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Experimental Medicine

Healing of Diaphyseal Fractures of Lower Limb Bones and Pathomorphological Studies of Tissues after Different Types of Intramedullary Locking Osteosynthesis

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(Presented by Academy Member Ramaz Khetsuriani)

The objective of this work is to determine the share of positive results of fractures' healing after the use of different types of intramedullary locking nailing (LIOS, IM nailing) and study the organization of tissues at the edge of tissues-implants border after implants' removal from a patient's body. The sampling of the study includes 60 patients with diaphyseal fractures of femoral and tibial bones. In three groups of patients (20 persons each), after the removal of IM nailing fixators with static, compression and dynamic locking of the nail, we studied the consolidation of fractures and conditions of tissues surrounding the fixing device. The mean age of patients was (43.9±6.5) years old. All patients underwent surgical removal of implants by their own will or upon their physician's recommendation. Among the patients, 56.7% were women. The analysis of fracture union was made for each group using radiological methods, considering 3 types of IM nailing. After the IM nailing, 50%, 55% and 75% of patients demonstrated approved fracture consolidation with static, dynamic, and compression locking of the nail, respectively. Using histological methods, we studied tissues around the nail and screws, as well as from the fracture area. The histological study covered only the patients with fracture consolidation without negative consequences like fractures of a fixator, slow consolidation or nonunion, infection, etc. The histological examination of the tissues, surrounding intramedullary fixing devices with all three types of locking has demonstrated, that by 18 months, a dense bone regenerate develops in the fracture areas, and its structural organization and the area of bone tissue were similar after 18 months. After 18 months, the density of bone tissue growth is statistically significant 18 months later, especially in areas of nails and screws placement, causing difficulties in the removal of the intramedullary nail. We have discovered destructive changes in the cortex. Thus, the results of the histological study confirmed, that the removal of intramedullary fixing devices in patients might be expedient in early terms after the fracture consolidation because the formation of large areas of bone tissue about the fixing device will significantly embarrass its removal. Clinical-radiological studies have shown that the largest share of fracture healing is related to IM nailing with the compression locking of the nail (75%). *© 2024 Bull. Georg. Natl. Acad. Sci.*

fracture, osteosynthesis, reparative osteogenesis, fracture healing, implant removal

Among the reasons for long-term temporary loss of workability and primary disability, a large share relates to diaphyseal fractures, growing every year in frequency and severity. Among the diaphyseal fractures, the first place belongs to shin fractures, corresponding to 13-21.4% of all musculoskeletal injuries or 64.3-70% of lower limb fractures [1]. Diaphyseal fractures of tibial bones comprise about 2% of all shin fractures in adults with a general frequency of approximately from 16.9 to 21.5 per 100,000 persons a year [2, 3]. Diaphyseal fractures of femoral bone make 6% of the totality of bone fractures, the occurrence – 18.2 per 100,000 persons a year [4].

The most frequent reasons for poor results of diaphyseal fractures are slow consolidation and nonunions [5]. In this connection, the search for optimal methods for fracture osteosynthesis continues. In recent years, IM nailing has been one of the most effective methods for diaphyseal fractures treatment, applied in many different states of the world [6]. It enables preservation of the periosteal blood flow, ensures reasonable redistribution of the loading on the injured limb, recovers the limb's axis and length.

However, the removal of the fixing structure used for osteosynthesis is, as a rule, the next stage of the surgical treatment. Implant removal is one of the most widespread surgical operations in bone and joint surgery, about 30% of all scheduled orthopaedic surgical procedures. This process could be rather traumatic and followed by the occurrence of complications like refractures, haematomas, injuries to nerves and vessels. Among the criteria for a fixing device removal were: fracture, migration, infection of an implant, or even the patient's desire. The most severe complication after bone plates in patients with open fractures are infectious complications, occurring more frequently than the same after intramedullary fixing devices and occurring in from 7 to 85% of cases, and from 5 to 23% after the close ones. [7]. The necessity of the scheduled removal of an implant after the fracture healing without negative consequences is ambiguous [8-11].

Even though metal fixing devices are widely applied in bone surgery for trauma injuries and orthopaedic surgery [12], the behaviour of a metal implant in the living tissue causes the response to the “foreign body”, which depends on the implant's material, shape and size, response of bone and soft tissue, duration of the stay, and specific features of a patient's body [13, 14]. Important information is provided by the studies dedicated to the effect of metal implants on the bone and surrounding tissues but observations of tissue response in the area of the metal fixing device are rare [15-18].

The study of the peculiarities of tissue organization around the implant may contribute to this issue.

Objectives of the study: to determine the share of positive fracture consolidations after different types of IM nailing and study the tissue organization at the edge of the “tissue-implant” border after the removal of the implant.

Materials and Methods

The perspective study was carried out at the premises of Zhytomyr Regional Hospital named after O.F. Herbachevskyi and the Institute of Traumatology and Orthopedics, NAMS of Ukraine, from March 2023 till January 2024. The research covered 60 patients who applied at the medical institution to remove the implant for desire of due to complications.

Criteria of inclusion into the study: patients applied at the hospital to remove their intramedullary fixing device without signs of disorders and in the absence of pain. Exclusion criteria: children and adolescents, patients with pathological fractures, patients with pain syndrome, impaired implant placement or its fracture, fracture nonunion, and those who refused to take part in the study.

The patients involved have given written informed consent. We have collected their anamnesis, carried out clinical and radiological examinations.

The examination plan has been approved by the commission on bioethics by the SI "ITO NAMS of Ukraine", minutes No. 1 of February 15, 2022.

The objects of study were fracture union and conditions of the tissues in 3 groups of patients after the fixation of long bones' diaphyseal fractures by intramedullary fixing devices with static, compression, and dynamic locking of the nail. The study covered 60 patients from different age groups, mean age of 43.9 ± 6.46 years old. Among the patients, women prevailed – 34 (56.66%). 20 patients, after fractures (in 35% – the middle third of the femoral bone diaphysis, 20% – the lower third of the femoral bone diaphysis, 15% – the upper third of the femoral bone diaphysis) at the age 36.5 ±2.79 (26-45) years old, passed surgical treatment with the implantation of a compression intramedullary fixing device. In 22.0 ± 2.96 (9-33) months, 75% of patients got their fixing devices removed after clinical and radiological confirmation of fracture healing and on their own desire or physician's recommendation. In 15%, fixing devices were removed due to their fracture, and in 15% – due to expressed pain syndrome. In 20 patients, after fractures (30% – the lower third of femoral diaphysis, 20% – proximal part of the femur, 20% – the middle third of the diaphysis, 10% – the lower third of the diaphysis, 15% the upper third of tibial diaphysis, 5% – the lower third of tibial diaphysis), at the age of 48.6 ± 5.91 (20-83) years old, surgical treatment included implantation of intramedullary fixing devices with static locking.

In 16.1±3.19 (1.5-32) months, in 40% of cases after clinically and radiologically confirmed consolidation of the fracture, the fixing device has been removed. In 5% of cases, after the fracture consolidation and in the absence of complaints, patients' plans to continue sports activities was an indication to remove the fixing device.

In 20 patients after the fractures (45% – the middle third of femoral diaphysis, 20% – the lower third of femoral diaphysis, 20% – the middle third of tibial diaphysis, 15% – the upper third of tibial diaphysis) at the age of 46.6± 4.07 (26-64) years old, surgical treatment included the implantation of an intramedullary fixing device with a dynamic type of fixation. In 19.6± 3.58 (3-38 months), in 55% of cases – after clinical and radiological confirmation of the fracture consolidation, the fixing device has been removed. In 20% of cases, the removal was due to consolidation of the fragments and revision osteosynthesis. In 10% of cases, the removal of fixing devices was indicated due to the expressed pain syndrome. In 10%, the removal was forced by the "conflict" with soft tissues.

For the research, histological materials of the patients with different types of IM nailing locking have been conditionally distributed into two groups – implant removal before and after 18 months. The time-lapse was obtained from AO's recommenddation to remove fixing devices within less than 18 months [19]. However, we haven't found any substantiation in dedicated scientific literature.

We examined the removed metal implants for deformities, fractures, corrosion signs. During the surgery, we visually assessed the presence of the metallosis in the surrounding tissues.

Histologic studies. Material for histologic study has been collected with a hollow drill from the area of fracture union. We accessed the target area in post-surgical scar under 1 cm long in the projection of the consolidated fracture, under the control of the E-O converter. For long bone fracture treatment, we used IM nailing with dynamic, static, and compression locking of the nail. Histologic study examined the samples, obtained in the projection of the fracture area and from the surface of the removed fixing device after the surgical operation in two series: before and after 18 months (from 19 to 27 months).

Samples from around the removed implant (in 3-6 places) were fixed in 10% neutral formalin. Bone fragments were decalcinated in the solution of the 5% formic acid. Tissues were processed in

paraffin. Serial sections 7-10 μm thick were made with a microtome (Thermo Scientific HM 325 Manual microtome). The deparaffinised sections were dyed with haematoxylin and eosin and examined with a microscope Micros (Austria) with the image transmitted to a monitor by a camera DCM 800 (Ukraine).

Statistic processing of the material. Using the software of the camera DCM 800, we measured the area of bone and connective tissue (objective 20, eyepiece 10) in the fragment of the tissue, obtained after the removal of the fixing device. The area was expressed in per cents. After the assessment of the rows' normality, we conducted statistical processing of the digital values. For this reason, we applied the Mann-Whitney non-parametric U criterion to compare the mean values of two independent selections and to determine statistical significance.

Studies and Discussion

The intramedullary nailing with a statically locked nail. In general, the use of IM nailing with a static locking of the nail ensured 50% of positive clinical and X-ray results, followed by the removal of the fixing device due to the fracture healing.

Conditions of tissues around the implant 18 months after the osteosynthesis. Histological examination of the fragments of tissues around the intramedullary fixing devices in the early period (1.5 months) demonstrated the formation of small areas of granulation and connective tissue of different maturity. The layers of granulation tissue included a network of thick fibres, separate fibroblasts, some of them with pipycnotic nuclei. The granulation tissue contained blood vessels with extended lumens. The specimens contained the areas of connective tissue with irregular collagen fibres with a high density of fibroblasts among them. In the projection of the fracture, we have discovered connective tissue, osteoids, and bone trabeculae. The maturity of the connective tissue and the formation of bone tissue grew within the period of the fixator's stay in the bone. As of a 3-month period, bone trabeculae, different in width, appeared among the connective tissue, having osteocytes on their surfaces. After 13-18 months, the regenerate appeared, represented by cancellous and lamellar bone tissue with areas of connective tissue. The layers of bone tissue were formed from the side of the intramedullary canal.

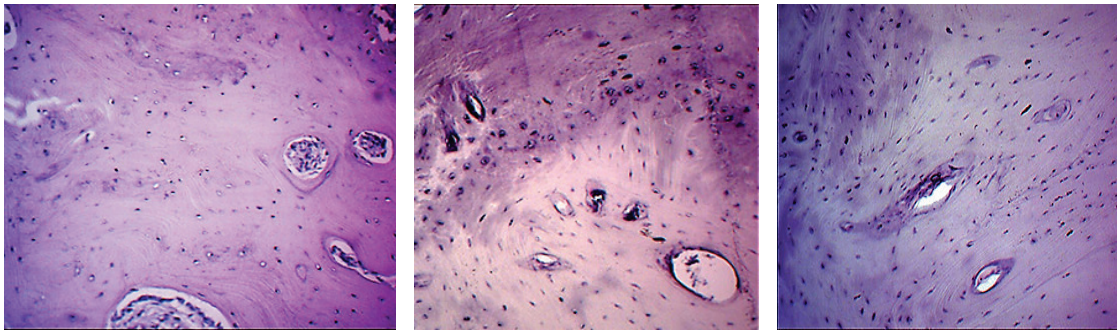
The IM nailing with a dynamic locking of the nail. For the complete period of observation, in 55% of cases, the complete transformation of bone tissue in the fracture area has been histologically confirmed.

Tissue conditions after the fixing device removal, up to 18 months. At early periods (3 months), tissue fragments around the fixing device demonstrated small areas of connective tissue varying in density, with irregularly located fibroblasts. After the longer stay of the fixing device in the bone, the areas in the connective tissue contained bone trabeculae with a high density of osteocytes; i.e. the density of bone tissue grows around the fixator. The regenerate is represented by the areas of cancellous and lamellar tissue.

IM nailing with a compression locking of the nail. Fracture healing was histologically confirmed in 75% of patients.

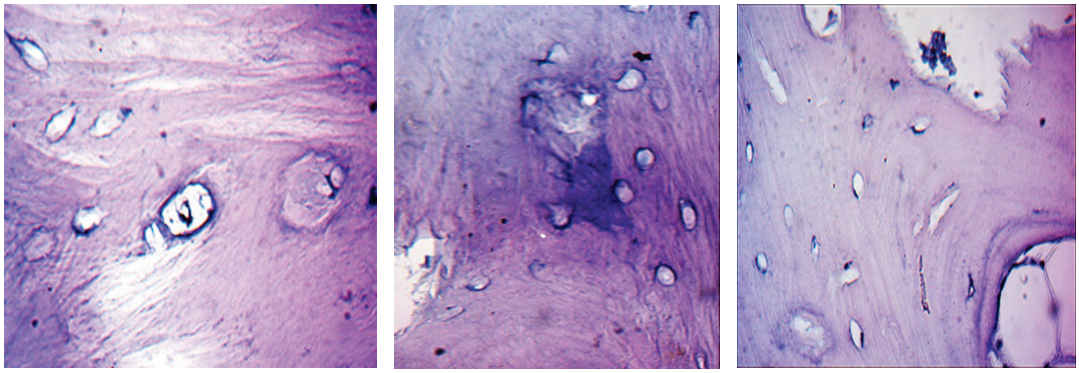
Conditions of tissues in 18 months after the fracture fixation. Histological study of the material, collected during the fixing device removal after the fracture healing (9-12 months) has demonstrated changes, similar to those discovered after the IM nailing with the dynamic locking of the nail. Jointly with small connective tissue areas, thick lamellar bone tissue was present in the projection of the regenerate.

Conditions of the tissues surrounding the IM nailing implants after 18 months in the intramedullary canal. Studying the fixing intramedullary devices, removed more than in 18 months, has demonstrated similar changes in



A B C

Fig. 1. Fragments of bone from the fracture area. High density of osteocytes. A. IM nailing with static locking of the screws. B. IM nailing with compression locking of the screws. C. IM nailing with dynamic locking of the screws. Haematoxylin and eosin. Amplification: 100.



A B C

Fig. 2. Bone tissue fragment. Matrix lamination. Lacunae without osteocytes. A. IM nailing with static locking of the screws. B. IM nailing with compression locking of the screws. C. IM nailing with dynamic locking of the screws. Haematoxylin and eosin. Amplification: 200.

tissues around the implant. We have discovered fibrosis changes in soft tissues. In the area around the intramedullary fixing devices and screws, we saw the areas of bone and dense connective tissue with thick collagen fibres and fibroblasts, located rarely among them. The samples from the regenerate area contained the areas of lamellar bone (Fig. 1. A, B, C), a network of bone trabeculae, different in width, located in edge portions, and small areas of connective tissue between them.

The assessment of the cortex of a diaphysis has shown the areas of lamination of the matrix with the unmasked collagen fibres with empty lacunae or remnants of detritus (Fig. 2. A, B, C).

The comparison of different types of IM nailing demonstrated that the bone tissue area in the projection of regenerate doesn't significantly differ within the period from 13 to 18 months and after 18 months (Table 1). At that, the area of the connective tissue decreases, evidencing the maturity of the regenerate. However, in the areas around the fixing devices and screws, the bone tissue area grew with a statistical significance after 18 months and the area of the connective tissue dropped.

Discussion

The research was based on studying two directions related to the removal of fixing devices for IM nailing: analysis of the conditions of regenerate and tissues around intramedullary implanted nail and screws to forecast optimal terms for the removal of IM implant with static, dynamic, or compression locking of the nail. In the research, we relayed upon AO recommendations for the optimality of the period of 18 months after the fracture consolidation

Table 1. Bone and connective tissue in the fracture area and around fixing devices for IM nailing

IM nailing with static locking of the screws			
	Bone tissue (%) from 12 to 18 months	Bone tissue (%) after 18 months	Statistical significance (P)
Fracture area Areas around a fixing device	78.2 ± 2,64 40.98 ± 1.99	80.18 ± 3.44 77.84 ± 2.22	> 0,05 < 0.01
	Connective tissue (%) from 14 to 18 months	Connective tissue (%) after 18 months	
Fracture area Areas around a fixing device	22 ± 2.62 59.02 ± 1.99	19.2 ± 3.44 24.16 ±2.98	> 0,05 < 0.01
IM nailing with static locking of the screws			
	Bone tissue (%) from 12 to 18 months	Bone tissue (%) after 18 months	Statistical significance (P)
Fracture area Areas around a fixing device	83.46 ± 3.69 62.29 ± 2.15	79.62 ± 3.18 84.36 ± 2.59	> 0,05 < 0.01
	Connective tissue (%) from 14 to 18 months	Connective tissue (%) after 18 months	
Fracture area Areas around a fixing device	16.54 ±3,69) 26.4±3.67	20.38 ± 3.18) 15.64 ± 2.59	> 0,05 < 0.01
IM nailing with dynamic locking of the screws			
	Bone tissue (%) from 12 to 18 months	Bone tissue (%) after 18 months	Statistical significance (P)
Fracture area Areas around a fixing device	80.36 ±3.65 42.7 ± .48	78.1 ±9.99 78.2 ± 2.22	> 0,05 < 0.01
	Connective tissue (%) from 14 to 18 months	Connective tissue (%) after 18 months	
Fracture area Areas around a fixing device	19.64 ±3.64 57.14 ± 5.61	21.9±3.98 21.8±2.53	> 0,05 < 0.01

[19] and extended our papers with the terms after 18 months. After the removal of the fixing IM devices, provided the consolidation of the fracture, histological study noted the formation of the fibrosis areas around the fixing devices, with a higher density after of use of statically locked IM nail. After the removal of the implants with static locking, it is expedient to reduce functional loading on the limb for up to 1 month to finish the functional transformation of the bones in the fracture area. In general, the development of the connective tissue layers around a metal fixing device complies with the classical law of histology "a body forms a fibrosis capsule around a foreign object". The peculiarity of the fixation is the proliferation of bone tissue, alternating with connective tissue. With time, while the fixing device remains in the body, the areas of bone tissue in the intramedullary canal grow. Biointegration and biocompatibility of implants are typical of the absence of inflammatory response on a microlevel for the studied periods on the background of the fracture consolidation.

The studies of conditions of the tissues after the IM nail removal, are rare. Fracture healing was studied on an experimental model of rabbits with the simulation of transverse osteotomy and further intramedullary fixation after intramedullary canal drilling. Bone callus formation was confirmed 2 weeks after the surgery, and 2 months after the operation, the biomechanical study of the animals showed no differences between the limb after the osteotomy and the contralateral one [20]. The collected data prove that intramedullary fixation of a transverse diaphyseal fracture doesn't interfere regeneration process.

One of the first studies examined tissue conditions in patients with femoral diaphyseal fractures, treated with intramedullary nailing, after 27 (15-44) months after the fixing device removal [21]. Using the CT, the authors observed the reduction in the density of bone trabeculae in femoral condyles and the area of the removed nail. Bone tissue density in femoral condyles and thickness of the cortex in this area dropped by 19% and 17%, respectively, compared to the contralateral limb. The cortex showed a slight decrease – by 4% in density and by 7% in thickness. A crossover longitudinal research on bone mineral density (BMD) analysed patients with tibial diaphyseal fractures after the IM nail removal by the method of double X-ray absorptiometry (DXA) on average, after 13 months [22]. It demonstrated, that in a proximal portion of femoral and tibial bones with a fracture, the BMD dropped by 3-11%, compared to the contralateral surface. At that, the distal portion of a tibial bone showed the largest loss in BMD (13-21%). A significant decrease of the BMD (5-6%) has been revealed also in the proximal femoral portion of the contralateral limb, declaring indirectly, that an intact limb may also suffer from the loss of bone mass after injury, thus after an intramedullary nail removal, restrictions in loading should be considered.

Thus, after IM nailing fixators removal according to histological results, we have discovered the formation of small areas of fibrosis around the fixing devices. The peculiarity of IM nailing is the proliferation of bone tissue around screws and nails with the extended fixation period (over 18 months) and the reduced connective tissue area. In the period after 18 months, the density of bone tissue around the fixing device grows, reflecting the integration of the implant with the fibrosis-bone tissue, able to cause negative consequences if the implant is removed. Revealed are destructive changes, connected with the matrix lamination and the death of osetocytes. Bio-integration and biocompatibility of implants are typical of the absence of inflammatory response on a microlevel in the background of the fracture healing.

Conclusions

- With the use of IM nailing, 50%, 55%, and 75% of patients have confirmed consolidation of the fracture after static, dynamic, and compression locking of the nail, respectively.
- Histological study of tissues around the three types of IM fixing devices demonstrated that before the 18th month, dense regenerate develops in the bone's fracture area, and after the 18th month, its density doesn't grow. After 18 months, the density of bone tissue demonstrates a statistically significant growth around fixing devices, especially in the areas of nails and screws location, having negative effects on the removal of the IM fixators.
- After 18 months, irrespective of the IM nail locking method, destructive changes progress in the cortex.

ექსპერიმენტული მედიცინა

ქვედა კიდურების ძვლების დიაფიზური მოტეხილობების მკურნალობა და ქსოვილების პათომორფოლოგიური კვლევები სხვადასხვა ტიპის ინტრამედულარული ბლოკირებით ოსტეოსინთეზის შემდეგ

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(წარმოდგენილია აკადემიის წევრის რ. ხეცურიანის მიერ)

ნაშრომის მიზანია ძვლის მოტეხილობების მკურნალობის დადებითი შედეგების წილის დადგენა სხვადასხვა ტიპის ინტრამედულარული ბლოკირების შტიფტის გამოყენებით და ქსოვილების ფორმირების შესწავლა ქსოვილ-იმპლანტის კიდეებზე პაციენტის სხეულიდან იმპლანტების ამოღების შემდეგ. კვლევაში მონაწილეობდა 60 პაციენტი ბარძაყისა და წვივის ძვლების დიაფიზური მოტეხილობით. პაციენტთა 3 ჯგუფში (თითოეულ ჯგუფში 20 ადამიანი), შტიფტის სტატიკური, შეკუმშვითი და დინამიკური ბლოკირებით ინტრამედულარული შტიფტის ფიქსატორების მოხსნის შემდეგ, შევისწავლეთ მოტეხილი ძვლის კონსოლიდაცია და ფიქსაციის გარშემო ქსოვილების მდგომარეობა. პაციენტების საშუალო ასაკი (43.9±6.5) წელი იყო. ყველა პაციენტს, თავისი სურვილით ან ექიმის რეკომენდაციით ამოუღეს იმპლანტები ქირურგიული გზით. პაციენტებს შორის 56.7% ქალი იყო. მოტეხილი ძვლის კონსოლიდაციის ანალიზი გაკეთდა თითოეული ჯგუფისთვის რენტგენის გამოყენებით, ინტრამედულარული შტიფტების 3 ტიპის გათვალისწინებით. ინტრამედულარული შტიფტის გამოყენების შემდეგ, პაციენტთა 50, 55 და 75%-ში გამოვლინდა ძვლის კონსოლიდაცია შტიფტის სტატიკური, დინამიკური და შეკუმშვითი ბლოკირებით, შესაბამისად. ჰისტოლოგიური მეთოდების საშუალებით შევისწავლეთ ქსოვილები შტიფტისა და ხრახნების გარშემო და ასევე, მოტეხილობის არეში. ჰისტოლოგიური კვლევა მოიცავდა მხოლოდ მოტეხილი ძვლის კონსოლიდაციის მქონე პაციენტებს უარყოფითი შედეგების გარეშე, როგორიცაა ფიქსატორის

მოტეხილობები, ნელი კონსოლიდაცია ან შეუხორცებლობა, ინფექცია და ა.შ. ძვლოვანი ქსოვილის ზრდის სიმკვრივე სტატისტიკურად მნიშვნელოვანია 18 თვის შემდეგ, განსაკუთრებით შტიფტისა და ხრახნების მოთავსების ადგილებში, რაც იწვევს ინტრამედულარული შტიფტის ამოღების სირთულეებს. ჩვენ აღმოვაჩინეთ დესტრუქციული ცვლილებები ქერქში. ამრიგად, ჰისტოლოგიური კვლევის შედეგებმა დაადასტურა, რომ პაციენტებში ინტრამედულარული ფიქსატორის მოცილება შესაძლოა მიზანშეწონილი იყოს მოტეხილი ძვლის კონსოლიდაციის შემდეგ ადრეულ პერიოდში, რადგან ფიქსაციის მექანიზმის გარშემო ძვლოვანი ქსოვილის დიდი უბნების წარმოქმნა მნიშვნელოვნად გაართულებს მის მოხსნას. კლინიკურ-რენტგენოლოგიურმა კვლევებმა აჩვენა, რომ მოტეხილობების შეხორცების ყველაზე დიდი წილი დაკავშირებულია შტიფტის კომპრესიული ბლოკირებით (75%).

REFERENCES

1. Anuar-Ramdhan IM., Azahari IM., Med Orth M. (2014) Minimally invasive plate osteosynthesis with conventional compression plate for diaphyseal tibia fracture. *Malays Orthop J.,* **8**(3): 33-36.
2. Court-Brown CM., Caesar B. (2006) Epidemiology of adult fractures: a review. Injury. **37**(8): 691-697.
3. Larsen P., Elsoe R., Hansen SH. et al. (2015) Incidence and epidemiology of tibial shaft fractures. *Injury,* **46**(4): 746–750.
4. Bäcker HC., Heyland M., Wu CH. et al. (2022) Breakage of intramedullary femoral nailing or femoral plating: how to prevent implant failure. *Eur J Med Res.,* **27**(1): 7.
5. Bondarenko AV., Guseinov RG., Gerasimova OA. et al. (2023) Chastota, factory riska, osobennosti diafizarnykh nesrashchenii dlinnykh kostei nizhnyh konechnostei (Occurrence, risk factors, specificity of diaphyseal non-unions of lower limbs' long bones) (in Russian). *Polytrauma,* S.l.(2):36-44. Access: https://polytrauma.ru/index.php/pt/article/view/439>
6. Wong WKN., Tan WPJ., Phua YMC. et al. (2021) Intramedullary nail: the past, present and the future - a review exploring where the future may lead us. *Orthop Rev (Pavia),* **13**(2): 25546.
7. Hrytsai MP., Kolov HB., Tsokalo VM. (2016) Infektsijni usklandennia pislia nakistkovoho ta vnutrishniokistkovoho osteosyntezu (Infectious complications after superficial and intramedullary osteosynthesis. In Ukrainian). Surgery, Orthopedics, Traumatology, 3 (25). Access: https://health-ua.com/article/6691-nfektcjn-uskladnennya-pslya-nakstkovogo-ta-vnutrshnokstkovogo-osteosintezu.
8. Barcak EA., Beebe MJ., Weinlein JC. (2018) The role of implant removal in orthopedic trauma. *Orthop Clin North Am.,* **49**(1): 45-53.
9. Scheider P., Ganger R., Farr S. (2020) Complications of hardware removal in pediatric upper limb surgery: a retrospective single-center study of 317 patients. *Medicine* (Baltimore), **99**(5): e19010.
10. Williams BR., McCreary DL., Parikh HR. et al. (2020) Improvement in functional outcomes after elective symptomatic orthopaedic implant removal. *J Am Acad Orthop Surg Glob Res Rev.,* **4**(9): e20.00137.
11. Lieber J., Dietzel M., Scherer S. et al. (2021) Implant removal associated complications after ESIN osteosynthesis in pediatric fractures [published online ahead of print]. *Eur J Trauma Emerg Surg.*
12. Szczęsny G., Kopec M., Politis DJ. et al. (2022) Review on biomaterials for orthopaedic surgery and traumatology: from past to present. *Materials* (Basel), **15**(10): 3622.
13. Carnicer-Lombarte A., Chen S-T., Malliaras GG., Barone DG. (2021) Foreign body reaction to implanted biomaterials and its impact in nerve neuroprosthetics. *Front. Bioeng. Biotechnol.,* 9: 622524.
14. Bandyopadhyay A., Mitra I., Goodman SB. et al. (2023) Improving biocompatibility for next generation of metallic implants. Prog Mater Sci., 133:101053.
15. Dapunt U., Giese T., Lasitschka F. et al. (2014) On the inflammatory response in metal-on-metal implants. *J Transl Med.,* 12:74.
16. Bondarenko S., Dedukh N., Filipenko V., Akonjom M., Badnaoui1 AA., Schwarzkopf R. (2018) Comparative analysis of osseointegration in various types of acetabular implant materials. *HIP International,* 1–7.
17. Richter M., Matusiewicz H. (2021) Review of the local tissue reaction to metallic spinal implant debris: ions and nanoparticles. *World Journal of Advanced Research and Reviews,* 09(03): 167-187.

18. Shrivas S., Samaur H., Yadav V. et al. (2024) Hard tissue integration around percutaneous bone-anchored titanium prostheses: toward achieving holistic biointegration. *ACS Biomater Sci Eng.,* **10**(4):1966-1987.
19. Twaddle B. (2013) Implant removal. Avail. from: https://aotrauma.aofoundation.org/-/media/project/aocmf/aotrauma/documents/education_pdf/orp_handout_english_implant-removal.pdf?la=en&hash=E4B40F4E0080A773FE860D1C6CF2EF0636E555E9.
20. Yoshino O., Brady J., Young K. et al. (2017) Reamed locked intramedullary nailing for studying femur fracture and its complications. *Eur Cell Mater.,* 34: 99-107. doi: 10.22203/eCM.v034a07.
21. Braten M., Nordby A., Terjesen T., Rossvoll I. (1992) Bone loss after locked intramedullary nailing. Computed tomography of the femur and tibia in 10 cases. *Acta Orthop Scand,* **63** (3): 31 0-314.
22. Kröger H., Kettunen J., Bowditch M. et al. (2002) Bone mineral density after the removal of intramedullary nails: a cross-sectional and longitudinal study. *J. Orthop. Sci.,* **7**(3): 325-330.

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