

## Treatment outcome of the Masquelet technique in 195 infected bone defects—A single-center, retrospective case series

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### ABSTRACT

**Background:** The Masquelet technique is a surgical procedure for the reconstruction of bone defects. During the first step, an osteosynthetically stabilized defect is filled with a cement spacer. The spacer induces a foreign body membrane, called a Masquelet membrane. In a follow-up procedure, the spacer is replaced by a bone graft, which ossifies in the subsequent phase.

**Material and Methods:** A total of 171 patients with 195 septic bone defects on the extremities that had been treated with the Masquelet procedure at the BG Klinikum in Hamburg, Germany, from 2011 to 2021 were retrospectively analysed, comparing patients who reached full weight and load bearing on the affected extremity to those who failed to do so. Defect size and configuration, microbiological results and treatment methods as well as comorbidities and epidemiologic data were analysed for factors influencing the treatment outcome.

**Results:** In all, 113[66%] of the patients were male, and 58[34%] were female, with an age distribution of 52 +/-16 years. Out of 171 patients, 24 patients had two defects. The number of patients that reached full weight bearing was 152[89%], the follow-up period was 2 +/-1 years (median +/- SD). Full weight bearing capability was negatively by the defect size as defects >62 mm tended to be less likely to reach full weight bearing than smaller defects. A secondary stabilization with an internal stabilization was applied in 58[34%] of all patients and positively influenced the attainment of full weight and load bearing.

**Discussion:** With 171 patients and 195 septic bone defects treated at a single centre with the Masquelet Technique, this study represents a comparably large cohort. Demographics, defect characteristics and treatment outcomes did not differ from those of other cohorts described in the literature. Defects larger than 62 mm showed lower chances to reach full weight bearing and can be defined as "critical defect size" for the Masquelet technique based on our data.

### Introduction

The restoration of biologically and biomechanically healthy bone after loss of substance due to trauma or resection of avital or infected bone tissue is often a time-consuming process fraught with complications [1–3]. Common techniques include segmental transport by means of an external fixator. This requires wearing of the construct for several weeks per centimetre of defect and a high level of patient compliance, often resulting in delayed healing and non-union at the docking site [4]. As a single-stage alternative, fibula transfer is available, but it is not recommended due to frequent infectious non-union [5] and the further requirement of a high level of microsurgical expertise when harvesting

and implanting the graft [6].

An alternative to the abovementioned methods is the Masquelet technique or 'Induced Membrane Technique'. It is a two-stage procedure developed by A. Masquelet in the 1980s and first scientifically described in 2000 [7,8]. After extensive debridement of the defect and internal or external stabilization as well as ensuring sufficient soft tissue coverage, a cement spacer is placed at the site of the defect. This usually antibiotic-loaded cement spacer induces a well vascularized foreign body membrane, also called a Masquelet membrane. After 4–6 weeks, the cement spacer is carefully removed, leaving the membrane intact, and the defect is filled with an autologous bone graft followed by careful closure of the membrane. In the subsequent phase of ossification of the

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defect area, the membrane serves as a physical barrier and supports the healing process in the presence of growth factors [9,10].

The technique is frequently carried out in the department of septic bone and joint surgery at the BG Klinikum in Hamburg, Germany. In this study, patients that had undergone the procedure were retrospectively analysed regarding factors influencing the treatment outcome, such as defect configuration and size, comorbidities, the surgical technique and pathogens isolated during surgery. The focus of this work is the functional outcome of full weight bearing and the need for additional surgical procedures with additional internal fixation of the defect area.

## Material and methods

### Study design and data acquisition

The study design was a retrospective, consecutive series, single-arm cohort study that included all patients treated with the Masquelet technique at the BG Klinikum Hamburg (BGKH) from July 2011 until June 2021.

In addition to clinical patient data, post-treatment data from electronic patient records were stored in a database that was used exclusively for study purposes. Names, addresses and dates of birth were not transferred, and ages were rounded in years. Other possibly identifying data, e.g. the period from the surgery date to the follow-up date, were calculated directly during extraction and stored only as a numerical indication of the period.

### Patient recruiting and inclusion criteria

For data evaluation, all patients aged 18 years and above were considered for data evaluation. The indication for using Masquelet rather than single-step autologous bone grafting was a defect size longer than 3 cm and at least 2/3 of the circumference, failed segment transport or lack of compliance by the patient [6] for segment transport.

After a positive vote by the ethics committee (April 15th, 2021, University of Lübeck EC, registration number 21–169), a request from the in-house hospital information system data bank followed in July 2021 to extract basic epidemiological and treatment data. All data were

pseudonymously registered on a spreadsheet saved on the inhouse IT infrastructure.

After literature research further parameters were defined to extract handedly from medical records:

- Age
- Sex
- Bone affected
- Defect configuration – semi-circular, circular and mixed (see Fig. 1)
- Work-related or private accident
- Indication for Masquelet technique
- Size of defect
- Pathogens isolated during each intervention
- Whether full weight and load bearing was achieved
- Time until full weight and load bearing was achieved
- Duration of follow up
- Secondary stabilization of the defect, defined as an intramedullary nail or a plate to reinforce the healed defect
- External fixation methods
- Concomitant diseases
- Complications
- Additive substances during surgery

### Routine treatment pathway in the investigated timeframe

#### Pre-surgical care

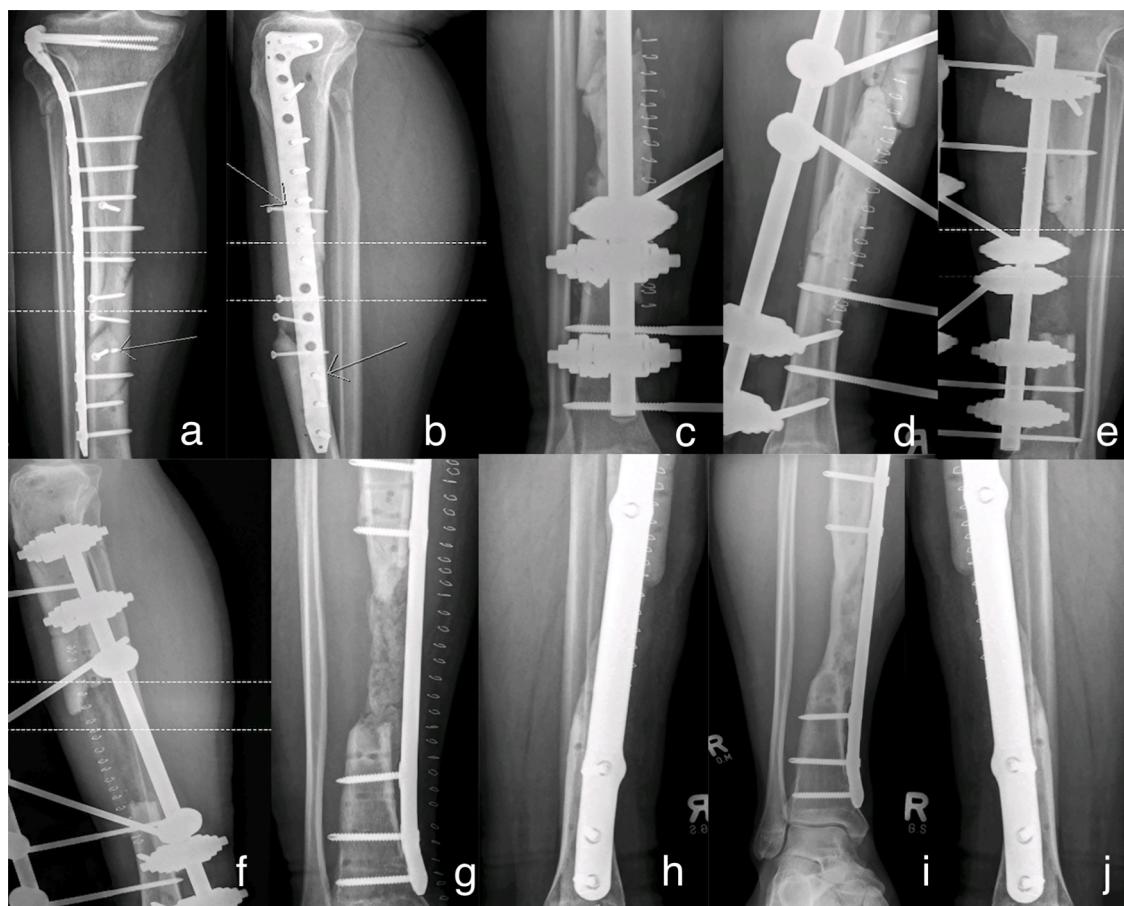
X-rays of the defect with the adjacent joints were taken in two planes, and an MRI was performed to delineate the extent of infection for sufficient debridement during the first step of the procedure.

#### The surgical procedure

The main steps of the procedure were carried out in the manner described by Masquelet et al. (2019) in their recently updated recommendations [7]. The procedure is briefly described as it was carried out at the BGK in Hamburg on a 34-year-old male patient suffering from a septic non-union after internal fixation of an II° open tibial fracture as shown in Fig. 2a and b. The defect had a total length of 8 cm, consisting



**Fig. 1.** X- rays with examples of defect configurations a) semicircular defect b) circular defect c) mixed semi- circular and circular defect.



**Fig. 2.** Example of a septic nonunion following a II° open fracture of the tibia treated with the Masquelet technique: a) and b) internal stabilization with a broken plate (barely visible, marked by upper thin arrow on the left image) and interfragmentary screws of which one is broken (lower thin arrows) c) and d) V-shaped external fixator and PMMA filled bony defect e) and f) visible ossification on defect side at week 6 after bone grafting g) and h) secondary stabilization of an ossifying defect zone using a fixed angle internal stabilization i) and j) final Consolidation of the defect zone one year after grafting.

of a 3 cm circular and 5 cm semi-circular component.

#### Debridement and spacer implantation

In the first step, all foreign material was removed, an extensive debridement of the defect site was carried out, an antibiotic-loaded

spacer made from Polymethylmethacrylate(PMMA) [7] was implanted to fill the defect (Fig. 2c and d) and external fixation was performed to secure the length, axis and rotation of the affected bone with either external fixation using an Ilisarow Ring-fixator (Fig. 3) or, as in the case of the abovementioned patient, with a tube fixator (Fig. 2c-f),



**Fig. 3.** Ilisarow ring fixator with a Hexapod feature.

mechanically counteracting soft-tissue interposition and supporting the fixation [11,12].

Microbiological samples were taken followed by an empirical treatment starting during the operation routinely using Ampicillin/Sulbactam 3 g intravenously or an alternative broad-spectrum antibiotic depending on microbial identification, allergies, pre-existing conditions, pharmacological compatibility and antibiotic sensitivity, continued for at least 5 days with possible prolongation of the interval depending on clinical and laboratory parameters.

Histological samples were also routinely taken to rule out malignancy, identify a chronic or acute stage of infection or hints of granulomatous diseases.

#### *Removal of the spacer and bone grafting*

Four to six weeks after the first procedure, patients underwent the second procedure. If the infection was not controlled, the first step was repeated. If the infection was successfully managed, the PMMA-Spacer was removed, preserving the Masquelet membrane. The surrounding tissue was carefully debrided to the bleeding bone. To preserve the integrity and function of the membrane as a physical barrier, a scraping of the membrane was not performed as described by Luangphakdy et al. [13], proven by Klaue et al. [10], in an experimental series in sheep.

The intramedullary canal was reconstructed with a gelatine sponge in accordance with Jae-Woo Cho et al. [14]. In the case of larger defects, vancomycin-augmented allografts such as Perossal® or donor cancellous bone were added. Bone grafts were obtained from either the pelvis or the proximal tibia. The site of harvesting was instilled with the local anaesthetic Ropivacaine, selected for its proven compatibility in orthopaedic interventions [15] to reduce postoperative pain.

The grafting material was placed at the site of the cortical defect, overlapping both ends of the defect (Fig. 2e and f). For larger defects, allografts were used, and bone marrow aspirate was added to the graft. Microbiological and histological regimens were identical to those in the first step.

#### *Ossification and transition to full weight and load bearing*

Radiological and clinical evaluation of the healing process was routinely carried out 4–6 weeks after grafting. Initial weight bearing was limited to 10 kg on the affected side. Upon radiological consolidation (Fig. 2g-j) weight bearing was increased successively.

Depending on the progress of ossification, the external fixation is removed starting 3 months after the grafting procedure. In accordance with clinical stability, either an internal secondary stabilization using a plate (Fig. 2g and h) or external load reduction by a brace [16] was used, successively increasing the load applied on the defect zone until consolidation of the defect zone was reached (Fig. 2i and j).

Smaller defects and those with a semi-circular configuration were not supplied with an additional secondary stabilization (Fig. 4).

#### *Statistical methods*

SAS statistical software [17] and R statistics [18] (version 3.5.1 and RStudio (both R Consortium, Boston, MA, USA), version 1.1.456.) were used for data analysis. Categorical data were expressed in absolute values as well as percentages. Nominal data were expressed in means with relative percentages and standard deviations. Differences between groups having nominal data formats were evaluated with the Student's *t*-test and categorical parameters with the chi-square test. The level of significance ( $\alpha$ ) was set to 5%; hence, p-values below 0.05 indicated significance. In concordance with the Declaration of Helsinki, the study was powered at 0.8.

#### **Results**

##### *Demographics*

Demographical and patient data subdivided into two groups, one that reached full weight and load bearing and one that did not, can be seen in Table 1. From 196 initially listed patients that had been treated with the Masquelet technique, 6 had to be excluded as their treatment was still ongoing. Fourteen patients were lost to follow-up, and 5



**Fig. 4.** a) Smaller defect with a semi-circular configuration with a PMMA spacer b) due to sufficient stability not supplied with an additional secondary stabilization after consolidation.

**Table 1**

Overview on demographic and treatment related data in relation to patients reaching full weight bearing versus failing to do so.

Overview on patient data divided by patients reaching full weight bearing versus not reaching full weight bearing				
	No (N = 18)	Yes (N = 153)	Total (N = 171)	p-value
<b>Sex</b>				0.611
Female	7 (39%)	51 (33%)	58 (34%)	
Male	11 (61%)	102 (67%)	113 (66%)	
<b>Age</b>				0.261
Mean (SD)	54 (16)	51 (16)	52 (16)	
Range	23 - 77	10 - 82	10 - 82	
<b>Complications</b>				
no complication	5 (28%)	72 (47%)	77 (45%)	
ossification	0 (0%)	1 (1%)	1 (1%)	
instability	1 (6%)	23 (15%)	24 (14%)	
re-infection	2 (11%)	38 (25%)	40 (23%)	
osteosynthesis related	3 (17%)	9 (6%)	12 (7%)	
soft tissue defect	7 (39%)	10 (7%)	17 (10%)	
<b>Secondary Stabilization</b>				0.523
no	14 (77.8%)	99 (64.7%)	113 (66.1%)	
intramedullary nail	0 (0.0%)	4 (2.6%)	4 (2.3%)	
plate osteosynthesis	4 (22.2%)	50 (32.7%)	54 (31.6%)	
<b>Localization of Defect</b>				
femur	2 (11%)	36 (24%)	38 (22%)	
foot	0 (0%)	1 (1%)	1 (1%)	
forearm	0 (0%)	3 (2%)	3 (2%)	
humerus	1 (6%)	8 (5%)	9 (5%)	
tibia	15 (83%)	105 (69%)	120 (70%)	
<b>Pneumologic comorbidity</b>				0.212
no	12 (67%)	124 (81%)	136 (80%)	
yes	6 (33%)	29 (19%)	35 (20%)	
<b>Cardiac comorbidity</b>				0.622
no	11 (61%)	82 (54%)	93 (54%)	
yes	7 (39%)	71 (46%)	78 (46%)	
<b>Metabolic comorbidity</b>				0.801
no	10 (56%)	92 (60%)	102 (60%)	
yes	8 (44%)	61 (40%)	69 (40%)	
<b>Polytrauma</b>				1.000
no	15 (83%)	125 (82%)	140 (82%)	
yes	3 (17%)	28 (18%)	31 (18%)	
<b>Vascular comorbidity</b>				0.181
no	13 (72%)	130 (85%)	143 (84%)	
yes	5 (28%)	23 (15%)	28 (16%)	
<b>Neurological comorbidity</b>				0.166
no	10 (56%)	112 (73%)	122 (71%)	
yes	8 (44%)	41 (27%)	49 (29%)	
<b>Immune System related comorbidity</b>				0.168
no	13 (72%)	131 (86%)	144 (84%)	
yes	5 (28%)	22 (14%)	27 (16%)	
<b>Psychiatric comorbidity</b>				0.615
no	9 (50%)	90 (59%)	99 (58%)	
yes	9 (50%)	63 (41%)	72 (42%)	
<b>Size of Defect</b>				0.167
Mean (SD)	78.1 (28.6)	56.5 (30.6)	58.8 (31.0)	
Range	30.0 - 130.0	20.0 - 180.0	20.0 - 180.0	
<b>Additional biomaterial fillers</b>				0.141
no	5 (28%)	19 (12%)	24 (14%)	
yes	13 (72%)	134 (88%)	147 (86%)	

patients died during treatment, leaving a total number of 171 patients. In all, 113[66%] of the patients were male and 58[34%] were female, with an age distribution of 52 +/- 16 (mean +/- SD) years of age, a maximum of 83 and a minimum of 18.

#### Comorbidities

Comorbidities were categorized into cardiac, immunological, metabolic, neurological, pneumological, psychiatric and vascular conditions.

Additionally, polytrauma was recorded as a relevant pre-existing condition. A summary of the occurrence of these conditions in pre-defined categories can be seen in Fig. 1.

Only 14[8%] patients had no pre-existing comorbidities, 36[21%] had only one comorbidity, 36[21%] two comorbidities, 55[32%] three, 17[10%] four, 10[6%] five and 2[1%] six comorbidities.

#### Defects

Out of 171 patients, 24 [14%] had two defects that had been treated with the Masquelet technique, resulting in a total number of 195 septic defects. The configuration of defects is shown in Fig. 1 with radiological examples. They were subdivided into semi-circular defects (Fig. 1a), circular defects (Fig. 1b) and mixed defects (Fig. 1c). The prevalence of semi-circular defects was N = 73 (37%), circular defects N = 87 (45%) and mixed N = 35 (18%).

In a non-parametric comparison of defect configurations using Bonferroni-adjusted p-values, no significant correlation of defect configurations to full weight and load bearing could be found, as seen in Table 2.

The mean length of all defects was 59 mm (+/-31 mm, min. 20 mm, max. 180 mm).

The localization of defects can be seen in Table 1, with 137[70%] of all defects located in the tibia followed by 43[22%] in the femur, 10 [5%] in the upper arm, 4[2%] in the forearm and 1[1%] in the foot.

#### Treatment

##### Indication for treatment

According to case notes, the indication for using the Masquelet technique was osteomyelitis in 125 [64%] cases followed by joint infections in 20[11%], non-compliance to treatment with other bone reconstruction modalities in 20 [10%], infected non-union in 12[6%], infected distraction osteogenesis in 10[5%] and soft-tissue loss in 8[4%] cases.

##### Primary stabilization of the defect

The method of surgical stabilization was an external tube fixator in 125[64%] follow by an Ilizarov ring-fixator in 45[23%] and a midi fixator in 4[2%] cases. No fixation due to existing stability was applied in 16[8%], and in 6[3%] cases the internal fixation system remained in situ.

During treatment, 39[23%] patients had to undergo a change of the fixation method with 21[54%] the patients changing an Ilizarow ring fixator, 9[22%] receiving an extension to a V-shaped external fixator configuration, 5[14%] receiving a tube external fixation system and 4 [10%] receiving a double tube system.

##### Additives used during bone grafting

During the first procedure, the following additives to PMMA were used: Perossal pellets (OSARTIS GmbH, Münster, Germany) with Vancomycin powder added in 78[40%], Perossal pellets without added Vancomycin in 4[2%], Gentacoll sponge (RESORBA Medical GmbH, Nürnberg, Germany) in 76[39%], MarrowStim (Orthob, Alc. Benito Juárez, México) in 25[13%], Refocoll (Zimmer Biomet Zug,

**Table 2**

Defect configurations compared in relation to reaching full weight and load bearing.

Defect configuration	Raw p-value	Bonferoni adjusted p-value
Semicircular vs. mixed	0,0199	0,0597
Semicircular vs. circular	0,0962	0,2886
Circular vs. mixed	0,3323	0,9969

Switzerland) in 25[13%], GelitaSpon (Novimed AG, Dietikon, Switzerland) in 35[18%], Vancomycin additive in the sponge in 10[5%], Cerament-G (BONESUPPORT HOLDING AB, Lund, Sweden) in 6[3%] and no additives in 35[18%] cases.

#### Results of microbiological analysis

The 10 most frequent individual organisms cultured during the first debridement and the first spacer removal are listed in [Table 3](#), with the respective rates of eradication. In total, 59 (35%) defects yielded no growth of bacteria despite clinical evidence of infection at first debridement. When the spacer was removed, 135 (79%) samples were sterile. Whether a single or multiple organisms were detected in culture is shown in [Table 4](#).

In all, 150[88%] patients that had a positive bacterial culture during the first spacer removal reached full weight and load bearing.

Besides the above mentioned, the following organisms appeared in single cultures: *Achrombacter xylosoxidans*, *Candida albicans*, *Corynebacterium aurimucosum*, *Enterobacter ludwigii*, *S. pettenkoferi*, *Stenotrophomonas maltophilia*, *Acinetobacter baumanii*, *Moraxella osloensis*, *Propionibacterium acnes* and *Bacteroides fragilis*.

#### Secondary stabilization

In all, 58[34%] patients needed a secondary stabilization of the defect. This was performed with a plate in 54[93%] cases and a nail in 4 [7%]. In all, 53 [92%] patients who had received a secondary stabilization reached full weight and load bearing.

#### Complications and revision rates

Complications were recorded for adverse events concerning the operated site and leading either to re-operation or to a prolonged hospital stay. The overall prevalence of complications amongst all patients was 54%[ $N = 92$ ]. The occurrence of specific complications can be seen in [Table 1](#). There was no statistically significant correlation between the number of pre-existing conditions and the development of complications with a p-value of  $p = 0.32$  in the Fisher exact test.

In all, 32[19%] patients needed one revision, 10[6%] two revisions and 1[1%] three revisions.

#### Follow-up and treatment outcome

The median for the follow-up period was  $2 +/ - 1$  years (median  $+/- SD$ ) years with a maximum of 9 years and a minimum of 8 weeks. Out of

**Table 3**  
Organisms cultured during first debridement and at the removal of the spacer.

Organisms	Prevalence at first debridement [%]	Prevalence when explanting the first spacer [%]
<i>S.aureus</i>	19,72	8,25
<i>S. epidermidis</i>	18,80	7,34
<i>E. faecalis</i>	6,88	2,75
<i>S. caprae</i>	5,04	0,92
Pseudomonas aeruginosa	5,04	5,04
<i>E. coli</i>	4,58	1,84
<i>S. iugdunensis</i>	3,21	—
<i>S. hemolyticus</i>	2,29	0,92
Enterobacter cloacae	1,83	—
<i>Serratia marcescens</i>	1,37	0,92
<i>Proteus mirabilis</i>	—	0,92
Klebsiella pneumoniae	—	0,92
Clostridioides intestinalis	—	0,92
<i>Citrobacter koseri</i>	—	0,92

**Table 4**

Number of different organisms in cultures from first debridement and from spacer removal.

Number of different species in one culture	Prevalence during debridement of the defect [N]	Prevalence during spacer removal [N]
0	77	157
1	111	52
2	29	11
3	3	2
4	2	0

all patients analysed, 152[89%] were reported to return to full weight and load bearing on the affected limb. The median time from treatment initiation to full weight and load bearing was  $20 +/ - 13$  months (median  $+/- SD$ ). When defect size and the ability to achieve full weight bearing are plotted against each other, an intersection point can be seen at 61 mm ([Fig. 5](#)), defining the cut-off point for a negative treatment outcome.

#### Discussion

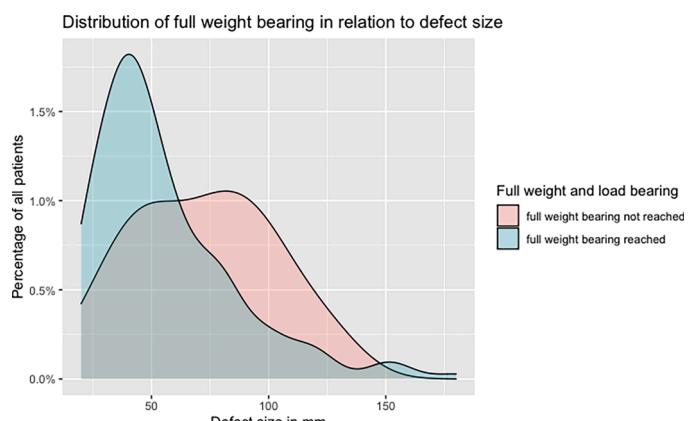
##### Demographics and patient characteristics

The mean age of the patients in our study was 52 years similar to Raven et al. [[19](#)] and Hsu et al. [[9](#)], all between the middle of the 5th and beginning of the 6th decade of life. A tendency towards predominantly male patients (66%) was also observed by Raven et al. [[19](#)] (67%) and Hsu et al. [[9](#)] (82%).

Study population sizes vary widely from  $N = 7$  to  $N = 84$  in meta-analyses by Hsu et al. [[9](#)] and Masquelet et al. [[7](#)] to a single-centre study by Raven et al. from 2019 describing treatment with the Masquelet in 150 patients [[19](#)] or by Karger et al. [[20](#)] comprising 84 patients. The strength of the current study is its high numbers with 171 patients with 195 infected defects.

A detailed analysis of comorbidities and the Masquelet technique could not be found in the literature. With only 8% of patients having no comorbidities, the Masquelet technique was applied in a difficult biological environment in our study population of the current study. By contrast, Roche et al. [[21](#)] found no statistically significant correlation between the number of comorbidities and the development of complications as the p-value in Fisher's exact test was  $p = 0.35$ . This may be explained by the elderly population examined by Roche et al., as age has an additional negative influence on regenerative capacity in osseous defects [[22](#)].

With 70% of all defects located in the tibia followed by 22% in the femur, 5% in the upper arm, 2% in the forearm and 1% in the foot, the patient collective fits well within the meta-analysis of a clinical series of  $>15$  patients summarized by Masquelet et al. in 2019 [[19](#)]. Karger et al.



**Fig. 5.** Defect size in relation to full weight and load bearing showing an intersection at 61 mm marking a point of critical size defects.

[20] published a series of 84 posttraumatic long bone defects with 73% in the tibia, 16% in the femur, 7% in the humerus and 5% in the forearm, with a similar prevalence of defects.

#### Defect configuration

In our study the overall defect size correlated positively with the time needed to attain full weight and load bearing ( $p = 0.0134$ ). The likelihood of a positive treatment outcome for reaching full weight and load bearing changed at 62 mm towards a negative outcome (see Fig. 5), a result that could not be found in literature. Hence, a defect measuring more than 62 mm can be seen as a critical size defect in patients undergoing bone reconstruction using the Masquelet technique.

This stands in contrast to the observation by Masquelet et al. that defect size was independent of the treatment result, which was not supported by statistical data [7]. Nauth et al. [24] analysed critical size bone defects in the literature with varying results ranging from 1 to 2 cm to 50% loss of bone circumference. Begue et al. [25] defined defects exceeding a length of 5 cm as critical and less likely to heal using conventional bone grafting, thus requiring the Masquelet technique.

The mean defect size reported by Raven et al. was 44 mm on average, the metanalysis by Hsu et al. reported 55 mm and showed comparable results to the 59 mm in this study [19].

The configuration of defects in this study was subdivided into three categories: circular, semi-circular and mixed defects. No significant correlation between defect configurations and reaching full weight and load bearing or development of complications was observed. Stafford et al. used a similar approach subdividing defects into conical and cylindrical with a focus on volumetric measurement [23].

Karger et al. subdivided their defects into segmented (86%) and bevelled (14%) defects [20]. A direct comparison cannot be made between studies and a universal nomenclature is needed.

#### Primary stabilization of the defect

In a recent paper by Masquelet et al., open questions and recommendations as to the optimal osteosynthesis construct are given in Table III [7], pointing towards limited evidence on the question [28]. By investigating changes in fixation methods, between every 4th and every 5th fixation system (23%) had to be changed, mostly to a ring fixator (52%) followed by a V-shaped construct (23%). It can be concluded that the system of maximal possible stability should be chosen for primary stabilization to spare additional operations.

#### Treatment outcome and its definition

With 89% full-weight and load bearing, the rate of adequate union was higher than the 80% reported by Raven et al. and slightly lower than the 90% union rate (range 79%–93%) reported by Masquelet et al. and the 90% reported by Hsu et al.

This study defined the point of reaching full weight bearing on the lower extremity and unrestricted load bearing for the upper extremity, short full weight and load bearing. The end point stands in contrast to the systematic review by Hsu et al. [9] and Masquelet et al. [7] as well as Raven et al. [19] who defined a successful treatment as a union of bone. No objective criteria or scoring system designed for the Masquelet technique exists to define this end point, which makes it difficult to compare the endpoints of this study to those of other publications. Existing radiographic healing scores, such as the RUSH Score for Hip Fractures [29], evaluate fracture healing in the absence of cancellous bone grafts and can therefore not be applied to patients treated with the Masquelet technique, as graft resorption is a problem occurring in these patients [30]. A histological scoring method for critical size bone defects by Han et al. exists but cannot be applied to this technique due to a lack of regular histological sampling during the healing process [31].

For the upper extremity, full load bearing was used as an endpoint in

this study. Outcome Scores for injuries of the upper extremity, for example, the DASH-score [32] and Oxford shoulder score [33] assess range of motion, level of pain and activities that can be executed with the affected arm without requiring load bearing. The Constant score evaluates load bearing at a 90° angle outstretched with a maximum of 25 pounds (11.34 kg). As the score mainly evaluates the shoulder where a certain weight has a physiologically limited force in relation to arm length, the location of an osseous defect may vary from the upper arm to the forearm. The load on the affected site can hence vary heavily, as the moment acting on the defect is a factor of force times distance  $M = F \cdot a$ , where 'M' is the moment in Newton meters, 'F' is the force in Newtons and 'a' is the distance in meters. Further, the load in the forearm is shared between the radius and ulna in a complex manner [34], which makes a defined load application less reliable as a tool for measuring the treatment outcome. Therefore, asking the patient whether full load bearing with the affected arm was possible and was therefore taken as an endpoint for treatment.

Time to union ranged between 3 and 94 months with no reported average in Hsu et al. [9], 14.4 months on average in the latest study by Masquelet et al. [7], 9.1 months for low-risk patients up to 15 months for high-risk patients. In this study the median time to full weight and load bearing was reported to be 20 months and thereby longer than that in other studies. This might be due to the set end point not being union of the defect but full weight and load bearing. This may be further explained by the fact that the Masquelet technique is partly used as a second-line treatment for osseous defects when segment transport has failed.

#### Harvesting of autografts

The main difference between our study and the three largest single-centre studies by Moghaddam et al. [26], ( $N = 50$ ), Raven et al. [19], ( $N = 150$ ) and Giannoudis et al. [27], ( $N = 43$ ) was that in the present study the RIA technique was not used to harvest autologous cancellous bone. According to a metanalysis by Careri et al. [8], the method of harvesting autologous bone grafts has no significant effect on the treatment outcome. Our study lends support to this observation, as the treatment outcomes of this study did not differ significantly from the results described in the literature.

#### Microbiological analysis–blind spots?

With *Staphylococcus aureus* and *Staphylococcus epidermidis* as the most common pathogens isolated, the present study agrees with other comparable studies [8,19,20]. In contrast to a study by Raven et al. [19], the present study did not distinguish infected from non-infected defects. Our approach was based on a study by Panteli et al. [35], who concluded in 2014 that despite 78% negative results in conventional screening for pathogens by culture, nearly 92% of tissue material showed positive DNA results for pathogens in bony defects. This is supported by Gille et al., who proved that 9% of non-unions are PCR positive for bacterial 16 s RNA [36], despite being negative on conventional culture. In this study, 35% of defects initially showed no growth on microbiological culture at the first debridement, with a suspected blind spot of possible septic non-unions and indicating a need for targeted, empiric antibiotic treatment.

As 88% of patients reached full weight bearing despite positive bacterial culture during the first spacer removal, no significant ( $p = 0.99$ ) was observed between the outcome of secondarily colonized spacers and the overall study population.

#### Difficult-to-treat organisms

The pathogen reduction rate was 60% on average, with a minimum of 0% for *Pseudomonas aeruginosa* and a maximum 100% for *S. lugdunensis*. Various pathogens (e.g., *Citrobacter koseri*, *Proteus*

*mirabilis, Clostridoides intestinalis*) were found for the first time during the revision procedure. *Pseudomonas aeruginosa* persisted over up to four revision procedures and can be identified as one of the most important ‘difficult-to-treat’ pathogens.

### Strengths and weaknesses

#### Weaknesses

Due to the retrospective study design functional scores were not systematically recorded. As the preoperative functional status was also missing, no information on functional development or the degree of recovery was available.

A patient-recorded outcome regarding the treatment and overall quality of life during treatment would have given the study a further perspective and should be considered for future studies.

The number of previous operations before treatment with the Masquelet technique could not be identified with certainty from medical files and should be recorded in future studies.

Regarding the treatment method, no control group was established, as the Masquelet technique is chosen as a last resort and only when segment transport could not be executed.

#### Strengths

The number of patients is the biggest strength of the study. With demographic and treatment-related data matching results already described in literature, the overall results gain further credibility and reliability. Besides bony healing, a functional outcome with full weight and load bearing is a further strength of this study and was described for the first time.

### Conclusion and outlook

The Masquelet technique remains a method with various factors influencing the treatment outcome displayed by the diamond concept, unknown parameters such as blind spots in microbiological analysis and unmodifiable factors like low patient compliance that make the technique difficult to study. Risk profiling of patients with the validated non-union-scoring-systems (NUSS Score) [37] and unvalidated risk profiling by Schmidmaier et al. [38], could be useful for prospective studies, yet did not find their way into clinical practice.

The radiologic healing process does not comply with objective criteria that could aid decision making on increasing weight and load bearing or whether to introduce a secondary stabilization of the defect with a plate or an intramedullary device. A scoring system to supplement expert opinions on radiologic bone healing would be helpful in to aid comparison between treatment results of different studies and in treatment adaptation. The end point of treatment for a defect should be defined as full weight and load bearing and not only as osseous consolidation.

Defects larger than 62 mm were defined as ‘critical size defects’ and special attention should be paid to them. Possible adaptations of the Masquelet technique, such as a three-step procedure firstly reducing the defect treated by two-step bone grafting with a secondary spacer, should be investigated.

### Declaration of Competing Interest

None of the authors declare any conflicts of interest.

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