

(ii) Diagnosis and management of infection after total knee arthroplasty

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Abstract

The incidence of infection after total knee replacement (TKR) has been reported variously between 0.4% to 2% in the current literature. As the numbers of TKR procedures are increasing annually, so are the numbers of prosthetic joint infections. Although the incidence of infection has been dramatically reduced over the last decade, an infected prosthetic joint still significantly adversely affects the outcome of TKR and adds undue financial burden on the healthcare system. This article aims to review the current literature regarding the factors associated with infected TKR, along with diagnosis and management of this serious potential complication.

Keywords debridement; infection; peri-prosthetic; revision; total knee replacement

Introduction

Infection after total knee replacement (TKR) remains a serious challenge faced by orthopaedic surgeons worldwide. The incidence of infection after TKR has been variously reported between 0.4% to 2% in the current literature.^{1,2} The National Joint Registry data from the year 2010 reported about 82 000 TKR procedures carried out in England and Wales, an increase of 5.7% from the year 2009.³ As the numbers of patients undergoing joint replacement procedures are increasing each year, so are the numbers of patients with infected prosthetic joints. An infected TKR can pose a serious threat to the limb or life of the patient, add significant morbidity to the patient, adversely affect the outcome of TKR and also impose financial strains on the healthcare system. The treatment options could include long-term antibiotic suppression with oral or parenteral antibiotics, surgical debridement with or without insertion of a new prosthesis, arthrodesis or amputation.⁴ This problem is further compounded by the emergence of new or resistant strains of microorganisms. Several organisms have been isolated from

infected TKRs, however *Staphylococcus aureus* is by far the most common organism responsible.¹

This article aims to review the current literature regarding the prevention, diagnosis and management of an infected TKR.

Risk factors associated with infected TKR

Several factors have been identified that are associated with an increased risk of infection after TKR (Table 1).

Obesity has often been implicated as a risk factor;⁵ however, this has not been proven conclusively,⁶ and whether or not to perform a TKR in an obese patient remains largely at the individual surgeon's discretion. Morbidly obese patients with poor nutritional status (measured as serum transferrin and albumin levels and total lymphocyte count) have been shown to be at higher risk of post-operative infection.¹ Of the other risk factors, as noted above, the majority can be screened for and identified prior to surgery. Strict pre- and peri-operative glycaemic control and electrolyte balance, screening and eradication of organisms like *Methicillin resistant S. aureus* (MRSA) and urinary tract infections, identification and treatment of skin ulcerations, and potential modification of immunosuppressive therapy prior to surgery remain a prerequisite pre-operatively. Similarly, effective peri-operative antibiotic prophylaxis, strict intra-operative aseptic technique and the use of laminar flow theatres also remain of paramount importance to try and minimize the risk of infection after TKR. The use of closed suction drainage after TKR has not been proven to increase the risk of infection post-operatively.⁷

Post-operative haematoma formation is a known risk factor for infection after TKR, and the risk of this is higher in patients with haemophilia or other bleeding disorders and those on anti-coagulation therapy. In a retrospective case-control study involving about 17 700 patients undergoing TKR, Galat et al reported that 13.6% of patients who underwent early evacuation of a haematoma within 30 days of TKR subsequently developed a deep infection.⁸ Similarly, in case-control study analyzing 78 patients with infected prosthetic joints, Parvizi et al found a direct correlation between excessive anticoagulation (International Normalised Ratio (INR) more than 1.5) and post-operative wound related problems that subsequently led to infected prostheses.⁹

Factors associated with an increased incidence of infection after TKR

| | |
|--------------------------------|---|
| Rheumatoid arthritis | Immunosuppressive therapy |
| Haemophilia | Excessive anticoagulation |
| Diabetes | Cancer |
| Obesity | Chemotherapy |
| Malnutrition | Multiple blood transfusions |
| Smoking | Peripheral vascular disease |
| Alcoholism | Bleeding disorder |
| Recent urinary tract infection | Hypokalemia |
| Oral corticosteroids | Previous knee surgery |
| Skin ulceration | Revision surgery |
| | Prolonged surgical time (more than 2.5 h) |

Table 1

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Classification

Several classification schemes have been described for infection after TKR, which help in deciding further management and prognosis, essentially whether to retain the implant or to proceed to a revision.¹⁰ That described by Tsukayama et al describes four groups:

- (A) Positive intra-operative culture (PIOC): this is usually seen in revision surgery for indications other than infection. The diagnosis of infection can only be confirmed when multiple specimens are positive for the same microorganism.
- (B) Early post-operative infection: this can be either superficial or deep and usually presents within the first month of the index procedure.
- (C) Acute haematogenous infection: these infections usually result from bacteraemia secondary to a dental, urological or similar surgical or medical invasive procedure. These patients usually present more than 4 weeks after the primary surgery; however, bacterial seeding of a prosthetic implant can also occur within first month of the surgery. Recent American Academy of Orthopaedic Surgeons (AAOS) guidelines recommend routine use of prophylactic antibiotics prior to any invasive procedures irrespective of the interval between the arthroplasty and the procedure.
- (D) Late chronic infections: these patients often present late after the primary procedure, with chronic pain with or without any obvious signs of infection. The treating clinician should have a high index of suspicion for diagnosing infection in any painful TKR.

Diagnosis and evaluation

The diagnosis and evaluation of a patient with a suspected infected TKR is based on the clinical features, laboratory investigations, imaging and further non-invasive and invasive procedures. Needless to say, the spectrum of presentation of a patient with an infected TKR can vary from a fulminant systemic sepsis to an indolent chronic low-grade infection. Clinically, the patient often presents with an acutely inflamed, painful, swollen knee joint with or without associated adjoining erythema or a discharging sinus. The patient may also complain of stiffness of the joint and difficulty in weight bearing on the affected limb. Any patient presenting with a suspected infection of a prosthetic joint should be evaluated comprehensively.

There are several diagnostic tests available to the physician to aid in the diagnosis of an infected prosthetic joint. However, these investigations should be used in a logical and meaningful way in order to confirm the diagnosis based on the associated risk factors and the clinical symptoms at the time of presentation.

Inflammatory blood markers

Several inflammatory markers have been used for the diagnosis of suspected prosthetic joint infection, including serum leukocyte/white cell count, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), Interleukin 6 (IL6), procalcitonin and tumour necrosis factor α (TNF- α). Serum leukocyte count as a diagnostic marker for prosthetic joint infection lacks sensitivity and specificity and is therefore of little value in diagnosing an infected TKR.¹¹ In a study analyzing various inflammatory markers in patients with suspected deep implant infection,

Bottner et al¹¹ found that procalcitonin was highly specific (specificity 0.98) but lacked sensitivity (0.33). TNF- α has been shown to be neither sensitive nor specific for diagnosing prosthetic infection.

IL6 is a cytokine produced by activated macrophages, monocytes and T cells as an inflammatory response and it induces production of acute phase proteins including CRP. Its level rises at 6 to 12 h after surgery or trauma and returns to baseline levels at 48 to 72 h.¹² IL6 has been found to be a very sensitive and specific marker for diagnosing infection after TKR.^{11,13} It can be particularly useful for diagnosing infection in the acute post-operative setting as it reaches its baseline level quickly, as opposed to CRP or ESR, which are generally still raised up to 3 weeks after the surgery. In absolute terms, a serum level of IL6 ≥ 12 pg/ml has been shown to be highly diagnostic of infection after TKR.^{1,11} In a recently conducted systematic review, IL6 was found to be the best diagnostic marker for infected TKR when compared to CRP and ESR.¹⁴ However, as the evidence is still evolving and the cost of routine IL6 testing is not known, the use of IL6 as a diagnostic marker is still developmental and hence it is not used routinely.

CRP is an acute phase protein produced in the liver as a response to systemic inflammation. It has been considered to be the most accurate diagnostic marker for infection after TKR^{1,11,13} owing to its high sensitivity (up to 0.96) and specificity (up to 0.92).¹⁵ A serum value of ≥ 3.2 mg/dl has been found to be highly sensitive (0.96).¹¹ However, it can give false positive values in an acute post-operative setting as the values can remain elevated for up to 3 weeks after surgery.

The sensitivity and specificity of ESR alone for diagnosing infected prosthetic joints has been found to be relatively low.¹¹ Recent guidelines from the American Academy of Orthopaedics Surgeons for diagnosing peri-prosthetic joint infections have recommended the combined use of ESR and CRP.² The combined use of ESR and CRP has been found to be highly sensitive (range 0.80–0.89) and specific (range 0.79–0.93), and hence has been recommended as the first choice of investigation in suspected cases.

Other inflammatory markers mentioned previously (TNF- α , IL8, IL10) have not been found to be reliably accurate for diagnosing peri-prosthetic joint infections and hence are not used routinely.

Joint aspiration

In high-risk patients with clinical features suggestive of infection and positive serum inflammatory markers (CRP and ESR), the next step in management should be aspiration of joint fluid. Needless to say, aspiration of a prosthetic joint should always be carried out with a strict aseptic technique, in the clean air of an operating theatre. The aspirated sample is analyzed for absolute and differential leukocyte cell count and culture of aerobic, anaerobic and fungal pathogens. An absolute leukocyte count of ≥ 1700 (range 1100–3000) leukocytes/ μ L and percentage neutrophils of $\geq 65\%$ carries a high specificity and sensitivity for infection.² If both are above the cut-off limit the positive predictive value can be as high as 98%.¹⁶ However, these absolute values cannot be used in the early post-operative period (within 6-weeks of arthroplasty surgery) due to higher false positive rates. Bedair et al, in a retrospective study, concluded

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