Unfractionated heparin is the standard anticoagulant used in interventional cardiology. Despite being used for the past 20 years in patients undergoing percutaneous coronary intervention (PCI), there are insufficient data from randomized trials to guide the optimal dose during the procedure. Two large studies have now been published that investigate this issue.

In the first study, published in *JAMA*, the FUTURA/OASIS-8 trial investigators compared two regimens of unfractionated heparin during PCI in patients with acute coronary syndromes treated with the synthetic factor Xa inhibitor fondaparinux. The investigators had shown previously that fondaparinux was noninferior compared with enoxaparin for the primary outcome, but halved rates of bleeding. However, there was an increase in catheter-related thromboses in patients receiving fondaparinux. "We specifically designed the FUTURA/OASIS-8 trial to find the optimal dose of heparin to prevent catheter thrombosis and ischemic events during PCI, without increasing major bleeding in patients treated with fondaparinux," says investigator Sanjit Jolly. Patients ($n=2,026$) were randomly assigned to receive low-dose unfractionated heparin (50 U/kg, regardless of glycoprotein IIb/IIIa blocker use) or standard-dose unfractionated heparin (85 U/kg, or 60 U/kg with glycoprotein IIb/IIIa blocker use). The primary outcome was a composite of per-PCI major bleeding, minor bleeding, or major vascular access site complications up to 48 h after PCI. No significant difference in the primary outcome was observed between low-dose and standard-dose heparin, and catheter thrombosis was rare in both groups; however, there was a trend for reduced efficacy with low-dose heparin, with an increased rate of ischemic complications.

The ISAR-REACT 3A trial was conducted in three German centers to evaluate whether a reduction in the dose of unfractionated heparin from 140 U/kg to 100 U/kg is associated with improved clinical outcomes in patients undergoing PCI. A total of 2,505 'biomarker-negative' patients received a single bolus of 100 U/kg after pretreatment with clopidogrel. The primary end point was the combined incidence of death from any cause, myocardial infarction, urgent target-vessel revascularization within 30 days, or major bleeding. This group of patients was compared with patients in ISAR-REACT 3 who received the higher dose of heparin (140 U/kg). At 30 days, the incidence of the composite end point was reduced in the lower-dose group compared with the patients administered the higher heparin dose (7.3% versus 8.7%, respectively). In addition, the lower heparin dose group was noninferior compared with the patients who received bivalirudin in ISAR-REACT 3.

Any data on heparin dosage is important, and both of these studies move us one step closer to finding the optimal heparin dose for patients undergoing PCI. "The FUTURA/OASIS-8 trial provides randomized trial evidence in support of current PCI guidelines, and should help physicians feel comfortable performing PCI in patients treated with fondaparinux," says Jolly. ISAR-REACT 3A shows that a single bolus of 100 U/kg heparin leads to a reduction in bleeding rates, but not at the expense of an increased risk of thrombotic events.

Helene Myrvang

Original articles The FUTURA/OASIS-8 Trial Group. Low-dose vs standard-dose unfractionated heparin for percutaneous coronary intervention in acute coronary syndromes treated with fondaparinux: the FUTURA/OASIS-8 randomized trial. *JAMA* 304, 1339–1349 (2010) | Schulz, S. *et al.* ISAR-REACT 3A: a study of reduced dose of unfractionated heparin in biomarker negative patients undergoing percutaneous coronary intervention. *Eur. Heart J.* doi:10.1093/eurheartj/ehq330