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Bivalirudin versus unfractionated heparin for percutaneous coronary intervention with radial access: A meta-analysis of randomized trials

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ABSTRACT

Background: Radial access for percutaneous coronary intervention (PCI) has been shown to be associated with better outcomes compared with femoral access. However, it is unknown whether bivalirudin would offer any further benefit when compared with unfractionated heparin for PCI with radial access.
Methods: A systematic search of electronic databases was conducted for randomized trials comparing bivalirudin with unfractionated heparin in patients undergoing PCI with a radial access. The primary safety outcome was major bleeding, while the primary efficacy outcome was major adverse cardiac events (MACE). Random effects overall risk ratios (RR) were calculated using DerSimonian and Laird model.
Results: A total of 8044 patients from 5 trials were included in the final analysis. The incidence of major bleeding was 1.8% in the bivalirudin group versus 2.2% in the unfractionated heparin group (RR 0.72, 95% CI 0.44–1.17, p = 0.18). Meta-regression analysis demonstrated that the risk of major bleeding was lower with bivalirudin when higher doses of unfractionated heparin were used in the control arm (p = 0.02). The incidence of MACE was 8.5% in the bivalirudin group versus 7.5% in the unfractionated heparin group (RR 1.15, 95% CI 0.81–1.64, p = 0.44). There were no significant differences in the incidence of all-cause mortality, and net adverse clinical events between both groups (RR 0.98, 95% CI 0.70–1.36, p = 0.89; and RR 0.79, 95% C I0.60–1.03, p = 0.08, respectively).
Conclusions: Bivalirudin might not be associated with better outcomes, when compared with unfractionated heparin in patients undergoing PCI with radial access.

1. Introduction

The benefit of bivalirudin compared with unfractionated heparin for percutaneous coronary interventions (PCI) has been a matter of ongoing debate [1]. Although bivalirudin has been shown by multiple trials to be associated with a reduction in the risk of major bleeding and net adverse clinical events (NACE) [2,3], this relative benefit was driven by the high dose of unfractionated heparin, and planned used of glycoprotein IIb/IIIa inhibitors in the unfractionated heparin arm in these trials [4].

Recently, multiple trials have demonstrated that radial access for PCI was associated with a reduction in the risk of major bleeding, and potential mortality benefit compared with femoral access [5]. The largest trial to date comparing radial with femoral access for PCI showed a reduction in the risk of NACE, that was driven mainly by the reduction in the risk of major bleeding [6]. However, it remains unknown whether bivalirudin might add any benefit compared with unfractionated heparin in subjects undergoing PCI with radial access. Therefore, we aimed to conduct a meta-analysis of randomized trials, comparing bivalirudin with unfractionated heparin in patients undergoing PCI with radial access.

2. Materials and methods

2.1. Data sources

A computerized search of the MEDLINE, Web of Science, and Central databases was conducted from inception until April 2016 for randomized clinical trials comparing bivalirudin with unfractionated heparin, with planned or bailout glycoprotein IIb/IIIa inhibitors use. The following keywords were utilized for this search: “bivalirudin”, “hirulog”,

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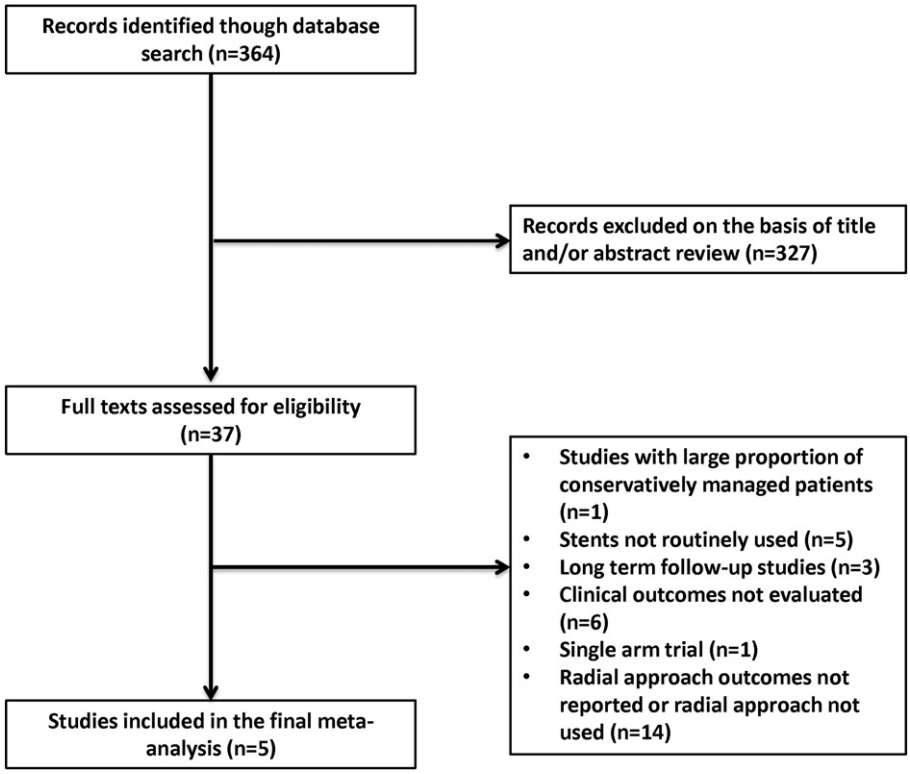

Fig. 1. Selection strategy for the included trials.

"angiomax", "heparin", "bleeding", "percutaneous coronary intervention", and "mortality" (Fig. 1).

2.2. Selection criteria

Trials were included if ≥80% of the patient population underwent PCI with radial access or if the published trial report performed a subgroup analysis for the outcomes for radial access. Outcomes from the reported radial subgroup were preferentially used whenever reported. For those trials in which ≥80% of the patients under PCI with radial access, the overall events were used.

2.3. Outcomes and definitions

The primary safety end point was major bleeding, while the primary efficacy outcome was major adverse cardiac events (MACE) as defined per the individual studies. Secondary outcomes included all-cause mortality and NACE.

2.4. Data extraction

Both authors extracted the data on study design, patients' characteristics, interventions strategies, and outcomes events, independently. Any discrepancies were resolved by consensus among the authors.

Table 1
Characteristics of the included studies.

Study	Year	Total population[a]	Indication	UFH dose, units/kg	GPIIb/IIIa use in the UFH arm	Primary outcome	Definition of MACE
MATRIX [12]	2015	3597	NSTEMI/STEMI	100	Planned or provisional	MACE, NACE	Death, MI or stroke
BRIGHT [13]	2014	1523	NSTEMI/STEMI	100	Planned or provisional	NACE	All-cause mortality, MI, ischemia-driven TVR, or stroke
ACRIPAB [14]	2014	100	NSTEMI/stable angina	60	Provisional	Major, minor bleeding	Cardiac mortality, TVR, ST or Post PCI ischemic events
HEAT-PPCI [15]	2014	1812	STEMI	70	Provisional	MACE, major bleeding	All-cause mortality, stroke, MI or TVR
EUROMAX [16]	2013	1012	STEMI	100	Planned or provisional	All-cause mortality, major bleeding	All-cause mortality, stroke, MI or TVR

GPIIb/IIIa = glycoprotein IIb/IIIa inhibitors.
MACE = major adverse cardiac events.
NACE = net adverse cardiac events.
NSTEMI = non-ST elevation myocardial infarction.
PCI = percutaneous coronary intervention.
STEMI = ST-elevation myocardial infarction.
TVR = target vessel revascularization.
[a] Numbers are of the patients who underwent PCI via a radial approach only except for ACRIPAB and HEAT-PPCI, which represent the total patient population. Data are formatted as bivalirudin arm/unfractionated heparin arm.