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Is heparin needed for patients with an intra-aortic balloon pump?

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Abstract

We addressed the question of whether or not the currently available evidence base supports heparinization in the context of a patient requiring cardiovascular support with an intra-aortic balloon pump (IABP). A best evidence topic was written according to a previously defined structured protocol. A literature search returned 443 papers, 3 of which were deemed relevant. Jiang *et al.* randomized 153 patients requiring IABP to heparin or no heparin, matched for age, sex and comorbidities. There was no significant difference in limb ischaemia; however, incidence of bleeding was significantly increased in the heparinized group (14.1 vs 2.4%). One cohort study compared two management strategies of IABP in which patients either received heparin universally or selectively with heparin only given for certain pre-defined indications. They reported increased bleeding with universal heparinization (39.2 vs 31.8%) but similar other complication rates. Another cohort study in which patients with IABP were initially treated with glycoprotein IIb/IIIa antagonists only, reported bleeding and ischaemia rates within accepted ranges for heparinized patients. The use of anticoagulation with IABP is intended to reduce the risk of thrombus, thromboembolus or limb ischaemia whilst generating an increased risk of bleeding as a side-effect. The aforementioned studies demonstrate that omitting or implementing a selective use strategy of heparinization during IABP counterpulsation can significantly decrease the incidence of bleeding without an increase in ischaemic events. One study also performed angiography prior to IABP insertion on some of their patients, selecting the less diseased side to insert the IABP. Current evidence on this topic is sparse, especially as relates to patients in the context of cardiothoracic surgery. Just one study specifically looked at surgical patients. However, the existing data suggest that it is safe to omit heparinization when using IABP counterpulsation. The decision to heparinize should be weighed in the context of other indications or contraindications rather than being an automatic response to the use of IABP.

Keywords: Intra-aortic balloon pump • Anticoagulation • Heparin • Heparinization

INTRODUCTION

A best evidence topic was constructed according to a structured protocol. This protocol is fully described in the *ICVTS* [1].

CLINICAL SCENARIO

Three days following coronary artery bypass grafting on a 70-year old man with a poor left ventricular function, he remains dependent on inotropes and intra-aortic balloon pump (IABP) counterpulsation. He has a previous history of bleeding from peptic ulcer disease and so you are not keen to anticoagulate him. You are unsure how strong the indication to anticoagulate him is in the context of continued IABP counterpulsation and resolve to check the literature.

THREE-PART QUESTION

In [patients who have an intra-aortic balloon pump in-situ] is [heparinization necessary] to [prevent thromboembolic complications]?

SEARCH STRATEGY

Search strategy using MedLine from 1950 to May 2011 using the Ovid Medline interface: (exp Intra-Aortic Balloon Pumping/OR IABP.mp OR counterpulsation.mp OR exp Counterpulsation/OR balloon pump.mp) AND (exp Heparin/or heparin.mp).

SEARCH OUTCOME

Four hundred and forty-three results were found using the reported search on Ovid Medline. From these, three papers were identified that provided the best evidence to answer the question. These are presented in Table 1.

RESULTS

Jiang *et al.* [2] reported the results of a randomized controlled trial of 153 consecutive patients requiring IABP counterpulsation. Of these patients, 50.3% received coronary artery bypass grafting surgery and the rest underwent percutaneous coronary intervention (PCI). Patients were randomized to receive either

Table 1: Best evidence papers

Author, journal, country Study type (level of evidence)	Patient group	Outcomes	Key results	Comments
Jiang *et al.* (2003), J Zhejiang Univ Sci, China Randomized trial (level 2)	153 consecutive patients requiring IABP at a single centre between 2001 and 2004 71 patients receiving anticoagulation with IV heparin with target aPTT 50–70 s vs 82 patients receiving no heparin 49.7% of patients underwent PCI, 50.3% underwent CABG surgery Patient demographics (heparin vs no heparin): • Age 58.7 ± 11.2, 59.6 ± 13.8 years • Male-to-female ratio 52:19, 52:30 • BSA 2 ± 0.3, 2 ± 0.2 m^2 • PVD 18 (25.4%), 24 (29.3%) • DM 43 (62.0%) ± 46 (56.1%) • AMI 36 (50.7%), 32 (39.0%) • PCI 35 (49.3%), 41 (50%) • CABG 36 (50.7%), 41 (50%) • IABPT 46.9 ± 19.4, 45.1 ± 22.4 h	 Limb ischaemia Bleeding IABP thrombus	 No statistical difference in demographics between the groups 4.2, 2.4% (ns) 14.1, 2.4% ($P < 0.05$) 0, 0	All patients catheterized with 8Fr heparin-free IABP catheter Anticoagulation was only checked every 24 h The accuracy of anticoagulation within therapeutic range is not commented on Minor limb ischaemia occurred in both the groups Other indications for anticoagulation were not considered
Cooper *et al.* (2008) Acute Cardiac Care, USA Prospective 'before and after' cohort study (level 3)	252 consecutive patients in a single centre, 2006–2007 102 patients received weight-based dosing of heparin to a target aPTTr 1.5–2.5 from September 2006–March 2007, followed by 150 patients who received heparin selectively only if there was another systemic indication for anticoagulation Of the 'selective' group, 53% had primary indication for anticoagulation (including large anterior MI, unrevascularized ACS, cardiac thrombus, AF, venous thromboembolism, on haemodialysis) and received heparin In total, 182 patients received heparin, and 70 were not heparinized Patient demographics (heparin, no heparin group), no significant difference unless indicated: • Age 62 ± 14, 62 ± 14 years • Female gender 34, 38% • White 59, 55% • BSA 2.0, 2.0 m^2 • Smoking history 32, 24% • Hypertension 57, 66% • DM 24, 18% • End-stage renal failure 4, 9% • CABG 6, 14% ($P = 0.03$) • PCI 19, 25% • Ejection fraction 34, 40% ($P = 0.005$) • Pulmonary artery catheter 48, 47% • Mechanical ventilation 30, 42% • IABPT 45.2 ± 38.8, 38.1 ± 33.3 h			All patients catheterized with either 7.5Fr or 8Fr catheter More patients in the 'selective' group were catheterized with 7.5Fr catheter, reflecting a temporal change in preference by physicians Heparin stopped at the discretion of physician if bleeding Incidence of major bleeding was higher at non-access sites in the universal heparin group than at the access site Universal heparin strategy increases risk of bleeding without reduced risk of ischaemia

Continued

Table 1: Continued

Author, journal, country Study type (level of evidence)	Patient group	Outcomes	Key results	Comments
		Limb ischaemia	0.5%, 0% (ns)	
		Access site bleeding	26.9%, 21.1% (ns)	
		Any bleeding	38.5, 25.4% ($P = 0.049$)	
		Major IABP-related complication	3.3, 5.6% (ns)	
Laish-Farkash *et al.* (2007) Clin Cardiol, Israel Cohort study (level 4)	97 patients with AMI who underwent primary PCI with IABP, treated initially with GP IIb/IIIa antagonist without heparin following initial heparin bolus. Once GP IIb/IIIa antagonist stopped, heparin titrated to aPTT 50–70 s GP IIb/IIIa antagonist used: eptifibatide (89.7%), tirofiban (6.2%), abciximab (4.1%) Patient demographics • Age 20–91 years (mean 63) • Male gender 79% • Previous MI 29% • Previous CVA 2% • Previous CABG 4% • Smoking 50 (51.5%) • Hyperlipidemia 4 (46.4%) • Hypertension 44 (45.4%) • DM 32 (33%) • Family history of heart disease 22 (22.7%) • IABPT≤ 48 h for 97% of patients			All patients were catheterized with 8Fr heparin-free IABP catheter Heparin bolus was given at PCI and restarted after GP IIb/IIIa antagonist stopped Incidence of ischaemic events resembles published numbers in existing literature for IABP with heparin There was considerable variation in length of GP IIb/IIIa antagonist treatment (not standardized across all patients) Mainly used agents other than AHA recommended (abciximab) due to non-availability in Israel
		Major bleeding	9.27%	
		Minor bleeding	15.50%	
		Limb ischaemia	2%	
Lazar *et al.* (1999) Ann Thoracic Surg, USA Randomized trial (animal trial)	25 pigs randomized to receive either heparin and IABP (Group A, $n = 5$), no heparin and IABP (Group B, $n = 10$), or no heparin and heparin-bonded IABP (Group C, $n = 10$)	Thrombus formation at IABP or insertion site (thrombus score from 0 (no thrombus) to 3 (thrombus >5 cm), mean ± SD) • Group A • Group B • Group C Thrombus formation in distal femoral artery • Group A • Group B • Group C	 0 1.55 ± 0.29 0 0 2.23 ± 0.23 0	Target ACT in heparinized group >200 s. Average ACT in nonheparinized groups 128 s (normal IABP), 125 s (heparin-bonded IABP group)

ACS: acute coronary syndrome; BSA: body surface area; PVD: peripheral vascular disease; DM: diabetes mellitus; AMI: acute myocardial infarction; PCI: percutaneous coronary intervention; CABG: coronary artery bypass grafting; IABPT: IABP treatment time.

intravenous heparin to an aPTT target of 50–70 s or no anticoagulation at all whilst on IABP. Patient groups were well matched in preceeding the procedure, demographics and comorbidities with no significant differences between the two. There was a significantly higher incidence of bleeding in the heparinized vs non-heparinized group, 14.1 vs 2.4% ($P < 0.05$), but no difference in incidence of limb ischaemia, with minor ischaemic complications, occurring in both groups, 4.2 vs 2.4% (*P*, not significant). No major ischaemic events occurred. Blood results (platelet count, d-dimer, plasminogen activator inhibitor-1 and fibrin degradation products concentrations) were also compared between the groups with no significant difference at IABP commencement, 24 or 48 h of continued therapy, or 24 h post-discontinuation of IABP. No macroscopic thrombus was seen on the catheter after the removal. The time of IABP support was not significantly different between the groups: 46.9 ± 19.4 h vs 45.1 ± 22.4 h. It is worth noting that 56 patients also underwent angiography of iliac and femoral vessels prior to catheterization of the less diseased side, which may help reduce the risk of limb ischaemia.

Cooper *et al.* [3] reported a 'before and after' cohort study in which they compared two different management strategies of anticoagulation in patients with IABP for 252 consecutive patients. The first 102 patients in the 'universal heparin' group all received heparin. The following 150 consecutive patients were managed with a selective strategy and given heparin only if indicated by an underlying condition (including unresolved acute coronary syndrome, anterior myocardial infarction, intracardiac thrombus, mechanical prosthetic heart valve and atrial fibrillation). Of this 'selective' group, 47% did not meet indication criteria for heparin and were not anticoagulated. There was a greater incidence of bleeding in the universal group, 39.2 vs 31.8% ($P = 0.049$), but no significant difference in ischaemic events, 1.0 vs 0%, or overall major IABP-related complications (major ischaemia, major bleeding or balloon leak), 2.9 vs 4.6%. A single major ischaemic event occurred in a patient in the 'universal heparin' strategy group. There was no difference in the length of stay in CCU, the total length of stay or in-hospital mortality rates. Groups were also well matched for demographics and comorbidities, except that there was lower incidence of hypertension in the universal group, 51 vs 65% ($P = 0.02$). There was no difference between groups in terms of the use of aspirin, clopidogrel or glycoprotein IIb/IIIa inhibitors. The mean duration of IABP support was similar in both groups with a mean of 43 ± 37 h. *Post hoc* analysis of those patients who received heparin (regardless of allotted group) against those who did not revealed any significant difference in major or minor limb ischaemia. However, major non-access-site bleeding was significantly more common among patients who received heparin than among those who did not (8.2 vs 1.4%, $P = 0.047$).

Laish-Farkash *et al.* [4] reported data from a cohort study of 97 patients following PCI with IABP *in situ*. Patients were treated with only a glycoprotein (GP) IIb/IIIa antagonist following a single heparin bolus at the start of PCI. Patients were only further heparinized if IABP was still required after the GP antagonist was discontinued (after 12–24 h for most patients, with the length of treatment determined by the hospital protocol). Minor bleeding (9.3%), major bleeding (15.5%), in-hospital mortality (13.4%) and limb ischaemia (2%) incidence were within the range of other published results for IABP with heparinization, suggesting no increase in ischaemic events or other complications with omission of heparin. Interpretation of these results is complicated by a wide variation in administration times of GP antagonists that were not standardized across the cohort. Following initial heparin bolus, some patients received a single bolus of GP antagonist before being recommenced on heparin, in which case the time 'off heparin' is likely to have been minimal, whereas others received GP antagonists for up to 48 h, without heparin.

Lazar *et al.* [5] conducted a trial in which 25 pigs were randomized to receive either IABP with heparinization, without heparinisztion, or a heparin-coated IABP without heparinization. After 9 h of counterpulsation, the pigs were sacrificed and the balloon catheters were analysed. There was no thrombus detected in either the heparinized group or the heparin-coated IABP group; however, thrombus was detected in the non-heparinized group at the insertion site, on the catheter itself, as well as in the distal femoral artery.

CLINICAL BOTTOM LINE

The use of heparinization with IABP is intended to reduce the risk of thrombus, thromboembolus or limb ischaemia whilst generating an increased risk of bleeding as a side-effect. The studies considered demonstrated that omitting or implementing a selective use strategy of heparinization during IABP counterpulsation can significantly decrease the incidence of bleeding without an increase in limb ischaemic events. The decision to heparinize should be weighed in the context of other indications or contraindications rather than being an automatic response to the use of IABP counterpulsation.

Conflict of interest: none declared.

BEST EVIDENCE TOPIC

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eComment. Sheathless intra-aortic balloon pump insertion

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We read with great interest the article by Pucher et al. regarding the systematic use of heparinization in patients requiring the insertion of an intra-aortic balloon pump (IABP) [1]. The authors reviewed a vast number of published articles and concluded that the decision-making process concerning the use of heparin in patients with IABP conterpulsation should be weighed in the setting of other indications or contraindications rather than being an automatic response.