By 2030, the demand for total knee arthroplasty (TKA) in the United States is expected to quadruple from current levels to nearly 3.5 million procedures annually. Although the safety and efficacy of TKA is well known, postoperative pain remains problematic and has been attributed to most poor outcomes after TKA. Recent reports suggest that 11% to 25% of patients treated with TKA are dissatisfied with their postoperative outcomes, largely because of pain. A study by Puolakka et al found that 36% of TKA patients reported daily pain. Hawker et al reported similar findings in patients treated with TKA at 2 to 7 years postoperatively. There is a lack of consensus regarding the effect of age and sex on pain after TKA. Although certain studies have cited female sex and younger age as important predictors of postoperative pain, other research, including the 2003 National Institutes of Health consensus statement, reported a lack of correlation between age, sex, and
Table 1
Potential Sources of Postoperative Pain After Total Knee Arthroplasty

<table>
<thead>
<tr>
<th>Intra-articular</th>
<th>Extra-articular</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection</td>
<td>Hip disease</td>
</tr>
<tr>
<td>Crystalline disease</td>
<td>Foot and ankle disease</td>
</tr>
<tr>
<td>Instability</td>
<td>Neurologic/spine disease</td>
</tr>
<tr>
<td>Component malalignment</td>
<td>Tendinitis/bursitis</td>
</tr>
<tr>
<td>Limb malalignment</td>
<td>Iliotibial band syndrome</td>
</tr>
<tr>
<td>Aseptic loosening</td>
<td>Psychological factors</td>
</tr>
<tr>
<td>Soft-tissue irritation</td>
<td>Heterotopic ossification</td>
</tr>
<tr>
<td>Component wear</td>
<td>Connective tissue disorders</td>
</tr>
<tr>
<td>Osteolysis</td>
<td>Material hypersensitivity</td>
</tr>
<tr>
<td>Extensor mechanism pathology</td>
<td>Unexplained pain</td>
</tr>
<tr>
<td>Recurrent hemarthrosis</td>
<td></td>
</tr>
</tbody>
</table>

Regardless of a patient’s risk factors, the diagnosis of an aseptic, painful TKA may be confounded by a myriad of potential intra- and extra-articular causes (Table 1). If preoperative symptoms are not relieved by TKA, extra-articular etiologies should be investigated. Ruling out infection should be the first step in diagnosing the source of postoperative pain after TKA, and the clinical practice guidelines on this topic from the American Academy of Orthopaedic Surgeons can help direct the evaluation. Obtaining a thorough history may aid in distinguishing between intra- and extra-articular pain sources, because a lack of pain relief immediately after TKA could suggest that the initial pain was not attributable to knee pathology. Additional symptoms, including delayed onset of postoperative pain, a sharp catching pain during movement, joint instability, or an abnormal radiographic finding, may indicate intra-articular causes. An intra-articular injection of a local anesthetic also can be used to rule out an intra-articular source of pain.

**Hip Disease**

Pain can be referred from the hip to the knee via the obturator and femoral nerves originating from L2-L4. Immunohistochemistry staining has been used to demonstrate the location of referred pain from the hip joint, and fluoroscopically guided diagnostic hip injections have been used to map patterns of referred pain to the knee.

Mechanical knee pain can result from increased knee torque resulting from decreased hip rotation or altered gait from various diseases affecting the hip joint. Patients with severe hip osteoarthritis who are awaiting hip arthroplasty may have pain that is localized to the anterior and posterior aspects of the knee. Several studies have demonstrated the association between various
forms of hip disease, including osteoarthritis, infection, hip fracture, and posterior hip dislocation, with ipsilateral knee pain. Other sources of hip disease, such as osteonecrosis, dysplasia, and implant loosening after total hip arthroplasty, can present as knee pain. Stress fractures, including femoral neck, pubic, and subtrochanteric stress fractures, are rare complications after TKA in patients with poor bone quality but can be secondary causes of pain. Generally, all patients who present with knee pain should have a physical examination of the ipsilateral hip to screen for pathology. If a painful or decreased range of hip motion is noted after TKA, radiographic studies are recommended.

**Foot and Ankle Disease**

Malalignment of the hindfoot resulting in excess valgus alignment of the heel secondary to posterior tibial tendon insufficiency or pes planus increases stress forces on the knee. This hindfoot valgus leads to increased lateral loading of the knee because of changes in ground reactive forces and an increased valgus thrust. Bhave et al reported that patients with planovalgus malalignment had substantial postoperative pain relief with shoe modifications. In addition to a physical examination, screening for malalignment of the hindfoot and ankle also can be performed during radiographic measurement of the weight-bearing axis. Numerous studies have noted the efficacy of including the hindfoot distal to the ankle and subtalar joint in an assessment of the ground mechanical axis deviation. A comprehensive radiographic evaluation of the rearfoot, ankle, and leg taken in multiple planes and angles may be appropriate before TKA in select patients and can be useful in ruling out foot and ankle-related etiologies in patients with pain after TKA.

**Vascular Disease**

Vascular diseases, such as lower extremity peripheral artery disease (PAD) or thrombosis, also have potential to contribute to symptoms of leg pain and are common in older patients. Although often useful as indicators for PAD, neither the presence of known risk factors (such as hyperlipidemia, cardiac disease, and diabetes) nor symptoms of claudication are definitive predictors of PAD. In a study of 50 consecutive patients referred to an orthopaedic surgeon for leg pain, Bernstein et al noted that 20% had undiagnosed PAD. Assessing for PAD via pulse volume recording or ankle-brachial pulse indexing (an index of <0.9 may indicate PAD) is neither invasive nor costly, especially given the frequency of PAD in patients without a history of trauma or claudication who present with leg pain. Indirect injury to arteries via compression can occur during TKA as external forces applied to diseased vessels during tourniquet application can lead to vascular damage, plaque disruption, and subsequent thrombus formation. Thrombosis is one of the most common causes of vascular insufficiency after TKA and can be confirmed with Doppler imaging secondary to a positive Homan sign. If an extra-articular source of pain after TKA is suspected, the presence of vascular diseases should be investigated.

**Lumbar Spine and Neurologic Disorders**

Lumbar spinal stenosis (LSS) has an incidence as high as 8% and is a common cause of leg pain in older adults. Nevertheless, patients with LSS who undergo TKA have been shown to have comparable outcomes to control patients with regard to revision rates and radiographic outcomes despite their lower preoperative functional scores. LSS is often idiopathic and presents as intermittent neurogenic claudication caused by the compression of the cauda equina, which results from enlargement of the bony and soft tissues associated with the spinal canal. In a study of 100 patients, Amundsen et al reported additional common symptoms of back pain, leg pain, weakness, and voiding disturbances. Double nerve root involvement is typical, and the L5 nerve root is the most commonly affected (prevalence of 91%), followed by S1 (63%), L1-4 (28%), and S2-5 (5%).

In patients with suspected LSS, a thorough physical examination should be conducted to rule out any other pathology that may be the source of referred pain to the legs. Sensory examination should include vibration, proprioception, and pin-prick testing in the appropriate nerve distribution regions. Loss of tendon reflexes, sciatic notch tenderness, and reduced lumbar lordosis may also be present in patients with suspected LSS. Motor weakness typically presents in the L5 nerve distribution. Amundsen et al reported sensory changes in 51% of patients with LSS, reflex changes in 47%, lumbar tenderness in 40%, reduced spinal mobility in 36%, a positive straight-leg–raising test in 24%, weakness in 23%, and perianal numbness in 6%. If a clinical diagnosis of LSS is indicated, imaging studies should be used for confirmation. Upright plain radiographs are useful for excluding other spine pathologies, and CT and MRI can confirm nerve compression.
Other neurologic disorders, such as complex regional pain syndrome (CRPS) and cutaneous neuroma, also have the potential to contribute to the incidence of pain after TKA. Previously referred to as reflex sympathetic dystrophy, CRPS symptoms include cutaneous hypersensitivity, abnormal skin color, edema, motor function impairment, and abnormal sudomotor activity.39,40 The occurrence of CRPS after TKA is rare; a diagnosis of CRPS was made in only 5 of 662 patients (0.8%) in a recent series.41 As a testament to the elusiveness of a CRPS diagnosis, the mean diagnostic time in this patient group was 5 months postoperatively.

Although the pathophysiologic mechanisms of CRPS remain unclear, the condition is thought to be initiated by sensitization of nociceptive nerve fibers by trauma.42,43 Regardless of etiology, the diagnosis of CRPS often consists of excluding other painful conditions. A variety of tests, including infrared thermography, quantitative sensory testing, sudomotor testing, and bone scintigraphy, can be used to rule out other painful conditions and differentiate CRPS. In TKA patients with suspected CRPS, orthopaedic disorders with CRPS-like symptoms (such as rheumatic arthritis, tendon infection, or migratory osteoporosis) should be ruled out first. Treatment of CRPS typically centers on therapeutic interventions. Sympathetic blockade by an anesthesiologist, electrotherapy, occupational therapy, physical therapy, and proper counseling are often necessary in managing patients with CRPS.

Cutaneous and subcutaneous neuromas are another rare neurosensory disorder that can cause pain after TKA and are often diagnosed by injecting lidocaine into the suspected neuroma site. Pain relief is often a confirmation of a cutaneous neuroma, which can be subsequently treated with a variety of nonsurgical interventions such as local anesthetics or spinal cord stimulation. If nonsurgical measures prove unsuccessful, cutaneous nerve resection may be warranted.41,44 In a series of patients who received a diagnosis of cutaneous neuroma after TKA, Katz and Hungerford41 found that 87% reported substantial improvement in visual analog scale pain scores after sympathetic blockade or sympathectomy by an anesthesiologist.

**Tendinitis, Bursitis, and Iliotibial Band Syndrome**

Posterolateral knee pain after TKA can arise from a variety of sources. Pandher et al45 reported a case of biceps tendinitis as the etiology of an acutely painful knee after TKA. Inflammation of the popliteus tendon also can present with posterolateral knee pain secondary to irritation from a laterally displaced femoral component, retained posterolateral osteophyte or cementophyte, or posterolateral tibial tray overhang. Alternatively, quadriceps and patellar tendinitis will present with anterior knee pain and typically result from a traumatic or overuse injury.

Semimembranosus tendinitis has been reported as a source of pain after TKA.46 It typically presents as pain in the posteromedial knee that radiates into the posterior thigh or calf region and worsens in deep knee flexion. Physical examination findings typically consist of tenderness to palpation at the semimembranosus bursal site. Pain relief is often a confirmation of a cutaneous neuroma, which can be subsequently treated with a variety of nonsurgical interventions such as local anesthetics or spinal cord stimulation. If nonsurgical measures prove unsuccessful, cutaneous nerve resection may be warranted.41,44 In a series of patients who received a diagnosis of cutaneous neuroma after TKA, Katz and Hungerford41 found that 87% reported substantial improvement in visual analog scale pain scores after sympathetic blockade or sympathectomy by an anesthesiologist.

Iliotibial band traction/friction syndrome should be considered in patients with a painful range of motion (specifically between 20° to 80°) and with pain localized to the lateral femoral epicondylar region.49,50 Luyckx et al49 reported a 7.2% incidence of iliobibial band traction/friction syndrome in a cruciate-substituting TKA design. The increased incidence was attributed to excessive lateral femoral condyle translation and internal rotation of the tibia, leading to excessive tension on the iliobibial band. This syndrome can be elicited using the Ober, Thomas, and Noble tests, and it typically presents as an overuse injury in conjunction with increased iliobibial band tightness.51 An Ober test is conducted with the patient lying on his or her side. After flexion of the knee to 90° and extension and abduction of the affected hip by the examiner, support of the knee is released.
Failure of the hip to adduct indicates a positive test. The Thomas test is conducted with the patient supine. After the examiner places his or her hand under the lumbar spine to prevent hyperlordosis, the unaffected hip and knee are fully flexed. The patient holds the knee. A positive sign is indicated by the affected leg raising off the table. Both legs can then be fully flexed, and the affected leg is slowly lowered back into extension. A lack of full extension may indicate iliopsoas tightness, and any external rotation may suggest iliotibial band tightness. With the patient supine, the Noble test is conducted by flexing the affected hip and knee to 90° and placing pressure on the lateral femoral epicondyle with the thumb. With continuing pressure, the leg is passively and slowly extended. A positive test is indicated by the presence of pain at 30° of flexion.

Many cases of iliotibial band traction/friction syndrome resolve with nonsurgical treatments, including anti-inflammatory medications or local steroid injections. If pain persists, surgical release of the iliotibial band may be necessary.

### Heterotopic Ossification

Oxidative stress from hypoxic environments often induces production of mast cells and fibroblast growth factor, which in turn undergo metaplastic transformation and leads to fibrocartilage formation with subsequent endochondral ossification and bone formation. Heterotopic ossification can be asymptomatic or associated with a loss of motion in addition to catching and snapping that is localized to the patellofemoral joint. The incidence of heterotopic ossification varies widely, with an increased incidence in heavier patients, men, and patients with larger preoperative deformities. Patients at elevated risk for heterotopic ossification include those with previous heterotopic ossification, bilateral hypertrophic osteoarthritis, and posttraumatic osteoarthritis with hypertrophic osteophytosis.

Radiographs and laboratory testing are rarely helpful in detecting early stages of heterotopic ossification because calcium deposition in the bone matrix and developmental alkaline phosphatase elevation do not occur until several weeks after the initial onset of heterotopic ossification. Bone scanning may be useful for a definitive diagnosis and is known to detect heterotopic ossification earlier than radiographs or laboratory testing.

Either a NSAID (such as indomethacin), diphosphonate (such as ethane-1-hydroxy-1,1-diphosphate), or local radiation therapy is recommended for the treatment or prophylaxis of heterotopic ossification.

### Fibromyalgia and Connective Tissue Disorders

Although the precise source of pain in fibromyalgia remains unknown, it clearly depends on peripheral nociceptive input as well as abnormal central pain processing. Some studies have suggested soft-tissue inflammation as the source of pain in fibromyalgia because pain and weakness of the muscles is one of its main symptoms.
indicating disturbed microcirculation, mitochondrial damage, and a reduction in high-energy phosphates all suggest an energy-deficient state in the resting, painful muscles of patients with fibromyalgia. Although fibromyalgia is characterized by allodynia and chronic pain, it should not be considered a contraindication for TKA because patients with fibromyalgia have shown improvement similar to that of control patients after TKA. Nevertheless, these patients have reported lower postoperative satisfaction, largely because of higher levels of persistent postoperative pain. The criteria set forth by the American College of Rheumatology are useful in diagnosing fibromyalgia; treatment typically consists of medications or therapy.

Rarer connective tissue disorders, such as Ehlers-Danlos syndrome, also have potential to cause chronic pain in TKA patients. Deficiencies of collagen production in TKA patients with Ehlers-Danlos syndrome has been shown to instigate pain via degeneration and destabilization of the knee joint. In a case series of 10 TKA patients with Ehlers-Danlos syndrome, approximately 30% reported dissatisfaction with TKA because of continued pain and instability. Although rare, a diagnosis of Ehlers-Danlos syndrome should be confirmed through genetic testing and treated with a combination of physical therapy and pain-relieving and anti-inflammatory medications.

**Psychological Factors and Pain Catastrophizing**

The potential for psychological factors to influence a patient’s perceptions of pain after TKA is well known, because pain catastrophizing has been designated a consistent and powerful psychological predictor of poor outcomes after TKA. Patients who catastrophize about their pain ruminate more often about their pain, magnify its perceived threat, and experience greater feelings of helplessness when dealing with pain. Patients with higher preoperative pain and anxiety levels typically report extended postoperative TKA pain and diminished function. It is imperative to carefully monitor and, if necessary, refer for further psychological treatment patients who may experience diminished postoperative outcomes because of anxiety, catastrophizing, or other psychological maladies known to intensify pain.

**Metal Hypersensitivity**

There is a paucity of clinical studies correlating positive hypersensitivity results with clinical TKA outcomes. Nevertheless, metal hypersensitivity has been described previously as a type IV immunologic reaction and also may be considered as an unlikely cause for a painful TKA if all other causes have been ruled out. Hypersensitivity reactions typically occur in the periprosthetic region in the months after TKA. Although rarely used, in vitro proliferation testing via lymphocyte transformation testing may be useful in assessing sensitivity to metal implants. Lymphocyte transformation testing consists of measuring lymphocyte proliferation after activation in vitro and comparing the findings with in vivo levels. Skin patch testing for nickel, cobalt, or chromium reaction may also be useful in detecting metal hypersensitivity in TKA patients, although the correlation between a positive test and symptoms remains unclear.

Hypoallergenic implants (specifically those that do not contain nickel) are warranted in a select subset of susceptible patients.

**Summary**

Determining the cause of pain after TKA can be a challenging task for an orthopaedic surgeon. With a thorough patient history, examination, and appropriate diagnostic approach, most sources of pain can be identified. After sepsis and intra-articular causes have been ruled out, extra-articular sources should be investigated. If the source of pain cannot be identified, revision arthroplasty alone is unlikely to relieve symptoms. By establishing an accurate etiology in a timely manner, unnecessary diagnostic testing will be avoided and the patient can be appropriately treated.

**References**

Diagnosis and Management of Extra-articular Causes of Pain After Total Knee Arthroplasty

Adult Reconstruction: Knee


