Perioperative Management of Patients with Connective Tissue Disease

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Abstract Diseases of the connective tissue are a varied group of disorders with major musculoskeletal manifestations such as joint pain and loss of function. As a consequence of the accompanying inflammatory joint disease, such patients often require surgery. Due to the protean organ-related consequences of these conditions, patients who suffer from chronic connective tissue disease are a highly challenging population in the perioperative context. This paper reviews the management of such patients in this clinical setting.

Keywords connective tissue disease · perioperative care

Surgery in the patient with connective tissue disease

Diseases of connective tissue are a varied group of systemic conditions. The symptomology of these diseases are dominated by musculoskeletal manifestations such as joint pain and loss of joint function. Although control of the inflammatory response, the hallmark of inflammatory arthritis, is generally achieved through increasingly successful medication regimens, there are some patients whose disease is not fully controlled. Such patients have persistent joint inflammation (synovitis) and, as a consequence, joint damage. Persistent synovitis, elevations in inflammatory

markers such as ESR, as well as persistently abnormal values on health assessment questionnaires (HAQ) predict joint destruction and increase the potential need for total joint arthroplasty (TJA). Additionally, some treatments, such as high dose corticosteroids, are often necessary for control of major manifestations of systemic lupus erythematosus (SLE) and myositis. This may result in osteonecrosis most often in the femoral head or head of the humerus leading to collapse, loss of function, and pain. When the femoral head is affected, total hip replacement is often required. As a consequence of these problems, rheumatologists work closely with orthopedic surgeons to determine when surgery is appropriate.

Patients with chronic connective tissue disease are among the most complex patients undergoing joint replacement surgery (TJA) and require close interdisciplinary collaboration to ensure optimal outcomes. Patients with rheumatic diseases and inflammatory arthritis have been shown to have excellent results from joint replacement surgery when pain relief is studied. However, if the restoration of function is the outcome of interest, such surgery is not always as successful [1]. When outcome measures such as the HAQ, which address functional capability, are used, patients with inflammatory arthritis lag behind osteoarthritis (OA) patients. Moreover, complications such as infection are increased in this population [2]. The increase in prosthetic joint infections seen in rheumatoid arthritis (RA) patients is further increased in revision surgery or in those patients with a prior history of prosthetic joint infection [3]. This is a population undergoing TJA more frequently, at a younger age, with more complications and worse outcomes when compared with patients with OA.

Patients with inflammatory rheumatic diseases have a high incidence of problems that require careful scrutiny in the perioperative period. Overt and subclinical cardiac disease, as well as renal and pulmonary disease, is common. These patients may be young and may have childbearing potential, factors that may influence the choice of implant materials. Further, such patients may have destruction of contiguous joints, which will create challenges in regard to

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surgical staging to optimize functional outcomes. Risk of postoperative thrombosis is magnified by the presence of the anti-cardiolipin antibody syndrome [4]. Finally, the medications used to control these diseases may impact wound healing or increase the risk of infection, are often discontinued during the perioperative period, and are held until early wound healing is complete. Withdrawal of these medications may permit disease flares, which can complicate postoperative rehabilitation [5, 6]. This review will identify the unique problems confronted in the care of these complex patients and describe some of the solutions currently in use to decrease the likelihood of perioperative complications such as cardiac ischemia and arrhythmias, renal functional impairment, pulmonary decompensation, thromboembolic events, and wound infection. We will also discuss the specific considerations relevant to surgery in young patients with childbearing potential and the unique risks of operating in patients with uncommon conditions such as pulmonary hypertension.

Cardiac disease

The increased mortality seen in RA and SLE over age-matched controls is largely attributable to cardiovascular disease and cannot be explained by the presence of concurrent traditional risk factors such as hypertension or hyperlipidemia [7]. The increase in cardiac deaths in SLE has been recognized since a large population study was published in 1976 [8], and more recently confirmed [9]. Young SLE patients may have a 50-fold increase in myocardial infarction (MI) over healthy controls. An increase in cardiovascular death, coronary artery disease (CAD), and congestive heart failure (CHF) is consistently recognized in patients with inflammatory diseases [10]. This increase is somewhat mitigated by therapy with DMARDs in the RA population and increased in the presence of persistent inflammation. The duration of the RA in association with persistent elevations of inflammatory markers such as CRP signify ongoing inflammation and

disease activity. Persistent elevations in CRP and other markers of inflammation correlate with the development of cardiovascular disease. The magnitude of increase is estimated to be as great as the increase in risk conferred by type 2 diabetes. The patients with poorly controlled inflammation are not only at risk for ongoing joint damage, which is likely to lead to joint replacement surgery, but are also at a high risk for concurrent cardiac disease.

Cardiovascular disease contributes significantly to overall risk in patients undergoing major surgery such as arthroplasty. Although perioperative cardiovascular risk has not been specifically studied in the rheumatic disease population, such risk has been well investigated for the general population. Algorithms have been developed by the American College of Cardiology/American Heart Association to assess perioperative cardiac risk [11, 12]. Total joint arthroplasty is rated as intermediate risk surgery, with a 1–5% incidence of cardiac death and non-fatal MI. Given the recognized increase in CAD in patients with inflammatory rheumatic diseases, the ACC/AHA recommendations can be applied (Table 1). Patients who are able to perform vigorous exercise may not need further formal testing to predict a low cardiac risk. Strenuous sports require an estimated 10 mets of energy, while walking up a flight of stairs is estimated to require four mets of energy. Patients with systemic rheumatic diseases may not be capable of vigorous exercise, so history alone may be an inadequate screen for the presence of significant cardiac disease. Additionally, these patients may not be able to perform adequately on a standard treadmill test. Resting echocardiography can assess overall left ventricular function and predict complications such as congestive heart failure and death when the left ventricular ejection fraction is less than 35%, but does not predict ischemic events [13]. Stress testing, performed either via echocardiogram or nuclear imaging, is preferable to predict ischemic risk. Cardiac stress testing, which provokes ischemia by increasing cardiac demand, permits stratification of ischemic risk by quantifying the vulnerability of cardiac muscle. When there are multiple or large ischemic regions, the risk of

Table 1 Predictors of increased cardiac risk [11]

Major predictors of increased cardiac risk	Intermediate predictors	Minor predictors
Recent (30 days) MI, unstable or severe angina, poorly compensated congestive heart failure (CHF), significant arrhythmias, severe valvular disease	Mild angina, prior MI by history or q waves, compensated or prior CHF, Diabetes Mellitus	Advanced age, abnormal EKG, rhythm other than sinus, low functional capacity, prior stroke, poorly controlled hypertension, prior cardiac revascularization, asymptomatic

perioperative ischemic events is high. Normal testing, while reassuring, does not suggest a complete absence of risk.

In rheumatic disease patients undergoing elective TJA, strategies for minimizing postoperative cardiac complications include risk stratification via imaging studies. Stress echocardiography has intuitive appeal given the dual information it provides about myocardial perfusion and valvular integrity. Although the benefit of the stress echocardiogram versus nuclear imaging remains unresolved, stress testing by either technique should be considered in patients who are incapable of vigorous exercise preoperatively. Beta-blockade slows the heart, improves myocardial contractility, and decreases myocardial oxygen consumption. Perioperative beta-blockade has been shown to decrease cardiovascular complications, but the initial observed benefit [14] has been offset by the more recent demonstration of an increase in hypotension and stroke in beta blocker-treated patients [15]. These observations have tempered enthusiasm for such therapy on a routine basis. Patients at high risk for ischemic events may benefit, but those with equivocal risk and baseline low blood pressures are probably best left untreated.

Renal disease

Renal function may be impaired in rheumatic disease patients and confers a significant risk to the patient in the perioperative setting. Intrinsic renal disease raises the risk of perioperative renal damage caused by hypotension or hypovolemia. Glomerulonephritis complicating SLE or use of nephrotoxic drugs such as NSAIDs can lead to a loss of renal function. Acute postoperative renal dysfunction, studied in hip fracture patients, is more common in patients with underlying renal disease, and is additionally associated with male sex, hypertension, and diabetes, as well as the preoperative use of nephrotoxic agents. A significantly higher complication rate and mortality have been reported in hip fracture patients undergoing surgery with postoperative renal dysfunction when compared with patients with stable renal [16]. Identification of patients at high risk for postoperative renal dysfunction in elective orthopedic surgery permits discontinuation of nephrotoxic medications such as NSAIDs and ACE inhibitors and ensures careful monitoring of fluid status.

Hypotensive anesthesia has advantages in THR including diminished blood loss and improved cement fixation, as well as playing a role in multimodal deep venous thrombosis (DVT) prevention strategies. The decrease in renal blood flow seen with hypotensive general anesthesia may precipitate renal failure [17] in patients with underlying renal disease. Hypotensive epidural anesthesia has been shown to be safe in patients with chronic renal disease who undergo total hip replacement when cardiac output is maintained by judicious fluid management and low-dose epinephrine infusion [18].

Certain hip implants with metal-on-metal articulations are felt to be more durable when compared with implants composed of metal or ceramic-on-polyethylene. These

components, however, shed metal ions that accumulate in the face of renal damage [19]. Although the long-term effect of metal ion accumulation is unknown, patients with underlying renal disease are not candidates for metal-on-metal prosthesis.

Pulmonary disease

Asthma and chronic obstructive pulmonary disease (COPD) are the most common causes of pulmonary disease and raise the likelihood of postoperative atelectasis or pneumonia, particularly when abdominal or thoracic surgery is performed. Smoking history or cardiac disease further increases this risk. In addition, rheumatic disease patients have a high prevalence of interstitial lung disease and pulmonary artery hypertension (PAH). Interstitial lung disease produces a restrictive defect with a decrease in lung volume as well as a decrease in diffusion capacity (DICO) on pulmonary function testing (PFT). PAH, when unaccompanied by left heart disease, can be caused by an increase in pulmonary vascular resistance with or without intrinsic pulmonary parenchymal disease. These entities frequently complicate the systemic connective tissue diseases such as scleroderma, SLE and mixed connective tissue disease, dermatomyositis (DM), and polymyositis (PM).

Restrictive lung disease may also reflect chest wall pathology. In scleroderma, the skin over the thorax may be thickened and bound down, preventing chest wall excursion. Similarly, DM and PM patients may have impaired inspiratory effort due to chest wall muscle weakness. Patients with ankylosing spondylitis may also have restricted chest wall expansion. Surgery performed under regional anesthesia is generally well tolerated. Careful assessment of pulmonary function is essential when scalene nerve block is employed such as in upper-extremity surgery. Such blocks result in ipsilateral diaphragmatic paralysis, which can further compromise lung function.

PAH is characterized by elevations of right heart pressures, which can lead to decreased venous return. This may lead to systemic hypotension and shock, when magnified by hypoxia-driven right-sided vasospasm. Anesthetic agents, which may have an anti-inotropic effect, may further aggravate this situation. In severe PAH, hypotension and decreased venous return which accompanies regional anesthesia can be catastrophic. Given the high mortality seen with PAH to minimize risk, careful preoperative assessment and perioperative management for patients with PAH requires close collaboration with cardiology, anesthesia, and pulmonary medicine as well as surgery [20, 21]. A comprehensive evaluation includes definition of right heart function by echocardiography or catheterization. Patients with severe pulmonary hypertension, given the high associated mortality, may not be suitable candidates for elective surgery.

Fat embolization, the presence of fat material in the circulation, frequently occurs during TJA when the cemented implant is inserted with pressurization [22]. The

majority of long-bone fracture patients, a well-studied surrogate group, demonstrate transient hypoxemia due to fat embolization, without clinical respiratory complications. Fat emboli syndrome refers to the development of clinical complications attributed to fat embolization and can include altered mental status, rash, as well as pulmonary compromise and hypoxemia. This may precipitate pulmonary decompensation in patients with underlying lung disease as the rise in pulmonary artery pressure contributes to increasing pulmonary vasospasm and worsens hypoxemia.

Upper airway compromise is reported in patients with RA due to involvement of the cricoarytenoid joints. These joints move with the vocal cords and may produce hoarseness when chronically affected in RA. Trauma at the time of intubation for anesthesia will produce swelling of the vocal cords and can lead to compromise of the airway sufficient to produce respiratory distress. Although this can be successfully treated with tracheostomy after re-intubation, preoperative pulmonary function studies, as well as fiber-optic laryngoscopy, can provide the definitive diagnosis and help plan anesthesia strategy.

Evaluation and management of patients with inflammatory arthritis or connective tissue disease frequently include detailed preoperative PFTs and echocardiography to anticipate perioperative challenges. Postoperative therapy with bronchodilators and nebulizer therapy and early mobilization can prevent atelectasis. Careful attention to bowel function is commonly overlooked and may contribute to respiratory compromise as the distended abdomen in the bed-bound patient prevents full chest expansion by compromising diaphragmatic excursion.

Pregnancy

Patients with systemic inflammatory diseases such as SLE, RA, and JRA may sustain joint destruction due to poorly controlled joint inflammation or due to avascular necrosis and require arthroplasty to maintain mobility and treat pain. Improvements in implant design and surgical technique have decreased the impact of age as a contraindication to arthroplasty. Nonetheless, concerns about safety arise when women under the age of 45 with childbearing potential undergo TJA. In a large retrospective survey of 343 women between the ages of 18 and 45 who underwent THA, 25% had inflammatory arthritis [23]. There were 47 (13.7%) successful pregnancies, of whom 30 delivered vaginally and 17 by caesarian section. There were no immediate complications such as dislocation or fracture in the patients delivered vaginally. Caesarian section was usually performed for obstetric reasons when the reason was known, or for concern about harm to the prosthesis. Although revisions are frequent when young patients undergo arthroplasty, pregnancy does not increase this rate. Groin pain, which is common in pregnancy, did predict later revision when the pain persisted after delivery. Smaller studies also support the safety of pregnancy after THA [24, 25]. There is more experience with THA in young women

in light of the increase in dysplasia in this group, providing more information than in TKA.

Hip resurfacing with metal on metal bearings are gaining popularity in younger patients because of their durability. Cobalt and chromium are the primary metal constituents of these devices. When metal ions are released systemically, normal renal clearance prevents excessive accumulation. The potential toxicity of metal ion accumulation in adults is not known, but there is concern for teratogenicity in the developing fetus. Although the placenta has been shown to modulate the trans-placental transfer of metal ions, some still occurs. Mothers with metal-on-metal implants had higher serum metal ion levels than controls, but cobalt and chromium ion levels in cord blood were decreased to 60% and 29%, respectively, of maternal levels [26]. Control mothers with lower absolute metal ion levels transferred 97% to 98% across the placenta. In spite of placental modulation of ion transfer, cord blood from mothers with metal-on-metal implants had higher absolute metal ion levels than controls. Prudence would suggest avoiding metal-on-metal implants until definitive studies delineating toxicity and teratogenicity are available in patients who have childbearing potential.

Staging of surgery in patients with polyarticular disease

Patients with multiple joint involvement require careful planning of their surgical procedures. Upper-extremity involvement may hinder the patient's ability to use assistive devices such as canes and walkers after lower-extremity procedures. In general, lower-extremity involvement takes priority over upper-extremity problems in order to keep the patient ambulatory. If patients stop walking for over 6 months, it is extremely difficult to regain the ability to walk.

In general, we address the most painful joint first, but given equal involvement of multiple joints, the surgery needs to be carefully planned. We recommend that bilateral hip and knee replacements be considered when patients have significant deformities including flexion contractures. If only one knee is straightened, the contracted knee will hamper the rehab and limit the motion of the operated knee. When patients have contractures at both the hip and knee, the hip should be addressed first with the knee is corrected shortly thereafter.

When faced with multiple joint involvement in the upper extremity, we usually prioritize procedures in the following order—wrist, hand, elbow, then shoulder. The first goal is to provide a stable, pain-free, well-aligned wrist. Next, function and alignment of the fingers and hand should be restored in order to give the patient incentive to use the hand. The elbow provides the patient the ability to position the hand in space and perform activities of daily living. Shoulder surgery can provide pain relief and rotation, but overhead motion may be unpredictable in patients with compromised rotator cuff muscles. Patients with inflammatory arthritis usually are more satisfied with their elbow replacements than they are with their shoulder

replacements due to the greater functional gains. If the patient has no rotation of the shoulder, sometimes the shoulder surgery should be performed before the elbow in order to avoid undue stress across the elbow.

In the lower extremity, given equal joint involvement, we usually reconstruct the ankle first, followed by the foot, hip, and knee. Restoring ankle alignment should be done before knee and foot surgery because a mal-aligned ankle will negatively impact the results of other joint surgery. If the foot is in equinus, the knee will be forced into hyperextension. If the foot is in valgus, uneven pressure will be placed on the forefoot. Once the ankle is aligned, the foot should be reconstructed as the results are very predictable and the patient requires a stable, well-aligned, pain-free foot in order to ambulate. Hip replacements are usually performed before knee replacement because the patient needs a pain-free, mobile hip in order to rehabilitate the knee. Also, referred pain from hip arthritis should be resolved before knee surgery is performed. In addition, if the patient has a flexion contracture of the hip, it should be corrected before the knee is replaced.

Although therapy for rheumatoid arthritis with DMARDs has decreased the incidence of severe cervical spine involvement, those patients with persistent disease activity and poor HAQ scores remain at risk. This may result in instability of the cervical spine with resultant myelopathy and sudden death. As the effects of cervical myelopathy may be misidentified due to peripheral joint involvement, we recommend screening flexion–extension radiographs of the cervical spine.

Medications

Patients with RA and SLE have an increased risk of infection when compared with the general population. In addition, some medications used in the treatment of rheumatic diseases are immunosuppressive, further increasing the risk of infection. These drugs may also have an impact on wound healing. Although there is little data addressing perioperative risk acquired via direct clinical trial, observations have been made from which we can extrapolate recommendations (Table 2).

Methotrexate (MTX) has been the most rigorously studied drug in RA patients undergoing TJA. On the basis of several

studies, including a prospective randomized trial [27], MTX appears to be safe in the perioperative period. In this prospective study, 388 patients undergoing orthopedic surgery were randomized to either continue their MTX (group A) or stop their MTX (group B). These patients were also compared with 228 patients (group C) who were not receiving MTX at the time of surgery. Group A patients had an infection or surgical complication rate of 2% and had no postop flares. Fifteen percent of group B patients had infections or complications and 8% of group B patients flared. Group C patients had infections or complications in 10.5%, and 2.6% flared.

Hydroxychloroquine and sulfasalazine have favorable toxicity profiles, but have not been studied in the perioperative period. Conflicting results have been published in regard to leflunamide use in this setting. A significant increase in wound healing complications has been reported in leflunamide-treated patients (40%) compared with MTX-treated patients (13.6%) [28]. However, a contrasting study found no difference comparing 41 patients given continuous leflunamide when compared with 41 patients in whom the leflunamide was stopped 1 month prior to surgery [29]. Pending definitive studies, we recommend holding leflunamide and sulfasalazine until normal postoperative bowel and renal function has been demonstrated.

Biologic agents such as the TNF inhibitors have been used in the treatment of RA now for over a decade. The major complication of therapy with TNF inhibitors is infection. Gram-positive organisms are the most commonly reported bacteria complicating TNF inhibitor therapy and are the predominant organisms seen in early surgical site infections. A single small prospective study by Bibbo et al. addressed surgical risk in patients undergoing foot and ankle procedures and found no increase in the 16 patients who were treated with continued perioperative TNF inhibitors, in contrast with the 15 patients treated with other DMARDs, who had delayed healing [30]. In a retrospective study of RA patients undergoing orthopedic surgery [31], 10 of 91 patients developed a serious postoperative infection. Seven of those 10 patients were receiving TNF inhibitor therapy. Other factors such as age, steroid use, or diabetes were not significantly different between the groups. Some information can also be extrapolated from the experience using TNF inhibitor therapy in inflammatory bowel disease patients. When operative complications in 40 patients with Crohn's disease

Table 2 Perioperative management of DMARDs

Medication	Continue/ discontinue	Time to discontinue prior to surgery	Time to restart postoperatively
Methotrexate, hydroxychloroquine Etanercept	Continue Discontinue	2 weeks	1–2 weeks postop, stitches out, wound without drainage
Infliximab Adalimumab	Discontinue Discontinue	4–6 weeks 2–3 weeks	1–2 weeks postop, stitches out, no wound drainage 1–2 weeks postop, stitches out, wound without drainage
Leflunamide, sulfasalazine, azathiaprin	Discontinue	2 days	1–2 days after normal GI and renal function has returned

(CD) treated with a TNF inhibitor, infliximab, at the time of bowel resection were compared with 39 CD patients not receiving infliximab, no significant differences were seen [32]. Until there are definitive studies addressing this question, given the known increase in infection with these agents, it seems prudent to discontinue TNF inhibitor therapy preoperatively. This position has also been advocated by European investigators [33, 34]. Rituxamab is a monoclonal antibody directed against the CD-20 cell surface marker, which is present on the surface of a subset of B- lymphocytes. Risk of infection with rituxamab is comparable with the risk seen with other biologic agents in clinical trials in RA, but there are no data regarding its use in the perioperative setting. Immunoglobulin levels are decreased, with a disproportionate decrease in autoantibody levels. Since the depletion of B cells can persist for up to a year, surgical planning to minimize risk is difficult.

Many rheumatic disease patients receive chronic glucocorticoid therapy. Concern about adrenal suppression in patients chronically given exogenous glucocorticoids with reports of adrenal insufficiency during periods of stress has led to the use of supraphysiologic doses of cortisone, or “stress dose steroids.” Glucocorticoid therapy is well recognized as a significant risk for infection and delayed wound healing. Patients have traditionally been given augmented doses if they have received low-dose steroid therapy for >6 months or moderate- to high-dose therapy for more than 3 weeks. However, the length of steroid therapy and dose are not reliable predictors of need in the perioperative period. Moreover, commonly used tests to assess adrenal function do not accurately predict steroid need. When 40 patients receiving chronic steroid therapy, 63% of whom had demonstrated adrenal insufficiency by the cosyntropin stimulation test, were hospitalized with significant stresses, none developed clinical adrenal insufficiency receiving only their usual daily dose of steroid [35]. Additional support for this comes from a prospective study of patients on chronic steroid therapy randomized to receive their usual daily dose of steroid or stress doses at the time of surgery [36]. Although all of these patients had demonstrated adrenal insufficiency by ACTH stimulation test, there was no difference clinically between the groups. The magnitude of the normal endogenous steroid response to various surgical procedures has been defined [37]. Thirty patients who had never received exogenous steroid undergoing either arthroscopy or unilateral knee arthroplasty

had serial cortisol levels measured. There was no significant increase over baseline cortisol levels in the arthroscopy patients, but there was a significant increase in endogenous steroid in the arthroplasty group. These studies support limiting the routine use of stress dose steroids in the perioperative setting. Patients undergoing minor procedures should take only their usual daily steroid dose. Patients undergoing major surgery, who are carefully monitored postoperatively, can receive their usual daily dose of steroid and be given additional steroid doses should they develop hemodynamic evidence of need, such as hypotension or tachycardia. Guidelines for perioperative steroid dosing are shown in Table 3.

Anticoagulation and DVT risk

DVT and pulmonary embolism (PE) are the most feared medical complications of TJA and can be life threatening. The reported incidence of DVT and PE increases with the sensitivity of the diagnostic study used. Studies utilizing venography report an incidence as high as 38% for DVT after knee replacement and an incidence of DVT of 16.4% after hip replacement surgery. In studies in which preventive techniques were not used, the incidence of fatal PE was 0.10%, and non-fatal PE was 3.2%; when preventive interventions are employed, the incidence of fatal and non-fatal PE drops to 0.05% and 2.2%, respectively. Although the risk of DVT and PE is consistently recognized in lower-extremity TJA, a recent study has found a significant risk in total shoulder arthroplasty (TSA) patients as well [38]. In a retrospective study an incidence of five DVT per 1,000 TSA versus 15.7 for THA and 26.9 for TKA was reported. The frequency of PE was 2.3 in TSA patients, compared with 4.2 and 4.4 in THA and TKA patients, suggesting the need to expand DVT/PE prophylaxis regimens to TSA patients.

There is considerable controversy in the literature debating optimal prophylaxis for thromboembolic events in the orthopedic literature arising in part from the choice of endpoints. The American College of Chest Physicians advocates the goal of elimination of all thromboembolic events, which requires an aggressive anticoagulation regimen including low molecular weight heparin with an expected increase in bleeding complications. The American College of Orthopedic surgeons regard non-fatal PE as a tolerable (though undesirable) endpoint for the postoper-

Table 3 Guidelines for perioperative steroid dosing

Stress	Target HCA equivalent	Preop steroid dose	Intraop steroid dose	Postop steroid dose	Postop day 1 steroid dose
Minor (arthroscopy, carpal tunnel)	25 mg/day for 1 day	Usual daily dose	None	None	Usual daily dose
Moderate unilateral arthroplasty	50–75 mg/day for 1–2 days	Usual daily dose	50 mg HCA	20 mg HCA every 8 h	20 mg HCA every 8 h
Major: anterior–posterior spine surgery, bilateral arthroplasty	100–150 mg/day for 2–3 days	Usual daily dose	50 mg HCA every 8 h	50 mg HCA every 8 h	50 mg HCA every 8 h

ative patient, a position that acknowledges the need to minimize bleeding complications which are associated with a higher risk of wound infections.

Risk stratification can be used to target populations at high risk for postoperative thromboembolic complications, thus identifying patients in need of aggressive anticoagulation. Screening for inherited procoagulant states as well as deficiencies in thrombolysis may be useful. Patients with PE following THR screened prospectively were more likely to have either the prothrombin G20210A gene mutation or a low anti-thrombin III level compared with patients without PE [39]. These tests are expensive and impractical to obtain as a screening strategy. Medical co-morbidities such as obesity, cancer, or a history of prior thromboembolic disease all increase risk. Intraoperative factors such as tourniquet time for TKA and operative time for THA also are associated with an increased risk of thromboembolic events.

A multimodal approach utilizing preoperative discontinuance of procoagulant medications such as estrogen, hypotensive anesthesia, venous pneumatic compression, intra-venous intraoperative heparin prior to femoral preparation, and low-intensity postoperative chemoprophylaxis with aspirin or Coumadin in conjunction with early mobilization has been successful [40]. The incidence of DVT after THA was 6.4%, and the incidence of symptomatic PE was 0.6%. Eighty-three percent of the patients received aspirin, of whom nine had PE, and 17% of the patients received Coumadin, of whom three had PE, a comparable outcome compared with more aggressive anticoagulant regimens.

Patients with the anti-phospholipid antibody syndrome are a high-risk group in whom aggressive anticoagulation is warranted. An approach to the perioperative management of these patients has been published based on the Hospital for Special Surgery experience [2]. Consideration of Greenfield filter placement to mechanically prevent PE should be made on a case by case basis and does not diminish the need for chemoprophylaxis. When a patient requires high-intensity anticoagulation, we withhold aggressive physical therapy to prevent wound complications, understanding the impact on mobility.

In summary, owing to the protean manifestations of the systemic connective tissue diseases, orthopedic surgery is not only frequently necessary but also presents significant challenges to the perioperative assessment and care in this subset of patients undergoing surgery. By anticipating potential complications through preoperative assessment, close collaboration with a team comprised of anesthesiologists, surgeons, rheumatologists, as well as cardiologists and pulmonary physicians when indicated has been successful in optimizing our patients preoperatively. Our collaborative approach permits identification of difficulties weeks before the date of surgery, permitting full evaluation and optimal therapy of problems, minimizing complications.

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