Original Article

Biological Reconstruction for Children with Osteosarcoma Around the Knee

Mark E Puhaindran, [1]*MBBS, MRCS (Edin), MMED (Surg)*, Robert WH Pho, [1,2]*MBBS, FRCS, MD*

Abstract

Introduction: Limb salvage in children with primary malignant bone tumours around the knee is challenging, with considerations such as shortening, bone and joint remodeling and high functional demands of active children. The ultimate aim for reconstruction is restoring a stable, painless and mobile joint. With improved survival rates from chemotherapy, reconstructive techniques should ideally last the child's lifespan. We adopted a biological approach by preserving the patients' native joint, with bony defects bridged by fibula grafts supplemented by autoclaved bone grafts infused with bone marrow. We conducted this retrospective review to determine if we were able to meet our objectives of reconstruction. Materials and Methods: A retrospective review of children with osteogenic sarcoma involving the distal femur or proximal tibia treated at our institution was done. Patients aged 13 years and below at the time of surgery who had undergone a limb salvage procedure that preserved the knee joint were included. Results: Nine patients were identified, 3 males and 6 females. The average age was 10.0 years (range, 7 to 13 years) at the time of surgery. Seven had tumours involving the distal femur while 2 had tumours involving the proximal tibia. There were no cases of local recurrence. Four of the 9 patients died from metastatic disease, the 5 surviving patients have no evidence of disease, and the average follow-up for survivors was 13.2 years. The average active range of motion for the knee joint was 96º (range, 50º to 130º). The average Musculoskeletal Tumour Society (MSTS) score was 26.3 (range, 23 to 30). Conclusion: We have observed this technique of limb salvage offers satisfactory limb function with long-term follow-up.

Ann Acad Med Singapore 2014;43:499-505

Keywords: Limb salvage, Malignant bone tumours

Introduction

Osteosarcoma is the most common primary malignant bone tumour in children. The most frequently affected joint is the knee, when tumours arise from the distal femur and proximal tibia.[1] Limb salvage is now widely accepted as an alternative to amputation to achieve local control of the tumour,[2,3] and the feasibility of limb salvage is dependent on tumour biology, anatomical site, age and socioeconomic factors.

In children, limb salvage is compounded with the challenges of shortening, bone and joint remodeling and high functional demands of active children.[4] The ultimate aim for reconstruction is the restoration of a mobile knee joint that is stable and painless. With the improved survival rates from chemotherapy, reconstructive techniques should also be durable and long lasting, if possible, for the child's entire lifespan. In the reconstruction following resections for osteosarcoma around the knee joints of children, many centres have advocated methods such as rotationplasty,[5,6] use of a growing prosthesis,[7-9] allografts,[10] epiphyseal distraction,[11] and distraction osteogenesis.[12] We have adopted a biological approach using a technique developed by the senior author.[13] The patient's native knee joint (including the epiphysis or physis) was preserved. Large bony defects were bridged by fibula grafts supplemented by autoclaved bone grafts infused with bone marrow in order to achieve immediate stability, early weight bearing and rehabilitation.

[1]Department of Hand and Reconstructive Microsurgery, National University Hospital, Singapore
[2]Yong Loo Lin School of Medicine, National University of Singapore, Singapore
Address for Correspondence: Dr Mark E Puhaindran, Department of Hand and Reconstructive Microsurgery, National University Hospital, 1E Kent Ridge Road, Level 11, NUHS Tower Block, Singapore 119228.
Email: mark_e_puhaindran@nuhs.edu.sg

We conducted this retrospective review of patients children with osteogenic sarcoma of the distal femur and proximal tibia that were treated at our institution over the past 20 years in order to assess the long-term functional outcomes and durability of this technique.

Materials and Methods

A retrospective case note review of children with osteogenic sarcoma involving the distal femur or proximal tibia who were treated at our institution was done. Patients aged 13 years and below at the time of surgery who had undergone a limb salvage procedure that preserved the knee joint were included. Those who underwent primary amputation or arthrodesis of the knee joint were excluded. Assessment of the patients were done during clinic reviews, and findings presented are based on the latest visits. For patients that had succumbed to disease, the best scores were taken and recorded.

Functional assessment was done using the Musculoskeletal Tumour Society (MSTS) score,[14] looking at 6 categories of pain, function, emotional acceptance, use of supports for walking and gait. A score of 0 to 5 was assigned to each category, with a score of 5 indicating the best function. The score was then added, with the highest possible score of 30. The active range of motion of the knee and limb length discrepancy were measured. For the surviving patients, we also asked their leisure activities, and noted the most physically demanding of these activities. Limb length discrepancy was also recorded, as well as the modifications required for coping with it.

Surgical Technique

All surgeries were performed by the senior author. The main criteria for joint preservation was the absence of intra-articular extension of the tumour on imaging, and the absence of an effusion. A good tumour response to preoperative chemotherapy was also essential for patients where the resection margin was expected to be close. This was assessed clinically by a decrease in the size of the swelling and pain from the tumour, and radiologically by increased ossification of the tumour seen on x-ray, decreased uptake on bone scan and a decrease of the oedema around the tumour on MRI.

In all cases, x-rays and MRI scans of the limbs and bone scans and computed tomography (CT) scans of the thorax were done before biopsy and after preoperative chemotherapy. CT scans of the legs were also done when necessary. Detailed imaging was essential to exclude trans-physeal and intra-articular extension (Fig. 1). At times, the margin of surgical resection had to be close to the tumour margin in order for the articular cartilage, sub-chondral

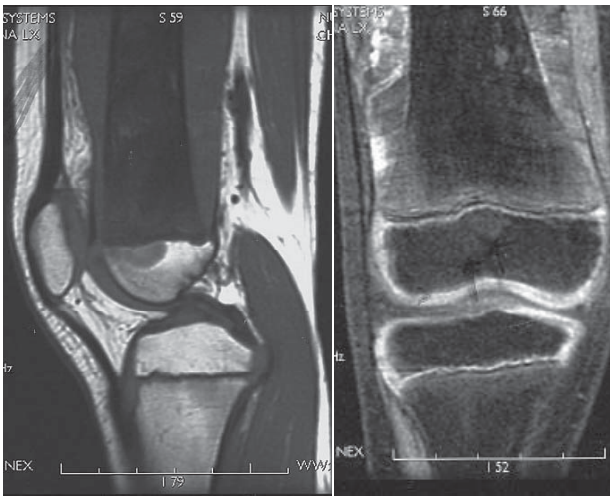

Fig. 1. MRI of the distal femur showing trans-physeal extension of the tumour (Patient 5).

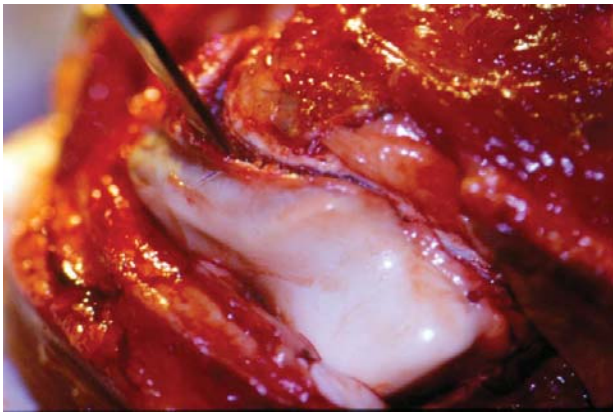

Fig. 2. Photograph showing resection of the distal femur performed through the subchondral bone using an osteotome (Patient 5).

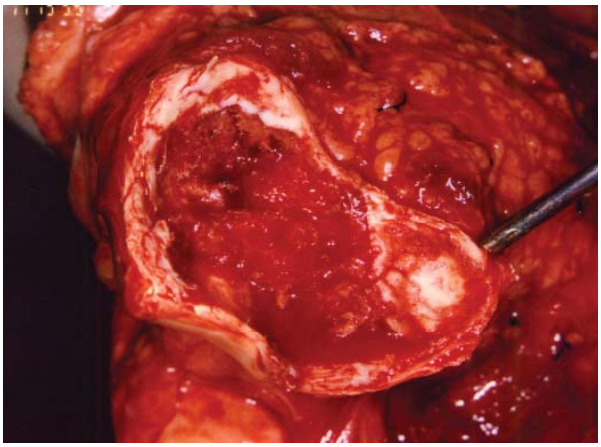

Fig. 3. Photograph showing the preserved subchondral bone and articular cartilage (Patient 5).

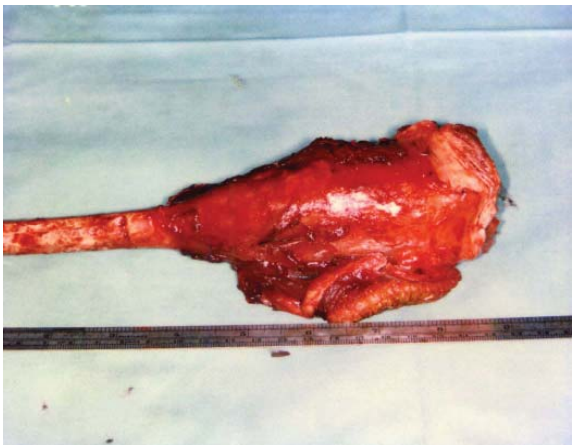

Fig. 4. Photograph showing the resected specimen. The tumour is then removed from the specimen on a separate table and the cortical bone autoclaved (Patient 5).

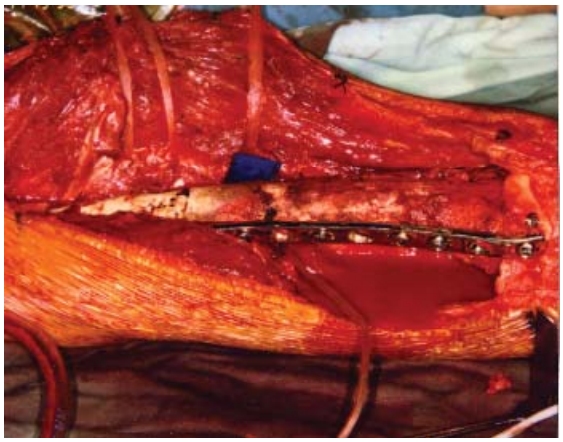

Fig. 5. Photograph showing the autoclaved bone with internal fixation done (Patient 5).

bone and ligaments to be preserved (Fig. 2).

At the start of surgery, iliac crest cortico-cancellous graft as well as bone marrow was harvested and stored. The donor site was then closed and dressed and re-draping was done. In patients with distal femur tumours, the fibular graft was harvested next and left on its vascular pedicle in situ. The ipsilateral fibular was used so that, in the event that the tumour recurred locally and amputation was required, there would be no donor morbidity affecting the contralateral normal limb.

Resection of the tumour was then performed, with the donor site sealed off. In proximal tibia lesions, resection was done prior to mobilisation of the ipsilateral fibular. Peri-articular resection was often performed using an osteotome (Fig. 2), allowing preservation of the articular cartilage, subchondral bone and ligaments that are critical to maintaining joint integrity and stability (Fig. 3).

The resected specimen was then brought to a separate table where the tumour and soft tissue were removed from the specimen and sent for histological assessment (Fig. 4). Sharp dissection was done using a knife to remove the soft tissue, while an osteotome was used to remove the osseous component of the tumour from the surface of the cortical bone. The bone was then placed in an autoclave and autoclaved at 132 degrees centigrade for 10 minutes before being removed. The harvesting of the fibular graft was then completed as the autoclaved graft cooled and closure of the donor site performed.

The cooled autoclaved graft was then infused with the harvested bone marrow and rigid internal fixation performed (Fig. 5). Fixation of the subchondral bone was always challenging, and at times had to be done using a combination of screws and staples (Figs. 6 and 7). The fibular graft was

Fig. 6. Postoperative x-ray showing the fixation done for a distal femur tumour (Patient 5).

Fig. 7. Postoperative x-ray showing the fixation done for a proximal tibia tumour (Patient 8).

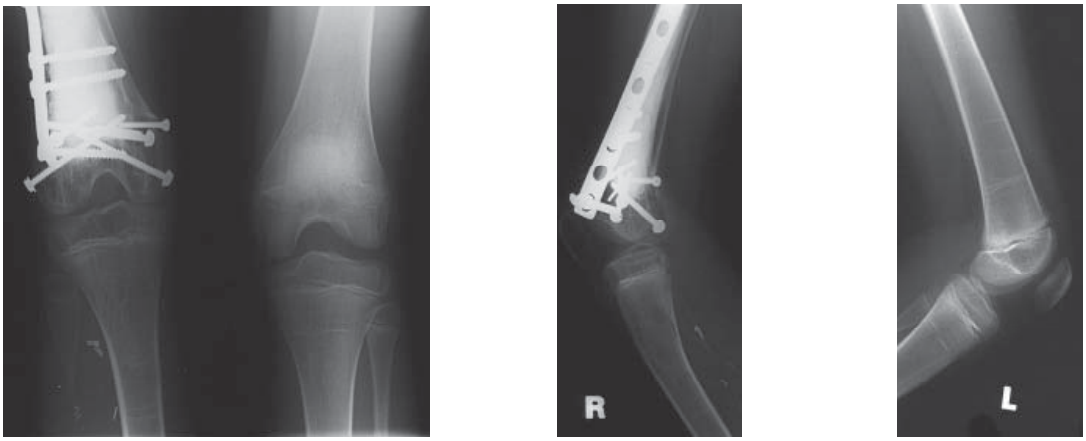

Fig. 8. X-rays taken 5 years following surgery showing continued development of the right knee joint despite sacrifice of the physis (Patient 5).

Fig. 9. X-ray showing hypertrophy of the vascularised fibular graft with incorporation of the autoclaved graft with the host bone, together with a photograph showing the range of motion of the knee joint (Patient 3).

inset into a trough and fixed with screws proximally and distally. Microsurgical anastomosis was performed and the wound closed. We did not harvest the fibular graft with a skin paddle and assessment of viability was done with a bone scan at postoperative day 5. A backslab was then placed and converted to a full cast after one week. Protected weight bearing was allowed in the cast and full weight bearing only after bony fusion was seen at both ends. Chemotherapy was recommenced within 3 weeks of surgery. Those with lung metastases underwent thoracotomy and excision of the pulmonary metastases soon after the limb salvage procedure.

There were variations in the technique used in 3 patients. In patients 1 and 7, non-vascularised fibular grafts were used as it was felt that the good muscle bed could revascularise and support the graft.[15] In patient 6, no autoclaved graft was used as it was too badly destroyed by the tumour and a vascularised fibular epiphyseal transfer was done instead to allow for growth.

Results

Nine patients were identified, 3 males and 6 females, and their average age was 10.0 years (range, 7 to 13 years) at the time of surgery. Seven of the patients had tumours involving the distal femur while 2 had tumours involving the proximal tibia. Also, 7 of them had Stage IIb disease while 2 had lung metastases at the time of diagnosis (1 distal femur, 1 proximal tibia).

There were no cases of local recurrence. Four out of the 9 patients died from metastatic disease, and the 5 surviving patients have no evidence of disease. The average follow-up from the time of surgery for survivors is 13.2 years (shortest 12 years, longest 16 years).

The average length of bone resected was 23.5 cm (range, 18.5 to 35 cm). The physis could be preserved in only one patient because it was involved with the tumour in the other patients. The largest limb length discrepancy was 10 cm, and this occurred in the 2 youngest patients with distal

Table 1. Patient Summary

No.	Age (years)	Sex	Site	Stage	Resection length	Growth plate	Surgery	Time to FWB	20 Procedures	Follow-up	Local recurrence	Oncologic outcomes	Limb shortening	MSTS score	Knee AROM	Recreational activities
1	13	F	DF	IIb	32 cm	Resected	NVFG + ABG	7 months	Nil	3 years	Nil	DOD 3 years	1 cm	25/30	0 – 900	NA
2	12	M	DF	IIb	18.5 cm	Preserved	VFG + ABG	11 months	Nil	12 years	Nil	CDF	Nil	30/30	0 – 1300	Running, basketball
3	11	F	DF	IIb	20 cm	Resected	VFG + ABG	9 months	Nil	18 months	Nil	DOD 18 months	Nil	30/30	0 – 1300	NA
4	8	F	DF	IIb	20 cm	Resected	VFG + ABG	9 months	Nil	4 years	Nil	DOD 4 years	6 cm	24/30	0 – 900	NA
5	7	F	DF	IIb	21 cm	Resected	VFG + ABG	9 months	Nil	12 years	Nil	CDF	10 cm	23/30	0 – 500	Walking
6	7	M	DF	IIb	21 cm	Resected	VFG (epiphyseal transfer)	17 months	1) Bone grafting, fixation revision 2) Limb lengthening	13 years	Nil	CDF	2.5 cm	24/30	0 – 600	Walking, kite flying
7	7	F	DF	III	24 cm	Resected	NVFG + ABG	24 months	Nil	6 years	Nil	DOD 6 years	10 cm	23/30	0 – 600	NA
8	13	M	PT	IIb	28 cm	Resected	VFG (pedicled) + ABG	11 months	Nil	13 years	Nil	CDF	1 cm	30/30	0 – 1300	Football, running
9	12	F	PT	III	27 cm	Resected	VFG (pedicled) + ABG	9 months	Sequestrectomy of infected ABG	16 years	Nil	NED (Metx)	Nil	28/30	0 – 1300	Walking, running

DF: Distal femur; PT: Proximal tibia; VFG: Vascularised fibular graft; NVFG: Non-vascularised fibular graft; ABG: Autoclaved bone graft; DOD: Died of disease; CDF: Continuously disease free; NED: No evidence of disease; Metx: Excision of metastasis; FWB: Full weight bearing; MSTS: Musculoskeletal Tumor Society Score; AROM: Active range of motion; NA: Not applicable

femur tumours that had the physis resected. However, we observed that while longitudinal growth is lost when the physis is sacrificed, latitudinal growth of the joint was still seen (Fig. 8).

The average active range of motion for the knee joint was 96º (range 50º to 130º) (Fig. 9). The average MSTS score was 26.3 (range, 23 to 30). Three of the 5 surviving patients were able to participate in running activities, while the others were able to swim and walk with a shoe raise, albeit with an altered gait. Some of the complications that we encountered included deep infection of the autoclaved graft in patient 9. There were fractures of the bone grafts in patients 6 and 7. Patient 6 was treated with revision of the fixation and bone grafting, while patient 7 was treated conservatively with prolonged casting. This resulted in a delay in return to full weight bearing for both patients. A summary of the results is presented in Table 1.

Discussion

We have found that biological reconstruction using autoclaved bone grafts infused with bone marrow that were reinforced with fibular grafts is a viable option in children with high grade osteosarcoma around the knee. It provides immediate stability, allowing early weight bearing and early rehabilitation. This construct is also durable, with none of our patients requiring revision surgery due to mechanical failure of the construct.

The disadvantage of this study is that it is a retrospective review of a small number of patients treated in a single centre. There were also different chemotherapy regimes used and not all patients underwent the exact same surgical procedure. However, the long period of follow-up has allowed us to demonstrate the durability of this construct.

Biological reconstruction is often technically more demanding then prosthetic replacement. Time to full weight bearing is longer than prosthetic replacement. However, once it works, the construct can be durable and further revision may not be required. Use of autoclaved bone grafts has the advantages of low cost, no rejection because the patient's own tissue is used, exact anatomical matching and no donor morbidity. The autoclaved bone, when infused with bone marrow, shows good bony union.[13] Over time, the fibular hypertrophies and incorporates with the autoclaved graft (Fig. 4). However, when there is bone loss and extensive destruction in the pathological bone, then autogenous bone graft should be used to bridge and fill this area of bone loss. Two of our patients developed fractures of the graft, with one of our patients requiring revision of the construct and bone grafting (Patient 6), and another (Patient 7) requiring prolonged treatment with a cast. Patient 7 had a non-vascularised fibular graft placed and on retrospect, a vascularised fibular should have been used instead. Patient 9 developed delayed deep infection of autoclaved tibia bone graft due to a prominent screw. She required repeated debridements and sequestrectomy of the infected autoclaved graft. However, the presence of vascularised graft allowed preservation of limb despite the infection due to its vascularity that made it resistant to infection.[16] It eventually underwent hypertrophy and took over the weight bearing from the infected autoclaved graft that was removed.

This technique that we have developed has several advantages over implant arthroplasty—it does not require revision once bone healing is completed and it is affordable in many developing countries, avoiding the costs of megaprosthetic implants.[7-9] It avoids the progressive wear and failure of osteoarticular allografts,[10] and while rotationplasty does result in good functional outcomes,[5,6] it is not culturally well accepted in our country. Other biological reconstructive techniques like distraction osteogenesis have also shown good results, though we have not adopted it in our practice because the physis has been shown as an inadequate barrier to local tumour spread,[17] and there might be a higher risk of local tumour recurrence. In preserving the native joint, our margins of resection will be closer when compared with intra-articular resections, hence we have had to carefully selected cases for whom it was technically feasible and who had what we assessed was a good response to preoperative chemotherapy. We have managed to achieve negative resection margins and avoid local recurrence in this group of patients.

When the physis is preserved, the limb can be expected to grow. When surgery is done towards the end of the growing period, limb length equality can be maintained despite sacrifice of the physis, while a short discrepancy is easily tolerated and managed with a shoe raise. However, when the distal femur physis is sacrificed in younger patients, the final limb length discrepancy can be significant. We have observed that while longitudinal growth is lost when the physis is sacrificed, circumferential growth of the joint is still seen. Distraction osteogenesis can be done at the end of the growing period to correct significant limb length discrepancies.

Conclusion

We have observed this technique of limb salvage offers satisfactory limb function with long-term follow-up. One disadvantage is that this is technically demanding with resection performed close to the tumour margin, hence good preoperative assessment and good response to chemotherapy is essential. The use of vascularised fibular grafts and application of microsurgical anastomosis often poses a great challenge to many orthopaedic oncologists, but with an experienced team, this technique can be readily applicable in most orthopaedic oncology centres.

REFERENCES

1. Unni KK (ed): Dahlin's Bone Tumors:General Aspects and Data on 11,087 Cases ed 5. Philadelphia, PA: Lippincott-Raven, 1996.
2. Simon MA, Aschliman MA, Thomas N, Mankin HJ. Limb-salvage treatment versus amputation for osteosarcoma of the distal end of the femur. J Bone Joint Surg Am 1986;68:1331-7.
3. Rougraff BT, Simon MA, Kneisl JS, Greenberg DB, Mankin HJ. Limb salvage compared with amputation for osteosarcoma of the distal end of the femur. A long-term oncological, functional, and quality-of-life study. J Bone Joint Surg Am 1994;76:649-56.
4. Futani H, Minamizaki T, Nishimoto Y, Abe S, Yabe H, Ueda T. Long-term follow-up after limb salvage in skeletally immature children with a primary malignant tumor of the distal end of the femur. J Bone Joint Surg Am 2006;88:595-603.
5. Hillmann A, Hoffmann C, Gosheger G, Krakau H, Winkelmann W. Malignant tumor of the distal part of the femur or the proximal part of the tibia: endoprosthetic replacement or rotationplasty. Functional outcome and quality-of-life measurements. J Bone Joint Surg Am 1999;81:462-8.
6. Hanlon M, Krajbich JI. Rotationplasty in skeletally immature patients. Long-term followup results. Clin Orthop Relat Res 1999;358:75-82.
7. Schindler OS, Cannon SR, Briggs TW, Blunn GW. Stanmore custom-made extendible distal femoral replacements. J Bone Joint Surg Br 1997;79:927-37.
8. Eckardt JJ, Kabo JM, Kelley CM, Ward WG Sr, Asavamongkolkul A, Wirganowicz PZ, et al. Expandable endoprosthesis reconstruction in skeletally immature patients with tumors. Clin Orthop Relat Res 2000;373:51-61.
9. Henderson ER, Pepper AM, Marulanda G, Binitie OT, Cheong D, Letson GD. Outcome of lower-limb preservation with an expandable endoprosthesis after bone tumor resection in children. J Bone Joint Surg Am 2012;94:537-47.
10. Muscolo DL, Ayerza MA, Aponte-Tinao LA, Ranalletta M. Use of distal femoral osteoarticular allografts in limb salvage surgery. J Bone Joint Surg Am 2005;87:2449-55.
11. San-Julian M, Dölz R, Garcia-Barrecheguren E, Noain E, Sierrasesumaga L, Cañadell J. Limb salvage in bone sarcomas in patients younger than age 10: a 20-year experience. J Pediatr Orthop 2003;23:753-62.
12. Tsuchiya H, Abdel-Wanis ME, Sakurakichi K, Yamashiro T, Tomita K. Osteosarcoma around the knee. Intraepiphyseal excision and biological reconstruction with distraction osteogenesis. J Bone Joint Surg Br 2002;84:1162-6.
13. Taguchi Y, Pereira BP, Kour AK, Pho RW, Lee YS. Autoclaved autograft bone combined with vascularized bone and bone marrow. Clin Orthop Relat Res 1995;320:220-30.
14. Enneking WF, Dunham W, Gebhardt MC, Malawar M, Pritchard DJ. A system for the functional evaluation of reconstructive procedures after surgical treatment of tumors of the musculoskeletal system. Clin Orthop Relat Res 1993;286:241-6.
15. Krieg AH, Hefti F. Reconstruction with non-vascularised fibular grafts after resection of bone tumours. J Bone Joint Surg Br 2007;89:215-21.
16. Low CK, Pho RW, Kour AK, Satku K, Kumar VP. Infection of vascularized fibular grafts. Clin Orthop Relat Res 1996;323:163-72.
17. Enneking WF, Kagan A 2nd. Transepiphyseal extension of osteosarcoma: incidence, mechanism, and implications. Cancer 1978;41:1526-37.