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ORIGINAL ARTICLE

A comparison of tumor prosthesis implantation and pasteurized autograft-prosthesis composite for proximal tibial tumor

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Abstract
Background and objectives Although previous reports on composite biologic reconstruction in the proximal tibial location vary, we hypothesized that this type of reconstruction may reduce the late infection rate and have advantages in terms of longevity by restoring bone stock.
Methods Primary analysis addressed differences between 62 tumor prosthesis (TP) and 25 pasteurized autograft-prosthesis composite (PPC) reconstructions in terms of survival rates, functional outcomes, and temporal patterns of infection.
Results The 10-year survival rates of the TP and PPC groups were 73.9 ± 11.7 and 68.7 ± 20.1 %, respectively ($P = 0.64$). Reconstructive failure occurred in 16 (25.8 %) in the TP and in 7 (28 %) in the PPC group. The cause of failures in the TP group was infection (16), whereas those of PPC group were infection (5), loosening (1), and local recurrence (1). The mean functional scores of TP (52) and PPC (20) patients that maintained a mobile joint were 24.2 (81 %) and 25.1 (83.6 %), respectively. Infection rates in the two groups were similar ($P = 0.328$), but infections occurred earlier in the PPC group ($P = 0.011$).
Conclusions This comparative study suggests composite biological reconstruction shows a comparable long-term survival rate to TP reconstruction; however, the composite method has a tendency to a lower rate of late infection.

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Introduction

Currently, three major reconstruction methods are used after tumor resection of the proximal tibia, namely, non-biologic [tumor prosthesis (TP)], biologic (osteoarticular allograft), and composite biologic [allograft- or pasteurized autograft-prosthesis composite (PPC)] reconstruction. Because of the problem of reconstructing the extensor mechanism, especially in TP reconstructions, biologic (allograft or pasteurized autograft) reconstruction has the advantage in terms of patella tendon reattachment. However, the use of osteoarticular allografts has been associated with high subchondral fracture rates and requires prolonged immobilization to achieve union of the capsuloligamentous structure [1–3]. In this respect, composite biologic reconstruction might be an ideal solution, as it combines the advantages of osteoarticular grafts with respect to the biologic insertion of soft tissue and the articular stability afforded by prosthetic reconstruction.

Although composite reconstruction may have theoretical and practical advantages, reported poor outcomes of patients with allograft-prosthesis composite (APC) raise questions about whether this type of reconstruction is appropriate in the proximal tibia [4–6]. Nevertheless, our pilot study on PPC reconstruction yielded a survival rate comparable to that of TP reconstruction, and most of the infected patients were within 1 year from operation [7]. Therefore, despite the pilot nature of this initial study, we hypothesized that PPC reconstruction would yield better results than the unsatisfactory ones of the allograft composite and have advantages over TP reconstruction in terms

of longevity, that is, it would restore bone stock and perhaps protect against late infection by improved coverage of the metallic surface. To test this hypothesis, we compared the outcomes of modular TP and PPC reconstruction in 87 patients treated for a proximal tibial tumor.

In particular, we asked (1) whether these two modalities differ in terms of reconstructive failure rates, complications, or functional outcomes, and (2) whether they differ in terms of temporal patterns of infection.

Materials and methods

We retrospectively identified 129 patients in our computerized database that had undergone proximal tibial resection and reconstruction for an aggressive benign or malignant bone tumor between January 1990 and March 2009. Sixty-two patients that underwent primary TP and 25 patients that underwent PPC reconstruction constituted the study cohort. Forty-two of the 129 patients were excluded for the following reasons: (1) switch from a temporary arthrodesis (29 patients), (2) fewer than 2 years of follow-up (10 patients), and (3) patients that experienced failure who had incomplete data (3 patients). Sixty-five of the 87 study subjects with primary high-grade sarcoma received chemotherapy, but no patient received local radiotherapy. In all study subjects, tumor extirpation involved intra-articular resection of the proximal tibia.

Pasteurized autograft-prosthesis composite reconstruction was used in patients (1) with less than 1/3 cortical bone destruction on axial MR images and (2) when the tumor was confined to one compartment. Lengths of pasteurized tibiae ranged from 8 to 22 cm (mean 12.6 cm), and percentages of tibial bone resected ranged from 23 to 63 % (mean 35.9 %). Preparation for and fixation of PPCs were performed as previously described [7]. Briefly, after tumor tissue was grossly removed, it was kept in preheated saline at 65 °C for 30 min. Pasteurized bone and long stem tibial components were assembled with cement. After polymerization of the cement, the assembled composite was fitted into the medullary canal. The Link Endo-Model Modular Knee Prosthesis System (Hamburg, Germany) was used throughout. Prosthesis stems were fixed with cement in 23 (92 %) cases, and the other 2 (8 %) patients underwent non-cemented fixation. Reconstruction of the extensor mechanism involved reattachment of the patella tendon to pasteurized bone with a non-absorbable suture (9 patients), wire (5 patients), or marlex mesh (3 patients), the latter of which was wrapped around the pasteurized bone. In 8 (32 %) of the 25 patients, salvaged anterior tibial cortical bone ligament or patella bone was fixed with screws or cables to the PPC. A medial gastrocnemius rotation flap was used to cover the autograft and to reinforce the extensor mechanism repair in 18 (72 %) patients, but the remaining 7 (28 %) did not receive a local muscle flap. Follow-up duration averaged 82 months (range 25–127 months).

Sixty-two patients underwent reconstruction using modular TP. Lengths of resected proximal tibiae ranged from 6 to 19 cm (mean 12.1 cm), and percentages of tibial bone resected ranged from 17 to 58 % (mean 35.4 %). In terms of hinge mechanisms, 18 (29 %) patients were implanted with a fixed hinge Kotz Modular Femur and Tibia Resection System (KMFTR®; Stryker Howmedica Osteonics, Rutherford, NJ, USA), and the remaining 44 (71 %) patients received a rotating hinge endoprosthesis [the MUTARS® (Modular Universal Tumour and Revision System, Implantcast, Buxtehude, Germany) system was used in 17 (27 %) patients and the Link® Endo-Model™ Modular Knee Prosthesis System (Hamburg, Germany) in 27 (44 %) patients]. The stems of all three prostheses were fixed with cement in 12 (19 %) patients, and the other 50 (81 %) patients underwent non-cemented fixation. Reconstruction of the extensor mechanism involved reattachment of the patella tendon to the anterior tibia prosthesis using a trevira tube [8] or marlex mesh in 35 (56.6 %), and in 6 (9.6 %) patients the tendon was fixed with a screw. In 6 (9.6 %) patients, the anterior tibia cortex/tuberosity was salvaged and secured to the tibial prosthesis with cables. In 15 (24.2 %) patients, the position of the patella was maintained using non-absorbable sutures to the gastrocnemius muscle flap. A medial gastrocnemius rotation flap was used in 57 (92 %) patients. Follow-up duration averaged 98 months (range 26–240 months).

Postoperatively, all 87 study subjects were immobilized in a cast/splint at 10° of knee flexion for 6 weeks. Thereafter, range of motion exercise using a continuous passive motion (CPM) machine was applied, and weight-bearing was gradually increased (as tolerated) to full weight-bearing at 12 weeks.

Plain anteroposterior and lateral radiographic examinations were performed monthly until 2 years postoperatively, at 3-month intervals until 5 years, and at 6-month intervals thereafter. After PPC reconstruction, junctional site radiographic union was judged by one radiologist (JYY) and two of the authors (WSS, CBK). Union was defined when callus was found to bridge >75 % of cortical thickness on serial radiographs [9]. Union was evaluated independently ($\kappa = 0.86$), and any discrepancy was resolved by consensus review. The radiographic interpretations of loosening were categorized into three grades as described by O'Neill and Harris [10].

Reconstruction failure was defined as the removal of the composite or prosthesis due to complications. Time to failure (months) was defined as the time elapsed between the first surgery and date of prosthetic removal.

Complications occurring within 1 year of index surgery were defined as early. Functional results were assessed at final follow-up visits using the Musculoskeletal Tumor Society (MSTS) System [11].

Demographic and treatment variables in the two study groups were compared using the *t* test and Fisher's exact test. Survival curves were determined using the Kaplan-Meier method, and inter-group survival differences were determined using the log-rank test. Analyses were performed using SPSS version 13.0 (SPSS Inc., Chicago, IL, USA), and *P* values of <0.05 were considered significant. This study was approved by our Institutional Review Board.

Results

No significant differences were detected between the TP and PPC groups for the following parameters: age, tumor size, use of chemotherapy, and percentage or length of resection. However, the TP group included more patients with a benign aggressive tumor ($P = 0.03$), a fixed hinge type prosthesis ($P < 0.001$), a gastrocnemius rotational flap ($P = 0.043$), and who had undergone non-cemented fixation ($P < 0.001$) (Table 1).

Ten-year reconstruction survival rates (calculated using failure for any reason) in the TP and PPC groups were 73.9 ± 11.7 and 68.7 ± 20.1 % ($P = 0.64$) (Fig. 1),

Table 1 Patient demographics of 62 TP and 25 PPC reconstructions

Variables	TP (%)	PPC (%)	*P* value
Age			
<20	28 (45.2)	15 (60.0)	0.210
≥20	34 (54.8)	10 (40.0)	
Gender			
Male	39 (62.9)	17 (68.0)	0.653
Female	23 (37.1)	8 (32.0)	
Diagnosis			
Osteosarcoma	41 (66.1)	22 (88.0)	0.037
Chondrosarcoma	0 (0)	2 (8.0)	
Bone MFH	3 (4.8)	1 (4.0)	
Ewing's sarcoma	1 (1.6)	0 (0)	
Multiple myeloma	1 (1.6)	0 (0)	
Soft tissue sarcoma	3 (4.8)	0 (0)	
Giant cell tumor	13 (21.0)	0 (0)	
Initial tumor volume (ml)			
Mean (range)	127 (17–509)	132 (18–304)	0.813
≤150	45 (72.6)	16 (64.0)	0.429
>150	17 (27.4)	9 (36.0)	
Chemotherapy			
Done	45 (72.6)	20 (80.0)	0.590
Not done	17 (27.4)	5 (20.0)	
Type of prosthesis			
Fixed hinge	18 (29.0)	0 (0)	0.001
Rotating hinge	44 (71.0)	25 (100)	
Stem fixation			
Cemented	12 (19.4)	23 (92.0)	<0.001
Uncemented	50 (80.6)	2 (8.0)	
Resection length (cm)			
Mean (range)	12.2 (6–19)	12.6 (8–22)	0.536
Resection percent (%)			
Mean (range)	35.6 (17.1–57.6)	35.8 (23.1–62.9)	0.895
Gastrocnemius flap			
Done	57 (91.9)	19 (76.0)	0.043
Not done	5 (8.1)	6 (24.0)	
Total	62 (100 %)	25 (100 %)	

TP tumor prosthesis, *PPC* pasteurized autograft prosthesis composite

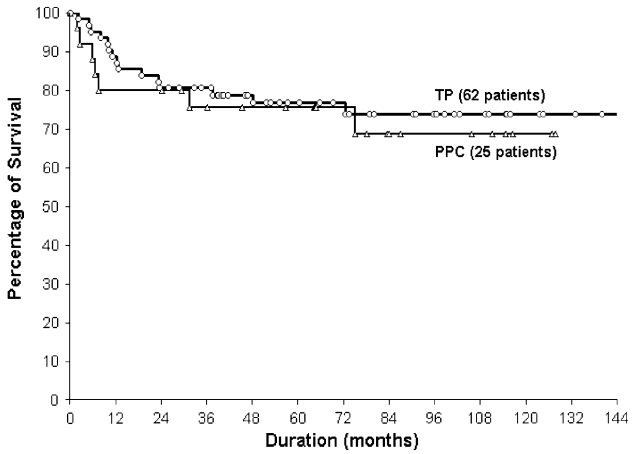

Fig. 1 Ten-year reconstruction survival rates (calculated using failure for any reason) of the TP and PPC groups were 73.9 ± 11.7 and 68.7 ± 20.1 % ($P = 0.64$)

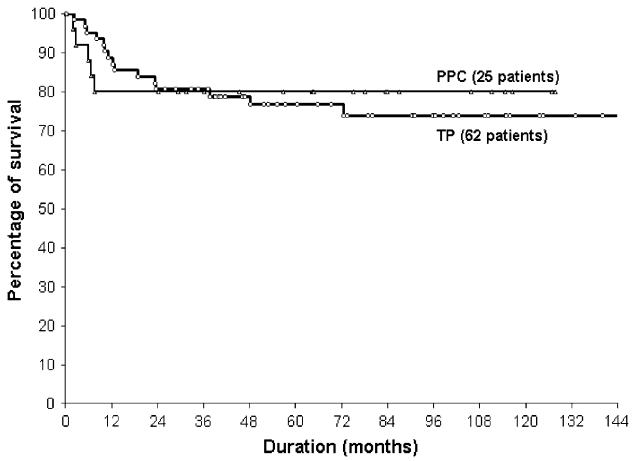

Fig. 2 Ten-year survival rates of revision due to infection in the TP and PPC groups were 73.9 ± 11.7 and 80.0 ± 15.7 %, respectively ($P = 0.819$)

whereas 10-year survival rates (calculated using revision due to infection) were 73.9 ± 11.7 and 80.0 ± 15.7 %, respectively ($P = 0.819$) (Fig. 2). Sixteen (25.8 %) reconstructive failures occurred in the TP group and 7 (28 %) in the PPC group. All failures except one in the TP group were due to infection; the exception was a patient with a giant cell tumor who developed concomitant local recurrence and infection at 240 months postoperatively. In the PPC group, five (71 %) of seven failures were secondary to infection and two to loosening and local recurrence, respectively.

Four of the 62 patients in the TP group required an additional surgical procedure for complications (2 bushing wear, 1 patella ligament rupture, 1 peri-prosthetic fracture) not requiring reconstruction removal, whereas 3 of 25 patients in the PPC group underwent 7 further operations due to local recurrence and wound problems. One superficial wound infection and one femoral condyle fracture occurred in the TP group, and two fractures occurred in the PPC group, which were managed conservatively. Union at the osteotomy site was observed in 18 (72 %) patients in the PPC group, and average union time for the 18 junctional sites was 18.9 months (range 12–43 months). Of the seven patients in the PPC group that experienced nonunion, five suffered a composite-related infection.

Final limb statuses of the 16 patients with failure in the TP group were arthrodesis in 7, mobile joint in 6, and amputation in 3, whereas those of the 7 failures in the PPC group were arthrodesis in 5 and mobile joints in 2. Functional outcomes, as determined using the MSTS system, of the 52 patients in the TP group and the 20 patients in the PPC group that maintained a mobile joint averaged 24.2 (81 %) (range 18–28) and 25.1 (83.6 %) (range 22–28), respectively. Thirteen (25 %) patients in the TP group had no extensor lag, and the remaining 39 (75 %) had an average residual extensor lag of 35° (range 10°–60°). On the other hand, 9 (45 %) patients in the PPC group had no extensor lag, and the remaining 11 (55 %) patients had an average residual extensor lag of 14° (range 10°–30°) ($P = 0.09$).

Although infection rates in the two groups were similar ($P = 0.328$), the mean time from index operations to infection development were different (5 vs. 34 months, $P = 0.011$), and the PPC group has a tendency ($P = 0.123$) to lower late (>1 year) infection (Table 2). Five patients in the PPC group developed infection at 2, 2.8, 6, 6.6, and 7.5 months postoperatively. Two of the five (infected at 2.8 and 6.6 months) were switched to resection arthrodesis immediately, while the remaining three underwent several episodes of debridement followed by arthrodesis at 21, 10.5, or 20 months postoperatively.

Discussion

Identifying an optimum reconstructive method after resection of bone sarcoma is important in terms of ensuring functional longevity. However, the proximal tibia has been reported to present a relatively high complication risk [12–14]; of the various complications that endanger reconstruction survival, infection is the leading cause of failure, and it can lead to limb loss [15, 16]. Although the majority of prosthetic failures due to infection occur only months after the initial surgery, TP reconstruction seems to present a risk of infection until reaching a plateau at approximately 10 years [17]. We presumed that biologic (pasteurized bone) composite reconstruction would have a lower risk of late infection than prosthesis reconstruction after the initial high-risk period. The present study confirms that the long-

Table 2 Complications, timing of infection, functional outcome, and final limb status

Variables	TP ($n = 62$)	PPC ($n = 25$)	P value
Number of infections	16 (25.8 %)	5 (20.0 %)	0.328
Timing of infection			
Mean (range)	33.6 (2–240)	5.0 (2–8)	0.011
<1 year	9 (14.5 %)	5 (20.0 %)	0.123
≥1 year	7 (11.3 %)	0 (0 %)	
Loosening	0 (0 %)	1 (4.0 %)	0.287
Local recurrence	1 (1.6 %)	1 (4.0 %)	0.495
Extension lag			
No	13 (25.0 %)	9 (45.0 %)	0.099
Yes	39 (75.0 %)	11 (55.0 %)	
MSTS score			
Mean (range)	24.2 (18–29)	25.1 (22–28)	0.102
Final limb status			
Mobile joint	52 (83.9 %)	20 (80.0 %)	0.329
Amputation	3 (4.8 %)	0 (0 %)	
Arthrodesis	7 (11.3 %)	5 (20.0 %)	

TP tumor prosthesis, *PPC* pasteurized autograft prosthesis composite

term survival of PPC reconstruction is comparable to that of TP reconstruction and that it has a tendency of lower late infection rates.

This study is primarily limited by the selection bias possibly introduced when we chose reconstructive methods. In particular, PPC group members may have had smaller tumors, and thus less extensive soft tissue and vascular damage. However, no difference was observed between the two groups in terms of initial tumor sizes or amounts of bone resected. Additional limitations included the non-standardized operation technique used and the unequal numbers of patients in the two groups. Thus, we acknowledge heterogeneities of prosthesis design, mode of stem fixation, and extensor mechanism reconstruction technique, including use of gastrocnemius flap.

The prosthesis survival rate and cause of failure in the TP group were comparable to those previously reported [18–20]. The frequency and nature of complications of APC or PPC involving the proximal tibia depend on the type of composite bone used (Table 3). Although Manabe et al. [21] and Ahmed et al. [9] reported a slightly higher rate of infection or graft fracture because of the various anatomic locations and disease entities included, their results were comparable to those in our study. Biau et al. used irradiated allograft composites in 26 patients and considered this procedure to be contraindicated in a proximal tibial location because of an unacceptably high rate of complications. In a smaller series of five patients provided with the same type of allograft composite, Wunder et al. also found a high rate of reconstructive failure. In contrast with two previous unfavorable results, Gilbert et al. reported no procedure-related failure among 12 patients (after excluding two patients with local recurrence) treated using a fresh frozen allograft and rigid fixation with a long-stemmed implant. In a larger series conducted on 62 patients treated with a fresh frozen allograft composite, Donati et al. reported a 5-year survival rate of 73.4 % and an infection rate of 24.2 %, which is comparable to those of the PPC group in the present study. In view of the relatively high infection rate encountered, they recommended this procedure for young patients with an aggressive benign or low-grade malignant tumor.

Despite the theoretical advantages of composite biologic reconstruction, its survival is endangered by complications, such as infection, graft fracture, graft resorption, non-union of osteotomy sites, and loosening. Infection is a major threat for composite biologic reconstruction, but as infection rates of osteoarticular allografts and of endoprostheses in this location range from 13 to 25 % [1, 22] or 16 to 20 % [18, 19, 23], infection seems to be an intrinsic problem at this location rather than a composite procedure-related problem. Furthermore, whether routine use of a gastrocnemius flap can reduce infection rates is controversial [5, 23, 24]. In our series, infection occurred in 4 (22.2 %) of 18 patients with rotation of the medial gastrocnemius as compared with 1 (14.2 %) of 7 patients with no flap rotation. Regarding the timing of infection, the PPC group showed a tendency of late infection. Although we cannot generalize our findings because of too small a sample size, previous studies also suggest a similar trend [4, 6]. We presume, by enveloping the prosthesis surface with bone of biologic potential, the biofilm mode of bacterial growth on the metallic surface is minimized [25].

Furthermore, in revision surgery for pasteurized autograft reconstruction, we often observe that the soft tissue surrounding pasteurized bone is attached firmly to the graft

Table 3 Comparison with previous studies

Author	Case no./ mean FU (years)	Type of surgery	Implant survival (%)		Loosening (%)	Implant/ graft fracture (%)	Infection (%)	Mean timing of infection (months)	Graft union (%)	LR (%)	Amputation (%)
			5 years	10 years							
Flint et al.	44/5.0	TP	73	NA	0	4.5	16	NA	NA	4.5	15.9
Gosheger et al.	42/3.8	TP	61.7	NA	7.1	2.4	16.7	NA	NA	NA	NA
Griffin et al.	25/9.3	TP	74	68	0	8.0	20	NA	NA	0	NA
Current series	62/7.5	TP	77	74	0	0	25.8	33.6	NA	1.6	4.8
Donati et al.	62/6.0	APC[a]	73.4	68	3.2	4.8	24.2	21	87.1	4.8	6.4
Gilbert et al.	12/4.0	APC[b]	79	–	0	0	0	0	100	16	8.3
Biau et al.	26/11.1	APC[c]	68	33	27	50.0	23	<12	30	7.6	11.5
Manabe et al.	13/6.1	PPC[d]	NA	NA	NA	7.7	30.1	NA	50	0	7.7
Ahmed et al.	17/6.1	PPC[e]	NA	NA	NA	5.8	29.4	NA	68	0	5.8
Current series	25/6.8	PPC	76.3	68.7	8.3	0	20	5	72	8.3	0

FU follow-up, *LR* local recurrence, *NA* not assessable, *TP* tumor prosthesis (modular, uncemented), *APC* allograft prosthesis composite, *PPC* pasteurized bone prosthesis composite (cemented fixation)

[a] Fresh frozen allograft and uncemented fixation

[b] Fresh frozen allograft and cemented fixation

[c] Irradiated allograft and cemented fixation

[d] Irradiated allograft and uncemented fixation

[e] Include whole anatomic sites with implant-pasteurized bone composite

and can see punctuate bleeding from the pasteurized bone surface. This may coincide with the histologic finding of pasteurized bone retrieved 3 years after implantation [26]. Kubo et al. stated that the architecture of the acellular cortical bones was still maintained without microfractures. Although we cannot expect revascularization of graft bone, the aforementioned findings may act positively in resisting infection.

Factors previously found to be related to allograft fracture or resorption are allograft irradiation, perforation of the allograft to allow reattachment of the extensor mechanism, and non-union [4, 27]. However, because irradiation affects the structural properties of allografts, these complications may be minimized by using fresh-frozen allografts [28, 29].

Union between the composite and host bone is another important factor for the success of this type of reconstruction, and non-union predisposes to loosening [4, 28]. To reduce non-union rates, primary bone-grafting at the osteotomy site and rigid fixation with a long stem have been advocated [5, 28]. However, the average union time of around 19 months based on our study and that of Gilbert et al. is too long. Therefore, we believe that the introduction of a novel method like the telescope allograft is required to enhance union rates and to reduce time to union [30].

In summary, pasteurized bone-prosthesis composite and TP reconstruction for proximal tibial tumor were found to be comparable in terms of survival and complication rates. Furthermore, pasteurized bone-prosthesis composite reconstruction has a tendency to lower late infection rates.

Conflict of interest The authors certify that they have no commercial associations (e.g., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might constitute a conflict of interest in connection with the submitted article.

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