European Journal of Orthopaedic Surgery & Traumatology
https://doi.org/10.1007/s00590-020-02862-5

ORIGINAL ARTICLE

Infected bone defects in the lower limb. Management by means of a two-stage distraction osteogenesis protocol

César Salcedo Cánovas[1,2] · Javier Martínez Ros[1,2] · Antonio Ondoño Navarro[3] · José Molina González[1,2] · Alicia Hernández Torres[2,4] · Encarnación Moral Escudero[2,4] · Manuel Medina Quirós[3]

Received: 24 November 2020 / Accepted: 25 December 2020

Abstract

Introduction Although bone transport is generally accepted as the gold standard for the treatment of segmental septic bone defects, some aspects of its practical application are still open to debate. We present our results in this field and compare them with the series published so far.

Material and methods We reviewed all our patients (2010–2018) that underwent a bone transport procedure in the lower limb due to a septic bone defect. We calculated the bone healing index (BHI), the external fixation index (EFI), the rate of complications and the clinical results. We statistically compared our results with 63 publications with a similar scope.

Results Thirty-five patients (30 M/5F) with a mean age of 40 years and a mean follow-up of 45 months were included. Bone segment was 24 T/11F and mean defect was 8.4 cm (7.34 T/ 10.73F). Mean global BHI was 45.62 days/cm (48.16 T/40.09F). Mean EFI was 2.37 months/cm. Results were excellent in 9 patients, good in 23 and bad in 3. Bone graft was used in 60% of the cases.

Discussion The size of our series is similar to previously published ones, although the mean age of our patients is higher and they present a larger bone defect. BHI of our series is similar to that of other series, although EFI is significantly higher. The number of complications is also in line with the existing literature.

Conclusion The use of a two-stage technique for managing segmental bone defects of septic origin in the lower extremity is a valid alternative. Our series shows results comparable to the current literature.

Keywords Bone transport · Lengthening · External fixation · Distraction osteogenesis · Infection

Introduction

The treatment of segmental bone defects of septic origin is a real therapeutic challenge that benefits from the existence of multidisciplinary reference units. By bringing together these difficult and infrequent cases, the professionals who integrate them gradually gain experience, which facilitates the journey through the demanding learning curve implied by these reconstruction procedures.

There are different options described in the literature [1, 2] for their management, which include the contribution of bone graft, microsurgical bone flaps or the Masquelet technique. Distraction osteogenesis is recognized as the gold standard for the treatment of segmental bone defects of septic origin. This technique makes it possible to regenerate a tubular bone tissue of optimal mechanical characteristics between the bone surfaces on which corticotomy has been performed and which have been subjected to gradual

César Salcedo Cánovas and Javier Martínez Ros have contributed equally.

✉ Javier Martínez Ros
javiermartinezros1985@gmail.com

[1] Unidad de Patología Séptica y Reconstructiva del Aparato Locomotor, Cirugía Ortopédica y Traumatología, Hospital Clínico Universitario Virgen de La Arrixaca, Murcia, Spain

[2] Grupo de Estudio de Enfermedades Infecciosas, Universidad de Murcia, Murcia, Spain

[3] Cirugía Ortopédica y Traumatología, Hospital Clínico Universitario Virgen de La Arrixaca, Murcia, Spain

[4] Medicina Infecciosas, Unidad de Patología Séptica y Reconstructiva del Aparato Locomotor, Hospital Clínico Universitario Virgen de La Arrixaca, Murcia, Spain

Published online: 08 February 2021

distraction, as well as the simultaneous adaptation of the surrounding soft tissues. [3–5]. Unlike other methods, these techniques can simultaneously address problems of limb asymmetry, deformities, joint contractures and even soft tissue defects.

From the first work of Codivilla [6] on bone lengthening in 1905, the technique has progressively evolved. Gavriil Ilizarov made a qualitative leap with the invention of his external fixator and the standardization of the osteogenesis process. His works laid the physiological and mechanical bases that govern the generation of new bone when faced with an adequate stress stimulus [7, 8].

The technique is well known, but it is not without risks [9, 10]. Some of the most common are intolerance or infection from fixator needles and screws, the appearance of stiffness caused by muscle transfixion, breaks in the synthetic material, axial deviations, neurological or vascular lesions, premature or late consolidation of the callus and the non-union of the docking point. The most frequent late complications are loss of length, the appearance of late deformities and re-fractures.

The quality of the regeneration depends on a huge number of factors [10, 11]. Among them, we can mention the intrinsic characteristics of the host and local factors of the affected limb, as well as the stability of the external fixation or technical aspects of the procedure, such as the type of osteotomy, its location, respect for soft tissues, the latency period, the rate and speed of distraction or the dynamization of the regenerate, as well as the mechanical load on said extremity.

They are long treatments, so in the recent literature, there are numerous studies that propose therapeutic strategies that can reduce them. The main key factor affecting therapeutic times is the consolidation of the docking point [12].

The objective of our study is to present and compare our results in the management of segmental bone defects of septic origin of the femur and tibia by distraction osteogenesis with the series published so far, as well as to present our docking point management protocol.

Material and method

A retrospective review of the database of our hospital was conducted to identify all patients who underwent a bone transport procedure in the lower limb between 1 January 2010 and 31 December 2018 because of a segmental bone defect of septic origin. All of them were operated by the staff of the Septic Unit (C.S.C, J.M.G. and J.M.R.).

The inclusion criteria were as follows:

- Patients treated by the adult hospital unit, older than 12 years.
- Segmental bone defects of septic origin in the femur or tibia greater than 3 cm that required treatment by distraction osteogenesis.
- Minimum follow-up of 12 months after the end of the treatment period.

Patients with follow-up of less than 12 months or incomplete follow-ups after surgery, those with bone defects due to tumours or congenital defects, and paediatric patients were excluded. Our hospital has an accredited national reference unit since 2010 for the treatment of resistant osteoarticular infection. The study has the approval of the corresponding ethics committee. In the cases that concern this study, those of segmental defects of septic origin, a two-stage treatment protocol is always performed. In the first surgical phase, the main objective is to eradicate the infection by extracting the osteosynthesis material, radical debridement of the devitalized bone tissue and the rest of the non-viable soft structures. Surgical ischaemia is not used in a protocolized manner and is only used in those cases that require a better visualization and dissection of noble structures at risk to then remove it and differentiate tissue viability. The devitalized bone tissue is resected until obtaining bone surfaces with haemorrhagic stippling and signs of vitality. Before the administration of intraoperative antibiotics, at least six samples were taken for culture and histological study. After the act of debridement, the surgery is completed by implanting an external fixation system of monolateral (LRS Advanced, Orthofix Srl, Verona, Italy), circular (TrueLok and TrueLokHex, Orthofix Srl, Verona, Italy) bone reconstruction. In some cases, due to the characteristics of the case, hybrid assemblies are performed with both systems. Whenever screws were used in the fixation, they had a hydroxyapatite coating (XCaliber screws, Orthofix Srl, Verona, Italy). After resection, the residual bone defect is evaluated, and a cement spacer enriched with antibiotic is placed for the management of the third space. During this first postoperative period, systemic antibiotic treatment is administered under the indication of the Infectious Diseases Unit, usually for a minimum of 6 weeks, although it was personalized in each case.

By protocol and for security, we wait 12 weeks before performing the second surgical stage. In that operation, after clinical and analytical resolution of the infection, the spacer is removed, and new debridement and sampling is performed. Next, an osteotomy is performed, which can be proximal to the bone defect (anterograde transport) or distal to it (retrograde transport). The osteotomy technique performed in all cases was the "De Bastiani" or "multi-drill" technique. After a small longitudinal skin incision, the periosteum is sectioned with a scalpel and raised bluntly with an osteotome. Multiple perforations are made in different planes from the point of entry until all cortical cells are weakened with a 4.8-mm drill bit to finally connect the

perforations with an osteotome and complete the osteotomy while maintaining the integrity of the periosteum.

Follow-up and distraction protocol

After the second surgical act, all patients were discharged from the hospital on the second or third postoperative day after explaining the correct care of the external fixator. Limb mobility was allowed from the first moment, as well as gradual partial load. The distraction phase in the osteotomy centre began between the seventh and tenth postoperative days. It was performed at a rate of 1 mm per day (0.25 mm every 6 h), with adjustments depending on the quality of bone regeneration. Once the bone segment completed the bone transport, it was continued at a rate of 0.5 mm/day to achieve complete compression contact for 7–10 days, except in those cases in which there was "navigation error", in which it was decided to perform surgery to achieve complete coaptation and seize the opportunity to provide a graft. However, this part of the protocol has been recently modified. Currently, we prefer to perform a graft contribution at the docking point unless we have a 100% coaptation in the metaphyseal region and with good quality of the local soft tissue. This variation of the protocol affected the last eight cases.

The patients were called to follow-up every two or three weeks, where they underwent clinical and radiological examinations to detect any common problem or complication, and the appropriate treatment was administered according to the needs of each case. The screw insertion points were assessed at each visit and treated when necessary. When the bone callus seemed mature radiologically, the dynamization phase was initiated using a DynaRing (Orthofix Srl, Verona, Italy) in the cases of monolateral fixator to favour bone consolidation. Once consolidation was achieved, the external fixator was removed, and physiotherapy was continued.

Definition of results

The bone healing index (BHI) was obtained by dividing the total treatment time (in days) by the total amount of elongation achieved (in centimetres). It gives us an expression of the number of days of treatment required for each elongated centimetre, from the beginning of the distraction until bone regeneration is achieved with three of the four mature cortical layers in two orthogonal radiographic projections.

The external fixation index (EFI) was obtained by dividing the total time with the fixator (in months) by the size of the bone transport (in centimetres). It gives us an expression of the number of days with the fixative required for each elongated centimetre.

The clinical results were assessed at follow-up using the criteria described by Cattaneo et al. [1]), who use three parameters for the evaluation: consolidation (no consolidation [U0] or solid consolidation [U1]), infection (without variations [I0], minimal persistent drainage [I1], complete clinical remission [I2]) and function (disability [F0], capable of performing all activities of daily life [F1], complete recovery [F2]).

The complications related to the fixation screws or needles were classified into four types, as described by Marsh et al. [13]: Type A, those that were resolved with local care or oral antibiotics, or after the planned removal of the fixative; Type B, those that required surgical intervention to establish new fixation elements; Type C, those that required removal of the external fixator before complete consolidation; Type D, which progressed to chronic osteomyelitis.

Statistical analysis

The data are summarized using arithmetic means and percentages. The dispersion is evaluated through the 95% confidence interval, and the comparisons between our series and the mean values found in the literature were carried out through parametric tests (Student's t test for unpaired data in the case of the quantitative variables and Pearson's chi-square for the qualitative variables). The level of significance was established for p values below 0.05. All calculations were performed using Stata v.14.0 software (StataCorp, Lakeway Dr College Station, USA).

Comparison with other studies

To analyse whether our results are in line with those of other similar publications, we have taken 62 studies collected in the two most recent meta-analyses published on the use of osteogenesis by distraction in septic bone defects [14, 15]. Additionally, we have included in the comparison a series recently published by another reference unit in our country that follows a treatment methodology very similar to ours [16]. We compared both the characteristics of the study and the demographic parameters of the patients and the results obtained.

Results

The summarized results are included in Table 1 and those detailed in Table 2. A total of 35 patients were included in the study, of which 30 were male (85.71%) and 5 were female (14.29%). The mean age of the series was 40.06 years (95% CI: 38.95–49.48). The affected segment was the tibia in 24 cases (68.57%) and the femur in 11 (31.43%). The mean follow-up was 45.31 months (95% CI: 36.27–54.35).

For the physiological classification of the host, we used the Cierny–Mader classification [17] and included 3 cases of type A, 18 of B (L), 11 of B (Ls) and 3 of C.

Table 1 Descriptive information

Number of patients	35
Male/female ratio	30/5
Age (years)	40.06 (95% CI 38.95–49.48)
Bone segment	
Tibia	24 (68.57%)
Femur	11 (31.43%)
Follow-up (months)	45,31 (95% CI 36.27–54.35)
Cierny–Mader classification	A:3; B(L):18; B(L-s):11; C:3
Previous surgeries	4.14 (95% CI 3.36–4.91)
Origin of the patient	
HCUVA	13 (37.14%)
Another hospital	22 (62.85%)
Defect size (cm)	8.40 (95% CI 7.02–9.78)
Tibia	7.34 (95% CI 6.15–8.51)
Femur	10.73 (95% CI 7.16–14.29)

The average number of previous interventions of the patients in the series was 4.14 (95% CI 3.36–4.91), with 62.8% ($n=22$) coming from another hospital and the remaining 37.2% ($n=11$) cases from our centre.

The mean bone defect size was 8.40 cm (95% CI 7.02–9.78). By segment, in the case of the tibia, the mean defect was 7.34 cm (95% CI 6.15–8.51), and in the femur, it was 10.73 cm (95% CI 7.16–14.29).

Regarding microbiology, the most common findings were Staphylococcus aureus in 37.14% of cases, Coagulase-negative staphylococci in 17.14% and isolated cases of other pathogens (14.29%) in the remaining cases.

Bone consolidation and limb restitution were achieved in 97.14% (34 patients), but only in one case (2.86%) were not achieved.

The mean global BHI was 45.62 days/cm (95% CI 42.19–49.06). By segment, the BHI in the tibia was 48.16 days/cm (95% CI 44.13–52.19) and 40.09 days/cm (95% CI 34.04–46.14) for the femur. Regarding the EF time, the patients in the series carried the fixative for a mean of 16.69 months (95% CI 15.26–18.11). The mean EFI was 2.37 months/cm (95% CI 2.13–2.61).

Regarding the function, and following the Cattaneo scale (Table 3), the distribution was 9 (25.71%) with excellent results, 23 (65.71%) with good results and 3 (8.57%) with bad results.

Results complications

Following the classification proposed by Marsh for the evaluation of complications, the most common was infection of the screw tract resolved with local cures and oral antibiotics (type A). This event occurred in 60% of patients. Complications of type B, requiring modification or removal of screws, occurred in 11% of patients.

The non-union of the docking point "per primam" was presented in 21 (60%) patients who required debridement and graft delivery. However, we must take into account that in the last 8 patients of the series, the docking point was systematically protocolized. But if we just consider the 27 patients that were treated following our old protocol, only 13 (48.15%) of them developed problems in the docking site.

No patients had to be re-operated for any other reason.

Results comparative with other studies

The mean values reported by the 62 selected studies, as well as those of our series, are reflected in Table 4. The results of the comparison are found in Table 5. The value of our series versus the kernel distribution of the set of studies considered is shown in Fig. 1.

The average number of cases in the articles was 24.19 (95% CI 20.96–27.42). Our series presents a significantly higher number of cases, with 35 patients ($p<0.001$).

Regarding the distribution of genders, the average of the articles presents a ratio between men and women of 74.75% (95% CI 68.40–80.74), which differs significantly from our ratio of 0.86% ($p<0.001$). There were also significant differences ($p<0.001$) between our mean age (40.06 years) and the mean of publications (36.07 years; 95% CI 34.76–37.38).

The mean follow-up of our series (45.31 months) was significantly higher ($p=0.044$) than the mean of the studies considered (38.67 months; 95% CI 32.21–45.14).

The number of previous interventions in the series presented here is 4.14. This differs significantly ($p=0.040$) from the mean of the set of studies, which amounts to 3.56 (95% CI 3.00–4.11).

There were also differences between the mean size of the bone defect ($p<0.001$), which was 8.4 cm in our series and 7.00 cm in the set of studies (95% CI 6.49–7.52).

Regarding the results obtained, our external fixation index (2.37 months/cm) was somewhat above the average of the studies considered (1.83 months/cm; 95% CI 1.45–2.20). The external fixation time, therefore, was also significantly longer (16.69 months compared to 11.21 months; 95% CI 9.20–13.21) ($p<0.001$). The percentage of cases in which the graft was used at the docking point was different ($p<0.001$) between our series (60%) and that of the set of studies (37.40%; 95% CI 27.75–47.05). There were also differences in the infection rate of the screws ($p=0.010$), with 0.285 infected screws per patient in our series and 0.74 (95% CI 0.41–1.08) in the set of studies.

Table 2 Detailed results

Id	Cierny–Mader classification	Bone segment	Previous interventions	Defect size (cm)	External fixator type	Bone graft	Follow-up (months)	BHI (days/cm)	IFE (months/cm)	External fixation time (months)	Cattaneo classification
1	C	Femur	8	4	Monolateral	Yes	90	44	2.5	10	U1 I2 F1
2	B (l-s)	Tibia	8	4	Monolateral	Yes	85	42	2.5	10	U1 I2 F1
3	B (l-s)	Tibia	6	10	Monolateral	Yes	86	47	2.2	20	U1 I2 F1
4	B (l-s)	Femur	4	12	Hybrid	No	83	36	3	15	U1 I2 F2
5	B (l)	Femur	3	8	Monolateral	Yes	85	47	2.5	20	U1 I2 F1
6	B (l-s)	Tibia	7	5	Monolateral	Yes	80	42	2.6	13	U1 I1 F1
7	B (l-s)	Tibia	7	4	Hybrid	Yes	72	45	3.75	15	U1 I2 F1
8	B (l-s)	Femur	10	8	Hibrido	No	70	42	1.9	15	U1 I1 F1
9	B (l)	Femur	7	18	Circular	Yes	60	32	2.6	26	U1 I2 F1
10	B (l)	Femur	6	6	Circular	Yes	59	45	3.5	14	U1 I2 F0
11	B (l-s)	Tibia	6	5	Circular	Yes	72	44.8	3.5	14	U1 I2 F0
12	B (l-s)	Tibia	4	11	Circular	Yes	44	38.1	1.5	17	U1 I2 F1
13	B (l)	Femur	3	20	Hybrid	No	55	30	1.1	22	U1 I2 F2
14	B (l-s)	Tibia	4	9	Circular	No	39	50	2.2	20	U1 I2 F1
15	B (l)	Tibia	3	12	Circular	No	30	50	2	24	U1 I2 F1
16	B (l)	Tibia	2	5	Circular	Yes	74	47	2.2	11	U0 I1 F0
17	C	Tibia	2	4	Monolateral	No	67	55	2.5	10	U1 I2 F2
18	B (l)	Tibia	3	12	Monolateral	No	52	28	1.16	14	U1 I2 F2
19	A	Tibia	2	11	Monolateral	No	37	35	1.54	17	U1 I2 F2
20	B (l)	Tibia	4	12	Circular	Yes	15	40	1.66	20	U1 I2 F2
21	B (l)	Tibia	5	6	Circular	Yes	36	50	2.66	16	U1 I2 F2
22	B (l)	Tibia	5	6	Circular	Yes	16	45	3	18	U1 I2 F1
23	B (l)	Tibia	4	6	Circular	Yes	18	45	3.5	21	U1 I2 F1
24	B (l)	Tibia	6	4	Circular	No	17	68	3.5	14	U1 I2 F1
25	B (l)	Femur	3	5	Circular	No	24	60	2.8	14	U1 I2 F1
26	B (l-s)	Femur	2	13	Monolateral	Yes	15	41	1.76	23	U1 I2 F1
27	B (l)	Tibia	2	7	Circular	Yes	25	62	2.7	19	U1 I2 F1
28	B (l)	Tibia	2	8	Circular	Yes	25	60	2.4	19	U1 I2 F1
29	B (l)	Femur	5	9	Monolateral	Yes	38	34	1.33	12	U1 I2 F2
30	A	Tibia	2	9	Circular	No	14	45	2	18	U1 I2 F2
31	A	Tibia	4	8	Circular	Yes	15	65	2.6	21	U1 I2F1
32	B (l)	Tibia	2	5	Circular	No	14	60	2.6	13	U1 I2 F1
33	B (l)	Tibia	1	7	Circular	Yes	18	46	2.1	15	U1 I2 F1
34	B (l-s)	Femur	1	15	Hybrid	No	30	30	1.33	20	U1 I2 F1

Table 2 (continued)

Id	Cierny–Mader classification	Bone segment	Previous interventions	Defect size (cm)	External fixator type	Bone graft	Follow-up (months)	BHI (days/cm)	IFE (months/cm)	External fixation time (months)	Cattaneo classification
35	C	Tibia	2	6	Circular	No	26	46	2.33	14	U1 I2 F1

From Cattaneo et al. [1]

Union: U0 non-union; U1 solid union

Infection: I0 no changes; I1 persistent minimal drainage; I2 complete clinical remission

Function: F0 invalid; F1 daily life activities; F2 complete healing

Table 3 Cattaneo classification

Type	*N*	%
Excellent (U1-I2-F2)	23	65.71
Good (U1-I2-F1 and U1-I1-F2)	9	25.71
Fair (U1-I1-F1)	0	0.00
Bad (U0-I0-F0)	3	8.57

Discussion

Distraction osteogenesis offers an effective and reproducible treatment for one of the most difficult problems in trauma: the resolution of bone defects of septic origin. It was initially developed by Gavril Ilizarov in Kurgan (Russia) in the 1950s but became popular in the West in the 1980s after he treated the Olympic medallist Valery Brummell for pseudoarthrosis of infected tibia.

The publications regarding the reconstruction of bone defects of septic origin do not present a very large series of patients. As shown in the review by Aktuglu et al. [15] and the meta-analysis of Papakostidis et al. [14], the mean number of patients was 24 patients per study, with a larger series such as that of Yin et al. [18] with 66 cases, or shorter, such as that of Ferreira and Marais [19] with only 7 patients. Our series includes 35 patients, which is within the range described. The average age of the patients collected in the studies selected for comparison is 36.1 years, with ours being the higher, 48.3, due in large part to the fact that in our study we included segmental defects secondary to complications of replacement arthroplasties that needed bone transport to be performed to cover the bone defect and achieve arthrodesis, which increases the average age.

In our series, we observed an average of 4.14 previous surgeries, which is slightly higher than that reported in the literature [14, 15, 20]. Therefore, we believe that we should reinforce the information to the different health centres and regional and national institutions as a national reference centre in reconstructive septic pathology so that they refer patients with less delay, since this can condition the patient's prognosis and outcome.

The average bone defect to be treated that we found in the literature is 7.00 cm [14, 15, 20]. We observed a mean of 8.4 cm (7.02–9.78), which is substantially higher and can affect clinical and functional results.

The quality of the regenerated bone can be objectified in terms of the external fixation index. In our series, we observed a bone healing index of 45.62 days/cm (95% CI 42.19–49.06), similar to other series, such as that of Makhdoom [21] (1.60 ± 0.34 months/cm [1.0–2.5], Lavini [22] (45.6 days/cm [74.8–26.6]), De Bastiani [23] (38 days/cm) and Harshwai [24] (1.42 months/cm).

Table 4 Studies used for comparison

Study	N	M/F ratio	Age (yr)	Tibia/Femur	Follow-up (months)	Previous interventions	Bone defect (cm)	IFE (months/cm)	External fixation time (months)	Bone graft	Pin infection
Martínez Ros	35	30/5	40.06	24/11	45.31	4.14	8.4	2.37	16.69	21	10
Abdel-Aal	15	12/3	30.4	15/-	–	–	10.6	–	–	2	–
Aboumira et al.	25	19/6	44.5	–	53	–	6.5	2.1	11.8	9	23
Aktuglu et al.	24	21/3	35.04	–	74.08	3.64	7.01	1.73	11.52	0	14
Atesalp et al.	43	43/0	24.7	43/-	50	–	9.7	–	–	0	–
Azzam et al.	30	30/0	32	–	18	–	7.4	1.3	7.5	30	2
Babar et al.	17	15/2	32.7	–	–	–	5.8	–	6	4	8
Barbarossa et al.	30	24/6	39.4	-/30	–	4.4	–	–	–	0	–
Bernstein et al.	30	24/6	43	–	31	–	5.9	2.5	11.03	–	–
Blum et al.	50	41/9	29.9	-/50	70.8	3.8	8.8	–	–	15	–
Bobroff et al.	12	–	32	12/-	15.3	3.2	9.5	–	–	9	–
Bumbasirevic et al.	30	29/1	30.4	30/-	99	1.3	6.9	1.48	9.7	1	14
Cattaneo et al.	28	22/6	34	28/-	27.4	3	–	–	–	0	–
Chaddha et al.	25	25/0	28.2	22/3	23.5	2.6	8.9	–	–	9	–
Cierny and Zorn	21	–		21/-	24 +	–	6.5	–	–	14	–
Corona Sánchez	54	44/10	49.06	32/22	28	3.21	8.58	3.54	24.5	–	–
Dendrinos et al.	28	23/5	37	28/-	39	4	6	–	–	3	–
Feng et al.	21	15/6	34.6	–	31	6	6.6	1.48	9.8	–	3
Fürmetz et al.	8	7/1	39	–	46	–	9	1.47	9.52	7	17
Green et al.	17	15/2	32.8	16/1	12 +	–	–	–	–	6	–
Hutson et al.	19	13/5	32	19/-	58	–	9.4	–	–	–	–
Khan et al.	24	21/3	38	–	11	2	3.2	4.2	8	0	5
Krappinger et al.	15	11/4	32	–	17.3	10.1	6.6	–	13.2	15	9
Krishnan et al.	20	17/3	38.4	-/20	63	4.4	6	–	–	1	–
Laursen et al.	16	11/5	36	16/-	42	5.6	3.6	–	–	1	–
Lin et al.	16	–	36	–	–	–	8	–	4.5	16	–
Lowenberg et al.	32	–	37	32/-	15	–	7.3	–	–	–	–
Madhusudhan et al.	22	18/4	37.2	22/-	13	3	4	–	–	0	22
Magadum et al.	27	27/0	39	27/-	27	2	10	–	–	–	–
Mahaluxmivala et al.	18	16/2	39.6	18/-	18 +	1.8	3.5	–	–	6	–
Maini et al.	30	27/3	34.7	24/6	28.9	2.2	7.4	–	–	3	–
Marais et al.	7	–	29	–	28	–	7	2.7	17.7	7	12
McKee et al.	11	8/3	43.7	11/-	41	4.5	–	–	–	3	–
Megas et al.	9	7/2	39.7	–	26.6	4.8	5	1.07	7.83	0	8
Mekhail et al.	19	14/5	36.4	16/3	68.7	2.5	7.2	–	–	18	–

Table 4 (continued)

Study	N	M/F ratio	Age (yr)	Tibia/Femur	Follow-up (months)	Previous interventions	Bone defect (cm)	IFE (months/cm)	External fixation time (months)	Bone graft	Pin infection
Morasiewicz et al.	16	11/5	35	-/16	60+	–	6.9	–	–	5	–
Morsy	12	10/2	36.5	–	9.2	–	4.6	1.52	6.8	4	40
Naggar et al.	11	10/0	36.5	9/1	–	2.6	6.7	–	–	2	–
Oostenbroek et al.	54	33/19	27	–	–	–	8.5	–	–	–	–
Paley and Maar	19	14/5	38	19/-	78	5	3.9	–	–	7	-
Paley et al.	25	19/6	34	25/0	–	3	7.3	–	–	0	–
Patil and Montgomery	41	35/5	41	36/5	61.1	3	–	–	–	34	–
Peng et al.	58	38/20	29	–	31	6.3	9.2	1.2	10.6	58	5
Pirwani et al.	16	16/0	32	–	16	–	4.5	3	16	2	16
Polyzois et al.	42	29/13	37.5	25/17	38	–	6	–	–	4	–
Ring et al.	10	6/4	34	10/-	72	2	4.3	–	–	3	–
Rohilla et al.	35	30/5	36.1	–	25.4	1.22	7.27	1.8	11.9	15	–
Rozbruch et al.	25	17/8	34	25/-	36	–	6	–	–	12	–
Rozbruch et al.	38	30/8	43	38/-	37	4	6.5	–	–	25	–
Sala et al.	12	8/4	44	12/-	24	3	8	–	–	10	–
Sanders et al.	19	12/7	45	19/-	39	3.6	8	–	–	5	–
Saridis et al.	13	10/3	34.6	-/13	42.4	3	8.3	–	–	2	–
Selim	10	10/0	30	–	28.8	–	9	0.28	2.5	2	1
Sen et al.	24	18/6	30.6	24/-	30	–	5	–	–	0	–
Shadid et al.	12	10/2	43.4	–	14.25	1.08	–	–	–	–	2
Smrke and Arnež	14	13/1	26.4	13/1	120	3.4	11.1	–	–	10	–
Song et al.	27	24/3	42	27/-	30	6	8.3	–	–	25	–
Spiegl et al.	25	22/3	46	–	29.4	1	5.3	1.9	23.2	25	9
Tetsworth et al.	21	18/3	38.2	–	25.5	4.5	7	1.8	12.5	–	25
Wani et al.	26	22/4	39	–	–	2.5	5.1	1.6	14.07	3	18
Xu et al.	30	21/9	34.1	–	29	6	6.4	1.36	10	–	3
Yilihamu et al.	14	11/3	35.9	–	96	–	–	1.51	9.8	4	8
Yin et al.	66	62/4	37.06	–	25.91	2.4	6.27	1.38	9.4	6	–
Zhang et al.	16	9/7	39.1	–	29.5	4.25	10.9	1.1	12	3	5

Table 5 Compared results

	HCUVA	Pool of studies ($n=62$)	p value
Number of patients	35	24,19 (95% CI 20.96–27.42)	<0.001
Male/female ratio	30/5 (0.86)	0.75 (95% CI 68.40–80.74)	<0.001
Age (years)	40.06 (95% CI 38.95–49.48)	36.07 (95% CI 34.76–37.38)	<0.001
Follow-up (months)	45,31 (95% CI 36.27–54.35)	38.67 (95% CI 32.21–45.14)	0.044
Previous surgeries	4.14 (95% CI 3.36–4.91)	3.56 (95% CI 3.00–4.11)	0.040
External fixation index (months/cm)	2.37	1,83 (95% CI 1.45–2.20)	<0.001
External fixation time (months)	16.69	11.21 (95% CI 9.20–13.21)	<0.001
Bone graft in docking site (%)	60	37.40 (95% CI 27.75–47.05)	<0.001
Defect size (cm)	8.40 (95% CI 7.02–9.78)	7.00 (95% CI 6.49–7.52)	<0.001
Screw infection (infection/patient)	0.285	0.74 (95% CI 0.41–1.08)	0.010

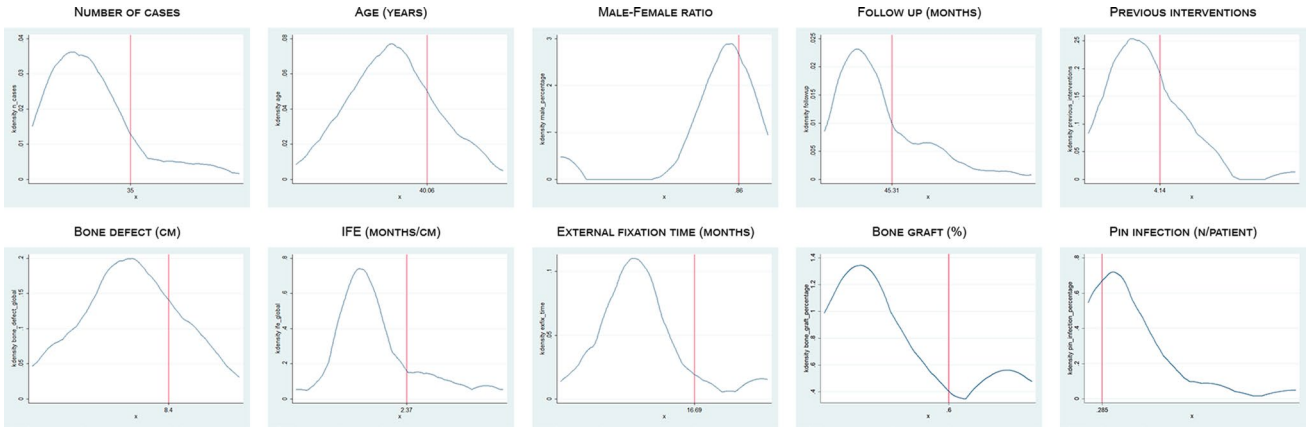

Fig. 1 Kernel charts for the different values of the set of studies considered for comparison and the value of our study. **a** Number of cases; **b** age (years); **c** male/female ratio; **d** follow-up (months); **e** previous interventions; **f** bone defect (cm); **g** EFI (months/cm); **h** external fixation time (months); **i** bone graft (%); **j** pin infection (number for patients)

Regarding therapeutic times, we observe certain differences with what is established in the literature. We observed a longer external fixation time and external fixation index with respect to those collected in the articles considered. We justify this increase in that in our treatment protocol, we systematically use two-stage management. An initial surgery in which the objective is to eradicate all non-viable tissue and provide satisfactory coverage of parts and skin by managing the third space with cement spacer enriched with antibiotic. In the second surgical stage, after being sure that we have managed to eradicate the infection, the objective is to restore bone integrity through distraction osteogenesis. Other authors do not do so systematically [25, 26]. For us, it is easier and more reproducible within the ortho-plastic management strategy in these severe bone and soft tissue injuries.

The main key factor affecting therapeutic times is the consolidation of the docking point, which is why it is currently recognized as one of the points on which to act to optimize the treatment time. The consolidation of the docking point is affected by many factors, such as the severity of the injury, the initial infection, the length of the bone defect or the interposition of soft tissues. In our series, we achieved the final consolidation of the docking point in 97.14% of the cases ($n=34$), but 60% of the patients required additional debridement and graft surgery ($n=21$).

The rate of non-union at the docking point varies from 0 to 83% according to different studies [27, 28]. The contribution of graft is collected in the literature as something "dogmatic" that goes from never to always [15, 29]. The group of Giotakis et al. [28] published in 2007 its protocol of action on the docking point based on the area of coaptation of bone surfaces. If there is a good coaptation of surfaces, they recommend performing closed techniques, either simple compression or the accordion technique in those cases in which no signs of consolidation are observed after 3 months. On the other hand, for those cases that fail with the above or that initially present poor bone coaptation, open debridement of surfaces and spinal recanalization followed by compression are recommended, providing graft only in those cases

in which the coaptation of surfaces is deficient. The group of Tetsworth et al. [30], published in 2017, given the poorly reproducible results of closed techniques, have incorporated into their protocol of bone transport treatment the systematic grafting of the docking site to make the consolidation more reproducible and fast. This strategy is controversial, finding support [31] and voices against it [27] in the literature. We have updated our action protocol and hope to present clarifying results in a while. We base it on the percentage of coaptation of bone surfaces, the state of local soft tissues, the characteristics of the host according to Cierny's classification [17] and the remaining months of maturation of bone regeneration (Fig. 2). Currently, we only give an opportunity for consolidation by simple compression or accordion technique if we have a bone coaptation close to 100%, with a good state of local soft tissues, on a type A individual and who have more than 5 months of maturation of the regenerated bone. (For example, in bone transports above 5 or 6 cm in which, taking as a reference a bone consolidation index of 45 days per cm, there are more than 5 months of treatment remaining and, therefore, waiting 3 months of consolidation of the docking point does not imply additional delay time in the removal of the fixative.) Our protocol is summarized in Fig. 3.

Another strategy on the docking point to reduce therapeutic times is acute shortening followed by lengthening. In this way, it is theoretically possible to convert the docking point into a focus of fracture in biological, biomechanical and consolidation terms (with the obvious limitations of not shortening more than 3–5 cm, so as not to compromise

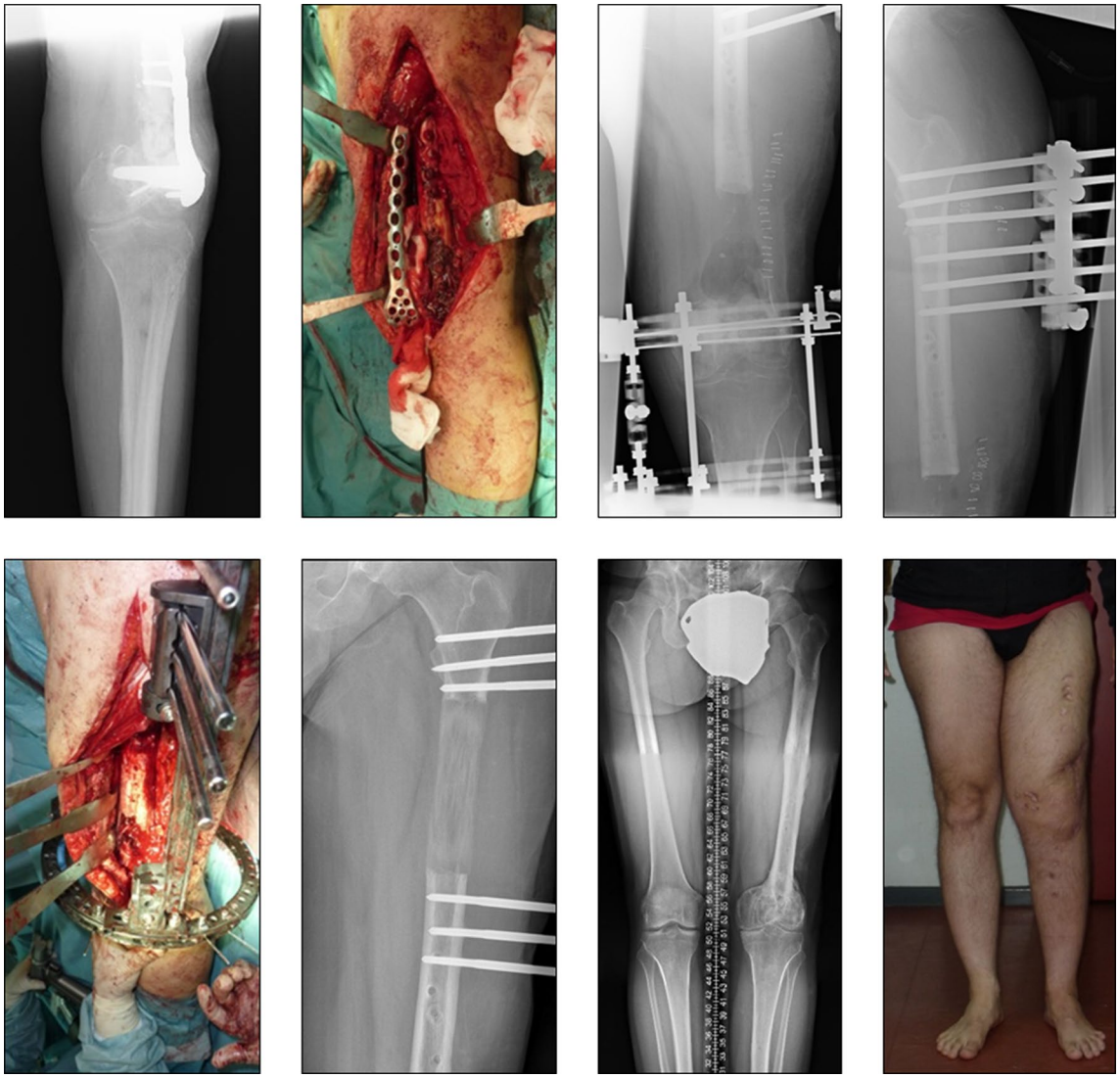

Fig. 2 Bone transport in a case of osteosynthesis infection in the distal femur. After resection, a spacer with antibiotics was used to treat the infection. The limb was stabilized by a hybrid fixator assembly. Finally, bone transport was performed in the proximal region of the femur

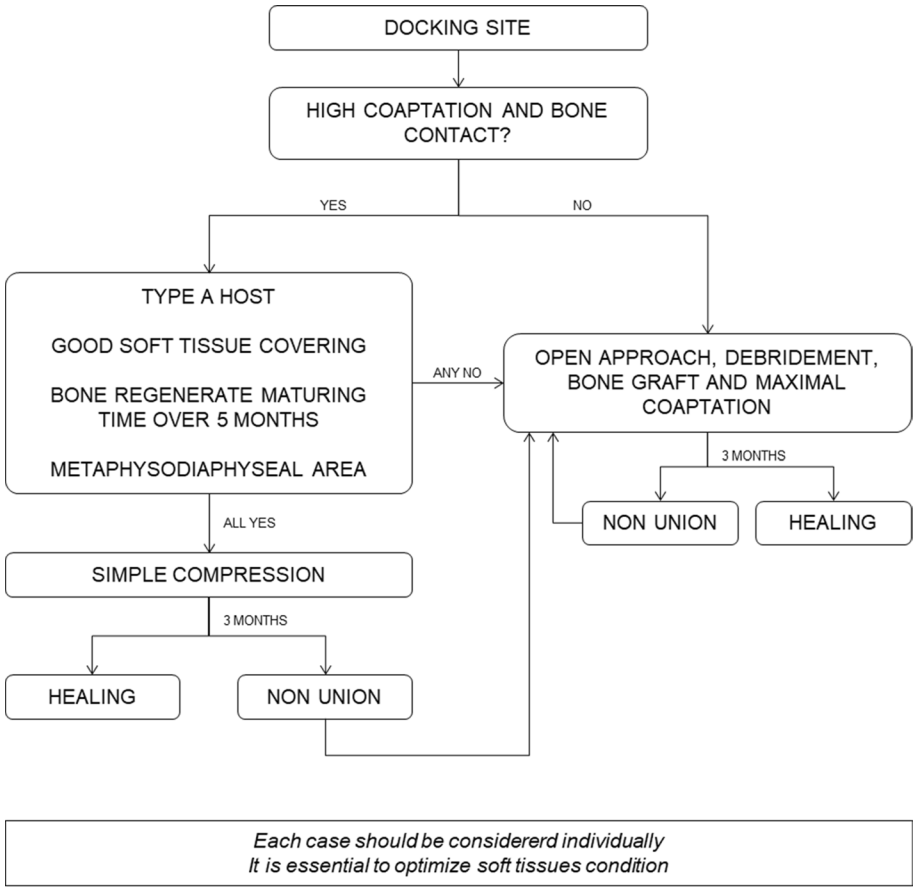

Fig. 3 Protocol of action on the docking point of our hospital

vascularization). The Tetsworth group [30] observed that in their acute shortening group, they presented 38% non-union. They justify this by explaining that, although this strategy attempts to imitate the healing pattern of a fracture, the bone and soft tissue injury far exceeds the damage threshold of a fracture. Therefore, they propose that, to optimize the results, grafting can also be provided, especially in cases that affect diaphyseal–diaphyseal junction points. In the same way, Wen et al. [12] conclude in their 2020 meta-analysis that acute compression strategies, followed by lengthening, improve bone transport times but, in turn, require graft delivery more frequently.

Our study has the inherent limitations of all prospective studies, such as the need to rely on clinical notes. Although both the number of cases and the extent of follow-up are limited, they are perfectly comparable to other published studies, presumably due to the unusual nature of bone reconstructive techniques. Therefore, our results, although comparable to others published in the literature, should be viewed with reserve, pending further studies.

Conclusions

The use of a two-stage technique that includes the management of the infection, followed by bone transport by distraction osteogenesis, is a valid alternative for the resolution of segmental bone defects of septic origin in the lower extremity. Our series presents results comparable to the current literature.

Acknowledgments The authors wish to thank the collaboration of Julio del Corral for his statistical help and that of Pablo Roza and María Rabanal in the preparation of the manuscript.

Compliance with ethical standards

Conflict of interest The author(s) declare that they have no competing interests.

Ethical approval Our study has been approved by the appropriate ethics committee and has therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Specific Spanish laws have also been observed.

References

1. Cattaneo R, Catagni M, Johnson EE. The treatment of infected nonunions and segmental defects of the tibia by the methods of Ilizarov. *Clin Orthop Relat Res*. 1992;(280):143–152. http://www.ncbi.nlm.nih.gov/pubmed/1611734.
2. Ashman O, Phillips AM (2013) Treatment of non-unions with bone defects: Which option and why? Injury. https://doi.org/10.1016/S0020-1383(13)70010-X
3. Goldstein RY, Jordan CJ, McLaurin TM, Grant A. The evolution of the Ilizarov technique: part 2: the principles of distraction osteosynthesis. *Bull Hosp Jt Dis*. 2013;71(1):96–103. http://www.ncbi.nlm.nih.gov/pubmed/24032589.
4. Gubin AV, Borzunov DY, Marchenkova LO, Malkova TA, Smirnova IL (2016) Contribution of G.A. Ilizarov to bone reconstruction: historical achievements and state of the art. Strateg Trauma Limb Reconstr. 11(3):145–152. https://doi.org/10.1007/s11751-016-0261-7
5. Polyzois VD, Stathopoulos IP, Lampropoulou-Adamidou K, Vasiliadis ES, Vlamis J, Pneumaticos SG (2014) Strategies for managing bone defects of the lower extremity. Clin Podiatr Med Surg. https://doi.org/10.1016/j.cpm.2014.06.008
6. Codivilla A (2008) The Classic: On the Means of Lengthening, in the Lower Limbs, the Muscles and Tissues Which are Shortened Through Deformity. Clin Orthop Relat Res 466(12):2903–2909. https://doi.org/10.1007/s11999-008-0518-7
7. Ilizarov GA. The tension-stress effect on the genesis and growth of tissues: part II. The influence of the rate and frequency of distraction. *Clin Orthop Relat Res*. 1989;(239):263–285. http://www.ncbi.nlm.nih.gov/pubmed/2912628.
8. Ilizarov GA. The tension-stress effect on the genesis and growth of tissues. Part I. The influence of stability of fixation and soft-tissue preservation. *Clin Orthop Relat Res*. 1989;(238):249–281. http://www.ncbi.nlm.nih.gov/pubmed/2910611.
9. Cánovas CS (2015) Bone elongation using monolateral external fixation: a practical guide. Strateg Trauma Limb Reconstr 10(3):175–188. https://doi.org/10.1007/s11751-015-0236-0
10. Catagni MA, Guerreschi F, Lovisetti L (2011) Distraction osteogenesis for bone repair in the 21st century: Lessons learned. Injury. https://doi.org/10.1016/j.injury.2011.04.004
11. Fischgrund J, Paley D, Suter C. Variables affecting time to bone healing during limb lengthening. *Clin Orthop Relat Res*. 1994;(301):31–37. http://www.ncbi.nlm.nih.gov/pubmed/8156692.
12. Wen H, Zhu S, Li C, Xu Y (2020) Bone transport versus acute shortening for the management of infected tibial bone defects: a meta-analysis. BMC Musculoskelet Disord 21(1):80. https://doi.org/10.1186/s12891-020-3114-y
13. Marsh JL, Nepola J V, Meffert R. Dynamic external fixation for stabilization of nonunions. *Clin Orthop Relat Res*. 1992;(278):200–206. http://www.ncbi.nlm.nih.gov/pubmed/1563155.
14. Papakostidis C, Bhandari M, Giannoudis PV (2013) Distraction osteogenesis in the treatment of long bone defects of the lower limbs: Effectiveness, complications and clinical results; a systematic review and meta-analysis. Bone Jt J. https://doi.org/10.1302/0301-620X.95B12.32385
15. Aktuglu K, Erol K, Vahabi A (2019) Ilizarov bone transport and treatment of critical-sized tibial bone defects: a narrative review. J Orthop Traumatol 20(1):22. https://doi.org/10.1186/s10195-019-0527-1
16. Corona PS, Ramirez-Nuñez LJ, Amat C, Carrera L (2017) Outcome of oscillating saw open osteotomy in two-stage lower extremity bone transport with monolateral frame. Injury 48(10):2285–2291. https://doi.org/10.1016/j.injury.2017.07.024
17. Cierny G, Mader JT, Penninck JJ (2003) The classic: a clinical staging system for adult osteomyelitis. Clin Orthop Relat Res 414:7–24. https://doi.org/10.1097/01.blo.0000088564.81746.62
18. Yin P, Zhang Q, Mao Z et al (2014) The treatment of infected tibial nonunion by bone transport using the Ilizarov external fixator and a systematic review of infected tibial nonunion treated by Ilizarov methods. Acta Orthop Belg. 80(3):426–435
19. Ferreira N, Marais LC (2015) Bone transport through an induced membrane in the management of tibial bone defects resulting from chronic osteomyelitis. Strateg Trauma Limb Reconstr 10(1):27–33. https://doi.org/10.1007/s11751-015-0221-7
20. Yin P, Ji Q, Li T et al (2015) A systematic review and meta-analysis of Ilizarov methods in the treatment of infected nonunion of tibia and femur. PLoS ONE. https://doi.org/10.1371/journal.pone.0141973
21. Makhdoom A, Kumar J, Siddiqui AA (2019) Ilizarov external fixation: percutaneous gigli saw versus multiple drill-hole osteotomy techniques for distraction osteogenesis. Cureus 11(6):e4973. https://doi.org/10.7759/cureus.4973
22. Lavini F, Dall'Oca C, Bartolozzi P (2010) Bone transport and compression-distraction in the treatment of bone loss of the lower limbs. Injury 41(11):1191–1195. https://doi.org/10.1016/j.injury.2010.09.030
23. Bastiani BD, Aldegheri R, Renzi-Brivio L, Trivella G (1987) Limb lengthening by callus distraction (Callotasis). J Pediatr Orthop 7(2):129–134. https://doi.org/10.1097/01241398-198703000-00002
24. Harshwal RK, Sankhala SS, Jalan D (2014) Management of nonunion of lower-extremity long bones using mono-lateral external fixator – Report of 37 cases. Injury 45(3):560–567. https://doi.org/10.1016/j.injury.2013.11.019
25. Yin P, Zhang L, Li T et al (2015) Infected nonunion of tibia and femur treated by bone transport. J Orthop Surg Res 10(1):49. https://doi.org/10.1186/s13018-015-0189-5
26. Zhang Y, Wang Y, Di J, Peng A (2018) Double-level bone transport for large post-traumatic tibial bone defects: a single centre experience of sixteen cases. Int Orthop 42(5):1157–1164. https://doi.org/10.1007/s00264-017-3684-y
27. Lovisetti G, Sala F, Miller AN, Thabet AM, Zottola V, Capitani D (2012) Clinical reliability of closed techniques and comparison with open strategies to achieve union at the docking site. Int Orthop. https://doi.org/10.1007/s00264-011-1260-4
28. Giotakis N, Narayan B, Nayagam S (2007) Distraction osteogenesis and nonunion of the docking site: Is there an ideal treatment option? Injury 38(1):S100–S107. https://doi.org/10.1016/j.injury.2007.02.015
29. Paley D, Maar DC (2000) Ilizarov bone transport treatment for tibial defects. J Orthop Trauma. https://doi.org/10.1097/00005131-200002000-00002
30. Tetsworth K, Paley D, Sen C et al (2017) Bone transport versus acute shortening for the management of infected tibial nonunions with bone defects. Injury 48(10):2276–2284. https://doi.org/10.1016/j.injury.2017.07.018
31. Hatzokos I, Stavridis SI, Iosifidou E, Karataglis D, Christodoulou A (2011) Autologous bone marrow grafting combined with demineralized bone matrix improves consolidation of docking site after distraction osteogenesis. J Bone Jt Surg - Ser A. https://doi.org/10.2106/JBJS.J.00514