplegia, a flexion position in the limb joints was observed, while the kinematics of its ankle joint did not differ significantly compared to healthy peers. Moreover, movements in the joints of the unaffected limb in children with hemiplegia were performed at greater energy consumption, especially in the knee and hip joints, while the power characteristics in the ankle joints were statistically lower than in healthy peers.

Discussion Significant increase, in comparison with the norm, and redistribution of power locomotor characteristics, as well as an increase in the GPS indicator of the total joint kinematic variability of the limb not involved in the pathogenesis indicate exclusively the compensatory nature of its behavior. Compensatory behavior is also shown by increased flexion angles in the joints and the sagittal tilt of the pelvis, which posturally eliminate the difference in leg length. Rotational positions of the pelvis and the femur, apparently, also serve to maintain the orientation of the foot.

Conclusion Compensatory behavior of the unaffected limb in children with hemiplegia during walking is manifested in kinetic and kinematic activity. Power locomotor characteristics are significantly redistributed compared to the normal values. Power indicators in the knee and hip joints increase, but power characteristics in the ankle significantly decrease. According to the GPS index, the total joint kinematic variability significantly increases, and the joint flexion angles and sagittal pelvic tilt increase to compensate for the difference in leg height. The procedure of early surgical lengthening of the triceps surae did not have a significant effect on the motor characteristics of the uninvolved limb.

Keywords: gait analysis, children, spastic hemiplegia, kinematics, kinetics

For citation: Mamedov UF, Dolganova TI, Smolkova LV, Trofimov AO, Gatamov OI, Popkov DA. Kinematic and kinetic features of an unaffected limb during walking in children with spastic hemiplegia. *Genij Ortopedii*. 2025;31(2):194-201. doi: 10.18019/1028-4427-2025-31-2-194-201.

INTRODUCTION

Hemiparetic forms of cerebral palsy are usually characterized by preserved motor functions and the ability to move independently [1, 2, 3]. The incidence of spastic hemiplegia in the structure of cerebral palsy does not exceed 15.3 % [4, 5]. Types of non-severe motor impairments according to the Gross Motor Function Classification System [6] prevail: 87.8 % of GMFCS level I, 7.1 % of GMFCS level II.

Kinematic and kinetic disorders, orthopedic problems of spastic hemiplegia on the affected side have been described and classified quite well [7, 8, 9]. However, there are only a few publications devoted to biomechanical studies of the features of movements of the uninvolved lower limb during walking [10, 11, 12, 13]. Known changes in the range of movements in the sagittal plane, rotation features of pelvic movements are considered compensatory, reflecting the degree of dysfunction on the contralateral, affected limb [14, 15, 16, 17]. Nevertheless, publications indicate the occurrence of orthopedic disorders in the foot of the unaffected limb [18, 19, 20].

The study of the problems of locomotor disorders on both sides in patients with spastic hemiparesis should contribute to the development of various aspects of medical rehabilitation [21]. Moreover, it is unknown whether there is a change in the adaptive age-related mechanisms of the uninvolved limb, and the impact of early isolated operations to correct ankle contractures on the kinematic and kinetic parameters of the unaffected limb is also unclear.

Purpose To determine the features of compensatory and adaptive behavior of the limb not involved in the pathogenesis in children with hemiplegia during walking and their dependence on age and previous surgical interventions on the triceps surae.

MATERIALS AND METHODS

This study included pediatric patients with spastic hemiplegia who were scheduled for surgical treatment at our institution. All patients underwent preoperative examination in the gait analysis laboratory.

Inclusion criteria were age under 16 years (open growth plates), GMFCS levels I–II, spastic hemiplegia.

Exclusion criteria were diagnosis of spastic diplegia, level greater than GMFCS II, age under 5 years, 16 years and older, previous multilevel interventions.

The study groups were formed according to the age criterion (5–9 years old and 10–15 years old), as well as to the criterion of performing triceps lengthening or so-called percutaneous fibrotomies (fibromyotomies) at an early age.

During the examination, patients walked independently or holding one hand of a parent, barefoot, on a 7-meter long platform at their usual speed. Kinematic data were recorded by Qualisys 7+ optical cameras with passive marker video capture technology; synchronized with six KISTLER dynamometric platforms (Switzerland). The IOR model was used for marker installation. Kinematics and kinetics analysis was performed with QTM (Qualisys) and Visual3D (C-Motion) software with automated calculation of values [17].

For statistical data processing, Microsoft EXCEL-2013 and AtteStat 12.0.5 were used. Quantitative characteristics of sample populations are presented in tables as medians with a percentile distribution level of 25 % ÷ 75 %. Based on the number of cases in groups, nonparametric statistics with a significance level of $p \leqslant 0.05$ were used to process the results. The statistical significance of differences in indicators between comparison groups was determined using the unpaired Wilcoxon test.

Permission to conduct the study was obtained from the institution ethics committee (protocol dated 07.10.2022 No. 2(72)). The study conducted in accordance with the ethical standards of the Helsinki Declaration of the World Medical Association "Ethical Principles of Medical Research Involving Human Subjects" with amendments of 2000, "Rules of Clinical Practice in the Russian Federation" approved by Order of the Ministry of Health of the Russian Federation dated 19.06.2003 No. 266. Parents of the subjects, authorized relatives or employees of social institutions confirmed their consent to conduct the study and publish its results without identifying the individual.

The locomotor characteristics of 78 children under 16 years of age with spastic hemiplegia and motor impairments corresponding to GMFCS levels I–II were compared with the data of 77 healthy peers. Based on age and the triceps surae lengthening surgery, all children were divided into 6 groups:

Group 1: 21 patients (21 limbs); age range — 5–9 years, mean age (7.2 ± 1.5) years; triceps surae lengthening was not performed previously;

Group 2: 8 patients (8 limbs); age range — 5–9 years, mean age — (7.7 ± 2.0) years; triceps surae lengthening was performed;

Group 3: 25 patients (25 limbs); age range — 10–15 years, mean age — (13.9 ± 1.6) years; triceps surae lengthening was not performed;

Group 4: 24 patients (24 limbs); age range — 10–15 years, mean age (12.4 ± 1.9) years; triceps surae lengthening was performed previously;

Group 5: 38 children (76 limbs); age range — 5–9 years, mean age — (6.9 ± 1.7) years; no gait pathology;

Group 6: 39 children (78 limbs); age range — 10–15 years, mean age — (12.7 ± 1.9) years; no gait pathology.

RESULTS

The data of the spatial and temporal characteristics of walking and the gait profile score show significant differences in the parameters of the unaffected limb from healthy peers (Table 1). In addition, we observed a significant increase in the stride width in group 2 (children under 10 years old with triceps lengthening performed) from both non-operated peers and healthy ones.

Table 1

Spatial and temporal characteristics of walking, GPS

Parameter	Group 1	Group 2	Group 3	Group 4	Group 5	Group 6
GPS, limb	12 (9.7 ÷ 13.7)	11 (8.7 ÷ 13)	10.2 (8.9 ÷ 11.1)	12.1 (10.2 ÷ 14.2)	**8.3* (6.4 ÷ 9.7)**	**7.8* (6.6 ÷ 9.0)**
General walking speed, m/sec	0.95 (0.78 ÷ 1.05)	0.9 (0.88 ÷ 0.97)	0.97 (0.9 ÷ 1.05)	0.91 (0.77 ÷ 1.05)	1.07 (0.81 ÷ 1.18)	1.2 (1.12 ÷ 1.31)
Stride width, m	0.11 (0.09 ÷ 0.12)	**0.15[1] (0.13 ÷ 0.18)**	0.13 (0.11 ÷ 0.16)	0.14 (0.11 ÷ 0.16)	0.09 (0.07 ÷ 0.1)	0.1 (0.08 ÷ 0.12)
Stride length, m	0.45 (0.42 ÷ 0.52)	0.44 (0.4 ÷ 0.48)	0.51 (0.47 ÷ 0.55)	0.49 (0.42 ÷ 0.53)	0.5 (0.45 ÷ 0.53)	**0.62* (0.56 ÷ 0.67)**
Stride duration, sec	0.47 (0.42 ÷ 0.5)	0.46 (0.43 ÷ 0.51)	0.52 (0.48 ÷ 0.54)	0.51 (0.45 ÷ 0.55)	0.47 (0.44 ÷ 0.49)	0.52 (0.49 ÷ 0.55)
% of stance from gait cycle duration	63.8 (61 ÷ 65.7)	62 (59 ÷ 64)	64.2 (62.2 ÷ 65.6)	65.2 (63.7 ÷ 66.4)	61.1 (60.7 ÷ 62.2)	61.7 (60.8 ÷ 62.6)
% of swing from gait cycle duration	36.3 (34.3 ÷ 39.2)	37.9 (36.5 ÷ 40.5)	35.7 (34.4 ÷ 37.8)	35 (34 ÷ 36.9)	38.5 (37.9 ÷ 39.3)	38.3 (37.4 ÷ 39.2)

Notes: * — significant differences according to the Wilcoxon criterion ($p < 0.05$) between the groups of healthy children and the cerebral palsy groups of the corresponding age; [1] — significant differences according to the Wilcoxon criterion ($p < 0.05$) between groups 1 and 2.

Tables 2 and 3 present the lower limb kinematics indices in the compared groups. In group of children with spastic hemiplegia, we can detect a pronounced flexion in the hip and knee joints from the moment of initial contact to the midstance of the gait cycle and high values of the flexion angle in the hip joint in the swing phase. However, no differences in ankle joint kinematics were found in comparison with healthy peers. A significant difference in the angle of foot orientation relative to the motion vector between the groups of healthy children reflects the physiological mechanism of torsional development of the hip as the child grows. An important finding is an increase in the angle of rotational position and the range of pelvic rotation on the side of the uninvolved limb, given that these indices, which differ from the healthy population, are present in both groups and in all the studied age ranges.

The indicators of the moments of forces arising during movements in the joints, as well as the generated power of movements indicate an increased energy consumption of the uninvolved limb gait, especially in movements in the knee and hip joints (Table 4). Moreover, the generated power of movements in the ankle joints of the uninvolved limb in children with spastic hemiplegia is significantly lower than in peers without movement pathology.

Table 2

Kinematics of the ankle and knee joints

Parameter	Group 1	Group 2	Group 3	Group 4	Group 5	Group 6
Maximum foot flexion in stance	11.04 (5.7 ÷ 16.5)	12.2 (11.2 ÷ 15.9)	14.8 (13.0 ÷ 17.0)	18.7 (15.1 ÷ 21.95)	11.9 (9.7 ÷ 14.5)	13.3 (10.5 ÷ 16.0)
Maximum plantar flexion	−19.8 (−28.6 ÷ −12.0)	−11.6 (−14.3 ÷ −8.9)	−11.2 (−13.5 ÷ −7.6)	−9.5 (−13.8 ÷ −5.1)	−15.1 (−18.7 ÷ −10.9)	−13.4 (−16.9 ÷ −8.8)
Foot position in swing	4.8 (0.0 ÷ 10.7)	5.7 (5.5 ÷ 8.7)	8.3 (7.2 ÷ 12.3)	8.7 (5.98 ÷ 10.3)	5.6 (2.7 ÷ 8.1)	7.3 (5.2 ÷ 8.8)
Foot inversion, max	16.1 (11.3 ÷ 21.1)	17.7 (14.4 ÷ 22.3)	14.8 (11.2 ÷ 18.7)	17.1 (10 ÷ 23.96)	15.8 (11.8 ÷)	13.3 (8.7 ÷ 15.7)
Range	15.6 (12.7 ÷ 17.6)	15.7 (12.5 ÷ 17.3)	14.3 (12 ÷ 16.3)	15.1 (12.6 ÷ 17.7)	15.2 (12.4 ÷ 17.5)	13.3 (11.3 ÷ 15.5)
Hind-foot clearance, cm	16.8 (15.7 ÷ 17.7)	16.2 (15.4 ÷ 17.8)	18.2 (16.6 ÷ 19.7)	18.6 (16.8 ÷ 19.95)	17.5 (16.4 ÷ 18.5)	20.8 (19.0 ÷ 23.0)
Knee joint position at contact, °	15.6 (12.0 ÷ 18.4)	15.7 (11.7 ÷ 17.4)	14.5 (11.6 ÷ 17.4)	22.981 (18.0 ÷ 30.8)	**7.0* (2.7 ÷ 11.2)**	**7.1* (4.0 ÷ 9.6)**
Max knee flexion in stance, °	29.3 (21.2 ÷ 34.2)	27.8 (22.1 ÷ 35.3)	27.6 (24.0 ÷ 31.5)	32.5 (26.3 ÷ 39.8)	**19.8* (13.7 ÷ 26.7)**	**18.5* (14.7 ÷ 23.5)**
Min flexion angle in stance, °	5.9 (1.4 ÷ 10.9)	11.0 (7.4 ÷ 15.1)	9.4 (6.4 ÷ 12.3)	13.8 (10.1 ÷ 18.98)	6.4 (3.4 ÷ 10.3)	**5.0[2] (1.2 ÷ 8.7)**
Knee flexion in swing, °	62.4 (54.5 ÷ 68.3)	63.0 (58.5 ÷ 67.3)	63.6 (58.7 ÷ 69.5)	68.3 (58.7 ÷ 71.8)	64.5 (60.7 ÷ 69.1)	60.9 (57.4 ÷ 65.1)

Notes: * — significant differences according to the Wilcoxon test ($p < 0.05$) between the groups of healthy children and the groups of the corresponding age with cerebral palsy; [1] — significant differences according to the Wilcoxon test ($p < 0.05$) between groups 3 and 4; [2]— significant differences according to the Wilcoxon test ($p < 0.05$) between groups 4 and 6.

Table 3

Kinematics of the hip and pelvis

Parameter	Group 1	Group 2	Group 3	Group 4	Group 5	Group 6
Femur position at initial contact, °	36.5 (30.1 ÷ 44.1)	33.5 (28.9 ÷ 37.5)	36.7 (30.0 ÷ 41.6)	38.1 (33.9 ÷ 44.2)	**27.9[1] (20.6 ÷ 34.3)**	**24,5* (16,9 ÷ 29,7)**
Max hip extension, °	−10.4 (−13.6 ÷ −6.3)	−7.3 (−10.6 ÷ −6.5)	−7.0 (−10.9 ÷ −2.7)	−6.4 (−13.0 ÷ −1.8)	−14.0 (−21.4 ÷ −8.0)	**−14,1* (−20,95 ÷ −10,2)**
Max hip flexion in swing, °	39.1 (31.8 ÷ 45.0)	37.3 (34.9 ÷ 39.6)	38.2 (31.3 ÷ 44.4)	41.4 (35.3 ÷ 46.7)	30.8 (25.6 ÷ 36.8)	**26,6* (21,1 ÷ 31,1)**

Table 3 (Continuation)

Kinematics of the hip and pelvis

Parameter	Group 1	Group 2	Group 3	Group 4	Group 5	Group 6
Sagittal pelvic tilt, ° Max values/range	16.5 (12.3 ÷ 20.4) 9.1 (6.5 ÷ 10.6)	14.0 (11.4 ÷ 16.8) 8.1 (6.6 ÷ 8.9)	15.8 (11.4 ÷ 19.9) 8.0 (5.9 ÷ 9.3)	14.4 (11.6 ÷ 19.4) 9.7 (7.6 ÷ 12.6)	**7.8*** **(3.7 ÷ 12.7)** **4.8** **(4.2 ÷ 5.3)**	**6,5*** **(0,9 ÷ 10,2)** **4,2** **(3,4 ÷ 4,6)**
Frontal pelvis inclination, ° Max values/range	2.5 (0.5 ÷ 4.2) 8.97 (7.0 ÷ 10.4)	3.0 (1.9 ÷ 5.0) 7.3 (6.5 ÷ 7.7)	3.7 (1.9 ÷ 6.1) 7.9 (6.0 ÷ 9.1)	4.0 (1.4 ÷ 6.3) 7.8 (6.2 ÷ 9.1)	3.5 (2.5 ÷ 4.6) 7.1 (5.8 ÷ 8.2)	3,3 (2,0 ÷ 4,5) 6,9 (5,2 ÷ 8,2)
Pelvis rotation, ° Max values/range	21.6 (14.9 ÷ 26.3) 21.8 (16.9 ÷ 29.0)	20.95 (15.0 ÷ 26.8) 19.9 (18.2 ÷ 22.2)	17.8 (13.8 ÷ 21.4) 17.96 (14.3 ÷ 20.8)	18.0 (12.5 ÷ 25.7) 20.6 (16.4 ÷ 26.1)	**8.4*** **(5.5 ÷ 10.95)** **15.51** **(12.1 ÷ 18.8)**	**7,2*** **(5,2 ÷ 9,3)** **13,42** **(10,1 ÷ 15,1)**
Femur adduction, ° Max values/range	9.3 (4.7 ÷ 13.7) 17.8 (15.5 ÷ 18.8)	7.2 (5.4 ÷ 10.2) 15.2 (13.3 ÷ 16.95)	8.8 (5.3 ÷ 11.4) 14.5 (11.7 ÷ 16.5)	7.9 (6.6 ÷ 9.8) 15.5 (13.1 ÷ 17.95)	9.0 (6.6 ÷ 11.2) 13.3 (11.7 ÷ 14.9)	7,5 (5,7 ÷ 9,8) 11,5 (9,6 ÷ 13,4)
Femur rotation, ° Max values/range	11.2 (9.1 ÷ 15.4) 21.1 (17.0 ÷ 23.7)	4.8 (0.1 ÷ 11.5) 19.8 (16.5 ÷ 20.95)	6.2 (−1.7 ÷ 11.7) 21.8 (14.2 ÷ 28.6)	11.8 (5.5 ÷ 22.3) 23.7 (19.5 ÷ 27.3)	9.6 (3.5 ÷ 15.2) 17.3 (14.7 ÷ 19.6)	11,3 (7,5 ÷ 15,8) 16,8 (13,7 ÷ 20,2)
Foot orientation, ° Max values/ minimum values	15.6 (7.4 ÷ 21.1) −5.1 (−10.2 ÷ −0.8)	14.2 (7.1 ÷ 21.7) −4.8 (−11.5 ÷ 0.55)	5.2 (−0.7 ÷ 14.6) −12.5 (−17.2 ÷ −4.0)	10.3 (3.9 ÷ 15.4) −8.3 (−14.7 ÷ −2.1)	23.5 (21.0 ÷ 26.8) −11.3 (−14.95 ÷ −6.5)	**3,7**[3] **(−0,3 ÷ 7,8)** **−11,6** **(−16,2 ÷ −6,5)**

Notes: * — significant differences according to the Wilcoxon test ($p < 0.05$) between the groups of healthy children and the groups of the corresponding age with cerebral palsy; [1] — significant differences according to the Wilcoxon test ($p < 0.05$) between groups 1 and 5; [3]— significant differences according to the Wilcoxon test ($p < 0.05$) between groups 5 and 6.

Table 4

Torque, useful power

Parameter	Group 1	Group 2	Group 3	Group 4	Group 5	Group 6
Hip extension, N×m	0.94 (0.73 ÷ 1.18)	0.78 (0.57 ÷ 0.93)	0.87 (0.7 ÷ 0.98)	0.88 (0.64 ÷ 1.17)	**0.73**[1] **(0.55 ÷ 0.99)**	0.77 (0.58 ÷ 0.92)
Femur abduction, N×m	0.61 (0.6 ÷ 0.72)	0.56 0.47 ÷ 0.68)	0.76 (0.7 ÷ 0.88)	0.7 (0.59 ÷ 0.87)	0.67 (0.59 ÷ 0.71)	0.85 (0.76 ÷ 0.92)
Knee extension, N×m	0.66 (0.47 ÷ 0.79)	0.7 (0.42 ÷ 0.96)	0.66 (0.41 ÷ 0.84)	0.87 (0.61 ÷ 1.17)	0.51 (0.31 ÷ 0.68)	**0.65**[2] **(0.43 ÷ 0.87)**
Plantar flexion, N×m	1.02 (0.87 ÷ 1.22)	1.1 (0.95 ÷ 1.28)	1.2 (1.09 ÷ 1.36)	1.25 (1.05 ÷ 1.45)	1.08 (0.91 ÷ 1.22)	1.45 (1.32 ÷ 1.55)
Hip power, W/kg	0.44 (0.24 ÷ 0.71)	0.27 (0.06 ÷ 0.38)	0.45 (0.19 ÷ 0.62)	0.36 (0.19 ÷ 0.47)	**0.27**[1] **(0.04 ÷ 0.42)**	0.21 (0.03 ÷ 0.34)
Knee power, W/kg	−0.49 (−0.81 ÷ −0.12)	−0.86 (−1.27 ÷ −0.3)	−0.71 (−1.07 ÷ −0.39)	−0.87 (−1.13 ÷ −0.48)	**−0.54**[3] **(−0.8 ÷ −0.26)**	−0.69 (−0.90 ÷ −0.45)
Ankle power, W/kg	0.95 (0.56 ÷ 1.62)	1.1 (0.67 ÷ 1.99)	1.49 (1.09 ÷ 1.97)	1.84 (1.10 ÷ 2.43)	**1.8*** **(1.24 ÷ 2.26)**	2.3 (1.60 ÷ 2.81)
Total useful power, W/kg	0.86 (0.17 ÷ 1.35)	0.60 (0.13 ÷ 1.74)	1.23 (0.57 ÷ 1.89)	1.34 (0.83 ÷ 2.195)	1.53 (0.82 ÷ 2.01)	1.83 (1.23 ÷ 2.39)

Notes:* — significant differences according to the Wilcoxon test ($p < 0.05$) between the groups of healthy children and the groups of the corresponding age with cerebral palsy; [1] — significant differences according to the Wilcoxon test ($p < 0.05$) between groups 1 and 5; [2] — reliable differences according to the Wilcoxon criterion ($p < 0.05$) between groups 4 and 6; [3] — significant differences according to the Wilcoxon test ($p < 0.05$) between groups 2 and 5.

DISCUSSION

Limb movement pathology on the affected side in spastic hemiplegia have been studied and classified quite well [7, 8, 22, 23].

The results of studies of movements and orthopedic condition of the unaffected limb in spastic hemiplegia in children are reported only in several works [10, 11, 12, 13, 24]. However, there is a risk of developing orthopedic pathology on the neurologically unaffected side [18, 19, 20], and correction of length discrepancy requires intervention of the controlled growth technique on the healthy limb [25, 26, 27, 28].

Increased flexion angles in the knee and hip joints during the stance phase of the gait cycle and in the swing phase are known and well described. The authors believe that the development of an adaptation mechanism to compensate for the inequality in limb lengths can explain this kinematic feature [10, 24, 29]. Our studies have also revealed such a feature of articulation in the joints, despite the fact that there are no differences in movements in the ankle joint compared to peers without movement pathology. We also believe that greater flexion angles in the knee and hip joints and excessive sagittal tilt of the pelvis are a mechanism for compensating for the inequality in limb length, especially since it does not disappear even after the elimination of ankle contracture in the early age (group 2 of our study). At the same time, movements in the hip and knee joints were accompanied by increased values of the resulting moments of force and generated power, which reflects the high energy consumption of such an adaptation mechanism. As for the kinetics of ankle joint movements, in contrast to the data of Cimolin et al. [24] on the absence of differences with healthy children, we noted a decrease in the strength characteristics of articulation in the ankle joint compared to the healthy population. This difference in the studies can be explained by the small sample in the work of Cimolin et al., which complicates the interpretation of the results. We see an explanation for the phenomenon we discovered in the general decrease in the motor activity of such children due to neurological pathology, in contrast to the healthy population [30].

Rotational positions of the pelvis and hip, increased range of motion on the part of both the involved and unaffected limbs can be explained by compensatory mechanisms for maintaining the orientation of the foot close to the motion vector [11, 14, 15]. Our studies confirm this statement, especially since high values of pelvic and hip rotation are accompanied by deviation of the foot axis within the physiological norm.

Finally, we note that our study did not reveal changes in the motor status of the uninvolved limb between the groups without early surgical intervention and with lengthening of the triceps surae at an early age. Progression of torsional deformities occurred equally in both groups, and compensatory flexion position in the knee and hip joints was present in all four studied groups of children with spastic hemiplegia in all age categories.

We believe that changes in the kinematics and kinetics of the unaffected limb, being compensatory, reflect the degree of the pathology of movements on the affected side, and their dynamics can serve as an indicator of the success of treatment and/or progression of motor disorders.

The results and conclusions presented in this study should be considered in view of the cross-sectional nature of the study of groups unrelated to each other and without dynamic observation. A study of the treatment results after multilevel interventions in combination with limb length correction may confirm the hypothesis of a decreased expression of compensatory indicators of the kinematics of the unaffected limb.

CONCLUSION

Compensatory behavior of the unaffected limb in children with hemiplegia during walking is reflected in kinetic and kinematic activity. Power locomotor characteristics are significantly redistributed compared to the normal values. Power indicators in the knee and hip joints increase, but significantly decrease in the ankle joint. According to the GPS index, the total joint kinematic variability significantly increases, and the joint flexion angles and sagittal pelvic tilt increase to compensate for the difference in the limb height. The procedure of early surgical lengthening of the triceps surae did not have a significant effect on the motor characteristics of the unaffected limb.

Conflict of interest *None.*

Funding *None.*

Ethical review *Approval was obtained from the institutional ethics committee to conduct the study (protocol dated 07.10.2022 No. 2(72)).*

Informed consent *The parents of the subjects, authorized relatives or employees of social institutions confirmed their consent to conduct the study and publish the results without identifying the individual.*

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The article was submitted 02.02.2024; approved after reviewing 02.08.2024; accepted for publication 05.02.2025.

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Original article
https://doi.org/10.18019/1028-4427-2025-31-2-202-209

Etiology of infectious spondylodiscitis: is there an associaton with successful treatment?

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Abstract

Introduction Infectious spondylodiscitis is rising in incidence and and is often a late diagnosis and identification of the causative agent.

The **objective** was to evaluate the treatment outcomes of patients with infectious spondylodiscitis depending on the positive/negative results of intraoperative microbiological culture.

Material and methods Treatment outcomes of 52 patients with infectious spondylodiscitis were retrospectively analyzed with no culture growth in the biological samples (group I, $n = 22$) and with identified pathogen (group II, $n = 30$). The diagnosis was verified using MRI imaging, intraoperative microbiological culture test, the clinical picture and blood inflammation markers (ESR and CRP). Poor outcomes were associated with death and/or recurrent spondylodiscitis.

Results Positive culture growth was detected in 57.7 % with staphylococci predominated in 57.2 % and *Staphylococcus aureus* detected in 42.9 %. Patients of group I were twice as likely to take antibiotics at the preadmission stage ($p = 0.0049$), had a 20 % longer delay in diagnosis ($p = 0.7286$), and had lower CRP and ESR levels than those in Group II ($p > 0.05$). Adverse events included one fatal case in each of the groups; recurrent infections occurred in 13.3 % of cases of group II ($p = 0.3814$) with three quarters of cases caused by *Pseudomonas aeruginosa*.

Discussion Poor prognostic factors in infectious spondylodiscitis include negative microbiological results, neurological impairment and concomitant endocarditis ($p \leqslant 0.05$). *S. aureus* associated spondylodiscitis is accompanied by increased mortality and morbidity. Patients with spondylodiscitis with a negative microbiological test result compared with patients with a culture-positive infection, had a better treatment outcome with minimum recurrent rate ($p > 0.05$).

Conclusion Spondylodiscites with a negative microbiological result compared with a culture-positive infection had a better treatment outcome with a minimum of relapses ($p > 0.05$).

Keywords: infectious spondylodiscitis, etiology of spondylodiscitis, spinal infection, causative agent of spondylodiscitis, recurrent spinal infection, outcomes of spondylodiscitis, antibiotic therapy

For citation: Lyubimova LV, Lyubimov EA, Pavlova SI. Etiology of infectious spondylodiscitis: is there an associaton with successful treatment? *Genij Ortopedii*. 2025;31(2):202-209. doi: 10.18019/1028-4427-2025-31-2-202-209.

INTRODUCTION

The problem of treating patients with infectious diseases of the spine (spondylodiscitis) has currently become increasingly relevant due to the increasing incidence of the pathology. The incidence of infectious spondylodiscitis (IS) in France for 2002–2003 was 0.2–2.4 per 100,000 population per year [1], increasing to 6.1 by 2010 and to 11.3 in 2019 [2]. According to the German registry, the annual incidence of IS in 2020 was 14.4 per 100,000 population per year [3].

Difficulty of diagnosis and low frequency of detection of the etiologic factor are other problems of infectious diseases of the spine. According to the French SPONDIMMO study, the median duration of symptoms before the diagnosis of IS is 25 (0–427) days [4]. By the time of diagnosis, outpatients are taking both nonsteroidal anti-inflammatory and antibacterial drugs, which may ultimately affect the detection of infectious agents.

The absence of microbial growth in biological material samples can reach 68 % [5]. Pola et al. reported negative microbiological culture as a statistically confirmed negative prognostic factor IS [6]. However, there is a paucity of studies that could provide or compare treatment outcomes of IS with the pathogen being detected or undetected.

Based on data from the Federal Trauma and Orthopedic Center, we undertook to review the treatment outcomes of patients with infectious spondylodiscitis depending on the results of microbiological examination of intraoperative culture.

The **objective** was to evaluate the treatment outcomes of patients with infectious spondylodiscitis depending on the positive/negative results of intraoperative microbiological culture.

MATERIAL AND METHODS

A continuous retrospective analysis of outcomes of patients with infectious spondylodiscitis was conducted at the Federal Center for Trauma, Orthopedics and Joint Replacement (Cheboksary, hereinafter referred to as the Center) between 2016 and 2022.

The study included all cases of conservative and surgical treatment of IS, with the exception of patients aged 18 years and younger (n = 52). The diagnosis of IS was based on clinical findings, MRI, blood inflammation markers (erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP)), the results of microbiological examination of intraoperative tissue biopsies and swabs from removed metal constructs. The delivery time of the biomaterial to the laboratory was 15–60 minutes.

The scoring system for spondylodiscitis termed SponDT (Spondylodiscitis Diagnosis and Treatment) based on the inflammatory marker C-reactive protein (CRP), the VAS scale of pain and magnetic resonance imaging (MRI) was used to monitor progression of the disease [7].

Blood sterility tests were performed in patients with signs of a systemic inflammatory reaction (increased blood procalcitonin levels of more than 1.0 ng/ml) who did not receive antibacterial therapy (n = 2).

Examinations included biopsy material (n = 4), intraoperative tissue biopsies (n = 48), swabs from removed metal constructs (n = 14). Biological material was taken from patients receiving conservative therapy in the operating room using needle aspiration from the disc space and the X-ray image intensifier.

Intraoperative tissue biopsy samples were collected in a quantity of at least three, followed by isolation of microorganisms in accordance with approved standards of microbiological research. Tissue samples were homogenized and then placed in thioglycollate broth. Subculture was performed

on dense nutrient media using Columbia, Chocolate and Schaedler agars for 1 day; Chocolate and Schaedler agars for 5 days and Schaedler agar for 10 days. Incubation using gas-generating bags was produced for aerobic, anaerobic and capnophilic microorganisms.

Metal constructs removed during surgery were processed in a BRANSON 8510 ultrasound machine (USA) for 5 min at a frequency of (40 ± 2) kHz to isolate microorganisms from microbial biofilms, followed by seeding of the swabs onto nutrient media and onto analyzer vials. The incubation period was 14 days.

Species identification of pathogens with determination of susceptibility was performed using a Vitec 2-compact automatic analyzer (Bio Merieux, France) and a Multiscan FC semi-automatic analyzer (Thermo Fisher, USA).

Patients with IS were divided into two groups: treatment group I (n = 22), with no culture growth in the biological samples; control group II (n = 30), with culture growth obtained. The groups were comparable by gender, age, BMI and comorbidity (Table 1).

Table 1

Characteristics of patients in the study groups

Description	Group I (n = 22)		Group II (n = 30)		$p < 0.05$
	abs.	%	abs.	%	
Male	12	54.5	16	53.3	1.0000
Female	10	45.5	14	46.7	
Comorbidities including:					
diabetes mellitus	4	18.2	7	23.3	0.7411
oncopathology	1	4.5	2	6.7	1.0000
HIV	0	0.0	2	6.7	0.5023
systemic diseases	2	9.1	2	6.7	1.0000
Localization of the infectious process in the spine, incl.:					
cervical	3	13.6	1	3.3	0.3053
thoracic	5	22.7	6	20.0	1.0000
lumbar or lumbosacral	14	63.6	23	76.7	0.3625
Scoring system for spondylodiscitis (SponDT):					
mild	0	0.0	1	3.3	1.0000
moderate	10	45.5	15	50.0	0.7852
severe	12	54.5	14	46.7	0.7793
The route of infection:					
primary (hematogenous)	14	63.6	23	76.7	0.1461
secondary (postoperative)	8	36.4	7	23.3	
Number of outpatients treated with antibiotics	19	86.4	13	43.3	0.0049*
Age, years	56.8 (50.2–60.8)		57.8 (56.4–64.6)		0.7564
BMI, kg/m^2	26.3 (23.2–29.4)		28.2 (26.1–30.4)		0.2977
Period from onset of disease to diagnosis, days	122.5 (64.3–180.7)		99.9 (64.9–134.3)		0.7286

* — statistically significant differences

Pain was assessed after surgery and at the follow-up using the visual analogue scale VAS, satisfaction with treatment results was evaluated using the EQ-5D and EQ VAS questionnaires [8, 9].

Complete healing of the postoperative wound and normal laboratory and radiological findings at the time of the study (even with persistent neurological deficit and/or chronic pain syndrome) were rated as favorable outcomes. Death and/or recurrence of spondylodiscitis with clinical and instrumentation signs of infection was rated as a poor outcome. The total observation period after debridement was 32.9 (24.9–35.1) months.

The data were recorded in the form of spreadsheets; visualization of the data structure and the analysis were produced using the MS Office Excel, 2007 (Microsoft, USA) and the Graf Pad software. For quantification, a test for the normality of distribution was performed using the Kolmogorov – Smirnov criterion. The mean value and standard deviation with 95 % CI were used to describe parameters in case of normal distribution. Comparison of quantitative characteristics between comparison groups was performed using the Mann – Whitney criterion. Categorical data (gender, outcome) were described by conditional codes of unmeasured categories that were not subject to ordering. Fisher's exact test was used to assess the effectiveness of the treatment in the groups. Differences in indicators between the groups were considered statistically significant at $p < 0.05$.

RESULTS

No growth of microorganisms in the intraoperative biological cultures ($n = 21$) and tissues during biopsy ($n = 1$) was observed in 42.3 % ($n = 22$) from 52 patients treated for IS. Patients with negative culture results (group I) received antibacterial therapy at the prehospital stage ($p = 0.0049$) more often as compared with group II and had a 20 % longer delay in diagnosis ($p = 0.7286$). The majority of patients in both groups suffered from lesions of the lumbar or lumbosacral spine. Although no statistically significant differences in the severity of spondylodiscitis were found in the observation groups severe spondylodiscitis was more common among patients of Group I (54.5 % versus 46.7 %).

Two cases of IS (6.7 %) with isolated microorganisms were classified as polymicrobial infections and were represented by microbial associations:

1) *Pseudomonas aeruginosa* + *Enterococcus faecalis* + *Enterococcus faecium* + *Staphylococcus epidermidis MRSE*;

2) *Staphylococcus epidermidis MRSE* + *Corynebacterium*.

Staphylococci (57.2 %) were the leading pathogens among the causative agents of monomicrobial infection (93.3 % of cases) with *Staphylococcus aureus* predominating. The second frequent occurrence was gram-negative microorganisms (21.4 %), represented by *Escherichia coli, Pseudomonas aeruginosa* and *Klebsiella pneumonia* (Fig. 1).

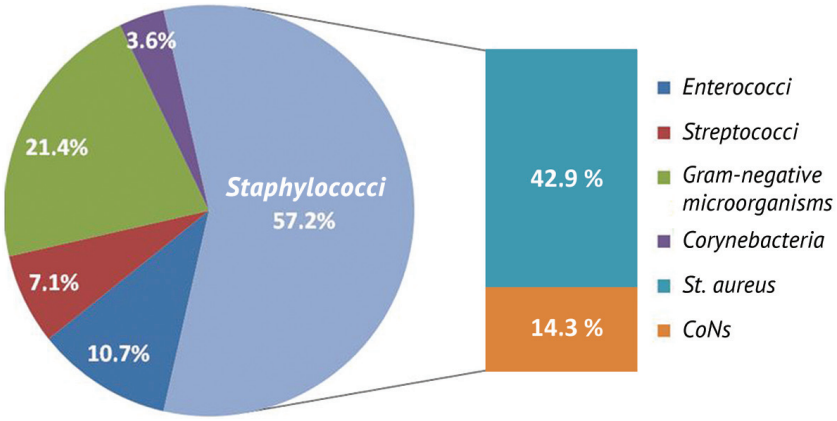

Fig. 1 Spectrum of spondylodiscitis pathogens with one isolated microorganism

A blood test for sterility showed a positive result in two control patients who received no antibacterial therapy at the outpatient stage: *Staphylococcus aureus* was detected in one case and *Streptococcus pneumoniae* was isolated in the other case. Inflammation blood test levels the were elevated in both observation groups at the prehospital stage, with a predominance of higher values of ESR, CRP and D-dimer seen in group II without statistically significant differences (Table 2).

Table 2

Blood test measurements in the groups prior to debridement

Description	Group I (n = 22)	Group II (n = 30)	$p < 0.05$
Blood WBC, 10^9/L	8.3 (7.0–9.5)	7.7 (6.6–8.9)	0.3152
ESR (mm/h)	35.1 (20.7–49.6)	52.9 (13.7–66.1)	0.0597
CRP (mg/L)	52.9 (14.4–83.8)	61.1 (42.3–80.0)	0.1802
D-dimer (ng/ml)	1137.9 (643.6–1632.0)	1305.9 (880.2–1732.0)	0.5104

MRI images indicated an abscess of various localizations detected in 54.5 % (n = 12) in group I and in 43.3 % (n = 13) of cases in group II (p = 1.0000). Conservative therapy included antibiotics (6–12 weeks) and spine fixation with a rigid corset and performed for one patient in group I and three patients in group II (p = 0.6288). The remaining patients with IS underwent surgical treatment (Table 3).

Table 3

Methods of surgical debridement in groups

Surgical interventions	Group I (n = 21)		Group II (n = 27)	
	abs.	%	abs.	%
Decompression with staged anterior and dorsal spondylodesis	2	9.5	–	
Anterior spondylodesis	2	9.5	2	7.4
Anterior fusion with plate fixation	2	9.5	–	
Posterior spondylodesis with TPF fixation	14	66.7	21	77.8
Debridement with decompression only	1	4.8	3	11.1
Posterior spondylodesis with autologous bone chips	–		1	3.7

The average duration of intravenous antibiotic therapy was (12.4 ± 3.8) days and (71.9 ± 55.4) days of oral antibacterial therapy. Empirical intravenous antibacterial therapy "glycopeptide + beta-lactam" was the most common intravenous regimen (54.5 %) in group II followed by the combination of "cefuroxime + amikacin" (22.7 %); monotherapy with third- and fourth-generation cephalosporins (13.6 %) and combination of cephalosporins with rifampicin (9.1 %). Fluoroquinolones combined with rifampin were the most common regimen of empirical oral antibacterial therapy (36.4 %); monotherapy with quinolones (18.2 %) or clindamycin (18.2 %), the combination of quinolone + doxycycline (13.6 %) or quinolone + co-trimoxazole (13.6 %) were other common oral regimens. Oral combination therapy with two or more antibiotics was used in 48.1 % of cases. In case of successful sanitation, no reliable differences in the quality of life of patients in the observation groups were found (Table 4). Patients were satisfied with the quality of life scored 75 on average.

Table 4

Patient satisfaction with the treatment performed at the follow-up stage

Description	Group I (n = 22)	Group II (n = 30)	$p < 0.05$
Assessment of quality of life using the EQ-5D questionnaire (scored from 0 to 1)	0.71 (0.61–0.80)	0.76 (0.67–0.86)	0.3083
Health assessment using the EQ-VAS “health thermometer” (scored from 0 to 100)	70.33 (59.23–81.43)	76.83 (69.83–84.14)	0.3256
VAS score	2.53 (1.58–3.49)	2.11 (1.43–2.80)	0.6184

The average observation period after debridement was 31.5 months (20.5–36.5) in group I and 34.0 months (23.0–37.0) in group II, p = 0.6397. Relapses in the form of deep spinal infection were not detected in group I, relapses were observed in 4 (13.3 %) patients in group II and debridement

was performed surgically ($p = 0.3814$). There was one fatal outcome in each observation group: due to tumor progression in group I and after conservative treatment of recurrent infectious spondylodiscitis due to mesenteric artery thrombosis in group II. Recurrent infections were observed in three out of four cases of spondylodiscitis caused by *Pseudomonas aeruginosa*.

DISCUSSION

Microbiological examination is a key element in the diagnosis and treatment of IS. However, it is not always possible to obtain cultural growth when examining biological material. The authors of several large prospective studies found that the pathogen could not be isolated in 21–34 % of cases [1, 10–12].

Stangenberg et al. reported the detection rate of bacterial pathogens through intraoperative sampling being 66.3 % and could be increased by the results of the blood cultures to a total of 80.6 % ($n = 170/211$) [13]. Pola et al. reported a microbiological diagnosis established in 74.3 % of cases; observed sensitivities of blood culture, CT-guided biopsy and surgical biopsy were, respectively, 55.5, 44.1 and 59.6 % [6]. Our results of searching for the causative agent of IS differ from those reported by our foreign colleagues, since we limited ourselves to microbiological examination of CT-guided biopsy and surgical biopsy, obtaining a positive result in 57.7 % of cases. The fact that 61.5 % of patients received antibacterial therapy preoperatively, sterility blood testing was not produced for them. The test as part of the screening diagnosis of IS could have clarified our results in the search for the infectious agent.

Assessing the structure of the pathogens isolated during the microbiological study, we obtained results similar to those of other studies, with *S. aureus* being the most common pathogen isolated in approximately 50 % of cases of spondylodiscitis [14, 15]. However, the incidence of spondylodiscitis in Germany reviewed over a ten-year period published in 2023 presented data indicating a decrease in the proportion of *S. aureus* in the overall microbial composition: coagulase-negative staphylococci were recorded in the majority of cases (27.1 %), followed by gram-negative bacteria (22.4 %), with *S. aureus* accounting for only 19. % [3].

A recent analysis of IS after implantation of metal constructs [16] showed that *S. epidermidis* was the most common pathogen (40.6 %) and has recently become prevalent in patients with implant-associated infection [17]. The growing importance of gram-negative pathogens in the etiology of IS is also evidenced by a study conducted in France in 2010–2019, with the frequency of isolation of the pathogens being 26.4 % (second place after staphylococci, 52.3 %) [2].

IS is a complex condition to treat and is caused by a wide range of organisms [18]. Searching for the causative agent of the infection is an important component of the treatment of patients with IS. According to our data, gram-negative microorganisms and coagulase-negative staphylococci are among the top three with an incidence rate of 21.4 % and 14.6 %, respectively. The trend of increasing gram-negative pathogens and coagulase-negative staphylococci can be associated with epidemiological problems caused by the aging population, an increased number of weakened patients with multiple comorbidities and an increase in invasive procedures and surgical interventions on the spine.

Despite the fact that control patients received etiotropic antibacterial therapy, the best treatment results, characterized by the absence of recurrent infection with similar indicators of satisfaction with the quality of life were obtained in the group with a negative bacteriological study. Data similar to ours were reported by Gillard et al. who described favorable outcomes under empirical two-drug

antimicrobial therapy including a fluoroquinolone given by the intravenous route, with no relapses or long-term recurrences versus controls with an established infectious agent and selected etiotropic therapy [19].

Stangenberg et al. reported S. aureus-associated spondylodiscitis being associated with an increased mortality and a higher complication rate with the pathogen due to the high frequency of detection in intraoperative specimens and in blood culture [13]. In contrast to the previously discussed works, Hopkinson et al. emphasized the importance of searching for the causative agent of IS (since the treatment outcome is worse if the causative agent is not detected) and showed a tendency for longer courses of antibiotic therapy. The authors also pointed out that these cases were more difficult to treat. The group of patients was represented by a small sample: 22 cases in the publication of 2021 and 23 in 2016 [21, 22].

In 2018, Pola et al. reported outcomes of 207 cases of IS and concluded that negative microbiological culture was a statistically confirmed negative prognostic factor, along with neurological impairment at diagnosis and underlying endocarditis [6]. Publications of Hopkinson (2001, 2016) and Pola (2018) were descriptive.

In our series, we attempted to analyze the outcome of IS treatment depending on the positive or negative result of intraoperative culture. The worse treatment outcomes of patients with an identified pathogen in our series could be due to undiagnosed bacteremia, since blood sterility testing was not produced for all patients with IS. Interestingly, 75 % of IS recurrent cases were associated with gram-negative pathogens (*Pseudomonas aeruginosa*, in particular), which may indicate an adverse effect of this pathogen on the outcome of IS treatment. Patients in Group I were significantly more likely to use antibiotics at the outpatient stage before culturing, although the optimal solution is to abstain from antibiotics until the microorganism is detected. We hypothesized that taking antibiotics at the outpatient stage increases their total course dose, which could also have a positive effect on the outcome of treatment of IS with a negative microbiological result.

The positive effect on the outcome of treatment of IS correlates with the study by Bhagat et al. who reported that starting antibiotics before detection of the microorganism may help reduce the risk of neurological deficit or spinal deformity [22]. Our study showed that empirical antibiotic therapy "glycopeptide + beta-lactam" used in most cases is no less effective than etiotropic treatment. The limitations of the study are the retrospective nature and small sample. We tested blood for sterility in only two patients, whereas 100 % coverage of this study could have increased the rate of pathogen isolation. The question of a reasonable time balance from the start of antibiotics to the identification of the pathogen remains open.

CONCLUSION

Patients with spondylodiscitis with a negative microbiological test result had a better treatment outcome with a minimum of relapses compared with patients with a culture-positive infection ($p > 0.05$).

Conflict of interest *The authors declare that there is no conflict of interest.*

Funding *The authors received no specific funding for this work.*

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The article was submitted 23.10.2024; approved after reviewing 27.11.2024; accepted for publication 05.02.2025.

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Original article
https://doi.org/10.18019/1028-4427-2025-31-2-210-217

Method of predicting the outcome of surgical treatment in Dupuytren's contracture based on leukocyte formula indices

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Abstract

Introduction World literature indicates the relevance of predicting the outcomes of Dupuytren's contracture (DC) treatment, including those based on laboratory methods. There are no comparative studies of the results of surgical DC treatment based on preoperative peripheral blood counts in the available literature.

The **purpose** of the work was to identify possible differences in preoperative leukocyte counts in DC with different outcomes of surgical treatment one year after surgery and to evaluate their prognostic significance.

Materials and methods The analysis of medical records of 52 DC patients operated on in the Hand Surgery Clinic of the Ilizarov Center in 2021–2022 was conducted. The results were assessed using the Khan scale, as well as by calculating the contracture reduction index (CRI). The subgroup included 111 patients with fair and poor results, the remaining 41 were included in subgroup 2 with good and excellent results.

Results According to the CRI values, the subgroups were in non-overlapping ranges. The percentage of eosinophils and basophils (B + E) in subgroup 1 was higher than in subgroup 2 ($p < 0.05$). ROC analysis of the "CRI — (B + E)" model revealed an area under the curve of more than 0.7 at $p < 0.01$, specificity of 100 %, sensitivity of less than 60 %. In patients with (B + E) < 1.2 %, the rate of excellent and good results one year after surgery was 95.23 %, with (B + E) ⩾ 1.2 % 70.00 % ($p < 0.05$).

Discussion The role of eosinophils and basophils in the development of fascial fibromatosis is unknown, but it has been established that interleukins IL-4 and IL-13 secreted by mast cells, basophils and eosinophils directly contribute to the activation of myofibroblasts and the development of fibrosis.

Conclusion In (B + E) < 1.2 %, a favorable outcome is predicted for both open and minimally invasive surgeries; at (B + E) ⩾ 1.2 % there is a high probability of progressive postoperative fibrosis, which justifies the choice of radical open interventions (hypodermectomy or dermofasciectomy) and the use of antifibrotic therapy in the postoperative period.

Keywords: Dupuytren's contracture, basophils, eosinophils, preoperative prognosis

For citation: Shchudlo NA, Sbrodova LI, Ostanina DA. Method of predicting the outcome of surgical treatment in Dupuytren's contracture based on leukocyte formula indices. *Genij Ortopedii*. 2025;31(2):210-217. doi: 10.18019/1028-4427-2025-31-2-210-217.

INTRODUCTION

Dupuytren's contracture (DC) is a consequence of palmar fascial fibromatosis (PFF), a ibroproliferative disease that primarily affects the fascial framework of the palms and fingers on the ulnar side of the hand. The main manifestations — nodes and fibrous chords — thicken and shorten the palmar-digital fascia and integumentary tissues, which leads to the formation of persistent flexion contractures of the finger joints. The majority of patients are males aged 40 to 80 years; about 3 % of them become disabled [1].

The etiology and PFF pathogenesis remain a matter of debate, with well-known risk factors including genetic predisposition, manual labor, alcohol and smoking, hypertension, and diabetes [2].

The most commonly used treatments for DC include collagenase injections, needle fasciotomy, and various types of open fasciectomy [3], which aim to destroy or remove pathological formations and correct hand deformity. Recurrence of contractures (growth in total extension deficit by more than 30°) is noted in 85 % of patients after needle fasciotomy and in 20 % after open partial fasciectomy over a five-year follow-up period [4].

Some authors classify contracture recurrences as late postoperative complications along with the spread and progression of fascial fibromatosis [5]. To optimize the treatment tactics for DC patients with, a technology for predicting late postoperative complications has been proposed based on the analysis of 39 factors that determine the patient's biological status and lifestyle, as well as the technical and surgical components of operations and rehabilitation treatment [6]. To develop a prognostic approach, a number of studies were conducted on potential laboratory markers of PFF activity: antibodies to connective tissue components [7, 8], matrix metalloproteinases [9], and circulating fibrocytes [10].

A study of 19 patients with DC found that the level of gene expression of matrix proteinases in tissue samples can be used to predict the outcome of treatment one year after surgery [11]. However, circulating matrix metalloproteinases did not correlate with postoperative extension deficit [12], so the problem of preoperative prediction of the outcome of DC treatment based on laboratory methods has not been solved to date. However, there are no data from comparative studies of surgical treatment outcomes based on preoperative peripheral blood parameters in the available literature.

The **purpose** of the work was to identify possible differences in preoperative leukocyte counts in DC patients with different outcomes of surgical treatment one year after surgery and to evaluate their prognostic significance.

MATERIALS AND METHODS

An analysis of preoperative leukocytograms and of treatment results was performed in 52 patients with DC, operated on at the hand surgery clinic of the Ilizarov Center in the period from 2021 throughout 2022.

The analysis of preoperative peripheral blood tests was performed based on the Nomenclature of the Ministry of Health of the Russian Federation (Order No. 804n): A12.05.121 "Differential leukocyte count (leukocyte formula)", which corresponds to the determination of the concentration of leukocytes in peripheral blood and differentiation of the main five types of leukocytes (neutrophils, eosinophils, basophils, lymphocytes, monocytes) by a hematology analyzer, as well as the calculation of their percentage. For the possible detection of immature leukocytes, atypical and blast cells, the automatic analysis is supplemented by "manual" microscopy of stained peripheral blood smears.

All patients underwent open partial fasciectomy with neurolysis and arteriolysis of the vascular-nerve bundles according to the indications (contracture of the metacarpophalangeal joint of 30° or more and contracture of the proximal interphalangeal joint regardless of the angle size [13]). In contracture of the proximal interphalangeal joint of more than 30°, fasciectomy was supplemented with arthrolysis [14]. In persistent contractures of grade II and grades III–IV, the operated rays were fixed in the Ilizarov mini-fixator during the healing period of the surgical wound. If full extension of the fingers was not achieved immediately during the operation due to contraction of the integumentary tissues and vascular-nerve bundles, dosed extension in the Ilizarov fixator was used, which started after the surgical wound healing. Once full extension of the joints had been reached, the fixator was blocked for at least 14 days, after which dynamic fixation was used: patients developed passive movements in the joints during the day, and the fixator was blocked at night. The duration of inpatient treatment varied from 9 to 14 days without fixator application and the fixation of the Ilizarov mini-apparatus was used from 17 to 42 days in the distraction application. After discharge, patients were recommended rehabilitation treatment.

The treatment results were assessed 6 and 12 months after surgery using the Khan et al. scale [15], as well as by calculating the contracture reduction index (CRI), expressed as a percentage of the difference between the initial sum of contracture angles and the sum of angles after surgery to the initial sum of angles [16].

Clinical and demographic characteristics of the studied group of patients are presented in Table 1. Based on the analysis of treatment results using the Khan et al. scale [15], patients with satisfactory and poor results were assigned to group 1 (n = 11), and patients with good and excellent results were included in group 2 (n = 41).

Table 1

Clinical and demographic parameters of studies patients

Parameter	Patients (n = 52)
Age — Me (Q1; Q2)	60 (58; 60)
Male to female ratio	5:1
Duration of disease since initial manifestations — Me (Q1; Q2)	8 (4; 14)
Contractures in stage III–IV, %	70.59
Patients under age of 50 years, %	49.02
Involvement of both hands, %	76.9
Interventions due to recurrence, %	23.53
Rate of multiple contractures (three or more digits), %	25.49
Contractures of ray V, %	74.51

The studies were conducted in accordance with the ethical standards of the World Medical Association Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects" with amendments.

Microsoft Excel 2010 spreadsheets and the Attestat computer program (version 9.3.1) were used for statistical processing of quantitative data. The Shapiro-Wilk criterion was used to test the hypothesis of normal distribution. In some samples, the distribution differed from normal, so the data in the tables are presented as medians and quartiles - Me (Q1; Q3). Hypotheses about differences were tested using the nonparametric Mann-Whitney test, applicable for comparisons of different-sized samples.

RESULTS

According to the CRI values, the groups were in non-overlapping ranges: patients with satisfactory and poor results had a contracture reduction index of 62 % or less, and in patients with good and excellent results, this indicator varied from 64 to 100 %.

The preoperative leukocytogram values (Table 2) did not differ from normal values, but a significant difference was revealed between the groups: the percentage of eosinophils and basophils in group 1 was higher than in group 2 ($p < 0.05$).

Table 2

Preoperative leukocytogram values (Me (Q1; Q3)) of patients based on the magnitude of the reduction index (RI) of Dupuytren's contracture one year after surgery

Group/ parameter	Whole sample	Group 1 (RI ⩽ 62 %)	Group 2 (RI 64 — 100 %)	*P*
	n = 52	*n* = 11	*n* = 41	
Leucocytes (× 10^9/l)	6.65 (5.31; 8.16)	5.91 (5.05; 8.67)	6.75 (5.45; 8.05)	0.66
Neutrophils (%)	56.50 (51.8; 62.4)	55.65 (55.45; 62.85)	56.50 (52.00; 6.40)	0.73
Lymphocytes (%)	35.00 (29.00; 39.95)	33.10 (29.30; 37.65)	35.00 (29.00; 40.00)	0.63
Monocytes (%)	7.15 (6.00; 8.20)	7.20 (6.50; 8.20)	7.15 (5.80; 8.20)	0.74
Eosinophils (%)	1.55 (0.70; 2.00)	2.05 (1.50; 3.05)	1.00 (0.00; 2.00)	0.02*
Basophils (%)	0.00 (0.00; 0.40)	0.35 (0.10; 0.50)	0.00 (0.00; 0.25)	0.01*

Note * — statistically significant differences according to the Mann – Whitney test ($p < 0.05$)

A similar intergroup difference was noted for the absolute content of eosinophils and basophils. Immature forms of leukocytes did not exceed reference levels; young, plasmatic and blast cells were absent in most patients, and did not exceed reference levels in solitary cases.

ROC analysis of the RIDC — (B + E) model revealed its good quality (area under the curve more than 0.7 at $p < 0.01$), high specificity (100 %), but only satisfactory sensitivity (less than 60 %).

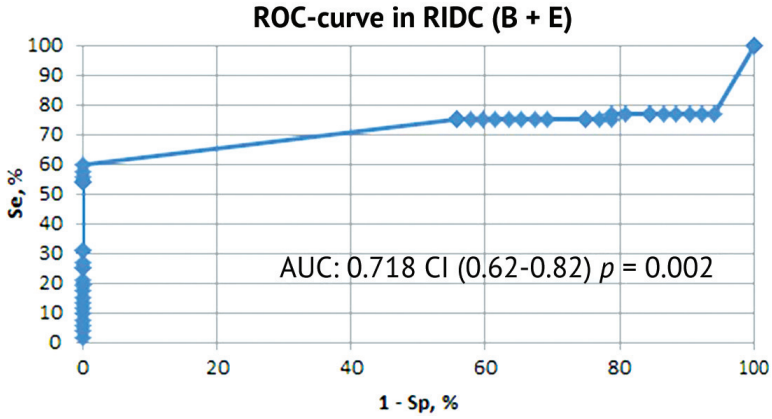

Fig. 1 Diagnostic value of preoperative total relative content of basophils and eosinophils (B+E) in the assessment of RIDC one year after surgery. Threshold 1.2 %; Sensitivity 59.62 %; specificity 100.0 %

At the next stage of the study, all patients were divided into groups based on the (B + E) value. There were 21 patients with a value lower than the threshold, and 31 patients with a value equal to or greater than the threshold. As shown by the data in Table 3, the groups did not have significant differences in clinical and demographic characteristics.

However, in patients with (B + E) < 1.2 %, the rate of excellent and good results one year after surgery was 95.23 %, and in patients with (B + E) ⩾ 1.2 % it was only 70 % ($p < 0.05$).

Table 3

Clinical and demographic characteristics of patients based on the value of the sum of basophils and eosinophils in peripheral blood before surgery

Parameters	Group		*p*
	(B + E) < 1,2 (*n* = 21)	(B + E) ⩾ 1,2 (*n* = 31)	
Age —Me (Q1; Q2) (min–max)	61.5 (58; 64) (51–71)	59 (54.5; 65) (23–75)	0.30
PFF duration	6.5 (5; 15) (1.5–20)	10 (4; 14.5) (2–40)	0.63
Patients under 50 years of age, %	40.90	53.57	0.52
Contracture severity — Me (Q1; Q2) (min–max)	3 (2; 3) (1–4)	3 (2.5; 3) (1–4)	0.77
Rate of patients with two-side involvement of PFF	81.82	78.57	0.79
Number of digits with impaired function — Me (Q1; Q2) (min–max)	1 (1; 2) (1–5)	2 (1;3) (1–4)	0.51
Patients that underwent second surgery, or more operations, %	27.27	46.43	0.18

DISCUSSION

The work presented, was the first comparative analysis of preoperative leukocytograms in patients with DC with different outcomes of surgical treatment one year after the operation. The studied pool of patients was characterized by a typical median age and gender ratio, typical duration of the disease, a high percentage of patients with severe contractures (more than 70 %), a large number of patients with signs of Dupuytren's diathesis (half of whom were affected at the age under 50 years and 77 % had lesions in both hands). More than 20 % of patients had operations for relapses, more than 25 % had contractures of three or more fingers and almost 75 % had contractures of the ray V.

Preoperative peripheral blood tests did not reveal any deviations in the absolute number of leukocytes. As is known, in such cases, the analysis of the leukocyte formula for relative content of the main types of leukocytes does not lead to erroneous results.

The results of surgical treatment were assessed using the qualitative scale of Khan et al. [15] and the quantitative indicator of the contracture reduction index. According to the qualitative scale, excellent and good results (*n* = 41) included complete restoration of motion or minor limitations of flexion-extension function that did not affect daily activities. The RIDC in such patients ranged from 64 to 100 %. None of those patients met the expert consensus definition of relapse as an increase in contracture of any treated joint by at least 20° within a year after surgery compared to six weeks after surgery [17]. In patients with fair and poor treatment results (*n* = 11), the contracture reduction index had negative dynamics within a year after surgery, confirming relapse.

According to some authors, DC relapses in the first year after surgery develop in cases where "operations were performed with violations of hand surgery guidelines" [18]. However, our study revealed significant differences in preoperative leukocytograms in groups of patients with different treatment outcomes. Apparently, the treatment outcome is also affected by the predisposition of patients to different patterns of wound healing.

As is known, eosinophils and basophils, along with mast cells, helper lymphocytes and macrophages, participate in inflammatory reactions of the second type, characteristic not only of allergies and parasitic invasions, but also of many other diseases. This type of immune reactions also regulates tissue reparation, including the restoration of epithelial barriers after damage [19, 20]

Eosinophils, comprising one to 5 % of peripheral blood leukocytes, are normally present in many tissues, performing homeostatic functions [21], including directly activating mast cells [22]. Basophil is the rarest blood cell, which normally comprises 0.5 % of leukocytes [23]. Unlike tissue basophils (mast cells), residents of connective tissue, short-life basophils of peripheral blood, are usually not present in tissues; their tissue traffic is associated with specific functions [24].

It has been previously established that the fascia of DC patients contains 12 times more mast cells than normal fascia [25], and not only their numerical density increases, but also their morphofunctional quantitative parameters, such as the area and index of degranulation with contractures of grades III–IV, compared with contractures of grades I–II, [26]. The role of eosinophils and basophils in the development of fascial fibromatosis is unknown, but it has been established that interleukins IL-4 and IL-13, secreted by mast cells, basophils, and eosinophils [27], directly contribute to the activation of myofibroblasts and the development of fibrosis [28].

As our study showed, patients with low and high total relative content of basophils and eosinophils in peripheral blood had no differences in clinical and demographic indicators. However, the proportion of fair and poor treatment results was significantly higher in the group with (B + E) ⩾ 1.2 %. Therefore, the total relative content of basophils and eosinophils in peripheral blood ⩾ 1.2 % in the preoperative period is an independent predictor of relapse of the fibroproliferative process in patients operated on for DC.

The results of ROC analysis indicate an average prognostic significance of this indicator due to a specificity of lower than 60 %; however, in combination with another leukocyte index (lymphocyte-monocyte ratio), which allows predicting the progression of DC and has a high prognostic significance [29], it can be used in preoperative prediction of treatment outcomes in DC patients [30].

Here are clinical cases with the use of this prediction method.

Case 1 Patient H., 71 years old, was admitted for treatment to the Ilizarov Center in November 2021 with the diagnosis: bilateral palmar fascial fibromatosis, acquired deformity of digits II-V of the left hand, DC stage IV (total deformity angle 190°). Concomitant diseases: stage 3 hypertension, chronic heart insufficiency, atrial fibrillation outside of paroxysm, late stage of Bechterev disease.

History of the disease: was ill for 8 years; initially, movement limitations and persistent contractures in the left hand developed, then in the right one; did not seek treatment for 5 years. On 07.03.18, he underwent surgery at the Ilizarov Center for acquired deformity of the fifth finger of the right hand, DC grade III. He was satisfied with the treatment result. According to the archival medical records, the lymphocyte-monocyte index was 5.8 (higher than the threshold value, which did not indicate a progressive nature of the disease at that time), the total content of eosinophils and basophils was 1 %, which indicates a probability of obtaining a good and excellent result of the operation of 95.23 %. At the time of the patient's admission due to the deformity of the left hand, the restoration of flexion-extension movements of the operated fifth finger of the right hand was almost complete.

The total contracture angle of ray V of the left hand before the operation was 190°. According to the preoperative blood test (2021), the lymphocyte-monocyte index was 5.75 (higher than the threshold value, which also does not indicate a progressive nature of the disease at the moment). The total content of eosinophils and basophils was 1.0 %, which indicates a probability of obtaining a good and excellent result of the operation of 95.23 %.

On 18.10.21, the following surgery was performed: excision of the fibrously altered palmar aponeurosis in the projection of rays II–V of the left hand, arthrolysis of the proximal interphalangeal joint of finger V, skin grafting of the palmar surface of ray V of the left hand with local tissues, osteosynthesis of ray V with the Ilizarov mini-fixator.

At the patient's follow-ups 6 and 12 months after the surgery, the total angle of deformation on the left hand decreased from 190° to 60° and 45°, respectively, and the contracture reduction index was 0.68 and 0.76. The latter value corresponded to an excellent result of surgical correction and coincided with the positive preoperative prognosis based on peripheral blood indices, despite the extreme severity of the disease (multiple contracture of digits II–V, grade IV).

Case 2 Patient U., 36 years old, was admitted for treatment to the Ilizarov Center with the diagnosis: palmar fascial fibromatosis, acquired deformity of the right hand, combined DC and digit V of the left hand in grade II–III (total deformity angle 90°).

According to the preoperative blood test, the lymphocyte-monocyte index was 5.39 (higher than the threshold value, which does not indicate a progressive nature of the disease at the moment). However, the total content of eosinophils and basophils was 2.8 % (higher than the threshold value of 1.2 %) and indicated that the probability of obtaining a good and excellent result of the operation is no more than 70.00 %.

On 26.01.22, the operation included excision of the fibrously altered palmar aponeurosis in the projection of ray V of the right hand, arthrolysis of the proximal interphalangeal joint of digit V, skin grafting of the palmar surface of ray V of the left hand with local tissues, osteosynthesis of ray IV with the Ilizarov mini-fixator.

A 6-month follow-up revealed a total contracture angle of 30°, and after 12 months it was 90°. The contracture reduction index one year after the operation was 0°, which corresponded to a poor result.

In this clinical case, the prognosis about a decreased probability of good and excellent results of the operation due to the high total content of eosinophils and basophils was confirmed.

CONCLUSION

Available prognostic criteria for detecting DC progression and recurrence have been developed. The lymphocyte-monocyte ratio and the total relative content of basophils and eosinophils were used as prognostic criteria. If the lymphocyte-to-monocyte ratio is more than 3.1, surgical treatment tactics (minimally invasive fasciotomy or open fasciectomy options) is chosen based on the local status, age, comorbidity and patient preferences. If the lymphocyte-to-monocyte index is less than 3.1, a prognosis is made about a high probability of fascial fibromatosis progression, which is an additional indication for radicalization of the surgical treatment method: open hypodermofasciectomy and dermofasciectomy. If the total relative content of eosinophils and basophils is less than 1.2 %, a prognosis is made about a favorable outcome of minimally invasive and open surgical interventions. If a total relative content of eosinophils and basophils is 1.2 % or more, there is a high probability of progressive postoperative fibrosis and the development of cicatricial contracture, therefore, in the immediate postoperative period, enhanced therapy of the edematous-inflammatory syndrome is necessary, and in the late period, antifibrotic therapy [31, 32].

The application of the developed criteria does not require material costs, but they have prognostic value and are important for refining treatment tactics, so it is advisable to use them in wide clinical practice.

Conflict of interest *Not declared.*

Funding *The research was funded within the framework of the state assignment for 2021–2023.*

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The article was submitted 09.10.2024; approved after reviewing 23.10.2024; accepted for publication 05.02.2025.

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Original article
https://doi.org/10.18019/1028-4427-2025-31-2-218-225

Dependence of serum procalcitonin level on microflora in the infection site in chronic osteomyelitis

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Abstract

Introduction The study of procalcitonin (PCT) levels simultaneously with blood cultures for sterility is an important addition to the diagnostic algorithm for chronic osteomyelitis detection.

Purpose of work is to study the relationship of serum PCT with the microflora isolated from blood, wounds and fistulas in patients with chronic osteomyelitis.

Materials and methods A retrospective analysis of wound microflora, blood cultures for sterility, and procalcitonin test results was performed.

Results Gram-positive microorganisms prevailed in the microbial tests from wounds, fistulas and blood in patients with PCT less than 0.5 ng/ml and from 0.5 to 2.0 ng/ml. In patients with PCT levels from 2.0–10.0 and above10 ng/ml, both gram-positive and gram-negative bacteria were isolated. Among positive blood cultures, S. *epidermidis* strains were the most frequently isolated, followed by S. *aureus*, K. *pneumoniae*, S. *agalactae*, and S. *hominis* isolates. PCT in the blood of seven patients was higher than 10 ng/ml; and six patients had it from 2.0–10.0 ng/ml. Two subjects had a low PCT level, but an infectious agent was detected in their blood.

Discussion In patients with PCT lower than 0.5 ng/ml, gram-positive microorganisms are most often found in the microflora of wounds and fistulas. The proportion of patients with PCT values ⩾ 2 ng/ml and gram-negative bacteria in the focus was higher compared to patients with gram-positive microflora. Nevertheless, the detected high correlation relationship between the microbiocenosis of patients' wounds and procalcitonin values confirms the leading role of gram-positive bacteria in the development of osteomyelitis.

Conclusion In positive blood cultures, the serum PCT level was usually higher than 2.0 ng/ml. The presence of gram-negative bacteria in the blood, as well as in the wound, was accompanied by PCT values higher than 10 ng/ml.

Keywords: chronic osteomyelitis, procalcitonin, microflora, resistance

For citation: Shipitsyna IV, Osipova EV, Shastov AL. Dependence of serum procalcitonin level on microflora in the infection site in chronic osteomyelitis. *Genij Ortopedii*. 2025;31(2):218-225. doi: 10.18019/1028-4427-2025-31-2-218-225.

INTRODUCTION

Chronic osteomyelitis is a complex and difficult to treat bacterial or fungal bone infection characterized by progressive inflammatory destruction, necrosis and proliferation in the area of bone damage that develop due to complications of the wound process if it communicates with the bone, surgical interventions or bacteremia [1–3]. As a rule, osteomyelitis is of exogenous origin, caused by microbial invasion, often with the formation of a biofilm [4–8]. Treatment of chronic osteomyelitis requires long-term and intensive antimicrobial therapy, which leads to the risk of resistance. Moreover, osteomyelitis is dangerous due to complications (sepsis, bacteremia, etc.).

In recent years, there has been renewed interest in studying the role of various biomarkers (C-reactive protein, interleukins 6 and 8, lactate, presepsin, procalcitonin, and others) in the diagnosis and risk assessment of inflammatory syndromes [9–11]. Among them, procalcitonin (PCT) stands out and is considered a specific marker of bacterial infection [12–16]. It is known that PCT levels in the blood serum of healthy people are lower than 0.1 ng/ml. In severe bacterial and generalized fungal infections, PCT concentration quickly grows, but remains low in viral infections and nonspecific inflammatory diseases [17].

An isolated test for PCT is not informative enough, since its level can be elevated not only in acute and chronic infectious processes, including osteomyelitis, but also in various non-infectious conditions, such as autoimmune diseases, major surgeries, injuries, burns, prolonged cardiogenic shock, stress [12, 13, 18].

A positive blood culture is considered the gold standard for diagnosing bacteremia; however, negative results do not always rule out its absence [14, 19, 20]. Microbiological blood testing takes time, which does not allow its use as a rapid test [21]. High PCT values with negative blood culture results may indicate the presence of local inflammation, while elevated levels and a positive culture result confirm a systemic infectious process.

There are only a few studies devoted to the study of PCT levels and blood culture results for sterility in patients with chronic osteomyelitis. According to the literature, PCT plays the role of a sensitive and specific marker in the diagnosis of bone and joint infections [22]. Positive blood culture results were detected in 53 % of patients with vertebral osteomyelitis, 19 % with bone infection, and 7 % with paraimplant infection [7].

Diagnosis of osteomyelitis is established with a combination of clinical signs and symptoms, instrumental and laboratory studies, including analysis of microflora with determination of sensitivity to antibiotics [23]. A study of serum PCT simultaneously with blood cultures for sterility can provide additional information to physicians that would allow them to predict the course and outcome of the disease in patients with chronic osteomyelitis.

The **purpose** of work was to study the relationship of serum PCT with the microflora isolated from blood, wounds and fistulas in patients with chronic osteomyelitis.

MATERIALS AND METHODS

The study included patients (n = 123) with chronic osteomyelitis, regardless of its location and mechanism of occurrence, who were treated at the Purulent Osteology Clinic of the Ilizarov National Medical Research Center of Traumatology and Orthopaedics in the period from 2021 to 2023. The average age of patients was 55 years (IQR 43–66) and 70.3 % (71/101) were males. There were no significant differences in age between the groups of males and females (p = 0.32).

A retrospective analysis of microbiological cultures ($n = 294$), including blood for sterility, was performed. The procalcitonin test was performed simultaneously with blood sampling for sterility and on the third day after surgery. In case of unsatisfactory results, the test was repeated on days 5 to 9 as prescribed by the physician.

For rapid cultivation of pathogenic microorganisms in blood, an automatic analyzer of the Juno® Labstar 100 series was used. Microbial cultures were identified to the species level on a BactoScreen bacteriological analyzer (NPF Litekh); determination of the sensitivity of bacteria to antibacterial drugs by the disk diffusion method on the Mueller-Hinton medium. Depending on the type of microorganism, various sets of antibiotics were used:

— for non-fermenting gram-negative bacteria: 1 — tetracycline (30 mcg), 2 — amikacin (30 mcg), 3 — gentamicin (10 mcg), 4 — tobramycin (10 mcg), 5 — ciprofloxacin (5 mcg), 6 — levofloxacin (5 mcg), 8 — meropenem (10 mcg), 9 — imipenem (10 mcg), 15 — piperacillin/tazobactam (30/60 mcg), 23 — cefepime (30 mcg);

— for enterobacteria: 1 — tetracycline (30 μg), 2 — amikacin (30 μg), 3 — gentamicin (10 μg), 5 — ciprofloxacin (5 μg), 6 — levofloxacin (5 μg), 8 — meropenem (10 μg), 9 — imipenem (10 μg), 13 — ceftazidime (10 μg), 14 — cefotaxime (5 μg), 15 — piperacillin/tazobactam (30/60 μg);

— for staphylococci: 1 — tetracycline (30 mcg), 3 — gentamicin (10 mcg), 5 — ciprofloxacin (5 mcg), 10 — vancomycin (5 mcg), 12 — cefoxitin (30 mcg), 16 — clindamycin (2 mcg), 17 — erythromycin (15 mcg), 18 — fusidine (10 mcg), 19 — linezolid (10 mcg); 21 — rifampicin (5 mcg);

— for enterococci: 3 — gentamicin (30 mcg), 10 — vancomycin (5 mcg), 11 — ampicillin (2 mcg), 27 — norfloxacin (10 mcg), 19 — linezolid (10 mcg);

— for streptococci: 11 — ampicillin (2 mcg); 14 — cefotaxime (5 μg), 16 — clindamycin (2 μg), and 20 — benzylpenicillin (1 μg).

The results were assessed using the EUCAST criteria (European Committee on Antimicrobial Susceptibility Testing, Version 9.0, valid from 2019–01–01). Moderately resistant strains were classified as resistant.

The concentration of PCT in the blood serum was determined by a semi-quantitative method using the ICA-procalcitonin test (Russia). The results were interpreted in accordance with the manufacturer's recommendations:

< 0.5 ng/mL — systemic infection is unlikely, although localized infection is possible;

0.5 – < 2 ng/mL — systemic infection is possible, but other conditions (major trauma, recent surgery, severe cardiogenic shock) can also cause significant increases in PCT;

2 – < 10 ng/mL — systemic infection is likely;

⩾ 10 ng/mL — severe bacterial sepsis or septic shock is highly likely.

The results of the study are divided into two groups: positive and negative. Positive results, depending on the isolated microorganisms in the blood culture or focus, are divided into two subcategories: gram-positive and gram-negative bacteria.

The Gnumeric 1.12.17 software program was used for processing and statistical analysis of the obtained results. Quantitative variables are presented as median and interquartile range (IQR), and qualitative variables are presented as percentages. The nonparametric Wilcoxon test was used to determine differences between the groups. To study the relationship between procalcitonin values and the species composition of bacteria isolated from wounds, the Spearman rank correlation coefficient was calculated. The obtained data were interpreted using the Chaddock scale. Differences were considered significant at $p < 0.05$.

The clinical study was approved by the Ethics Committee of the Ilizarov National Medical Research Center of Traumatology and Orthopedics; it was conducted in accordance with the ethical standards of the Declaration of Helsinki.

RESULTS

Blood PCT concentrations lower than 0.5 ng/ml were observed in 52.0 % of the examined patients, from 0.5 to 2.0 ng/ml — in 19.5 % ($p = 0.13$), from 2.0–10.0 ng/ml — in 12.3 % ($p = 0.049$), and more than 10 ng/ml — in 16.2 % ($p = 0.049$). Gram-negative microflora in the blood was detected only in patients with PCT values greater than 10 ng/ml (Table 1).

Table 1

Number of patients with chronic osteomyelitis in dependence on PCT level

PCT, ng/ml	Количество пациентов по годам								Positive blood sterility test in the period from 2021 to 2023
	2021 ($n = 35$)		2022 ($n = 31$)		2023 ($n = 57$)		2021–2023 ($n = 123$)		
	n	%	*n*	%	*n*	%	*n*	%	
< 0.5	11	31.4	16	51.5	37	64.9	64	52.0	S. *epidermidis* ($n = 3$)
0.5–2.0	12	34.2	6	19.4	6	10.5	24	19.5* $p = 0.13$	S. *aureus* ($n = 1$), S. *hominis* ($n = 1$)
2.0–10.0	4	11.5	4	12.8	7	12.3	15	12.3* $p = 0.049$	S. *aureus* ($n = 3$), S. *pidermidis* ($n = 3$), *Streptococcus* spp. ($n = 2$)
⩾ 10.0	8	22.9	5	16.3	7	12.3	20	16.2* $p = 0.049$	S. *pneumoniae* ($n = 3$), S. *epidermidis* ($n = 2$)

Note: * — level of significance of differences between the number of examined patients with PCT values lower than 0.5 ng/ml

In the microbial landscape from the pathological focus in patients with PCT lower than 0.5 ng/ml and in the range 0.5–2.0 ng/ml, gram-positive microorganisms prevailed (Table 2). In patients with PCT from 2.0–10.0 ng/ml and above 10 ng/ml, both gram-positive and gram-negative bacteria were isolated. Among gram-negative bacteria from wounds and sinuses, enterobacteria were most often isolated, mainly strains of K. *pneumoniae*, and among gram-positive bacteria, strains of S. *aureus*. In five patients, there was no growth of microorganisms in the focus, while the PCT level was 0.5–2.0 ng/ml ($n = 4$), 2.0–10.0 ng/ml ($n =$). In one patient, bacteriological examination of wound culture did not reveal growth of pathogenic bacteria, but the test for blood sterility revealed the pathogen *Streptococcus* spp., while PCT was in the range of 2.0 to 10.0 ng/ml. In 10 patients, the microflora of wounds and fistulas did not match the results of blood cultures for sterility. The proportion of patients with PCT values ⩾ 2 ng/ml and gram-negative bacteria in the lesion was higher compared to patients with gram-positive microflora.

The correlation coefficients between the microbiocenosis of patients' wounds and the procalcitonin values indicate an inverse relationship between the studied features. The closeness of these relations was noticeable ($r = –0.57$ for gram-negative microflora) and high ($r = –0.74$ for gram-positive microflora) according to the Chaddock scale.

A positive blood sterility test was obtained in 17 patients. In two patients, K. pneumoniae strains were isolated during the initial blood test, with serum PCT values exceeding 10 ng/ml (Table 3). A repeated blood test showed a change in microflora to gram-positive with a simultaneous decrease in PCT to 0.5 ng/ml (patients No 1 and No 2, Table 3).

Table 2

Frequency of bacterial occurrence based on PCT values

Microorganism	PCT, ng/ml			
	0.5	0.5–2.0	2.0–10.0	More than 10
NFGNB	11	5	4	4
Enterobactereaceae	25	10	5	17
Total:	**36 (44.4 %)**	**15 (18.5 %)**	**9 (11.1 %)**	**21 (25.9 %)**
S. *aureus*	35	11	4	10
CoNS	15	6	2	7
Enterococcus sp.	8	2	–	5
Streptococcus sp.	1	1	–	1
Corynebacterium sp.	2	1	1	–
Total:	**61 (55.5 %)**	**21 (19.1 %)**	**7 (6. 4 %)**	**21 (19.1 %)**
No growth:	9	4	1	0

Note: NFGNB — non-fermenting gram-negative bacteria; CoNS — coagulase negative bacteria

Table 3

Active antibacterial drugs against bacteria isolated simultaneously from blood and wounds

No*	Blood microflora	Effective antibiotics	Microflora of wound and fistula	Effective antibiotics	PCT, ng/ml
1	K. *pneumoniae*	1	K. *pneumoniae*	1	> 10.0
	S. *epidermidis (MRSE)*	10	S. *epidermidis (MRSE)*	10	< 0.5
2	K. *pneumoniae*	2, 3	K. *pneumoniae*	2, 3	> 10.0
	S. *aureus*	All tested	S. *aureus*	All tested	< 0.5
3	K. *pneumoniae*	1	K. *pneumoniae*	1	> 10.0
			E. *faecalis*	1, 21	
4	K. *pneumoniae*	1–3, 6, 8, 9, 15, 22	E. *cloacae*	2, 9	> 10.0
			E. *faecalis*	7	
5	S. *epidermidis (MRSE)*	3,10, 16–18, 21	E. *coli*	2–6, 8, 9, 15, 22	< 0.5
			S. *aureus*	All tested	
6	S. *epidermidis (MRSE)*	10, 18, 19, 21	S. *epidermidis (MRSE)*	10, 18,19,21	2.0–10.0
7	S. *epidermidis (MRSE)*	1, 10, 18, 19, 21	S. *aureus (MRSA)*	1,10,18,19,21	> 10.0
8	S. *epidermidis*	All tested	S. *aureus*	All tested	2.0–10.0
9	S. *epidermidis*	All tested	P. *aeruginosa*	2, 3, 5, 8, 9, 15, 23	< 0.5
			A. *baumannii*	4, 8, 9, 15	
			S. *aureus*	All, but 16, 17	
10	S. *epidermidis (MRSE)*	1, 10, 18, 19, 21	S. *epidermidis (MRSE)*	1, 10, 18, 19, 21	2.0–10.0
			K. *pneumoniae*	2, 3, 8	
11	S. *epidermidis (MRSE)*	10, 18, 19, 21	E. *cloacae*	1–4, 6, 8, 23	> 10.0
12	S. *hominis (MRSH)*	10, 18, 19, 21	K. *pneumoniae*	1, 2, 3, 8	0.5–2.0
			P. *aeruginosa*	2, 3, 5, 8, 9, 15	
			E. *faecalis*	2, 10, 19	
13	S. *agalacteae*	All, but 1	No growth	–	2.0–10.0
14	S. *agalacteae*	11	E. *cloacae*	2, 6, 8, 9	> 10.0
			S. *epidermdis (MRSE)*	10, 19, 18, 21	
			E. *faecalis*	3, 10, 19	
15	S. *aureus*	All, but 5	P. *aeruginosa*	1, 3, 4	2.0–10.0
			A. *baumannii*	1, 4, 8, 9	
16	S. *aureus*	All tested	S. *aureus*	All tested	0.5–2.0
17	S. *aureus*	All tested	S. *aureus*	All tested	2.0–10.0

Note: * —numbers of patients with positive blood cultures. In the column with effective drugs, the antibiotics listed in the Materials and Methods section are marked with numbers.

Among positive blood cultures (*n* = 19), the most frequently isolated strains were S. *epidermidis* (*n* = 8, including 6 MRSE), followed by isolates of S. *aureus* (*n* = 4), K. *pneumoniae* (*n* = 4), S. *agalacteae* (*n* = 2), and methicillin-resistant S. *hominis* (*n* = 1).

Blood PCT was higher than 10 ng/ml in seven patients, and 2.0–10.0 ng/ml in six patients. Two patients had low PCT levels, and an infectious agent was detected in their blood. In six patients, the blood microflora and bacterial sensitivity to the tested antibacterial drugs coincided with the wound microflora. Gram-positive bacteria isolated from the blood were sensitive to most of the tested drugs. MRSE strains were isolated from the blood of six patients, two of whom had PCT above 10 ng/ml.

Bacterial strains belonging to the same taxon, isolated simultaneously from blood and wounds, were characterized by the same sensitivity to antibacterial drugs. Among the most effective antibacterial drugs against K. pneumoniae were tetracyclines and aminoglycosides, against bacteria of the genus *Staphylococcus* — glycopeptides, linezolid, rifampicin and fusidin.

In eight patients with PCT higher than 10 ng/mL, the value decreased to normal values within 7–9 days. In seven patients (in three of whom microorganisms were isolated from the blood), PCT did not decrease. In 13 of 15 patients with initial PCT values from 2.0 to 10.0 ng/mL, it decreased to normal values within 5–6 days.

DISCUSSION

According to the results of the study, gram-positive microorganisms, mostly S. aureus, were isolated from the focus in the patients with PCT less than 0.5 ng/ml. The rate of gram-negative bacteria was 1.7 times lower. At the same time, in patients with PCT values above 10 ng/ml, both gram-negative and gram-positive microorganisms were equally isolated from the lesion (wounds, sinuses, blood). Moreover, in all patients in who K. *pneumoniae* strains were isolated from the blood the PCT level was above 10 ng/ml. K. *pneumoniae* and MRSE bacteria detected together in the blood and wounds were characterized by a high level of resistance to most of the tested antimicrobial drugs.

Many studies described a correlation between high serum PCT levels and gram-negative bloodstream infection [24]. PCT concentrations were significantly higher in patients with positive blood cultures [25]. High blood PCT levels are significantly influenced by gram-negative bacterial endotoxin, which is an obligate lipopolysaccharide of the bacterial wall.

Studies showed that bloodstream infection caused by gram-negative bacteria results in significantly higher PCT levels than gram-positive bacteria. This is due to the fact that gram-negative and gram-positive bacteria recognize Toll-like receptor 4 and Toll-like receptor 2 on the cell surface using lipopolysaccharide and lipoteichoic acid, respectively, and subsequently induce the release of different cytokines and different PCT levels [26].

There are also reports of similar PCT values in gram-negative and gram-positive bacteremia [27]. Oksuz et al. could not demonstrate a statistically significant difference between gram-negative and gram-positive bacteremia in terms of PCT levels [28]. A correlation was established between the PCT value and microflora, provided that the infection site and the bloodstream infection are caused by the same pathogen [29].

According to the literature data, 40–90 % of patients with suspected systemic infection have negative blood culture results [30]. In our study, there was no microbial growth in five cases, while the PCT level was higher than 0.5 ng/ml but lower than 10 ng/ml. The PCT level above 2 ng/ml was observed in 35 subjects, while the pathogen was detected in the blood of only 13 patients.

At the same time, microflora was isolated from the blood of two individuals with a low PCT value (lower than 0.5 ng/ml).

To date, PCT is one of the most studied biomarkers for rational use of antibiotics [31]. PCT threshold values < 0.5 μg/L or reduction by 80–90 % from the peak level are considered a sign of recovery, which is a ground for completing the course of antibiotic therapy. In our study, PCT decreased to threshold values within 5–9 days. In three cases, no decrease in PCT was observed. We assume that the dynamics of PCT concentration during antibacterial therapy can serve as a criterion for the effectiveness of antibiotic use [31–32].

CONCLUSION

In patients with PCT lower than 0.5 ng/ml, gram-positive microorganisms were most often found in the microflora of wounds and sinuses. The proportion of patients with PCT values ⩾ 2 ng/ml and gram-negative bacteria in the focus of infection was higher compared to patients with gram-positive microflora. Nevertheless, the detected high correlation relationship between the microbiocenosis of patients' wounds and procalcitonin values confirms the leading role of gram-positive bacteria in the development of osteomyelitis.

In positive blood cultures, the serum PCT level was, in most cases, higher than 2.0 ng/ml. The presence of gram-negative bacteria in the blood, as well as in the wound, was accompanied by PCT values higher than 10 ng/ml. If the same pathogen was detected in wounds and blood, high resistance of bacteria to most of the tested drugs was noted.

The obtained results showed that a blood test for PCT simultaneously with microbiological studies may be an additional tool in the diagnosis of chronic osteomyelitis.

Conflict of interest *Not declared.*

Funding *None.*

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The article was submitted 16.10.2024; approved after reviewing 09.01.2025; accepted for publication 05.02.2025.

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Original article
https://doi.org/10.18019/1028-4427-2025-31-2-226-236

Experimental evaluation of $CA_3(PO_4)_2$ based bone substitutes using rat femoral defect models

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Abstract

Introduction Replacement of bone defects is an important issue of modern traumatology and orthopedics. With increasing technological advances there is a spectrum of bone-substituting materials, and the choice of the effective option is essential for biomedical research.

The **objective** was to determine the effect of the three-dimensional structure and pore size of tricalcium phosphate based bone substitute materials on osteoconduction using a critical diaphyseal defect of the rat femur.

Material and methods A monocortical 7 mm defect was simulated in the middle third of the rodent femoral shaft under anaesthesia and filled with blocks of one of four tricalcium phosphate based materials differing in the number, size and direction of pores. Eight rats from each group were sacrificed at 3 and 6 months, and the newly formed bone was histologically examined and the results compared using statistical methods.

Results The bone tissue was shown to grow into the defect area through the pores of the material in all the groups at 3 and 6 months, The newly formed bone measured (11 ± 4) % and (31 ± 6) % of the defect area in the Cylinders group, (14 ± 5) % and (29 ± 4) % in the Gyroid group; (39 ± 5) % and (41 ± 7) % in the Gyroid-150 μm group and (17 ± 7) % and (27 ± 8) % in the Gyroid-50 μm group, respectively. The area of newly formed bone was statistically greater in the Gyroid-150 μm group compared to that in the other groups ($p < 0.05$, Kruskal – Wallis test).

Discussion The effect of the type of architecture of the bone substitute material, the pore size and their relationships are reported in many studies with larger diameter pores (more than 600 μm) improving osteoconduction, and the upper limit of porosity being limited by a decrease in the mechanical properties of the block. The advantages of the Gyroid structure over other types of architectures are described in theoretical and applied research. Structures with pores of different sizes were examined in few studies, and our findings demonstrated the feasibility of using the complex structures and the role in replacing bone tissue.

Conclusion The three-dimensional structure of bone substitute materials based on tricalcium phosphate was shown to have an effect on osteoconductive properties, with an additional pore mode with a diameter of 150 μm added to the Gyroid structure leading to significantly greater experimental bone tissue ingrowth in the sample.

Keywords: traumatology, bone repair, bone substitute, 3D-printing

For citation: Shcherbakov IM, Evdokimov PV, Larionov DS, Putlayev VI, Shipunov GA, Danilova NV, Efimenko AYu, Novoseletskaya ES, Dubrov VE. Experimental evaluation of $CA_3(PO_4)_2$ bbased bone substitutes using rat femoral defect models. *Genij Ortopedii*. 2025;31(2):226-236. doi: 10.18019/1028-4427-2025-31-2-226-236.

INTRODUCTION

Replacement of bone defects is an important issue of modern traumatology and orthopedics [1–5]. Autologous bone grafts are limited in supply and allo- and xenograft bone is an attractive alternative [6–11]. With increasing technological advances there is a spectrum of bone-substituting materials, and the choice of the effective option is essential for biomedical research [3, 7, 12–17].

Various chemical substances differing in the mechanical properties and bioresorbability are used to develop new bone-substituting materials [12, 18–21]. Three-dimensional structure of the material is important for bone replacement to determine the process of new bone formation and the rate [22, 23]. However, there are no criteria reported in the literature to allow the choice of the material architecture to accelerate bone ingrowth. Spongy bone tissue is a complex irregular three-dimensional structure with a porosity of 50 to 90 % and a pore size of 300 to 500 μm with non-homogeneous anisotropic properties [24]. A structure based on a gyroid-type triply periodic minimal surface is one of the optimal structures in terms of compromise between permeability and strength having high relative rigidity [25].

The **objective** was to determine the effect of the three-dimensional structure and pore size of tricalcium phosphate based bone substitute materials on osteoconduction using a critical diaphyseal defect of the rat femur.

MATERIAL AND METHODS

Bioresorbable materials are new-generation macroporous ceramic 3D structures based on calcium orthophosphate $Ca_3(PO_4)_2$. Photocurable emulsions were used to synthesize highly porous ceramic materials. The method used to obtain them was reported [25]. The Cylinders material was used as the initial architecture. The material was characterized by the total porosity of about 55 % with the size of the main pores of 300 μm, the transitions of 50 μm, while the pores were disarranged. Stereolithographic 3D printing using an Ember DLP printer (Autodesk, USA) was employed to form materials with Gyroid architecture and three-dimensional models of the structures were created using the Monolith (Autodesk, USA) and Fusion 360 (Autodesk, USA) software. The total porosity of the material (Gyroid material) was about 70 % with the main channels of 1250 μm and the transitions of 750 μm between them to provide maximum permeability of the architectures (Fig. 1, left). The use of photocurable emulsions allowed an additional pore mode to be initiated in a given ceramic 3D framework. In this series, materials with an additional pore mode and an average size of 50 (Gyroid-50 μm material) and 150 μm (Gyroid-150 μm material) were examined (Fig. 1, right). The total porosity of the created materials by volume was about 85 %.

The study received a favourable opinion from the relevant Research Ethics Committee of the Lomonosov Moscow State University (approved at the meeting on 11.02.2021, reg. No. 123-zh). Animal care and all experimental procedures were in accordance with the "Guidelines for the Maintenance and Care of Laboratory Animals" (Interstate Standard GOST 33216-2014 "Rules for the Maintenance and Care of Laboratory Rodents and Rabbits"). The experimental study involved 66 male Wistar rats Rattus norvegicus aged 20–22 weeks from the SPF Vivarium of the ICG SB RAS (Institute of Cytology and Genetics SB RAS). The animals were housed three to a cage in a vivarium where rats had unlimited access to water and food. The defect was simulated and filled with the material to be examined (Fig. 2) using the method previously reported [16].

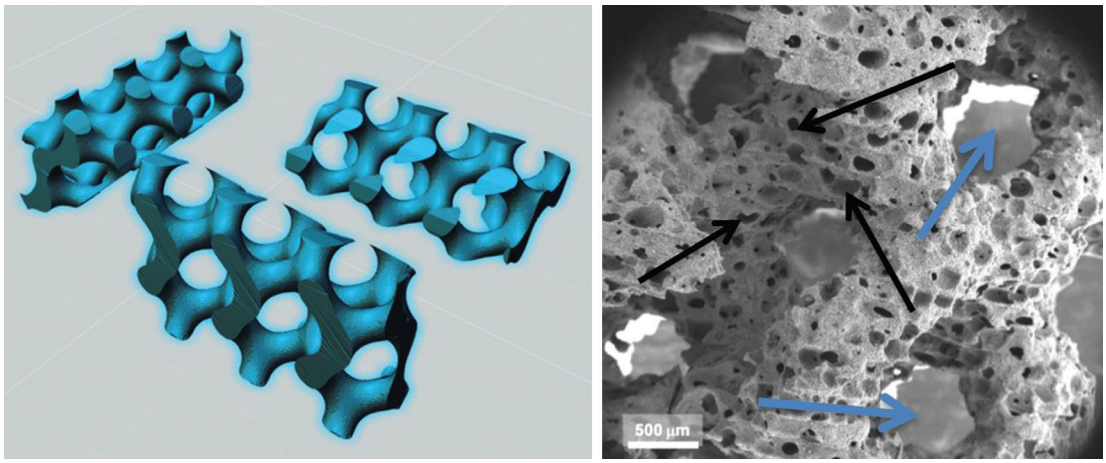


Fig. 1 Three-dimensional structure of the bone-substituting materials created. A graphic computer model of the Gyroid material structure is on the left. A scanning electron micrograph of the Gyroid-150 µm material is on the right (magnification 50 times). A view from the main pore. Transitions between the main pores with a diameter of 750 µm (blue arrows) and additional mode pores with a diameter of 150 µm (black arrows) can be seen

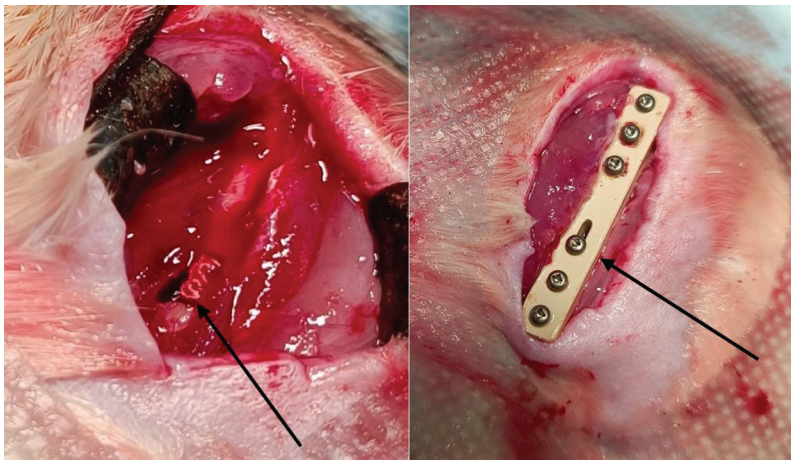


Fig. 2 Progress of the operation: a view of the surgical wound with a defect filled with implanted material (left, indicated by the arrow) and the bone fixed with a polyetheretherketone plate and titanium screws (right, the plate is indicated by the arrow)

The animals were divided into 4 groups of 16 animals each, depending on the implanted material. Eight rats from each group were euthanized using a standard method and a CO_2-chamber at 3 and 6 months after the operation with the material collected (femur with a defect) for histological examination. Samples for histological examination were prepared using a standard technique [16]. Blind histometric analysis was performed to evaluate the results. Images of histological preparations were obtained using a Leica DM LB2 light microscope (Carl Zeiss) and an AxioCam ICc3 digital camera (Carl Zeiss). The digitized images were converted to JPEG format. Histometric evaluation was performed using the Fiji program [26] at a magnification of 10 times and the area of newly formed bone measured in the lacunae of the materials as a percentage of the total area of the defect. For each sample, calculations were performed using two preparations; a total of 16 values were obtained for each period in each group. The results of each group were presented as the mean and standard deviation. To establish the statistical significance of differences, the nonparametric Kruskal-Wallis criterion was calculated using the StatSoft Statistica 10.0 (2011) program separately for the groups with a withdrawal period of 3 months and with a withdrawal period of 6 months.

RESULTS

Two animals died during the experiment from complications associated with anesthesia. The remaining animals underwent surgery and survived uneventful to the euthanization. The average weight of rats was (488 ± 54) g at the time of introduction to the experiment, (611 ± 32) g at 3 months

and (653 ± 56) g at 6 months. No significant difference in weight and the increase was recorded between the groups (Table 1).

Table 1

The weight of animals at the time of the operation and withdrawal from the experiment

Group	Body weight at the time of inclusion in the experiment, g	Body weight at the time of withdrawal from the experiment, g	
		at 3 mo	at 6 mo
Cylinders	460 ± 38	606 ± 59	649 ± 71
Gyroid	453 ± 42	616 ± 45	645 ± 83
Gyroid-50 microns	513 ± 26	620 ± 34	709 ± 72
Gyroid-150 microns	507 ± 36	589 ± 40	692 ± 74

No changes were seen in the behavior of the animals postoperatively, the rats moved on four legs without attempts to limit the load. Neither wound infection nor mechanical complications from the implant and the bone were detected.

Histological sections of the defect area revealed a rectangular gray formation structured as the implanted material in the **Cylinders** group at 3 months. There were rounded areas at the implant site with no fillings that indicated material resorption. Areas of bone tissue ingrowth were detected in the pores of the implant (Fig. 3). There was an increase in the no-fillings areas at the implant site at 6 months indicating material resorption, in the half adjacent to the soft tissues, in particular. Vague smooth implant contours were noted due to resorption. Areas of bone tissue ingrowth were detected in the implant pores (Fig. 3) with the maximum concentration seen noted at the site of the bone-substituting material adjacent to the bone marrow canal. An increase in bone ingrowth in the pores of the material could be noted in dynamics, compared with 3 months.

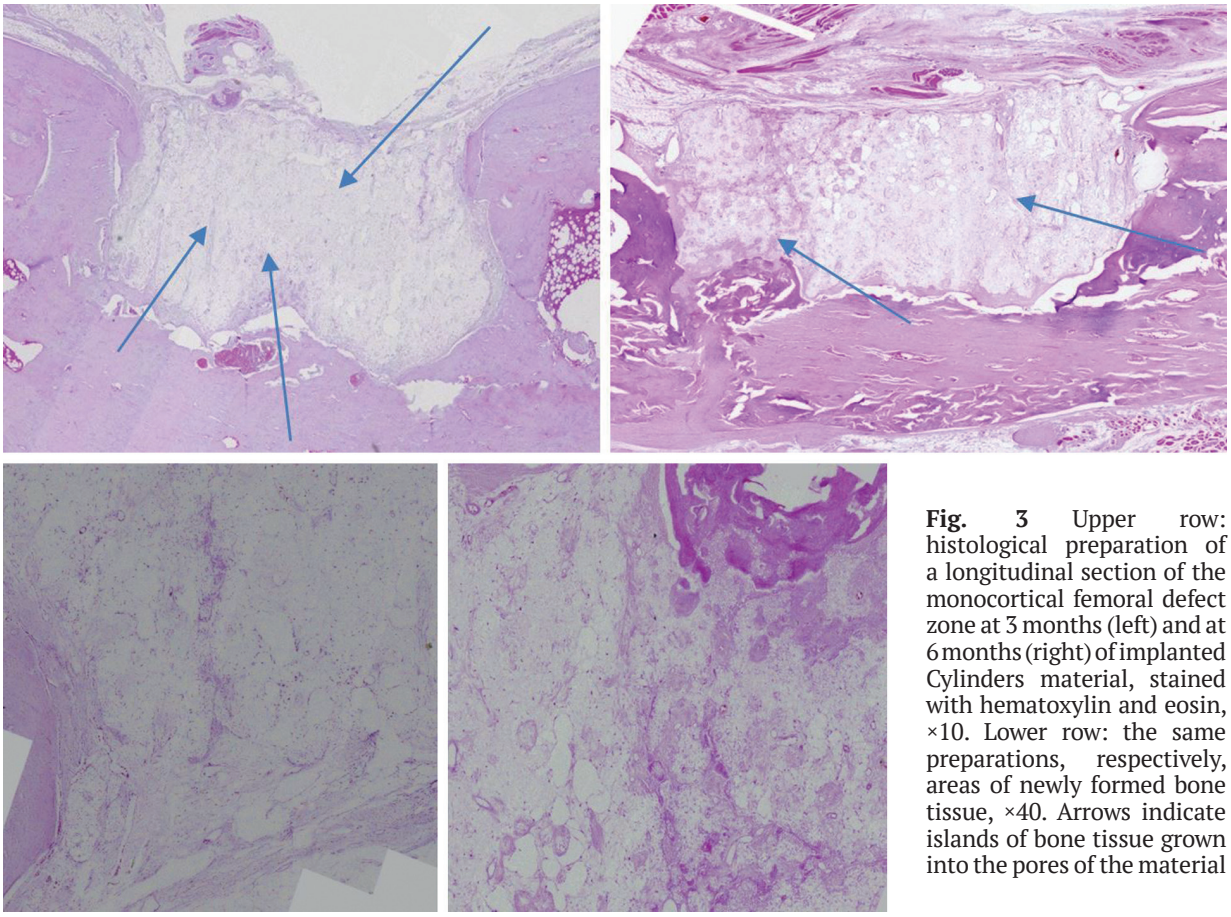


Fig. 3 Upper row: histological preparation of a longitudinal section of the monocortical femoral defect zone at 3 months (left) and at 6 months (right) of implanted Cylinders material, stained with hematoxylin and eosin, ×10. Lower row: the same preparations, respectively, areas of newly formed bone tissue, ×40. Arrows indicate islands of bone tissue grown into the pores of the material

Zones of preserved structure of the material were noted at the defect site at 3 months and were represented by gray fields with single cells along the perimeter and large pores at the site of material resorption in the **Gyroid** group. Fat and connective tissue grew into the implant from the soft tissue side, and compact bone tissue grew into the implant from the bone side. The material pores were filled with connective tissue and single bone tissue ingrowths. The material was limited by compact bone tissue on the side of the medullary canal (Fig. 4). A large-mesh network of voids could be seen in the defect area at 6 months and remained in place of the material after decalcification. Bone tissue ingrowth was noted as small islands over the whole section area repeating the contours of the pores (Fig. 4).

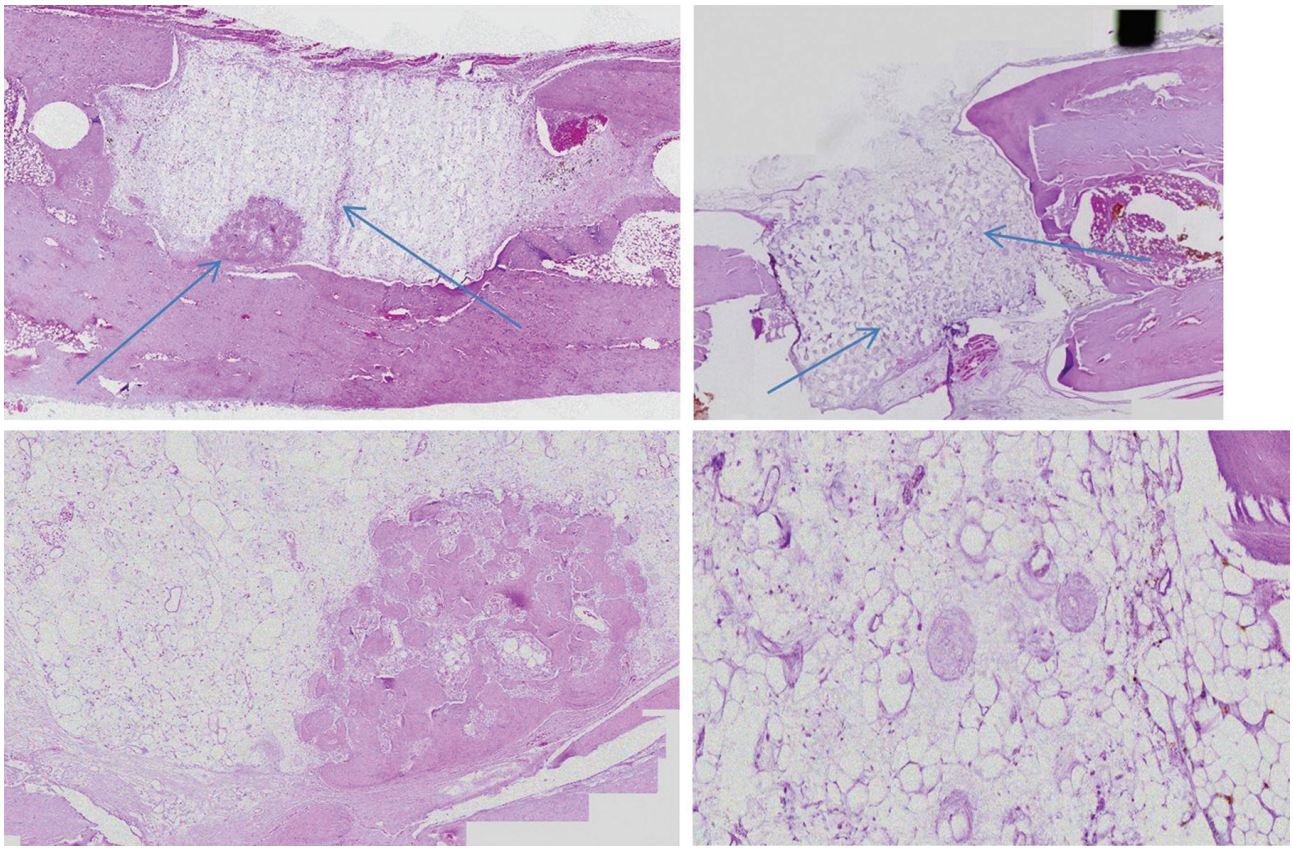


Fig. 4 Upper row: histological preparation of longitudinal section of the monocortical defect zone of the femur at 3 months (left) and at 6 months (right) of implanted Gyroid material, stained with hematoxylin and eosin, ×10. Lower row: the same preparations, respectively, areas of newly formed bone tissue, ×40. Arrows indicate foci of bone tissue ingrowth in the implant

Bone ingrowth into the pores was noted between the elements of the material in the **Gyroid-150 μm** group at 3 months, repeating the architecture of the implant. Massive resorption of the material and the replacement with mature bone tissue was noted in the zone adjacent to the bone marrow canal. Bone ingrowth into the pores of the material was noted at 6 months with signs of resorption, and no statistically significant difference was found at the site of newly formed bone tissue compared to 3-month samples (Fig. 5).

The implanted material was clearly visible in the **Gyroid-50 μm** group at 3 months with ingrowth of bone tissue islands seen from the side of the medullary canal (Fig. 6). Ingrowth of connective tissue into the material was noted on the defect side.

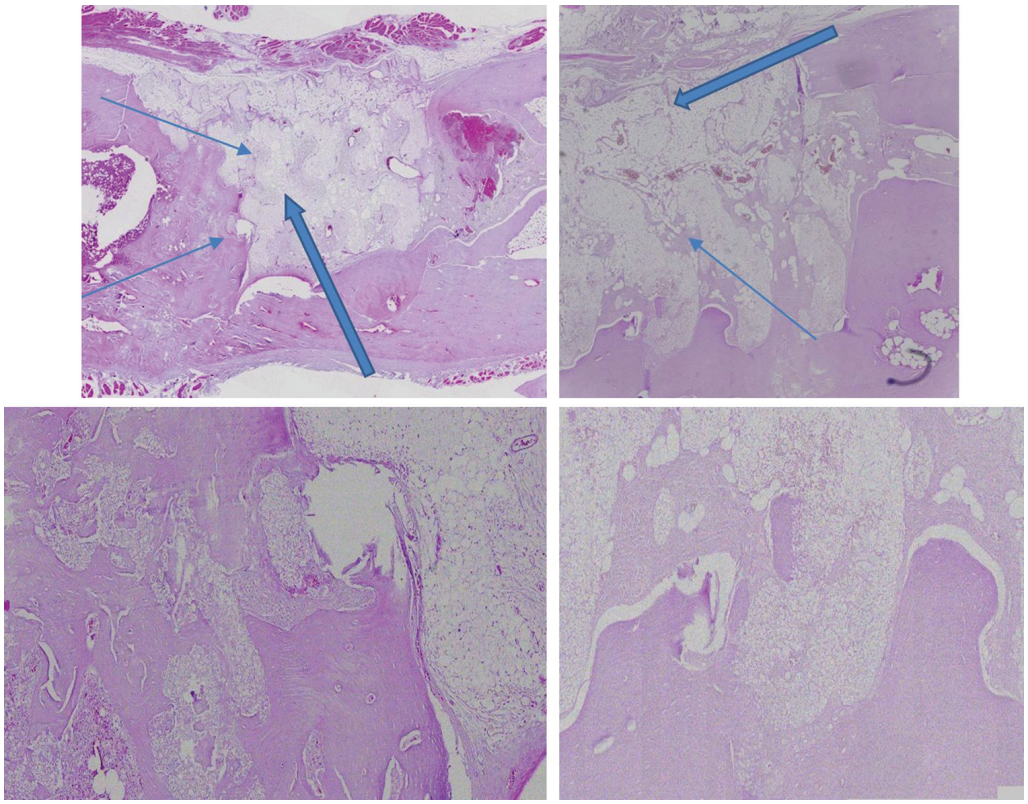
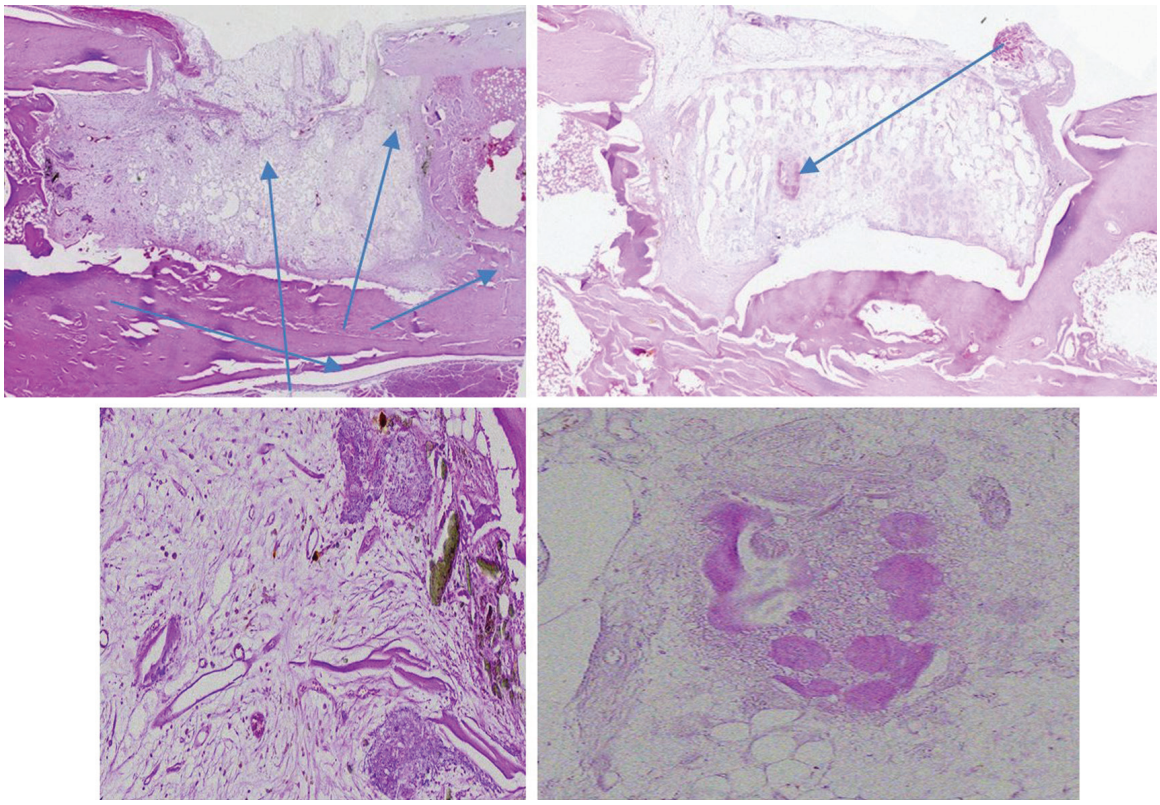


Fig. 5 Upper row: histological preparation of a longitudinal section of the monocortical defect zone of the femur at 3 months (left) and at 6 months (right) of implanted Gyroid-150 μm material, stained with hematoxylin and eosin, ×10. Lower row: the same preparations, respectively, areas of newly formed bone tissue, ×40



Fid. 6 Upper row: histological preparation of a longitudinal section of the monocortical defect zone of the femur at 3 months (left) and at 6 months (right) of implanted Gyroid-50 μm material, stained with hematoxylin and eosin, ×10. Lower row: the same preparations, respectively, areas of newly formed bone tissue, ×40. Thin arrows indicate islands of bone tissue grown into the pores of the material

An increase in the number and area of bone islands was noted in dynamics deep in the implant, with zones of material resorption observed as rounded voids in the Gyroid-50 μm group at 6 months. The implant was overgrown with bone tissue on the side of the bone marrow canal and structured as the cortical bone (Fig. 6).

Summarized data on the area of newly formed bone tissue are presented in Table 2.

Table 2

New bone tissue formed at the defect site distributed between the study groups: percentage of the total area, mean ± sample standard deviation

Group	Area of newly formed bone tissue at the time of withdrawal from the experiment, %	
	at 3 months	at 6 months
Cylinders	11 ± 4	31 ± 6
Gyroid	14 ± 5	29 ± 4
Gyroid-50 microns	17 ± 7	27 ± 8
Gyroid-150 microns	**39 ± 5***	**41 ± 7***

Note: values marked with * are significantly different from those in other groups for an observation period, Kruskal – Wallis test, $p < 0.05$,

The area of newly formed bone tissue was statistically greater in the Gyroid-150 μm group compared to that in the other study groups. Bone ingrowth into the material was observed over time in all other groups indicating the presence of osteoconductive properties in all the materials examined.

DISCUSSION

Critical size bone defects that cannot self-repair are a challenge. Autologous bone grafts, cadaveric bone and animal bone are limited in supply for various reasons including limited quantity, risk of infection, immune reactions, and the use of synthetic bone-substituting materials is an attractive alternative in modern regenerative medicine. Over the past 10 years, 3D printing has experienced significant advancements in building materials with a controlled structure, and there is a search for the most effective samples to be used for bone replacement bone, which is the subject of numerous studies in recent years. Our study aimed to establish the influence of three-dimensional pore organization on the osteoconductive properties of bone-substituting material. The influence of the structure of porous material on the osteoconductive properties of bone-substituting blocks created from them has been widely discussed in the literature in recent years [27–31]. Small pores have been recognized to facilitate cell adhesion and the primary differentiation, but hinder vascular growth and impair the nutrition of newly formed tissues. Very large pores reduce the mechanical properties of the material blocks, which may lead to the premature destruction and disruption of ingrowth, which is important for repair of segmental diaphyseal bone defects [32]. Creation of pores of different diameters in one sample can be practical for the problem solution providing high porosity and maintaining the mechanical properties of the material, which is what our work was devoted to.

The choice of the Gyroid architecture relies on our previous works and the studies reporting theoretical advantages of the architecture for the process of cell migration. Seehanam et al. [33] compared the Gyroid and Diamond structures on various biomechanical parameters and the ability to stimulate cell growth and suggested the advantage of the Gyroid architecture with a main pore size of 500 μm. The results of using the materials in vivo in our series are comparable with those reported by other researchers. Wu at al. [34] compared osteoconductive properties of a ceramic material based on Mg-substituted vallostonite with a pore diameter of 200, 320, 450 and 600 μm and a cubic cell structure using a model of a critical size defect of the rabbit femoral

condyle at the time intervals of 2 to 16 weeks. The Cylinders group in our series corresponded to a material with a pore size of 320 μm, and the Gyroid group was compliant to a pore size of more than 600 μm. As reported by the above authors, the best osteoconductive and osteoinductive properties were shown by structures with a larger pore diameter. The amount of bone tissue formed for the material with pores of 400 and 600 μm in a period of about 3–4 months (30–35 %) corresponds to that of the Gyroid group with an additional pore mode of 150 μm [34]. The authors used a defect in the spongy bone of the femoral metaepiphysis close to the red bone marrow zone, and we reported the defect located in the diaphysis. The specific feature of our series was the use of a Gyroid-type structure with the addition of another pore level, that showed a significant increase in the ingrowth of bone tissue into the material with a diameter of 150 μm.

Wang at al. [35] reported positive results in increased porosity of a tricalcium phosphate-based material in the form of increased sectional bone formation at the middle level of the material. A cranial vault defect bones with membranous osteogenesis was simulated by the authors, and the material was obtained by foaming a mixture of tricalcium phosphate powder, i.e. without a clear 3D organization of pores. Large longitudinal pores of 1 mm in diameter were formed by drilling in the original block with the original pores of 550 μm in diameter and the total porosity of 80 %. The block thickness was 1.5 mm and the diameter measured 8 mm. The authors reported the level of bone tissue formation in the material up to 40-50 % at 3 months, however, the bone tissue areas imitated the pore sizes, and the differences between the porous blocks and the non-porous material were seen in the middle.

Lim et al. [36] examined hydroxyapatite tricalcium phosphate ceramic scaffolds implanted in rabbit calvarial models. The animals were observed for eight weeks, and six animals were euthanized in the fourth and eighth weeks. The material contained only large main pores ranging in size from 0.8 to 1.4 mm with a step of 0.2 mm without additional interconnectivity. The authors reported 10 % bone tissue growth by two months with no relationship observed between pore size and bone regeneration at the stage. Compared to our series, the authors used shorter observation periods, a simple scaffold shape and absence of pores in the materials, a model of a calvarial defect, which could caused inferior histological results.

Shibahara at al. [37] examined the effect of micropores on the osteoconductive properties of a ceramic bone-substituting material (carbonate apatite in the study). However, the main pores sized smaller (about 300 μm) having linear structure as honeycomb, and micropores of about 1 μm located randomly. This material corresponds to the architecture of the Cylinder in our series. The *in vivo* properties were tested on a rabbit ulna defect model with additional fixation using a plate and screws at 1 and 4 months. The area of newly formed bone tissue was only 12 % the group with large pores and large micropores even after 4 months,and was less than 10 % in the groups with smaller pore sizes, which is comparable with our results in the Cylinders group. This indicates the need to create a main group of pores with a diameter greater than 1 mm for faster tissue ingrowth, and modification should be carried out in the pore interconnectivity and micropores to create conditions for cell differentiation and accelerate resorption of bone-substituting material.

Jiao et al. [32] studied the effect of different porosities (60 %, 70 % and 80 %) of bone-mimicking tantalum scaffolds on the osteoconductive capacity. The size of the main pores was 450, 600, and 800 μm, respectively, with interconnectivity of 100 μm. The authors reported the bionic bone trabeculae structure and 3D conformation of the porous tantalum scaffold having comparable mechanical properties to human cancellous bone. A model of a non-critical metaphyseal defect of the rat femoral condyle measuring 3 mm in diameter and 5 mm in height was used for *in vivo*

studies at 6 and 12 weeks after implantation. The authors reported that the groups with 60 %, 70 % and 80 % porosity had 14.3 %, 28.6 %, and 23.3 % of new bone area at 12 weeks, respectively, which was inferior to the results in the Gyroid group measuring 150 μm after 3 months, and greater than the area of newly formed bone tissue in the other groups. The explanation for the fact could be the greater overall porosity of our material (about 85 %) and a more complex pore structure, which had a fundamental effect on the osteoconductive properties of the material.

Metal (titanium, tantalum and their alloys) is not associated with resorption and can maintain a constant pore size throughout the osseointegration period. We agree with the authors who suggest there are no unified approaches to the study of bone substitute materials in animal models, which would hamper comparison of results and development of recommendations for clinical practice [32]. We conclude that there is a positive effect with a Gyroid structure with larger diameter of the main pores (more than 1 mm) and with additional connecting channels with an average diameter of 150 μm added to the material structure during printing. This facilitates the increase of newly formed bone tissue and improve the osteoconductive properties of the ceramic-based bone-substituting material. The phenomenon may occur due to the pore surface with a certain curvature effecting the differentiation of progenitor cells along the osteoblastic pathway, which is reflected in a larger amount of ingrowing bone tissue. However, the absence of an increase in the amount of newly formed bone tissue when comparing observation periods of 3 and 6 months indicates an insufficient capacity for resorption of the selected substance (tricalcium phosphate), since the maximum germination is achieved in the early stages and is subsequently limited by the preservation of the material in the defect volume. Therefore, improved osteoconduction can be associated with optimization of the material architecture and the choice of a substance with greater resorption capacity for its construction.

CONCLUSION

An additional pore mode of 150 μm in diameter added to the structure of ceramic materials based on Gyroid tricalcium phosphate can facilitate a statistically significant increase in the amount of newly formed bone tissue and improvement of the osteoconductive properties of the material.

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

Funding *The research was performed as part of the RSF grant 20-79-10210. The results presented in the work were obtained using the equipment purchased at the expense of the Moscow University Development Program.*

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The article was submitted 18.03.2024; approved after reviewing 06.12.2024; accepted for publication 05.02.2025.

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Original article
https://doi.org/10.18019/1028-4427-2025-31-2-237-244

Prediction of impaired consolidation of limb long-bone fractures using neural network analysis

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Abstract

Introduction Impaired reparative regeneration in patients with fractures is the most common complication; immunogenetic mechanisms play a leading role in its pathogenesis. Many researchers are engaged in the search for an "ideal" diagnostic marker. For this purpose, neural networks have been increasingly used, which allow not only to predict various pathological conditions but also to determine reliable options for prevention and treatment.

The **purpose** of the study was to evaluate the effectiveness of predicting impaired consolidation of long-bone fractures of the extremities using the neural network data analysis.

Material and methods We examined 108 young patients (WHO classification) with fractures of lower limb long bones. The clinical comparison group consisted of 62 patients without complications at the age of 34.5 [18; 44] years. The study group included 46 patients of similar age (36 [18; 44]) years and gender with delayed consolidation. The control group included 92 practically healthy individuals. Exclusion criteria from the study were any concomitant disease, other location and nature of injuries, alcoholism, as well as inaccurate reduction of bone fragments, and repeated operations. Patients who received antiresorption therapy and calcium supplements in the prehospital stage were also excluded. Laboratory (genetic) studies included determination of carriage of polymorphic molecules — *TNFRSF11B-1181(G>C), IL6-174(C>G)*, *TGFβ1-25(Arg>Pro), EGFR-2073(A>T)* and *VDR(BsmI283G>A)*. Amplification was carried out using primer sets Litekh-SNP (Russia). The risk of developing delayed consolidation was assessed using SPSS Statistics Version 25.0 (Neural Networks module). The predictive performance of the neural network was assessed using ROC analysis.

Results For determining the importance of the independent variable, the following gradation was noted: *TGFβ1-25(Arg>Pro)* gene polymorphism — 100 %; gene polymorphism *TNFRSF11B-1181(G>C)* — 97.1 %, gene polymorphism *VDR-BsmI283(G>A)* — 34.7 %; *IL6-174(C>G)* gene polymorphism — 31.5 %; polymorphism of the *EGFR-2073(A>T)* gene — 15.3 %. The percentage of incorrect predictions was 8.3 %. Area under the curve of ROC analysis (AUC) = 0.91[0.85–0.98], $p < 0.001$. The specificity of the resulting model is 0.95 %, sensitivity is 0.87 %, accuracy is 91.7 %.

Conclusion The use of the neural network for predicting delayed consolidation of fractures using data on the carriage of certain gene polymorphisms has a sufficient degree of accuracy (91.7 %), which indicates that the introduction of the neural network analysis into practical medicine is promising.

Keywords: consolidation disorder, genetic markers, polymorphism, neural network analysis, neural network

For citation: Miromanov AM, Gusev KA, Staroselnikov AN, Mudrov VA. Prediction of impaired consolidation of limb long-bone fractures using neural network analysis. *Genij Ortopedii*. 2025;31(2):237-244. doi: 10.18019/1028-4427-2025-31-2-237-244.

INTRODUCTION

Despite advances in surgical treatment of patients with musculoskeletal injuries, slow bone tissue reparation processes are quite frequent, and about 10 % of fractures end in nonunion [1, 2, 3]. The issue of reparative regeneration disorders in patients without systemic and local risk factors remains open. Currently, studies have been conducted that show the leading role of human immunogenetics in this complication, and certain variants of polymorphic gene carriage and their abnormal expression can be decisive in the mechanism of consolidation disorders [4, 5, 6, 7]. However, the range of such studies is still not so wide and requires further research.

In the modern world, the role of innovative technologies for analyzing the data obtained is increasing. The use of neural networks and artificial intelligence (AI) in contemporary healthcare may solve many problems, in particular, not only predict various diseases/complications but also to determine reliable options for the prevention and treatment of these pathological conditions [8, 9, 10].

The **purpose** of the study was to evaluate the effectiveness of predicting impaired consolidation of long-bone fractures of the extremities using the neural network data analysis.

MATERIALS AND METHODS

The ethical principles of the Helsinki Declaration of the World Medical Association (amended in 1964, 2011) were followed in the work with the subjects of this study.

This report was prepared as part of the comprehensive research work RK 034 (02, 03), registration number AAAA-A16-116063010015-6.

A total of 108 young patients (according to WHO grading of age) with long-bone fractures of the lower extremities were examined. The clinical comparison group consisted of 62 patients without complications aged 34.5 years [18; 44], the main study group were 46 patients of the same age (36 [18; 44]) with delayed consolidation, the control group included 92 practically healthy people comparable in age (35.0 [18; 44]) and gender. The criteria for non-inclusion in the study were any concomitant diseases, other locations and nature of injuries, alcoholism, as well as incomplete alignment of bone fragments during reduction and repeated operations. Patients who received antiresorptive therapy and calcium preparations at the prehospital stage were also excluded.

The diagnosis of delayed consolidation was made based on the RUST consolidation assessment [11] and radiographic criteria described in the clinical guidelines. Patients were treated in accordance with the clinical guidelines approved by the Russian Ministry of Health (Femur fractures (except for the proximal femur), 2021; Tibial fractures, 2021).

The material for molecular genetic analysis was DNA samples isolated from the peripheral blood leukocytes of the study subjects. For the study of SNV (Single Nucleotide Variant) point mutations of tumor necrosis factor receptor (TNFRSF11B) at position 1181 (G>C), interleukin-6 (IL6) at position 174 (C>G), transforming growth factor β_1 ($TGF\beta_1$) at position 25 (Arg>Pro), epidermal growth factor receptor (EGFR) at position 2073 (A>T) and vitamin D (VDR) (BsmI 283G>A) were selected. Amplification of gene fragments was performed in a Bis-M111 thermal cycle (Bis-N Ltd, Novosibirsk). Litekh-SNP primer sets (Russia) were used in the work. Visualization of amplification products was performed using electrophoresis in 3 % agarose gel with the addition of ethidium bromide in transmitted ultraviolet light. The results were interpreted according to the manufacturer's instructions.

The risk of delayed consolidation was assessed using SPSS Statistics Version 25.0 (Neural Networks module). The prognostic characteristics of the neural network were assessed using ROC analysis. For conducting statistical analysis, the authors were guided by the principles of the International Committee of Medical Journal Editors (ICMJE) and the recommendations on Statistical Analysis and Methods in Published Literature (SAMPL) [12].

To test the significance of differences in quantitative parameters between the groups, descriptive statistics methods and a number of nonparametric criteria were used. The distribution law of that considers the sample number in groups was assessed using the Shapiro – Wilk criterion. The analysis of differences in quantitative parameters of the studied samples was performed using the Mann – Whitney U-test. Qualitative data were described as absolute (*n*) and relative (%) values. To compare the nominal data of the two study groups, the Pearson χ^2 criterion was used. If the number of expected cases was less than 10, the Pearson χ^2 test with Yates's correction for continuity was used for comparison; if less than 5, the Fisher exact test was used. A value of $p < 0.05$ was considered statistically significant [13].

RESULTS

The prediction model used only genotypes of the studied gene polymorphisms (*TNFRSF11B, IL6, TGFβ$_1$, EGFR, VDR*) (Table 1, Table 2).

Table 1

Frequency of carriage of the studied SNVs among healthy individuals and groups of patients with long bone fractures

Genotype		Control group (*n* = 92)	Comparison group (*n* = 62)	Main study group (*n* = 46)
TNFRSF11B-1181G>C	Genotype GG OR [95 % CI]	0.511	0.161 0.18 [0.08–0.41]	0.696 2.19 [1.03–4.63]
	Genotype GC OR [95 % CI]	0.326	0.452 1.7 [0.88–3.30]	0.196 0.5 [0.22–1.17]
	Genotype CC OR [95 % CI] χ^2 *p*	0.326	0.387 3.24 [1.53–6.88] 21.12 < 0.001	0.109 0.63 [0.21–1.84] 4.3 0.12
IL6-174C>G	Genotype CC OR [95 % CI]	0.326	0.323 0.98 [0.49–1.96]	0.174 0.44 [0.18–1.05]
	Genotype CG OR [95 % CI]	0.467	0.468 1.00 [0.53–1.91]	0.391 0.37 [036–1.5]
	Genotype GG OR [95 % CI] χ^2 *p*	0.207	0.210 1.02 [0.46–2.25] 0.00 1	0.435 2.96 [1.37–6.39] 8.63 0.01
TGFβ$_1$-25Arg>Pro	Genotype ArgArg OR [95 % CI]	0.630	0.581 0.81 [0.42–1.57]	0.282 0.23 [0.11–0.5]
	Genotype ArgPro OR [95 % CI]	0.240	0.371 1.88 [0.93–3.79]	0.196 0.77 [0.32–1.85]
	Genotype ProPro OR [95 % CI] χ^2 *p*	0.130	0.048 0.34 [0.09–1.26] 4.91 0.09	0.522 7.27 [3.14–16.82] 25.47 < 0.001
EGFR-2073A>T	Genotype AA OR [95 % CI]	0.315	0.306 0.96 [0.48–1.93]	0.13 0.33 [0.12–0.85]
	Genotype AT OR [95 % CI]	0.598	0.597 1.00 [0.52–1.92]	0.37 0.39 [0.19–0.82]
	Genotype TT OR [95 % CI] χ^2 *p*	0.087	0.097 1.13 [0.37–3.42] 0.05 0.98	0.5 10.5 [4.15–26.54] 30.48 < 0.001
VDR-BsmI283G>A	Genotype GG OR [95 % CI]	0.359	0.468 1.57 [0.82–3.03]	0.196 0.43 [0.19–1.01]
	Genotype GA OR [95 % CI]	0.446	0.435 0.96 [0.5–1.84]	0.5 1.24 [0.61–2.53]
	Genotype AA OR [95 % CI] χ^2 *p*	0.196	0.097 0.44 [0.16–1.18] 3.43 0.18	0.304 1.8 [0.8–4.05] 4.44 0.11

Note: *p* — statistical significance of differences with control group

Table 2

Frequency of carriage of the studied SNVs among groups of patients with long bone fractures

Genotype		Group I (n = 62)	Group II (n = 46)	χ^2	p	OR [95 % CI]
TNFRSF11B-1181G>C	Genotype GG	0.161	0.696	32.06	< 0.001	11.89 [4.72–29.92]
	Genotype GC	0.452	0.196			0.3 [0.12–0.71]
	Genotype CC	0.387	0.109			0.19 [0.07–0.56]
IL6-174C>G	Genotype CC	0.323	0.174	6.99	0.03	0.44 [0.17–1.12]
	Genotype CG	0.468	0.391			0.73 [0.34–1.59]
	Genotype GG	0.210	0.435			2.9 [0.89–6.75]
TGFβ$_1$-25Arg>Pro	Genotype ArgArg	0.581	0.283	23.73	< 0.001	0.05 [0.01–0.17]
	Genotype ArgPro	0.371	0.196			2.42 [0.99–5.92]
	Genotype ProPro	0.048	0.522			3.51 [1.55–7.95]
EGFR-2073A>T	Genotype AA	0.306	0.13	22.25	< 0.001	0.34 [0.12–0.94]
	Genotype AT	0.597	0.37			0.4 [0.18–0.87]
	Genotype TT	0.097	0.5			9.33 [3.36–25.92]
VDR-BsmI 283 G>A	Genotype GG	0.468	0.196	11.94	0.003	0.28 [0.11–0.67]
	Genotype GA	0.435	0.5			1.3 [0.6–2.79]
	Genotype AA	0.097	0.304			4.08 [1.43–11.67]

Note: p — statistical significance of differences with control group

The analysis of SNV genotypes carriage frequency in patients with delayed consolidation revealed a prevalence of the mutant genotype of the *IL6* gene *(C174G), TGFβ$_1$ (A25P), EGFR (A2073T)* and *VDR (BsmI G>A)* by 2.1, 10.1, 5.1 and 3.1 times, respectively, in comparison with the clinical comparison group. In contrast, determination of the distribution frequency of the genotype of the *TNFRSF11B (G1181C)* gene polymorphism in the group with delayed consolidation revealed a significant prevalence of the normal homozygous variant in comparison with the first group by 4.3 times (Tables 1, Table 2).

Model of predicting consolidation disorders

In order to verify the obtained results of delayed consolidation prediction, we additionally performed neural network data analysis. As a model, we used a multilayer perceptron system based on the dependent variable (delayed consolidation), which is determined during the analysis of independent data (possible predictors). As independent variables (15 input neurons), we used the genotypes of the studied SNPs that have significant prognostic value. During the calculation, the neural network showed an architecture with an optimal number of hidden layers (5 and 4, respectively), which realize the prediction (Fig. 1). The creation of a relationship between the weighted sums of objects with the subsequent layer of values of these objects in both hidden layers is carried out by activating the sigmoid function. A similar function is recorded in the output layer (0; 1), which corresponds to the original study design. The sum of squares served as the error function. The output layer contained 1 target (dependent) variable (delayed consolidation is present / not present) (Fig. 1).

By determining the importance of an independent variable, the following gradation is noted: gene polymorphism *TGFβ$_1$-25(Arg>Pro)*; gene polymorphism *TNFRSF11B-1181(G>C)*; gene polymorphism VDR-BsmI283(G>A); gene polymorphism *IL6-174(C>G)*; gene polymorphism *EGFR-2073(A>T)* (Fig. 2).

The normalized importance was 100 %, 97.1 %, 34.7 %, 31.5 %, and 15.3 %, respectively. The percentage of incorrect predictions was 8.3 %.

The prognostic value of this neural network was assessed using ROC analysis (Fig. 3).

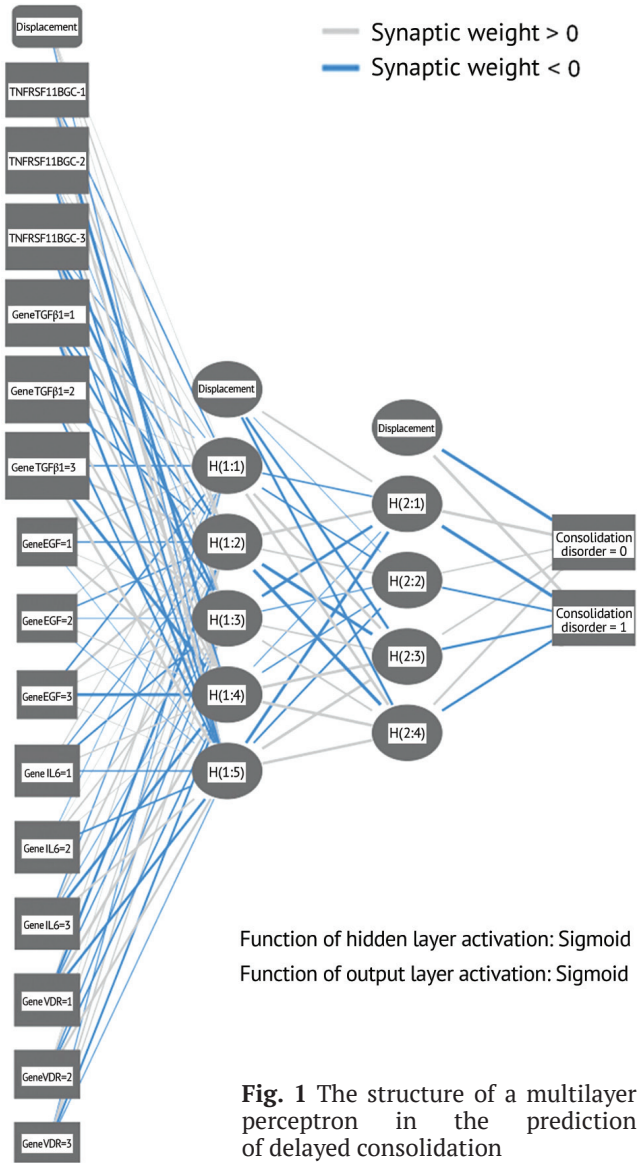

Fig. 1 The structure of a multilayer perceptron in the prediction of delayed consolidation

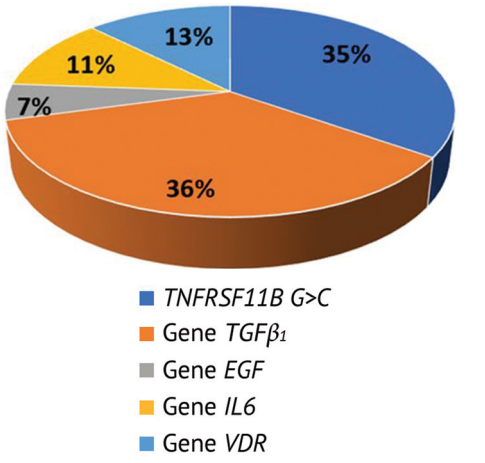

Fig. 2 Gradation in determining the importance of the independent variable

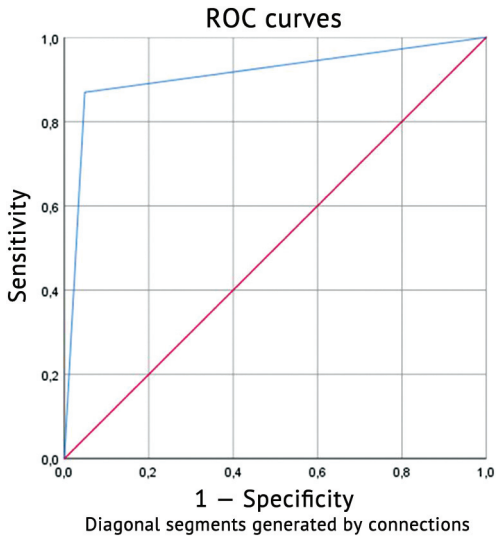

Fig. 3 ROC analysis of the possible delayed consolidation based on neural network data analysis

The area under the curve (AUC) = 0.91 (95 % CI = 0.85–0.98). The prediction accuracy of the prognostic model was 91.7 %, sensitivity was 0.87 %, specificity was 0.95 %. AUC was 0.91 (95 % CI = 0.85–0.98), $p < 0.001$.

DISCUSSION

Dominance of the mutant genotype of the gene I*L6(C174G), TGFβ$_1$(A25P), EGFR(A2073T), VDR (BsmI G>A)* and normal homozygous variant *TNFRSF11B(G1181C)* in the group with delayed consolidation indicate a high risk of consolidation disorders in case of their carriage [4].

The results of scientific works of the last decades show that hereditary factors play an important role in the development of improper functioning of the immune system. Programmed, genetically reduced or increased production of proteins in the macroorganism contributes to the ability of the immune system to respond differently to pathogens [4, 14]. In particular, the role of gene polymorphism of many cytokines was proven both in the development of pathological conditions and in their protective effect [15, 16].

However, these studies are not so many and they do not reveal the immunogenetic mechanisms of diseases and/or complications of the musculoskeletal system sufficiently [4].

To date, there are few studies where SNV genes act as "markers" of the risk of consolidation disorders. In particular, SNV of the SMAD6 transcription factor gene (T/T rs2053423) and the gene of the protein inhibitor of some morphogenetic proteins NOGGIN (G/G rs1372857) are associated with the development of atrophic pseudoarthrosis. Nonunion of the femoral and tibial diaphysis is more often observed in carriers of the platelet-derived growth factor (PDGF) haplotype A (rs1800814, rs62433334, rs13309625; CCG). A predisposition to inflammatory complications and impaired bone tissue reparation has been established in the carriage of the allele T and C/T codon 10 of the gene of the transforming growth factor-β (TGF-β) and the mutant gene of toll-like receptor-4 (TLR4) W/1. Also, the risk factors for consolidation disorders include carriage of the T/T genotype of the IL1β gene (rs2853550) and the nitric oxide synthase gene NOS2 (rs2297514). Moreover, the disruption of normal reparative regeneration is facilitated by the carriage of the haplotype A of the gene of the morphogenetic protein BMP4 (rs2761884, rs17563, rs2071047, rs762642; GTAA), the T/G genotype of the gene of the angiogenic inducer, rich in cysteine CYR61 (rs3753793), as well as the C allele of the gene of the fibroblast growth factor receptor FGFR1 (rs13317) [17].

The work of Zimmermann et al. shows the role of gene expression in normal fracture consolidation and its disorders. Thus, excessive expression of the genes of cysteine dioxygenase-1 (CDO1), cartilage oligomeric matrix protein (COMP), fibromodulin (FMOD), fibronectin 1 (FN1), clusterin (CLU), two-component signaling pathway system (TCS22), actin (ACTA2) and phosphodiesterase 4D-interacting protein (PDE4DIP) contributes to an imbalance in the work of the structure and function of cells during reparative regeneration, which leads to consolidation disorder of the nonunion type [18].

Experimental studies of Waki et al. demonstrate the role of microRNA (miRNA) in reparative regeneration and bone tissue remodeling. It was found that consolidation disorders are noted with increased expression of miR-31a-3p, miR-31a-5p, miR-146a-5p, miR-146b-5p and miR-223-3p [19].

In contrast, the study by Wang et al. noted that bone morphogenetic protein receptor type Ib (BMPR1b) is a potential target of miR-125b, inhibits it and promotes better restoration of bone tissue defects [20]. Thus, eleven miRNAs that can contribute to the disruption of reparative regeneration processes were experimentally identified [21].

There are also data on the carriage of SNV that is protective. It was established that the carriage of the G/T and G/G genotype of the neuronal specific retinoic acid-induced gene (FAM5C (rs1342913)), the G/G genotype of the bone morphogenetic protein 6 gene (BMP6 (rs270393)) and the G/G genotype of the matrix metallopeptidase gene 13 (MMP13 (rs3819089)) is associated with a favorable course of consolidation [22].

However, in order to confirm the significant role of the above SNVs in the processes of impaired fracture consolidation, the above data require further studies with a large number of patients and strict inclusion/exclusion criteria regarding concomitant pathology.

It has been shown that AI can fulfill key healthcare tasks, including disease diagnostics. A mathematical model based on sample data (training) is built using machine learning (ML) algorithms, which leads to the construction of predictions and/or specific solutions [23, 24, 25]. In particular, ML algorithms are most frequently used in personalized medicine. Such ML programs necessarily require supervised learning using an outcome variable [23].

Complex forms of ML, such as neural networks, are now increasingly used in medicine. Such technologies are also used in the diagnosis (prediction) of various pathological conditions [26]. As for the multilayer perceptron used in this work, it is classified as a feedforward network (from layer

to layer). The final calculation result is formed as a result of the difference between the responses of each layer. The accuracy of this model increases with an increase in the number of perceptron layers [27].

Thus, further studies of personalized immunogenetic mechanisms in a unfavorable course of the traumatic disease in fractures of long bones of the extremities, including the use of modern digital systems, can serve as a basis for detecting a predictor of complications and will allow making the necessary preventive corrections to treatment, which will contribute to a significant decrease in adverse outcomes.

Currently, the use of such technological solutions in practice is limited due to the lack of universal software and the initial stages of digitalization in the medical sphere. However, the creation of a unified digital contour and the introduction of AI which is gaining momentum within the framework of the federal project "Digital Healthcare Services" demonstrates the importance of digitalization of scientific medical technologies in all fields. In the near future, with the development of research on genetic predisposition to various diseases/complications, this technology, in our opinion, will be widely used.

The data we obtained are preliminary. We hope that further full-scale studies will substantiate the introduction of immunogenetic markers based on digital services in the diagnosis of complications in the pathology of the musculoskeletal system.

CONCLUSION

The use of a neural network to predict delayed fracture consolidation using data on the carriage of certain gene polymorphisms has proven to be quite effective, since it has a high degree of accuracy (91.7 %). It indicates the prospects for introducing neural network analysis into the field of traumatology and orthopaedics.

Conflict of interest *None declared.*
Funding *No sponsorship.*

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The article was submitted 18.09.2024; approved after reviewing 10.10.2024; accepted for publication 05.02.2025.

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Original article
https://doi.org/10.18019/1028-4427-2025-31-2-245-251

The diagnostic value of IL-6 and thymidine phosphorylase in the progression of osteosarcoma

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Abstract

Introduction Thymidine phosphorylase (TP) is known to be correlated with the pathogenesis of solid tumors. IL-6 is overexpressed in osteosarcoma, and data exist showing that high concentrations of IL-6 are linked to a poor prognosis.

The **aim** of this study is to investigate the diagnostic role of thymidine phosphorylase and IL-6 in the pathogenesis and progression in patients with osteosarcoma.

Materials and methods Thirty patients diagnosed with osteosarcoma (with age ranging between 15–44 years) were included in the current study. Those patients were distributed as 6, 15, 5 and 4 subjects for stages AI, BI, II and III respectively.

Results Statistical analysis pointed out that IL-6 tends to be increased patients in stage III (3.89 ± 0.34 ng/ml) compared to stage AI, BI and II: 1.48 ± 0.22 ng/ml, 1.55 ± 0.24 ng/ml and 2.45 ± 0.45 ng/ml respectively. Regarding thymidine phosphorylase, the current study also found that it tends be increased patients in stage III 8.3 ± 0.33 ng/ml comparing to stage AI, BI and II: 7.2 ± 0.92 ng/ml, 6.82 ± 1.14 ng/ml and 7.8 ± 0.22 ng/ml, respectively. The area under the curve (AUC) for thymidine phosphorylase was 0.87, with high significant difference $p < 0.001$, at a cut-off point 2.44, while the sensitivity and specificity ratios were 0.85, and 0.71 respectively. Regarding IL-6, the area under the curve (AUC) was 0.75, with significant difference $p < 0.038$, at a cut-off point 6.32, while the sensitivity and specificity ratios were 0.81, and 0.69 respectively. These biomarkers can also be used in the diagnosis and progression of osteosarcoma.

Discussion High levels of TP are expressions of tumor aggressiveness and poor prognostic factors. Some separate studies focus on TP expression at different osteosarcoma stages but their numbers are few, arguing that there is a gap in the current available literature. TP more recently has attracted significant attention for its involvement in cancer biology, especially with regard to its influence on disease pathogenesis and prognosis, according to available studies, TP plays a major part in the development of most malignant diseases, and particularly bone-related malignancies. It has been observed that TP promotes angiogenesis, is expressed in tumor-associated macrophages within the tumor stroma. TP expression has been studied in different types of cancer as a predictive body. New prognostic models for patients with bone cancer can be developed based on literature data.

Conclusion It is suggested that thymidine phosphate activity and IL-6 have a significant high diagnostic power in the diagnosis and progression of osteosarcoma.

Keywords: thymidine phosphorylase, IL-6, diagnosis power, osteosarcoma

For citation: Abdul Azeez BA, Abd Alhussain GS, Salman RS, Al-Fahham AA. The diagnostic value of IL-6 and thymidine phosphorylase in the progression of osteosarcoma. *Genij Ortopedii*. 2025;31(2):245-251. doi: 10.18019/1028-4427-2025-31-2-245-251.

INTRODUCTION

Osteosarcoma (OS), the most common primary bone malignancy, has a worldwide annual incidence of 3.4 per million population. The main pathophysiological mechanism includes multiple possible genetic drivers of the disorder associated with bone formation, leading to a progressive and metastatic malignant transformation. Although significant steps have been made towards the prognosis of patients with localized forms having the event-free survival rate above 60 % it generally remains grim in cases of those with metastatic versions and stays below 30 % [1]. The pathogenesis of osteosarcoma is polygenic and compiles genetic, molecular, and cellular aspects. While these sources do not straightly talk about osteosarcoma, knowledge of cancer genetics from other cancers can help direct views, including the genetic foundation for myeloproliferative neoplasms commented on by Vainchenker et Kralovics to the landscape of osteosarcoma at the molecular level [2]. Mutation of specific genes acting as tumor suppressors, for instance tumor protein p53 (TP53) and retinoblastoma 1 (RB1), defines most of the tumorigenic pathways in osteosarcoma. Experience has also shown that two to three driver gene mutations can transform osteoblasts to become osteosarcomas. This event likely follows loss of the p53 and Rb pathways based on what transformation has been shown to use across tumor types. Loss of differentiation may help explain why normal differentiation is blocked and sarcomas have primitive-appearing cells. The findings here are consistent with the strong genetic evidence indicative of the critical role of TP53 as a major tumor suppressor gene in human tumorigenesis and sarcoma genesis specifically [2]. Osteosarcoma is the third most common cancer in adolescence, after lymphomas and brain tumors, with an annual incidence of 5.6 cases per million children below 15 years of age. Osteosarcoma incidence is bimodal, peaking at 18 and 60 years of age, and is slightly more common in males. Peak incidence is in the second decade of life. Before the age of five, OS is rare. OS arises sporadically, with few cases related to known inherited defects in cell cycle regulation, but about 70 % of tumor specimens show a chromosomal abnormality. Some key mutated genes drive the initiation and progression of osteosarcoma [3]. Thymidine phosphorylase (TP) is a rather interesting enzyme that performs functions in nucleosides metabolism that executes salvage of pyrimidine with its functional activities in the pathway. First described in 1953, stimulated by TP is the reversible bioconversion of thymidine (TdR) into thymine and 2-deoxy-α-D-ribose-1-phosphate (dRib-1-P), as well as deoxy uridine phosphorolysis into uracil and 2-deoxy-α-D-ribose-1-phosphate. However, this reaction is reversible; TP's major function is catabolic. There are two different names for one molecule: angiogenic factor platelet-derived endothelial-cell growth (PD-ECGF) and TP. That metabolic role aside, TP plays an essential role in angiogenesis. The reaction is catalyzed by TP expressed as: TdR + H_2O ↔ thymine + 2-deoxy-α-D-ribose [4, 5]. The reversible nature of the reaction has arisen some debate as to the reality of TP catalyzing that reaction to any appreciable extent, such a view seems to dismiss a good body of consistent evidence, which is becoming available, that supports a catalytic function for this enzyme in pyrimidine degradation both *in vitro* and *in vivo* within the large majority of cells that TP is the primarily source of this activity [6–7]. Furthermore, several human cancers overexpress TP. The human TP gene is located on chromosome 22q13. TP is a dimer protein composed of two identical subunits non-covalently associated with a dimeric molecular mass of 51 kD [8]. Thymidine phosphorylase (TP) levels are expressed in some epithelial, glial cells, macrophages, and stromal cells. It is manifested in the nucleus. Here it regulates the supply of pyrimidine nucleosides that are necessary for DNA synthesis as well as in the cytoplasm, where it exhibits enzymatic activities [9]. IL-6 is a pleiotropic cytokine, synthesizing from various cells, including endothelial cells, keratinocytes, fibroblasts, and tumor cells; it is considered as the most important cytokine responsible for induction of events-ranging over many biological processes. IL-6 is a key inflammatory mediator implicated in the procession and advancement of osteosarcoma.

IL-6 binds with a receptor complex having α-gp80 (or IL-6R) and then further association with gp 130 [10]. IL-6 exerts inflammatory responses and has been impugned in the pathogenesis of a variety of cancers. High levels of this cytokine within the tumor microenvironment are also well documented to underlie the poor prognosis and aggressive nature of the tumor; Fisher et al., in 2014, focus their assertions that IL-6 may have paradoxical effects within the tumor microenvironment, dichotomously acting not only as a growth promoter but also as an apoptosis inhibitor. This duality perfectly underscores the complexity surrounding attempts to target this cytokine in cancer therapy [11]. In 2016, Tanaka et al. expound on how IL-6 contributes to inflammation-driven carcinogenesis, a process that takes place in colorectal cancer as basic mechanisms work similarly in osteosarcoma. This leads to expression in the tumors' proximity of factors like IL-6 that further enhance chronic signaling through pathways like JAK/STAT to advance and support tumorigenetic processes [12].

The **aim** of this study is to find out the diagnostic role of thymidine phosphorylase and IL-6 in the pathogenesis and stages progression in patients with osteosarcoma.

MATERIAL AND METHODS

Patients and data collection

A prospective study was performed at Al-Forat Al-Awsat Oncology Center in Najaf and Oncology Center in Baghdad/Iraq in the period from September 2023 to June 2024. Thirty patients diagnosed as having osteosarcoma, aged between 15–44 years were included in the present study. The general information (age, gender, and stage) was collected from the records of the patients in the Oncology Center. An amount of 5 milliliters venous blood samples were collected. The blood samples were allowed to coagulate in the gel tube at room temperature for 20 minutes. After coagulation, the samples were centrifuged at 2000xg for 20 min to obtain the serum, which was stored at (−20 °C) until assayed. IL-6 and thymidine phosphorylase were estimated in the serum by ELISA kit (My BioSource, USA) for serum thymidine phosphorylase and IL-6 determination. The Enneking system for staging classifies according to grade (I or II), intra- or extra-compartmental location (A or B), and the presence of metastases (III). So, stage IA is a low-grade intra-cortical tumor, IB is a low-grade extra-cortical tumor, IIA is a high-grade intra-cortical tumor, and IIB is a high-grade extra-cortical tumor. Metastatic disease instantly catapults to III stage [3].

Statistical Analysis

The SPSS software version 25.0 (SPSS, Chicago) was used for all the appropriate statistical analyses, the normality test which was used to test who want to continuous data for Shapiro Wilk test. All normally distributed data are acted as mean ± standard deviation. ANOVA test was used to find out the statistical difference in TP and Il-6 with patients' groups classified by tumor stages. The receiver operating characteristic curve (ROC) was used to test the predictive value of thymidine phosphorylase and IL-6 in predicting relapse among osteosarcoma patients. A *p*-value less than .05 was considered to indicate a statistically significant difference.

RESULTS

Patients who participated in the current study have a wide range of age (15–44 years) with a mean of (26.25 ± 6.22) years; the majority of them (43.33 %) within the interval (15–24) years, while those within (24–34) years constitute (40 %) of the sample. It seems that osteosarcoma is more common in male (60 %) compared to female (40 %). The distribution of patients according to the stage of osteosarcoma was as follows 6, 15, 5 and 4 individuals for stages AI, BI, II and III respectively (Table 1).

Table 1

Statistical distribution (frequency and percentage) of patients by their general characteristics

Items	Sub-group	Patients N = 30	
		Freq.	%
Age	15–24	13	43.33
	25–34	12	40
	35–44	10	33.33
Mean ± SD 26.25 ± 6.22			
Sex	Male	18	60
	Female	12	40
Stage	AI	6	20
	BI	15	50
	II	5	16.67
	III	4	13.33

Data regarding thymidine phosphorylase and IL-6 were found to follow normal distribution. Accordingly, these data were expressed as mean and standard deviation. The statistical analysis pointed out that thymidine phosphorylase tends to be increased in patients in stage III (3.89 ± 0.34 ng/ml) compared to stage AI, BI and II: (1.48 ± 0.22 ng/ml), (1.55 ± 0.24 ng/ml) and (2.45 ± 0.45 ng/ml) respectively (Fig. 1). Regarding IL-6, the current study also found that IL-6 tends to be increased in patients in stage III (8.3 ± 0.33 ng/ml) compared to stage AI, BI and II: (7.2 ± 0.92 ng/ml), (6.82 ± 1.14 ng/ml) and (7.8 ± 0.22 ng/ml) respectively (Fig. 2).

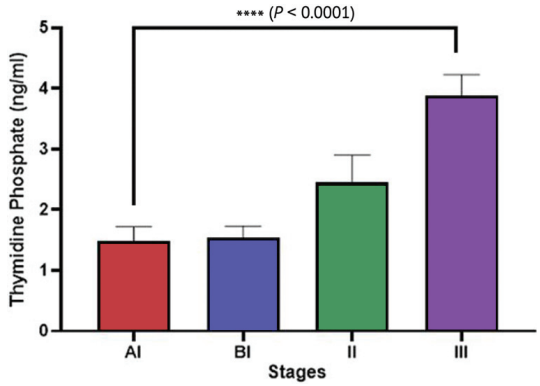

Fig. 1 Differences in serum thymidine phosphorylase in different stages of osteosarcoma

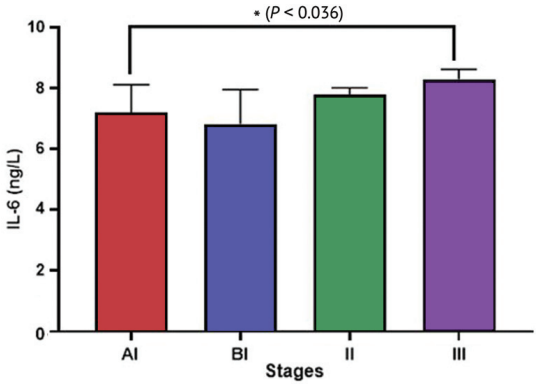

Fig. 2 Differences in serum IL-6 in different stages of osteosarcoma

The receiver-operating characteristic (ROC) curve analysis of thymidine phosphorylase and IL-6 was used in predicting relapse in patients with osteosarcoma. The area under the curve (AUC) for thymidine phosphorylase was 0.87, with high significant difference $p < 0.001$, at a cut-off point 2.44, while the sensitivity and specificity ratios were 0.85, and 0.71 respectively. Regarding IL-6, the area under the curve (AUC) was 0.75, with significant difference $p < 0.038$, at a cut-off point 6.32, while the sensitivity and specificity ratios were 0.81 and 0.69 respectively, as shown in Table 2 and Fig. 3.

Table 2

The areas under the curve (AUC), sensitivity and specificity of the biomarkers for the diagnosis of osteosarcoma

Biomarkers	(AUC)	Sig. p-value	Cut-off Point	Sensitivity (%)	Specificity (%)
TP	0.87	0.01	2.44	0.84	0.71
IL-6	0.75	0.038	6.32	0.81	0.69

TP — Thymidine phosphorylase; AUC — Area Under the Curve.

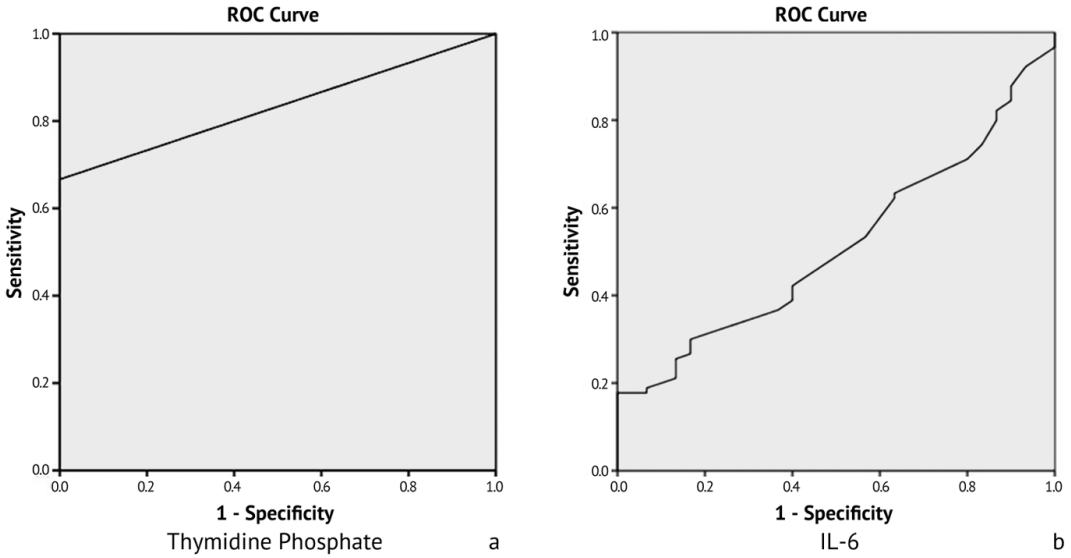

Fig. 3 Diagonal segment of the Receiver operating characteristic (ROC) curve for (a) thymidine phosphorylase and (b) IL-6 in for the diagnosis of osteosarcoma

DISCUSSION

Thymidine phosphorylase activity in 30 cases of osteosarcoma was analyzed by ELISA, including (6 cases at Stage AI, 15 at Stage BI, 5 at Stage II, 4 at Stage III). Thymidine phosphorylase is upregulated in a broad set of solid tumors and enhances progression of tumor via anti-apoptotic activity. High levels of TP are expressions of tumor aggressiveness and poor prognostic factors. The presence of high intracellular levels of this enzyme indicates increased chemosensitivity to pyrimidine antimetabolites [13–14]. This study exhibited that thymidine phosphorylase is present in high concentration in patients with higher stages of osteosarcoma. Although some separate studies focus on TP expression at different osteosarcoma stages, their numbers are few, arguing that there is a gap in the current available literature. Thymidine phosphorylase is an enzyme that acts in thymidine metabolism and more recently has attracted significant attention for its involvement in cancer biology, especially with regard to its influence on disease pathogenesis and prognosis [15]. Indeed, according to available studies, TYMP plays a major part in the development of most malignant diseases, and particularly bone-related malignancies [16]. Thymidine phosphorylase significantly promotes bone lesion formation by inhibiting osteoblast activity and stimulating osteoclast activity. This reaction models TYMP as a facilitator of myeloma-induced bone lesions and thus argues for its potential contribution to other inflammatory events accompanying bone cancer [16]. The other striking feature is TYMP's contribution to angiogenesis. It has been observed that TYMP, it promotes angiogenesis, is expressed in tumor-associated macrophages within the tumor stroma. This correlation between TYMP expression, angiogenesis, and poor prognosis underscores its potential as a key player in the tumor microenvironment: influencing both tumor growth and metastasis [17]. TYMP expression has been studied in different types of cancer as a predictive body. Thus, TYMP expression was found to be higher with a high systemic immune-inflammation index, suggesting that TYMP levels are related to patient outcomes [18]. This relationship is especially significant in the sensitivity of TYMP as a biomarker to postoperative patients with gastric cancer, which means that it has the potential to be developed as a clinical prognostic biomarker. The expression in tumor tissues with high SII values was much higher compared with those with low SII values, indicating their association with poor prognostic factors in various cancers other than bone cancer [19]. Xu et al. successfully isolated exosomes related to chemotherapy responses in osteosarcoma containing differentially expressed microRNA and mRNA. In view of this trend,

highly increased TYMP may indicate a more aggressive tumor phenotype and subsequently become a prospective aim for therapeutic intervention [20]. The present study highlighted that IL-6 is found in high concentration in patients with higher stages of osteosarcoma. Specific research on IL-6 in osteosarcoma is scanty, though several inferences can be made from those done in other malignancies. Increased levels of IL-6 have been documented in several inflammatory conditions as observations by Conti et al. (2020), who reported a significant increase of IL-6 in patients critically ill. In line with this, the author observed that proinflammatory cytokines like IL-6 could contribute to an immunosuppressive tumor microenvironment — a situation not suitable for effective anti-tumor immunity [21]. This association provided further insights into the role of IL-6 as a mediator of systemic inflammatory responses in disease severity, as might be relevant with osteosarcoma. There is accumulating evidence that IL-6 plays an essential role in regulating immune responses in cancer [22]. Data by Mazzoni et al. (2020) show the defect of immune cell cytotoxicity in severe COVID-19 patients that depends on IL-6. Secretion of such high levels of IL-6 would, therefore, skew the immune response to a more tolerogenic state. This leads to questioning whether analogously it could do so in immunotherapeutically treated osteosarcoma patients by providing room for immune response, thus lowering effectiveness of the strategy [23]. On the one hand, IL-6 is one of the pleiotropic cytokines that are surely critical in many physiological processes and simultaneously steers pathogenetic processes, especially inflammation and cancer. CAF-derived IL-6 is indeed strongly pro-tumorigenic and contributes significantly to stroma-dense growth in several cancer entities, including pancreatic ductal adenocarcinoma. Reports show recurring interplay between IL-6 and CAFs to create a pro-tumorigenic environment that supports further tumor growth and metastasis [24]. In line with this, it seems that IL-6 is not just a byproduct of the disease but takes on the form of an active player in the tumor microenvironment that per se influences the behavior of malignant cells. Through this, dysregulated IL-6 signaling in bone cancer may result in increased tumor growth and, therefore, increased survival [25]. The prolonged activation of the STAT3 pathway, which is driven by IL-6, has been implicative of cancer progression and chronic inflammatory diseases. This persistent STAT3 activation underscores, directly, the importance of IL-6 maintaining an inflammatory state that is conducive to cancer development. One of the critical prognostic values of IL-6 in cancer is its well-known relationship to poor prognosis and the growth of many tumors, such as prostate, which leads to a negative correlation with regards to survivals and responses to chemotherapy [26–27]. The negative correlation of IL-6 might make it a good biomarker for the progression of the disease, which in turn would give clues about the likelihood of response to treatment and general outcome in patients. In this regard, whether similar relationships exist between IL-6 levels and clinical outcomes in bone cancer will underpin further attempts. IL-6, by promoting cancer cell growth and blocking apoptosis, seems to be essential for the switch from tumor types to more aggressive phenotypes [27]. New prognostic models for bone cancer patients could be developed based on that information.

CONCLUSION

It is suggested that thymidine phosphorylase activity and IL-6 have a significant high diagnostic power in the diagnosis and progression of osteosarcoma.

Conflict of interest *Not declared.*

Funding *The authors rely only on their own financial support.*

Ethics approval *The project in this study was approved by the ethical committee of the Medical College in the University of Kufa (No. 135 in 2024).*

Consent to participate *Prior to collecting samples, all patients involved in the study were required to provide written consent for their participation.*

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The article was submitted 03.10.2024; approved after reviewing 29.10.2024; accepted for publication 05.02.2025.

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Review article
https://doi.org/10.18019/1028-4427-2025-31-2-252-262

Proximal femoral nail antirotation versus bipolar hemiarthroplasty for intertrochanteric fractures: a meta-analysis

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Abstract

Introduction Intertrochanteric fractures account for almost half of all hip fractures, with a mortality rate of 15 to 20 % within one year following fracture, primarily in elderly patients aged 65 years old and older.

The **purpose** of this study is to compare the operative time, intraoperative blood loss, intraoperative blood transfusion, hospitalization time, weight-bearing time, Harris Hip Score at 1, 3, 6, 12 months follow-up, and complications after proximal femoral nail antirotation versus bipolar hemiarthroplasty for intertrochanteric fracture in elderly patients based on the published literature of their comparison.

Methods We conducted a comprehensive search in the electronic databases such as PubMed, Scopus, and Google Scholar. Original articles up to November 2024 were screened, focusing on retrospective or prospective cohort studies.

Results and Discussion The initial search yielded 702 studies. Six cohort studies with a total of 495 participants were assessed. The Proximal Femoral Nail Antirotation (PFNA) showed statistically significant shorter operative time (p = 0.006), lower intraoperative blood loss ($p < 0.0001$) compared with bipolar hemiarthroplasty. Bipolar Hemiarthroplastty had statistically significant better Harris Hip Score at 1- and 3- month follow-up post-operatively ($p < 0.00001$), (p = 0.001). It provides early weight-bearing (p = 0.003) and helps mobilize post-operative patients. Blood transfusion, hospitalization time, Harris Hip Score after 6- month follow-up, and complications had balanced results between two apporaches.

Conclusion PFNA and bipolar Hemiarthroplasty have comparable results in intertrochateric fractures in the elderly. PFNA has the advantages of shorter operative time, and lower intraoperative blood loss. Bipolar hemiarthroplasty has the advantages of better Harris Hip Score at 1- and 3-month follow-up and earlier weight-bearing.

Level of Evidence: I.

Keywords: Proximal Femoral Nail Antirotation, Bipolar Hemiarthroplasty, Intertrochanteric Fracture, Elderly, Harris Hip Score, Complications.

Acknowledgements The authors also acknowledge the contribution of the Department of Orthopaedic and Traumatology, Udayana University, Bali, Indonesia for the supports given.

For citation: Damara IGAD, Wijaya NSN, Dusak IWS. Proximal femoral nail antirotation versus bipolar hemiarthroplasty for intertrochanteric fractures: a meta-analysis. *Genij Ortopedii*. 2025;31(2):252-262. doi: 10.18019/1028-4427-2025-31-2-252-262.

INTRODUCTION

Intertrochanteric hip fractures are common and often fatal injuries, especially among the elderly. Intertrochanteric fractures account for almost half of all hip fractures, with a mortality rate of 15 to 20 % within one year following fracture [1]. By 2050, Asia is expected to account for more than half of all hip fractures worldwide, owing to an ageing population and increased life expectancy. In Japan, the chance of lifetime hip fractures for people over the age of 50 is stated to be 5.6 % for men and 20 % for women. Hip fracture cases in China are expected to increase sixfold, from 0.7 million in 2013 to 4.5 million by 2050 [2].

The number of hip fractures in the United States alone is expected to rise from approximately 320,000 per year to 580,000 by 2040. This growing demand puts tremendous strain on the health-care system in terms of staffing and resources needed to manage these patients. In the United States, healthcare expenses for the management of hip fractures are anticipated to surpass $10 billion annually [3–8], while the impact on the UK healthcare system is expected to be $2 billion per year [9]. These expenditures are driven not just by the acute surgical treatment, but also by post-acute care, such as rehabilitation. While hip fracture surgery is very effective, patients are likely to endure severe morbidity in terms of pain, discomfort, and limited mobility during their recovery, and in many cases are unable to restore pre-fracture levels of function [3, 6, 9]. Studies also reveal that there is a relationship between hip fracture and higher rates of mortality, with 30 % more deaths seen than the age-matched populations with and without hip fracture [9–14]. However, such findings should be interpreted with caution, as those who have had a hip fracture may be more vulnerable and prone to illness.

The optimum surgical method for intertrochanteric fracture should restore the patient's mobility to preoperative levels while minimising intra- and postoperative morbidity and death. Although proximal femoral nail antirotation (PFNA) has been widely used by orthopaedic specialists for patients with intertrochanteric fractures, PFNA failure has been reported due to extensive comminution, osteoporosis, implant cutout, femoral medialization, and lateral migration of proximal screws or helical blades [15, 16]. As a result, bipolar hemiarthroplasty, which allows for early weight-bearing while reducing the chance of osteosynthesis failure, has become a popular option for older patients with intertrochanteric fractures [17].

The proximal femoral nail antirotation (PFNA) has acquired widespread approval for its minimally invasive nature and biomechanical advantages, which allow for early weight-bearing [18]. This treatment comprises closed fracture reduction under fluoroscopy and the subsequent insertion of an intramedullary nail with a helical blade into the femur, minimising surgical time and blood loss while improving outcomes in terms of fracture union and functional recovery [19, 20]. However, problems such as blade migration and fixation failure have been reported, motivating efforts to identify and mitigate risk factors through continuous research and advancements in surgical procedures and implant designs [21].

For older patients with unstable intertrochanteric femur fractures, hemiarthroplasty with a bipolar prosthesis improves early postoperative ambulation. This would have a direct impact on both postoperative rehabilitation and general health [22].

The **objective** of this study was to compare the operative time, intraoperative blood loss, intraoperative blood transfusion, hospitalization time, weight-bearing time, Harris Hip Score at 1, 3, 6, 12 months follow-up, and complications after the proximal femoral nail antirotation versus bipolar hemiarthroplasty for intertrochanteric fracture in elderly patients, so that it can help the physician to choose the right treatment for the intertrochanteric fracture in the elderly.

MATERIALS AND METHODS

The Cochrane Handbook for Systematic Reviews of Interventions was used to perform this systematic review and meta-analysis, which was then reported using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Search Strategy

Two researchers (IGADD and NSNW) conducted literature search using three databases including PubMed, Scopus, and Google Scholar. The focus of the search was on the topic "proximal femoral nail antirotation versus bipolar hemiarthroplasty for intertrochanteric fracture in elderly". The study used only retrospective and prospective cohort studies. The literature search was performed using the keywords "proximal femoral nail antirotation" OR "PFNA" OR "bipolar hemiarthroplasty" OR "BHA" AND "Intertrochanteric Fracture". Applying filters to English language papers, human studies and cohort (retrospective or prospective) studies. The literature search ensuring inclusion of the terms in titles, abstracts, and keywords for study design and publication year. All search results were evaluated based on titles and abstracts to ensure relevance to the inclusion criteria.

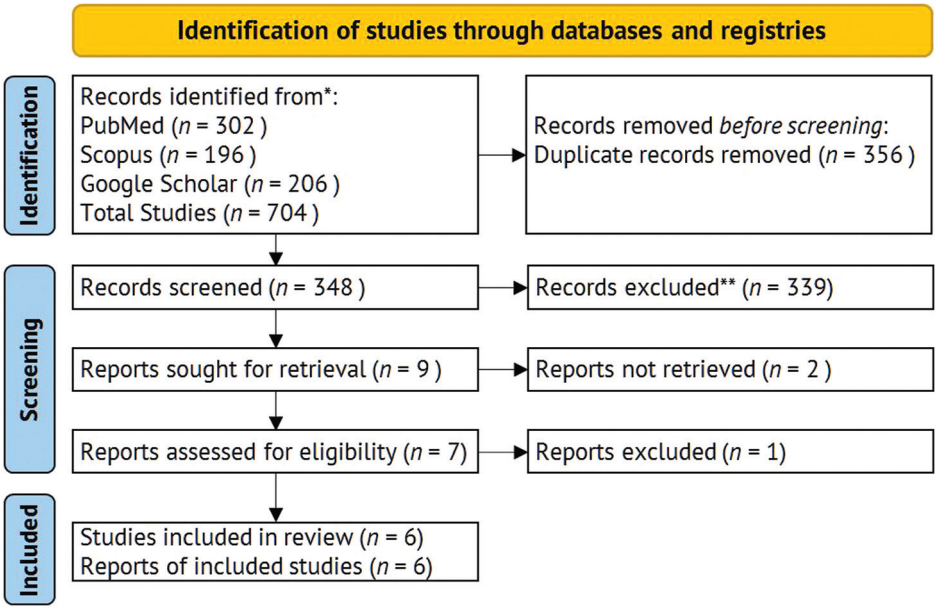

Fig. 1 PRISMA Flowchart 2020

Inclusion and Exclusion Criteria

The Inclusion criteria

(1) retrospective or prospective cohort studies comparing the use of the proximal femoral nail antirotation (PFNA) and bipolar hemiarthroplasty (BHA) in patients with intertrochanteric fractures;

(2) studies reporting at least one of the following outcomes: operative time, intraoperative blood loss, intraoperative blood transfusion, hospitalization time, weight-bearing time, Harris Hip Score, and complications;

(3) the study population included participants aged above 65 years old diagnosed with intertrochanteric fractures;

(4) articles published in English;

(5) with full texts available.

Exclusion criteria

(1) studies design were other than cohort (case report, case series, randomized controlled trials, literature review);

(2) studies that did not distinguish outcomes between PFNA and BHA;

(3) studies with fewer than 15 patients for each group;

(4) article data that could not be quantitatively analysed.

All articles meeting the inclusion criteria were assessed for methodological quality using the Newcastle Ottawa Scale (NOS).

Study Selection

Two reviewers (IGADD and NSNW) independently reviewed the title and abstract of all studies generated from the literature search to exclude irrelevant studies. For potentially eligible studies, 2 reviewers (IGADD and NSNW) independently reviewed the full text of articles (up to November 2024) using the inclusion criteria. The references in the retrieved articles were also carefully searched. Inconsistencies were resolved by discussion by a third author (IWSD). The reviewers were not blinded to the authors, journals, or sources of financial support.

Data Extraction and Quality Assessment

Data extraction and quality assessment were conducted by two reviewers (IGADD and NSNW). Key information for data extraction was collected from each study, including the first author's name, year of publication, retrospective or prospective cohort studies, sample size, demographic characteristics of participants, fracture classification (Evan-Jensens), treatment groups (proximal femoral nail antirotation and bipolar hemiarthroplasty). Quality assessment of included studies was performed using the Newcastle Ottawa Scale (NOS). NOS used for evaluating three domains: selection of participants, comparability of study groups, and assessment of outcomes. Studies with score ⩾ 6 on the NOS were considered of high methodological quality. Disagreement during data extraction was resolved through discussion with a third reviewer (IWSD).

Statistical Analysis

Statistical analysis was conducted employing Review Manager (RevMan) version 5.4.1. Dichotomous data were condensed using odd ratio (OR) with 95 % confidence interval (CI), for continuous data were evaluated using standard mean difference (SMD) and Mean Difference (MD) to define for variation in measurement scale across studies. Heterogeneity was evaluated using the Chi^2 test and quantified with the I^2. If I^2 test > 50 % using random effect model indicating high heterogeneity, if I^2 test < 50 % using fixed effect model indicating low heterogeneity. Forest plots were generated to visually provide the pooled effect estimate for each outcome. Statistical significance was set using *p* value ⩽ 0.05. All analyses adhered to PRISMA guidelines for systematic reviews and meta-analysis.

RESULTS

Selection of the Studies

The PRISMA flow diagram shows the study selection process in Figure 1. The initial research obtained a total 704 studies, and through the elimination of duplication 348 studies underwent independent screening and 339 were excluded due to subsequent reason: irrelevant title and abstract, non PFNA and BHA procedures. After exclusion, 7 full-text studies were assessed for the eligibility. At the end, 6 studies (original articles up to November 2024) were included in our data synthesis.

Table 1

Baseline Characteristics of the studies

Study	Country	Design	Study Period	Ages (Mean ± SD)		Intervention to patients		
				PFNA	BHA	PFNA	BHA	Total
Cai, et al., 2022 [29]	China	Retrospective Cohort	2014–2019	80.88 ± 4.90	82.19 ± 3.96	34	36	70
Lu, et al., 2023 [30]	China	Retrospective Cohort	2006–2021	92.3 ± 2.7	92.1 ± 2.5	36	77	110
Saraf, Munot, 2018 [31]	India	Retrospective Cohort	2016–2017	82.4 ± 3.9	80.8 ± 4.3	20	20	40
Song, et al. 2022 [32]	China	Retrospective Cohort	2012–2016	79.9 ± 6.1	81.0 ± 9.1	32	30	62
Zhou, et al., 2019 [33]	China	Retrospective Cohort	2008–2012	83.5 ± 4.8	83.8 ± 6.4	61	47	108
Zhou, et al., 2024 [34]	China	Retrospective Cohort	2012–2018	78.00 ± 6.95	80.04 ± 6.39	52	50	102

Table 2 represents the results of the New Castle Ottawa Scale. Of all included studies, one study has a score of 7, three studies have a score of 8, one study has a score of 9, and one study has a score of 10. It can be concluded that all studies have high quality studies.

Table 2

Newcastle-Ottawa Scale (NOS)

Study	Selection				Comparability	Outcomes			Total
	Representativeness ofexposed cohort	Selection of nonexposed cohort	Ascertainment of exposure	Outcome not present at the start of the study		Assessment of outcomes	Length of follow-up	Adequacy of follow-up	
Cai, et al., 2022 [29]	+	+	+	–	+	+	+	+	8
Lu, et al., 2023 [30]	+	+	+	+	+	+	+	+	9
Saraf, Munot, 2018 [31]	–	–	+	+	+	+	+	+	7
Song, et al. 2022 [32]	–	+	+	+	+	+	+	+	8
Zhou, et al., 2019 [33]	–	+	+	+	+	+	+	+	8
Zhou, et al., 2024 [34]	++	+	+	+	+	+	+	+	10

Operative Time

Of the 6 included studies, 5 reported the operative time [29–31, 33–34]. The forest plot analysis found that BHA had statistically significant difference in longer operative time, compared with PFNA (SMD –1.45, 95 % CI –2.49 to –0.42, $p = 0.006$) A random effects model was used because of the clinical heterogeneity ($I^2 = 94$ %, Fig. 2).

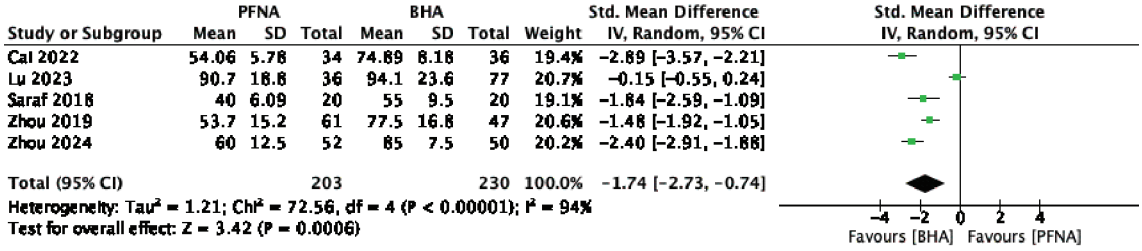

Fig. 2 Comparison of PFNA vs BHA on Operative Time

Intraoperative Blood Loss

All the included studies reported the intraoperative blood loss [29–34]. The forest plot analysis found that BHA statistically significant difference in intraoperative blood loss, compared with PFNA (SMD –2.34, 95 % CI –3.50 to –1.19, $p < 0.0001$) A random effects model was used because of the clinical heterogeneity ($I^2 = 96$ %, Fig. 3).

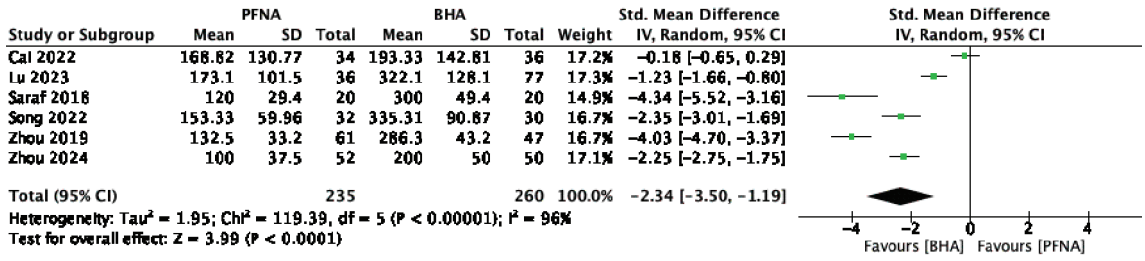

Fig. 3 Comparison of PFNA vs BHA on Intraoperative Blood Loss

Blood Transfusion

Of the 6 included studies, 2 reported the blood transfusion [29–30]. The forest plot analysis found that there was no statistically significant difference in blood transfusion between two groups (SMD –0.10, 95 % CI –1.11 to 0.90, $p = 0.84$) and low heterogeneity ($I^2 = 31$ %, Fig. 4).

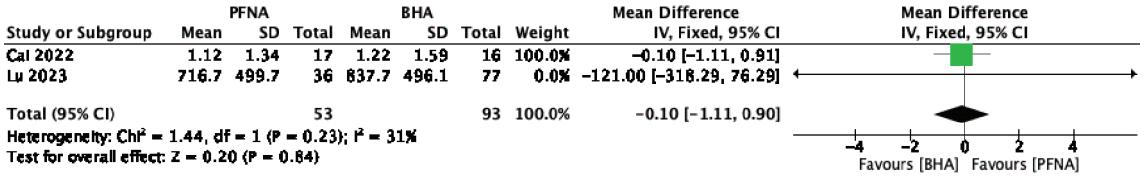

Fig. 4 Comparison of PFNA vs BHA on Blood Transfusion

Hospitalization Time

Of the 6 included studies, 5 reported the hospitalization time [29, 31–34]. The forest plot analysis found no statistically significant difference in hospitalization time between the two groups (SMD –0.16, 95 % CI –0.59 to 0.27, $p = 0.47$) A random effects model was used because of the clinical heterogeneity ($I^2 = 76$ %, Fig. 5).

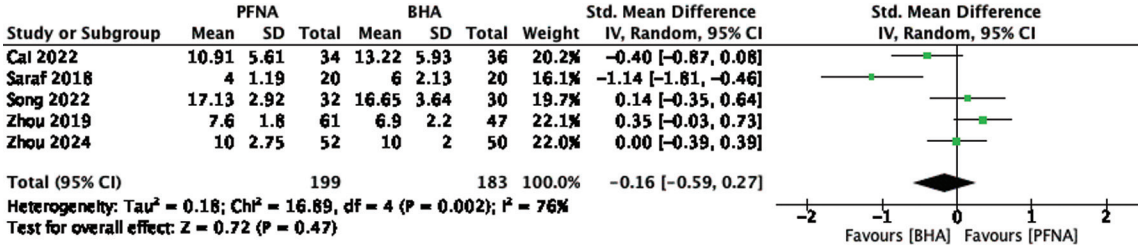

Fig. 5 Comparison of PFNA vs BHA on Hospitalization Time

Weight- Bearing Time

Of the 6 included studies, 3 reported the weight-bearing time [32–34]. The forest plot analysis found statistically significant difference that that PFNA was slower in early weight-bearing time, compared with BHA (SMD 5.16, 95 % CI 1.81 to 8.50, $p = 0.003$) A random effects model was used because of the clinical heterogeneity ($I^2 = 98$ %, Fig. 6).

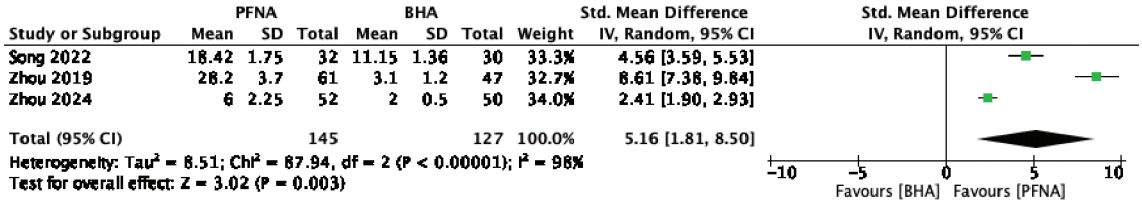

Fig. 6 Comparison of PFNA vs BHA on Weight-Bearing Time

Harris Hip Score at 1 Month Follow Up

Of the 6 included studies, 2 reported Harris Hip Score at 1-month follow-up [31, 34]. The forest plot analysis found that BHA statistically significant difference more superior in Harris Hip Score at 1-month follow-up, compared with PFNA (SMD –3.39, 95 % CI –3.91 to –2.86, $p < 0.00001$) and no heterogeneity ($I^2 = 0$ %, Fig. 7).

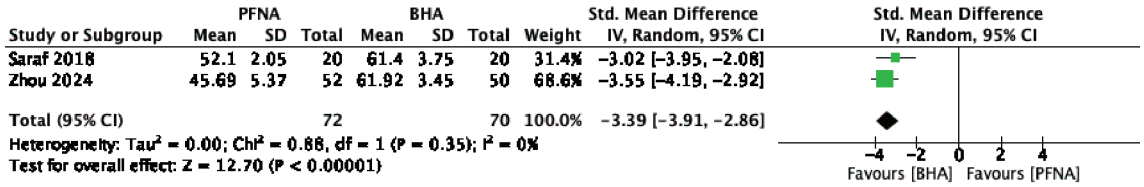

Fig. 7 Comparison of PFNA vs BHA on Harris Hip Score at 1-Month Follow-up

Harris Hip Score at 3 Month Follow Up

Of the 6 included studies, 4 reported Harris Hip Score at 3-month follow-up [29, 31, 32, 34]. The forest plot analysis found that there was statistically significant difference and BHA was more superior in Harris Hip Score at 3-month follow-up, compared with PFNA (SMD –1.80, 95 % CI –2.90 to –0.70, $p = 0.001$). A random effects model was used because of the clinical heterogeneity ($I^2 = 93$ %, Fig. 8).

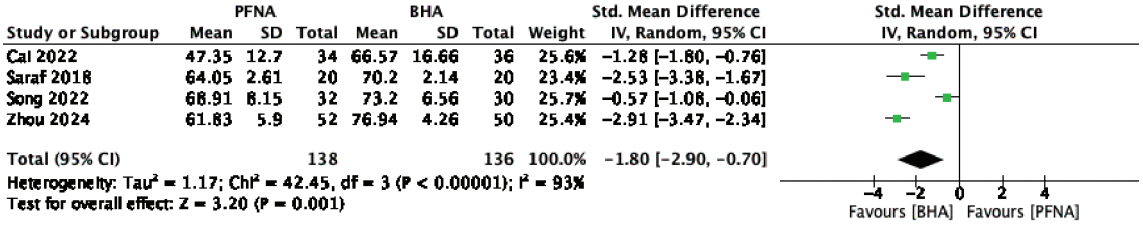

Fig. 8 Comparison of PFNA vs BHA on Harris Hip Score at 3-Month Follow-Up

Harris Hip Score at 6 Month Follow Up

Of the 6 included studies, 3 reported Harris Hip Score at 6-month follow-up [31, 32, 34]. The forest plot analysis found that no statistically significant difference in Harris Hip Score at 6-month follow-up between two groups (MD –0.29, 95 % CI –1.16 to 0.59, $p = 0.52$) and no heterogeneity ($I^2 = 0$ %, Fig. 9).

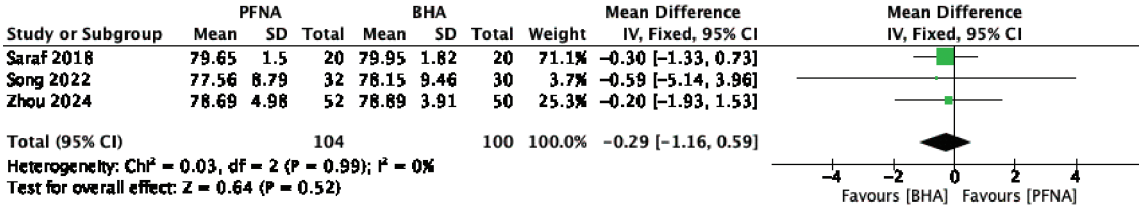

Fig. 9 Comparison of PFNA vs BHA on Harris Hip Score at 6-Month Follow-Up

Harris Hip Score at 12 Month Follow Up

All of the included studies reported Harris Hip Score at 12-month follow-up [29, 31–34]. The forest plot analysis found that there was no statistically significant difference in Harris Hip Score at 12-month follow-up between two groups (MD –0.50, 95 % CI –1.81 to 0.81, $p = 0.45$) and low heterogeneity ($I^2 = 34$ %, Fig. 10).

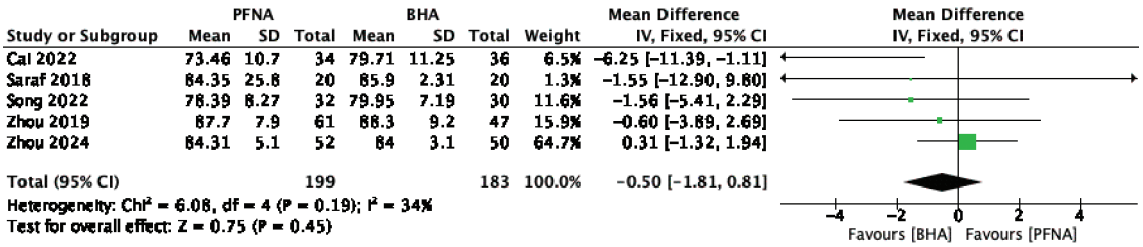

Fig. 10 Comparison of PFNA vs BHA on Harris Hip Score at Final Follow-up

Complications

Our findings show that there are 5 major groups of complications that occur in patients undergoing BHA and PFNA. There was no statistically difference in re-fracture complications (OR 1.14, 95 % CI, [0.40, 3.31], $p = 0.80$, $I^2 = 0$ %) and no heterogeneity. Re-operation rate was similar and showed no statistical difference (OR 2.06, 95 % CI [0.60, 7,08], $p = 0.25$, $I^2 = 51$ %) and moderate heterogeneity, wound infection (OR 0.49, 95 % CI [0.15, 1,58], $p = 0.23$, $I^2 = 38$ %) and low heterogeneity, deep vein thrombosis (OR 1.60, 95 % CI [0.18, 1.16], $p = 0.10$, $I^2 = 0$ %) and no heterogeneity, urinary tract infection (OR 1.60, 95 % CI [0.37, 6.88], $p = 0.53$, $I^2 = 0$ %) and no heterogeneity (Fig. 11) [29–34].

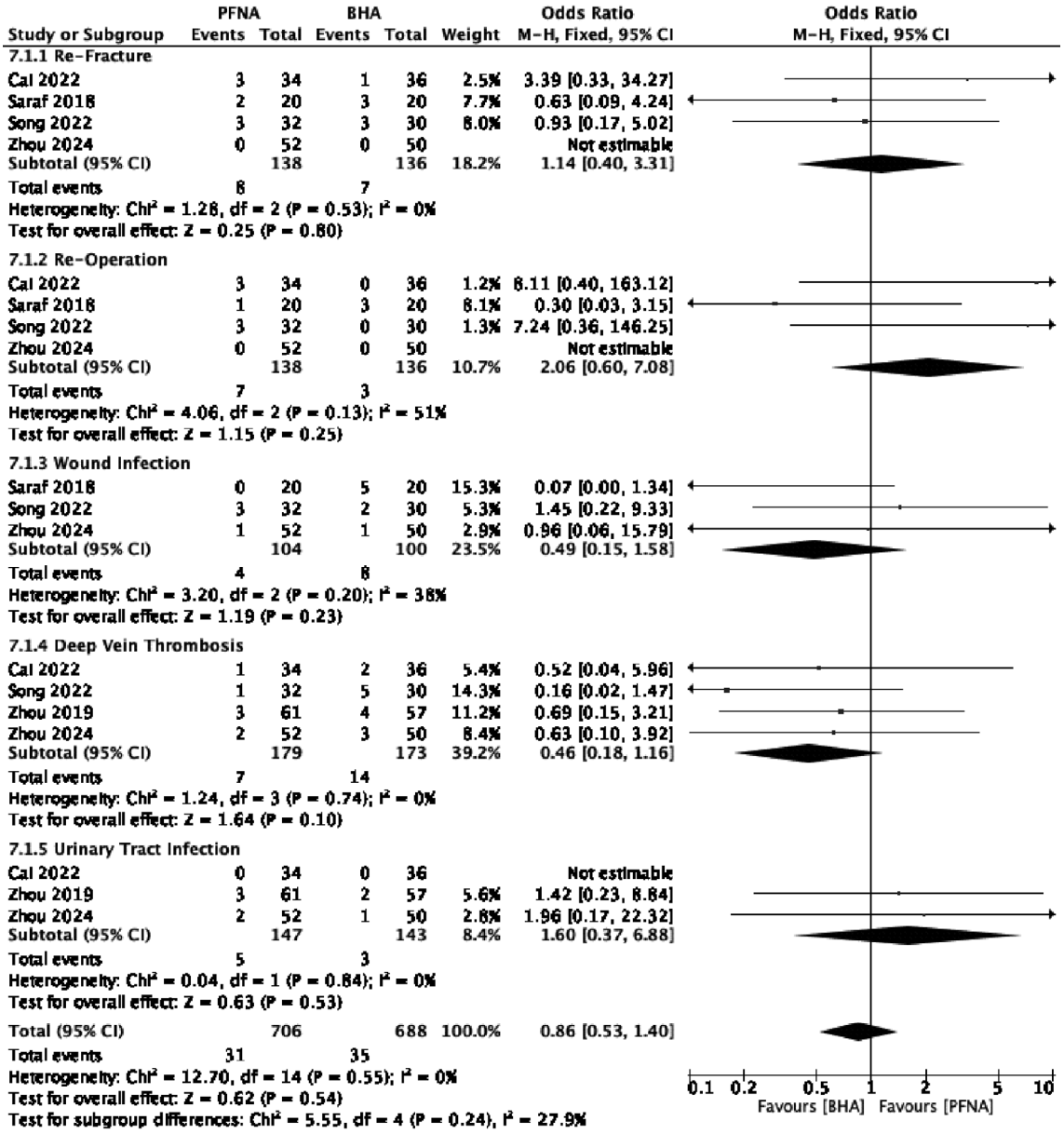

Fig. 11 Comparison of PFNA vs BHA on Complications

DISCUSSION

Our study results on the use of proximal femoral nail antirotation versus bipolar hemiarthroplasty in intertrochanteric fractures in elderly showed statistically significant results on operative time, intraoperative blood loss, early weight-bearing time, and Harris Hip Score at 1 and 3 months after surgery. There was no statistical difference in hospitalization time, blood transfusion, Harris Hip Score 6 and 12-months after surgery, and complications.

In our study, PFNA had the advantage of shorter operative time compared to BHA. Consistent with the studies of Cai et al (2022), Saraf et Munot (2018), Zhou et al. (2019), Zhou et al. (2024). This is because there is no complicated prosthesis placement and the procedure is minimally invasive. PFNA also avoids the extensive soft tissue dissection and precise prosthetic alignment required in BHA. BHA usually necessitates a longer surgical time due to the intricacy of arthroplasty operations, which involve the removal of the femoral head, femoral canal preparation, and appropriate prosthesis fixation [29, 31, 33, 34].

Given that osteoporosis is more common in the elderly and causes a more comminuted intertrochanteric fracture pattern, this has important ramifications for improving the prognosis of elderly patients with intertrochanteric femoral fractures. The surgical intervention with BHA requires not only performing the femoral head osteotomy but also repeatedly broaching the medullary and even repositioning and fixing the great trochanteric fragment, which may be more traumatic for elderly patients than patients with PFNA internal fixation and may explain the higher intraoperative blood loss in the BHA group compared to the PFNA group. This result is similar with the results of a prior study revealing that PFNA therapy leads to less blood loss and shorter operating time than BHA treatments [23].

Our study demonstrates significantly lower intraoperative blood loss in proximal femoral nail antirotation (PFNA) compared to bipolar hemiarthroplasty (BHA). This result is consistent with Saraf et Munot (2018), Song et al. (2022), Zhou et al. (2019), and Zhou et al. (2024) that PFNA reduced bleeding due to a less invasive approach compared with BHA. The increased blood loss in BHA is due to the significant soft tissue dissection and femoral canal preparation necessary during the surgery [31, 32, 33, 34].

There were no significant differences in intraoperative blood transfusion between PFNA and BHA. Song et al. (2022) and Zhou et al. (2024) discovered that patient specific factors including preoperative anaemia and comorbidities had a greater impact on blood loss and transfusion during surgery [32, 34].

The analysis of hospitalization time shows no significant difference. The primary premise of postoperative functional exercise for unstable intertrochanteric fractures is to begin out-of-bed activities as soon as feasible, but the affected leg cannot bear full weight. As a result, the patient bears weight on one leg and walks using crutches or other walking aids. Patients with limited upper limb strength or poor body balance cannot follow this training plan. As a result, many patients remain in bed for extended periods of time following PFNA surgery [24]. Unfortunately, this raises the likelihood of bed-related issues, medical expenses, and longer hospital stays.

The forest plot indicates that BHA allows significantly earlier weight-bearing compared to PFNA. BHA, which is favourable in terms of less operation time and permitting early weight-bearing, was initially utilised in 1978 and subsequently employed by other surgeons for intertrochanteric fracture treatment with satisfying results [25]. It has been suggested as an alternate approach for older intertrochanteric fracture patients [26, 27]. BHA is advised as a primary treatment for intertrochanteric fracture with poor stability in the elderly with severe osteoporosis, poor prognosis after internal fixation, and a short life expectancy [28].

The Harris Hip Score (HHS) has been widely utilized to evaluate hip functional outcome in elderly patients with intertrochanteric fractures treated with bipolar hemiarthroplasty (BHA) or proximal femoral nail antirotation (PFNA). Studies constantly highlight that both techniques can achieve good functional outcomes, but the results vary in magnitude and timeline.

In our study, the Harris Hip Score after 1 month and 3 months postoperatively was better in the bipolar hemiarthroplasty group compared to PFNA. However, after 6 months and at the end of follow-up, BHA and PFNA produced functional HHS outcomes which differences were not statistically significant. In line with the research of Saraf et Munot (2018), Song et al. (2022), Zhou et al. (2024) that the Harris Hip Score in the early postoperative period was better in the BHA group compared to PFNA, but after 6 months postoperatively there was no statistically significant difference. However, it is necessary to consider age and type of fracture as a therapeutic modality used for intertrochanteric fractures [31, 32, 34].

PFNA is appropriate for treating unstable intertrochanteric fractures, although BHA is better for treating comminuted fractures in individuals with severe osteoporosis, particularly those with an intertrochanteric fracture. Zhou et al. (2019) recommend the following indications for BHA in the treatment of intertrochanteric fractures: age > 75 years with severe osteoporosis; severe comminuted fracture; the presence of internal diseases and the inability to tolerate long-term bed rest; implant failure or non-union; femoral head disease; and voluntary arthroplasty [33].

PFNA may be more appropriate for younger, more active patients because of its capacity to preserve the native hip joint. BHA, on the other hand, is generally chosen for older, weak patients or that with poor bone stock because it eliminates the requirement for fracture healing and reduces the risk of problems like implant failure.

Complications including re-operation rates, re-fracture, wound infection, deep vein thrombosis, urinary complications between proximal femoral nail antirotation (PFNA) and bipolar hemiarthroplasty (BHA) for intertrochanteric fractures are generally comparable, as indicated by the forest plot and supporting studies.

The advantages of this study are:

(1) comprehensive evidence synthesis, by pooling data from multiple studies, this study improves the statistical power and provides more potent evaluation of the relative efficacy and safety of PFNA and BHA, which addresses the variations that may exist in each studies;

(2) evaluation of multiple outcomes, such as operative time, intraoperative blood loss, intraoperative blood transfusions, hospitalization time, weight-bearing time, Harris Hip Score and complications, allowing a holistic approach of the risks and benefits of each procedures.

The results of this study confirm previous studies that reported PFNA had a longer operative time and greater intraoperative blood loss. BHA had the advantage of better Haris Hip Score at 1- and 3-month follow-up, and could be early weight-bearing.

This study has some limitations. These limitations include:

(1) the number of articles that meet the inclusion criteria is only 6 articles, due to the lack of cohort studies discussing PFNA versus BHA;

(2) high bias in the results of forest plots of several subgroup analyses, this can occur due to various factors, namely patient demographics, clinician experience in performing surgery, and varying pre-operative to post-operative protocols;

(3) the number of participants is small so it can cause bias.

CONCLUSION

PFNA and BHA have comparable results. PFNA and BHA each have advantages and disadvantages. PFNA has the advantages of: (1) shorter operative time, (2) lower intraoperative blood loss. However, the disadvantage of PFNA is later weight-bearing than BHA. BHA has the advantages of: (1) better Harris Hip Score in 1 and 3 month follow-up post-operatively, (2) early weight-bearing and helps mobilize post-operative patients. However, the disadvantages of BHA are longer operative time and higher intraoperative blood loss which can increase the risk in elderly patients. It is necessary to consider performing BHA in patients with unstable intertrochanteric fractures or patients with osteoporosis so that patients can be immobilized as soon as possible. Blood transfusion, hospitalization time, Harris Hip Score at 6 and 12-month follow-up, and complications had balanced results between PFNA and BHA.

***Conflicts of interest**. The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.*

***Funding**. The authors did not receive any grant or funding for this research from any funding agency in the public, commercial or not for profit sectors.*

***Ethics approval**. Not applicable.*

***Consent for publication**. Not applicable.*

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The article was submitted 04.04.2024; approved after reviewing 11.09.2024; accepted for publication 21.02.2025.

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Anatoly Grigorievich Kaplunov
(12.11.1936 – 16.03.2025)

Anatoly Grigorievich Kaplunov passed away on March 16 at the age of 89. He was an honored doctor of Russia and one of the first disciples of academician G.A. Ilizarov.

Anatoly Grigorievich Kaplunov was born on November 12, 1936. In 1960, he graduated from the Stalingrad Medical University (currently, the Volgograd State Medical University) and chose the specialty of trauma- and orthopaedic surgeon for his entire life. At that time, a delegation from the Kurgan Hospital for War Veterans arrived in Volgograd to recruit young specialists for a new department opened for a then unknown orthopaedic surgeon, and later the famous academician G.A. Ilizarov.

Young doctor Kaplunov moved to Kurgan and began working with Ilizarov. In 1969 he headed the new department for the study of compression-distraction osteosynthesis in the treatment of diseases and deformities of the musculoskeletal system in adults at the Kurgan branch of the Leningrad Research Institute for Traumatology and Orthopaedics named after Vreden. G.A. Ilizarov wrote about his disciple: "... Anatoly Kaplunov, a tall, imposing young man, immediately won over the hospital staff. He won them over with his enthusiasm, diligence, good dedication to work, delicacy towards patients and staff...".

In 1972, Dr. Kaplunov successfully defended his candidate of medical sciences dissertation entitled "Treatment of pseudoarthrosis of the lower leg with the Ilizarov transosseous compression-distraction osteosynthesis". In his work, he summarized the experience of using the Ilizarov apparatus and method on a large clinical material for treating patients with the most complex pathology, proving its significant advantages compared to other methods of treatment.

Kaplunov A.G. continued his work at the Ilizarov Center for 20 years, being the deputy director for clinical activities for the last 10 years, and made a huge contribution to the development of the institution. Anatoly Grigorievich personally participated in the treatment of many famous patients of the Center: composer D.D. Shostakovich, Olympic champion V. Brumel, army general A.P. Beloborodov and others.

In 1979, Dr. Kaplunov returned to Volgograd, where he created and headed the regional orthopaedic center. Under his leadership, the Ilizarov method began to be widely used in the region. He headed the created by him center until 2006, but even after leaving his position, he continued to consult patients daily for many years. Anatoly Grigorievich cured thousands of patients and saved their limbs, and returned people to normal life.

In 2008, Kaplunov's book "Unknown Ilizarov: Sketches to a Portrait" was published, in which he tells us about his joint work with Academician Ilizarov: "...I had the rare fortune of being an acquaintance, a student, an associate, to a certain extent a friend and confidant person of this very extraordinary personality... He was a genius and at the same time an ordinary human, and I found myself involved in his Genius, in his human joys and weaknesses... Such personalities are a rare product in the historical process."

Anatoly Grigorievich Kaplunov himself was such a special person who left wonderful memories about him. His name will forever remain in our memory and in the history of the Ilizarov Center.

The staff of the Ilizarov Center and the editorial board of the journal "Genij Ortopedii" express sincere condolences to the family and friends of Anatoly Grigorievich.

Главный редактор А.В. Бурцев

Компьютерная верстка М.А. Беляева

Журнал зарегистрирован Федеральной службой по надзору в сфере связи,
информационных технологий и массовых коммуникаций
ПИ № ФС77-68207 от 30 декабря 2016 года

Территория распространения: Российская Федерация, зарубежные страны

Подписано в печать 17.04.2025. Дата выхода 28.04.2025
Формат 60 × 84 1/8. Усл. печ. л. 14,65
Тираж 75 экз. Заказ № 14739. Свободная цена

Адрес издателя, редакции журнала «Гений ортопедии»
640014, Россия, г. Курган, ул. М. Ульяновой, 6
http://ilizarov-journal.com

Отпечатано в Типографии «Эталон». 198097, г. Санкт-Петербург, ул. Трефолева, 2 литера БН, помещение 3-Н, офис 1