Evaluation of patients with a painful total knee replacement

V. Mandalia, K. Eyres, P. Schranz, A. D. Toms
From the Royal Devon & Exeter Hospital, Exeter, England

Evaluation of patients with painful total knee replacement requires a thorough clinical examination and relevant investigations in order to reach a diagnosis. Awareness of the common and uncommon problems leading to painful total knee replacement is useful in the diagnostic approach. This review article aims to act as a guide to the evaluation of patients with painful total knee replacement.

Following total knee replacement (TKR) some patients continue to have pain or develop a new pain which may be accompanied by other symptoms such as instability, stiffness or swelling. There is often significant delay in establishing the cause of persistent pain after TKR. This article describes a logical evaluation of the assessment and care of patients with a painful knee replacement. A thorough history and careful examination must be undertaken since clinical evaluation will provide the diagnosis in the majority of cases. Imaging studies and laboratory tests provide additional support to the diagnosis.

Differential diagnosis
The causes of a painful knee replacement can be broadly divided into extrinsic and intrinsic (Tables I and II). The common causes are infection, instability, patellofemoral problems, osteolysis and prosthetic loosening.

Clinical evaluation
The first step is to identify the main symptom, which could be pain, instability, stiffness or swelling. The most frequent is pain, and this is the most troublesome to the patient. Patients with associated symptoms such as instability or stiffness are more likely to have an intrinsic rather than an extrinsic problem.

It is important to establish if the pain is the same or different compared with before operation. Pain which is unchanged following operation is likely to be caused by an extrinsic problem related to the hip, nerve entrapment in the spine or of vascular origin. The next step is to distinguish between pain which began in the early post-operative period rather than that which occurred after a period free of symptoms. Common causes of early post-operative pain include acute infection, instability because of inadequate balancing of the soft tissues, prosthetic malalignment and soft-tissue impingement. Pain of delayed onset is more likely to be caused by loosening of a component, wear of the polyethylene, late ligamentous instability, late haematogenous infection or a stress fracture.

Irrespective of whether the pain is of early or late onset, it is imperative to establish its characteristics including the nature, onset, duration, intensity, exact location, radiation, association with rest or activity and aggravating or relieving factors. A visual analogue scale (VAS) is helpful in documenting the intensity of the pain and in assessing the response to treatment. The anatomical location of the pain indicates the probable site of the underlying problem. A sharp catching pain is usually the result of a mechanical problem such as impingement, whereas pain at rest is less likely to be mechanical. Rest pain or pain at night should raise concerns about infection or referred neurogenic pain. A history of pain or hypersensitivity due to contact with bedclothes or clothing implicates a cutaneous neuroma. Radiating pain may be of extra-articular aetiology related to the hip, lumbar spine or of vascular origin. Pain related to activity rather than rest is likely to be due to a loose component, instability, impingement or tendonitis. Systemic symptoms such as fever, chills or lethargy may accompany infection. There must be an awareness of the increased risk of infection in patients with a background history of diabetes, psoriasis, rheumatoid arthritis (RA) and an immunocompromised status. Other sources of infection in the body such as urinary tract, den-
tal or chest infection and breaches of the skin must be sought. It is also important to establish the level of activity which the patient is undertaking, as overenthusiastic activity may be the cause of underlying discomfort.

The indication for the original operation should be reconsidered. Pain following TKR may be due to other underlying pathology, such as Paget’s disease, pigmented villonodular synovitis or RA, rather than problems with the knee replacement itself. It is important to identify which prosthesis was used and whether or not the patella was resurfaced. Were the components cemented or uncemented and was the prosthesis stemmed? Any navigation used should be noted as the sites for insertion of the pins can be a source of stress fracture and pain. Problems or complications at operation and during the early post-operative recovery period must be identified. It should be established whether the patient complied with the programme of rehabilitation.

The severity of the pre-operative pain must be established and psychological disorders and other comorbid conditions such as diabetes mellitus, RA and fibromyalgia noted. Brander et al1 studied prospectively the natural history and typical pain pattern after TKR and identified factors which predicted excessive post-operative pain for up to 12 months following knee replacement. Of 116 patients studied, significant pain was reported in 44.4%, 18.4% and 13.1% of patients at one, six and 12 months, respectively. Moderate to severe pain was seen in one in eight patients at one year after surgery despite an absence of clinical or radiological abnormalities. Pre-operative depression and anxiety were the best predictors of heightened pain at this time.

In a recent study involving more than 8000 patients Baker et al5 reported that 19.8% had persistent pain one year after operation. A further prospective study6 of 860 patients with TKR showed that those who had marked functional limitation, severe pain, a low mental health score and other comorbid conditions before operation were more likely to have a worse outcome after one and two years.

The use of medication, including non-steroidal anti-inflammatory drugs, anxiolytic drugs, opiate analgesia, antidepressant or any other treatment by pain specialists must be clearly defined.

### Clinical examination

A thorough examination helps to confirm the provisional diagnosis made from the history. Assessment of the painful TKR should include a review of the pattern of gait, identifying any thrust resulting from instability. Surgical scars should be noted. Erythema, increased temperature, swelling or obvious sinuses suggest infection. Atrophic, dusky skin or discoloration over the knee and leg may be associ-
ated with chronic regional pain syndrome or vascular disease. An assessment of limb alignment is important and can be further confirmed by long-leg radiographs. Excessive external or internal rotation of the foot may be indicative of rotational malposition of the tibial component, which can be confirmed by CT scan.

The knee should be checked for swelling and effusion which, if present, again points to an intrinsic knee problem. An effusion can be secondary to haemarthrosis. Recurrent haemarthrosis after TKR is uncommon with a reported incidence of between 0.3% to 1.6% \(^9\) and has been described in patients with proliferative synovitis, pigmented villonodular synovitis, haemophilia, defects of platelet function and in patients on anticoagulants. \(^9,10\) In the absence of a coagulopathy, impingement of the proliferative synovium between the joint surfaces is the most frequent cause of recurrent haemarthrosis. Other reports have described false aneurysms, erosion of an atherosclerotic vessel by a prominent flare on the femoral component and loose components, leading to bleeding from the underlying bone, as a cause of recurrent haemarthrosis. \(^11-14\)

Careful palpation should be undertaken. Tenderness along the lateral border of the patella can occur with a lateral facet syndrome due to an undersized patellar component. Tenderness on the medial aspect of the knee can be caused by either overhanging of the tibial component causing irritation of the medial collateral ligament or pes anserinus bursitis. Tenderness with or without a clicking or snapping sensation over the posterolateral aspect of the knee should raise the suspicion of either impingement of the popliteus tendon or problems with the fabella secondary to impingement or stress fracture. \(^15-20\) The popliteus tendon may catch over a retained lateral femoral condylar osteophyte or over the overhanging edge of the metallic posterior femoral condyle. \(^15,20\) Patients usually complain of painful snapping on flexing and extending the knee and will demonstrate tenderness on direct palpation of the posterolateral aspect of femur with varus stress on the knee. Cutaneous neuromas are most commonly noted in the infrapatellar branch of the saphenous nerve just medial to the tibial tuberosity, and in the medial cutaneous nerve of the thigh medial to the patella. The diagnosis of a cutaneous neuroma can be further confirmed by a local anaesthetic nerve block or a lignocaine patch.

The active and passive range of movement and the stability of the knee should be checked. Hyperextension, fixed-flexion deformity or an extensor lag may produce problems following TKR. The knee joint should be assessed for mediolateral stability with valgus and varus stress testing in various positions of flexion. The knee should be examined for a mismatch of the flexion/extension gap.

Problems related to the patellofemoral joint are common following TKR. Was the patella resurfaced or not? Any defect along the course of quadriceps or patellar tendon should raise suspicion of disruption of the extensor mechanism which should be confirmed by weakness of active extension of the knee. Patellofemoral compression and the general mobility of the patella should be checked. The lateral facet of the patella should be examined for impingement. Patellar tracking should be carefully examined, noting any clunk or crepitus. A clunk is produced by impingement of a mobile nodule of fibrous tissue which displaces out of the notch of the prosthesis as the knee is extended, producing a palpable and painful catch. \(^21\) Impingement of soft tissue in the patellofemoral joint and the patellar clunk syndrome are associated with the design of the femoral component, inflammation following operation, altered extensor mechanics, a low lying patella and anterior placement of the tibial tray. \(^21,22\)

Examination of the lumbar spine, hip, foot and ankle should be part of the routine assessment of patients with a painful TKR. Disorders in the hip commonly present as anterior thigh or knee pain. Any pain or limitation of movement, especially of internal rotation of hip, should raise suspicion of this joint. Severe planovalgus deformity of the foot may produce pain and eventually laxity of the medial collateral ligament and valgus instability of the knee joint.

**Imaging**

**Radiographs.** Good quality radiographs must be obtained. The standard radiological series should include a weight-bearing anteroposterior (AP), lateral skyline and long-leg alignment views, which should be scrutinised for limb alignment, component size and any overhang, positioning, stress fracture, loosening, luencies, osteolysis, wear of the polyethylene insert with loss of joint space or an unequal joint space, and heterotopic ossification. Overhang of the tibial component, especially on the medial side, is a common cause of pain.

The lateral view will disclose overfilling of the patellofemoral joint as a result of inserting a too large femoral component, anterior translation of the femoral component or inadequate resection of the patella. These errors will lead to pain and decreased flexion at the knee. The lateral view will also identify the position of the patella in relation to the joint line (Fig. 1) and occasionally a large fabella which may cause impingement and posterolateral pain. \(^15,16\)

A skyline view is particularly important to assess the patellofemoral joint. \(^23\) Unresurfaced patellae are often blamed for post-operative pain but this should be a diagnosis of exclusion. Any obvious malalignment, tilting, fracture or luency of the patella is also best identified on the skyline view (Fig. 2).

If standard radiographs are inconclusive, oblique or fluoroscopically-positioned films can be useful. Fluoroscopically-positioned radiographs provide optimal visualisation of the prosthesis-bone interface, and are especially helpful in the imaging of uncemented prostheses.

Usually stress radiographs merely clarify the findings on clinical examination and are rarely necessary. Serial radiographs are important in identifying subtle loosening, but it must be realised that minor differences in
the rotation of the limb greatly alter the visualisation of radiolucencies. Radiological signs of loosening include a progressive increase in a radiolucent line, change in component position and subsidence, fracture or reaction around the tip of the component. Loosening most commonly involves the tibial component which may shift into varus alignment (Fig. 3). Femoral loosening typically results in a progressive increase in flexion of the component.

The clinical significance of thin radiolucent lines at the prosthesis-bone interface is uncertain.24,25

Acute infection is diagnosed by clinical evaluation, serological investigation, diagnostic imaging and microbiological analysis.26 There are few common or reliable radiological signs and low-grade chronic infection may present without any obvious radiological changes. However, chronic infection may produce resorption of bone at the interfaces, a periosteal reaction, soft-tissue swelling, lysis and premature loosening of the component (Fig. 4). Differentiation of mechanical from septic loosening cannot be made solely on conventional radiographs.

**Bone scan.** The uptake of radionuclide is influenced by blood flow, osteoclastic activity and the sympathetic tone. The first phase, the blood flow phase, demonstrates perfusion of a lesion and consists of serial images of two to five seconds, obtained during injection of the isotope. The second, blood pool phase, involves images obtained within five minutes of injection and for the third, delayed, phase images are obtained about three hours later, when urinary excretion has decreased the amount of radionuclide in the soft tissue. In general, the first phase demonstrates perfusion to a lesion, the second demonstrates the relative vascularity of the lesion and the third the relative bone turnover.

The most commonly-used scans include triple-phase technetium 99-m-HDT bone scan, indium-111 leukocyte scan, and the technetium sulphur colloid bone marrow scan. The majority of scans are highly sensitive but not very specific. A negative scan is highly predictive of the absence of significant component loosening or infection.

**Three-phase technetium bone scan.** The triple-phase bone scan has a high sensitivity but poor specificity. Increased uptake on the first and second phases of the scan signifies hyperaemia and increased blood pool uptake, respectively, but these findings are non-specific.27

Following total hip replacement the scan typically returns to normal six to 12 months after operation while after TKR, increased peri-prosthetic uptake on the third phase may persist indefinitely.28,29 The characteristic findings with an infected TKR are increased uptake in all three phases of the scan. The lack of increased uptake in the first two phases is an important negative finding that would militate against the diagnosis of infection.28 Osteolysis from polyethylene wear debris usually gives rise to the same appearances on the bone scan as infection which it may
mimic clinically. It is thought that the uptake surrounding the tibial or femoral stems is more indicative of loosening than uptake underlying the tibial tray.\textsuperscript{30}

\textbf{Indium-111 leukocyte scan.} Indium-labelled leukocytes accumulate in areas of inflammation or infection and in healing wounds after operation. The marrow surrounding the implanted components has been shown to have hyperplastic elements which may result in a physiological increase in the uptake of indium around the prosthesis after operation. The sensitivity and negative predictive value of the indium leukocyte scan for infection are both very high, approaching 95\% and 100\%, respectively,\textsuperscript{31,32} although this technique is rarely used. Thus, a negative indium scan is a strong predictor of the absence of an infected TKR, but a positive scan is of limited value.

\textbf{Technetium sulphur colloid bone marrow scan.} Sulphur colloid accumulates throughout the reticuloendothelial system, in the bone marrow, in the liver and in the spleen. Therefore, the hyperplastic marrow normally encountered surrounding joint replacements which gives rise to an increased indium uptake, should have a corresponding matching increase in uptake on the marrow scan.\textsuperscript{33} However, if infection is the cause of increased peri-prosthetic uptake of indium, the uptake of sulphur colloid by the infected marrow is inhibited or diminished, resulting in relatively less uptake on the marrow scan in areas of peri-prosthetic infection.\textsuperscript{34} If the indium and marrow scans match, they are considered ‘congruent’, indicating a low likelihood of infection. If there is a mismatch, where the areas of increased uptake on the indium scan are normal or ‘cold’ on the marrow scan, the findings correlate with a high likelihood (90\%) of infection.\textsuperscript{32} The combination of these scans may improve the specificity for the diagnosis of infection.

\textbf{Computerised tomographic scan.} This can be helpful for evaluating patients with a painful TKR, and advances in multi-detector CT have improved the image quality by further minimising metal artefact. Computerised tomography can show the extent and width of peri-prosthetic lucencies which may be underestimated or not apparent on plain films. A CT scan is also useful to assess the rotational alignment of the prosthesis relative to bone\textsuperscript{35} and can help to detect any subtle peri-prosthetic fractures.

\textbf{Magnetic resonance imaging.} The magnetic susceptibility artefact associated with metal prostheses has limited the role of MR scans in patients with TKR. Techniques such as increasing the imaging bandwidth, reducing time to echo (TE), using fast spin echo train, avoiding chemical fat saturation and gradient echo imaging have been shown to improve the quality of the image after joint replacement.\textsuperscript{36,37} As some of the more recent technological advances are made more widely available, the role of MR may increase.

\textbf{Laboratory investigations}

\textbf{Serological investigation.} The erythrocyte sedimentation rate (ESR) and the level of C-reactive protein (CRP) are widely used as serum markers for assessing bacterial infection in patients with total joint arthroplasty.\textsuperscript{38} After joint replacement, the ESR typically increases, with a peak at five to seven days after operation, and then slowly decreases to pre-operative levels in approximately three months. However, some studies have shown that the ESR can remain elevated for as long as one year.\textsuperscript{39-41} An ESR > 30 mm per hour has been shown to have a sensitivity of 82\%, a specificity of 85\%, a positive predictive value of 58\% and a negative predictive value of 95\%.\textsuperscript{42} The CRP level is a better indicator of infection as it is more sensitive, with an early peak at two to three days after surgery, returning to normal within the first three weeks after operation.\textsuperscript{39-43} A CRP value > 10 mg/l has been associated with a 96\% sensitivity, a 92\% specificity, a 74\% positive predictive value and a 99\% negative predictive value. Greidanus et al\textsuperscript{44} in their study reported high sensitivity (0.93 and 0.91) and high specificity (0.83 and 0.86), respectively, for ESR (> 22.5 mm/hr) and CRP (> 13.5 mg/L) for the diagnosis of infection in patients with painful TKR. They also suggested that when ESR and CRP levels are measured together as a screening battery the sensitivity is 0.95 and the negative predictive value is 0.97. When a combination of positive ESR and CRP was used, specificity increased to 0.93.
Another serological test that has shown promise for diagnosing infection is the measurement of the serum level of interleukin 6 (IL-6). In one study, this was found to be consistently elevated (> 10 pg/mL [10 ng/L]) in patients with peri-prosthetic infection, and it had a higher predictive value than most other serological markers. It exhibits a more rapid increase and quicker return-to-normal than either the CRP level or the ESR, suggesting that the IL-6 level may be a superior indicator of post-operative inflammatory response. Interleukin-6 levels peak in the first six to 12 hours after surgery and fall back to their baseline range by 48 to 72 hours. A combination of CRP and IL-6 has recently been shown to provide excellent sensitivity in the assessment of infection after TKR. Interleukin-6 is not likely to be elevated in patients with aseptic loosening, but may be in patients with an underlying inflammatory arthropathy.

**Aspiration of synovial fluid.** This is a valuable diagnostic tool in suspected infection. The synovial fluid is subjected to gram stain, leukocyte count and aerobic and anaerobic culture. Although this may be performed on fluid aspirated pre-operatively or intra-operatively, this test in general has a relatively poor sensitivity and specificity.

**Leukocyte count.** Setting aside the inconsistencies in units, there are still discrepancies in the literature with regard to the level at which the cell count in fluid from the site of a prosthetic joint may be considered abnormal.

**Culture.** The aspirate should be sent for aerobic and anaerobic culture and sensitivity in conjunction with close liaison with the microbiology department. Patients should have not received antibiotics for a minimum of two weeks prior to aspiration. Such investigations have revealed a sensitivity of 55% and a specificity of 96%, although one author reported up to 100% sensitivity and specificity for aspiration.

**Summary**

The clinician reviewing patients with a painful TKR should be aware of both the common and rare underlying causes and have an algorithm to reach the diagnosis. The approach outlined in this article with assessment involving clinical evaluation, serological investigation, diagnostic imaging and microbiological analysis helps to find the underlying cause of the painful TKR. Pain after operation occurs in one in eight patients despite an absence of clinical or radiological abnormalities. This should be explained to the patient during the consenting process before operation. A multidisciplinary approach involving the physiotherapist and pain team often helps in overall management even where the exact aetiology of the painful TKR is identified.

There are a number of associated pre-operative features to identify high-risk patients. These patients benefit from early multidisciplinary intervention but require a significant amount of time and thought when they are seen in clinic.

**References**