

disorders, such as renal insufficiency, organ transplantation, graft versus host disease, inflammatory bowel disease, HIV, and acute lymphoblastic leukemia.^{122 246} Bisphosphonate therapy may mitigate this risk.²⁴⁷

Accelerated OA progression

Rapid progressive OA (RPOA), also called rapid destructive hip disease or rapid destructive OA, is a rare condition with rapid loss of joint space on X-rays that is beyond the anticipated rate; defined as a joint space loss of >2 mm within a 12-month period.¹²²

A report of 307 patients undergoing hip IACS noted 23 patients (7%) developed RPOA, and of the 152 patients undergoing knee IACS, 6 (4%) were observed to experience RPOA.¹²² This study was limited by retrospective review of the clinical care. Radiographic follow-up was incomplete, obtained only when clinically indicated, and this would result in conservative estimates. Selection bias (referral to the radiology department for image-guided injections) may have been selected for patients with more progressive OA (independent of IACS).

A recent two-part study documented an association between hip CSI and RPOA.²⁴⁸ In the case-control portion, the authors showed an association between CSI and RPOA, with the risk increased with higher dosage and number of injections. The risk was low with a single 40 mg triamcinolone injection and higher with higher doses (80 mg or higher) and multiple (two or more) injections. The minimum effective dose is 40 mg TA (see box 7). In the retrospective portion, the investigators noted a rate of 5.4% (37 of 688 cases) after injection. Diagnosis occurred at an average of 5 months after injection and was characterized by rapid narrowing of the joint space, osteolysis, and collapse of the femoral head.

SYSTEMIC EFFECTS OF CS INJECTIONS

Blood glucose

An IA corticosteroid is known to elevate blood glucose in patients with and without diabetes mellitus, although not necessarily with adverse clinical consequences in patients without diabetes. Shoulder IACS (triamcinolone 40 mg) for the treatment of ACs elevated fasting blood glucose (FBG) by 17 mg/dL in both patients with and without diabetes, resulting in higher levels at day 1 (attributable to higher baseline FBG); FBG was observed to remain above baseline up to 2 weeks following injections for both groups.²⁴⁹ Among 60 patients with diabetes mellitus who received IACS, fasting and postprandial blood glucose were observed to be elevated up to 3 days after injection among the entire cohort.²⁵⁰ However, when analyzed according to site, upper extremity injections were not found to be associated with increased fasting or postprandial blood glucose, knee injections were associated with significantly elevated fasting and postprandial blood glucose, and paradoxically, injections at multiple sites were not associated with elevated fasting or postprandial blood glucose on days 1 through 7. In multivariate analyses, high baseline glycosylated hemoglobin (HbA1c) was significantly associated with elevated blood glucose following IACS, while factors including body mass index, insulin use, and corticosteroid dose were not associated with elevated blood glucose. In this study, one patient had FBG as high as 493 mg/dL, but no patient experienced diabetic ketoacidosis.²⁵⁰ A study of 23 patients with diabetes undergoing IACS shoulder injection reported similar findings, namely no significant elevation of blood glucose above baseline following injection.²⁵¹ One RCT of patients with diabetes on oral agents undergoing IA knee

Box 7 Statements and recommendations on adverse events from intra-articular corticosteroid (IACS) injections

Statements

1. Clinically significant increases in blood glucose may follow IACS injection, particularly in patients with diabetes mellitus. These effects are noted within hours of IACS, but peak blood glucose may be delayed for up to 2 days after IACS.
Level of certainty: high
2. Extended-release corticosteroid preparations may mitigate the impact of IACS on systemic blood glucose in patients with diabetes.
Level of certainty: moderate
3. Adrenal suppression may follow an intra-articular corticosteroid injection.
Level of certainty: moderate
4. For warfarin, in patients with an international normalization ratio (INR) in the therapeutic range (2.0–3.0), the risks of withholding anticoagulation prior to IACS related to the development of a thromboembolic event are greater than the risks of bleeding
Level of certainty: low
5. When there is strict adherence to standard infection control practices, the risk of infection due to IACS is low.
Level of certainty: moderate
6. There is an increased risk of postoperative deep joint infection when IACS is administered within 3 months prior to that joint replacement surgery, especially if IACS is performed within 1 month of surgery.
Level of certainty: moderate
7. There is a trend toward increased risk of postoperative deep joint infection when IACS is administered within 3 months prior to that joint replacement surgery.
Level of certainty: low

Recommendations

1. Patients with diabetes mellitus should be advised to monitor blood glucose carefully postinjection for at least 48 hours, until blood glucose normalizes (possibly up to 7 days).
Grade A
2. Monitoring of cortisol levels pre-IACS or post-IACS is not recommended routinely.
Grade D
3. In the right clinical setting, adrenal crisis should be considered as a possible etiology in the hypotensive patient in the days or weeks following IACS.
Level of certainty: low
4. For patients on chronic stable warfarin therapy with good control (no bleeding symptoms), anticoagulation therapy need not be withheld for IACS; patients on warfarin may be in therapeutic INR range.
Grade A
5. Providers should adhere to standard infection control practices, including strict aseptic technique when performing IACS.
Grade A
6. Avoid IACS within 3 months of planned total replacement of that joint, notably within 1 month of planned surgery.
Grade D
7. Discuss with the surgeon the risks/benefits when considering IACS in a joint planned for replacement surgery within 3 months.
Grade C