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Should Intravenous Heparin Be Administered During Total Knee or Total Hip Arthroplasty?

Armita A. Abedi, MD [a, b], Ibrahim Tuncay, MD [c, d], Mohamed M. Adi, MD [e], Samih Tarabichi, MD [f], Stavros Memtsoudis, MD, PHD, MBA [g], Martin Buttaro, MD [h], Javad Parvizi, MD [i]

[a] International Consensus on Orthopedic Infections Organization, Philadelphia, Pennsylvania, USA
[b] Department of Clinical Medicine, University of Copenhagen Faculty of Health and Medical Sciences, Copenhagen, Denmark
[c] Department of Orthopedics and Traumatology, Acibadem Mehmet Ali Aydınlar University, Istanbul, Turkiye
[d] International Joint Centre (IJC), Acibadem Maslak Hospital, Istanbul, Turkiye
[e] Orthopedics Division at Burjeel Medical City, Abu Dhabi, United Arab Emirates
[f] Alzahra Hospital, Dubai, United Arab Emirates
[g] Department of Anesthesiology, Critical Care & Pain Management, Hospital for Special Surgery, New York, New York
[h] Hip Surgery Unit, Institute of Orthopaedics "Carlos E. Ottolenghi", Italian Hospital of Buenos Aires, Buenos Aires, Argentina
[i] International Joint Center, Acibadem University Hospital, Istanbul, Turkey

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Should intravenous heparin be administered during total knee or total hip arthroplasty?

Response/Recommendation: There is insufficient high-quality clinical evidence to support the routine use of intravenous intraoperative heparin in total joint arthroplasty.

Level of Evidence: moderate.

Vote: Agree 93.2%, disagree 4.7%, abstain 2.1%.

Rationale

The risk of venous thromboembolism (VTE) increases after total hip arthroplasty (THA) and total knee arthroplasty (TKA) [1]. While most VTE prophylaxis regimens are instituted postoperatively, the activation of the coagulation system starts during surgery. In THA, this activation is evidenced by increased levels of thrombin–antithrombin complex, prothrombin fragment 1 + 2, fibrinogen peptide A, and D-dimer following femoral reaming for prosthesis insertion [2]. Intraoperative heparin significantly reduces fibrinopeptide A and prothrombin F1.2, indicating decreased synthesis of thrombin and fibrin, but does not affect the thrombin–antithrombin complex [2,3]. Studies have investigated the potential of intraoperative heparin to reduce the incidence of early postoperative VTE. Unfractionated heparin (UFH) has been utilized due to its established efficacy in cardiac bypass surgery and the ability to reverse its effects with protamine in cases of excessive bleeding.

Several randomized controlled trials (RCTs) have investigated intraoperative intravenous (IV) UFH compared to placebo in patients undergoing THA and TKA. In a study by Sharrock et al. [4] 1,000 units of IV UFH were administered, before incision, to patients undergoing THA, followed by 500 units every 30 minutes until completion of surgery. In another study by Westrich et al. [5],

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from the same institution, 15 units/kg of IV UFH were administered to patients at high risk of VTE, during acetabular reconstruction for patients undergoing THA. In both studies, patients received aspirin at 650 mg for 11 to 30 days to prevent VTE. In the former study by Sharrock et al. there was a reduction in the incidence of deep venous thromboembolism (DVT) and pulmonary embolism in patients receiving IV UFH, but also an increase in intraoperative blood loss. In the study by Westrich et al. [5] the rate of VTE and blood loss was the same in both groups. In an RCT conducted by Huo et al. [6], patients undergoing THA were randomly assigned to different doses of intraoperative UFH, compared to a control group receiving saline. The study reported a significant decrease in the overall incidence of DVT ($P < 0.001$). No adverse effects from heparin were noted, and there were no significant differences between groups in postoperative drainage, hematocrit levels, or transfusion requirements. The antithrombotic effect of heparin was observed to last for approximately 30 minutes, and additional boluses before surgery did not provide added benefit. Another RCT investigating coagulation parameters in THA patients found reduced levels of D-dimer and other coagulation markers with intraoperative IV UFH [7]. In a study by Giachino et al. [8] 100 units/kg of UFH were administered to patients, before tourniquet inflation, in patients undergoing TKA. They measured the embolic load in the right atrium of patients and found no differences between the groups in embolic material, interpreted as fat emboli, after the release of the tourniquet. Another prospective study in patients undergoing TKA was a single-arm cohort without any comparator [9], the patients received 1,000 IU of IV UFH before surgery and a second IV bolus of 500 units was given at the end of surgery and right before deflation of the tourniquet. Patients then received enoxaparin, 30 mg subcutaneously, every 12 hours for 6 to 8 days following surgery. The study reported an incidence of DVT at 50% [9]. In another study, Reitman et al. [10] observed a notably low incidence of DVT among patients who received a multimodal approach to DVT prophylaxis, excluding those who have predisposing factors. A total of 1,308 patients undergoing TKA received intraoperative prophylaxis, including 1,000 units of IV UFH before tourniquet inflation, hypotensive epidural anesthesia maintaining mean arterial pressures of 70 to 90 mm Hg, followed by postoperative external pneumatic compression, and 325 mg aspirin twice daily for 6 weeks. The incidence of DVT detected by duplex venous ultrasound was 4%. However, definitive conclusions regarding the effectiveness of intraoperative IV UFH cannot be drawn from this study as multiple modalities were implemented.

Several studies have been published, comparing smaller cohorts with or without intraoperative administration of UFH for patients undergoing THA [11] or TKA [12] or comparing cohorts with historical studies that did not use intraoperative UFH [13]. These studies found no clear difference in the incidence of symptomatic VTE. A retrospective review included two extensive cohorts undergoing THA and TKA, where patients received 1,000 IU of UFH at skin incision, with an additional 500-unit dose intraoperatively [14]. The study found no significant differences in the incidence of fatal pulmonary embolism compared to historical controls. Another retrospective cohort study investigated intraoperative IV UFH in THA patients who had a history of DVT [15]. Patients received 10 units/kg IV UFH intraoperatively, before femoral canal preparation. The study lacked a comparator group and patients received varied postoperative antithrombotic regimens, precluding definitive conclusions from the findings.

In a retrospective cohort study of patients undergoing THA due to femoral neck fracture, the administration of 10 IU/kg of UFH intraoperatively before cementation was compared to no UFH [16]. The study revealed a significant increase in intraoperative bone cement implantation syndrome among patients who received UFH (35 versus 3%) ($P < 0.001$). No association was found between bone cement implantation syndrome and thromboembolic events at 30 days, 90 days, or 1 year postoperatively.

Regarding safety, only one study demonstrated significantly increased bleeding with intraoperative heparin [4]. The study used repeated doses of 500 units of heparin every 30 minutes during surgery, resulting in a higher total heparin dosage than any subsequent regimen in the other studies. Therefore, intraoperative IV UFH may be regarded as safe. Regional anesthesia was utilized in almost all studies involving THA, and epidural anesthesia has been associated with a lower DVT rate than general anesthesia [17,18]. This may have reduced the incidence of VTE and have served as a confounding variable. In addition, hypotensive anesthesia has the added advantage of reducing intraoperative blood loss, serving as another confounding variable in the majority of studies.

CRediT authorship contribution statement

Armita A. Abedi: Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Data curation, Conceptualization. **Ibrahim Tuncay:** Writing – review & editing, Supervision, Methodology, Formal analysis, Conceptualization. **Mohamed M. Adi:** Writing – review & editing, Supervision, Methodology, Formal analysis. **Samih Tarabichi:** Writing – review & editing, Supervision. **Stavros Memtsoudis:** Writing – review & editing, Supervision. **Martin Buttaro:** Writing – review & editing, Supervision. **Javad Parvizi:** Writing – review & editing, Supervision, Methodology, Formal analysis, Data curation, Conceptualization.

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