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First mid-term results after cancellous allograft vitalized with autologous bone marrow for infected femoral non-union

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Summary

Background Surgical treatment of infected femoral non-union is challenging. Only few reports exist including autologous bone grafting (ABG) from the iliac crest promoting union. Vitalized allogeneic bone grafting (VABG) is an alternative promoting osseous healing and reconstructing bone defects. VABG contains allogeneic cancellous bone, impregnated with autologous bone marrow puncture harvested from the iliac crest. Yet, no systematic trial exists summarizing the results of septic femoral non-union using VABG analyzing the infection eradication rate, rate of osseous integration with union, and osseous remodeling.

Methods In this prospective non-randomized cohort study, 18 patients treated by nailing or plating for femur fractures that subsequently developed a septic non-union were included. The surgical intervention included a standardized protocol by eradicating infection first, followed by implantation VABG to promote osseous union. Main outcome measurements were radiographic union and clinical parameters.

Results Mean follow-up was 5.9 years (range: 2–8 years). Infection eradication was achieved for all patients, while union was achieved in 15 out of 18 cases (83.3 %). Mean time for union took 16.9 weeks (range: 12–24). Radiographic analysis proved osseous remodeling and full integration of VABG within 12 months for 15 patients. No infection recurrence occurred at final follow-up.

Conclusions VABG demonstrated a high union rate without donor site morbidity as the main advantage over ABG. Sufficient osseous integration within 3 months and remodeling within 12 months are promising aspects, as no late fatigue fractures occurred. However, further trials are necessary due to the limitations of this study.

Keywords Septic non-union · Femoral pseudarthrosis · Osteomyelitis · Bone defect · Allograft · Autologous bone graft

Introduction

The treatment of infected long bone non-union remains challenging. Surgeons are confronted with osteomyelitis, bone and soft tissue loss, reduced bone quality caused by osteopenia and impaired blood supply, adjacent joint stiffness, and complex axial or torsional deformities [1–3]. The main goals of surgical treatment are therefore to: (1) eradicate infection, (2) restore bone length, torsion, and alignment, (3) achieve union, and (4) gain optimal function. Many colleagues have focused on the treatment of infected non-union of long bones, with the majority addressing the tibia or including different anatomical regions [1–9]. The reported results of treating femoral non-union are of lesser extent [10–17]. Consensus prevails that specific systemic antibiotic therapy, sequestrectomy with thorough debridement and intense irrigation are essential to achieve sufficient local blood supply and cure infection [2, 3, 5, 18, 19]. Many authors recommend staged autologous bone grafting (ABG) from the iliac crest to promote union, being aware of the disadvantages of limited availability and explantation morbidity including chronic complaints [1, 5, 6, 20].

In a detailed literature search, we were able to locate only four retrospective series specifically analyzing success rates for septic femoral non-union treatment with or without ABG [21–24]. The key questions involved in these studies and their treatment protocols are whether

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to remove all osteosynthetic implants including nails and plates or to retain them in the presence of an active or subacute infection, and the timing of bone grafting. Chen et al. [24] recommended specific antibiotic treatment and retention of intramedullary nails if the bone-osteosynthetic construction is stable and the infection under control. External fixation is most suitable for uncontrollable osteomyelitis or infected non-union [24]. Prasarn et al. [23] suggested a single-stage treatment protocol with an antibiotic holiday in preparation for one surgical procedure with adequate intra-operative cultures, aggressive debridement, stable fixation with correction of anatomical deformities, and ABG. Ueng et al. recommended a two-stage protocol: the first stage consisted of radical debridement with antibiotic bead chains and external fixation. The second stage called for ABG and the use of external fixation until osseous union was achieved [21].

In light of these limited reports with different treatment protocols using ABG, we present our multi-staged protocol for treatment of infected femoral non-union, which consists of first eradicating the infection with or without external fixation and then performing staged bone grafting with a vitalized allograft (VABG). This protocol has been applied successfully in cases of infected tibial non-union [3]. The aim of this trial was to analyze success rates for infection eradication, union, remodeling of VABG, potential late fatigue fractures, and late onset of infection recurrence when treating infected femoral non-union, as to our knowledge a careful literature search failed to localize a comparable study.

Patients and methods

All patients who underwent VABG were prospectively registered in our clinic without randomization. From 2003 to 2007, 18 patients underwent VABG for infected femoral non-union. Inclusion criteria were a diagnosis of femoral non-union, documented infection, definitive internal fixation, and adequate clinical and radiographic follow-up for a minimum of 1 year. In our routine clinical work infected non-union is defined as a state of union failure lasting a minimum of 6 months after injury and as the previous or current occurrence of an infection with a positive bacteriological culture [3, 5]. A total of 18 patients met the inclusion criteria and were included in this trial. The patient collective consisted of 13 men and 5 women with an average age of 51.8 (range: 19–81) years at first presentation. The study patients were referred to our Level 1 trauma center with a specialized separate septic unit from other institutions due to persistent infection and/or non-union of the femur. Our standardized multi-staged protocol involved infection eradication followed by staged VABG to promote bony union:

As a first step, the non-union site was revised with radical debridement of the femur and the soft tissue coverage with the aim of obtaining good blood supply and eradicating infection. Multiple specimens were taken for microbiological culture including aerobic and anaerobic organisms and fungi. The bone-osteosynthetic construction was assessed for biomechanical stability and possible improvements for each individual case. When required by the grade of infection severity, the implant was removed to control infection and the femur was stabilized with temporary external fixation with the aim of later stabilizing the non-union by plating. If the infection grade was suitable, the implant was left in place but drains were placed to eliminate inflammatory secretion at the non-union site. All patients received a regimen of specific antibiotics for at least 6 weeks. Infection parameters such as local symptoms (swelling, redness, and hyperthermia), fever, white blood cell count, and C-reactive protein concentration were monitored. After achieving an infection-free local environment, while using external fixation, VABG and plating were performed at the non-union site to promote bone consolidation under specific antibiotic coverage for three further weeks. This surgical procedure has been described previously [3]. In brief, industrially prepared allogeneic cancellous bone was rehydrogenated for approximately 20–30 min and then impregnated with autologous bone marrow harvested from the ipsilateral iliac crest. Via a minimal incision of approximately 1 cm, a Yamshidy needle was placed in the iliac crest. It is important to move the needle in the iliac crest during aspiration to obtain real bone marrow and not blood. This bone marrow was immediately injected into the cancellous femoral head before agglutination, thus impregnating the allogeneic cancellous bone (Figs. 1, 2, 3). Before transplanting this VABG, the non-union site must be macroscopically free of signs of infection and provide sufficient local blood supply. Our protocol involved the use of so-called continuous long-term drains at the site of the non-union and the implant. To avoid infection recurrence such drains have to be mobilized every day to avoid adhesions and drain obstruction and thus ensure sufficient elimination of potentially inflammatory secretion that could create a surgical fistula. The drains remained in place until union was achieved. The standardized postoperative aftercare included partial weight bearing of 20 kg with no restrictions on knee motion for a period of 6 weeks. Thereafter, increased weight bearing was allowed without any limitations following radiological serial control. After removing the drains, specific antibiotic medication was administered for 2 weeks. X-rays in two planes were performed at intervals of 4 weeks as part of the routine clinical controls. Clinical follow-up included a radiographic investigation in two planes and measurement of the circumference of each limb to check the range of motion of the hip and knee joint. Local tenderness, swelling, redness, and the ability to walk without or only with walking aids were recorded. All patient charts were analyzed with regard to microbiological cultures, internal diseases like diabetes, coronary or peripheral vascular disease, nicotine consumption, etc. Infection severity was classified according to Cierny-Mader classification [3]. Late onset of infection recurrence was noted and a final clini-
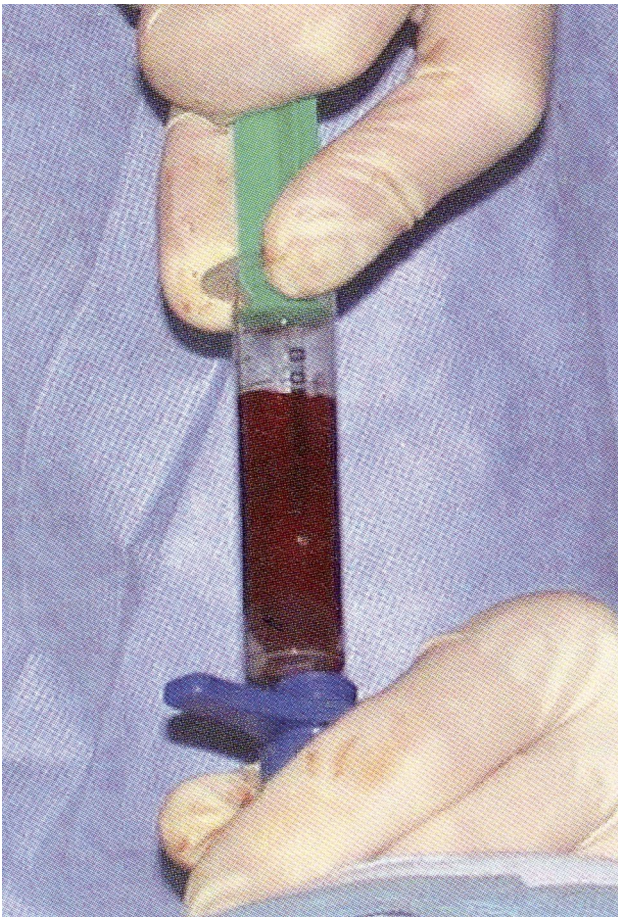
Fig. 1 Bone marrow aspiration via a Yamshidy needle from the iliac crest

Fig. 2 Industrially prepared allogeneic femoral head (lyophilized and radiated) is shown, which was rehydrogenated for approximately 20–30 min
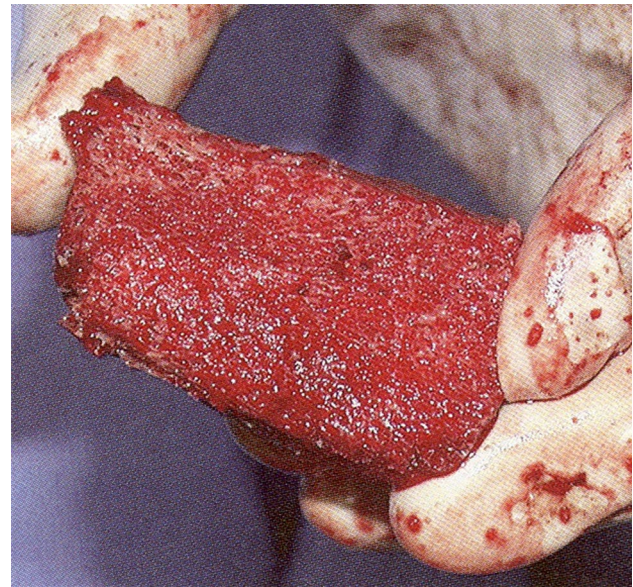

Fig. 3 This figure shows an impregnated cancellous femoral head, which was chopped into small bone chips before implantation

Table 1 Modified Merchant-Dietz Score

Function	Does housework or job without difficulty	8
	Climbs stairs: foot over foot	6
	Any manner	4
	Carries heavy objects, such as a suitcase	4
	Is able to run, participates in athletics, or work at heavy labor	4
	Walks enough to be independent	8
	Does yard work, gardening, lawn mowing	4
	Has no difficulty getting in or out of an automobile	6
Freedom of pain	No pain	40
	Pain only with fatigue or prolonged use	30
	Pain with weight-bearing	20
	Pain with motion	10
	Pain with rest or continuous pain	0
Gait	No limp	10
	Antalgic limp	8
	Uses cane or one crutch	2
	Uses wheelchair or cannot walk	0
Range of motion	Total amount of flexion (normal 140°); assign 2 points for every 20°	10
Results	90–100 points	Excellent
	80–89 points	Good
	70–79 points	Fair
	<70 points	Poor

cal scoring was calculated according to a modified Merchant-Dietz Score (see Table 1) [25]. The modification is a suggestion made by the authors for use in the femur, with the only difference being that the range of motion of the knee joint is noted, but not of the ankle [25].

The serial X-ray controls were checked for time to union and to analyze remodeling of the VABG as well as new identifiable sequestral bone formations.

This study was approved by the appropriate ethics committee. All patients submitted a written declaration of consent for anonymous acquisition and processing of the measured and analyzed results.

Results

With this protocol, we treated 18 patients for infected femoral non-union from 2003 to 2007. Mean follow-up for this analysis was 5.9 (range: 2–8) years. The patients needed on average 3.2 (range: 2–7) staged surgical debridement procedures to achieve infection control before vitalized bone grafting was performed. Culture analysis showed seven cases of *Staphylococcus aureus* alone and two cases of methicillin-resistant *Staphylococcus aureus*. All culture results are summarized in Table 2. At time of first presentation, 12 intramedullary nails and 6 extramedullary plates including two dynamic hip screws were in situ. In 14 of the 18 study patients, the original implant (nail or plate) had to be removed first, with temporary external fixation to eradicate infection. In these 14 cases, definitive plate stabilization was performed concomitantly with VABG. In the remaining four cases, the original implants were retained, and after infection eradication the final procedure consisted of implanting a vitalized allograft alone to promote union. Union was achieved in 15 (83.3%) of the 18 cases. The Cierny-Mader classification is presented in Table 2. A total of 2 of the 3 cases with a persistent non-union required an above-knee amputation. These patients had several concomitant internal diseases and impaired bone vascularity, which would have required an Ilizarov procedure at the age of 65 and 81 years (Table 2). The remaining case involved a 77-year-old woman with a symptomatic femoral non-union of the proximal femoral shaft and concomitant hip arthrosis. This case was treated by implanting a cemented hip replacement. Following hip replacement, no late recurrence of infection or loosening of the endoprosthesis occurred. Consolidation of the former non-union was achieved at a mean of 16.9 (range: 12–24) weeks. The continuous long-term drain remained in place in all patients until union with weight bearing was radiographically documented (mean: 16.9 weeks). A slight circumferential resorption of the transplanted cancellous bone graft was detected, namely approximately 5–9 mm. This remodeling took place within the first 12 months and showed no further changes. No secondary development of sequestral formation was radiographically detected with regard to the vitalized bone graft. The average clinical scoring calculated according to the modified Merchant-Dietz Score was 76.7 points. Further details are given in Table 2. Mean range of motion of the knee joint was 125° (range: 110°–140°).

A case of a 27-year-old male patient is shown in the Figs. 4, 5, 6, 7, 8.

Discussion

It is essential to work according to a reliable surgical treatment protocol in difficult situations such as infected femoral non-union. The treatment goals are infection eradication, osseous union with appropriate function achieved within a reasonable treatment time, with a minimum of surgical procedures and the lowest possible morbidity rate.

These hard to achieve goals are complicated by the dilemma confronting surgeons, namely whether to remove or retain osteosynthetic implants, in view of the fact that intramedullary nails are more problematic than extramedullary fixation systems. Systematic antibiotic medication cannot eradicate intramedullary bacterial infection after nailing, although the purulent infection may be diminished. Some authors have advocated retaining the nail despite an infection, with subsequent nail removal and reaming debridement after the fracture has healed. The ensuing dispute is known as the "union first" strategy versus the "infection first" strategy.

The majority of authors recommend first achieving infection-free conditions via debridement, organism-specific antibiotics, and stable fixation and then promoting union by ABG [3, 6, 21, 24, 26]. Remaining disadvantages of ABG are well known and include harvesting morbidity and limited availability [3, 6, 27]. Therefore, the use of a VABG seems to be an interesting alternative. We published the first positive results achieved in infected tibial non-unions following the same strategy, namely eradicating the infection first and subsequently promoting union by means of VABG [3]. Schmid et al. [28] published the first description of VABG in 2007. In this series, no complications or chronic complaints were observed due to harvesting bone marrow from the iliac crest by puncture, which is a remarkable advantage over harvesting autologous bone from the iliac crest. Our multi-staged protocol achieved infection eradication in all 18 cases. The microbiologic biopsy samples at the non-union site were negative when performing the VABG. In 14 cases, the original implant had to be removed for infection eradication due to persistent macroscopic infection signs with purulent secretion and local necrosis, which was routinely re-assessed during second-look revision and debridement. These cases received temporary external fixation to stabilize the non-union. Following infection eradication, staged internal fixation was performed by means of plating and implanting VABG. In the remaining four cases, the second-look revision and debridement demonstrated no further signs of infection (including negative microbiologic culture), thus allowing us to retain the original implant in situ and perform VABG to promote union.

The fact that infection eradication was achieved in all patients without early recurrence is probably due not only to the radical staged debridement, administration of organism-specific antibiotics, and stable fixation, but also to our postoperative regimen using a continuous long-term suction drain at the implant and graft site to ensure

Table 2 Overall results are summarized to allow a tightly arranged overview

| Case	Age/sex	Lesion site	Gustilo-Anderson classification	Cierny-Mader classification	Last osteo-synthesis	Bone defect (cm)	Bacteria	Weeks for bony union	Postoperative follow-up in months	Merchant Dietz Score	Complications
1	76/Male	Proximal 1/3	Closed	IV BL	Condylar plate	None	OSSA - oxacillin sensible staphylococcus aureus	20	84	68	None
2	66/Female	Middle 1/3	Closed	IV BL, BS	Condylar plate	None	OSSA - oxacillin sensible staphylococcus aureus	24	62	70	None
3	48/Male	Proximal 1/3	Closed	IV BL	Wagner plate	None	Staphylococcus epidermidis	14	96	84	None
4	60/Female	Proximal 1/3	Closed	IV BL	Dynamic hip screw	1	Staphylococcus epidermidis	16	94	74	None
5	34/Male	Proximal 1/3	Closed	IV BS	Condylar plate	None	Methicillin-resistant Staphylococcus aureus (MRSA) and Staphylococcus epidermidis	22	70	69	None
6	19/Male	Proximal 1/3	Closed	IV BL	Wagner plate	None	OSSA - oxacillin sensible staphylococcus aureus	12	94	88	None
7	74/Female	Proximal 1/3	Closed	IV BL	Condylar plate	None	OSSA - oxacillin sensible staphylococcus aureus, Enterococcus faecalis	14	92	64	Persistent non-union, therefore implantation of a cemented hip replacement
8	56/Male	Proximal 1/3	Closed	IV BL, BS	Condylar plate	1	OSSA - oxacillin sensible staphylococcus aureus	14	86	84	None
9	67/Male	Distal 1/3	Closed	IV BL	Condylar plate	3	Enterococcus faecalis, Pseudomonas aeruginosa, Staphylococcus epidermidis	24	92	75	None
10	27/Male	Proximal and middle 1/3	IIIA	IV BL	Wagner plate	4	OSSA - oxacillin sensible staphylococcus aureus	12	84	82	None
11	68/Male	Proximal 1/3	Closed	IV A	Condylar plate	1	OSSA - oxacillin sensible staphylococcus aureus	14	83	70	None
12	81/Female	Middle 1/3	Closed	IV BL	LCDC plate	None	MRSA - methicillin resistent staphylococcus aureus	None	29	–	Above-knee amputation, died 2 years after amputation due to internal diseases
13	65/Male	Distal 1/3	Closed	IV BL	LISS	None	Enterococcus faecalis, Escherichia coli, Pseudomonas aeruginosa	None	29	–	Above-knee amputation, died 1 year after amputation due to internal diseases
14	22/Male	Middle 1/3	Closed	IV BL	LCDC plate	None	OSSA - oxacillin sensible staphylococcus aureus, Lactobacillus	14	64	84	None
15	54/Male	Distal 1/3	Closed	IV BL	LISS	None	Staphylococcus epidermidis	14	64	74	None
16	41/Male	Middle 1/3	Closed	IV BS	LCDC plate	4	Enterococcus faecalis, Staphylococcus epidermidis	16	60	76	None
17	53/Female	Middle 1/3	Closed	IV BL	LCDC plate	None	OSSA - oxacillin sensible staphylococcus aureus	12	56	75	None
18	23/Male	Middle 1/3	Closed	IV BL	Condylar plate	None	Enterococcus faecalis, Staphylococcus epidermidis	12	56	90	None
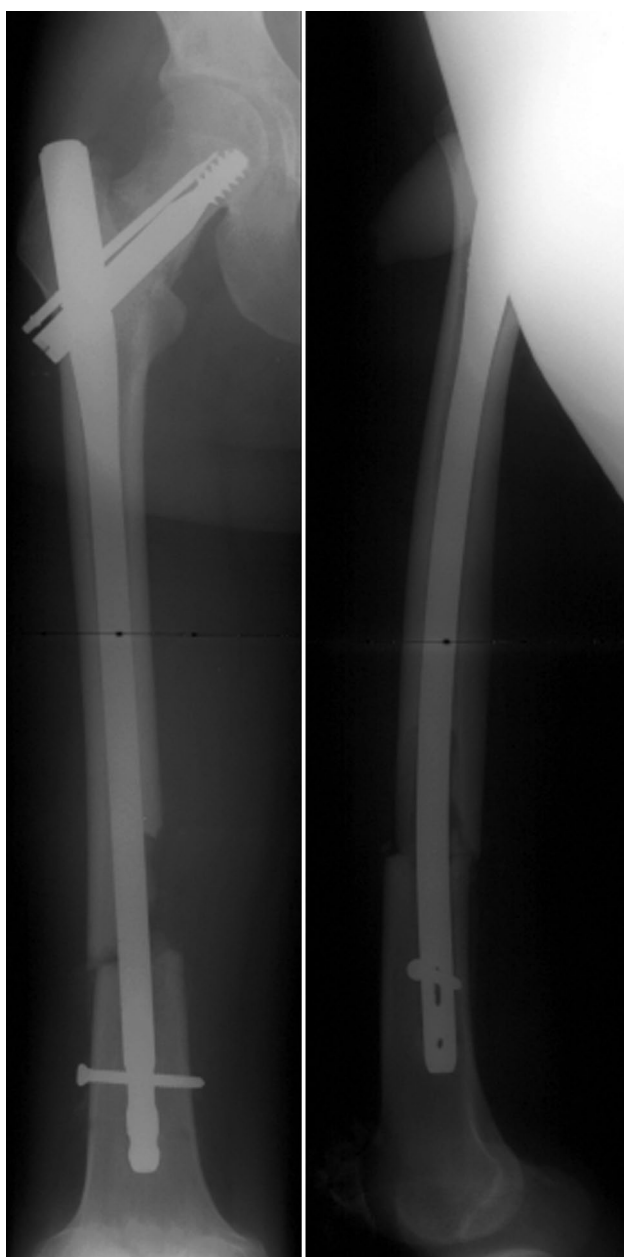
Fig. 4 X-rays of a 27-year-old man with a stabilized pertro-chanteric and diaphyseal femoral fracture including a multi-fragmentary patellar fracture with an Intrasys™ nail (Zimmer®)

Fig. 5 X-ray showing septic loosening of the nail with a diaphyseal defect 6 months after stabilization. The pertrochanteric fracture had healed at that time

elimination of potentially inflammatory secretion until union was achieved. The latter is an approach, which was described before [3]. This principle is that the long-term drain evacuates secretion at the recipient non-union site so that the VABG is not surrounded by a postoperative seroma providing good soft tissue (muscle) contact to enhance incorporation of the VABG. If the draining secretion quality would have turned from clear to turbid and suspicious indicating a potential infection, our consequence is to debride the recipient site surgically, which was not necessary in this case series. The microbiologic specimens were all negative at the time of VABG, so that we stated an infection eradication of 100 %. We observed a postoperative rate of infection recurrence of 0 %, while the continuous drain was in situ and after removing the drain. Our postoperative routine did not show any infection signs controlling the local clinical aspect (without signs of redness, swelling, or draining sinus), performing sonography (ruling out seromas), and analyzing blood results. But we have to admit critically that this postoperative routine has the weakness that a low-grade infec-

Fig. 6 X-rays showing the revised femur after nail removal with temporary external fixation and plate stabilization with a large vitalized allogeneic bone grafting (two femoral heads) to reconstruct the bone defect and promote union

Fig. 7 X-ray controls 3 months after final revision showing remodeling and integration of the vitalized allogeneic bone grafting

tion cannot be ruled out with certainty, especially for the three cases that developed a persistent non-union. It must be kept in mind that detailed patient instructions and compliance are obligatory to ensure proper drain care. If this is not possible, daily outpatient wound care to mobilize and clean the drain must be organized (in our treatment group $n = 3$ for elderly patients). Once union is achieved, the drain can be removed because the implant can be removed if the infection recurs. We believe that this surgical aftercare can be an alternative for retaining stable plates by avoiding infection recurrence or exacerbation after surgical debridement and VABG. Cases involving infected nails in the medullary cavity should be treated by removing the nail with reaming and fenestration of the distal medullary cavity to eliminate all infectious intramedullary tissue through the distal fen-

estration under simultaneous suction to avoid systemic bacteremia. These goals can also be achieved by using the Reamer-Irrigator-Aspirator (RIA) Tool [29]. Stabilization is possible by means of external fixation or secondary internal fixation using plates or renailing of the femur. However, it must be remembered that the rate of infection recurrence after renailing of formerly infected femoral non-unions is remarkably high [30, 31]. Only Prasarn et al. [23] and Chen et al. [24] reported on cases in which the implant was retained or replaced, while Prasarn recommended a single-stage procedure, but with a strict regimen of medication and surgical technique. Interestingly, Prasarn et al. [23] reported that 14 secondary surgical procedures were necessary in their series of total 11 cases. In four cases, ABG and antibiotic bead removal were necessary. The initial surgical procedure achieved a union rate of 91%, and in all patients the former fractures ultimately healed using internal fixation. They noted no late infection recurrence, with a mean follow-up of 5.6 (range: 2–12) years and a mean time to union of 13.1 (range: 3.5–34) months. Mean knee flexion was limited to 97°, whereby it must be remembered that of the 11 patients 7 had a non-union located in the distal third of the femur. The authors attribute their success rate to the replacement of infected hardware. Retaining implants in a situation of active infection makes the bacteria 1000 times more resistant, and the infection will likely recur when antibiotics are discontinued [32]. Rightmire et al. showed that only 68% of infected fractures treated with antibiotic infection suppression while retaining hard-

Fig. 8 X-ray controls at 5-year follow-up demonstrating complete union without sequestral formation and complete osseous integration of the former vitalized allogeneic bone grafting

ware will unite. Thus, they recommend that the initial hardware should be removed [33]. Nevertheless, the authors did not use long-term drains to ensure sufficient secretion elimination and thus prevent infection recurrence, which disturbs union. Our treatment protocol shows that infection recurrence during osseous healing can be avoided. The question remains whether this can be attributed to repeat debridement and organism-specific antibiotic medication, temporary external fixation with staged internal re-osteosynthesis by plating (in the majority of our patients), or to additional use of the continuous drain to improve the incorporation of the VABG and avoiding postoperative seromas and potential infection recurrence.

Chen et al. [24] treated two groups of patients. Group I consisted of 12 patients with a retained infected nail and a further heterogeneous procedure: in 8 cases debridement and drainage, followed in 2 cases by reinsertion of the nail, and in 2 other cases by external fixation after debridement failure and nail retention. Antibiotic beads

were placed at the former fracture site in seven cases. All fractures united in this group after a mean of 9 (range: 5–15) months. No infection recurrence was noted after an average follow-up of 25 (range: 12–76) months. Group II consisted of 11 patients treated with nail removal and external fixation. In all patients, antibiotic beads were placed at the former fracture site after debridement and drainage. In two patients, a decision was made to use external fixation. All patients underwent staged ABG to promote union. In all, 7 out of 11 non-unions healed (63.6%) at an average of 10 (range: 4–24) months. In total, 2 patients received an above-knee amputation due to limb non-function as the sequelae of head injury, and two additional patients because of persistent infection of the non-union site.

Ueng et al. [21] applied a two-staged protocol using external fixation and ABG to achieve a union rate of 100% in 15 cases. Following the second stage, three patients developed postoperative infections that required repeat debridement and antibiotic therapy. External fixation was necessary for a mean of 9.5 (range: 7–15) months. A total of 7 patients developed pin track infections that required further treatment. Remarkable is the mean postoperative range of knee motion with 100° flexion, although no distinction was made for fracture localization. These results, which agree with our experience in the past, are arguments against long-term use of external fixation for the femur. Our treatment protocol that uses long-term drains to delay internal plate fixation is an option that provides fair knee motion, fewer restrictions on patient quality of life, and a low likelihood of infection recurrence. Our patient survey revealed that all our patients preferred to carry a continuous drain that needs daily mobilization and cleansing, rather than to use an external fixation with more restrictions and local complaints. It must be remembered that soft tissue coverage of the thigh with sufficiently vascularized muscles made internal replating possible, while the same treatment protocol for infected tibial non-union made external fixation indispensable for the majority of patients until union was achieved [3].

Our union rate of 83% (15 out of 18 patients) can probably be attributed to the promoting effect of VABG. The union rate reported in our trial is lower than the results of Ueng et al. [21] with 100%, Prasarn et al. [23] with 91%, and Chen et al. [24] with 100% in group I but higher than in group II with 63% who all used ABG as the gold standard. In conclusion, our union rate with 83% using VABG is comparable with the results using ABG. A promising alternative to ABG is the RIA-harvested bone grafting, which has been used with an increasing frequency in the past decade. Systematic comparisons between ABG and RIA have been made by Dawson et al. [27]. They compared union and complication rates between ABG and RIA as well as donor site complaints and the possible grafting volume in a total number of 133 patients. Their Investigation revealed that RIA ($n=56$) yielded a greater volume than from the anterior iliac crest ($n=57$) and had a shorter operating time compared with harvesting

bone from the posterior iliac crest. Union rates between ABG and RIA were comparable with 86 and 82 %, respectively. The mean time for union was 22.5 weeks for ABG and 25.8 weeks for RIA [27] demonstrating equivalent results between the treatment modalities of ABG, RIA, and VABG. RIA had furthermore the advantage of significantly less complaints at the donor site over ABG [27], so that RIA can be favored over ABG from the iliac crest due to the aforementioned advantages including cost aspects [27].

Union is the result of well-orchestrated interactions between cytokines, cells, osteo-conductive matrix, sufficient stability with a good local blood supply, according to the "diamond concept" [20]. Therefore, several clinical trials using bone morphogenetic proteins (BMPs) were performed. These gave evidence of increased healing rates with BMP compared with usual care control in acute tibial fractures, but observed that osseous healing for non-unions was similar to bone graft substitutes [20]. ABG and RIA are the safest and most effective procedures, due to that fact that it contains patient's own bone growing cells (osteogenesis) and proteins (osteoinduction) while providing a frame for the new bone to grow into (osteoconduction). However, ABG and RIA are limited in quantity: approximately 20 cm^3 are available from the anterior iliac crest, 36 cm^3 from the posterior iliac crest, and 37 cm^3 for RIA [27]. Its harvesting is associated with additional comorbidities and donor site complaints with significantly less complaints after RIA [3, 20, 27]. In view of these facts, allogenic bone from tissue banks has the advantage of unlimited availability without donor site compilations. Different forms of allogenic bone are available: fresh-frozen, dried, or lyophilized. This solution provide denaturized matrix proteins and apoptotic cells, thus it only guarantees osteoconductive properties. Moreover, fresh frozen allogenic bone may transfer disease or lead to immunological rejections [3, 20], so we prefer the lyophilized allogenic bone graft. The consequent development is to combine cancellous allograft with autologous mesenchymal stem cells as we proposed it here during surgery or to concentrate bone marrow, as has been proposed in bone defects after revision hip surgery [3, 20]. The advantage to impregnate the allogenic cancellous bone in one single step is to save time and costs in comparison with concentrate mesenchymal stem cells by a specialized working process. In summary, the biological principle of VABG is to mimic autologous cancellous bone from the iliac crest with avoiding comorbidity by harvesting bone marrow from the iliac crest via puncture avoiding donor site complications.

The important key points of our multi-staged protocol with overall positive results are radical repeat debridement, culture-specific antibiotics, and, if necessary, temporary external fixation to first eradicate the infection. After infection eradication, our protocol includes stable definitive fixation by means of plating and a vitalized bone grafting impregnated with autologous bone marrow to promote union. The use of a postoperative continuous drain to prevent infection recurrence until union has been achieved within 3 months or the secretion is less than 10 ml per day is an additional treatment option to prevent early infection recurrence. We have to underline that this is an institutional postoperative mode rather than an accepted published regime. The relevant shortcomings of this study are the small sample number, the lack of a comparative control group, which would be inherently difficult to provide, and the heterogeneous patient population. The main strengths of this trial are the mean follow-up of 5.9 years, the standardized treatment protocol for all patients, and the prospective approach. Although union was not achieved in all patients in our series, infection eradication was successful in every patient. Functional overall results were good to fair. Therefore, we believe our multi-staged treatment protocol utilizing VABG to promote osseous union is a potential alternative to RIA and ABG that is worth being evaluated in further prospective clinical trials and long-term analysis.

Ethical standard statement

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008 (5).

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