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Hip and Knee Arthroplasty in the Patient with Inflammatory Arthritis

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1. Introduction

The term inflammatory arthritis refers to an inflammatory arthropathy in patients suffering from one of a number of chronic inflammatory conditions including rheumatoid arthritis (RA), and the seronegative spondyloarthropathies of ankylosing spondylitis (AS), psoriatic arthritis (PsA), spondyloarthritis associated with inflammatory bowel disease and undifferentiated spondyloarthritis. This chapter will focus on a review of the surgical management of patients with RA, AS, and PsA, as these represent the most common of the inflammatory arthropathies.

Knowledge of the inflammatory arthritides is important for lower limb arthroplasty surgeons as awareness of both the local changes within the affected joints and how extra-articular manifestations can adversely affect anaesthesia, surgery and rehabilitation is necessary to ensure good surgical outcomes. In addition to the local and systemic manifestations of the inflammatory diseases, patients may be prescribed multiple medications, including disease modifying anti-rheumatic drugs (DMARDs) or biological therapies that may affect the local surgical site or affect the patient systemically and have an impact on rehabilitation and patient outcome. In addition, quality of life and functional outcome of patients with chronic inflammatory arthropathies may also be reduced compared to simple osteoarthritis because of the chronicity and systemic nature of the inflammatory disease. Finally, the choice of implant and the method of fixation may affect implant survival and revision burden.

The term inflammatory arthropathy covers a wide spectrum of diseases which ultimately manifest themselves with joint destruction, systemic features and disability. In the following section the pathophysiology, presentation, diagnosis and medical treatments for the inflam-

matory conditions will be considered separately to the treatment of hip and knee 'inflammatory arthritis'.

2. Rheumatoid arthritis

2.1. Epidemiology and pathophysiology

Rheumatoid arthritis (RA) is the most common chronic inflammatory condition and affects 3% of women and 1% of men, and has its peak age of onset between 35 and 45 years. The aetiology of RA remains unclear but involves environmental and heritable factors. Several susceptibility loci reside in the HLA region on chromosome 6 and within this region, normal genetic variation may increase a patient's susceptibility to or severity of rheumatoid disease. Although many genetic variants have been identified [1-4], the impact of individual variants on the risk of developing RA is low. Research into the functional mechanisms by which these genetic variants confer disease susceptibility is on-going, with the ultimate goal of identifying discrete biological pathways which pathologically induce chronic inflammation. From this research, medical therapies to specifically target RA may be further developed. Environmental triggers which may increase the risk of RA include smoking, high alcohol intake, coffee, vitamin D levels and low socio-economic group [5-10].

The underlying pathophysiology of RA is of over-activation of intra and extra-cellular inflammatory cascades including over the expression of tumour necrosis factor and other inflammatory cytokines including interleukin (IL) 6 and IL-1 [11-14]. The cells that drive the inflammatory response include B and T lymphocytes, macrophages and synovial cells [15]. The activation of inflammatory pathways result in persistent synovial inflammation with subsequent joint and periarticular bone destruction.

2.2. Presentation

2.2.1. Joint features

Patients with RA typically present with a persistent symmetrical polyarthritis. The small joints of the hand and foot are most commonly affected, although any synovial joint may be involved. The natural history of the affected joint is one of low grade chronic inflammation with periods of intense pain and stiffness during a 'flare.' Between flares, joint stiffness is usually worst in the morning or after a period of rest.

2.2.2. Systemic features

Extra articular manifestations (EAM) of RA affect many organ systems and can be classified by the Malmö criteria [16] into severe and non-severe (Table 1). EAM may be present in up to 41% of patients with RA and up to 22% of patients may develop the severe EAMs [17]. These EAMs must be considered in any patient presenting to the orthopaedic surgeon and investigated further in conjunction with rheumatology and anaesthetic specialists prior to any

surgery. In addition, patients with RA may suffer from general malaise, anorexia, anaemia, weight loss and depression.

Affected tissue or organ	EAM		Co-morbidities
	Not severe	Severe	
Skin	Nodules Raynaud's phenomenon	Petechiae, purpura, ulcers, gangrene	Cancer
Pulmonary system	Bronchiolitis obliterans Organizing pneumonia	Pleuritis Interstitial lung disease	Lung carcinoma
Heart	Valvular heart disease Myocarditis Arrhythmias	Pericarditis Coronary vasculitis and aortitis	Hypertension Heart failure Ischaemic heart disease
Nervous system	Non identified	Mono/polyneuritis multiplex Central nervous system vasculitis	Depressive syndrome Cervical myelopathy
Eyes	Secondary Sjögren's syndrome Sicca syndrome	Episcleritis or scleritis Retinal vasculitides	None identified
Haematological system	None identified	Felty's syndrome	Non-Hodgkin lymphoma Lymphadenopathy Splenomegaly
Kidneys	None identified	Glomerulonephritis Interstitial nephritis Amyloid deposition	None identified
Bone	None identified	None identified	Osteoporosis

Table 1. Extra-articular manifestations (EAM) in rheumatoid arthritis (RA). (Reproduced with permission from Prete M *et al* [17]).

2.3. Diagnosis

Diagnostic criteria have been designed to differentiate RA from other joint diseases. In 1987 the American College of Rheumatology (ACR) published seven diagnostic criteria to aid the diagnosis [18]. For a patient to be diagnosed with RA, four of the seven criteria have to be present and morning stiffness, arthritis in three or more joints, symmetrical arthritis and hand arthritis had to be present for at least 6 weeks (Table 2).

ACR Criteria for Rheumatoid Arthritis	
1	Morning stiffness (present for at least 1 hour)
2	Arthritis of 3 or more joints.
3	Arthritis of hand joints (>1 swollen joint)
4	Symmetrical arthritis
5	Rheumatoid Nodules
6	Serum Rheumatoid factor
7	Radiographic changes

Table 2. The American College of Rheumatology diagnostic criteria for Rheumatoid Arthritis [18].

However, the ACR classification has been criticised for its low sensitivity and specificity for early RA [19], a time which is critical since early pharmacological intervention increases remission rate. Further, early treatment can limit the severity of the disease and prevent bony destruction [9]. This has led to the development of another classification system by the ACR and the European League Against Rheumatism (ELAR) (Table 3) [20]. This more recent classification system assesses joint involvement, and duration of symptoms along with serological markers including acute-phase reactants and detection of antibodies against citrullinated peptides (ACPA). The detection of ACPA antibodies increases the sensitivity of the serological tests greater than the detection of rheumatoid factor. The common radiographic features of RA are shown in Table 4.

ACR/EULAR 2010 criteria	
1	Joint involvement (0-5) One medium to large joint (0) Two to ten medium to large joints (1) One to three small joints (large joints not counted) (2) Four to ten small joints (large joints not counted) (3) More than ten joints (at least one small joint) (5)
2	Serology (0-3) Negative RF and negative ACPA (0) Low positive RF and low positive ACPA (2) High positive RF or high positive ACPA (3)
3	Acute-phase reactants (0-1) Normal CRP and normal ESR (0) Abnormal CRP or abnormal ESR (1)
4	Duration of symptoms (0-1) Less than 6 weeks (0) Greater than 6 weeks (1)

Table 3. The 2010 American College of Rheumatology &European League Against Rheumatism classification criteria for Rheumatoid Arthritis [20].

Soft tissue overlying the joint
Swelling
Effusion
Rheumatoid nodules
Intra-articular changes
Global joint space narrowing
Marginal erosions
Secondary osteoarthritic change (osteophytes, sclerosis, cysts)
Peri-articular changes
Juxta-articular osteoporosis
Metaphyseal cysts (geodes)
Periostitis (common at the digits, rare at large joints)
Joint mal-alignment (alignment abnormalities due to ligament incompetence, joint subluxation, joint dislocation)

Table 4. Common radiographic features in rheumatoid arthritis [48]

2.4. Medical management

The classes of medication therapies used in rheumatoid and in other inflammatory arthropathies include simple analgesics non-steroidal anti-inflammatories (NSAIDs), disease modifying anti-rheumatic drugs (DMARDs), glucocorticosteroids and biological agents.

In RA, reduction of pain and stiffness may be achieved with the use of simple analgesics and NSAIDs. However, the long-term use of NSAIDs is limited by their cardiac and renal toxic effects and their lack of impact on disease progression [9]. DMARDs are the first line of treatment for rheumatoid disease. Although they are a heterogeneous group of drugs, they all decrease pain and stiffness, improve function, and may limit disease progression and induce disease remission. The most frequent DMARD used in RA remains methotrexate. Others include sulfasalazine, leflunomide, hydroxychloroquine, and gold. Serious adverse effects are associated with these potential agents and require careful monitoring. Hepatotoxicity, pancreatitis, interstitial lung disease, blood dyscrasias, marrow aplasia, induction of autoimmune diseases and acute kidney injury are all adverse effects of DMARDs. In particular, methotrexate can induce bone marrow suppression, induction of liver enzymes and folic acid depletion, necessitating concurrent folic acid supplementation.

Glucocorticosteroids may be used as an effective local treatment when given intra-articularly. They may also be administered systemically for controlling acute flares, as they reduce synovitis, however with longer term use the adverse effects of osteoporosis, increased risk of infection and chronic adrenal suppression limit their use.

To date, five anti-tumour necrosis factor (anti-TNF) antibodies have been licenced as biological therapy for RA. They act in one of two ways, Enterocept blocks the effect of TNF by acting as a soluble TNF receptor whereas Infliximab, Golimumab, Adalimumab and Certolizumab are monoclonal antibodies which bind and block TNF. A recent meta-analysis of the efficacy of

the TNF blocking agents concluded that TNF blockers as a monotherapy were efficacious but only as much as the DMARD methotrexate [21]. Combination therapy of methotrexate and an anti-TNF were more efficacious than either of the treatments in isolation. Adverse reactions and complications of anti-TNF treatment has been widely reported and includes local injection site reactions, infusion reactions, reactivation of latent infections, especially tuberculosis and an increased risk of sepsis, both local and systemic. Other biological approaches to disease modification include depletion in B cell numbers that drive inflammation using Rituximab, a monoclonal antibody to a protein found on the surface of B cells.

3. Ankylosing spondylitis

3.1. Epidemiology and pathophysiology

Ankylosing spondylitis (AS) is a chronic seronegative autoimmune arthropathy and is the most common of the spondyloarthritis subtypes. It predominantly affects the axial skeleton especially the sacroiliac joints and the spine, however the lower limb joints, the entheses and peripheral joints may be affected. AS typically starts in the third decade of life, has a prevalence of up to 1.2% and is 2.5 times more common in men than women [22, 23]. All of the spondyloarthropathies have a strong heritable component to susceptibility, most strongly with the HLAB27 variant on chromosome 6. 90-95% of patients with ankylosing spondylitis are positive for HLAB27. However, only 5% of subjects carrying this variant develop a spondyloarthropathy.

3.2. Bony features

Bony changes in AS commonly include new bone formation which arises from the cortical surfaces. Bony spurs from the vertebral bodies (syndesmophytes) extend vertically and may bridge across the intervertebral disc ultimately leading to a rigid 'bamboo' spine appearance. Entheses are also affected by new bone formation and patients may develop bony spurs in the Achilles tendon or plantar fascia. In addition, patients with AS have an increased risk of osteoporosis which can lead to devastating spinal fractures and cord compromise. The hip joint is more commonly affected than the knee joint in AS, 20% of patients who develop AS during adolescence go onto total hip arthroplasty (THA) [24].

3.3. Systemic features

AS is a systemic disease and extra-articular features (EAMs) are present in up to 40% of patients [25]. The most common EAMs include anterior uveitis, inflammatory bowel disease, lung disease, cardiac abnormalities (including conduction defects, valvular disease and cardiomyopathy) and renal disease secondary to deposition of IgA and renal amyloid [25].

3.4. Diagnosis

The main clinical manifestations of AS are pain and stiffness within the axial skeleton. A number of radiographic grading systems have been developed in AS, however magnetic

resonance imaging (MRI) is more sensitive and can detect inflammation within the sacroiliac joints before radiographic changes are apparent [26, 27]. The clinical diagnosis of AS can approach a sensitivity of 70% and a specificity of 81% if two of the four criteria developed by Rudwaleit *et al* are present [28] (Table 5). Other investigations that aid the diagnosis include typing for HLAB27 and C-reactive protein however this may be elevated in only 50% of cases [27]. Serum alkaline phosphatase is elevated in severe disease.

In established disease, lumbar spine and pelvis plain radiographs may show squaring of the lumbar vertebrae (a consequence of inflammatory bone remodelling), syndesmoses and structural changes within the sacroiliac joint. MR imaging reveals bony oedema, inflammation and bony erosions within the sacroiliac joints before radiographic changes are apparent.

New criteria for inflammatory back pain in young to middle-aged adults (<50 yrs) with chronic back pain
Morning stiffness >30 minutes
Improvement in back pain with exercise but not with rest
Awakening because of back pain during the second half of the night only
Alternating buttock pain
The criteria are fulfilled at least two of four of the parameters are present (sensitivity 70.3%, specificity 81.2%).

Table 5. Clinical criteria for the diagnosis of Ankylosing Spondylitis [25].

3.5. Medical management

Simple NSAIDs and cyclooxygenase-2 inhibitors are used to control pain and stiffness. In addition NSAIDs may limit the osteoprolific component of the disease as they block the osteoblastic effects of prostaglandin E2. Again the adverse effects of long term NSAIDs however limit protracted use. Intense physiotherapy may assist individual patients but its role has not been proven to be of benefit when evaluated in Cochrane systematic reviews [29].

As with RA, AS is a systemic disease and the DMARDs methotrexate, sulphasalazine and leflunomide have been used to treat symptoms and prevent or slow disease progression. Clinical results and results from RCTs unfortunately have been disappointing. Methotrexate may be effective at treating the peripheral joint disease but its use for axial disease has not been proven. Similar results are seen with other DMARs as well perhaps reflecting a different pathophysiology in AS compared to RhA.

The recent introduction of anti-TNF biological agents has greatly aided the medical management of AS. RCTs have shown that these agents control symptoms, improve function and limit or halt disease progression. The adverse reactions of these drugs have been previously documented but in selected patients therapy is well tolerated both in the short term and up to 6 years [30, 31].

4. Psoriatic arthritis

4.1. Epidemiology and pathophysiology

Psoriatic arthritis (PsA) is usually a seronegative spondyloarthropathy associated with psoriasis. Five subsets were described by Moll and Wright in 1973 [32] and are widely used in clinical practise, these include; distal interphalangeal arthritis, asymmetrical oligoarthritis, symmetrical arthritis, spondylitis and arthritis mutilans. The prevalence of psoriasis in Western Europe is 2-3% and up to 30% of patients with psoriasis develop an arthritis [33]. However this prevalence varies considerably due to geographic variation and variation in diagnostic criteria.

PsA has a strong genetic component to susceptibility, and has been linked to the MHC region and HLA-B28, HLA-B39 and HLA-B27. This latter association is much weaker in PsA than ankylosing spondylitis [34, 35]. As with the other major spondyloarthropathies, upregulation of the T-cells and increased expression of inflammatory cytokines are features of the disease. A bacterial or traumatic environmental trigger has been proposed with PsA, however no conclusive evidence for this has been found to date [36, 37].

4.2. Presentation

PsA differs from RA in that fewer joints are affected, and the pattern of joint involvement is commonly asymmetric, and involves the distal interphalangeal joints and nail lesions [38]. Dactylitis, spondylitis and sacroiliitis are common features of PsA, the involved joints are tighter, contain less fluid and are less tender than those in RA [38]. The systemic features of PsA are less significant than RhA but patients may still suffer from EAMs of anterior uveitis and a disease pattern similar to SAPHO (synovitis, acnes, pustulosis, hyperostosis and osteitis). The incidence of and mortality from cardiovascular complications is increased in patients with PsA which is thought to be secondary to an increase in atherosclerosis [39, 40].

4.3. Diagnosis

Many diagnostic criteria have been used to detect psoriatic arthropathy, the most recent in 2006 by the Classification Criteria for Psoriatic Arthritis (CASPAR) group [41] (Table 6). The sensitivity and specificity for psoriatic arthritis may reach 98.7 and 91.4 respectively [42]. No single laboratory finding in PsA is diagnostic however acute phase reactants are elevated in approximately 50% of cases [43].

4.4. Medical management

Methotrexate, retinoids and psoralen combined with ultraviolet A (PUVA) treatment appear to be most effective at treating skin and joints together [43]. The role of biological agents remains unclear with limited data evaluating their use in PsA [33].

Category	Point
Current psoriasis	2
Personal history of psoriasis	1
Family history of psoriasis	1
Typical psoriatic nail dystrophy (onycholysis, pitting, hyperkeratosis)	1
Negative rheumatoid factor	1
Current dactylitis or history of dactylitis (recorded by a rheumatologist)	1
Hand or foot plain radiography: evidence of juxta-articular new bone formation, appearing as ill-defined ossification near joint margin (excluding osteophytes)	1

Table 6. Caspar Classification of Psoriatic Arthritis [41]

5. Surgical interventions for inflammatory arthritis

Optimal management of the patient with inflammatory arthropathy requires a multidisciplinary approach both in primary and secondary care. The hospital management of the inflammatory arthropathies is predominantly led by the rheumatologist with support from physiotherapy, occupational therapy, the surgeon, dieticians, social workers, orthotists and chiropradists. Community care is also paramount to maintain and optimise pain control and function. The multidisciplinary approach comprises general practitioners, district nursing, occupational therapy and social workers. Patients also often require support through housing agencies for home adaptation, community care workers and employment services [44].

In the lower limb, patients with inflammatory arthritis can present with a combination of progressive pain, restricted movement, instability particularly in the knee joint and progressive loss of function. Arthroplasty should be considered when optimal medical and non-drug supportive therapies have failed.

5.1. Pre-operative assessment

The systemic features of RA and the spondyloarthropathies need to be thoroughly identified through a detailed history, examination and appropriate investigations (Table 7). Abnormalities which may affect fitness for surgery or rehabilitation need to be discussed with the anaesthetist, rheumatologist and where necessary other relevant medical and allied professionals. Cardiovascular pathology maybe silent because of low physical demand. The incidence of silent myocardial infarction is six times that of the general population and is responsible for much of the 10 year reduced life expectancy in the rheumatoid population versus the background population [45]. Any abnormalities within the history in a patient with inflammatory arthritis therefore need to be investigated further.

History	Disease onset Pattern and temporal sequence of joints involved Presence and persistence of joint swelling Pain: site, severity and radiation Morning stiffness and duration Functional difficulties Presence of non-articular features (e.g. nodules) Systemic features (e.g. anorexia, fatigue, weight loss) Psychological effects Full review of systems Previous anaesthetic and surgical history Drugs and allergies
Examination	Complete medical Evidence of joint inflammation Joint damage, range of motion, and previous surgical scars Tendon and ligamentous damage Presence of extra-articular features (e.g. plenomegaly, leg ulcers, vasculitis) Grip strength General health, anaemia, muscle atrophy Dental inspection, assessment of mouth opening ability, dysphonia Neurological assessment for cervical myelopathy and peripheral neuropathy
Investigations	Full blood count, urea, creatinine, electrolytes, and liver function tests Chest radiograph, lateral cervical spine flexion and extension radiographs Electrocardiogram Urine dipstick; culture to exclude occult infection Pulmonary function tests in patients with limiting lung disease Echocardiogram in patients with limiting cardiac involvement

Table 7. Preoperative assessment of the Rheumatoid Patient, Wilkinson *et al* [48]

Airway management in the rheumatoid patient may also present difficulties because of laryngomalacia and atlanto-axial subluxation (AAS). AAS may be anterior, posterior, vertical, lateral/rotatory and sub-axial. The less common posterior and lateral subluxations place the spinal cord in jeopardy during extension of the neck. Cervical pathology is common. In a review of rheumatoid patients awaiting orthopaedic surgery, Neva *et al* found that 44% of patients had cervical spine subluxation or previous fusion [46]. Interestingly, they found no difference in neck pain, headaches or upper limb radiculopathy between patients with or without cervical spine instability. Flexion and extension views of the cervical spine or computed tomography (CT) scanning may aid AAS diagnosis and although this diagnosis may not change anaesthetic practise it will ensure that neck handling is kept to a minimal and ensure that staff with adequate training are present for anaesthesia [45]. Further cervical spine difficulties are encountered in the AS patient who may have fixed spinal deformities. These

fixed deformities in the presence of osteoporosis place patients at high risk of fracture and subsequent neurological deficit. The anaesthetist needs to be made aware of these issues before surgery. Cervical spine involvement is not common in psoriatic arthritis and the most common clinical feature is a decrease in range of movement secondary to apophysial joint ankylosis [47]. Radiographically, the prevalence of anterior atlanto-axial instability is less than 10%. Published data with regards to the incidence of cervical spine involvement with spondyloarthritis secondary to inflammatory bowel disease is extremely limited.

Finally, patients with chronic inflammatory disease often have anaemia both as a result of their disease or secondary to medication. Optimising pre-operative haemoglobin levels, intraoperative cell salvage and reinfusion post-operative drains should be planned before surgery is undertaken.

5.2. The order of surgery

Patients with inflammatory arthritis often present with many symptomatic joints of both the upper and lower limbs. Careful consideration to the order of surgical intervention requires assessment on an individual level. Surgical priority should be given to structures that are at high risk of failure (for example symptomatic cervical spine instability or imminent tendon rupture). In general, lower limb surgical procedures precede those of the upper limb as post-operative rehabilitation using crutches can compromise upper limb reconstructive surgery. Within the lower limb, total knee arthroplasty implant positioning and rotational alignment is simpler once femoral length and rotation have been restored with a total hip arthroplasty [48], however generally the order of surgery should be dictated by managing the most painful and functionally limiting joints first. In patients with severe forefoot disease, consideration should be given to undertaking forefoot arthroplasty prior to hip or knee joint replacement (Figure 1).



Figure 1. Soles of the feet in a patient with rheumatoid arthritis. There is distal subluxation of the forefoot pad pad with exposure of subluxed metatarsal heads and resultant callosity formation.

5.3. The perioperative management of medical therapies

The adverse effect profile of many of the medications used to control symptoms and influence disease progression in inflammatory arthropathy may affect a wide variety of organ systems and an awareness of these and of their potential drug interactions is required.

NSAIDs increase the risk of gastric ulceration and patients may benefit from perioperative gastric protection with proton pump inhibitors. Long term use may also impair renal function increasing the risk of acute kidney injury secondary to post-operative dehydration.

The risk of an Addisonian crisis, an insufficient adrenal response to stress, is increased in patients with long term glucocorticosteroid use. Exogenous steroid use results in adrenal atrophy secondary to suppression of corticotropin-releasing hormone and adrenocorticotrophic hormone (ACTH). Patients in Addisonian crisis may present with symptoms ranging from lethargy, abdominal pain and syncope to coma. Biochemically, hypoglycaemia, hyponatraemia, hyperkalaemia and hypercalcaemia may be present. Local practice governs the regimen of hydrocortisone supplementation in the perioperative period, however typical dosing includes 100mg of intravenous hydrocortisone at induction of anaesthesia and 100mg 6 or 8 hourly for 3 days. Lower dosing regimens with a total of 150mg per day are also used [48].

While the effects of NSAIDs and glucocorticoids are well understood, there is no consensus on the perioperative management of the DMARDs. A randomised controlled trial in RA patients revealed that the infection rate was lower in patients continuing methotrexate versus those who stopped methotrexate prior to surgery (2% versus 15% respectively) [49]. A recent systematic review of the use of methotrexate in RA patients undergoing elective orthopaedic surgery found that continuing methotrexate was not associated with increasing risk of surgery complications, and led to fewer disease flares in the perioperative period [50]. Disease activity is also better controlled when methotrexate weekly administration remains uninterrupted [51]. Also, a study examining late infection rates with uninterrupted methotrexate use found no evidence of increased risk of late deep infection in 65 patients undergoing elective orthopaedic surgery over 10 years of follow up [52].

There is, to date, no clear evidence on the perioperative risk of orthopaedic infections in patients receiving biological agents, such as anti-TNF therapy [53]. A review of the limited published data in this area reveals much heterogeneity. RA patients have shown no increase in superficial wound infection rates following arthroplasty surgery with the continued use of biological agents [54, 55]. Conversely other studies have shown an increased rate of post-operative infection [56]. In a retrospective review of 81 total hip arthroplasties (THA) and 339 total knee arthroplasties (TKA), there was an increased odds ratio for superficial skin infection of up to 9.8 with continued use of anti-TNF therapy [57]. In a much larger Japanese study [58], 1626 patients treated with biological agents versus 29,903 patients not on a biological agent, reported an odds ratio for superficial infection of 2.1 with the use of biological agents even when these were stopped prior to surgery. The general recommendations of the American College of Rheumatology (ACR) guidelines in 2008 [59] and its update in 2012 [60] on the perioperative management of DMARDs are as follows:

- i. Methotrexate: continue perioperatively for all procedures.
- ii. Sulfasalazine: discontinue 1 day before surgery, resume 3 days after surgery.
- iii. Leflunomide: discontinue 2 days before surgery, resume 2 weeks after surgery.
- iv. Hydroxychloroquine: continue perioperatively for all procedures.
- v. Biological agents (eg. Anti-TNF- α): discontinue 1 week before surgery, resume 2 weeks after surgery. The ACR guidelines also recommend that the time period for cessation of biological agents is dependent upon the half-life of the biological agent used. Gilson et al. [110] recommends that the cessation of anti-TNF therapy should allow levels to fall by 5 half-lives prior to surgery in order to ensure that the drug has been eliminated.

6. Surgical challenges and choice of implant in inflammatory arthritis

Patients with inflammatory arthritis may be regular attenders to primary and secondary care. A good rapport and doctor-patient relationship is essential to gain trust and understanding and help to manage patients expectations. Some orthopaedic challenges stem from the general chronicity of the inflammatory disease or from the medications used to treat it. Others are joint-specific.

6.1. General features

Many patients will have had previous hip or knee procedures or had surgery at other sites. The overall function of these sites, as well as the presenting joint, must be assessed as they may affect rehabilitation and outcome. Soft tissue pathology may manifest as joint contracture, tendon attenuation or rupture, ligamentous instability, skin loss, chronic ulceration, vascular or neurological insufficiency, or a combination of these features (Figure 2). Previous surgical scars, especially around the knee, may affect planning, exposure and outcome after surgery. Bony disease can result in extensive bone loss secondary to erosive disease, avascular necrosis, or osteoporosis with increased fracture risk and deformity and challenges in establishing primary implant fixation.

6.2. Surgical challenges for hip arthroplasty

Surgical challenges at the hip include acetabular protrusio, focal bone loss and osteoporosis. Flexion contractures may be present in patients who have been chair-bound for a considerable time prior to seeking treatment for their joint disease.

Protrusio may be primary, or secondary, and can occur with or without medial wall defects and is common in all inflammatory arthritides (Figure 3). Protrusio was first recognised by Otto in 1816 [61] and it was 1935 when Overgaard [62] presented the first useful classification into primary and secondary, since modified by Gilmour [63]. Other classifications have also emerged e.g. Charnley [64] and Hirst [65].



Figure 2. Thin skin, ligamentous damage, infection, and soft tissue loss at the wrist in a patient with rheumatoid arthritis. Similar problems at the foot are common, and may impact on hip and knee reconstructive options.



Figure 3. Plain radiograph of the pelvis in a patient with rheumatoid arthritis. On the right side there is protrusio acetabuli, on the left this has been treated with cemented total hip arthroplasty plus impaction of morsellised allograft to the protrusio defect.

Charnley graded protrusio acetabuli by measuring the distance between the medial wall of the acetabulum and the iliopectineal line. In Grade I protrusio the medial acetabular wall is medial to the line by 1-5mm, Grade II 6-15mm and Grade III greater than 15mm. Edstein and Murphy recognised that using the ilioischial line as a reference point that there was sex specific variation of the medial wall of the acetabulum, in males the medial wall was 2mm lateral to the line and females were 1mm medial [66]. Hirst graded the protrusio taking into account this sex related variation [65](Table 8).

Grade	Men	Women
I	3-8 mm	6-11 mm
II	8-13 mm	12-17 mm
III	>13 mm	>17 mm with fragmentation

Table 8. Protrusio acetabuli classification by Hirst [65]

In Grade III cases dislocation of the femoral head may be difficult and the surgeon should be confident with his/her ability to divide the femoral neck in situ and remove the femoral head as a secondary procedure. The normal anatomy of the sciatic nerve may also be altered and it should be actively sought for in posterior approaches to the hip. Anatomical restoration of the centre of hip rotation lateral to Kohler's line is essential. Anatomical restoration optimises hip biomechanics and prevents impingement; therefore further deepening of the acetabulum should be avoided. Medial wall supplementation and anatomical restoration can be achieved with the use of bone grafting or metal augmentation. Hirst [65] initially described the use of 2mm thick femoral head slices impacted into the medial acetabular wall and Rosenberg *et al* have reported a 90% survival rate at 12 years using morsellised impaction bone grafting [67]. Larger defects require medial wall supplementation. The clinical results of support with metal mesh in these large defects is poor [68] and therefore cage supplementation prior to impaction bone grafting is needed. These systems report good outcomes, up to 95% survival at 9 year follow-up [69], in revision surgery for large defects. However there are few long term studies assessing the clinical and radiographic outcomes of primary hip arthroplasty in Grade III protrusio defects in inflammatory arthritis. Studies utilising trabecular metal supplementation are awaited.

6.3. Choice of implant for hip arthroplasty

Cemented or cementless THA components may be used in patients with RA. A study from the Finish Arthroplasty register found comparable long-term results between cemented and cementless components in 4,019 patients who were over 55 years when revision for any reason was used as an end point [70]. Similarly, in a study of 2,557 patients under the age of 55 years there were no significant differences in overall survival between different components [71]. The 15-year survival rate for cementless proximally circumferentially porous-coated stems was 87% and for cemented stems was 81%. However, the 15-year survivorship for cementless cups was poorer than cemented cups, 67% versus 80%, respectively.

In another study from the Danish Hip Arthroplasty registry [72], 1,395 (1,661 primary hips) patients with RA were followed for up to 14 years and results were compared with 64,858 patients with osteoarthritis (RA: cemented cups 47%, cemented stems 73%, OA: cemented cups 43%, cemented stems 68%). There was no difference in survival of cups between primary THAs in rheumatoid versus osteoarthritis patients. In contrast, there was better overall survival of stems in rheumatoid versus osteoarthritis patients, both for revision due to aseptic loosening

(adjusted relative risk = 0.58; 95% CI: 0.34-0.99) and for any reason (adjusted relative risk = 0.63; 95% CI: 0.45-0.88).

In a 10-year follow up study of 75 patients with RA (106 hips) who received a cemented THA, stem survival was 98% and cup survival was 92% [73]. In cemented Charnley THA in young patients with rheumatoid arthritis (63 patients, 100 hips) versus osteoarthritis (54 patients, 66 hips), 25-year survivorship of the femoral component was 85% in patients with rheumatoid arthritis versus 74% in patients with osteoarthritis, and of the acetabular component was 79% versus 59%, respectively [74]. Finally, in a recent systematic review of 23 small case series and 5 national implant registers of THA in rheumatoid patients there was no evidence in favour of cemented components over cementless ones [75].

The role of resurfacing arthroplasty in RA remains unclear. In a recent international register study, 47 rheumatoid patients (54 hips) were gender and age matched with 131 osteoarthritis patients (138 hips) and all had uncemented acetabular and cemented femoral hip resurfacing with Birmingham Hip Resurfacing implant. At 8-year average follow up, the survival rate was 96.3% in the RA group and 97.8% in OA group [76]. In another small series of 10 patients (13 hips) who had metal-on-metal resurfacing, no failures were reported at short term 3-year follow up [77]. However, recent data on the survival of resurfacing prostheses in general suggests avoiding this type of prosthesis in women, and in smaller men, phenotypic characteristics that are common in the rheumatoid population.

6.4. Surgical challenges for Total Knee Arthroplasty (TKA)

Soft tissue destruction leading to ligamentous instability, focal bone loss particularly of the femoral condylar bone leading to loss of height within the lateral compartment and fixed valgus deformity (Figure 4a and b), and periarticular osteoporosis are common features in the rheumatoid knee [48]. Valgus deformities with a variable degree of hyperextension rather than fixed flexion are commonly seen. Varus deformities are often secondary to osteoarthritic changes with a degree of fixed flexion [78]. The surgical challenge is to ensure correct soft tissue balance to avoid unequal loading and asymmetric stresses on the implant and eventual loosening. A stepwise approach to the release of contracted tissue is required [79-81]. A medial parapatellar or a lateral approach is used and structural bone grafting or prosthetic augmentation blocks may be required to restore large bone defects [48, 82]. Soft tissue insufficiency and ligamentous imbalance often favours the use of a cruciate sacrificing, rather than a posterior cruciate-retaining prosthesis. The survivorship of cruciate retaining prostheses is reported as poor in some series [83][84]. In cases of ligamentous incompetence a fully constrained prosthesis may be required [85]. The role of patella resurfacing in the rheumatoid patient is unclear. In a randomised controlled trial of 26 patients with RA who had bilateral TKA and patellar replacement performed in one randomly selected knee in each patient demonstrated improved pain and function in the patella resurfacing group [86].

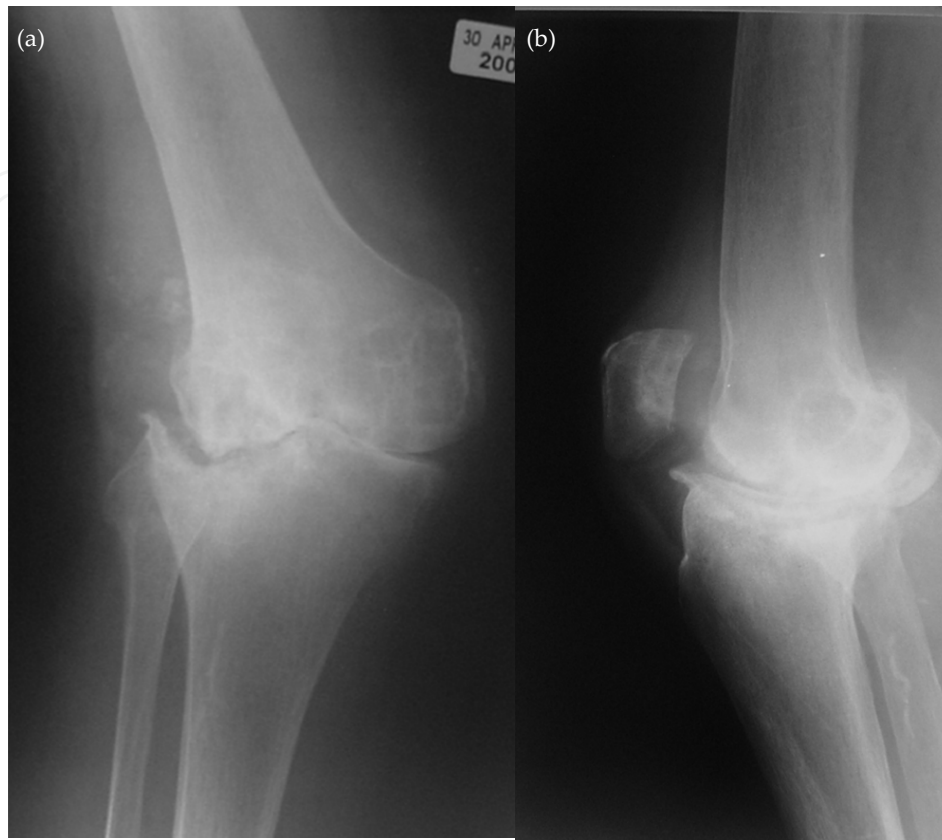


Figure 4. Plain anteroposterior (a) and lateral (b) radiographs of the knee in a patient with rheumatoid arthritis. Degenerative changes are present in all 3 joint compartments. There is collapse of the lateral compartment with resultant valgus deformity. Erosion of the anterior aspect of the distal femoral metaphysis due to pannus is also seen.

6.5. Choice of implant for knee arthroplasty

Cemented TKA has been considered the gold standard prosthesis for the rheumatoid patient. The 10-year revision rate of cemented TKA between 2001 and 2010 in rheumatoid patients reported to the Swedish Knee Arthroplasty register was 4% [87]. Fifteen-year survival rate of cemented Kinematic TKA was 93.7% in 25 rheumatoid patients (36 knees) [88]. However, recent survivorship data on cementless TKA also show good results, with a survival rate of 96.8 % at 10 years in a cohort of 112 patients (179 knees) [89]. The cementless Hi-Tech Knee II cruciate-retaining prosthesis was evaluated in 31 Japanese patients with RA with an average 8-year follow up and a reported survival rate 96.9% [90]. Similarly, 16-year survival rate of cementless low contact stress TKA in 47 patients was 94% [91]. Unicompartamental prostheses are not appropriate for RA patients as the degenerative changes are pan-articular, and their use is associated with high failure rates [92].

7. Complications of hip and knee arthroplasty in inflammatory arthritis

When compared to the general arthroplasty population, patients with inflammatory arthritis have more comorbidities and are taking more prescription medication. This is reflected by the higher risk of systemic and surgery specific complications. Mortality rates in rheumatoid patients are 1.5-1.6 fold higher than in the general population [93]. In a ten-year survivorship analysis from the Scottish register, greater mortality rate was associated with rheumatoid disease. Cardiovascular disease is the most commonly attributed cause of death, although other complications, such as infection, pulmonary and renal disease, are also more prevalent in the rheumatoid population [94].

In a population based study on risk of revision for infection in THA and TKA from the Norwegian Arthroplasty register, data from 6,629 (2,462 TKA, 4,167 THA) patients with RA were compared with 102,157 osteoarthritis patients (21,832 TKA, 80,325 THA). On an average 8-9 year follow up, rheumatoid patients with TKA had a 1.6 times higher risk of revision for infection than osteoarthritis patients, whereas there was no difference in the THAs [95]. In a population based study from Mayo clinic, 462 patients with RA (657 total joint replacements) the prosthetic infection rate at 4 years follow up was 3.7% [96]. Da Cunha *et al* [97] found no significant difference in infectious complications when compared perioperative infections in 49 rheumatoid patients (28 TKA, 47 THA) with 75 gender and age matched osteoarthritis patients (56 TKA, 75 THA).

A retrospective review of nearly 5 million patients demonstrated that RA was an independent risk factor for pulmonary embolism and deep vein thrombosis (DVT) in hospital patients, with a relative risk of 2.25 and 1.9 respectively [98]. In a recent comparative study, the risk of DVT was compared in 199 patients (238 knees) with RA and 156 patients (169 knees) with osteoarthritis and was found to be higher in the osteoarthritis group [99]. Earlier studies have also demonstrated lower risk in rheumatoid patients, which has been attributed to the use of NSAIDs [100]. The use of NSAIDs is also believed to cause lower incidence of heterotopic ossification in the rheumatoid patient as compared with those with osteoarthritis [101].

The risk of dislocation is also reported as higher in RA patients in a recent population based study from the Scottish National arthroplasty register, 62,175 total hip arthroplasties performed from April 1989 to March 2004 [102]. This is supported by the results of a prospective study assessing dislocation 2-years following THA in inflammatory arthritis patients [103]. Finally, periprosthetic fractures are reported more common in RA patients compared to OA, this can be explained by the poor bone quality and comorbidities [104, 105]

7.1. Functional outcomes

Successful functional outcome requires realistic understanding of goals and expectations of surgery with active inclusion of the patient in the decision making process [109]. In measuring the success of lower limb arthroplasty in patients with inflammatory arthritis, condition-specific outcome measures should be used. Scoring systems have been developed to measure disease activity and functional deficit. The American College of Rheumatology has developed

the “ACR20 response score” [106], this was modified and adapted by the European League Against Rheumatism “EULAR score” [107]. The ACR score is considered the gold standard and it is based on seven clinical end points: swollen joint count, tender joint count, the physician’s assessment of disease activity, the patient’s assessment of disease activity, pain, and physical function, and levels of an acute-phase reactant (either the C - reactive protein levels or the erythrocyte sedimentation rate). The “ACR20 response” [106], defined as at least 20% improvement in both the tender joint count and the swollen joint count and at least 20% improvement in 3 of the 5 other core set measures listed above. ACR20 aims to provide an objective assessment of disease status and is used in longitudinal studies to measure the effectiveness of medical and surgical interventions. The use of these scores helped to provide objective assessment of patients outcomes, better preoperative scores are associated with better surgical outcome [108].

The outcome of surgery is influenced by the local pathology, nature of the procedure and the severity of the disease [53, 88, 110]. In a systematic review of patients characteristics affecting the surgical outcome of total joint arthroplasty, older age was related to worse function particularly among women, whilst age and sex did not influence the outcome of pain [111]. There is good evidence that an increase in joint damage is associated with an increase in functional disability [112] and joint surgery has improved the function and quality of life of patients with RA [113].

However, when compared to patients with osteoarthritis, those with inflammatory arthritis have a slower, more gradual functional improvement in clinical outcomes scores [114]. Functional outcomes following THA are poorer in rheumatoid compared with non-inflammatory arthritis [73], this is perhaps explained by the multiple joints involvement in this group and its effects on functional outcomes [115]. Nevertheless, following THA in 50 rheumatoid patients, Harris hip score improved from 22 to 82 at 9 years mean follow up [116], and from 25 to 89 at 11 years follow up in another cohort of 20 patients [117].

Studies on TKA in rheumatoid patients have also reported good long term functional outcomes. When using the knee society score, 46 patients (71 knees) achieved 77% ‘Good’ or ‘Excellent’ at 10 years follow up [118]. In another study, 25 patients (36 knees) achieved 78% ‘Good’ or ‘Excellent’ at 15 year follow up [88]. However, when compared with osteoarthritis patients who had TKA, 207 rheumatoid patients younger than 55 years achieved less postoperative improvement [119]. On the other hand, when assessing patient satisfaction following TKA, there was a significantly better subjective outcome in rheumatoid versus osteoarthritis patients [120].

8. Conclusions

Hip and knee reconstruction are important surgical interventions in the management of the patient with inflammatory arthritis. Evidence to date suggests that both cemented and cemented prosthesis give good long term results. The functional benefit achieved in an individual patient will be affected by the systemic nature of the disease, and other

joint involvement. Because inflammatory arthropathy involves the whole joint, partial and uni-compartmental joint replacement should be avoided. The perioperative management of the patient with inflammatory arthropathy requires multidisciplinary input, and recognition and appropriate management of comorbidities that are common in this patient group. Finally, an awareness of the pharmaceutical and biological agents taken by the patient, and their appropriate peri-operative management is important to minimise the risk of iatrogenic complications.

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