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Surgical treatment of critical size bone defects with Masquelet technique versus bone transport: a systematic review and meta-analysis of comparative studies

Lucrezia Allesina[1] · Mattia Alessio-Mazzola[2] · Alberto Belluati[3] · Salvatore Mosca[1] · Giacomo Placella[1] · Vincenzo Salini[1]

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Abstract

Introduction To date, the management of critical-sized bone defects lacks a universally accepted approach among orthopedic surgeons. Currently, the main options to treat severe bone loss include autologous grafting, free vascularized bone transfer, bone transport and induced-membrane technique. The purpose of this study is to critically compare the outcomes of Masquelet technique and bone transport to provide a higher level of evidence regarding the indexed techniques.

Material and methods The authors conducted a systematic search on several databases according to the PRISMA guidelines. English-written reports comparing outcomes of the Masquelet technique versus the bone transport technique in patients with critical-sized defects in lower extremities were included.

Results Six observational studies involving 364 patients were included. The systematic review and meta-analysis of pooled data showed no significant difference in most outcomes, except for ASAMI bone outcomes and residual deformity, which showed better results in the bone transport group. The 64% of patients treated with Masquelet technique obtained excellent/good bone ASAMI results compared to 82.8% with bone transport ($p = 0.01$). Post-operative residual deformity was 1.9% with the bone transport method versus 9.7% with the Masquelet technique ($p = 0.02$).

Conclusions Both the Masquelet technique and bone transport showed comparable results for the management of critical-sized bone defects of the lower limb. However, these findings must be carefully interpreted due to the high risk of bias. Further prospective randomized controlled trials are necessary to better clarify the strengths and limitations of these two techniques and to identify the variables affecting the outcomes.

Keywords Masquelet technique · Induced-membrane technique · Distraction osteogenesis · Bone transport · Critical-size bone defects

Introduction

Critical-sized bone defects pose a major challenge for both patients and surgeons in the orthopedic field. Overall, defects exceeding 2.5 cm and affecting more than 50% of bone circumference can be considered as critical. However, such a definition lacks shared consensus among experts [1–3], as it might be influenced by the anatomical location, the soft tissue conditions, vascular and neurological status of the extremity, the presence of infection as well as other patient-related factors [4].

The management of critical-sized bone defects is complex and leads to uncertain results, with neither guideline nor universal consensus to properly guide the orthopedic treatment [3, 5]. Historically, amputation was the only solution

Lucrezia Allesina and Mattia Alessio-Mazzola co-first authorship, the authors equally contributed to this research.

Giacomo Placella and Vincenzo Salini co-last authorship, the authors equally contributed to this research.

✉ Mattia Alessio-Mazzola
mattia.alessio@hotmail.com

1 Università Vita-Salute San Raffaele, Milan, Italy

2 Orthopaedic and Trauma Unit, IRCCS Ospedale San Raffaele, Via Olgettina 60, 20132 Milan, Italy

3 Orthopaedic and Trauma Department, Hospital Santa Maria delle Croci, Viale Vincenzo Randi, 5, 48121 Ravenna, Italy

in case of severe bone loss, but the ongoing advancement of new technologies and surgical techniques led to the development of limb salvage procedures. Currently, autologous grafting is widely used for small defects, but it may be inadequate to manage defects exceeding 5 cm, due to its high rate of graft resorption [6]. Other options to treat wider bone defects include free vascularized bone transfer, bone transport through distraction osteogenesis and induced-membrane technique [1–6].

The purpose of this study is to systematically review and meta-analyze comparative studies investigating the outcomes of the Masquelet technique and bone transport technique to manage critical-sized bone defects of lower limb.

Material and methods

Evidence acquisition

Comparative studies reporting the outcomes of Masquelet technique versus bone transport technique in patients with critical-size defects in lower extremities were considered eligible for inclusion. Study types include prospective and retrospective cohort studies assessing at least one radiological or clinical outcome.

The primary endpoint is to measure the bone union rate, while secondary results include time to bone union, time to full weight bearing, ASAMI bone and functional scores, need for soft tissue coverage, general complication rate and prevalence of specific complications (infection rate, leg-length discrepancy > 2 cm, hardware failure or stress refracture, joint stiffness, need for re-intervention, residual deformity and late amputation).

Search methods for identification of studies

A systematic literature review has been conducted in agreement with the Cochrane Handbook of Systematic Reviews of Interventions [7] and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [8] for study selection (Fig. 1).

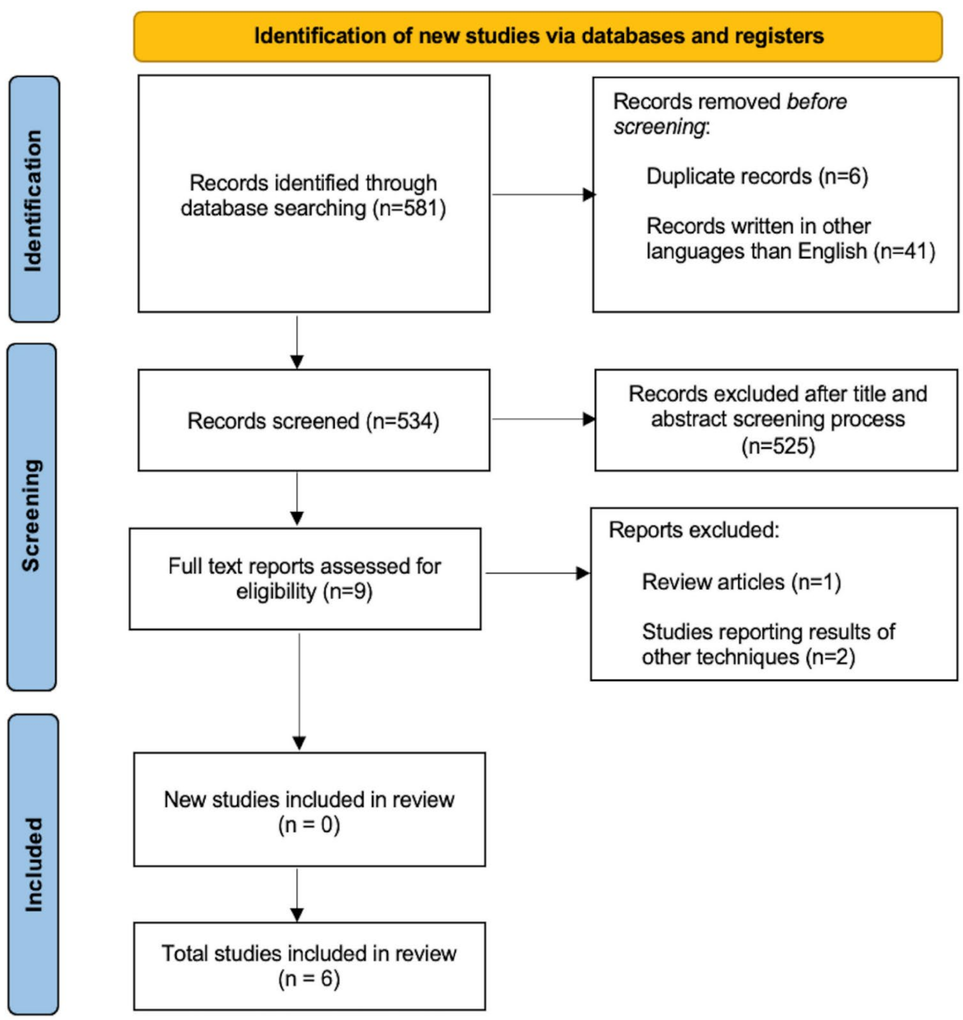

Fig. 1 Study selection for updated systematic reviews according to the PRISMA guidelines

Relevant studies were systematically searched from several databases using the following keywords alone and in all the various combinations: “Masquelet technique” OR “induced membrane” AND “Ilizarov technique” OR “bone transport” OR “distraction osteogenesis”. The databases used to identify pertinent records included the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE/PubMed, Embase, Scopus, the Science Citation Index Expanded from Web of Science and ScienceDirect.

Non-Chinese language original articles from January 2000 to May 2023 reporting comparative results of Masquelet technique and bone transport were included. The selection process was based on the participants, intervention, control, outcome, and study design (PICOS). After excluding the duplicates, two reviewers (AL, AM) independently screened the title and abstract of each identified article resulting from the primary electronic search. The selected publications were then subjected to a full-text analysis to determine their final inclusion.

All references of each study were accurately screened to look for any additional relevant study that was potentially missed with the first review process. The two reviewers followed the same checklist to screen all studies and evaluate the eligibility criteria. Disagreements were resolved by consensus agreement with a third reviewer (PG). At the end of the process, six studies were included with 364 patients.

Data collection and analysis

The level of evidence of included research studies was assessed through the adjusted Oxford Centre For Evidence-Based Medicine 2011 Levels of Evidence [9]. The quality of the studies was defined using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system [10] rating the quality of evidence in systematic reviews. After the evidence was collected and summarized, the GRADE system provided explicit criteria for rating the quality of evidence that includes study design, risk of bias, imprecision, inconsistency and indirectness (Table 1). The risk of bias was analyzed with the revised tool to assess the risk of bias in non-randomized studies of intervention (ROBINS-I) [11] (Fig. 2).

Each reviewer conducted an independent stepwise analysis on basic information about each study, including study design, aim of the study, level of evidence, year of publication, country, number of procedures, mean follow-up and population features (mean age at surgery, gender, site of injury, length of bone defect and diagnosis of inclusion). Discrepancies in data extraction were discussed and resolved by a consensus meeting between the authors. All these data are accurately summarized in Tables 2 and 3. The assessment of primary and secondary endpoints was conducted for each study. Data about bone union, time to bone union, time to weight bearing, bone and functional ASAMI scores, need for soft tissue coverage are summarized in Table 4, while data on general and specific complications are reported in Table 5.

Statistical analysis

All analyses were completed with Review Manager 5.4.1 software (Cochrane Collaboration, Oxford, UK) and IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA) and a p value funnel plot was used to assess the existence of publication bias for the primary outcome measure.

For each included study, mean differences (MD) and 95% CI were calculated for continuous outcomes, while risk ratio (OR) and 95% CI were calculated for dichotomous outcomes. Statistical heterogeneity among the studies was assessed using the χ^2 test and I^2. A fixed-effect model was applied when $I^2 < 40\%$, and a random-effect model when $I^2 \geq 40\%$. A p value of less than 0.05 was considered statistically significant.

The amount of heterogeneity (i.e., tau^2), was estimated using the Hunter–Schmidt estimator. In addition to the estimate of tau^2, the Q test for heterogeneity and the I^2 statistic were reported. In case any amount of heterogeneity is detected, a prediction interval for the true outcomes was also provided. Studentized residuals and Cook’s distances are used to examine whether studies may be outliers and/

Table 1 GRADE quality assessment of included studies

Author	Apriori GRADE	Risk of bias	Inconsistency of results-value	Indirectness of evidence	Imprecision	Reporting bias	Final grade
Tong 2017 [12]	Low	Y	N	Y	Y	Y	Very low
Wen 2019 [13]	Low	Y	Y	N	Y	Y	Very low
Gupta 2022 [14]	High	Y	Y	N	Y	Y	Low
Rohilla 2022 [15]	High	Y	N	Y	Y	Y	Low
Abou-Seif 2020 [16]	Low	Y	Y	N	Y	Y	Very low
Koti 2016 [17]	Low	Y	Y	N	Y	Y	Very low

N = NO, Y = YES

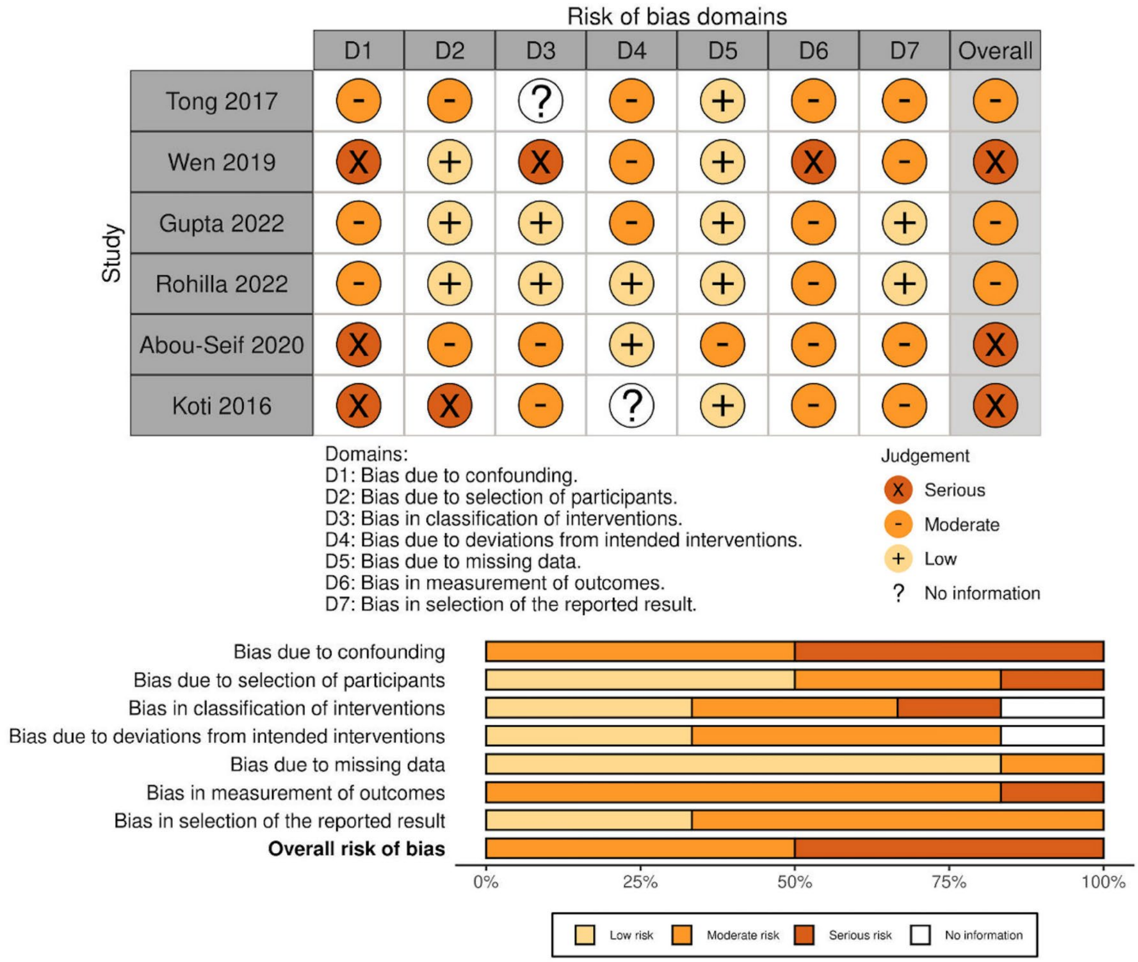

Fig. 2 Visual expression of risk of bias assessment with ROBINS-I tool

or influential in the context of the model. Studies with a studentized residual larger than the 100 × (1 − 0.05/(2 × *k*))th percentile of a standard normal distribution were considered potential outliers. Studies with a Cook's distance larger than the median plus six times the interquartile range of the Cook's distances are considered to be influential. The rank correlation test and the regression test, using the standard error of the observed outcomes as predictor, are used to check for funnel plot asymmetry.

Evidence synthesis

A total of 216 records were identified from the initial electronic database research. After initial screening, 9 studies underwent a full-text assessment and 6 comparative studies were included at the end of the process [12–17], involving a total of 470 patients. One-hundred-six patients were excluded from the meta-analysis as treated with other techniques (free vascularized fibular transfer FVFT), resulting in 364 patients eventually being included. Precisely, 153 patients underwent the Masquelet technique, and 211 patients were treated with the bone transport technique. The selection process in agreement with the PRISMA guidelines is reported in Fig. 1.

The risk of bias assessment with the Robins-I tool revealed that 3 studies [12, 14, 15] had a moderate risk of bias and 3 studies [13, 16, 17] had a serious risk of bias as shown in Fig. 2. According to the GRADE system, the quality of study resulted in low in 2 studies [14, 15] and very low in 4 studies [12, 13, 16, 17] (Table 1).

Results

Bone union

Among the 6 investigations, all 6 studies [12–17] reported complete data on union rate and involved 364 participants: 153 in the Masquelet group and 211 in the bone transport

Table 2 General characteristics of included studies

Author	Year	Country	Number of patients	Intervention MT/BT	Study design	Level of evidence	Measured outcomes	Mean follow-up (months)
Tong et al. [12]	2017	China	39	MT $n = 20$ BT $n = 19$	Comparative retrospective study	Level III	Bone outcomes (bone union, deformity, infection and leg-length discrepancy LLD) and functional outcomes (significant limping, joint contracture, soft tissue dystrophy, pain and inactivity) according to the ASAMI score and presence of complications	23.1 ± 9.5 27.5 ± 10.1
Wen et al. [13]	2019	China	317	FVFT $n = 106$ MT $n = 79$ BT $n = 132$	Comparative retrospective study	Level III	Radiological healing/consolidation time, clinical outcomes (time to non-protected weight bearing, unrestricted walking distance and monopedal weight bearing), need for soft tissue coverage, complications, VAS score and SIP score	27 / 29 / 24
Gupta et al. [14]	2022	India	24	MT $n = 12$ BT $n = 12$	Prospective double-blinded study	Level II	Post-operative activities of daily living, pain, dystrophy, knee and ankle joints contracture, loss of knee and ankle joint motion, LLD, bone union, infection, limb deformity, need for soft tissue coverage, functional outcome (ASAMI score) and radiological healing/consolidation time	18.3 ± 5.6 18.2 ± 3.9
Rohilla et al. [15]	2022	India	25	MT $n = 12$ BT $n = 13$	Prospective randomised study	Level II	Bone outcomes (bone union, deformity, infection and leg-length discrepancy LLD) and functional outcomes (significant limping, joint contracture, soft tissue dystrophy, pain and inactivity) according to the ASAMI score and presence of complications	30.4 ± 4.8 31.7 ± 3.7
Abou-Seif et al. [16]	2020	Egypt	40	MT $n = 20$ BT $n = 20$	Prospective observational study	Level III	Bone outcomes (bone union, deformity, infection and leg-length discrepancy LLD) and functional outcomes (significant limping, joint contracture, soft tissue dystrophy, pain and inactivity) according to the ASAMI score and presence of complications	18.3 ± 5.6 18.2 ± 3.9
Koti et al. [17]	2016	India	25	MT $n = 10$ BT $n = 15$	Prospective observational study	Level III	Radiological healing/consolidation time, time to achieve bone union, post-operative infection rate	NR

BT bone transport, *FVFT* free vascularized fibular transfer, *MT* Masquelet technique, *NR* not reported

Table 3 Patients' pre-operative data

Author	Number of patients	Intervention MT/BT	Mean age (years)	Gender (M/F)	Site of injury	Length of bone defects (cm)	Diagnosis	
							Infected	Non-infected
Tong et al. [12]	39	MT $n=20$ BT $n=19$	39.8 ± 15.0 38.5 ± 11.0	15/5 15/4	Femur $n=13$ Tibia $n=26$	6.7 ± 3.8 6.8 ± 3.4	20/19	0/0
Wen et al. [13]	317	FVFT $n=106$ MT $n=79$ BT $n=132$	36.5 ± 5.9 35.2 ± 5.0 35.7 ± 5.6	74/32 97/35 53/26	Long bones of lower limbs $n=317$	11.5 ± 9.1 10.5 ± 8.4	39 / 37	40/95
Gupta et al. [14]	24	MT $n=12$ BT $n=12$	43.8 ± 9.3 38.1 ± 9.8	11/1 11/1	Tibia $n=24$	< 5 cm = 1/3 > 5 cm = 11/9	6/4	6/8
Rohilla et al. [15]	25	MT $n=12$ BT $n=13$	39.7 ± 14.1 31.8 ± 14.9	12/1 11/1	Tibia $n=25$	3.8 ± 1.2 3.9 ± 0.9	12/13	0/0
Abou-Seif et al. [16]	40	MT $n=20$ BT $n=20$	35.2 35.2	NR	Tibia $n=24$ Femur $n=16$	> 4 cm $n=20/20$	10/10	10/10
Koti et al. [17]	25	MT $n=10$ DO $n=15$	37.8 ± 9.1 40.9 ± 9.9	8/2 13/2	Tibia $n=25$	5.5 ± 1.8 5.4 ± 1.4	4/10 7/15	5/10 6/15

BT bone transport, *DO* distraction osteogenesis, *F* female, *FVFT* free vascularized fibular transfer, *M* male, *MT* Masquelet technique, *NR* not reported

group. Statistical heterogeneity was $\chi^2 = 8.43$; $I^2 = 53\%$; $p = 0.08$, and a random-effect model was used for analysis.

Four studies [12–14, 17] showed no significant difference in bone union rate between the two techniques. On the other hand, 2 studies [15, 16] demonstrated significantly better results for bone transport in terms of consolidation. The meta-analysis of pooled data confirmed no significant difference in union rate between Masquelet and bone transport techniques (OR 0.30; 95% CI 0.05–1.65; $p = 0.17$) (Fig. 3). Precisely, the union rate of Masquelet group was 88.2% versus 95.7% of bone transport group.

Publication bias

A funnel plot including 6 studies [12–17] was performed with the bone union rate as the indicator to identify the presence of bias (Fig. 4). The observed log odds ratios ranged from − 3.3 to 2.1, with the majority of estimates being negative (50%). The estimated average log odds ratio based on the random-effects model was − 1.0 (95% CI − 2.4 to 0.4). Therefore, the average outcome did not differ significantly from zero ($z = -1.4$, $p = 0.2$). A 95% prediction interval for the true outcomes was given by − 3.4 to 1.4. Hence, although the average outcome was estimated to be negative, in some studies the true outcome may in fact be positive. An examination of the studentized residuals revealed that none of the studies had a value larger than ± 2.6 and hence there was no indication of outliers in the context of this model. According to the Cook's distances, none of the studies could be considered overly influential. Neither the rank correlation nor the regression test indicated any funnel plot asymmetry ($p = 1.000$ and $p = 0.416$, respectively).

Time to bone union (weeks)

Only 4 studies [13–15, 17] reported complete quantitative data on the mean time to achieve bone union and involved 285 participants (113 in the Masquelet group and 172 in the bone transport group). Statistical heterogeneity was $\chi^2 = 12.46$; $I^2 = 76\%$; $p = 0.006$, and a random-effect model was used for analysis.

Three studies [13–15] found no statistical difference in terms of bone union time, while Koti et al. [17] reported a significantly longer consolidation time with Masquelet technique. Meta-analysis highlighted no significant difference on time to bone union between the two methods (MD = 0.71 weeks; 95% CI = − 5.55 to 6.97; $p = 0.82$) (Fig. 5).

Time to full weight bearing (weeks)

Due to the large variability of measured variables and lack of quantitative data, a meta-analysis of time to full weight bearing was not feasible, as only 2 studies [12, 13] measured this outcome.

Both studies agree that full-weight bearing is significantly lower in Masquelet group than in bone transport group. Precisely, Wen et al. [13] evaluated the time from surgery to total non-protected weight bearing reporting 46.5 ± 19.2 weeks for bone transport and 46.5 ± 19.2 weeks for induced-membrane technique. Tong et al. [12] evaluated the finite fixation time, which was significantly shorter in Masquelet group. The finite fixation time was 40.6 ± 6.6 weeks for Masquelet technique and 68.8 ± 15.2 weeks for bone transport.

Table 4 Measured outcome values

Author	Bone union	Mean time to bone union (weeks)	Time to full weight bearing (weeks)	Need for soft tissue coverage	Bone results (ASAMI score)				Functional results (ASAMI score)			
					Excellent	Good	Fair	Poor	Excellent	Good	Fair	Poor
Tong et al. [12]	19/19	NR	40.6 ± 6.6 68.8 ± 15.2	7/6	5/7	10/9	4/2	1/1	8/3	9/6	3/2	0/0
Wen et al. [13]	79/126	38.1 ± 21.2 44.7 ± 19.5	56.6 ± 18.9 46.5 ± 19.2	4/17	NR	NR	NR	NR	NR	NR	NR	NR
Gupta et al. [14]	12/12	21.4 ± 4.3 21.4 ± 4.3	NR	7/1	9/11	3/1	0/0	0/0	6/7	6/5	0/0	0/0
Rohilla et al. [15]	6/12	28.8 ± 7.2 29.2 ± 10	NR	4/3	3/9	3/3	6/1	0/0	2/8	6/4	3/0	1/1
Abou-Seif et al. [16]	12/20	NR	NR	NR	4/6	4/7	4/7	8/0	4/8	5/8	3/4	8/0
Koti et al. [17]	7/13	35.8 ± 9.6 51.7 ± 16.4	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR

ASAMI Association for the Study and Application of the Method of Ilizarov; *NR* not reported

Need for soft tissue coverage

Only 4 studies [12–15] reported complete data on the need for soft tissue coverage performed at the same time as indexed procedures. These studies involved 298 participants, including 123 in the Masquelet group and 175 in the bone transport group. Statistical heterogeneity was $\chi^2 = 8.61$; $I^2 = 65\%$; $p = 0.04$, and a random-effect model was used for analysis.

Wen et al. [13] reported less interventions in the Masquelet group, while the opposite was described by Gupta et al. [14]. The other 2 studies [12, 15] demonstrated no significant difference on need for soft tissue procedures between the assessed techniques. Results from pooled data indicated 17.9% of patients treated with Masquelet technique needed soft tissue coverage versus 15.4% of patients who underwent bone transport without significant differences (OR 1.36; 95% CI 0.36 to 5.11; $p = 0.65$) (Fig. 6).

ASAMI bone outcome (excellent and good)

Bone results are evaluated in agreement with the ASAMI classification, which considers bone union, the presence of infection, the degree of residual deformity and the limb length discrepancy. More details on ASAMI bone criteria are reported in Table 6.

Four studies [12, 14–16] reported complete data and involved 128 participants including 64 in the Masquelet group and 64 in the bone transport group. Statistical heterogeneity was $\chi^2 = 1.79$; $I^2 = 0\%$; $p = 0.41$, and a fixed-effect model was used for analysis.

Two studies [12, 15] did not evidence any statistical difference in bone results, but Abou-Seif et al. [16] demonstrated that bone outcome was significantly more favourable among patients treated with bone transport. The meta-analysis of pooled data demonstrated superior bone ASAMI score (excellent or good) with bone transport technique. Precisely, 64% of patients treated with Masquelet technique obtained excellent/good bone ASAMI outcome versus 82.8% with bone transport (OR 0.32; 95% CI 0.13–0.77; $p = 0.01$) (Fig. 7).

ASAMI functional outcome (excellent and good)

Functional outcomes were evaluated in accordance with ASAMI classification, whose criteria include the ability to return to pre-injury daily life activities, the presence of limping, the degree of knee and ankle stiffness, the reflex sympathetic dystrophy, and the pain severity. The functional score is further discussed in Table 7.

Only 4 investigations [12, 14–16] reported complete qualitative data on functional results assessed using ASAMI criteria. These studies involved 128 participants including 64

Table 5 General and specific complications

Author	Overall complication rate	Infection at the site of fracture	LLD > 2 cm	Implant failure or refracture	Joint stiffness (loss of knee, ankle or both motion)	Residual deformity > 7°	Non-union	Need for re-intervention	Late amputation
Tong et al. [12]	NR	1/0	2/1	0/1	NR	NR	1/0	1/3	0/0
Wen et al. [13]	21/34	0/1	5/3	3/0	6/8	4/2	0/6	4/2	0/0
Gupta et al. [14]	NR	0/1	0/0	NR	2/3	3/0	0/0	1/4	0/0
Rohilla et al. [15]	NR	0/0	0/0	0/0	4/5	3/1	6/1	4/2	2/0
Abou-Seif et al. [16]	NR	6/1	NR	NR	NR	NR	8/0	9/3	11/17
Koti et al. [17]	NR	4/2	NR	NR	NR	NR	3/2	NR	NR

LLD leg-length discrepancy, *NR* not reported

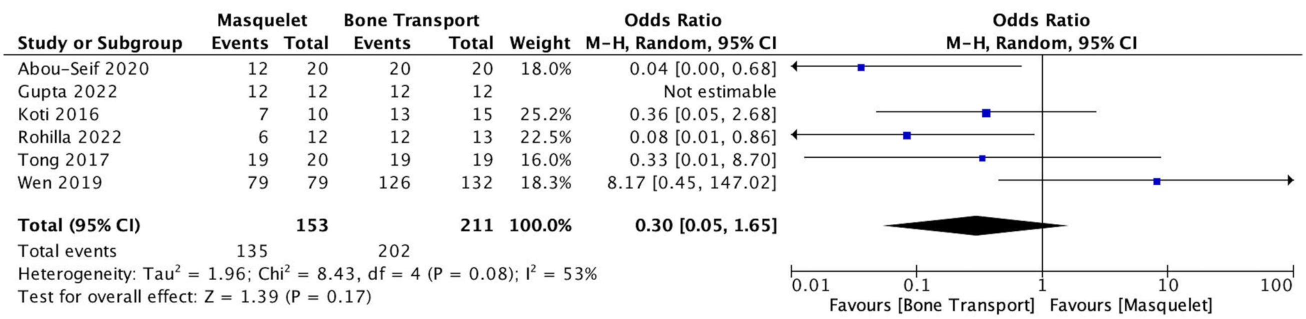

Fig. 3 Bone union forest plot

in the Masquelet group and 64 in the bone transport group. Statistical heterogeneity was $\chi^2 = 12.35$; $I^2 = 84\%$; $p = 0.002$, and a random-effect model was used for analysis.

The functional outcomes were variable among three different investigations. Rohilla et al. [15] found no significant difference between Masquelet and bone transport groups, while Tong et al. [12] described more favourable functional recovery in patients treated with induced-membrane technique. Eventually, Abou-Seif et al. [16] highlighted a significant difference in favour of bone transport group. The meta-analysis of pooled data showed no significant difference between the two techniques (OR 0.64; 95% CI 0.05–7.46; $p = 0.72$) (Fig. 8).

General complication rate

Due to the large variability of measured variables and lack of complete data, a meta-analysis of the overall complication rate was not feasible. General complications should be intended as the sum of specific complications, which were not evaluated uniformly thus not allowing a reliable comparison of data.

Wen et al. [13] was the only study referring to the overall complication rate, but they did not report any significant difference between the two methods. Specifically, they reported 26.6% complication rate for the Masquelet group against 25.8% for the bone transport group.

Infection rate

All included studies [12–17] reported complete data on the infection rate. The data analysis was performed on a total of 364 patients, 153 belonging to the Masquelet group and 211 to the bone transport group. Statistical heterogeneity was $\chi^2 = 3.79$; $I^2 = 0\%$; $p = 0.44$, and a fixed-effect model was used for analysis.

Rohilla et al. [15] reported that no patients suffered from infection recurrence at the site of fracture, and 3 studies [12, 13, 17] that both techniques had similar infection rates. Conversely, Abou-Seif et al. [16] reported a significantly higher infection rate in the Masquelet group.

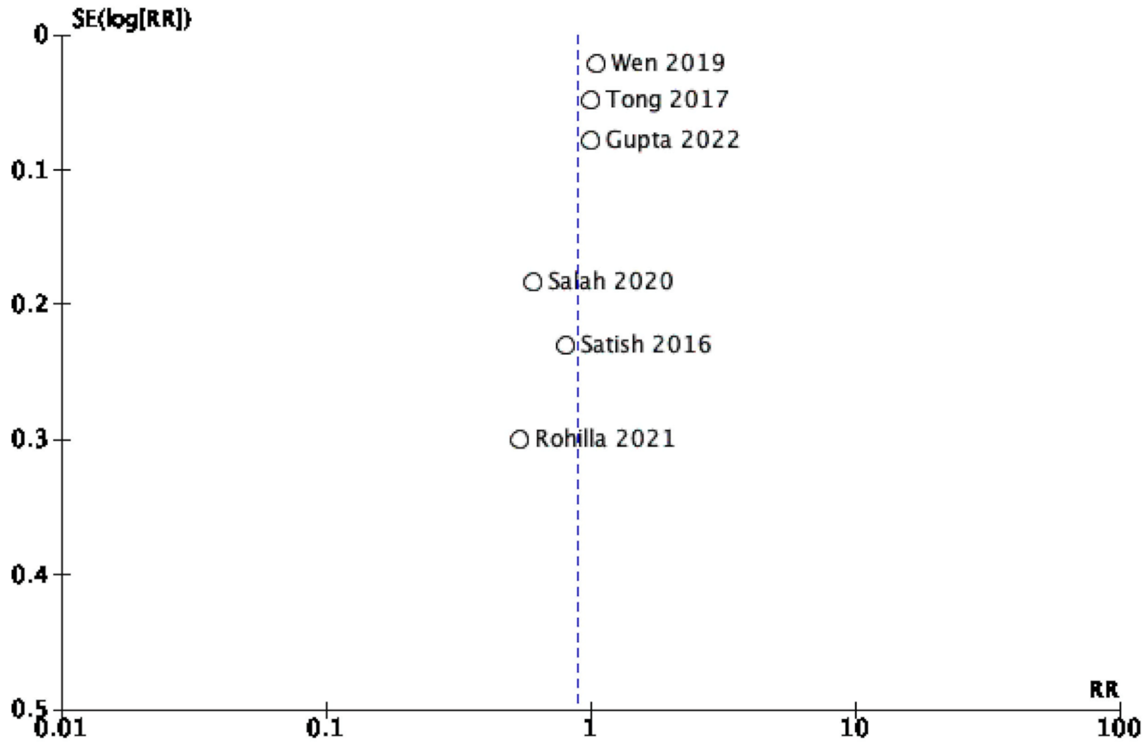

Fig. 4 Bone union funnel plot

Study or Subgroup	Masquelet Mean	Masquelet SD	Masquelet Total	Bone Transport Mean	Bone Transport SD	Bone Transport Total	Weight	Mean Difference IV, Random, 95% CI
Gupta 2022	21.4	4.3	12	21.4	4.3	12	31.7%	0.00 [−3.44, 3.44]
Koti 2016	51.7	16.4	10	35.8	9.9	15	16.3%	15.90 [4.57, 27.23]
Rohilla 2022	28.8	7.2	12	29.2	10	13	24.8%	−0.40 [−7.19, 6.39]
Wen 2019	38.1	21.2	79	44.7	19.5	132	27.1%	−6.60 [−12.34, −0.86]
Total (95% CI)			**113**			**172**	**100.0%**	**0.71 [−5.55, 6.97]**

Heterogeneity: Tau² = 29.06; Chi² = 12.46, df = 3 (P = 0.006); I² = 76%
Test for overall effect: Z = 0.22 (P = 0.82)

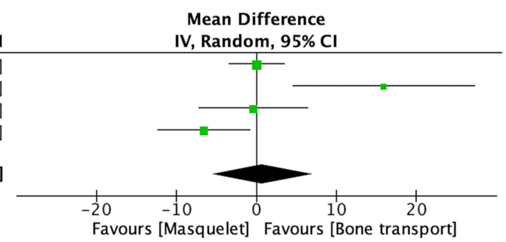

Fig. 5 Time to bone union forest plot

Study or Subgroup	Masquelet Events	Masquelet Total	Bone Transport Events	Bone Transport Total	Weight	Odds Ratio M-H, Random, 95% CI
Gupta 2022	7	12	1	12	17.7%	15.40 [1.47, 160.97]
Rohilla 2022	4	12	3	12	23.2%	1.50 [0.25, 8.84]
Tong 2017	7	20	6	19	28.3%	1.17 [0.31, 4.43]
Wen 2019	4	79	17	132	30.8%	0.36 [0.12, 1.11]
Total (95% CI)		**123**		**175**	**100.0%**	**1.36 [0.36, 5.11]**
Total events	22		27			

Heterogeneity: Tau² = 1.15; Chi² = 8.61, df = 3 (P = 0.04); I² = 65%
Test for overall effect: Z = 0.45 (P = 0.65)

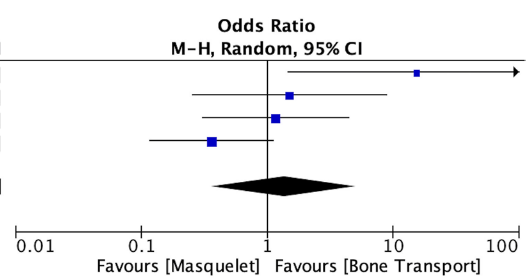

Fig. 6 Need for soft tissue coverage forest plot

Interestingly, all the cases presenting an infection recurrence were already infected at the diagnosis. The current meta-analysis showed no significant difference on infection rate between Masquelet technique and bone transport (OR 2.63; 95%CI 0.95–7.25; $p = 0.06$) (Fig. 9).

Table 6 ASAMI scoring system for the evaluation of bone outcomes

Bone results	Criteria
Excellent	Union, no infection, deformity < 7°, limb-length discrepancy (LLD) < 2.5 cm
Good	Union plus at least two of the following: absence of infection, deformity < 7°, LLD < 2.5 cm
Fair	Union plus at least one of the following: absence of infection, deformity < 7°, LLD < 2.5 cm
Poor	Not applicable

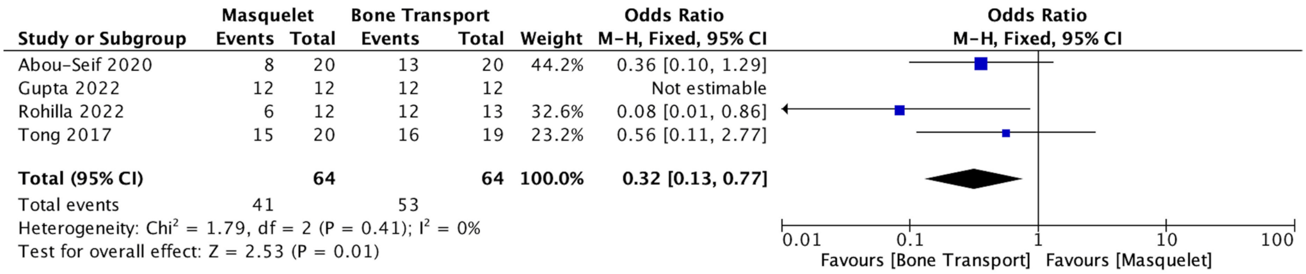

Fig. 7 Bone ASAMI score forest plot

Table 7 ASAMI scoring system for the evaluation of functional outcomes

Functional results	Criteria
Excellent	Active, no limp, minimum stiffness (loss of < 15° knee extension/ < 15° ankle dorsiflexion), no reflex sympathetic dystrophy (RSD), insignificant pain
Good	Active plus one or two of the following: limp, stiffness, RSD, significant pain
Fair	Active plus three or all of the following: limp, stiffness, RSD, significant pain
Poor	Inactive (unemployment or inability to return to daily activities because of injury)
Failure	Amputation

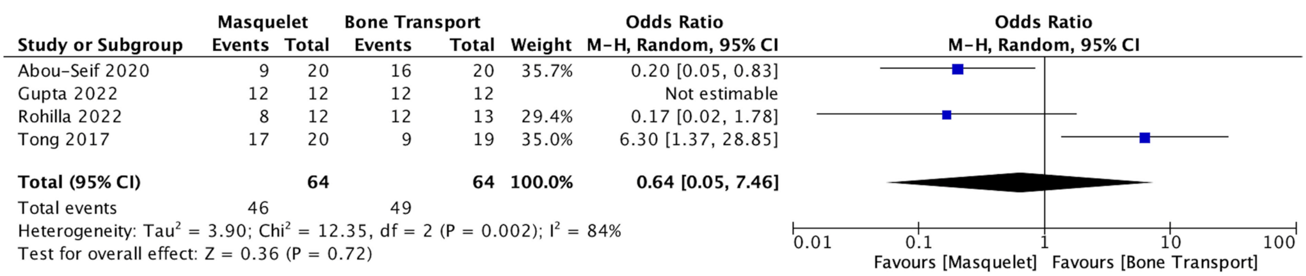

Fig. 8 Functional ASAMI score forest plot

Leg-length discrepancy (LLD) > 2 cm

Four studies [12–15] reported complete data regarding LLD > 2 cm after indexed techniques. These studies included 299 patients: 123 individuals were treated with Masquelet method, while the remaining 176 underwent bone transport. Statistical heterogeneity was $\chi^2 = 0.06$; $I^2 = 0\%$; $p = 0.80$, and a fixed-effect model was used for analysis.

None of the included studies reported significant difference in LLD > 2 cm and meta-analysis of pooled data confirmed no significant differences between the two techniques (OR 2.63; 95% CI 0.74–9.28; $p = 0.13$) (Fig. 10).

Implant failure or refracture

Only 3 studies [12, 13, 15] reported complete data on implant failure or refracture and involved 275 participants, including 111 in the Masquelet group and 164 in the bone transport group. Statistical heterogeneity was $\chi^2=2.71$; $I^2=63\%$; $p=0.70$ and a random-effect model was used for analysis.

None of the included studies reported significant difference of incidence of postoperative refracture/implant failure between the two techniques, which was confirmed by the present meta-analysis (OR 2.03; 95%CI 0.05–76.65; $p=0.70$) (Fig. 11).

Joint stiffness

Only 3 studies [13–15] reported complete data on joint stiffness and involved 260 participants (103 in the Masquelet group and 157 in the bone transport group). Statistical heterogeneity was $\chi^2=0.51$; $I^2=0\%$; $p=0.78$ and a fixed-effect model was used for analysis.

All included studies [13–15] did not report significant differences between the two techniques, which was confirmed by the meta-analysis of pooled data (OR 0.99; 95% CI 0.43–2.27; $p=0.98$). Specifically, 9.7% of patients treated with Masquelet technique experienced joint stiffness against 10.2% of cases in the bone transport group (Fig. 12).

Need for re-intervention

Five studies [12–16] reported complete data regarding the need for re-intervention and included 339 patients, 143 individuals were treated with Masquelet technique, while the remaining 196 underwent bone transport. Statistical

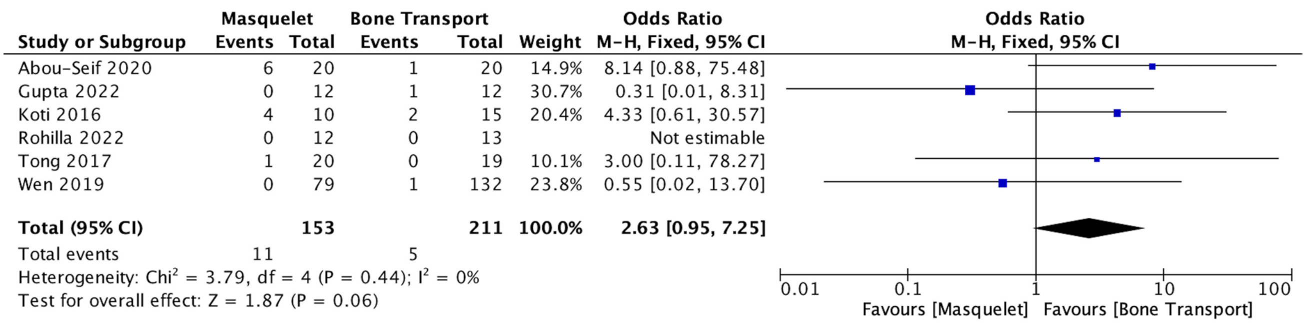

Fig. 9 Infection rate forest plot

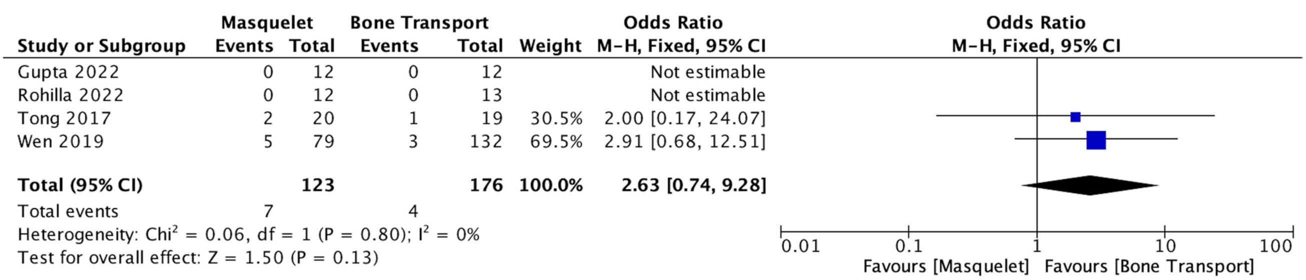

Fig. 10 Leg-length discrepancy > 2 cm forest plot

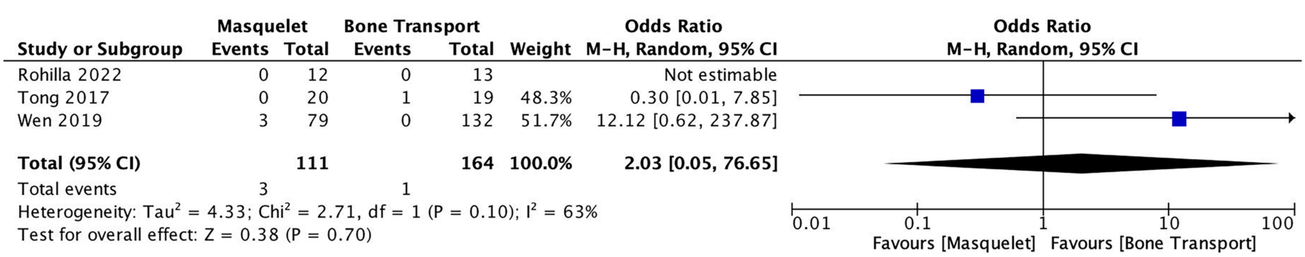

Fig. 11 Implant failure/refracture forest plot

heterogeneity was $\chi^2 = 8.30$; $I^2 = 52\%$; $p = 0.08$ and a random-effect model was used for analysis.

Re-intervention was considered as any additional surgical procedure following the indexed treatments in the attempt to achieve acceptable bone and functional results. Additional procedures in Masquelet group included bone transport ($n = 3$), repeated plastic coverage ($n = 1$), functional cast bracing ($n = 2$), secondary osteotomy ($n = 4$) and amputation ($n = 2$). For the bone transport group, re-interventions were fibula osteotomy ($n = 1$), re-debridement of bone margins and fixator adjustment ($n = 4$), bone grafting ($n = 4$) and secondary osteotomy ($n = 2$). Overall, the present meta-analysis showed no significant differences in the need for intervention after the indexed procedures (OR 1.47; 95% CI 0.42–5.09; $p = 0.55$) (Fig. 13).

Residual deformity

Only 3 studies [13–15] reported complete data regarding the residual deformity after indexed procedures and included 260 patients (103 individuals in the Masquelet group and 157 in the bone transport group). Statistical heterogeneity was $\chi^2 = 0.30$; $I^2 = 0$; $p = 0.86$ and a fixed-effect model was used for analysis.

None of these studies report a significant difference in residual deformity > 7° between the two techniques. However, the meta-analysis of pooled data demonstrated that residual angular deformity is significantly higher in patients treated with Masquelet technique (OR 4.46; 95% CI 1.26–15.72; $p = 0.02$). Specifically, 9.7% of patients from the Masquelet group presented postoperative residual angular deformity versus 1.9% of cases treated with bone transport (Fig. 14).

Study or Subgroup	Masquelet Events	Masquelet Total	Bone Transport Events	Bone Transport Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Gupta 2022	2	12	3	12	22.3%	0.60 [0.08, 4.45]
Rohilla 2022	4	12	5	13	28.5%	0.80 [0.16, 4.12]
Wen 2019	6	79	8	132	49.3%	1.27 [0.43, 3.82]
Total (95% CI)		**103**		**157**	**100.0%**	**0.99 [0.43, 2.27]**
Total events	12		16			

Heterogeneity: Chi² = 0.51, df = 2 (P = 0.78); I² = 0%
Test for overall effect: Z = 0.03 (P = 0.98)

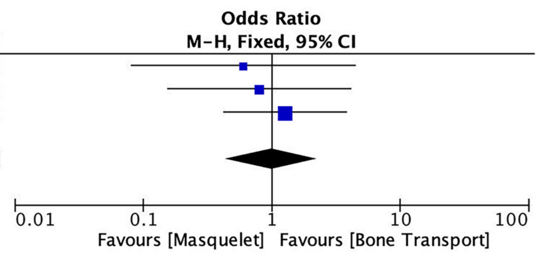

Fig. 12 Joint stiffness forest plot

Study or Subgroup	Masquelet Events	Masquelet Total	Bone Transport Events	Bone Transport Total	Weight	Odds Ratio M-H, Random, 95% CI
Abou-Seif 2020	9	20	3	20	24.9%	4.64 [1.02, 21.00]
Gupta 2022	1	12	4	12	16.2%	0.18 [0.02, 1.95]
Rohilla 2022	4	12	2	13	20.2%	2.75 [0.40, 18.88]
Tong 2017	1	20	3	19	16.3%	0.28 [0.03, 2.97]
Wen 2019	4	79	2	132	22.4%	3.47 [0.62, 19.38]
Total (95% CI)		**143**		**196**	**100.0%**	**1.47 [0.42, 5.09]**
Total events	19		14			

Heterogeneity: Tau² = 1.03; Chi² = 8.30, df = 4 (P = 0.08); I² = 52%
Test for overall effect: Z = 0.60 (P = 0.55)

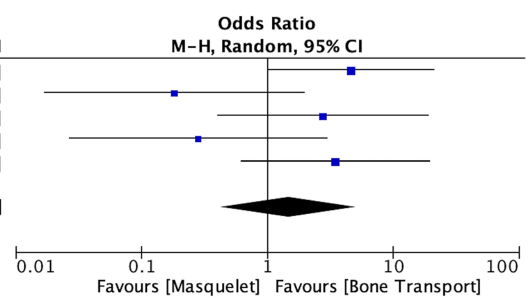

Fig. 13 Need for re-intervention forest plot

Study or Subgroup	Masquelet Events	Masquelet Total	Bone Transport Events	Bone Transport Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Gupta 2022	3	12	0	12	14.6%	9.21 [0.42, 200.59]
Rohilla 2022	3	12	1	13	28.7%	4.00 [0.35, 45.10]
Wen 2019	4	79	2	132	56.7%	3.47 [0.62, 19.38]
Total (95% CI)		**103**		**157**	**100.0%**	**4.46 [1.26, 15.72]**
Total events	10		3			

Heterogeneity: Chi² = 0.30, df = 2 (P = 0.86); I² = 0%
Test for overall effect: Z = 2.32 (P = 0.02)

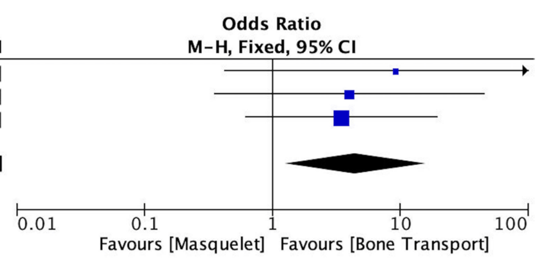

Fig. 14 Residual angular deformity > 7° forest plot

Late amputation

Five studies [12–16] reported the incidence of late amputation after the indexed procedure and included 339 patients, 143 treated with Masquelet technique and 196 with bone transport. Statistical heterogeneity was $\chi^2 = 12.42$; $I^2 = 68\%$; $p = 0.01$ and a random-effect model was used for analysis.

Most of the included studies did not investigate thoughtfully the prevalence of late amputation as post-operative complication. However, a meta-analysis of reported data was still possible since data could be deducted from ASAMI functional scores. Comprehensively, this meta-analysis did not report any significant difference between the two techniques (OR 0.89; 95% CI 0.03–24.85; $p = 0.94$) (Fig. 15).

Details of all analyzed dichotomic outcomes are reported in Table 8.

Discussion

The main finding of this study is that both the Masquelet technique and bone transport are reliable procedures with comparable consolidation rates, time to bone union, functional results and complications. Nonetheless, analysis of pooled data showed that distraction osteogenesis had better outcomes in terms of bone ASAMI scores and residual limb deformity.

Since the current literature is mostly based on low-quality, non-randomized and often retrospective studies with a serious risk of bias, there is lacking evidence and no clear consensus on the treatment of critical-sized bone defects of the lower extremities. Furthermore, several articles are only found in Chinese language, preventing an exhaustive evaluation and comparison of data.

Benulic et al. [18] provided a systematic review of the literature showing that distraction osteogenesis had superior

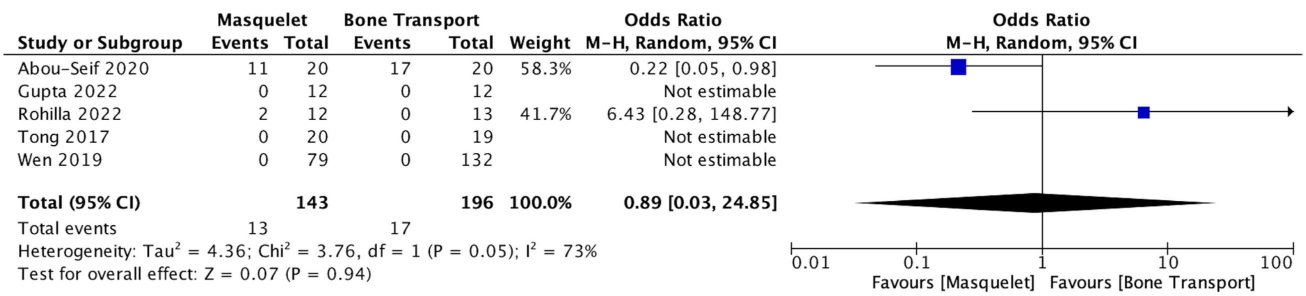

Fig. 15 Late amputation forest plot

Table 8 Sub-group analysis of the outcomes reported in the Masquelet and bone transport with number of participants, reported odd ratio (OR), 95% confidence interval (95% CI), and the relative *p* value

Outcome	Number of studies	Participants (MT/BT)	Prevalence (MT/BT)	OR [95% CI]	*p* Value
Bone union	6 [12–17]	364 (153/211)	88.2%/95.7%	0.30 [0.05, 1.65]	0.17
Soft tissue coverage	4 [12–15]	298 (123/175)	17.9%/15.4%	1.36 [0.36, 5.11]	0.65
ASAMI bone outcomes	4 [12, 14–16]	128 (64/64)	64.0%/82.8%	0.32 [0.13, 0.77]	0.01*
ASAMI functional outcomes	4 [12, 14–16]	128 (64/64)	71.9%/76.6%	0.64 [0.05, 7.46]	0.72
General complication rate	1 [13]	211 (79/132)	26,6%/25,8%	NR	> 0.05
Infection	6 [12–17]	364 (153/211)	7.2%/2.4%	2.63 [0.95, 7.25]	0.06
LLD > 2 cm	4 [12–15]	299 (123/176)	5.7%/2.3%	2.63 [0.74, 9.28]	0.13
Implant failure or refracture	3 [12, 13, 15]	275 (111/164)	2.7%/0.6%	2.03 [0.05, 76.65]	0.70
Joint stiffness	3 [13–15]	260 (103/157)	9.7%/10.2%	0.99 [0.43, 2.27]	0.98
Re-interventions	5 [12–16]	339 (143/196)	13.3%/7.1%	1.47 [0.42, 5.09]	0.55
Residual deformity	3 [13–15]	260 (103/157)	9.7%/1.9%	4.46 [1.26, 15.72]	0.02*
Late amputation	5 [12–16]	339 (143/196)	9.1%/8.7%	− 0.01 [− 0.10, 0.08]	0.85

ASAMI Association for the Study and Application of the Method of Ilizarov, *BT* bone transport, *LLD* limb-length discrepancy, *MT* Masquelet technique, *NR* not reported

*Highlight significant values

outcomes over Masquelet technique in terms of bone union and infection rate. However, the authors summarized the results of retrospective case series without a direct comparison of outcomes through a meta-analysis. Ren et al. [19] published the first systematic review and meta-analysis comparing the Masquelet technique and the bone transport with Ilizarov external fixation reporting superior results of the induced-membrane technique in most of the assessed outcomes. However, authors did not assess the bone union rate and 12 out of the 13 included articles were non-English publications, hence precluding a more comprehensive and updated review with the present study.

To the best of our knowledge, this is the first study to meta-analyze the bone union rate and the most recent paper summarizing the bone and functional results obtained with Masquelet technique versus bone transport for the treatment of critical-sized bone defects of lower limb. This study critically compared the efficacy and limitations of these two methods and demonstrated that both techniques have overlapping outcomes.

One of the main advantages of bone transport with Ilizarov external fixation is the high rate of union and the possibility to achieve early weight-bearing [20]. However, bone transport is inevitably dependent on the patient compliance, and the social implications and psychological stress experienced by patients undergoing distraction osteogenesis are important aspects to consider when deciding the best treatment strategy in critical-sized bone defects [21]. Furthermore, circular frames require periodical consultations and constant adjustments with considerably higher costs and resources for the healthcare system [23, 24]. Finally, complications such as pin site infection, chronic skin irritation, broken wires and ankle stiffness are specific to this technique [24].

The Masquelet technique was developed to overcome some limitations of bone transport maintaining adequate results in terms of union rate [25]. The technique presents the advantage of internal fixation and theoretically shorter recovery time, as shown by Kanakaris et al. [22], also significantly reducing the associated healthcare costs. Despite initial satisfactory outcomes, some investigations showed concerns related to bone union and infection recurrence [26, 27, 28], although the poor outcomes could be related to technical issues and non-strict adherence to the "diamond concept" [24].

The present research demonstrated that bone transport had significantly lower residual deformities, but this is intrinsic to distraction osteogenesis, which is well known to be applied in the correction of three-dimensional bone deformities [28]. Furthermore, this meta-analysis showed that bone transport had significantly better bone outcomes in agreement with ASAMI criteria. Specifically, the meta-analysis of data from 128 patients demonstrated that 82.8% of cases treated with the bone transport versus 64% of patients treated with the Masquelet technique obtained excellent or good results in terms of bone union, LLD, residual deformity and infection ($p=0.01$). Despite the lack of data regarding mechanism of injury and severity of the lesion, no statistical difference in the need for soft tissue coverage between the two groups highlighted similar pre-operative baseline conditions hence providing consistency to these findings.

In terms of overall functional results, no significant difference emerged between the induced-membrane technique and bone transport making them comparable. Nevertheless, the lack of qualitative data prevented a meta-analysis on the mean time to full functional recovery, which would have been indicative of the length of treatment. Ren et al. [19] that patients treated with the Masquelet procedure had a shorter mean time to full weight bearing if compared to bone transport.

Complications remain a common contributor to treatment failure and persistent non-union, especially when referring to infection. According to the results of this meta-analysis, postoperative complications including infection, residual deformity, hardware failure, need for re-intervention and late amputation had a similar prevalence in the two groups. However, these findings partially disagree with those presented by Ren et al. [19], who showed that patients in the Masquelet group had a lower post-operative complication rate. By contrast, the analysis of data conducted by Benulic et al. [18] demonstrated that the infection rate was significantly higher in patients treated with the induced-membrane technique. However, potential confounding factors such as the mechanism of injury, the degree of contamination and possible intra-operative technical issues (i.e., insufficient debridement) were not clearly stated in most of the published articles.

This systematic review has a precise design and strict inclusion and exclusion criteria but presented several limitations. One of the main limitations was the high heterogeneity of data due to mixed populations, different assessment methods, pre-operative diagnosis and the absence of patient-specific details. Furthermore, all the investigations included presented a moderate-to-serious risk of bias and a low quality of evidence, which is mostly related to study design and retrospective nature of current literature.

Several confounding factors may influence the assessed outcomes, potentially biasing the reported results. First of all, it is pivotal to provide a precise diagnosis of inclusion, distinguishing between septic and aseptic bone loss and reporting sub-population results that are often missing in the included articles. Similarly, the initial management of fracture, the severity of injury and the conditions of soft tissue must be considered with quantitative scoring data. Further prospective randomized controlled trials are necessary to better clarify the strength and drawbacks of these two techniques and to identify the variables affecting the outcomes.

Conclusions

Masquelet technique and bone transport are both reliable solutions for the management of critical-sized bone defects of the lower limb and presented comparable results in most of the assessed outcomes. Meta-analysis of pooled data showed a superior outcome of the bone transport technique in bone ASAMI score and residual deformity that should be carefully interpreted and investigated with further prospective randomized studies.

Data availability All data supporting the findings of this study are available within the paper and its Supplementary Information.

Declarations

Conflict of interest The authors have no conflict of interests to declare.

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