occur.[122 217–226] Systemic effects from CSI may include hyperglycemia, decreased bone marrow density, and adrenal suppression (though no cases of clinical adrenal insufficiency have been described).

Bleeding

In a retrospective study of 514 patients on therapeutic anticoagulation with warfarin who underwent a total of 640 joint injections and/or arthrocentesis, a single incident of clinically significant bleeding in an anticoagulated patient (international normalization ratio (INR) 2.3) was found (rate of 0.2%).[227] A total of 456 procedures were performed when INR was >2.0, and 184 procedures were performed with INR <2.0. Another single-center retrospective study of adult patients on novel oral anticoagulants found no incidents of bleeding among 1050 consecutive procedures, with the authors concluding that holding oral anticoagulation prior to joint injections is not warranted.[228]

The ASRA PM recommends that patients on anticoagulant and antiplatelet medications without additional complicating coagulopathic conditions (advanced liver disease or cirrhosis, advanced renal disease, old age, history of bleeding/hemophilia, or multiple anticoagulant medications) may continue their anticoagulant or antiplatelet treatments without interruption for low bleeding risk procedures (such as peripheral joint injection) as the risk for stopping these medications likely outweighs the low risk of bleeding for those on therapeutic dose.[229] Indeed, even patients with knee pain due to hemophilic arthropathy have been shown to derive benefit from IACS, and knee injections have been shown to be performed safely in this population with use of US and power Doppler.[230]

Cartilage, ligament, and tendon health

One of the concerns with IACS for the knee is the potential AE of IACS on cartilage health. Potential detrimental effects include catabolic effects on cartilage proteins including aggrecan, type II collagen, and proteoglycans, chondrocyte availability, and gross cartilage morphology.[231–234] Animal studies investigated the effects of corticosteroids on cartilage with inconsistent and conflicting results.[231 232 235–237] Some of these studies demonstrated cartilage disruption, while others showed cartilage preservation during acute inflammatory events. For commonly employed corticosteroid preparations, such as MP, betamethasone, and triamcinolone, basic science and animal studies have demonstrated a dose-dependent detrimental effect on cartilage.

A 2-year randomized placebo-controlled, double-blind trial of IA TA versus saline for symptomatic knee arthritis in 140 patients using annual knee MRIs, IACS resulted in greater cartilage volume loss than saline injection.[238] In this study, the intervention (saline or 40 mg triamcinolone without IA local anesthetic administration) was administered every 12 weeks for 2 years. Patients received MRIs at 0 (baseline), 12, and 24 months, and mean cartilage thickness was computed. The cartilage loss was more significant with the corticosteroid, and a corresponding response with pain improvements did not occur, raising concern about the value of frequent repeat IACS for the knee.

As noted previously, cases of tendon rupture were reported after injection into the biceps tendon or into the iliotibial band.[93 94 168] The long-term risks of repeated injections of the tendon sheath have not been reported, but in vitro studies indicated damage to chondrocyte viability after exposure to MP.[239] Single doses of USG injections of the biceps tendon do not appear to cause changes in tendon elasticity.[240] Practitioners may choose to exercise caution in performing repeated CSIs of the biceps tendon or iliotibial band.

Accelerated joint space narrowing and osteonecrosis

An IACS knee RCT study (40 mg IA TA injections administered every 3 months vs saline placebo for up to 2 years) used X-rays (rather than MRI) to examine radiological progression of joint space narrowing.[241] The study was powered (34 patients per group) to detect a difference of 0.125 mm progression of joint space narrowing between the two treatment groups at 2 years. No difference between the groups was detected at either 1-year or 2-year follow-up.

A study used radiographic findings to assess progression of joint space narrowing or joint destruction (semi-quantitative 0–4 scale) in 30 individuals with OA and 35 with RA who underwent a minimum of 15 knee CSIs over a 4-year period and a maximum of 167 injections over a 12-year period.[242] Fifty percent (36) knees showed no or minimal progression between radiographs (duration not described). Ten knees showed marked deterioration (marked narrowing with some collapse of a condyle and/or lateral subluxation). Two knees (same patient) revealed gross deterioration (Charcot's type joint), over 7 years after 82 and 85 IACS provided for each knee. However, there was no correlation between the number of injections and the rating of joint deterioration. Again, follow-up radiographs were done for clinical indications (not by protocol) with variable follow-up (not described). The total number of injections rather than frequency per year were described; laterality was not addressed. The authors concluded that repeated IACS do not lead to rapid joint destruction.

An updated Cochrane review of IACS for knee OA found that corticosteroids had no effect on joint space narrowing compared with control interventions (SD −0.02; 95% CI −0.49 to 0.46).[243]

Two retrospective studies showed progression of OA with IACS (based on Kellgren-Lawrence radiographic grading of OA) compared with non-injected controls. One is a small retrospective study with hip OA, and[244] the other is a bigger multi-institutional study of 684 patients with knee OA.[245] The retrospective study of 70 patients with hip OA compared with a matched control group showed that 44% (31 of 70) of patients who were given injections of corticosteroids with local anesthetics had radiographic progression of their OA, and 17% (12 of 70) experienced collapse of the articular surface.[244] The two radiologists, blinded to receipt of hip injection, found osteonecrosis in eight to nine images prior to injection and new osteonecrosis in 16–19 images postinjection. There was a very high prevalence of X-ray defined osteonecrosis in both the IACS group (37%) and comparator group (24%).[244] The larger multicenter longitudinal observational study followed 684 propensity-score matched participants. Using either an increase in the Kellgren-Lawrence grade by >1 or a decrease in joint space by >0.7 mm for knee rapid OA progression, the authors noted an association between IACS and knee radiographic OA progression.

Finally, there is also a case report of collapse of the superior femoral head articular surface after IACS administration in a patient with osteonecrosis but with preserved femoral head contours.[122] This progression has to be kept in mind since patients with painful non-collapsed osteonecrosis of the femoral head are frequently referred for IACS. The case also demonstrates value in radiographic imaging before IACS hip injections.

The risk factors for osteonecrosis include a history of BMD compromise; chronic corticosteroid exposure; and underlying