■ INSTRUCTIONAL REVIEW

The management of an infected total knee arthroplasty

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Periprosthetic joint infection (PJI) is one of the most feared and challenging complications following total knee arthroplasty. We provide a detailed description of our current understanding regarding the management of PJI of the knee, including diagnostic aids, pre-operative planning, surgical treatment, and outcome.

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Periprosthetic joint infection (PJI) is one of the most feared and challenging complications following total knee arthroplasty (TKA). Despite all efforts to prevent this complication, infections occur in about 0.5% to 1.9% of primary TKAs and in 8% to 10% of revision TKAs.[1-3] While the definitive diagnosis of PJI remains the key to success, thorough pre-operative evaluation, careful surgical planning and rigorous adherence to the principles of treatment are essential. Treatment may involve irrigation and debridement (I & D) with retention of the components, and exchange arthroplasty either as a one- or two-stage procedure. In patients who fail all reconstructive endeavours, salvage operations include resection arthroplasty, fusion and above-knee amputation.

A one-stage exchange offers the advantages of only one operation, reduced treatment with antibiotics, reduced hospitalisation and reduced costs.[4]

Although the two-stage technique has been considered to be the 'gold standard' for the management of PJI, there is no high-level evidence that it has a higher success rate than a one-stage revision.[5] Moreover, many aspects of a two-stage procedure remain unknown, including the optimal timing of the second stage. A reliable biomarker of the elimination of infection is yet to be discovered.[6,7]

Classification

Current guidelines of the American Academy of Orthopaedic Surgeons (AAOS),[8] the Infection Disease Society of America (IDSA)[7] the International Consensus on PJI,[9] and the Liestal Algorithm from Switzerland[10] make a clear distinction between early and late PJIs: an early infection is considered to occur within three weeks of the procedure, or in the case of a late haematogenous infection, within three weeks of the development of symptoms. Any PJI which develops thereafter is considered to be late, irrespective of the stability of the components. It is important to realise that PJI does not only reflect an infection of the prosthetic interface, but also an infection of the surrounding bone and soft tissues.

An early infection may be treated with aggressive debridement, exchange of modular parts, and retention of the fixed components. Late infection necessitates the removal of the components. Other factors, besides the timing of the infection, may influence the outcome of treatment and should be taken into consideration. We advocate the concept introduced by McPherson et al,[11,12] which consists of considering the timing of the infection, the systemic medical and immune status of the patient, and the local compromising factors (Table I).[13]

The distinction between early and late PJI is based on the assumption that within three weeks organisms can form a biofilm on the surface of the components, necessitating their removal. However, it has recently been shown that organisms can form a biofilm within hours and at most a few days.[14-16] Thus, we need to re-examine the logic behind the older classification and consider the fact that the formation of the biofilm is the detrimental step that needs to be addressed in the surgical management of PJI.

Variable outcomes have been reported following I & D, with the success rates varying between 21% and 100%, for further infection occurring within a month of the operation.[17] This variation may be because of factors related to the patient, the surgery or the pathogen.

Diagnostics

A painful TKA should be considered to be infected until proved otherwise. Therefore, even without obvious signs of infection, such

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Table I. Staging system for periprosthetic joint infection (adapted from McPherson et al[11])

Category/Grading	Definition	Considerations
Infection Timing		Early and late PJI were originally defined as within and after 4 weeks following the index surgery, respectively, as per classification of Tsukayama et al[13]
I	Early	
II	Acute hematogenous	
III	Late	
Systemic factors		Systemic compromising factors:
		- Age > 80 years
		- Alcoholism
		- Nicotine use (inhalational or oral)
		- Chronic indwelling catheter
		- Chronic malnutrition
		- Diabetes mellitus
A	No compromising factors	- Liver insufficiency
B	1 to 2 compromising factors	- Pulmonary insufficiency
C	≥ 3 compromising factors or presence of presence of one of the following:	- Renal insufficiency
	- Absolute neutrophil count <1000/mm^3	- Systemic inflammatory disease (rheumatoid arthritis, systemic lupus erythematosus)
	- CD4 T cell count < 100/mm^3	- Systemic immune compromise from infection or disease (human immunodeficiency virus, acquired immunodeficiency virus)
	- Intravenous drug abuse	- Chronic active dermatitis or cellulitis
	- Chronic active infection other site	- Malignancy (history of, or active)
	- Dysplasia or neoplasm of immune system	- Immunosuppressive drugs
Local factors		Local compromising factors
		- Active infection present
1	No compromising factors	- Multiple incisions (creating skin bridges)
2	1 to 2 compromising factors	- Soft-tissue loss from prior trauma
		- Subcutaneous abscess > 8 cm^2
		- Synovial cutaneous fistula
		- Prior periarticular fracture or trauma about joint (especially crush injury)
		- Prior local irradiation to wound area
3	≥ 3 compromising factors or presence of immune deficiency	- Vascular insufficiency to extremity (absent extremity pulses, chronic venous stasis disease, significant calcific arterial disease)

as redness or swelling, a low-grade infection should be ruled out in all patients with a painful TKA. The presentation often involves insidious symptoms and the threshold for the clinical suspicion of infection should be particularly low in patients with predisposing factors for PJI, such as those with a history of wound drainage and those with comorbidities such as diabetes mellitus or immunosuppressive conditions.[6,7]

The AAOS and the International Consensus Group on PJI have provided an algorithm for making the diagnosis of infection that we endorse and follow.[6,17] This involves performing laboratory tests and aspiration of the joint. The tests should include:

- C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR).[18-20]

- Analysis of the joint fluid, should include the white cell count, neutrophil percentage, leukocyte esterase, and culture.[21-23] If the initial aspiration is unsuccessful it should be repeated. Repeat aspiration should also be considered if there is a discordance between the clinical presentation and the findings following analysis of the joint fluid.

- If repeat aspiration is still negative, a white-cell-labelled bone scan may be undertaken, although this has a limited role in the diagnosis of PJI because of its low specificity and inconsistent results.[8] Tissue from the joint may be analysed using an open or arthroscopic approach.[24]

The value of serum markers such as procalcitonin, interlukin-6, and others in the diagnosis of PJI remains controversial.[17] There is a desperate need for serum markers of PJI and our respective institutions are currently pursuing such a test.

Recent analyses of the data in our institutions have shown that the sensitivity of the serum CRP level is much lower than previously assumed. We have also recently noted that the levels of serological and synovial markers are affected by the administration of systemic antibiotics.[25] Table II[26-33] presents the characteristics of the diagnostic tests for PJI.

Joint aspiration

Aspiration of the joint is far the most important test in the investigation of a patient with painful TKA. The analyses performed on the aspirate provide the information that allows the categorisation of patients, based on the Musculoskeletal Infection Society (MSIS) criteria,[34] and culture of the fluid also allows isolation of the infecting

Table II. Test characteristics of common laboratory tests used in the diagnosis of periprosthetic joint infection of the knee

	Sensitivity (%)	Specificity (%)
Blood tests		
Erythrocyte sedimentation rate*[26]	75	70
C-reactive protein*[26,27]	*82* to *88*	*74* to *77*
Synovial tests		
Leucocyte esterase[28,29]	*81* to *93*	*87* to *100*
White cell count[30,31]	*84* to *99*	*80* to *94*
Neutrophil percentage[30,32]	*84* to *93*	*69* to *83*
Fluid culture[24]	*12* to *100*	*81* to *100*
Tissue culture[24,33]	100	*95* to *98*

* Values represent the results of pooled analyses by meta-analyses

organism in up to 93% of patients.[35] However, culture of the aspirate may be negative in up to 45% of patients[20,36] which does not rule out infection. The isolation of the infecting organism and the corresponding antibiotic profile are essential for antibiotic-loaded cement to achieve a high level of elution at the surgical site during a one-stage procedure.[37]

Following this algorithm is the gold standard for every revision TKA in our hospital, including all those with an early or late PJI. Furthermore, we expand this regimen to all patients with persistent pain of unknown origin or malfunction after primary or revision TKA. A study from the Endoklinik showed that between 4% and 7% of patients initially planned for an aseptic TKA revision had evidence of a low-grade infection.[38]

Another study from the Rothman Institute showed that 12% of patients undergoing so called 'aseptic' revision had evidence of PJI that had either not been appropriately evaluated, or had escaped the available diagnostic modalities.[39] Aspiration should always be undertaken after antibiotics are withheld for 14 days to avoid false negative results.[36]

Furthermore, we recommend that bacteriological cultures are performed for ten to 14 days because of slow growing organisms or small colony variants.[36] It has been shown, for example, that *Propionibacterium acne* and *Peptostreptococci* may be detected on routine culture plates only after incubation for between ten and 12 days.

Irrigation and debridement

Aggressive debridement and irrigation with exchange of the polyethylene liner should only be undertaken for patients with an early PJI.[40] It should not be used in patients with risk factors for persistent or recurrent infection such as those with poor local soft tissues, those who are immune compromised and those with resistant pathogens because of the risks of persistent colonisation and polymicrobial infection.[41]

The International Consensus Group provided a detailed protocol on how I & D should be performed.[42] An aggressive debridement of the periarticular tissues and the components should be undertaken to reduce the bioburden of the pathogens and to improve the efficiency of the patient's immune system and antibiotics against the surviving pathogens. Thus, all non-bleeding soft- or osseous tissues should be removed. In order to access the posterior capsule of the knee, the liner must be removed, and preferably exchanged. All the components should also be inspected for loosening; thus, the interfaces of the components should be exposed.[43,44]

Specific protocols for the irrigation have been described, which should include about nine litres[41] although it remains unclear which irrigation protocol gives the best outcome.[45] There is little consensus regarding use of low-pressure (< 15 pounds per square inch) or high-pressure (> 45 pounds per square inch) lavage. High-pressure lavage provides rapid and effective removal of necrotic tissues, but may cause tissue damage or penetration of bacteria into deeper soft-tissue layers.[45]

Post-operatively, long-term combined intravenous (IV) antibiotic treatment of between four and six weeks followed by oral rifampin for six months is recommended in patients undergoing I & D.[7] The outcome may be adversely affected by the time interval between the initial operation and the development of infection. The success rate of I & D dropped to 40% when the infection started > six weeks after the TKA.[46]

Some authors have suggested a combined protocol consisting of debridement, antibiotic treatment for > one year, and implant retention (DAIR) for the treatment of PJI. However, there is risk of recurrence following discontinuation of the antibiotics. The risks of this happening are increased four-fold according to Byren et al[47] suggesting that this form of treatment does not eradicate the pathogen but postpones its reactivation. It has also been suggested that the outcome of a two-stage revision TKA is adversely affected by a prior failed I & D.[43,48] The results of recent publications regarding I & D and DAIR treatment are shown in Table III.[42,45,49-54]

Two-stage exchange arthroplasty

In patients with late PJI, exchange TKA is recommended. A two-stage exchange procedure involves the removal of all material, including the cement, and aggressive debridement of the soft tissues and bone at the first stage. A spacer is introduced and systemic antibiotics are administered for between four and six weeks. When the knee is subsequently deemed to be free of infection, the second stage is undertaken to introduce new components. However, if there is any suspicion of persistent infection, a repeat debridement with exchange of the spacer should be undertaken.

Very extensive debridement is essential for both one- and two-stage procedures. While it is mandatory to remove all components - femoral, tibial and patellar, bone cement, cement restrictors, screws and wires, in a two-stage procedure, meticulous debridement is also required. Further debridement may also be undertaken at the second stage. During the debridement, all septic membranes must be

Table III. Outcome of irrigation and debridement. Only studies with > 20 patients with minimum one-year follow-up and published after 2000 are reported

	Sample size*					
Publication	**Early**	**Late**	**Definition of failure**	**Follow-up (yrs)†**	**Success rate (%)**	**Considerations**
Fehring et al[49]	30	16	Return to the operating room for an infection-related problem	4 (2 to 9)	37	- Hip and knee PJI within 90 days of the index surgery were included. - Success rate represents overall outcome including patients with knee PJI occurring within one month (acute) or 31 to 90 days (chronic) after index surgery. - Success rates were not specified per joint-chronicity subgrouping (e.g. acute knee PJI) but they were not significantly different between acute and chronic PJI (25/57 *vs* 7/29, respectively) for both knees and hips.
Lora-Tamayo et al[50]	267	78	Death related to infection	> 2	55	- 345 joints (including 195 knees) with PJI due to methicillin-sensitive (264) or resistant (81) *Staphylococcus aureus* were included.
			Implant removal Persistence or relapse of infection Extra I & D within 30 days of the first I & D Long term suppressive antibiotic treatment			- Success rates were not specified per joint-chronicity.
Koyonos et al[44]	102	36	Need for surgery or long-term suppressive antibiotics	> 1	35	- Included 78 knees (57%) and 60 hips (43%). - Success rate for all knee PJIs (acute and chronic) was 38%. Success rates for acute and chronic PJIs were 37% and 28%, respectively (both knees and hips). Success rates per joint-chronicity subgrouping (e.g. acute knee PJI) were not specified.
Odum et al[51]	47	102	Reoperation for PJI	> 2	31	- Included both knees (65%) and hips (35%). - Success rate for acute and chronic PJIs was 16 and 29%, respectively. One-third of patients did not have 2-year follow-up.
Azzam et al[52]	104		Resection arthroplasty or recurrent microbiologically proven infection	6 (2 to 10)	44	- Included 52 patients with knee and 52 patients with hip PJI. - Success rates per joint grouping were not specified.
Byren et al[47]	NS	NS	Recurrence of PJI with positive culture	> 2	75	- All patients underwent DAIR therapy included 51 patients with knee PJI. - Chronicity of PJI was not specified. - Mean duration of antibiotic was 1.5 years.
			Recurrence of wound drainage/sinus for three months beyond index I & D Requirement for revision surgery (repeat I & D was not considered as failure)			- Failure was more common following arthroscopic procedures compared with open procedures
Marculescu et al[53]	NS	NS	Occurrence of any PJI, death or indeterminate clinical failure	> 2	60	- Included 99 cases of hip and knee infection undergoing DAIR treatment. - Chronicity was not specified. - 78 episodes received long-term antibiotic treatment. - Success represents 2-year treatment free survival rate.
Deirmengian et al[54]	31		Recurrence of infection or need for implant removal	4 (2 to 10)	35	- Success rate includes 5 patients (16%) with indefinite suppressive antibiotic therapy.

* Represents number of knees with periprosthetic joint infection (PJI)
† Represents mean follow-up duration with the range in parentheses
DAIR, debridement, antibiotics and implant retention; I & D, irrigation and debridement; NS, not specified

radically excised. Special care needs to be taken to debride the posterior capsule, since it might be the source of re-infection.

Cortical windows may be required for the removal of well-fixed uncemented components. High-speed burrs and curved saw blades may be needed. Removal of well-fixed components carries the risk of destruction of bone and the adjacent soft-tissues.

All efforts should be made, however, to minimise bone loss. This involves patiently working around the cement and the interface with the components. The tibial component, for example, is best removed by using an oscillating saw first to cut into the cement mantle and then using a 'stacked osteotome' technique to loosen the interface further. Narrow, straight osteotomes with symmetrically coned blades should be used to remove all bone cement. This may be less destructive than aggressive extraction using a mallet and special extraction devices. Special or universal extraction forceps are sometimes required in order to remove the components. Curved chisels, long rongeurs, curetting instruments, long drills, and cement taps are used to remove the cement. General debridement of bone and

posterior soft tissues must be as radical as possible, including all areas of osteolysis and necrotic bone.

Many tissue samples from different areas should be sent for microbiological examination. We recommend taking between three and six samples from areas that should include the intramedullary canals of the femur and the tibia, and the posterior capsule.

We usually use pulsatile lavage throughout the procedure, although the literature regarding the benefits of its use is inconclusive.[45] A copious amount of liquid must be used. After the removal of all foreign material and debridement, the intramedullary canals are packed with swabs soaked with antibacterial solutions such as polymeric biguanide hydrochloride (Lavasept, Fresenius-Kabi AG, Bad Homburg, Germany), although the most efficacious antimicrobial solution for irrigation remains unknown.[45]

The antibiotic-impregnated cement spacer

After extensive debridement and irrigation, an antibiotic-loaded cement spacer is introduced.[55] The role of the spacer is to preserve the joint space and reduce soft-tissue contracture, while delivering high doses of antibiotic.[56,57]

Ideally, it should also allow for an optimised exposure for the second stage. The high level of local bactericidal antibiotics allows the residual organisms that may remain after the debridement to be killed.[58,59]

The spacer may be dynamic (articulating) or static (non-articulating).[60] While a general improvement of function before the second stage may be achieved with an articulating spacer, the range of movement at a mean follow-up of two years after the second stage did not significantly vary (< 5°) after the use of static or dynamic spacers.[19] No clear contraindications have been described for the use of either type of spacer, although many authors believe that massive bone loss, lack of functioning collateral ligaments and the need for soft-tissue reconstruction such as local flaps, are relative contraindications for the use of an articulating spacer.[17] Neither is there evidence that one type of spacer provides a better control of infection over the other. There is also no evidence that premade (manufactured) spacers have any superiority over 'homemade' spacers.[17] The advantages of manufactured spacers are the smoother surfaces that may allow for better articulation and the time that is saved in making the spacers intra-operatively.

Antibiotic-loaded spacers may contain water soluble, heat resistant antibiotics in crystalline form; the powder should be mixed together with the powder of the polymethylmethacrylate before liquid is added. The amount of antibiotic may be up to 20% of the total mass of the spacer, as the mechanical strength of the spacer is not a major issue. However, care should be taken with the amount of antibiotics used to prevent systemic toxicity.[61] Although rarely described, topical antibiotics may be nephrotoxic. In comparison, when using antibiotic-loaded cement for the fixation at the second stage, a maximum of 10% by weight of antibiotic should be added to the cement in order to retain its biomechanical properties.[62,63]

In patients with recurrent infection or delayed wound healing between the two stages, an exchange of the spacer may be indicated. Based on the results of intra-operative microbiological testing at the first stage, a new antibiotic combination may be considered for this subsequent spacer.[64,65]

Antibiotic treatment

The choice of antibiotics is based on the results of cultures. An infectious disease expert should be consulted to help determine the type and duration of treatment and to monitor the patient during treatment.[61]

Treatment is started during the first stage procedure, and is commonly continued for between four and six weeks post-operatively as recommended by the IDSA[7] and International Consensus on PJI.[66] The treatment should be individualised, taking into account the infecting organism and the patient. In the first two weeks, IV administration is recommended, after which oral treatment may be continued depending on the resistance profile of the organism and the availability of an appropriate agent.[67]

Currently, no tests or measurements are available to determine the optimal timing of the second stage.[65] Most surgeons allow a period of two weeks, during which no antibiotics are used before this stage. There is, however, no evidence to support this. The ESR and CRP levels may be measured before the second stage. However, it has been shown that although these levels reduce following the first stage, the levels at the time of the second stage remain variable and are not representative of control in infection,[68,69] nor do they predict subsequent failure.[70] Aspiration of the knee before the second stage may be undertaken. The microbiological culture of the aspirate before the second stage has been shown to be specific (92% to 100%) but the sensitivity is inconsistent (0% to 100%).[71,72] In order to minimise the rate of false negative cultures before the second stage, aspiration should be performed at least two weeks after completion of systemic antibiotics.[18] Moreover, the thresholds for the cell count and neutrophil percentage in the synovial fluid in patients with a spacer in place are not currently known. Other biomarkers of the synovial joint such as interleukin-6 have also been proposed but more robust data are required to determine its use in planning the timing of the second stage.[73]

Re-implantation

The second stage is performed when the wound is healed, the knee appears to be clinically (and/or by laboratory parameters) ready for further surgery, and the patient is medically fit. However, as mentioned above, determination of the optimal timing of this stage remains unsupported by robust evidence. Typically, it takes place between two and three months after the first stage.[69] During the procedure, further antibiotics are administered and a further aggressive debridement is performed.[74] Some surgeons prefer to perform an anterior synovectomy, before the preparation of the

tibia, and then approach the posterior aspects of the knee, including a posterior synovectomy. The femoral preparation is relatively specific to the design of the component, which may be semi- or fully-constrained. The mode of fixation of the stems remains controversial. Cementing allows the delivery of antibiotics while diaphyseal engaging uncemented stems might improve alignment and the ease of removal if there is re-infection. Hybrid techniques have also been described using diaphyseal-engaging uncemented stems on the femoral and tibial components. Cement is applied to the undersurface of the components at the metaphysis.[75] However, the available evidence shows that the rate of re-infection is similar with different types of fixation, according to one comparative study (20% *vs* 24% for cemented and hybrid components, respectively)[75] and several non-comparative studies (8% to 14% for cemented and 6% to 17% for uncemented and hybrid components).[76-80]

The second stage procedure should be seen as another opportunity to perform aggressive debridement. Post-operative antibiotics are continued until the microbiological results of the intra-operative cultures are available. If these cultures are positive, consideration should be given to prolonged antibiotic treatment.

One-stage exchange arthroplasty

One-stage exchange arthroplasty has many advantages. This form of treatment is performed in up to 85% at specialised centres in Europe,[38,81] and is gaining popularity in North America. This approach is a viable option for most patients with a PJI. The infecting organism and its sensitivity need to be established pre-operatively,[4] allowing the delivery of local antibiotics from the cement.

In our opinion, the following are contraindications to a one-stage exchange arthroplasty:

- Sepsis with substantial systemic manifestations (such as haemodynamic decompensation), which mandates prompt reduction of bio-burden of the causative pathogen and hardware removal.
- Failure of two or more previous one-stage procedures.
- Infection involving the neurovascular bundles, precluding radical debridement.
- Culture-negative PJI where appropriate antibiotic treatment cannot be determined.
- Extensive soft-tissue involvement preventing closure of the wound.
- Infection with a highly virulent organism, especially if appropriate antibiotics for addition to cement are unavailable.

Operative technique

The outcome of a one-stage exchange arthroplasty relies on appropriate patient selection, meticulous surgical technique and strict peri-operative multidisciplinary management. This procedure, like the two-stage exchange, is largely dependent on the efficiency by which debridement and reduction of the bioburden is performed.

The debridement begins by excising the previous scar. The sinus, if present, should be integrated into the incision and radically excised down to the capsule of the joint. The use of a tourniquet is generally not recommended during debridement surgery to allow the identification of non-bleeding soft and osseous tissues, which need radical excision. After completion of debridement and removal of the components, a tourniquet may be used to minimise blood loss and during cementation, to achieve better fixation. Between three and six tissue samples are sent for microbiological culture and histopathology evaluation during the procedure.[24,36]

For removal of long and cemented stems special instruments such as curved chisels, long forceps, curretting instruments, long drills, and cement taps are needed. All cement and restrictors need to be removed. Debridement of bone and soft tissues must be radical and include all areas of osteolysis and non-viable bone. If resection of the collateral ligaments becomes necessary, we use fully cemented long stemmed revision components with a higher level of constraint such as a rotating hinge.[82] Pulsatile lavage is used throughout the procedure; however, after removal of the components and debridement, the intramedullary canals are packed with swabs that are soaked with polymeric biguanide hydrochloride (Lavasept). After the completion of the resection, the wound is temporarily closed and the surgical team rescrubs. New instruments are used for the re-implantation. A second dose of antibiotic is given at this time.

Re-implantation

The re-implantation proceeds as with other types of revision. We prefer not to use allograft bone to address bone loss, although favourable outcomes have been described by Winkler et al with the use of antibiotic-impregnated allografts. They reported a 96% rate of control of infection following uncemented hip and knee revision for PJI in 45 patients at a mean follow-up of 3.2 years (1 to 7).[83,84] We fill the defect with cement and/or trabecular metal cones. Variations in the depth and width of the cones allow for appropriate satisfactory reconstruction.[85] It has been suggested that tantalum may have a protective effect against infection.[86] It is essential that the antibiotic added to the cement has activity against the infecting organism, be in powder and not liquid form, and be bactericidal. In addition, the maximum weight of the antibiotic should not exceed 10% of the weight of the PMMA powder to prevent biomechanical weakness. Systemic antibiotics are continued ten to 14 days post-operatively.[38,61]

Post-operative care

Functional exercises and weight-bearing may be undertaken early based on an individualised physiotherapy plan, whose aims are to restore movement. We generally recommend mobilisation within the first post-operative days

Table IV. Outcome of one- and two-stage revision arthroplasty. Only studies with > 20 patients with a minimum two-year follow-up and published after 2000 are reported

Study	Sample size*	Definition of failure	Follow-up (yrs)†	Success rate (%)
One-stage exchange arthroplasty				
Zahar et al[82]	70	Revision surgery for infection or any other cause	10 (9 to 11)	*93*
Haddad et al[90]	28	Major surgery or chronic suppression antibiotic therapy for control of infection	6 (3 to 9)	*100*
Tibrewal et al[91]	50	Revision for recurrent infection	10 (2 to 24)	*98*‡
Jenny et al[92]	47	Occurrence of any infection	3 (0.5 to 6)§	*87*
Singer et al[99]	63	Recurrence of infection	3 (2 to 6)	*95*
Two-stage exchange arthroplasty				
Haddad et al[90]	74	Major surgery or chronic suppression antibiotic therapy for control of infection	6 (3 to 9)	*93*
Macheras et al[93]	31	Recurrence of infection	12 (10 to 14)	*91*
Gooding et al[94]	115	Presence of symptoms of infection as well as raised inflammatory markers	9 (5 to 12)	*87*
Mortazavi et al[100]	117	Any further surgical treatment for PJI	3 (2 to 9)	*72*
Kurd et al[95]	96	Any further surgical treatment for PJI	3 (2 to 7)	*73*
Hsu et al[96]	28	Re-infection	8 (5 to 10)	*89*
Hart et al[97]	48	Persistence of infection	4 (2 to 7)	*88*
Haleem et al[77]	96	Reoperation	7 (2 to 13)	*84*
Emerson et al[98]	48	Re-infection	6 (3 to 13)	*79*

* Number of knees with periprosthetic joint infection (PJI)
† Mean follow-up duration with the range in parentheses
‡ The success rate included three patients (6%) with recurrent infection who did not require surgery and nine other patients (18%) who underwent further revision for aseptic loosening (negative intra-operative cultures)
§ Cases with no repeat infection were followed for at least three years

using walking aids and full weight-bearing within two weeks.

Outcomes

Persistent or recurrent infection remain the most important complications.

Although the indications for one-stage arthroplasty are more limited, the outcomes which have been reported for both procedures are comparable (Table IV).[87-100] Comparative prospective randomised studies are, however, required to compare the control of infection and function following these procedures.

Alternative forms of treatment

Long-term antibiotic suppression. The goal of antibiotic suppression is to allow for infection control rather than eradication. Chronic antibiotic suppression may be used in elderly, frail patients who may not be able to withstand a surgical procedure. If chronic suppression is considered, it is important to ensure that the prosthesis is well-fixed, the pathogen is not virulent, and oral antibiotics against the organism are available. Using these indications a success rate of 86% at a mean follow-up of five years has been described in a series including 36 patients.[101] However, this form of treatment depends highly on the selection criteria, as other authors with larger numbers of patients only reported good outcomes in between 18% and 24% of patients.[102,103] Relative contraindications of this form of treatment include the presence of other implants that are not infected and the presence of an artificial heart valve.

Excision arthroplasty. The indications for this procedure which involves removal of the components with soft-tissue and bone debridement and without the re-implantation of new components, are very limited and might include low-demand patients who simply require to sit comfortably as this is easier after an excision arthroplasty than after arthrodesis of the knee. As a salvage procedure the infection may be eradicated in between 50% and 89% of patients.[104,105]

Arthrodesis. This has been used traditionally for the treatment of PJIs. The number which are undertaken has declined over the past decades with the improved results of one- and two-stage revision procedures. Good candidates for arthrodesis are young active patients in whom reconstructive alternatives have failed, particularly those with loss of the extensor mechanism and compromised bone stock, or PJI caused by multi-resistant pathogens that have proved to be uncontrollable.

Different techniques have been described to achieve arthrodesis of the knee, including external fixation, double plating, and intramedullary nailing, which is the preferred form of treatment at our hospital. It may be performed as a one-stage procedure. During surgery, extensive debridement is performed and the knee is prepared to accept the intramedullary device. Then the instruments are changed and personnel rescrub and new drapes are used. We prefer to add powdered local antibiotics with activity against the infecting organism to the knee before closure. Supporting evidence for this strategy mainly originates from spine literature where direct application of vancomycin powder into the wound at posterior lumbar has been associated with a significant decrease in infection rate, without affecting the rate of fusion.[106] While successful in most patients, the complications of arthrodesis of the knee include persistent

infection, pain, limb-length inequality, and rotational malalignment. The success rate in achieving control of infection and fusion have been reported to be between 88% and 94% and 75% and 88%, respectively.[107-109] Comparing two different techniques of arthrodesis, external fixation proved to be less susceptible to recurrent deep infection than intramedullary nailing (4.9% *vs* 8.3%); however, the rate of successful fusion was higher when intramedullary nailing was used (23/24 (95%) *vs* 41/61 (67%) with a mean follow-up of 13 months). The rate of complications in this series was 40%.[107] Based on a recently published review of literature, following a failed two-stage revision TKA, arthrodesis was found to be the optimal form of treatment to control infection and gain function, compared with repeat two-stage exchange revision, chronic antibiotic suppression and amputation.[110]

Amputation. Above-knee amputation is truly a last option for management of PJI after TKA and is rarely indicated (0.1%).[111] It might be the only form of treatment in patients with life-threatening systemic sepsis. However, in our experience, these situations are best handled with open debridement, continuous lavage, and the suction drains. The indication for amputation is a patient with extensive involvement of soft tissues, massive bone loss, and persistent infection with many failed attempts at control of infection. The presence of massive bone loss precludes performing arthrodesis. Above-knee amputation is very occasionally preferred to arthrodesis, especially in tall patients who may have difficulty fitting into a car or travelling on a plane.

The outcome of amputation may be poor owing to the need for higher levels of energy that are required for walking. In one series of 25 above-knee amputations including 19 cases with failed PJI management with a mean follow-up of 4.5 years, only 30% of the patients with above-knee amputation could walk regularly, and 52% were confined to a wheelchair.[112]

In conclusion, although there are various surgical and non-surgical options for the management of PJI after TKA, the outcomes of all of these procedures are far from perfect. Most patients with PJI require protracted treatment. There is a desperate need for novel forms of treatment and improvement in the care for these patients.

Exciting research is in progress including attempts to determine the genetic susceptibility of patients to infection, the design of many techniques for disrupting biofilms and the introduction of infection-resistant implants.

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