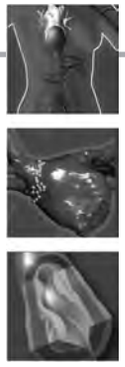

Bleeding avoidance strategies among patients undergoing percutaneous coronary intervention

Evaluation of: Marso SP, Amin AP, House JA *et al.*: Association between use of bleeding avoidance strategies and risk of periprocedural bleeding among patients undergoing percutaneous coronary intervention. *JAMA* 303(21), 2156–2164 (2010). Major bleeding during percutaneous coronary intervention (PCI) is associated with an adverse outcome. While a number of models exist to identify patients at risk of bleeding during PCI, it is not known whether targeted bleeding avoidance strategies lead to a reduction in major bleeding rates in these patient groups. This study aimed to address this knowledge gap and examined the use of two bleeding avoidance strategies: vascular closure devices and bivalirudin. Periprocedural major bleeding rates were obtained from a very large national registry of 1,522,935 patients undergoing procedures at 955 US centers. Bleeding occurred in 2% of patients. Use of one or more of these strategies resulted in reduced bleeding rates in both high- and low-risk cohorts. When both strategies were used together, the rates of bleeding were especially low. Importantly, those at highest preprocedural risk were least likely to receive either therapy. There are substantial and accumulating data from randomized studies and real-world registries regarding the adverse effects and prognostic importance of periprocedural bleeding in patients undergoing PCI. The study makes a powerful case for preprocedural risk stratification of patients undergoing PCI and for the utilization of specific and widely available bleeding avoidance strategies to reduce these effects.

KEYWORDS: ACS ▪ acute coronary syndrome ▪ bleeding ▪ mortality ▪ PCI ▪ percutaneous coronary intervention ▪ vascular access

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This paper reviews the recent study by Marso *et al.*, demonstrating that in a large national percutaneous coronary intervention (PCI) registry, the use of vascular closure devices (VCDs) and bivalirudin were associated with significantly lower bleeding rates, particularly if applied among patients considered to be at greatest risk of bleeding following PCI [1]. Bleeding is the most common noncardiac complication in patients undergoing PCI, and major bleeding independently predicts both increased in-hospital and 1-year mortality, with the predominant source being access-site related [2–11]. Adjuvant antithrombotic and antiplatelet drugs used during PCI are effective in preventing recurrent ischemia in patients with acute coronary syndromes (ACS), but are also associated with a higher bleeding risk [12]. A reduction in the incidence of ischemia following PCI has been achieved at the expense of major bleeding complications [13,14]. Elderly female patients and those undergoing emergent procedures and receiving intense antithrombotic regimens are at a higher risk of major bleeding [13]. In these subgroups, the risk of major bleeding can reach up to 5%, potentially negating any benefit that PCI might offer in this subgroup [14,15]. This study utilizes a clinical risk model to calculate periprocedural bleeding risk (previously developed and validated using the American College of Cardiology National Cardiovascular Data Registry [NCDR] CathPCI Registry®) [16].

Study design, setting & patients

The investigators retrospectively analyzed nationally representative PCI data (NCDR CathPCI Registry) from over 1,522,000 patients at 955 US centers undergoing PCI over a 4-year period [1].

Exclusion criteria included a nonfemoral access site (radial or brachial), undergoing more than one PCI procedure during the same hospital episode, patients with incomplete data or missing information on bleeding.

Bleeding avoidance strategies consisted of VCD alone, bivalirudin alone or VCD plus bivalirudin. Patients who received manual compression hemostasis served as the reference group. Periprocedural bleeding (requiring blood transfusion or >3 g hemoglobin loss) was the main outcome measure.

Results

Of the 1,759,408 patients who underwent PCI in the study period, 236,473 were excluded. Overall bleeding occurred in 2% of patients.

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Bleeding was reported in 2.8% of patients who received manual compression, compared with 2.1% with VCD only, 1.6% with bivalirudin only and 0.9% receiving both strategies ($p < 0.001$). The observed bleeding rates in low-, intermediate- and high-risk groups were 0.72, 1.73 and 4.69%, respectively. In high-risk patients, manual compression resulted in an observed bleeding rate of 6.1%. With VCD alone, this was 4.6%, and with bivalirudin alone it was 3.8%. Use of both strategies resulted in a much lower rate of 2.8% ($p < 0.001$).

In this registry, the use of VCD and bivalirudin were associated with significantly lower bleeding rates, particularly in the high-risk population who were least likely to receive both strategies when compared with the low-risk group (14.4 vs 21%, respectively; $p < 0.001$).

Significance

Periprocedural bleeding remains the most common noncardiac complication of PCI, and independently predicts short- and long-term mortality. A meta-analysis of data from several large studies indicates a fivefold increase in the risk of death in patients with ACS who experience major bleeding [2,12,17].

The current study highlights the importance of applying clinically validated risk models to identify the risk of peri-PCI bleeding, and of adopting necessary bleeding avoidance strategies. It also suggests that clinical outcomes may be improved in patients where a targeted bleeding avoidance strategy is utilized. There are important caveats to the study, many of which are acknowledged by the authors. Although large, this is an observational study and can only be regarded as hypothesis-generating. Importantly, the use of adjunctive pharmacology, particularly GpIIb/IIIa inhibitors (GPIs), is not stated in the manuscript, despite this being a major driver of periprocedural bleeding. Potential confounders include local practice and differences in case mix between centers. Finally, although not recorded, the periprocedural use of other antithrombotics such as fondaparinux may also have had an effect on bleeding [8,18].

Adverse outcomes observed following periprocedural bleeding may also be related to transfusion itself. Important transfusion-related pathophysiological effects may explain the adverse effects [7,19], and recent data have demonstrated that red cells stored for prolonged periods have a direct effect on short- and long-term outcome [20].

Future perspective

■ Other strategies to reduce periprocedural bleeding

Periprocedural bleeding following PCI can be broadly categorized into access-site and non-access-site bleeding. A number of patient- and procedure-related factors may increase the risk of bleeding. Broadly speaking, the main target areas for the avoidance of bleeding are vascular access and the use of adjunctive pharmacotherapy.

Vascular access: is there an advantage to trans-radial over femoral access?

More than two-thirds of bleeding occurrences are often attributed to femoral access site complications [5,10,21]. Randomized trials and registries have demonstrated that trans-radial PCI is associated with a lower risk of bleeding and need for blood transfusion when compared with femoral access, translating into a mortality benefit [11,22]. In this era of stringent antithrombotic and anticoagulant use, trans-radial access offers a major advantage by virtually eliminating access-site-related complications and reducing periprocedural bleeding. However, this is a more technically demanding procedure with a significant learning curve, which probably underlies its comparatively limited use.

Adjunctive pharmacotherapy

Antithrombotic and anticoagulant pharmacotherapy regiments have constantly been refined in order to decrease bleeding risk. Strategies that maintain the benefits of currently available antithrombotic therapies but result in less bleeding, are of distinct clinical relevance. Unfractionated when compared with low-molecular-weight heparin reduces nonfatal outcomes in ACS with or without ST-segment elevation, but increases major bleeding [23,24]. Therefore, newer agents are required that are safer and work effectively across the whole spectrum of patients undergoing PCI [8,21].

Fondaparinux – a factor Xa inhibitor – reduces the risk of ischemic events in patients with ACS (non-ST-segment elevation myocardial infarction [STEMI]) undergoing PCI, and also substantially reduces major bleeding, leading to a reduction in mortality at 30 days [8].

Bivalirudin – a direct thrombin inhibitor – has been demonstrated to reduce both major and minor bleeding compared with GPIs, with similar efficacy following PCI in both elective and acute settings [9,25]. Elderly patients undergoing PCI following ACS exhibit significantly fewer bleeding complications when assigned to bivalirudin instead of a heparin plus GPI strategy [26].

In patients undergoing primary PCI for STEMI, assignment to bivalirudin as compared with heparin plus GPI resulted in significantly lower rates of major bleeding at 30 days and a mortality advantage at 1 year [27,28].

Vascular closure

Several VCDs have been developed over the last decade or so and have been variably used around the world. Despite their popularity and ease of use, their use has not generally been associated with a reduction in femoral access-site complications and a number of studies have shown an increase in complications [29,30]. This study by Marso conversely suggests that their use may be associated with a reduction in bleeding in higher risk groups, an observation that certainly merits further study.

Financial & competing interests disclosure

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

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Executive summary

Background

- Bleeding remains the most common noncardiac periprocedural complication during percutaneous coronary intervention (PCI). Major bleeding is an independent predictor of short- and long-term mortality.

Methodology

- A retrospective observational study of nationally representative PCI population data from over 1,522,000 patients undergoing PCI procedures via femoral access, carried out in all 955 US centers over 4 years.

Results

- Periprocedural bleeding occurred in 2% of the cases. The use of bivalirudin with a vascular closure device was associated with a 3.8% absolute reduction in PCI-related bleeding in high-risk patients, who were paradoxically the least likely to receive both strategies.

Future perspective

- New antithrombin agents combined with radial access for PCI potentially offer an optimal strategy to significantly reduce bleeding following PCI.

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