Clinical Outcome of Total Knee Megaprosthesis Replacement for Bone Tumors

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Introduction

Amputation used to be the most common treatment for malignant bone tumors. However, tremendous advances in medical therapy and surgical reconstruction techniques and materials over the last three decades have allowed for limb salvage in the majority of patients.

The most common malignant bone tumors are chondrosarcoma, osteosarcoma and Ewing's sarcoma [1]. Chondrosarcoma is a bone malignancy of adulthood, resistant to chemotherapy and radiotherapy; thus wide excision with negative margins is the suggested treatment option [1]. Osteosarcoma and Ewing's sarcoma mainly develop in children and young adults [1]. These pathologies frequently develop around the knee joint, as the distal femur and proximal tibia growth plate demonstrate a high growth rate [2, 3]. Both of these sarcomas are considered chemosensitive and most of the suggested treatment protocols include neoadjuvant chemotherapy followed by tumor wide resection and post operative chemotherapy based on the degree of tumor necrosis induced by chemotherapy [1].

Marcove was one of the pioneers of limb salvage for tumors around knee in the 1970s [4]. At that time, custom-made prostheses were used. After biopsy and tissue diagnosis of malignancy, 4–6 weeks were required for prosthesis manufacture and Rosen introduced the concept of preoperative chemotherapy in the waiting period [5].

Currently, for patients at skeletal maturity and with a primary malignant bone tumor around the knee, limb salvage is indicated when resection to negative margins can be achieved and remaining soft tissues are adequate for wound closure and function. Contamination of the knee synovial fluid with malignant cells, either from intra-articular extension of a malignant tumor or an intra-articular hematoma caused by a pathologic fracture or incorrect intra-articular biopsy, may be an indication for amputation. In such cases an alternative to above knee amputation is a Van Ness rotationplasty or an extra-articular knee resection [6–8]. For patients who have not reached skeletal maturity, limb salvage and reconstruction with an adult type mega-prosthesis can be performed when limb length discrepancy is anticipated to be less than 3 cm [3]. As distal femur or proximal tibia oncological resection sacrifices collateral ligaments, a degree of constraint is required in total knee mega-prosthesis. Initially tumor megaprostheses were cemented, custom made, with fixed hinge mechanisms. The

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principal mode of failure was the high rate of aseptic loosening [9].

In 1982, the Kotz Modular Femur Tibia Reconstruction (KMFTR) System was introduced. The KMFTR prosthesis used uncemented stems and a fixed hinge system. The next step in the evolution of knee megaprostheses was the rotating hinge mechanisms that compensated for ligamentous instability but allowed for knee rotation, resulting in better functional outcome and lower loosening rates [10–12]. Several studies have documented comparative oncological outcomes between limb salvage and amputation and limb salvage offers better functional outcome [13, 14]. Bernthal et al. evaluated 24 patients (7 proximal femoral replacements, 9 distal femoral replacements, and 8 proximal tibia replacements) in a gait laboratory at a mean of 13.2 years after their reconstruction [15]. Median O_2 consumption and walking speed among the endoprosthesis groups was not different from the control patients. Patients with proximal tibia replacements had reduced knee extension and flexion strength compared with patients in other reconstruction groups. All groups had an efficient gait and were active at home and in the community at a mean of 13.2 years after surgery.

Although endoprosthetic reconstruction for bone tumor defects allows for a functional limb, an increased number of complications are encountered. Unwin et al. in 1993 classified failure of tumor endoprosthesis as biological (infection), biomechanical (loosening and fracture) or mechanical (prosthesis breakage and servicing procedures such as change of bushings) [16]. A multicenter study in 2010 followed 2,174 skeletally mature patients who received a large endoprosthesis for tumor resection. Five modes of failure were identified and classified: soft-tissue failures (Type 1), aseptic loosening (Type 2), structural failures (Type 3), infection (Type 4), and tumor progression (Type 5). The relative incidences are significantly different and dependent on anatomic location [17].

There is debate over the most appropriate method for fixation of the medullary stems: cemented vs uncemented. Obviously, cemented stems offer the advantage of immediate stability

of the prostheses which allows for full weight bearing after soft tissue healing. Uncemented prostheses need protected weight bearing until osseointegration is achieved. However, patients with malignant bone tumors frequently receive prolonged chemotherapy regimens, develop quadriceps muscle atrophy after biopsy and protected weight bearing and may have limited life expectancy. On the other hand, first generation cemented megaprostheses had a high revision rate due to aseptic loosening with bone loss. Compress implants are newer designs which use a spring-loaded component that exerts continuous high compression forces, inducing bone hypertrophy at the bone–prosthesis interface [18, 19]. The functional results as well as the complications encountered for knee mega-prosthesis reconstructions are not the same for distal femur and proximal tibia bone resections. Indeed, endoprosthetic survival seems to be better for tumors of the distal femur compared to the distal tibia [9, 20].

Distal Femur Endoprostheses

Proximal tumors can be resected with an anterolateral or more commonly an anteromedial approach that facilitates major vessel identification and protection (Fig. 20.1). Malignant bone tumor can invade the cortex and extend to soft tissue (extra-compartmental tumors T2, on the Enneking classification system) [21]. However, popliteal vessels and nerves are infrequently involved by the tumor. In such a case, after the vessels are dissected out, an envelope of quadriceps musculature covering the soft tissue extension should be excised with the distal femur. The rectus femoris muscle is rarely infiltrated by tumor extension and thus can be spared for retention of the extension mechanism. Remaining musculature can be rearranged to cover the prosthesis and enhance rotational stability and strength of knee extension [22]. The length of bone resection is an important factor for aseptic loosening of the prosthesis as resection of more than 40 % of the distal femur has a negative influence on prosthetic survival [9, 23].

Cemented Fixation

Unwin et al. in 1996, reviewed 1,001 Stanmore cemented custom made prostheses with fixed hinge mechanisms, inserted before 1992 as a primary replacement for bone tumor [9]. The probability of avoiding aseptic loosening for 10 years was reported as 93.8 % for the proximal femur, 67.4 % for the distal femur and 58 % for proximal tibia replacements. The amputation rate due to complications for the entire group was 8.6 %. Myers et al. in 2007, reported on 335 patients who underwent distal femoral replacement [24]. A total of 192 patients remained alive with a mean follow-up of 12 years. All prostheses were custom made. One hundred and sixty two patients had a fixed-hinge design and 173 a rotating-hinge of which 143 had a hydroxyapatite (HA) collar. Only 15 prostheses were uncemented. Patellar resurfacing was not routinely performed. Early failure was usually due to infection or breakage of the prosthesis whereas late failure was more likely to be due to aseptic loosening. If aseptic loosening was taken as the endpoint, the rotating-hinge
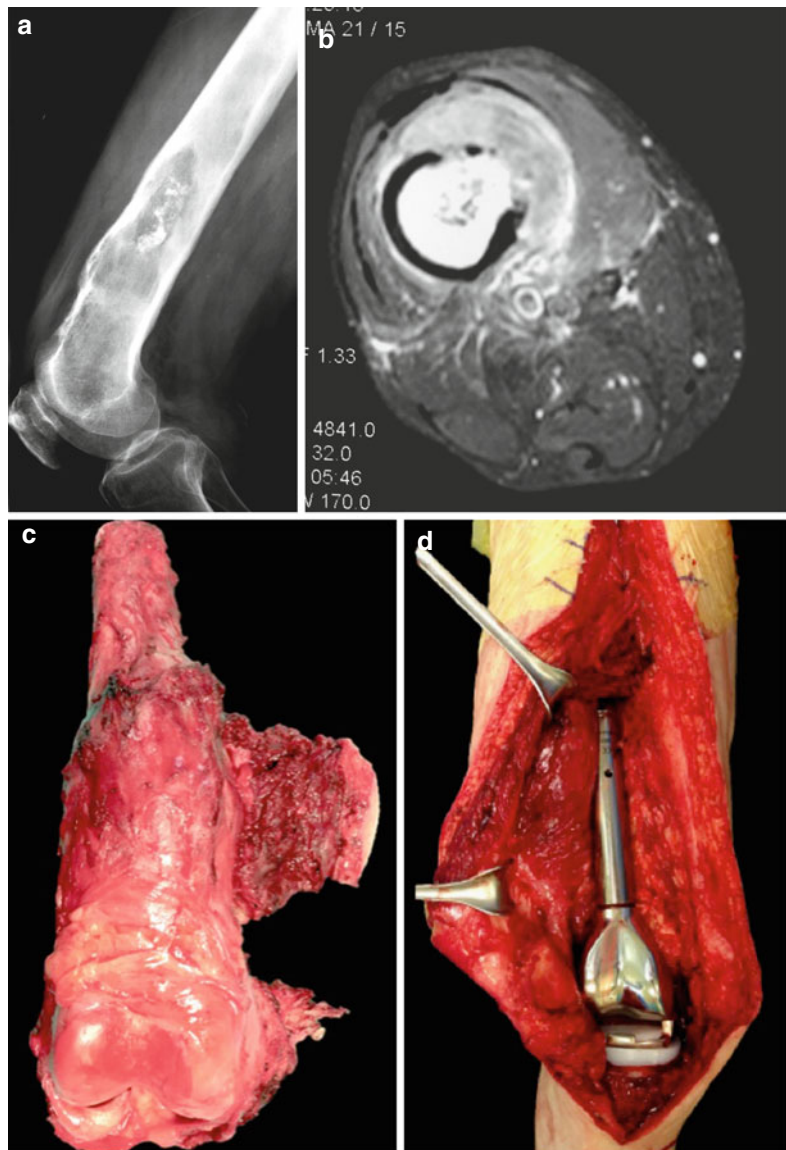
Fig. 20.1 A 70 years old male presented with progressive knee- distal femur pain over 3 months. (**a**) X-ray reveals a predominantly lytic lesion with intra-lesional calcifications of the distal metaphysis- diaphysis of the femur. (**b**) MRI axial T2 FS image reveals cortex erosion and soft tissue extension. Closed biopsy was consistent with high grade chondrosarcoma. (**c**) The patient underwent wide tumor resection. Distal femur specimen. (**d**) Cemented rotating hinge prosthesis was inserted. (**e**, **f**) X-rays 3 months post operatively

Fig. 20.1 (continued)

design with an HA collar was least likely to fail. The risk of revision for aseptic loosening of a fixed-hinge was 35 % at 10 years compared with 24 % for a rotating-hinge without an HA collar and 0 % for a rotating-hinge with an HA collar. Rebushing of the primary endoprosthesis was needed in 55 prostheses (45 fixed-hinge, 10 rotating-hinge). The overall infection rate was 9.6 %. Amputation was performed in 6 % for local recurrence and in 4.5 % of patients due to infection. Schwartz et al. in 2009, compared 85 modular distal femoral implants to 101 custom-casted designs [12]. All prostheses were cemented with a rotating hinge mechanism. The modular components had a greater 15-year survivorship than the custom-designed implants: 93.7 % versus 51.7 %, respectively. 9.7 % of the patients ultimately required amputation. The authors conclude that long-term survivors should expect at least one or more revision procedures in their lifetime. Bergin et al. in 2012, published the results of 104 distal femoral reconstructions [25]. They focused their analysis on the impact of the bone/stem ratio on aseptic loosening rate. All patients received a cemented modular prosthesis. Survival for 104 stems from aseptic loosening was 94.6 % at 10

and 15 years and 86.5 % at 20 years. The bone/stem ratio independently predicted aseptic failure. Patients with stable implants had larger stem sizes and lower bone/stem ratios than those with loose implants (14.5 mm versus 10.7 mm and 2.02 versus 2.81, respectively). The largest cause of failure in this study was infection (11.7 %) while 5.8 % of the implants were revised because of stem fracture.

Uncemented Fixation

Batta et al. has reported a high rate of aseptic loosening for custom-made uncemented, distal femoral endoprosthetic replacements [26]. Nine out of 69 implants (13 %) had to be revised due to aseptic loosening. All aseptically loose implants were diagnosed within the first 5 years. Capanna et al. in 1993, reports the results of 95 modular uncemented KMFTR tumor prostheses for distal femoral resections [27]. The femoral stem had two lateral flanges at right angles to each other, each with three holes to allow the passage of a total of six screws through the stem and cortex. Clinical results were excellent or good in 75 %.

Local recurrence of the tumors developed in five patients. The polyethylene bushes failed in 42 % of cases at an average of 64 months postoperatively, causing varus-valgus instability or locking, usually painless. The infection rate was 5 % for primary cases and was correlated to the extent of quadriceps excision. Bone remodeling around the femoral stem was evaluated on X-rays using the Rizzoli system. According to this system, in grade A there is no change, Grade B there is cortical sclerosis, Grade C there is cortical cancellation, Grade D there is distal sclerosis and proximal atrophy and in Grade E there is proximal osteolysis. In their series Grade D remodeling occurred in 47 % of the prostheses fixed with six screws and in only 11 % with three screws. Stem breakage occurred in 6 % and was associated with the use of narrow stems and extensive quadriceps excision. Most of the fractures occurred though the proximal screw hole. Lan et al. used dual-energy X-ray absorptiometry (DEXA) to evaluate the extent of periprosthetic bone remodelling around the KMFTR prosthesis for distal femoral reconstruction [28]. Bone loss around the KMFTR prosthesis was maximal at the distal end of the femur and progressively decreased towards the proximal end of the stem. Ten patients with implants fixed by screws were found to have a mean loss of bone mineral density (BMD) of 42 % in the most distal part of the femur, while the 13 without screw fixation had a mean loss of 11 %. Mittermayer et al. in 2002, reported on 251 uncemented reconstructions with the KMFTR system or the Howmedica Modular Reconstruction System (HMRS) [29]. Aseptic loosening rate at 10 years was 4 % for proximal femur, 24 % for distal femur replacements and 15 % for proximal tibia. The first radiological signs of aseptic loosening were always seen at the most proximal or distal part of the anchorage stem at a mean of 12 months after the first implantation. Griffin et al. in 2005, examined the risk factors associated with prosthetic failure for the KMFTR uncemented tumor prosthesis of 74 distal femoral [30]. For the distal femoral prosthesis the aseptic loosening rate was very low (2.7 %), the infection rate was 6.8 %, tumor local recurrence was 6.8 %, and the stem fracture rate 5.4 %.

All stem fractures occurred through components with six holes for transverse screw fixation produced before 1994. No fractures occurred through newer components with only three holes.

Proximal Tibia Replacements

For proximal tibia resections the common surgical approach is the anterior with proximal medial femoral extension, allowing for popliteal space exploration, identification of the popliteal neurovascular bundle, the trifurcation of the popliteal artery, arterial branches to gastrocnemius heads and common peroneal nerve (Fig. 20.2).

The reported results for proximal tibia replacement megaprostheses are frequently inferior to the distal femur. Two inherent characteristics of proximal tibia resection surgery are considered to be the principal causes for this outcome: defective attachment of the patellar tendon and the lack of available soft tissue. The attachment of the patellar tendon should be resected at least a few millimeters from the tibial tubercle in cases of malignancy, in order to achieve a clear oncological margin, thus resulting in a shortened tendon stump. In order to restore the continuity of the extensor mechanism, augmentation of the stump with synthetic or biological material is frequently necessary. This is the weak point for this step of reconstruction as reliable and effective long-term attachment of the tendon to the implanted prosthesis is not always successful. We frequently observe a gradual proximal migration of the patella on a lateral X-ray and a clinical lag of active, but full passive knee extension. Colangeli et al. in 2007, performed gait analysis of knee megaprostheses for proximal tibia tumors [31]. Functional performance during gait was abnormal in moss cases, consistent with weakness of the extensor apparatus and knee extension lag. Knee stability was supported by the intrinsic prosthesis biomechanics. The inadequacy of surrounding soft tissue for tension free coverage of the prosthesis (especially the metaphyseal part of the prosthesis) is the other major issue. Frequently, the

proximal tibia has to be resected en block with the proximal fibula and an envelope of soft tissue for safe negative tumor margins. An important step in the evolution of limb sparing surgery for proximal tibia tumors was the concept of a local rotational flap of gastrocnemius head for prostheses coverage and anchorage of the patellar tendon [32, 33]. More recently the use of the Trevira attachment tube has been introduced to enhance joint capsule stability and tendon attachment [34]. The tube is directly attached to the tibial prosthesis with non-absorbable sutures. Fibroblasts migrate into the tube's mesh, so that attachment of soft tissue takes place. In Hardes et al.'s series most of the patients were able to actively extend their knee [35].

Cemented Fixation

Myers et al. in 2007, reported on 194 patients who underwent a cemented proximal tibial replacement, with 95 having a fixed hinge design and 99 a rotating-hinge with a hydroxyapatite collar [10]. The median age of the patients was 21.5 years. At a mean follow-up of 14.7 years, 115 patients remained alive. Rebushing of the primary endoprosthesis was needed in 36 patients (20 fixed-hinge, 16 rotating-hinge). The risk of revision for aseptic loosening in the fixed-hinge knees was 46 % at 10 years. This was reduced to 3 % in the rotating-hinge knee with a hydroxyapatite (HA) collar. Amputations were carried out in 17.5 % of patients either for local tumor recurrence or

Fig. 20.2 A 12 years old female had right vague proximal tibia pain for a month. (**a**) anterior posterior x-ray reveals mixed sclerotic and lytic areas at the metaphyseal area. (**b**) MRI T1 coronal image shows a low to iso-intense signal to muscle lesion of the metaphysis extending to proximal tibial epiphysis. Biopsy of the lesion diagnosed osteosarcoma. The patient followed neo-adjuvant chemotherapy (**c**) Intraoperative view. Popliteal artery is dissected and the branch of the anterior tibial artery (*arrow*) is identified and ligated. (**d**) The proximal 14 cm of the tibia with proximal fibula 5 cm was resected en block. (**e**) A cemented modular hinge rotating prosthesis is inserted 1 cm longer. (**f**) The patellar tendon is sutured with heavy sutures over the porous coated anterior surface of the prosthesis. The medial gastrocnemius head is dissected and ready to rotate over the prosthesis and tendon attachment. (**g**) Lateral x-ray 6 months post operatively. The patient had 10° extension lag
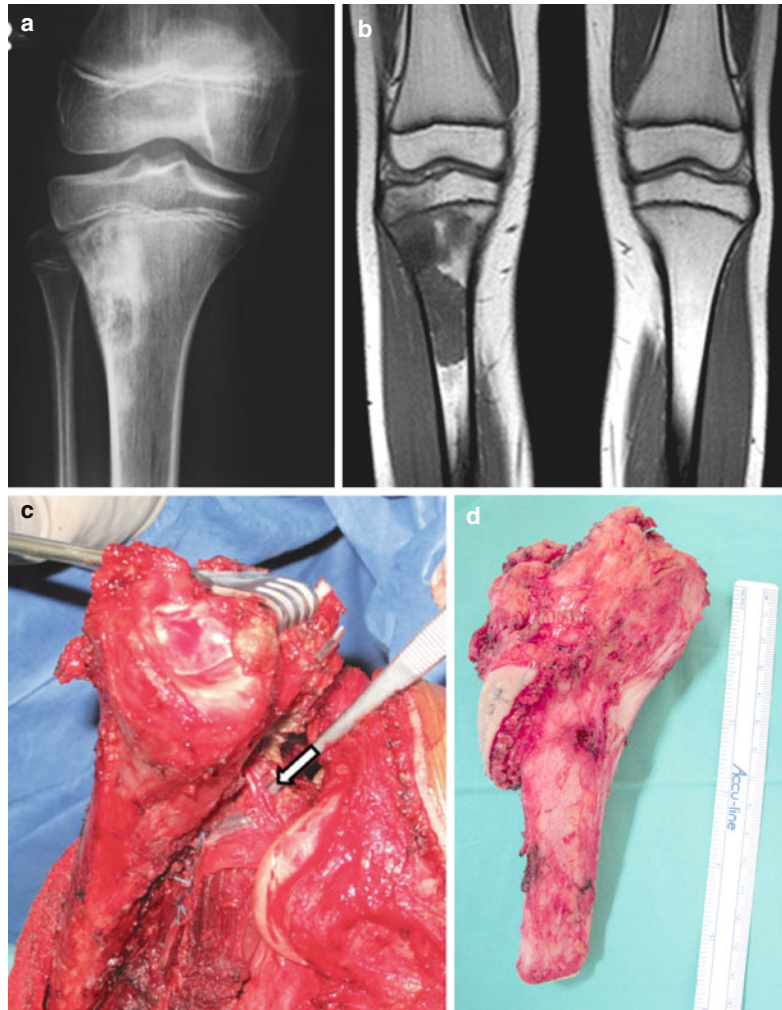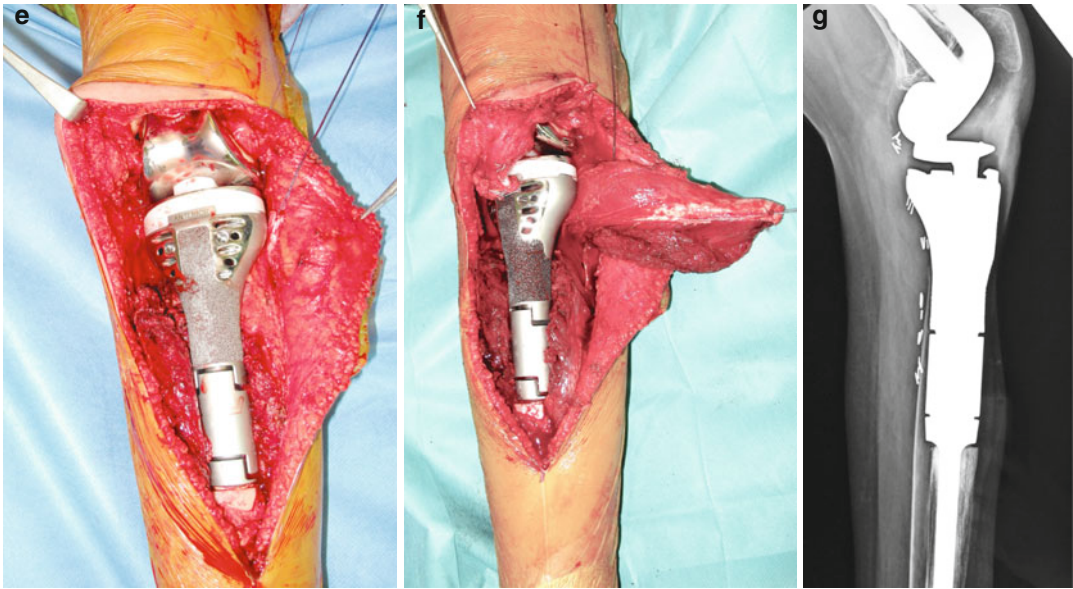
Fig. 20.2 (continued)

infection. Before gastrocnemius flaps were used the risk of amputation at 10 years following surgery was 28 %. Since the introduction of flaps, this has fallen to 14 %. Schawrtz et al. in 2010, retrospectively reviewed 52 cemented proximal tibial endoprosthetic reconstructions [12]. All prostheses had rotating hinge mechanisms; in 98 % this was the Kinematic rotating-hinge mechanism. Post-operatively all patients had their knee immobilized for a month. The failure of the rotating-hinge mechanism necessitating replacement of the bushings, axle, tibial bearing, or polyethylene was 23.1 % at a mean of 8.9 years postoperatively. Delayed wound healing or minor postoperative wound dehiscence was observed in 13.5 % of patients. The incidence of deep infection and local recurrence rate was 5.8 % and 5.8 % respectively while amputation had to be performed in 9.6 % of the patients. The use of an extramedullary porous ingrowth surface was associated with a lower incidence of aseptic loosening [12, 36]. The 29 modular implants demonstrated a trend toward improved survival compared to the 23 custom-designed components, with a 15-year survivorship of 88 % versus 63 %. The final mean postoperative Musculoskeletal Tumor Society score at was 82 % of normal function [12].

Uncemented Fixation

Griffin et al. in 2005, examined the risk factors associated with prosthetic failure for the KMFTR uncemented tumor prosthesis in 25 proximal tibial implants [30]. For the proximal tibia prosthesis the aseptic loosening rate was 0 %, the infection rate 20 % and stem fracture rate 8 %. Flint et al. in 2006, reported on 44 uncemented proximal tibia reconstructions [37]. Although they had no case with aseptic loosening, 24 % of the prosthesis failed either due to infection, local tumor recurrence, stem fracture, rotational instability or vascular compromise. In 16 % of the patients amputation was carried out. The mean knee extension lag was 6° and the MSTS score was 75 %. Mavrogenis et al. in 2013, reviewed 225 patients with proximal tibial tumors treated with proximal tibial resection from 1985 to 2010 [38]. The prostheses used in this series were KMFTR, HMRS and the rotating hinge Global Modular Reconstruction System (GMRS). Fixation of the prosthesis was cementless in 209 and cemented in 16 patients. The overall survival of patients with sarcomas was 62 % at 10 years, while survival of megaprosthetic reconstructions was 78 % at 10 years, without any difference

between fixed and rotating hinge megaprostheses. The overall complication rate was 25 %. The most common complications were infection (12 %), aseptic loosening (6 %), and extensor mechanism rupture (3 %). Infection rate was almost double in patients who had been administered chemotherapy. The mean extension lag from full active extension was 12°. MSTS function was significantly better in multivariate analysis for rotating compared to fixed hinge megaprostheses.

Infection

Infection is a frequent complication of knee megaprosthesis reconstruction ranging from 3.6 % to 37.5 %, and it is a leading cause for amputation [12, 39–44] (Fig. 20.3). Body image is significantly worse for patients undergoing late amputation after failed limb salvage [45]. Hardes et al. in 2006, reported on 30 patients with an infection associated with a tumor endoprosthesis [46]. Limb salvage related to the complication infection was achieved in 63.3 %. The mean number of revision operations per patient was 2.6. No patient receiving chemotherapy with a poor soft tissue condition had limb salvage surgery. A poor soft tissue condition was a significant risk factor for failed limb salvage. Jeys and Grimer, in 2009, stated that the risk of infection is life-long although infection most frequently occurs within 12 months from the last surgical procedure [43]. The most common pathogenic organism is coagulase-negative Staphylococcus and the most effective treatment for deep infection is two-stage revision [43, 47]. Previous radiotherapy increases the infection rate [47]. Flint et al. in 2007, reported on 11 patients who underwent removal of the prosthesis for infection [48]. They concluded that two-stage revision of uncemented tumor endoprostheses with retention of a well-ingrown stem could be associated with successful eradication of infection. Racano et al. in 2013, conducted a systematic review of the literature for clinical studies that reported infection rates in adults with primary bony malignancies of the lower extremity treated with surgery and endoprosthetic reconstruction [49]. This review
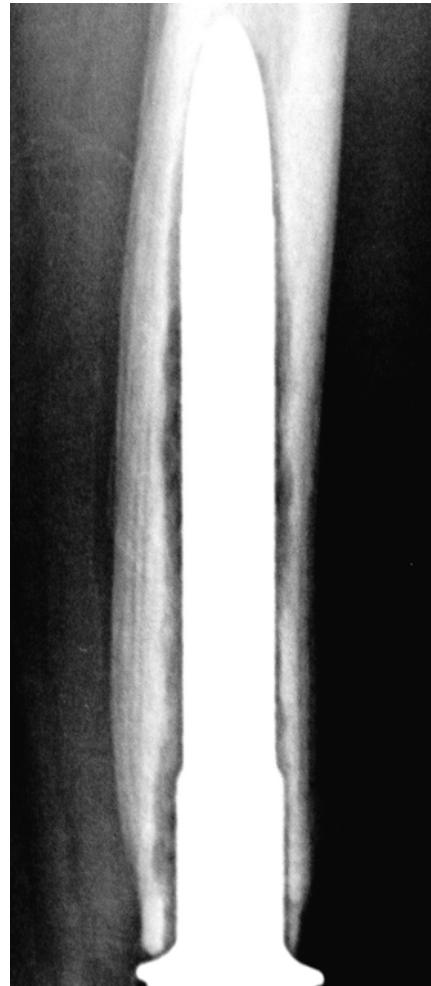
Fig. 20.3 X-ray of a distal femur uncemented stem with deep infection. Multiple solid periosteal reactions and intramedullary radiolucencies around stem

yielded 48 studies reporting on a total of 4,838 patients. The overall pooled weighted infection rate for lower-extremity LSS with endoprosthetic reconstruction was approximately 10 % with the most common causative organism reported to be Gram-positive bacteria in the majority of cases. The pooled weighted infection rate was 13 % after short-term postoperative antibiotics and 8 % after long-term postoperative antibiotics. Silver is well known for its anti-microbial properties. Silver coated megaprostheses are currently under investigation regarding their effect on incidence of deep infection and possible side effects [50, 51]. An in-vivo study in a rabbit model concludes that the silver coated Mutars megaprosthesis

resulted in reduced infection rates without toxicological side effects [52]. Hardes et al. demonstrated a lower infection rate and less aggressive treatment of infection in patients treated with silver coated megaprostheses compared to titanium prostheses [53]. Shirai et al. in 2014, performed a clinical trial of iodine-coated megaprostheses to evaluate their safety and antibacterial effect [54]. Abnormalities of thyroid gland function were not detected. The authors conclude that the iodine-supported titanium megaprostheses were highly effective and showed promise in the prevention and treatment of infections in large bone defects.

Advances in chemotherapy have substantially increased the overall survival of patients for most of the primary bone malignant tumors. Limb salvage is currently the rule for most patients as it is associated with improved function without compromising oncological outcome [13, 14]. Massive allograft transplantation around the knee used to be an attractive treatment option. However, over the last decade massive allografts have gone out of favour because of prolonged time to union and a high number of complications: namely infection, nonunion and allograft fracture [55, 56].

Length of bone resection seems to be related with prosthesis longevity for both proximal tibia and distal femur resections [9]. The first designs of custom made cemented prostheses for tumors around the knee were characterized by a high rate of aseptic loosening. The original uncemented KMFTR prostheses with two flanges and six screw holes had a high rate of fatigue stem fractures because of increased stress shielding and stress resorption of bone under the flanges of the prosthesis. Thus the prosthesis has been modified from six to three screw holes. The rotating hinge mechanism is a significant development as it reduces rotational stress around the stem. Rotating hinge mechanisms seem to improve knee function and reduce aseptic loosening and stem breakage rates. However, metal ion cobalt (Co) and chromium (Cr) release is significantly higher in patients with megaprostheses compared to a standard rotating-hinge knee device [57]. Nowadays, the use of a fixed hinge mechanism should be considered in cases with large soft tissue resections and total femur replacements as

fixed mechanisms facilitate closed reduction in case of dislocation of the hip replacement. The use of a hydroxyapatite collar seems to reduce osteolysis from polyethylene particles as bone formation around the HA collar seals the medullary path for wear debri migration. Currently the use of modular replacement systems with rotating hinge mechanisms, either with cemented or uncemented stems, for reconstruction of bone and joint defects is not only limited for reconstruction after tumor surgery but is also extended for difficult post-traumatic or cases of infection. Patients close to skeletal maturity and older can be treated with available modular adult type endoprostheses. Modular prostheses offer the advantage of immediate availability. Additionally, the surgeon can adjust the length of bone resection based on the principles of oncological surgery and intra-operatively construct and implant the prosthesis. Although modularity of implanted endoprosthesis raises concerns about increased aseptic loosening, newer prostheses have shown very good survival rates compared to older custom designs [12]. Custom made prosthesis manufacturing should be reserved for unusual tumor location, large bone defects, skeletal immaturity and difficult revision cases.

Infection is still a major problem for megaprosthesis reconstruction. The incidence is much higher compared to conventional prosthesis. Development of deep infection with poor soft tissue quality frequently results in amputation. The use of a gastrocnemius rotation flap for coverage of the proximal tibia prosthesis seems to reduce the infection rate and increase the function of the extensor apparatus. Use of silver coated or iodine-supported prostheses may also help to reduce infection rates.

Conclusion

The overall complication rate for megaprostheses reconstruction for the distal femur and proximal tibia is relatively high but limb salvage is feasible in the vast majority of patients. The overall oncological and functional outcome with newer prostheses is satisfactory, although long-term survivors will probably undergo prosthesis revision in their lifetime.

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