



# Comparative Effectiveness of the Masquelet Technique, the Ilizarov Method, and Vascularized Bone Flaps in the Reconstruction of Extensive Long-Bone Defects of the Limbs: A Systematic Review and Meta-Analysis

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## Abstract

**The aim of this meta-analysis** – to compare clinical outcomes and complications of the reconstruction of extensive long-bone defects of the limbs of various etiologies in patients older than 18 years using the Masquelet technique, the Ilizarov bone transport, and reconstructive procedures with vascularized bone flaps.

**Methods.** Publications were searched in the eLIBRARY, PubMed, Embase, Cochrane Central Register of Controlled Trials, and Google Scholar databases for the period 2015–2025. Randomized controlled trials and cohort studies addressing the reconstruction of extensive bone defects of the limbs using different techniques (the Masquelet technique (MT), bone transport (BT), and free vascularized flaps (FVF), particularly the fibular graft) were included in the analysis.

**Results.** Nine publications involving a total of 375 patients were included in the meta-analysis to assess the effectiveness and safety of the techniques. The majority of cases involved long bones of the lower limbs ( $n = 332$ ; 87%), most commonly the tibia ( $n = 284$ ; 74%), followed by the femur ( $n = 48$ ; 13%). Among upper limb injuries, extensive bone defects of the forearm were reported in 44 cases (12%) and of the humerus in 4 cases (1%). The overall duration of fixation did not differ significantly between MT and FVF groups, nor between MT and BT groups ( $p = 0.76$  and  $p = 0.40$ , respectively). The proportion of patients achieving complete bone union without additional surgical interventions was significantly higher with BT compared to MT (86% vs. 61%,  $p = 0.02$ ). The analysis of surgical site infection (SSI) rates revealed the following patterns: the proportion of patients with superficial SSI was significantly lower with MT compared to BT (11% vs. 23%,  $p = 0.0004$ ). Conversely, the incidence of deep SSI was significantly higher with MT compared to BT (15% vs. 8%,  $p = 0.04$ ). No statistically significant differences were found regarding nonunion rates or the conversion of surgical treatment to amputation. The proportion of patients with excellent or good outcomes according to the ASAMI score was 85% for MT and 71% for BT; however, the difference was not statistically significant ( $p = 0.48$ ).

**Conclusion.** The systematic literature review confirmed the effectiveness of all three methods: the Masquelet technique, the Ilizarov bone transport, and free vascularized flaps. The meta-analysis did not reveal a significant advantage of any single method in terms of fixation time or time to union; however, distinct safety profiles were identified and should be considered when selecting the surgical strategy. When choosing a technique for the reconstruction of large segmental bone defects, it is essential to take into account the defect location and length, soft tissue status, the presence and activity of infection, as well as individual patient characteristics, particularly treatment adherence and expectations regarding the quality of life.

**Keywords:** Masquelet technique; induced membrane; bone transport; free vascularized bone flap; open fracture; nonunion; osteomyelitis; bone defect.

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## Сравнение эффективности методик Masquelet, костного транспорта по Илизарову и кровоснабжаемых лоскутов при замещении обширных дефектов длинных костей конечностей: систематический обзор и метаанализ

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### Реферат

**Цель метаанализа** — сравнить клинические результаты и осложнения при замещении обширных дефектов длинных костей конечностей различной этиологии у пациентов старше 18 лет с помощью техники Masquelet, методики костного транспорта по Илизарову и реконструктивных вмешательств с применением свободных кровоснабжаемых костных лоскутов.

**Материал и методы.** Поиск публикаций осуществлен в базах данных eLIBRARY, PubMed, Embase, Cochrane Central Register of Controlled Trials, Google Scholar за период с 2015 по 2025 г. В анализ включены РКИ и когортные исследования, посвященные замещению обширных дефектов костей конечностей с помощью различных техник: Masquelet (ТМ), костного транспорта (МКТ) и свободных кровоснабжаемых лоскутов, в частности малоберцового кровоснабжаемого трансплантата.

**Результаты.** Для метаанализа с целью оценки эффективности и безопасности методик было отобрано 9 публикаций, включавших данные о 375 пациентах. Преобладали описания повреждений длинных костей нижних конечностей ( $n = 332$ ; 87%), наиболее часто — большеберцовой кости ( $n = 284$ ; 74%), на втором месте по частоте — поврежденная бедренной кости ( $n = 48$ ; 13%). Среди повреждений верхних конечностей описаны обширные костные дефекты предплечья ( $n = 44$ ; 12%), плечевой кости ( $n = 4$ ; 1%). Общая продолжительность фиксации в группах пациентов после ТМ и СКЛ, а также ТМ и МКТ статистически значимо не различалась ( $p = 0,76$  и  $p = 0,40$  соответственно). Доля пациентов с полной консолидацией, достигнутой без дополнительных хирургических вмешательств, при применении МКТ в сравнении с ТМ была статистически значимо выше (86% против 61%,  $p = 0,02$ ). При оценке частоты распространенности инфекций области хирургического вмешательства (ИОХВ) были выявлены следующие особенности: доля пациентов с поверхностной формой ИОХВ была ниже ( $p = 0,0004$ ) для ТМ в сравнении с МКТ (11% и 23% соответственно). И напротив, частота глубокой ИОХВ для ТМ оказалась выше ( $p = 0,04$ ) в сравнении с МКТ — 15% и 8% соответственно. Статистически значимые различия по частоте несращения и конверсии хирургического вмешательства в ампутацию выявлены не были. Доля пациентов, достигших отличных и хороших результатов по шкале ASAMI, составила 85% для ТМ и 71% для МКТ, различия не были статистически значимыми ( $p = 0,48$ ).

**Заключение.** Систематический обзор литературы подтвердил эффективность всех трех методов: техники Masquelet, костного транспорта по Илизарову и использования свободных кровоснабжаемых лоскутов. Метаанализ не выявил значимого преимущества ни одного из методов по срокам фиксации и консолидации, однако обнаружил характерные профили безопасности, которые должны учитываться при выборе тактики. При выборе метода замещения крупных сегментарных дефектов следует учитывать локализацию и протяженность дефекта, статус мягких тканей, активность инфекционного процесса, а также индивидуальные характеристики пациента, в частности его приверженность лечению и ожидания в отношении качества жизни.

**Ключевые слова:** техника Masquelet; индуцированная мембрана; костный транспорт; свободный кровоснабжаемый костный лоскут; открытый перелом; несращение; остеомиелит; дефект кости.

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## INTRODUCTION

According to the literature, the annual number of patients with extensive bone defects of various etiologies exceeds 20 million and shows a tendency to increase [1, 2].

Particular difficulty is presented by segmental defects of the long bones of the limbs classified as type C according to the Universal Classification of Long Bone Defects [3]. As a rule, such defects occur in the setting of high-energy injuries and are often associated with massive microbial contamination of the wound, which necessitates prolonged multistage treatment and is related to a high risk of complications, predominantly infectious in nature [4].

Current treatment methods for this pathology include the reconstruction of bone defects using distraction osteogenesis according to the Ilizarov technique (bone transport – BT), the use of an osteoinductive membrane, or the Masquelet technique (MT), and free transfer of vascularized osteomuscular tissue complexes (predominantly the free fibular flap – FFF), as well as various options of actively developing bioengineering technologies [5, 6].

Despite the availability of thematic review articles, including systematic reviews and meta-analyses [6, 7, 8, 9], there is currently no unified scientifically substantiated approach to selecting the optimal strategy for the reconstruction of extensive defects of the long bones of the limbs. Therefore, the problem of treating patients with extensive segmental bone defects remains extremely relevant.

*The aim of this meta-analysis* – to compare clinical outcomes and complications in the reconstruction of extensive long-bone defects of the limbs of various etiologies in patients older than 18 years using the Masquelet technique, the Ilizarov bone transport technique, and reconstructive procedures with free vascularized bone flaps.

## METHODS

### Search strategy

The systematic literature review was performed in accordance with the international guidelines for Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) [10]. The key questions and objectives of the review, the information search strategy, inclusion

and exclusion criteria, screening algorithms, methods for source evaluation, data synthesis and assessment of the risk of bias, as well as approaches for resolving disagreements were defined prior to performing the review, reflected in a predeveloped study protocol, and were not subject to modification during its implementation. The protocol of the planned review was not previously published or registered in any registry.

The search for relevant publications was carried out in the databases eLIBRARY, PubMed (MEDLINE), Embase (Ovid), Cochrane Central Register of Controlled Trials (CENTRAL), and Google Scholar using logical operators and keywords. For English-language sources, the following search query was used: (“Masquelet” OR “induced membrane”) AND (“Ilizarov technique” OR “bone transport” OR “distraction osteogenesis”) OR (“vascularized bone graft” OR “vascularized fibula graft”). For Russian-language sources, a similar search strategy was applied. The search for publications, study selection, and data extraction were performed independently by two investigators in parallel. In case of disagreement regarding the inclusion of a publication in the meta-analysis, the decision was made through discussion involving the entire group of authors. The search time frame was 10 years (2015–2025). The last search date was May 20, 2025.

The next step after screening titles and abstracts in the aforementioned databases was the manual selection of relevant full-text publications that met the inclusion criteria. The search strategy and the number of excluded publications with the reasons for exclusion are presented in Figure 1.

### Study selection

Clinical studies that met the criteria listed below, defined using the PICOS algorithm [11] (Table 1), were included in the review.

#### *Inclusion criteria:*

1) patients aged 18 years and older who underwent the reconstruction of an extensive bone defect (more than 2 cm) using the Masquelet technique, regardless of the etiology and location of the bone defect; the comparison group included reconstruction using a free vascularized flap or the Ilizarov technique;

2) study type: randomized controlled trials (RCTs), retrospective and prospective cohort studies (level of evidence 1–2);

3) availability of data on at least one of the following treatment outcomes: duration of fixation, time to consolidation, time to restoration of limb weight-bearing capacity, functional assessment, postoperative complications.

No restrictions were imposed regarding the sex of study participants, the type of fixation, the presence of randomization, blinding, or other aspects of study design beyond those listed above.

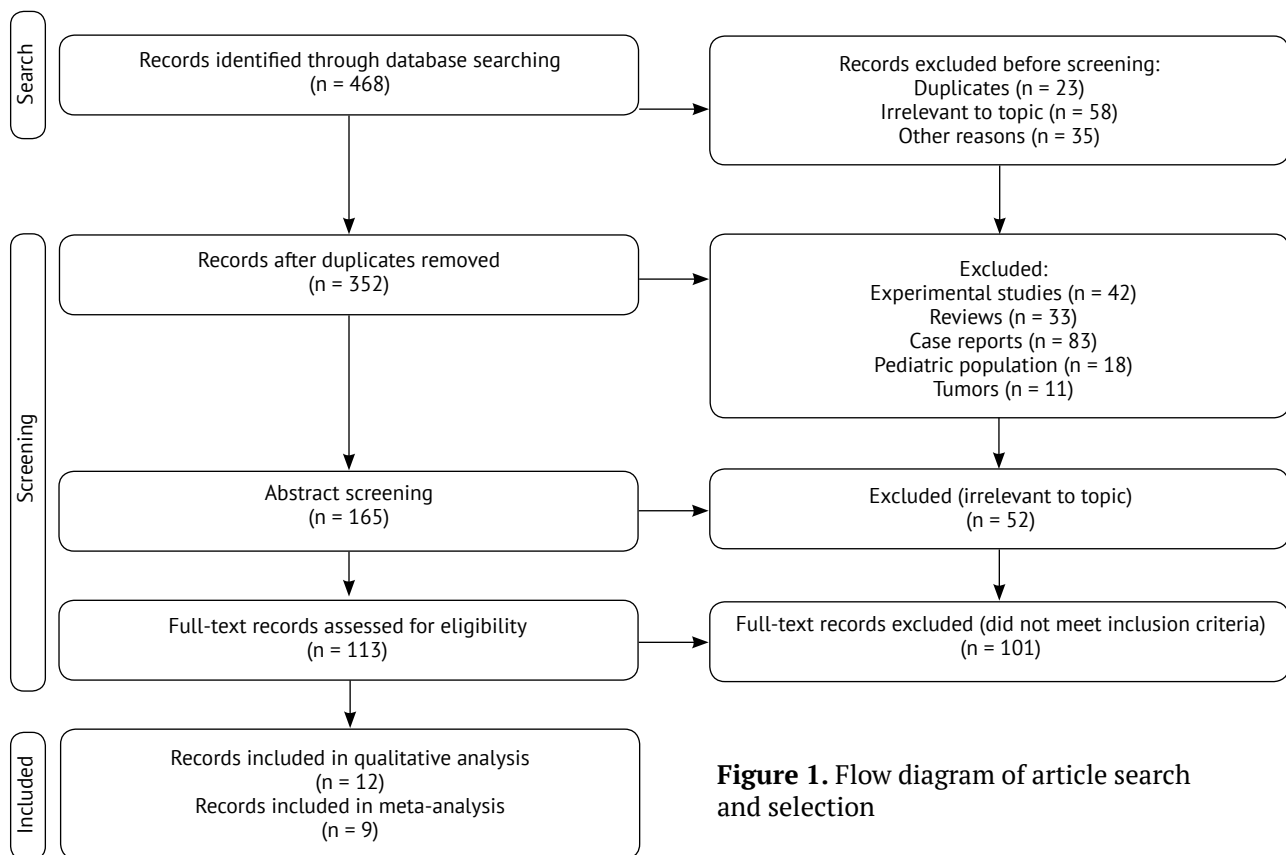
Publications meeting at least one of the following criteria *were excluded*:

- 1) conference proceedings, review articles, clinical guidelines, and meta-analyses;
- 2) incomplete presentation of data in the study;
- 3) duplicate studies containing previously used data;
- 4) presence of an extensive bone defect following surgical treatment of a malignant neoplasm;
- 5) preclinical studies on animals and *in vitro* studies.

### Data extraction and assessment of study quality

The screening of the publications was performed independently by two authors (A.A.I. and F.Yu.A.) without the use of automation tools. The following extracted data were entered into a pre-prepared table: first author’s name, year of publication, study type and level of evidence, general characteristics of the sample (number of patients, sex, age), localization and size of the bone defect, etiology of the condition, intervention performed, postoperative follow-up period, functional outcomes, and complications. In the presence of discrepancies, conflicts of interpretation were resolved through collegial discussion.

The assessment of study quality with the determination of the risk of bias was carried out using the following methodological tools: for non-randomized studies — ROBINS-I [12], and for randomized controlled trials — RoB 2 [13].



**Figure 1.** Flow diagram of article search and selection

Table 1

**Inclusion criteria for studies in the systematic review according to the PICOS framework**

Parameter	Inclusion criterion
<i>P – Patients</i>	
Condition	Extensive defect of a long bone of a limb (more than 2 cm) regardless of the etiology and location of the defect
Age	Older than 18 years
<i>I – Intervention</i>	
Intervention	Masquelet technique regardless of the type of fixation
<i>C – Comparison</i>	
Comparison groups	Ilizarov bone transport technique OR bone defect reconstruction using vascularized flaps
<i>O – Outcome</i>	
Endpoints	Time to bone union Duration of fixation Time to restoration of limb weight-bearing capacity Presence of complications Need for additional/revision procedures
<i>S – Study type</i>	
Study Design	Prospective or retrospective cohort study OR randomized clinical trial

**Statistical analysis**

Statistical analysis was performed using RevMan 5.4 software (Cochrane Collaboration, Denmark).

For the description of quantitative parameters (duration of external fixation, time to consolidation), pooled mean values with 95% confidence intervals (CI) were used. For categorical outcomes (assessment of bone union and complications), odds ratios (OR) with 95% CI were calculated.

Heterogeneity among studies was assessed using the Cochran's Q test and Higgins' I<sup>2</sup> test. Heterogeneity was considered statistically significant at  $p \leq 0.1$  for the Q test due to the low power of the test when the number of studies is small. I<sup>2</sup> values were interpreted as follows: 0-40% – low heterogeneity, 30-60% – moderate heterogeneity, 50-90% – substantial heterogeneity, and 75-100% – considerable heterogeneity.

Given the expected clinical and methodological heterogeneity among studies, a random-effects model was used in the meta-analysis. In cases of low heterogeneity, a fixed-effects model was applied. Forest plots were used for the graphical presentation of the meta-analysis results.

To assess the risk of publication bias, funnel plots were constructed and Begg's and Egger's tests were performed. Given the small number of included studies, the results of these tests were interpreted with caution; funnel plot asymmetry and/or  $p \leq 0.1$  in Begg's and Egger's tests were considered possible evidence of publication bias due to the low statistical power of these methods when the number of studies is small.

To pool data from different sources, the median and interquartile range were converted into mean values and standard deviations using approximation methods proposed by X. Wan et al. [14].

**RESULTS****Results of study selection**

The initial search identified 468 publications (see Figure 1). After the removal of duplicates, 352 studies remained for screening. Following abstract review and the assessment of eligibility according to the inclusion criteria, 9 studies were selected for full-text analysis and included in the meta-analysis to evaluate the effectiveness and safety of the techniques [15, 16, 17, 18, 19, 20, 21, 22, 23]. The characteristics of these studies are presented in Table 2.

Additionally, for a comprehensive qualitative assessment of the data reported in the literature, three more studies were taken into account [24, 25, 26], presented in Table 3.

Thus, the total number of publications included in the qualitative and quantitative analysis was 12.

### Characteristics of the included studies and assessment of their quality

Of the 12 studies included in the analysis, 10 (83%) were cohort studies. Among the selected publications, there were also 2 randomized controlled trials (17%) [16, 17].

The selected publications included data on 375 patients. Among them, the reconstruction of extensive bone defects was performed using the Masquelet technique in 238 cases (63%), Ilizarov bone transport in 92 cases (25%), and a free vascularized fibular flap in 45 cases (12%).

Male patients predominated in the sample (305 of 375; 81%). The pooled mean age of patients was 40±23 years in the Masquelet group, 37±11 years in the vascularized flap group, and 38±25 years in the bone transport group. The pooled mean defect length was 57±28 mm, ranging from 2 cm [15, 18, 25] to 12 cm with the use of the osteoinductive membrane technique [26] for the Masquelet group; 56±29 mm in the Ilizarov bone transport group; and 75±46 mm in the group treated with free vascularized fibular flaps.

The descriptions of the injuries of the long bones of the lower limbs predominated (n = 332; 87%). The most common localization of extensive bone defects was the tibia (n = 284; 74%), followed by the femur (n = 48; 13%). Among upper limb injuries, extensive bone defects of the forearm were described (radius and ulna or their combination; n = 44; 12%), as well as the humerus (n = 4; 1%).

Table 2

#### Studies included in the quantitative analysis

Authors	Year	Study type*	Level of evidence	The technique compared**	Number of patients
Sadek A.F. et al. [15]	2016	RC	2c	BT	30
Tong K. et al. [16]	2017	RC	2c	BT	39
Abdou S.A. et al. [17]	2020	RC	2c	BT	14
Gupta G.K. et al. [18]	2022	RCT	1b	BT	24
Lan C. et al. [19]	2022	RC	2c	FFF	44
Rohilla R. et al. [20]	2021	RCT	1b	BT	25
Whitlock K.G. et al. [21]	2025	RC	2c	BT	46
Zhang Q. et al. [22]	2024	RC	2c	BT	65
Zhou M. et al. [23]	2024	RC	2c	FFF	43

\* RCT — randomized controlled trial, RC — retrospective cohort.

\*\* BT — bone transport, FFF — free fibular flap.

Table 3

#### Additional studies included in the qualitative analysis

Authors	Year	Study type *	Level of evidence	Compared groups	Number of patients
Borzunov D.Yu. et al. [24]	2022	AC	2c	Presence/absence of infection	24
Liu X. et al. [25]	2022	RC	2c	Type of fixation	23
Zhang Q. et al. [26]	2023	RC	2c	Type of fixation	63

\* AC — ambidirectional cohort, RC — retrospective cohort.

In 5 of the 12 studies (41%), the postoperative follow-up period was not clearly specified. One study reported a follow-up duration of 6 months or more [15], while another publication indicated a follow-up period of more than 12 months without specifying the exact duration [21]. The maximum reported duration of postoperative follow-up exceeded 66 months [23].

**Assessment of publication bias**

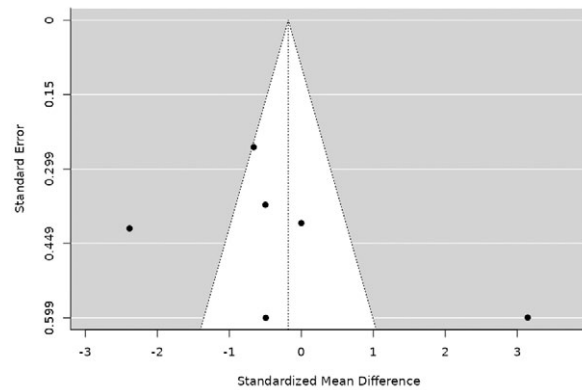
For the visual and statistical assessment of the risk of publication bias, funnel plots were constructed and Begg’s and Egger’s tests were performed for the parameter of fixation duration (Figure 2).

Visual inspection did not reveal pronounced asymmetry. Statistical analysis also did not demonstrate significant evidence of publication bias (Begg’s test,  $p = 1.000$ ; Egger’s test,  $p = 0.230$ ). It is important to note that the interpretation of these tests is limited by the small number of included studies, which reduces their statistical power. Therefore, the interpretation of the obtained data requires caution.

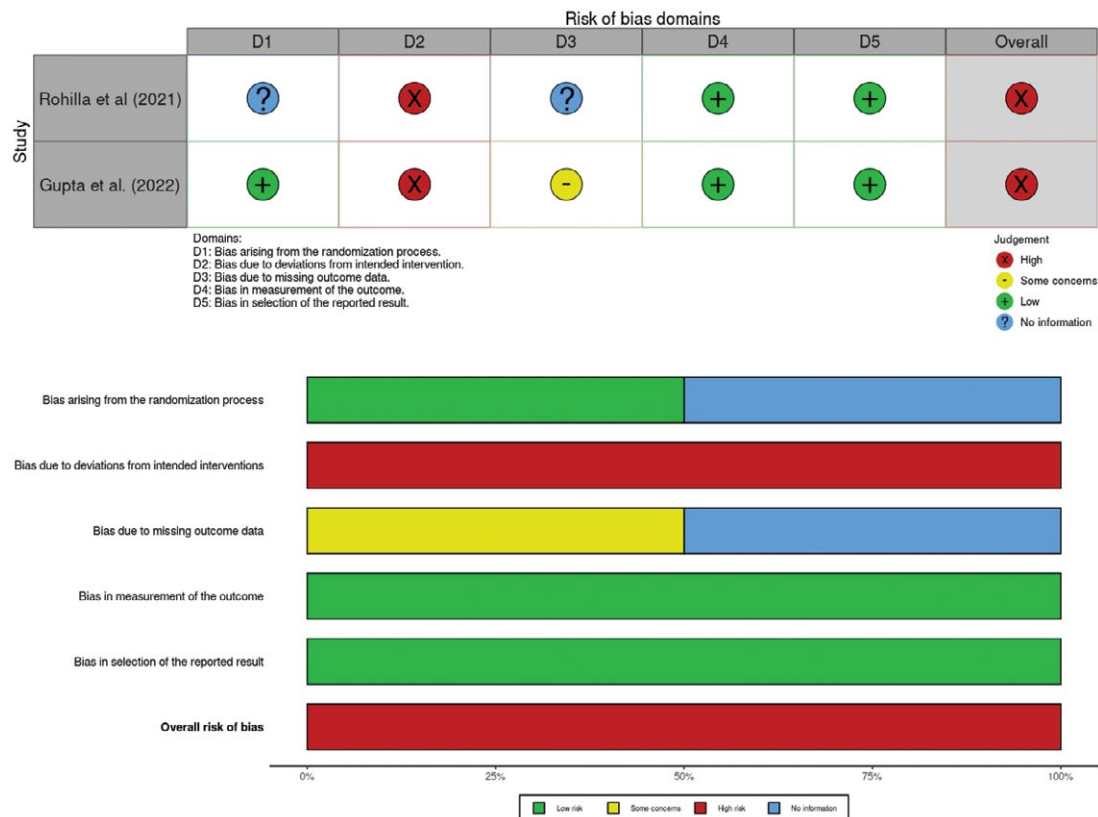
**Assessment of the risk of bias**

The results of the assessment of the risk of bias for the studies included in the meta-analysis are presented in Figures 3 and 4.

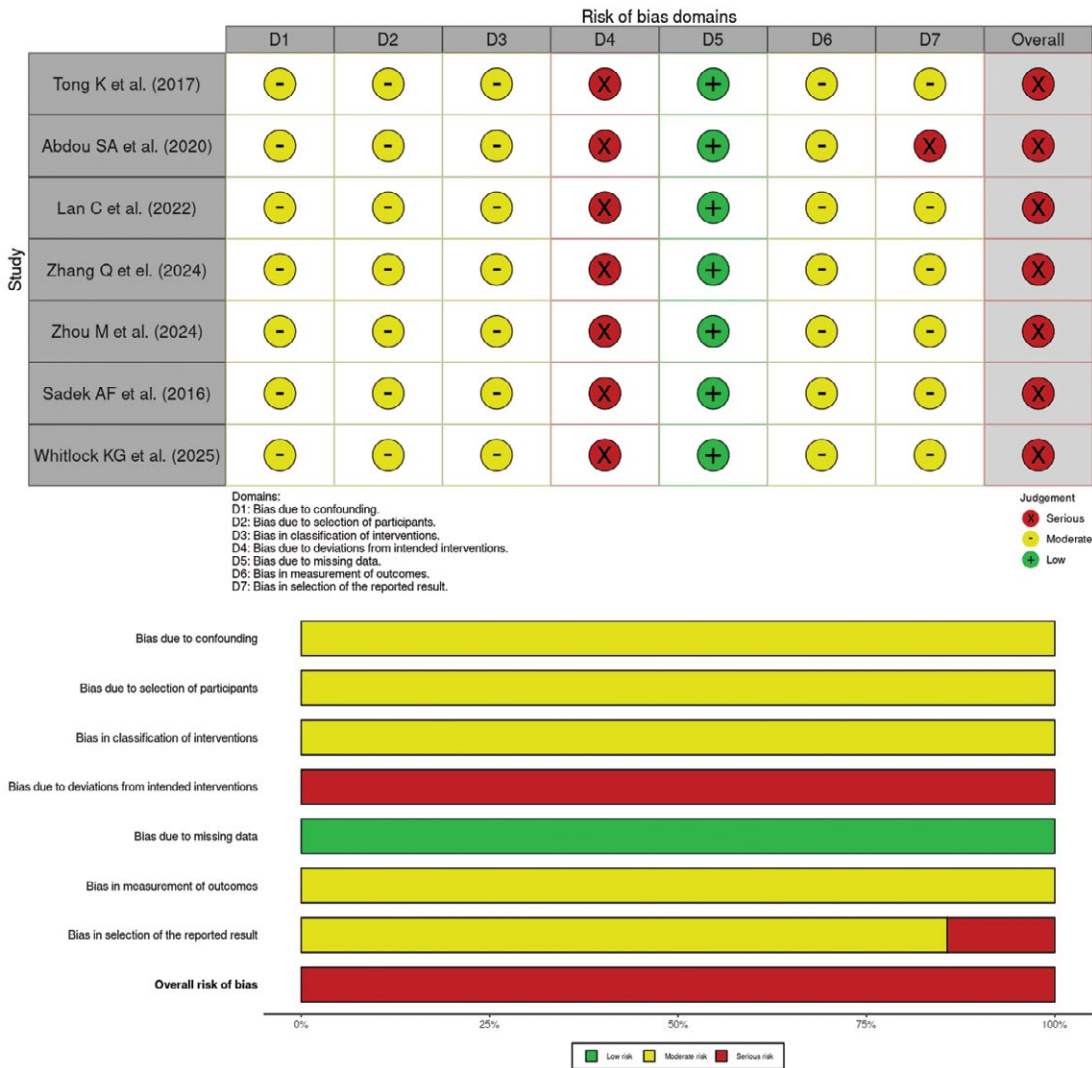
Thus, the evaluation of the methodological quality of the analyzed clinical studies, performed by two experts, demonstrated a high potential probability of bias in the interpretation of the meta-analysis results.



**Figure 2.** Funnel plot for studies assessing the mean duration of fixation with the Masquelet technique and bone transport



**Figure 3.** Risk of bias assessment for randomized controlled trials included in the meta-analysis (RoB 2 tool)



**Figure 4.** Risk of bias assessment for non-randomized clinical studies included in the meta-analysis (ROBINS-I tool)

### Mean duration of fixation

In cases where the primary data on total fixation duration were presented in days [15, 16, 24], the values were converted into months.

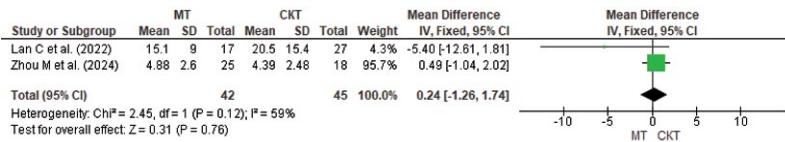
A meta-analysis of two eligible studies using a fixed-effects model did not reveal statistically significant differences ( $p=0.76$ ) in the total duration of fixation in patients who underwent the reconstruction of bone defects using the Masquelet technique compared with the use of free vascularized flaps (Figure 5). At the same time, moderate but statistically non-significant heterogeneity between the studies was observed ( $I^2 = 59\%$ ;  $p = 0.12$ ).

Given the critically small number of studies, the high risk of bias, and the low sensitivity of heterogeneity assessment, the interpretation of

the meta-analysis results comparing the mean duration of fixation for these techniques requires considerable caution.

In some studies, the primary data were presented as the median and interquartile range; therefore, for the purposes of meta-analysis, measures of central tendency were converted to mean values with standard deviation using the method proposed by X. Wan et al., assuming an approximately normal distribution of the data [15, 16, 21].

The comparison of the results of the meta-analysis of six studies after data approximation demonstrated trends similar to those obtained in the preliminary analysis of three studies in which the measures of central tendency had originally been reported as mean and standard deviation (Figure 6).



**Figure 5.** Mean duration of fixation (months) with the Masquelet technique and free vascularized flaps

Thus, a meta-analysis of eligible studies using a random-effects model did not reveal statistically significant differences in the total duration of fixation in patients who underwent the reconstruction of bone defects using the Masquelet technique compared with the Ilizarov technique (p = 0.40). Heterogeneity between studies was high (I<sup>2</sup> = 96%; p < 0.001).

None of the studies had an excessive influence on the model; however, the study by R. Rohilla et al. was identified as a potential outlier [20].

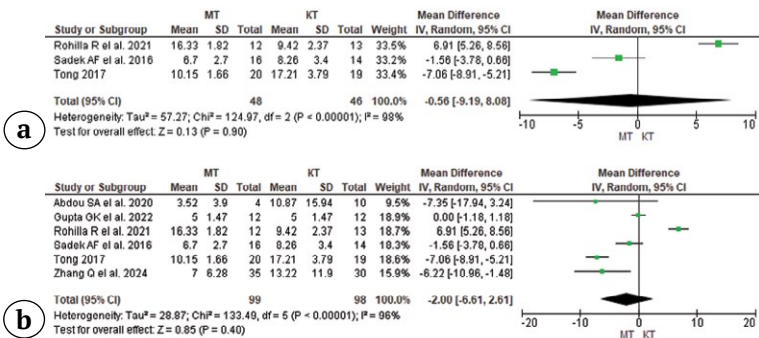
### Proportion of patients achieving complete bone union without additional surgical interventions

A meta-analysis of eligible studies demonstrated a statistically significantly higher proportion of patients achieving complete bone union without additional surgical interventions when

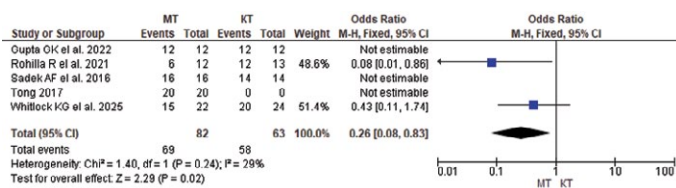
the bone transport was used compared with the Masquelet technique (32 of 37; 86% vs. 21 of 34; 61%; p = 0.02) (Figure 7). Heterogeneity between studies was low (I<sup>2</sup> = 29%, p = 0.24).

### Conversion of the initial surgical intervention to amputation

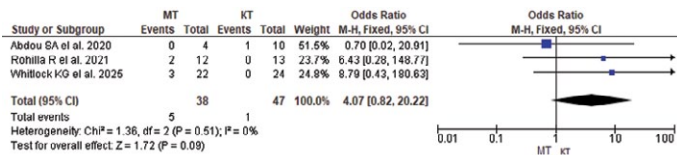
The proportion of patients who underwent limb amputation was 13% (5 of 38) for the Masquelet technique and 2% (1 of 47) for the bone transport. However, a meta-analysis of three eligible studies did not reveal statistically significant differences in the rate of conversion of the surgical treatment to amputation among patients treated with the induced membrane technique compared with the Ilizarov technique (p = 0.09) (Figure 8). Heterogeneity between studies was low (I<sup>2</sup> = 0%; p = 0.51).



**Figure 6.** Mean duration of fixation (months) with the Masquelet technique and bone transport: a – based on studies reporting measures of central tendency as mean and standard deviation; b – after inclusion of publications with primary data converted according to the method of Wan et al.



**Figure 7.** Proportion of patients achieving complete bone union without additional surgical interventions with the Masquelet technique and bone transport



**Figure 8.** Rate of conversion of the primary surgical procedure to amputation with the Masquelet technique and bone transport

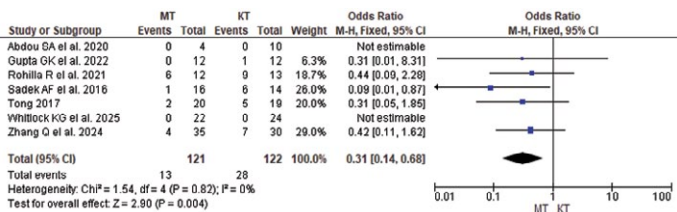
Comparable data for the technique using free vascularized bone flaps were not reported in the literature.

### Incidence of postoperative complications

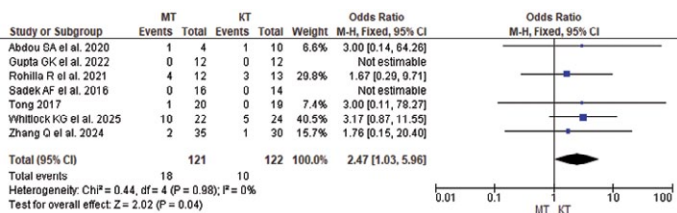
#### Superficial SSI

The proportion of patients with superficial surgical site infection (SSI) was 11% (13 of 121) for the Masquelet technique and 23% (28 of 122) for the bone transport. Meta-analysis demonstrated a statistically significantly higher rate of superficial infectious complications among patients who underwent the reconstruction of bone defects using the Ilizarov technique compared with the Masquelet technique (p = 0.004) (Figure 9). Heterogeneity between studies was low (I<sup>2</sup> = 0%, p = 0.82).

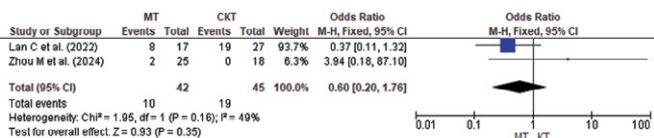
Data on superficial SSI when using vascularized flaps compared with the Masquelet technique were not reported in the publications in sufficient volume for analysis.



**Figure 9.** Proportion of superficial infectious complications with the Masquelet technique and bone transport



**Figure 10.** Proportion of deep infectious complications with the Masquelet technique and bone transport



**Figure 11.** Proportion of deep infectious complications with the Masquelet technique and free vascularized flaps

The proportion of patients with nonunion during treatment was 7% (3 of 42) for the Masquelet technique and 16% (7 of 45) for free vascularized bone flaps ( $p=0.38$ ) (Figure 13). Heterogeneity between studies was low ( $I^2 = 0\%$ ;  $p=0.81$ ).

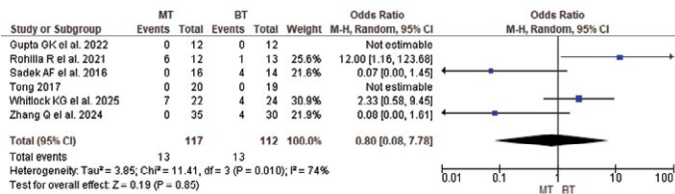
**Functional outcomes according to the ASAMI scale**

The proportion of patients with excellent and good outcomes according to the ASAMI scale was 85% (51 of 60) for the Masquelet technique and 71% (41 of 58) for Ilizarov bone transport. A meta-analysis of three eligible studies did not reveal statistically significant differences in the proportion of patients with excellent and good functional outcomes according to the ASAMI scale when bone defect reconstruction was performed using either the Masquelet technique or the Ilizarov technique ( $p=0.48$ ). Heterogeneity between studies was high ( $I^2 = 72\%$ ;  $p=0.03$ ) (Figure 14).

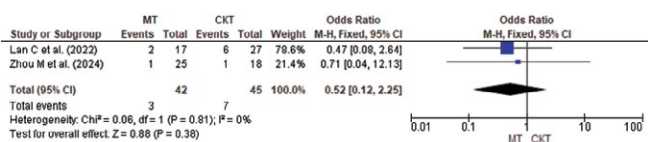
Data on functional outcomes assessed using this scale for the patients treated with free vascularized flaps were not reported in the publications.

**DISCUSSION**

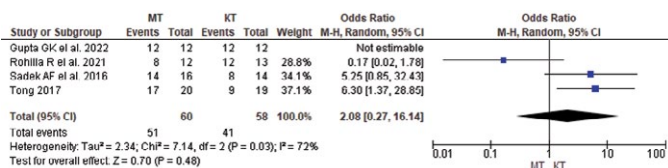
Modern trends characterized by the technological progress and parallel increase in the number of local armed conflicts inevitably lead to a rise in the incidence of complex high-energy injuries accompanied by extensive defects of the long bones of the limbs. Despite advances in surgical technologies, the problem of selecting the optimal method of reconstruction remains relevant in the context of decreased quality of life in patients with large segmental defects of the long bones of the limbs in the long term [27]. Extensive soft-tissue detachment, as well as the frequently open nature of the fracture, create conditions associated with a high risk of infectious complications, which itself represents a serious challenge [28]. Considering the above-mentioned features, a segmental defect may form following primary surgical debridement of the injured bone segment, and the reconstruction of such defects has long been and remains a highly complex task [29]. Historically, the gold standard for the treatment of this pathology has been the method of distraction osteogenesis according to Ilizarov [30, 31]. However, according to the study by K.G. Whitlock et al., the incidence of pin tract osteomyelitis alone during the reconstruction of such defects may exceed 60%, which forces clinicians to turn to other techniques [21]. This circumstance stimulates the search for and development of alternative surgical strategies.



**Figure 12.** Proportion of nonunions with the Masquelet technique and bone transport



**Figure 13.** Proportion of nonunions with the Masquelet technique and free vascularized flaps



**Figure 14.** Proportion of excellent and good outcomes according to the ASAMI score with the Masquelet technique and bone transport

One of the methods of choice for the treatment of infected segmental defects of the long bones is the two-stage technique proposed by the French orthopedic surgeon Alain Masquelet [32]. At the first stage, radical surgical debridement of the defect area is performed with stable fixation of bone fragments and filling of the defect with bone cement containing an antibacterial agent at a concentration of up to 10 wt% (1-4 g of vancomycin per 40 g of bone cement) [33]. At the second stage, after 6-8 weeks, the cement is removed followed by bone grafting of the defect zone [34]. Despite more than a 30-year history of using this technique, the results reported in the literature remain contradictory [35]. However, given the high contamination of the bone defect area and surrounding soft tissues with infectious agents, it is difficult to imagine a more effective approach than radical surgical debridement combined with filling the defect with a cement spacer containing an antibacterial agent [33]. According to the study by E. Liidakis et al., a polymethylmethacrylate spacer with an antibiotic concentration of up to 10 wt% promotes the formation of a connective tissue membrane with the most favorable osteoinductive properties [36]. At the same time, *in vitro* experiments demonstrate insufficient duration of antimicrobial activity of bone cement containing 10 wt% antibiotic [37]. This may lead to low efficacy in pathogen eradication and may be a reason for the higher rate of deep SSI compared with Ilizarov bone transport, which was also demonstrated in our meta-analysis. Other commonly cited disadvantages of the Masquelet technique include its staged nature as well as limitations related to the length and localization of the defect [38]. On the other hand, according to D. Pederiva et al., the rate of repeated interventions during the reconstruction of bone defects using bone transport techniques and free tissue complex transplantation reaches 30%, while the rate of nonunion is 17% [8].

In the context of the present study, the prospect of combining different techniques for the reconstruction of long-bone defects of the limbs in the presence of infection appears particularly interesting. Thus, in the study by

D.Yu. Borzunov et al., the authors note the feasibility of adequate debridement of the infectious focus with the implantation of large spacers containing a prophylactic dose of antibiotic, followed by delayed reconstruction of the defect using the Ilizarov external fixator as a possible treatment option for this category of patients that combines the advantages of both techniques [24]. The results of the experimental study by T.N. Varsegova et al. also demonstrate the importance of adequate pharmacotherapy and rehabilitation at each stage of reconstruction of long-bone defects of the limbs [39]. This approach undoubtedly appears promising but requires further studies with a clearly structured methodology.

### Study limitations

This systematic review has several limitations that may affect the interpretation of the obtained results. Significant clinical and methodological heterogeneity of the included studies, manifested in differences in study design, fixation methods (plates, intramedullary nails, external fixators), postoperative protocols, and outcome assessment criteria, limits the reliability of pooled estimates in the meta-analysis and explains the high statistical heterogeneity observed. The small number of studies, particularly for the comparison of the Masquelet technique with free flaps, reduces the statistical power of the conclusions and does not allow for a reliable assessment of the risk of publication bias. The main sources of methodological bias are predominantly retrospective cohort studies with a high risk of selection bias, in which the choice of treatment method largely depended on the clinical situation, as well as the absence of blinding in randomized studies. The inability to perform stratification according to key clinical factors, such as the initial infectious status and the exact length of the defect, due to incomplete reporting of data in the primary publications, does not allow the formulation of detailed recommendations. Additional prognostic variables (soft-tissue condition, comorbidities, characteristics of the bone graft) also could not be fully accounted for in the analysis. Considering these

limitations, the results should be interpreted with caution. They confirm the complexity of direct comparison between the techniques and emphasize the need for large prospective multicenter studies with a unified protocol to minimize the sources of bias.

## CONCLUSION

The conducted systematic review confirms the high clinical effectiveness of the three main methods for the reconstruction of extensive segmental defects of the long bones of the limbs — the Masquelet technique, Ilizarov bone transport, and the use of free vascularized flaps. The meta-analysis did not reveal a significant advantage of any method with respect to the key temporal parameters (duration of fixation and time to consolidation); however, characteristic safety profiles were identified that should be taken into account when selecting the treatment strategy. The Ilizarov technique is associated with a higher risk of superficial infections, whereas the Masquelet technique is associated with a higher incidence of deep infectious complications, which may reflect insufficient antimicrobial activity of cement spacers in patients with infected wounds. At the same time, the Masquelet technique may potentially be associated with better treatment adherence and functional outcomes. Free vascularized flaps demonstrated effectiveness comparable to the Masquelet technique with respect to the main parameters evaluated.

Thus, when selecting a method for the reconstruction of large segmental defects, it is necessary to consider the localization and length of the defect, the status of the soft tissues, the activity of the infectious process, as well as individual patient characteristics, including treatment

adherence and expectations regarding the quality of life. The predominance of retrospective studies and their methodological heterogeneity limit the existing evidence base and determine the need for prospective multicenter randomized studies to develop more specific clinical recommendations, including the evaluation of promising combined techniques.

## DISCLAIMERS

### **Author contribution**

*Avdeev A.I.* — study concept and design, data acquisition and processing, drafting and editing the manuscript.

*Fedorova Yu.A.* — study concept and design, data acquisition and processing.

*Malashicheva A.B.* — data interpretation, editing the manuscript.

*Serdiukova D.A.* — data interpretation, editing the manuscript.

*Docshin P.M.* — data interpretation, editing the manuscript.

*Bozhkova S.A.* — drafting the manuscript, scientific guidance.

All authors have read and approved the final version of the manuscript of the article. All authors agree to bear responsibility for all aspects of the study to ensure proper consideration and resolution of all possible issues related to the correctness and reliability of any part of the work.

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