Review

Application and Development of Megaprostheses in Limb Salvage for Bone Tumors Around the Knee Joint

Cancer Control
Volume 29: 1–9

DOI: 10.1177/10732748221099219
journals.sagepub.com/home/ccx
SAGE

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Abstract

In recent decades, limb-salvage surgery has replaced amputation as the first choice for the treatment of bone tumors around knee. After tumor resection, there are a variety of reconstruction methods for us to choose, including autograft or allograft, inactivation and reimplantation, artificial prosthesis replacement, and allograft-prosthesis compound reconstruction. Compared with other reconstruction methods, artificial prosthesis reconstruction has some advantages: relatively simple, early weight bearing, fewer early complications, and good function in the early and mid-term follow-up. After decades of continuous improvements, the design of tumor prosthesis has reached a relatively mature stage, and the failure rate of prosthesis has also been declining year by year. However, artificial prostheses also have multiple complications such as infection, aseptic loosening, prosthetic breakage, and patients sometimes face the risk of revision or amputation. Therefore, clinicians need to deeply understand the characteristics of related complications and the principles of treatment.

Keywords

megaprosthesis, limb salvage, failure mode, complication, prosthetic design

Introduction

In limb-salvage surgery for bone tumor, there are 3 main ways to reconstruct the bone defect after tumor resection: autograft or allograft, inactivation and reimplantation, and artificial prosthesis replacement. Due to the advantages of artificial prosthesis, such as relatively simple, early weight bearing, fewer early complications, and good function in the early and mid-term follow-up, artificial prosthesis replacement has gradually become the mainstream method in the reconstruction of structural bone defects.[1-4]

With the developments of prosthesis movement patterns, surface biological coatings and biological fixation methods, the low long-term survival rate of artificial prostheses has gradually improved. In order to explore the long-term clinical outcome of tumor prostheses, Pala et al[5] followed up 687 cases of distal femoral tumor prostheses, and the results showed that the failure rate of prosthesis was 27%, the 10-year survival rate of prosthesis was 70%, and 91.4% of patients were satisfied with the functional recovery with a mean functional score of 23.3. These conclusions all confirm that the rapid development of artificial prostheses makes most patients no longer need to undergo cruel amputation, and can obtain ideal functional recovery and quality of life.

It is worth noting that there are still many complications following artificial prosthesis replacement, such as periprosthesis infection, aseptic loosening, and fractures around prosthesis.[6,7] It has been reported in the literature that the incidence of complications after tumor knee replacement is 5–10 times higher than that of conventional knee replacement, which is due to the peculiarities of bone tumor surgery.[2,8] Many patients with bone tumor are younger, and they have a higher level of activity and exercise intensity, which will undoubtedly subject the prosthesis to greater torsional and shear stress, and ultimately lead to periprosthetic fractures and

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prosthesis loosening. Patients with bone tumor often require perioperative radiotherapy and chemotherapy, which makes these patients in a state of immunosuppression for a long time, thus affecting the healing of the prosthesis-bone interface and wound.[9] A final consideration is the enormous trauma associated with bone tumor surgery, including greater bone and soft tissue resection, greater blood loss, and longer operative time. Extensive resection of bone results in longer reconstructed prostheses, which are more prone to loosening;[10] extensive soft tissue resection and blood loss make postoperative infections more common.[11] The existence of these complications makes many patients face the potential risks of secondary revision or amputation, so it is very important to further improve the treatment effects of limb-salvage reconstructions.

There have been several literature focusing on prosthetic reconstruction of bone tumors, however, none of these literatures describe and analyze prosthetic complications according to the newly published classification of prosthetic complication.[12-14] In current review, we discuss prosthetic complication rates, causes, and risk factors based on classification of prosthetic failure, and update some recently published literature. We believe that these introductions will help clinicians to use tumor prosthesis reasonably and ensure acceptable effects after surgery.

Development History of Tumor Artificial Prosthesis

The advancement of tumor prosthesis reconstruction is inseparable from the joint development of imaging, orthopedic materials science, adjuvant therapy, and surgical technology, but the improvement of prosthetic design has played a decisive role in this. The development of tumor prosthesis design is a long, dynamic and gradual process, which is reflected in some aspects such as prosthetic assembly, prosthetic fixation mode, and prosthetic movement mode.

Prosthetic Assembly Mode

The original prosthesis was customized prosthesis, which required clinicians to predict the extent of osteotomy based on preoperative imaging data, and then with the cooperation of engineers, a prosthesis matching the size of the patient's bone defect and medullary cavity could be manufactured. This is undoubtedly time-consuming and expensive. The most frightening thing is that the patient with bone tumors may miss the best treatment opportunity.

With the increase in the amount of tumor prosthesis replacement surgery, custom-made prostheses that take several weeks to produce gradually cannot meet clinical needs, and modular prostheses appear. The literature comparing the clinical efficacy of custom-made and modular prostheses have shown that the modular prosthesis has better results for the survival rate of prosthesis and the postoperative function of patients.[12,15]

Since the extent of osteotomy varies among patients with bone tumors, it is very important to prepare modular components of various sizes before surgery. The modular prosthesis is mainly composed of a prosthetic stem, an extension piece, a joint part, a rotating hinge axle, and a polyethylene liner. The Kotz modular femoral tibial reconstruction system (KMFTR) released in 1986 is a typical representative of knee joint modular prostheses. This system uses a Morse taper to connect the various components of prosthesis. Its 26 main components can ensure that the patient could be reconstructed from the femoral head to the distal third of the tibia. In a multicenter cohort study including 187 Mutars modular tumor prostheses, 76.5% of patients had implant retention at the last follow-up. The overall prosthesis failure rate was 23.5%, with a mean time to failure of 1.7 years. The overall implant survival rates for all types of failure were 68% and 52% at 5 and 10 years, respectively.[10] Our recent study published in 2020 has also demonstrated the advantages of modular prostheses in postoperative survival and complications.[16] At our institution, the risk of failure of custom prostheses is 80% higher than that of modular prostheses.

However, the high flexibility of the modular prosthesis has also caused some new problems: because the components of the modular prosthesis are connected by tapers or screws during the operation, in the cases of improper assembly during the operation or postoperative trauma, the prosthesis may dislocate or disintegrate; due to the increase in the number of components, the micromotion between the various components may cause more wear particles to be produced, which could lead to subsequent osteolysis and aseptic loosening. In addition, if the patient's bone defect is extremely large or the bone is severely deformed and cannot be reconstructed with existing components, then a customized prosthesis that meets the patient's conditions will still be needed.

Prosthetic Fixation Method

Cement fixation has been widely accepted and has become the most common way of prosthetic fixation. Bone cement plays a kind of micro-interlocking effect by effectively filling the cancellous bone, which can not only fix the prosthesis but also strengthen the bearing strength of cancellous bone. However, cement fixation often leads to frequent aseptic loosening and osteolysis, and it is extremely difficult to completely remove the bone cement during revision surgery.[17-19] A study including 115 patients with bone metastases in the extremities who underwent resection and reconstruction with cemented or uncemented endoprostheses showed the stem loosening rates of the cemented and uncemented groups did not differ statistically. On the other hand, significantly higher number of stem loosening areas was observed after cemented reconstructions compared to uncemented endoprostheses at last follow-up. In addition, the time of stem loosening was significantly longer in the cemented group compared to the uncemented group.[20]

Biological fixation does not require bone cement as a medium, but relies on the geometry (polygonal shape) and the surface coating (porous or biological coating) to achieve the initial fixation and secondary osseointegration.[17,21] The introduction of hydroxyapatite and tricalcium phosphate stem coatings promotes osteogenic adhesion to metallic surfaces and has positively impacted tumor prosthesis fixation and survival.[17]

However, the biological prosthesis relies heavily on the initial stability of the prosthesis during limb-salvage surgery. If a sufficient press-fit is not achieved, the subsequent micromotion will interfere with bone ingrowth and promote the generation and migration of wear particles.[22] It is reasonable to believe that biological fixation is simple and reliable under the premise of ensuring sufficient intraoperative press-fit.

Because bone tumor surgery is often accompanied by huge bone defects, conventional prosthetic stems often cannot meet the needs. The compress fixation method that appeared in recent years provides ideas for solving this problem.[18] It is different from the previous fixation method but uses the pressure generated by a spring to fix the residual bone and prosthesis. In theory, this fixation method can greatly reduce the stress shielding and prevent wear particles from entering the distal end of medullary cavity. And because of its short stem design, this prosthesis is particularly suitable for situations where there is little residual bone. The literature shows that compress prosthetic fixation after distal femoral tumor resection exhibits long-term survivorship. Implant failure was associated with patient nonadherence to the recommended weight-bearing proscription or with bone necrosis and fracture.[23,24]

Prosthetic Movement Mode

The addition of a rotating hinge structure to the knee tumor prosthesis is a major design improvement, which greatly reduces the rotational stress carried by the prosthesis itself and the polyethylene bushing (Table 1).

Earlier knee tumor prosthesis was a fully restricted structure, with only flexion and extension movements. This structure is to meet the needs of knee joint stability in patients with bone tumors after surgery because part of the stable structure of the knee joint may be removed during the operation. Long-term follow-up found that the incidence of aseptic loosening was high.[5,25] With the in-depth understanding of biomechanics of knee joint, the rotating hinge prosthesis appeared in the late 1970s, in which the hinge component provides stability and the rotating component provides axial rotation. The rotating hinge prosthesis allows moderate internal and external rotation of knee joint and reduces the stress on the host bone-prosthesis interface, so it has fewer mechanical complications and better postoperative function than the fixed hinge prosthesis.[5] A study conducted by Zhang et al[25] in 2019 showed that the rate of aseptic loosening of fixed hinge prostheses was 4 times higher than that of rotating hinge prostheses, and they believed that the movement mode of the prosthesis was the most important factor among factors related to aseptic loosening.

However, due to the complexity and flexible structure of the rotating hinge prosthesis, when the direction of movement suddenly changes or the movement is suddenly stopped, rotating hinge prosthesis is prone to loosening caused by shear force and impact force. And when most of the stable structures such as muscles and ligaments are removed, the rotating hinge prosthesis cannot provide sufficient joint stability. Therefore, the fixed hinge prosthesis is still retained in clinical practice due to its excellent self-stability. It is mainly used for patients with extremely poor muscle strength, such as patients with extensive quadriceps resection or with total femoral reconstruction.

Prosthetic Survival Rate and Complications

Although there have been many improvements in materials and designs of tumor prostheses, the complication rates reported in the literature are still 5 to 10 times higher than that of conventional total knee arthroplasty.[8] This is due to the particularity of bone tumor surgery: patients are younger and active; patients are often accompanied by immunosuppression, more bone and soft tissue removal, and longer operation time. Compared with biological reconstruction, the complications of artificial prostheses tend to gradually increase with the prolongation of implantation time, which results in young patients who may need 1 or even multiple revisions in their lifetime.[1,26]

The definition of prosthesis failure varies greatly in different literature. Most scholars believe that prosthesis failure includes: complete or partial revision of prosthesis, fixation of the fracture around prosthesis, reconstruction of soft tissue to restore joint stability, removal of the prosthesis, and amputation. A large multicenter retrospective study showed that the overall failure rate of tumor prostheses was 24.5%, and it varied greatly with the implantation site. The failure rates of distal femoral replacements and proximal tibial replacements were 27% and 34%, respectively.[27]

The classification standard for complications of tumor prosthesis was released by Henderson and colleagues in 2011, and the content of extensible prosthesis was added in 2014.[7,27] Generally, complications can be divided into 2 categories: mechanical complications and non-mechanical complications. Mechanical complications include the loss of normal function and/or the poor relationship between the prosthetic components and adjacent bone and soft tissue. These complications may threaten function, but rarely threaten life and limbs. Non-mechanical complications include the prosthesis must be removed or revised without impairing the structure of prosthesis and the surrounding soft tissue. These complications are serious and may eventually lead to amputations. Prosthesis

Table 1. Literature review of different outcome on tumor surrounding the knee reconstructed with tumor prosthesis in the past 10 years.

Study	Publication year	Location and no	Cemented/cementless	Fx/RT-H	Follow-up (mo)	Implant survival (%)			Complications, n (%)				
						5y	10y	15y	Type 1	Type 2	Type 3	Type 4	Type 5
Schwartz et al[15]	2010	186 dF	186 cemented	186 RT-H	96	87.7	77.2	61.6	13 (7)	22 (11.8)	10 (5.4)	6 (3.2)	13 (7)
Matsumine et al[30]	2011	69 dF	69 cemented	69 RT-H	57	85	60	/	7 (10)	7 (10)	8 (11.6)	7 (10)	10 (14.5)
Bergin et al[28]	2012	104 dF	104 cemented	104 RT-H	67	76.1	73.3	62.8	/	5 (4.8)	6 (5.7)	12 (11.5)	1 (1)
Coathup et al[39]	2013	61 dF	61 cemented	61 RT-H	102	88.5	84.4	/	8 (13)	5 (8.2)	3 (4.9)	3 (4.9)	6 (9.8)
Healey et al[24]	2013	82 dF	82 cementless	82 RT-H	43	85	80	/	/	8 (9.8)	5 (6.1)	0 (0)	0 (0)
Batta et al[22]	2014	69 dF	69 cementless	69 RT-H	124	72.7	64.6	54.8	3 (4.3)	9 (13)	3 (4.3)	5 (7.2)	2 (2.9)
Nakamura et al[31]	2014	82 dF	17 cemented; 65 cementless	82 RT-H	61	80	57	/	6 (7.3)	5 (6.1)	6 (7.3)	7 (8.5)	11 (13.4)
Pala et al[2]	2015	187 dF; 60 pT	22 cemented; 225 cementless	247 RT-H	48	68	/	/	21 (8.5)	14 (5.7)	0 (0)	23 (9.3)	14 (5.7)
Müller et al[47]	2016	23 pT	10 cemented; 13 cementless	23 RT-H	62	78.8	78.8	/	1 (4.3)	0 (0)	0 (0)	3 (13)	1 (4.3)
Pala et al[5]	2016	687 dF	687 cementless	491 Fx-H; 196 RT-H	95	76	70	57	41 (6)	33 (4.8)	26 (3.8)	57 (8.3)	28 (4.1)
Hu et al[21]	2017	82 dF; 24 pT	56 cemented; 50 cementless	106 RT-H	89	83	68	63	1 (.9)	5 (4.7)	7 (6.6)	7 (6.6)	3 (2.8)
Zhang et al[38]	2018	76 dF; 32 pT	108 cemented	108 RT-H	53.2	77.7	54.4	/	1 (.9)	8 (7.4)	3 (2.7)	5 (4.6)	4 (3.7)
Yilmaz et al[36]	2019	49 dF; 26 pT	/	75 RT-H	96	/	/	/	22 (29.3)	5 (6.7)	6 (8)	8 (10.6)	19 (25.3)
Zhang et al[25]	2019	119 dF; 58 pT	177 cemented	19 Fx-H; 158 RT-H	92	/	/	/	2 (1.1)	22 (12.4)	3 (1.7)	12 (6.8)	5 (2.8)
Piakong et al[37]	2020	195 dF	195 cemented	/	78	74	64	49	/	14 (7.2)	/	19 (9.7)	/
Zhang et al[16]	2020	142 dF; 72 pT	214 cemented	27 Fx-H; 187 RT-H	85	88.6	74.1	48.3	2 (.9)	26 (12.1)	4 (1.9)	13 (6.1)	5 (2.3)
Bukowski et al[33]	2021	115 dF	115 cemented	115 Fx-H	/	88.3	80.7	/	4 (3.5)	3 (2.6)	14 (12.2)	13 (11.3)	5 (4.3)
Karaismailoglu et al[19]	2021	77 dF; 41 pT	63 cemented; 55 cementless	66 Fx-H; 52 RT-H	/	78	/	/	/	7 (5.9)	19 (16.1)	/	/
Ogura et al[34]	2021	214 dF	76 cemented; 138 cementless	214 RT-H	/	77.4	69.9	65.7	0 (0)	39 (18.2)	26 (12.1)	40 (18.7)	3 (1.4)
Gusho et al[35]	2021	57 dF	52 cemented; 5 cementless	57 RT-H	45.7	88	63.5	/	0 (0)	3 (5.3)	3 (5.3)	3 (5.3)	0 (0)

Fx/RT-H, fixed/rotating hinge; dF, distal femoral; pT, proximal tibial.

failure can be further divided into 5 types according to etiology.

Soft Tissue Complications

Soft tissue complications are divided into functional failure and coverage failure. Functional failure includes joint dislocation or subluxation, tendon rupture, and instability caused by excessive soft tissue resection; Coverage failure includes aseptic wound dehiscence. Soft tissue complications are the least common type of all complications, but they usually appear first.[27] Soft tissue complications mostly occur in shoulder and hip joint reconstructions.[4] The incidence of upper limbs is also higher than that of lower limbs. The reason may be due to the destruction of the integrity of joint capsule and the greater range of joint motion.

However, this complication does not necessarily lead to failure of the prosthesis. For example, aseptic wound dehiscence can be treated by debridement and skin grafting without revision of the prosthesis. Joint dislocation or subluxation is mostly related to insufficient soft tissue reconstruction or improper movement of tumor patients. Therefore, the surgeon should pay attention to ensuring the balance of surrounding soft tissues and the correct assembly of prosthetic components during the operation. Doctors should also remind patients and their families to protect the affected limbs and avoid intense confrontational sports and accidental injuries.

Aseptic Loosening

Aseptic loosening is the most common cause of prosthetic failure during long-term follow-up, and it increases with the prolonging of implanting time whether the prosthetic stem is cemented or uncemented.[27] Due to differences in tumor site, fixation technique, and type of prosthesis, the incidence of aseptic loosening varies widely among studies, ranging from 0 to 27.5%.[2,5,22,27-35]

Patients with aseptic loosening are often accompanied by increasing weight-bearing pain, and different degrees of displacement of the prosthesis and the formation of radiolucencies around prosthesis can be seen on the X-ray film. If the aseptic loosening is only visible in the imaging examination and the patient has no obvious symptoms of discomfort, clinician can choose not to intervene. However, clinician should inform the patient of the high risk of aseptic loosening, and advise the patient to pay attention to the protection of prosthesis and avoid falls and high-intensity exercise. If the patient has clinical symptoms and signs of aseptic loosening on imaging, a revision surgery should be performed as soon as possible to avoid damage function. Generally speaking, patients can recover good limb function after revision surgery.

Aseptic loosening is caused by a variety of variable and invariable factors. This multi-factor nature requires us to understand the impact of related factors on aseptic loosening as much as possible to minimize the risk of loosening.

The site of prosthesis replacement is an important factor affecting the risk of prosthesis loosening.[36] Henderson et al[27] found that aseptic loosening of the distal femoral prosthesis accounted for 6.8% of all failures, which was the highest among all anatomical locations. Piakong et al followed up 246 patients who underwent a knee reconstruction with a modular cemented endoprosthesis after resection of a musculoskeletal tumor between 1997 and 2017.[37] Aseptic loosening involving the femoral stem occurred in 4.6% of the patients and aseptic loosening involving the tibial component occurred in 2.6%. The mean time to revision for aseptic loosening of the femoral stem was 59 months.

The stress on the prosthesis-bone interface is mainly concentrated on the tip of the prosthesis stem. For the distal femoral prosthesis, the deviation of the anatomical axis and the force line is large at the tip of prosthesis stem, and the bending stress borne by the prosthesis is also large. In contrast, the offset of the proximal tibial stem is relatively small, and the medullary cavity resembling a triangle rather than a circle is also more conducive to the firm fixation of the prosthetic stem.[1] Piakong et al noted the weight of the limb is transferred through the stem to the proximal femoral bone, resulting in a radiolucent area at the bone-prosthesis junction. When the radiolucent area develops, contact at the bone-prosthesis area decreases and the load at the stem tip increases. The cortex at the stem tip thickens in response, resulting in cortical expansion remodeling.[37]

The rotating hinge structure helps to reduce the occurrence of aseptic loosening, which has been reported in many literatures.[1,2,25] Rotating hinge prosthesis allows knee joint to obtain flexion, extension, and axis rotation, thereby dispersing the torsional stress on the prosthesis stem.[30,32] In contrast, in patients using fixed hinge prostheses, the stress cannot be properly distributed around the knee joint, which may lead to subsequent aseptic loosening.[5,38] Our recent study showed that the risk of aseptic loosening of fixed hinge prosthesis is 4 times that of rotating hinge prosthesis (HR = 4.11, CI 95% 1.74–9.70, P = .001).[25] This reminds us that, except for the elderly with poor muscle strength and patients with extensive muscle resection, the rotating hinge prosthesis should be routinely used in reconstruction after resection of tumor around the knee joint.

In recent years, there has been a collar design that adds hydroxyapatite (HA) or porous coating to the joint between the prosthesis and the host bone. This structure can induce bone and soft tissue to grow in, thereby "sealing" the distal medullary cavity to prevent the entry of wear particles. Coathup et al[39] followed up 61 cases of cemented distal femoral prostheses with HA collar, and the results showed that revisions caused by aseptic loosening were less (8%). During the follow-up period of 2 to 18 years, 70% of patients showed imaging evidence of osseointegration, and histological analyses of 4 prostheses confirmed bone ingrowth and direct bone-prosthesis contact.

The degree of anastomosis between the stem and medullary cavity is an important factor affecting the long-term stability of tumor prosthesis. This involves 3 parameters of the stem: diameter, length, and curvature.[40] Bergin et al[28] followed up 104 cemented modular prostheses with a mean follow-up of 5.6 years. They pointed out that the greater the bone/stem ratio, the greater the risk of aseptic loosening. Batta et al[22] pointed out that an increase in the ratio of total length of prosthesis/stem length would increase the risk of aseptic loosening. Piakong et al[37] noted no aseptic loosening was observed in patients with implants with curved stems that were 13 mm or greater in diameter. One of our studies determined that the length of intramedullary stem is an independent risk factor for aseptic loosening (HR = 2.84, CI 95% 1.13–7.12, $P = .026$), and shorter stems have a higher rate of loosening.[25] Some anatomical positions, such as the femur, have a certain physiological curvature. In these cases, a straight stem has poor resistance to rotation. The use of a prosthetic stem with a matching curvature can obtain better initial stability.

Many patients with bone tumors are young, so high-intensity exercise is inevitable in these patients, but these activities have little benefit to the prosthesis itself.[16] Clinicians need to give necessary warnings to overweight patients and young patients with high activity, and reasonably recommend them to control their weight and adjust the intensity of physical activity to minimize the load.

Structural Complication

Structural complications are divided into prosthetic fracture and periprosthetic fracture. Compared with the upper limbs, the structural complications of the lower limbs are easier to be observed, which may be related to the weight-bearing function of lower limbs.

The factors affecting prosthetic fracture include size and geometry of prosthesis, design of prosthesis, material of prosthesis, manufacturing technology of prosthesis, and the remaining muscle strength. Matsumine et al[30] attributed the fracture of prosthetic stem to the small diameter, and they suggested that the stem with a diameter of less than 12 cm should not be used in the weight-bearing part of the lower limb. In patients with progressive junctional radiolucencies without cortical thickening for stabilization of the stem, a periprosthetic fracture, broken stem, or aseptic loosening might occur.[37]

Periprosthetic fractures generally occur during prosthesis replacement surgery or after trauma, and the fracture locations are mostly at the tip of the prosthetic stem. Risk factors include local osteoporosis around prosthesis, loosening of stem, non-neutral position of stem, straight stem, mismatch between the stem and medullary cavity, and intraoperative violent operation.

Periprosthetic Infection

Because bone tumor surgery is often accompanied by longer operation time, more soft tissue removal, larger exposure range, immunosuppressive status caused by radiotherapy and chemotherapy, and poor general condition of patients, the incidence of infection is high.[4,41,42] A multicenter study noted that periprosthetic infections accounted for 34% of all failure modes following megaprosthetic replacement, and they were the most common failure type for all anatomical positions except for the proximal femur.[27] Periprosthetic infections put patients at risk of repeated operations, pain, dysfunction, long-term recovery, delayed adjuvant therapy, and amputation. Several studies have shown that infection is 1 of the main reasons for amputation after prosthesis replacement, and the risk of amputation is second only to tumor recurrence.[43,44]

The diagnosis of infection is challenging because the symptoms are variable and the detection methods are non-specific, which requires clinicians to judge by combining clinical symptoms, laboratory indicators, and microbiological examinations. The gold standard for diagnosis is the positive bacterial culture of fluid obtained by paracentesis from the diseased site. Clinical symptoms include fever, local redness and swelling, elevated skin temperature, night pain and resting pain. Although some laboratory indicators such as C-reactive protein, erythrocyte sedimentation rate and white blood cell count lack specificity, they can provide reference for diagnosis.

The treatment methods of infection include conservative treatment, debridement, one-stage revision, two-stage revision, arthrodesis, and amputation. The literature shows that the most successful treatment method to eradicate infection is amputation (successful in 98% of patients), followed by two-stage revision (72%) and one-stage revision (42%). Other methods such as antibiotics, arthroscopic washout, debridement, and arthrodesis have a low success rate.

One-stage revision included debridement of the joint, change of modular components, retaining the prosthetic stem, prolonged antibiotic therapy.[45] One-stage revision has been recommended for patients with early or low-grade infections, caused by low-virulence microorganisms, patients with a short duration of symptoms and early diagnosed infection and high antibiotic-sensitive pathogens, well-fixed implants, poor general condition of the patient, and long delay of chemotherapy.[41] The advantages of one-stage revision surgery are the avoidance of larger bone defects, less joint stiffness, lower cost, and shorter hospital stay.[46]

Two-stage revision of infected tumor prostheses included the complete removal of all prosthetic components, antibiotic-loaded cement spacer and long-time use of systemic antibiotics. Two-stage revision is recommended for patients with persistent, higher-grade infections, extensive osteolysis with prosthesis loosening and bone loss, poor soft tissue envelope, antibiotic-resistant pathogens, and a failed one-stage procedure.[41,46] After a long period of administration of systemic antibiotics, a second stage surgery for reimplantation of a new prosthesis, 2 or more months later is performed.[44] Antibiotic-loaded cement spacers serve 2 functions in two-stage revisions. First, the spacer provides a mechanical support during removal of the prosthesis. This maintains proper joint position, prevents muscle contractures, and enhances patient comfort between the first and second stages. The second function is to provide topical antimicrobial therapy, as well as enhance systemic antibiotic therapy between the first and second phases.[47]

Tumor Recurrence

Tumor recurrence can be divided into soft tissue recurrence and bone recurrence. Both types of recurrence require revision surgery. The difference is that soft tissue recurrence only needs to be treated with local resection and adjuvant therapy, while bone recurrence requires further osteotomy. Tumor recurrence accounts for about 17% of all failure types, and the mean time to failure is 26 months. The distributions of this complication in different anatomical sites are similar, and it is not related to the type of prosthesis.[27]

Risk factors related to tumor recurrence include insensitivity to radiotherapy or chemotherapy, aggressive tumors and positive margins.[20] For tumors that are sensitive to adjuvant therapy, preoperative and postoperative radiotherapy and chemotherapy should be standardized, which is of great significance for improving the prognosis of these patients. If the frozen pathological section finds positive margins after tumor resection, the resection range must be expanded again to ensure complete tumor resection.[20] A study including 82 patients who underwent limb-salvage surgery for primary and metastatic bone tumors of the lower extremity showed the local recurrence rate of 5.8% (2 in 34 sarcomas) seen in this series compared favorably with previous reports for primary bone sarcomas. The authors suggested that achieving a favorable chemotherapy response and tumor-free margins may explain the acceptable local recurrence rate.[4] Tumor recurrence is associated with poor prognosis even with aggressive measures including amputation and systemic chemotherapy.

Outlook and Perspectives

After decades of development, tumor megaprostheses have been widely used in limb-salvage reconstructions all over the world. However, there are still complications such as infection, loosening, and periprosthetic infection, which may force patients to undergo multiple revision surgeries or even amputations. The emergence of some new technologies in recent years, such as 3D printed prostheses, provides new ideas for solving these problems.

Custom-made prostheses have been used since the 1990s with success in the reconstruction of large-sized bone defect[48] and tumor prostheses.[1,6] Close collaboration between the surgeon, technician and medical engineer is needed and considerable time and resources are dedicated to preoperative planning. Typical production cycles are measured in weeks to months. Conventional computer numerical control subtractive manufacturing techniques typically yield products with favorable longevity using high-quality alloy elements. Constructs can be tested to be able to sustain physiological loads and optimized using finite element modeling simulation before the design is completed.[49] Many of these established computer assisted design and computer assisted manufacturing techniques are applied to the modern metal 3D printing workflow.

The use of custom-made titanium alloy prostheses manufactured by metal 3D printing technology, such as direct metal laser sintering or electron beam melting technologies, is increasingly popular and arguably cheaper and faster. In keeping with the objectives of immediate and long-term stability, metal 3D printing can produce implants with complex shapes and porous internal structures controlled to the micrometer level for bone ingrowth. Customizable textured surfaces and regional stiffness can minimize irritation to overlying soft tissues, stress concentration and stress shielding. 3D printed prostheses are typically implanted with 3D printed patient-specific instrumentation and surgeons are provided with 3D printed models to aid resection and implantation. The technologies of 3D printing and computer navigation can be easily made complimentary, since 3D digital models in stereolithography format are readily transferred between systems.[49]

A prime concern for metal 3D printed prosthesis is the unknown likelihood of fatigue failure compared to conventional computer numerical control manufactured prosthesis, and this remains to be observed in larger case series and implant registries.[50] Early reports of customized metal 3D printed prosthesis for repairing the bone defect after bone tumor resection are encouraging. Angelini et al conducted a study to investigate the feasibility of surgical reconstruction with these prostheses in oncologic and non-oncologic settings. The results showed 7 complications occurred in 5 patients (38.5%) and functional outcome was good or excellent in all cases with a mean score of 80.3%.[51] Fan et al[52] used 3D printed titanium prostheses manufactured by electron beam melting technology to reconstruct huge bone defects in patients with bone tumors. The results showed that there were no surgical complications such as limb length discrepancy, screw loosening, and implant breakage in all patients.

In the above series, although usual complications and periprosthetic fractures were encountered, metallic failure of 3D printed prosthesis was not reported. 3D printed custom-made prostheses represent a promising reconstructive technique in musculoskeletal oncology surgery. Further studies are needed to evaluate prosthetic design, fixation methods, and stability of the implants at long-term.

Acknowledgments

Sincerely thank my dear Zhuo for supporting and helping my life and writing.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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