Review article
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Failed distractional bone regeneration as a complication of distraction osteosynthesis: risk factors, preventive diagnosis, treatment

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Abstract

Introduction Despite the large number of articles on complications associated with surgical lengthening, information about such a complication of transosseous distraction osteosynthesis as failed bone regenerate (called hypoplastic in foreign literature) is extremely rare. There are no methods for predicting the restructuring of the regenerate and clinical recommendations for the management of patients at various stages of reconstruction of the distraction regenerate. This entails a long period of immobilization and severe complications.

The objective of the work was to define the notion of inadequate ("ischemic"/hypoplastic) bone regeneration and the problem of its formation as a complication during surgical limb lengthening

Material and methods The PubMed database and the eLIBRARY scientific electronic library were used to select sources for a systematic literature review. The sources published between 1997 and 2020 were selected

Results and discussion Ineffective distraction bone regenerate is a complication of surgical segment lengthening with the shape and/or structure of the newly formed bone preventing functional load on the segment. There is a general tendency with bone elongations being greater than 15-20 % to significantly reduce biomechanical properties of the distractional regenerate bone. Patients' age at surgical lengthening is not reported as a risk factor for distraction regenerate fractures and a history of adverse events and complications is regarded as an additional risk factor. Inadequate (unstable) distraction regenerate bone includes morphotypes III-V and structural types 1, 5, 7 as classified by Ru Li. There are no clinical guidelines for operational strategy. Failed distraction bone regeneration as a complication of distraction osteosynthesis was reported by different authors between 1997 and 2020. There are conflicting statistically unreliable data regarding a risk for regenerate bone to develop into a less stable type. The surgical options presented have no statistical significance (occasional case reports) and do not describe all possible clinical scenarios.

Conclusion The problem of failed distraction regeneration and impaired organotypic restructuring remains one of the most important problems in limb lengthening. Inadequate formation and restructuring of newly formed bone can be caused by many factors including anatomical, physiological and technological aspects that would require further comprehensive study.

Keywords: hypoplastic/ischemic/atrophic distractional regenerate bone, complications of distraction osteosynthesis, classification of distraction regenerate bone

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INTRODUCTION

There are no statistical data on the number of limb lengthening surgeries performed worldwide due to the lack of the national healthcare reports with no possibility to authenticate the information. With a large number of articles and reports on complications associated with surgical limb lengthening there is a paucity of publications reporting failed bone regeneration, called hypoplastic in foreign literature, as a complication of transosseous distraction osteosynthesis (1-4.8 % of all surgical limb lengthening cases). There is no clear definition of the adverse event which cannot be prevented due to the lack of methods for predicting the restructuring of the regenerate bone into an unstable type. There are no recommendations for management of patients at various stages of reconstruction of the distraction bone regeneration to be followed by a long period of immobilization and severe complications (muscle atrophy, joint contracture, severe decrease in the mobility and quality of life, mental health adverse effect).

The objective was to define the notion of inadequate ("ischemic"/hypoplastic) regenerate bone and explore the phenomenon as a complication of surgical limb lengthening based on literature data.

MATERIAL AND METHODS

An internet search of eLIBRARY and PubMed databases using the search terms: bone regenerate complications during lengthening, ischemic regenerate bone, classification of distraction bone regeneration, treatment of ischemic bone regenerate, fractures after bone lengthening was performed.

Exclusions included publications reporting maxillofacial surgery (mandibular lengthening, maxillar bone correction), animal experiments, lengthening of short cancellous bones, case/control reports and paid content.

Overall, 1207 contributions were identified including 808 with eLIBRARY and 399 with PubMed. 37 sources were selected, including 5 patents.

RESULTS

Definition of the term

The definition of ischemic distraction regenerate in their study was given by D. Borzunov et al. [1]. The authors used the radiological classification offered by R. Li to evaluate hypoplastic types of distraction regenerate [2]. This classification includes five callus shapes of distraction osteogenesis:

– Fusiform (the regenerate is wider than the original bone);

– Cylindrical (the regenerate is the same width as the original bone);

– Concave (the regenerate tends to produce an hourglass appearance);

– Lateral (the regenerate show a callus defect);

– Central (the regenerate is a thin pillar in the central portion).

According to the authors, types 3 and 5 can be classified as "ischemic" distraction regenerate formed as a hypoplastic type. Type 4 (with the formation of a marginal defect and a hypoplastic bone formation) cannot be classified as an "ischemic" regenerate. It is usually associated with an impaired integrity of the bone due to the osteotomy. The authors differentiate between "ischemic" regenerate and "hypoplastic" regenerate based on the following characteristics: a) the connective tissue area prevailing over the osseous area of the regenerate; b) the the original bone area prevailing over the regenerate area; c) no tendency to increasing the length and area of bone sections (according to radiological investigations in dynamics); d) formation of endplates at the ends of the osseous regenerate parts with signs of nonunion (like an atrophic nonunion); e) disparity between organotypical restructuring of the regenerate and bone fixation length in combination with

maintained pathological mobility observed with clinical testing; f) formation of a soft tissue defect in the projection of the "ischemic" regenerate. In the treatment of patients with this pathology. The authors suggested osteotomy to be produced in the proximal and distal original bone to be followed by compression and compaction [1].

F. Schiedel et al. reported 67 patients (101 cases of femoral lengthening) with 11 developing unstable regenerate between 2008 and 2010. The authors reported no cases where intramedullary reinforcement could not be used. The appearance of the regenerate using the Li classification scheme was not a predictive value for the probability of a fracture after frame removal. The authors classified morphotypes 4 and 5 and structural types 1-4 of the regenerate as "unstable" types [3]. J. Kenwright et al. classified fractures after surgical lengthening of the segment and identified 4 types: Ia, compression of the regenerate zone; Ib, fracture of the regenerate and displacement; II, fracture in the "base" of the regenerate; III, fracture of the parent bone proximally/distally off the regenerate zone; IV, fracture of the adjacent bone segment [4].

Preventive diagnosis and risk factors

In 2003, G.V. Dyachkova et al. reported outcomes of 149 patients who underwent distraction osteosynthesis, and found that if the height of the radiolucent zone (connective tissue layer) was more than 20 % of the height of the diastasis, the reasons for that were to be identified and adjustments made during the distraction; if the diameter of the regenerate at the "growth radiolucent zone" was 20 % less than the diameter of the bone fragments, the reasons for that were to be identified and adjustments made to the elongation process due to the risk of an hourglass regenerate [5].

A.L. Shastov reported a history of repeated and unsuccessful surgical interventions, angioneurological disorders, cicatricial degeneration of soft tissues, traumatic disruption of bone integrity during osteotomy, inadequate distraction rate, lack of timely monitoring as risk factors of "ischemic" distraction regenerate [6].

The C-reactive protein level was practical for predicting poor regeneration during Ilizarov segment lengthening. The serum CRP of less than 6 mg/l in the first 10 days of distraction was a prognostic sign indicating high probability of poor regeneration [7].

Outcomes of lower limb lengthening in patients with systemic skeletal diseases and pathologically short stature showed that the rate of poor results increased with repeated segment lengthening in patients aged 14 years and older, in adults aged 20 years and older, with the length gain of more than 50 % of the initial segment length, with osteosynthesis index (OI) being less than 20 days/cm with the femur lengthened secondarily at the cross-lengthening stage, and in patients with Shereshevsky-Turner syndrome [8].

K.A. Dyachkov suggested that the regenerate "growth zone" should not exceed 23-33 % of the total regenerate area during the distraction period, otherwise it would result in complications in most cases [9].

White blood cells CD3++ and CD19++ more than 6.6 units and the serum immunoglobulin A of more than 3.3 would slow down fracture healing and transosseous distraction osteosynthesis with the Ilizarov healing [10].

K.N. Devmurari et al. explored radiographs of 28 cases of femoral lengthening by 30-55 % of the original length and reported callus fractures in 14 patients within 440-545 days of frame removal. No callus fracture was seen in segment lengthening of 30 %; the atypical shape of the callus and its optical properties corresponded to the parameters of the femur [11].

L. Zaka et al. reviewed outcomes of 19 patients who underwent lower limb lengthening with intramedullary nail. The mean age of the patients was 43 years with a mean distraction distance of 38.9 mm. There was no relationship between the effectiveness of distraction osteosynthesis and the patient's age [12].

In contrast, other authors [13] retrospectively studied 63 patients (aged 3 to 57 years) who had 74 distraction osteogenesis procedures between 2004 and 2009 using circular and monolateral external fixators. Adult age and bone healing index were the most important predictors of complications associated with the distraction regenerate restructuring into unstable types. The use of the cure index as such was uninformative. The index was calculated by dividing the number of days from the beginning of treatment to the patient's complete recovery by absolute or relative length gain (it can be calculated at the end of treatment, and not at the beginning or in the mid, and cannot be used for prediction). Another study [14] indicated 72 cases of segment elongation with 17 fractures observed in 25 patients and occurred in different morphotypes of the regenerate without distinct correlation with the relative segment elongation (from 39 to 66 %).

K.P. Venkatesh et al. [15] reviewed the results of 20 patients who underwent bilateral lengthening with a monolateral external fixator. The patients were divided into 2 groups: 12 patients had lengthening of less than 50 % of the original segment length and 8 of more than 50 % of the initial femoral length. All patients developed stable types of regenerate (70 % fusiform and 30 % cylindrical) in the initial phase of distraction. The regenerate transformed into a less stable type in 85 % of cases of the first group and in 62 % of the second group with 25 % of them restructured into unstable types during advanced distraction phases. The ratio maintained during the consolidation stage.

The regenerate was shown to restructure into a less stable type in all cases of elongation greater than 10 cm. The authors reported a correlation between the regenerate structure and the risk of fracture. Fractures were not associated with a "transparent" regenerate and cylindrical shape (types 4 and 8 as classified by R. Li's and is characterized by a radiological transparent layer in the projection of the growth zone of the regenerate). Li type III regenerate fractures were treated using re-osteosynthesis with an external fixation device; patients with regenerate types IV and V with external transosseous compression-distraction osteosynthesis added by bone grafting with no dynamics for more than 4 months of frame removal.

In 2012, F. Launaya et al. [16] reported retrospectively 111 cases of lower limb lengthening (40 femurs, 71 tibiae in patients aged 5 to 32 years) performed between 2000 and 2010 with a higher rate of femoral fractures compared to the tibia. Most of the fractures were classified as Simpson – Kenwright type II. The incidence of fractures was higher with the surgery performed for patients aged 9 years and younger and with distraction started earlier than 7 days of osteotomy. There was no statistical correlation between the beginning of lengthening and the patient's age.

N. Muzaffar et al. reported 15 cases of femoral lengthening in 15 patients aged 12 to 32 years with 3 "false" cylindrical regenerates and the volume (measured in pixels) risky because if diagnosis is untimely or inaction on the part of the attending physician, the biomechanical properties of the newly formed bone can be completely lost, and repeated surgical intervention would be required [17].

A review of 319 Ilizarov lengthening procedures was performed in 2013 to include patients aged 3 to 50 years and showed a strong relationship between the lengthening index (month/cm of lengthening) and the length of the regenerate (i.e., the greater the lengthening of the segment, the longer the fixation with the frame on). The lowest lengthening index was in younger patients. A significant difference in the lengthening index in different segments was also revealed (16 % less in the femur than in the tibia). The authors were unable to statistically prove longer periods for repeated segment lengthenings [18].

M. Kenawey et al. reported 37 cases of femoral lengthening using the ISKD system with poor regenerate noted in 8 cases (no description of the cases and the definition of the concept provided). Important risk factors were a distraction rate greater than 1.5 mm/day (9.1 times higher risk), age 30 years or older, smoking, and lengthening greater than 4 cm. [19].

In his work N.G. Burkel et al. [20] reported 178 cases of femoral lengthening in 108 patients and a 4.5 % incidence of distraction regenerate fractures. They found no statistically significant relationship between the incidence of fractures and the age of patients, gender, and time of surgery. Lengthening of greater than 5 cm were considered a statistically significant risk factor.

The bone and the structural components of the limb segment are involved in the process of limb lengthening, and the success of treatment depends on their condition. The muscles has an important role. T.I. Menshchikova [21] reported the use of ultrasound diagnosing the reserve capabilities of muscles (echo density) for the maximum lengthening gain without negative consequences.

Treatment options

Upbringing the distraction regenerate and stimulation of distraction osteosynthesis is emphasized by many authors.

S.S. Leonchuk et al. [22] reported an hourglass-shaped regenerate with a height of the middle layer of 10 mm or greater and low bone mineralization as indications for stimulation of osteogenesis. Mechanical stimulation was considered as a simple and most effective method (gradual or immediate compression of the regenerate by 7-10 mm with a certain force applied). The technique ensured compression of the bone regenerate with ischemic connective tissue stimulating angiogenesis. The method facilitated restoration of the regenerate integrity with the diameter and the mechanical strength increasing. The "rotational" compression of the distraction regenerate could be more effective. The bone was subjected to a dosed external rotation of 15-20º during gradual segment lengthening and correction of the limb axis with the apparatus, after 5-7 days of longitudinal-axial bone alignment. Rotation was produced at a rate of 2-3º/day. Biomechanical stimulation was performed using automatic high-frequency distraction. The "accordion maneuver" was used to stimulate osteogenesis by distraction by 0.25 mm in the morning to be followed by compression of 0.25 mm in the afternoon and distraction of 0.25 mm to be produced in the evening. Good results have been shown with use of bioactive implants (combined osteosynthesis using intramedullary wires coated with hydroxyapatite), hyperbaric oxygenation, local application of low-frequency pulsed ultrasound on the regenerate and electrical stimulation of the limb muscles.

A.L. Shastov reported compaction of the regenerate including an additional osteotomy, minimally invasive introduction of autologous bone chips and medullary components or paired fibula as methods of choice for treatment of an "ischemic" distraction regenerate [6].

A retrospective analysis performed by V.I.Shevtsov et al between 1976 and 2020 included 213 literature sources [23] and 564 patients featuring (1) the use of auto- and heteroplasty for bone defect repair; (2) fibular bone grafting to repair bone defects; (3) the use of artificial materials to repair bone defects; (4) application of tissue engineering and cellular technologies. The method developed by G.A. Ilizarov has been recognized as the most biological method for bone defect repair with the effectiveness of 97.7-100 % but it cannot be used for short bone fragments, the need of long-term treatment, limited in-hospital stay, for patients living far from medical centers, etc.).

V.D. Balayan et al. reviewed treatment outcomes of 120 patients aged 23 to 72 year. They were treated with revascularizing osteoperforation, X-shaped longitudinal osteotomy, bone grafting with auto- and allografts in combination with fixation of fragments with a bone fixator, external fixation device, intramedullary osteosynthesis with locking screws (BIOS) and intraosseous Fixion rod to stimulate reparative osteogenesis shortening the period of limb external fixation from 115 ± 12 days to 85 ± 12 days [24].

T.I. Dolganova et al. [25] reported ischemic distraction regenerate observed during polyfocal bone lengthening in patients with long bone defects (ultrasound examination) with distraction regenerates developing independently during sequential multi-level bone lengthening. An additional bone osteotomy and subsequent discrete bone transport can improve reparative processes at the site

of the “ischemic” distraction regenerate with the closure of the marginal defect with newly formed bone tissue and accelerated organotypic restructuring (the latter should be taken into account when choosing surgical treatment strategy).

Methods for stimulation of distraction regeneration that can be used for preventive and therapeutic purposes included a longitudinal split left along the posterior surface of the bone as a source of osteoinductive cells [26], HBOT to address vascular, neurological and biomechanical complications [27],platelet-rich plasma introduced into the distraction regenerate to prevent poor regeneration [28], gradual elongation with spiral longitudinal deflection of fragments to ensure formation of a good volumetric bone regenerate [29], accelerated distraction rate in the first 10 days after osteotomy and the slowdown 10 days before the end of distraction leading to bone regeneration being comparable with the maternal bone fragments [30].

J.J. Jauregui et al. [31] performed meta-analysis of 192 cases of segmental lengthening showing that the use of LIPUS (low-frequency ultrasound stimulation) and PEMF (pulsated electromagnetic field) reduced the HI (healing index) from 45.4 days/cm of lengthening to 33.7 days/cm.

In contrast, A.H.R.W. Simpson et al. [32] conducted a study (32 patients using stimulation with the LIPUS system and 30 placebo) showed no effect of ultrasound on distraction osteoneogenesis. Smoking increased the cure rate by 50 %.

H.I. Balci et al [33] reported the optimal distraction rate of 0.564 mm/day for good morphological quality callus based on the experience of twenty-seven patients with congenital pseudarthrosis of the tibia who underwent limb lengthening surgery between 1997 and 2016.

K.-W. Park et al. [34] reported a higher incidence of complications during femoral lengthening in 148 achondroplasia patients who underwent lower limb lengthening. Tibial lengthening had a significantly lower complication rate and a higher callus formation rate than femoral lengthening. The authors gave an example of the formation of a Li type V regenerate (treatment option included reinforcement with wires and use of an autograft from the iliac crest with a satisfactory result).

DISCUSSION

Ineffective distraction bone regenerate is a complication of surgical segment lengthening when the shape and/or structure of the newly formed bone does not allow functional load on the segment. The complication is a fracture after surgical segment lengthening (types III, IV complications according to Donnan). The reported incidence of fractures after surgical segment lengthening averages 2.9 % (1–4.8 %, with one study reporting a rate of 40 %) [35, 36]. A review of 11 series including 1065 segments of patients of different ages, with various nosologies, different lengthening values included 117 fractures and deformities at the regenerate level amounting for 10.99 % of which patients must be aware signing consent for surgical lengthening intervention.

The trends that can be observed in the majority of publications include: lengthening greater than 15-20 % is associated with higher complication rate (including failed distraction bone regenerate). Data regarding the performance situation are conflicting. In most articles, the age at which surgical lengthening is performed is not a risk for the development of an incompetent distraction regenerate; a history of problems and persistence during previous surgical lengthening of segments is an additional risk factor (the significance of the indicator of its underdevelopment). There are conflicting data regarding the effect of age on the incidence of complications. The age at which surgical lengthening is performed is not a risk factor for the development of a failed distraction regenerate; a history of adverse events during previous surgical segment lengthening is an additional risk factor (the significance is not indicated numerically).

The pathology can be treated surgically and conservatively (plaster/plastic bandage, osteosynthesis with a plate/TEN with/without grafting, bifocal osteosynthesis with an external fixation device).

No uniform recommendations for clinicians have been developed at the moment. Like other researchers, we suggest that R. Li's classification is the most practical grading system for assessing distraction regenerate to identify 5 morphotypes and 10 types of regenerate structure [37]. Most authors evaluate morphotypes III-V and structural types 1, 5, 7 as a failed distraction (unstable) regenerate (if these structures are identified on radiographs, measures should be taken to stimulate regeneration).

CONCLUSION

Failure of the distraction regenerate and impaired organotypic restructuring has been one of the most important problem of limb lengthening. Poor regeneration and restructuring of newly formed bone can be caused by anatomical, physiological and technological events that remain controversial and require further comprehensive study.

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