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ORIGINAL PAPER

Clinical outcomes of Kyocera Modular Limb Salvage system after resection of bone sarcoma of the distal part of the femur: the Japanese Musculoskeletal Oncology Group study

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Abstract
Purpose The Japanese Musculoskeletal Oncology Group have developed an original prosthesis called the Kyocera Modular Limb Salvage system (KMLS system). This prosthesis has a semi-rotating hinge joint and is particularly designed for people with an Asian body type. The metallic parts of the prosthesis are made entirely of titanium alloy. The purpose of this study is to evaluate the clinical outcomes of treatment using this system following tumour resection of primary bone sarcoma of the distal femur.
Methods Between 2002 and 2010, 82 patients with primary bone sarcomas of the distal femur were treated. Seventeen patients underwent stem cementation, while 65 patients were treated with cementless prostheses. The mean follow-up period after surgery was 61 months.
Results Complications were observed in 28 of the 82 patients. Forty-one complications occurred in these 28 patients. Thirteen prostheses (16 %) required revision surgery due to complications, including five cases of stem breakage, three deep infections, three cases of aseptic loosening, one case of displacement of the shaft cap and one case of breakage of the tibial tray. The five-year overall prosthetic survival rate was 80.0 %. Four of the 82 patients underwent subsequent amputation due to local recurrence. The five-year limb salvage rate was 94.5 %. The mean function score according to the scoring system of the Musculoskeletal Tumour Society was 21.8 points (72.5 %).

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Conclusions Although further follow-up is required to determine the performance, this prosthesis is considered to be satisfactory for reconstruction of the distal femur after resection of bone sarcoma.

Keywords Prosthesis · Bone sarcoma · Distal femur

Introduction

Over the last few decades, limb salvage has become the standard procedure for treating the majority of patients with bone sarcomas of the extremities, as there have been considerable advances in the management of such patients due to improved imaging techniques, neoadjuvant chemotherapy, radiotherapy planning, delivery and surgical expertise [1]. The distal femur is a common site for primary bone sarcoma [2]. However, most types of prostheses are designed for the Caucasian body type and are frequently too large and heavy for Asian-Pacific patients. Therefore, the Japanese Musculoskeletal Oncology Group (JMOG) have developed an original prosthesis (KYOCERA PHK III) which requires bone cement to fix the femoral stem [3]. Matsumine et al. [3] investigated the short-to-medium term follow-up clinical results of this prosthesis and demonstrated that aseptic loosening is the primary reason for failure of cemented stems after long-term follow-up [4, 5]. Moreover, some authors have suggested that the cementless-type of prosthesis reduces the risk of fat embolism or venous thromboembolic disease [6–8]. Therefore, the JMOG developed a new cementless stem in addition to PHKIII series, and brought out the prosthesis as the Kyocera Modular Limb Salvage (KMLS) system in 2002. In the KMLS system, we can make a choice between cemented and cementless-type stem according to the situation of the patients. The purpose of this study was to evaluate the clinical outcomes of treatment with the KMLS system following tumour resection of bone sarcoma of the distal femur in 82 Japanese patients.

Patients and methods

Patients

Between 2002 and 2010, 82 patients with primary bone sarcoma of the distal femur were treated by surgeons of the JMOG using the KMLS system at 19 institutions.

The records of all patients were collected using a questionnaire administered to the members of the JMOG. The collected data included the demographic details, histological diagnosis, surgical stage, adjuvant therapy, surgical methods, size of the prosthetic components, complications, postoperative limb function and oncological outcome at the final follow-up. Patients treated with the KMLS system for revision surgery were excluded from this study. There were 38 males and 44 females, with a mean age of 32 years. The primary malignant bone tumours included 67 conventional osteosarcomas, six chondrosarcomas, five parosteal osteosarcomas and four others. The surgical stage according to the Enneking surgical staging system [9] was as follows: stage IA, one patient; stage IB, one patient; stage IIA, nine patients; stage IIB, 62 patients; stage IIIA, two patients; stage IIIB, seven patients. Chemotherapy was administered in 66 patients and irradiation was administered in five patients. Informed consent was obtained from all patients according to the guidelines of the institutional ethics review board.

Procedure for tumour resection and reconstruction

Wide tumour resection was performed in 80 patients, and marginal tumour resection was performed in two patients. Extra-articular resection was performed in 16 patients, while intra-articular resection was performed in 66 patients. The length of the resected femur varied from 11 cm to 30 cm, with a mean size of 16 cm. More than three segments of the quadriceps femoris muscle were resected in 17 patients.

Seventeen patients underwent stem fixation using cement-type femoral components and bone cement, while 65 patients were treated using cementless-type stem. A local musculocutaneous flap was required in 14 patients and a free vascularised musculocutaneous flap was required in three patients to cover defects in the soft tissue and skin following prosthetic reconstruction. The mean follow-up period after surgery was 61 months.

Prosthesis

The KMLS Total Knee system is an original prosthesis of JMOG and is designed especially for people with an Asian body type (Fig. 1). This prosthesis has a semi-rotating hinge joint, and the metallic parts are made entirely of titanium alloy. The general architecture of the prosthesis including semi-rotating hinge mechanism is exactly the same as PHK III [3]. But, an alternative choice can be made between the cement-type femoral stem and the cementless-type femoral stem according to the situation of the patients in the KLS system. The cementless-type femoral stem component has three unique partial-holes with screw thread and a side plate with three screw holes. To gain initial implant fixation, three side bolts must be inserted through the screw holes of the side plate. The interface of femoral stem component is processed by porous proofing to promote bone ingrowth. The diameter of the femoral stem is 11–13 mm for the cement-type and 12–15 mm for the cementless type.

Fig. 1 The detailed features of the KMLS system. *Left* Cement-type femoral stem and cementless-type femoral stem and prosthesis. *Right* Three unique partial-holes and a side plate with three screw holes of the cementless-type femoral stem component

Statistical analysis

The statistical associations between the clinicopathological factors were evaluated using the Mann-Whitney U-test for quantitative data and the chi-square test for qualitative data. The duration of survival was defined as the interval between the date of initial treatment for the primary tumour and the date of death. Patients who died from non-tumour-related causes were uncensored at the time of death in this study. The prosthesis survival rate was calculated as the time from surgical reconstruction using the KMLS system to revision surgery due to prosthetic failure. Prosthetic failure was defined as replacement of any part of the prosthetic components, including minor parts of the prosthesis, due to local recurrence, polyethylene bushing failure, breakage of the prosthesis, aseptic loosening or infection. The limb salvage rate was calculated as the time from surgical reconstruction using the KMLS system to amputation. Survival curves were constructed using the Kaplan-Meier method. The log-rank test was used to compare the survival of the patients. A value of $p < 0.05$ was considered to be significant in all statistical analyses.

Results

At the time of the review, 58 patients were alive and free of disease, four were alive with disease, 19 had died of disease and one had died of another disease. The five-year overall survival rate was 74.8 %. Eleven patients developed local recurrence. Four patients underwent amputations for local recurrence. The remaining seven patients underwent re-excision of the recurrent tumours without amputations.

Complications were observed in 28 of the 82 patients (Table 1). Forty-one complications occurred in these 28 patients. Intraoperatively, failed insertion of one side of the bolt was found in nine patients and a fracture occurred in the proximal part of femur when the femoral stem was inserted in one patient. Postoperatively, major complications included infection in seven patients, followed by aseptic loosening in five patients, stem breakage in five patients, patella tracking abnormalities in four patients and loosening or breakage of side bolt in three patients. Thirteen prostheses (16 %) required revision surgery due to complications, including five cases of stem breakage, three deep infections, three cases of aseptic loosening, one case of displacement of the shaft cap and one case of breakage of the tibial tray (Table 2). While cement-type femoral stem breakage occurred at the bone–prosthesis junction, cementless-type femoral stem breakage occurred through the distal fixation hole. The five-year overall prosthetic survival rate was 80.0 % (Fig. 2). The log-rank test showed no statistical differences between the prosthetic survival rate and the following factors: patient age, gender, diameter of the femoral stem, stem fixation (cemented stem or cementless stem), resection of the joint capsule (intra-articular resection or extra-articular resection) and the administration of chemotherapy (Table 3).

The five-year limb salvage rate was 94.5 % (Fig. 3). Four of the 82 patients underwent subsequent amputation due to local recurrence. The mean function score according to the classification system of the Musculoskeletal Tumour Society [10] was 21.8 points (72.5 %) (Table 4).

Table 1 Complications in 82 patients

Complications	n (%)
Intraoperative complications	
Failed insertion of side bolt	9 (11)
Fracture	1 (1)
Postoperative complications	
Infection	7 (9)
Aseptic loosening	5 (6)
Stem breakage	5 (6)
Patella tracking abnormality	4 (5)
Loosening or breakage of side bolt	3 (4)
Skin necrosis	2 (2)
Fracture	2 (2)
Peroneal nerve palsy	1 (1)
Haematoma	1 (1)
Metal allergy	1 (1)

Table 2 Details of patients who underwent revision surgery

Case	Age/ gender	Primary tumour	Type of stem component (stem diameter)	Cause of revision	Time to revision (months)
1	13/F	Osteosarcoma	Cementless (12 mm)	Deep infection	26
2	18/M	Osteosarcoma	Cementless (12 mm)	Aseptic loosening	47
3	16/F	Osteosarcoma	Cement (11 mm)	Deep infection	54
4	40/F	Parosteal OS	Cementless (12 mm)	Deep infection	32
5	12/F	Osteosarcoma	Cement (11 mm)	Breakage of tibial tray	110
6	17/F	Osteosarcoma	Cementless (12 mm)	Aseptic loosening	60
7	38/F	Parosteal OS	Cementless (12 mm)	Stem breakage	40
8	22/F	Osteosarcoma	Cementless (12 mm)	Stem breakage	11
9	62/M	Fibrosarcoma	Cement (12 mm)	Aseptic loosening	48
10	16/F	Osteosarcoma	Cementless (12 mm)	Stem breakage	18
11	40/F	Osteosarcoma	Cementless (12 mm)	Dislocation of shaft cap	19
12	18/M	Osteosarcoma	Cementless (13 mm)	Stem breakage	22
13	14/F	Osteosarcoma	Cement (10 mm)	Stem breakage	59

F female, M male, OS osteosarcoma

Discussion

Limb salvage surgery has replaced amputation as the first-line treatment for primary bone sarcoma of the distal femur [11, 12]. This transition has been achieved without adversely affecting survival, primarily owing to improvements of chemotherapy [11, 12]. However, the complication rate after prosthetic replacement remains high. Thus, we developed a novel type of tumour prosthesis system, the "KMLS system", which can be used for reconstruction of distal femoral defects following tumour resection. In this study, we evaluated the prosthetic and functional outcomes of the newly developed system, and showed that this prosthesis is satisfactory for reconstruction of the distal femur after the resection of bone sarcoma.

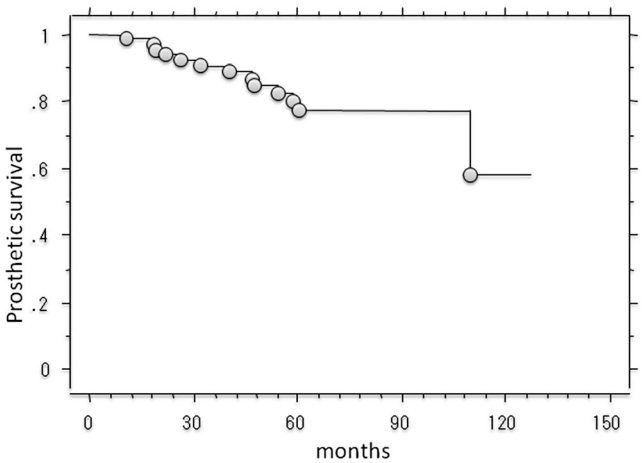

Fig. 2 Kaplan-Meier curve showing prosthetic survival rate in the 82 patients

In the KMLS system, a choice can be made between the cement-type femoral stem and the cementless-type femoral stem according to the situation of the patients. Nine of 65 patients who were treated using cementless-type femoral stem had failed insertion of one side bolt intraoperatively. The cementless-type femoral stem component has three unique partial-holes and a side plate with three screw holes. To gain initial implant fixation, three side bolts must be inserted through the bolt holes of the side plate. We noticed that there are two causes which prevent screw insertion to femoral stem. The first cause is that bone debris produced by the drilling prevents the insertion of side bolt into the partial-holes of the stem. Because the partial-holes of the stem tend to accumulate bone debris compared to through-holes, scrubbing of the drill hole before bolt insertion is necessary. The second cause is that bending of the side plate created by the insertion of the first and second side bolt sometimes prevents the insertion of the third bolt, especially when the patient has a thin femoral cortex. Thus, it is important to fasten the stem component bit by bit and evenly with the side bolts.

Our results showed that, overall, 16 % of the patients required revision of their prosthesis. In this study, the prosthetic survival rate of 80.0 % at five years is generally in keeping with the findings of most reports published in the literature [3, 5, 11, 13, 14]. Directly comparing the survival results of the current series to those of these previous studies is difficult due to the heterogeneity of the patient population. However, our results are comparable to those previously reported in the literature.

Revision for stem breakage was required in five cases (6.1 %) within five years after the primary surgery. Stem breakage occurred in one ten millimetre cement stem, no 11-

Table 3 The relationship between prosthetic survival and patient characteristics

Variables		n	Five-year survival (%)	p value
Age	≥ 20	43	83.0	0.66
	< 20	39	78.0	
Gender	Male	38	87.9	0.12
	Female	44	73.6	
Administration of chemotherapy	Yes	66	78.6	0.86
	No	16	80.1	
Resection of quardriceps femoris	≥ 3 segment	17	49.5	0.13
	< 3 segment	65	84.9	
Stem diameter	≥ 13 mm	22	94.4	0.1
	<13 mm	60	74.8	
Fixation of femoral stem	Cement	17	59.3	0.24
	Cementless	65	84.2	
Resection of joint	Intra-articular	66	82.6	0.82
	Extra-articular	16	71.6	

to 13-mm cement stems, three 12-mm cementless stems, one 13-mm cementless stem and no 14-mm stems. This suggests that smaller stems are more subject to fatigue stress regardless of whether the stem was fixed with or without cement. Capanna et al. reported that six of 95 cases of femoral stem breakage occurred at an average of 43 months [15]. Their system involves an intramedullary stem with two lateral flanges to allow the passage of a total of six screws through the stem and cortex. They suggested that consideration should be given to using the largest possible stem in order to reduce the possibility of stem breakage. Although the KMLS system currently excludes the ten millimetre cement stem component, further careful follow-up is needed for the remaining smaller stems. Concerning cementless-type stem, stem breakage occurred through the most distal partial-holes, suggesting the convergence of the mechanical stress at the most distal partial-holes. Recently, we have started to improve the femoral stem design to avoid stem breakage. The new cementless femoral stem will employ the press fit system with taper shape design.

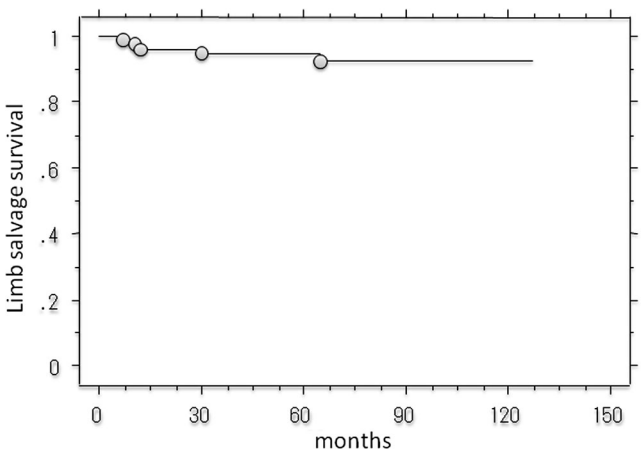

Fig. 3 Kaplan-Meier curve showing limb salvage rate in the 82 patients

In our study, five prostheses (6 %) were identified as radiographically loose, and three of the five loose prostheses required revision surgery. Aseptic loosening remains a major problem after prosthetic replacement of large bone defects. Some authors favour the use of cementless fixation, reporting the incidence of aseptic loosening in 7.7–11 % of cases [14, 16, 17]. Our results show that the KMLS system exhibits stable performance, although further long-term follow-up is needed.

The rate of infection was 8.5 % in our series and ranges from 8 % to 15 % in previous reports [18]. Providing adequate soft tissue coverage after reconstruction is one of the most critical factors for reducing infection. Insufficient muscle coverage of the prosthesis can be improved with vascularised muscle or free muscle flap transfer.

Amputation following prosthetic replacement was required in four patients (4.9 %). In all cases, amputation was needed due to local recurrence of disease. The risk of a patient requiring amputation is related to the rate of local recurrence as well as the risk of deep infection [12]. In our cases, revision surgery was needed in three patients due to deep infection, although amputation was not performed.

The mean Enneking score of 72.5 % observed in our study indicates a functionally acceptable outcome that is comparable to the results reported in the literature, ranging from 63 % to 88 % [18]. The patients had better scores for pain (mean, 4.3), with a reduced function (mean, 3.1). This may be because the patients often focused their emotional and physical efforts on saving the extremity due to the fear of disrupting the prosthesis [19].

In conclusion, the KMLS system is considered to be a satisfactory prosthesis for reconstruction of the distal femur after resection of bone sarcoma. However, further follow-up is required to determine the performance of this system. In

Table 4 Functional score after surgery

Measure	Mean score	Number of patients (%)		
		Excellent (A score of 5)	Good (A score of 3 or 4)	Poor (A score of 0–2)
Pain	4.3	45 (59)	27 (36)	4 (5)
Function	3.1	13 (17)	44 (58)	19 (25)
Acceptance	3.4	18 (24)	43 (57)	15 (19)
Support	3.5	36 (47)	18 (24)	22 (29)
Ability	3.9	34 (45)	37 (49)	5 (6)
Gait	3.5	18 (24)	48 (63)	10 (13)

particular, careful follow-up is needed for the smaller cementless stems due to the risk of stem breakage.

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Conflict of interest statement We declare that we have no conflicts of interest.

References

1. Torbert JT, Fox EJ, Hosalkar HS, Ogilvie CM, Lackman RD (2005) Endoprosthetic reconstructions. Results of long-term follow up of 139 patients. Clin Orthop Relat Res 438:51–59
2. Dofman HD, Czerniak B (1988) General considerations. In: Dorfman HD, Czerniak B (eds) Bone Tumors. CV Mosby, St Louis, pp 1–33
3. Matsumine A, Ueda T, Sugita T et al (2011) Japanese musculoskeletal oncology group. Clinical outcomes of the KYOCERA Physio Hinge total knee system type III after resection of a bone and soft tissue tumor of the distal part of the femur. J Surg Oncol 103:257–263
4. Horowitz SM, Lane JM, Otis JC, Healy JH (1991) Prosthetic arthroplasty of the knee after resection of a sarcoma in the proximal end of the tibia: a report of sixteen cases. J Bone Joint Surg Am 73-A: 286–293
5. Unwin PS, Cannon SR, Grimer RJ et al (1996) Aseptic loosening in cemented custom-made replacements for bone tumors of the lower limb. J Bone Joint Surg Br 78-B:5–13
6. Ereth MH, Weber JG, Abel MD et al (1992) Cemented versus noncemented total hip arthroplasty: embolism, hemodymanics, and intrapulmonary shunting. Mayo Clin Proc 67:1066–1074
7. Francis CW, Marder VJ, Evarts CM (1986) Lower risk of thromboembolic disease after total hip replacement with non-cemented than with cemented prostheses. Lancet 1:769–771
8. Kim YH, Suh JS (1988) Low incidence of deep-vein thrombosis after cementless total hip replacement. J Bone Joint Surg Am 70:878–882
9. Enneking WF, Spanier SS, Goodman MA (1980) A system for surgical staging of musculoskeletal sarcoma. Clin Orthop Relat Res 153:106–120
10. Enneking WF, Dunham W, Gebhardt MC et al (1993) A system for the functional evaluation of reconstructive procedures after surgical treatment of tumors of the musculoskeletal system. Clin Orthop 286: 241–246
11. Rougraff BT, Simon MA, Kneisl JS, Greenberg DB, Mankin HJ (1994) 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 76:649–656
12. Henderson ER, Pepper AM, Marulanda G, Binitie OT, Cheong D, Letson GD (2012) Outcome of lower-limb preservation with an expandable endoprosthesis after bone tumor resection in children. J Bone Joint Surg Br 94:537–547
13. Myers GJC, Abudu AT, Tillman RM, Grimer RJ (2007) Endoprosthetic replacement of the distal femur for bone tumours. Long-term results. J Bone Joint Surg 89:521–526
14. Mittermeyer F, Krepler P, Dominkus M et al (2001) Long-term follow up of uncemented tumor prostheses for the lower extremity. Clin Orthop Relat Res 388:167–177
15. Cappana R, Morris HG, Campanacci D, Del Ben M, Campanacci M (1994) Modular uncemented prosthetic reconstruction after resection of tumours of the distal femur. J Bone Joint Surg Br 76-B:178–186
16. Plotz W, Rechl H, Burgkart R et al (2002) Limb salvage with tumor endoprostheses for malignant tumors of the knee. Clin Orthop Relat Res 405:207–215
17. Gosheger G, Gebert C, Ahrens H, Streibuerger A, Winkelmann W, Hardes J (2006) Endoprosthetic reconstruction in 250 patients with sarcoma. Clin Orthop Relat Res 450:164–171
18. Hardes J, Gebert C, Schwappach A et al (2006) Characteristics and outcome of infections associated with tumor endoprostheses. Arch Orthop Trauma Surg 126:289–296
19. Hillmann A, Hoffmann C, Gosheger G, Krakau H, Winkelmann W (1999) 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 81-A:462–468