TITLE: Procedure Site Bleeding Complications Following Percutaneous Coronary Interventions or Angioplasty: A Review of Clinical Evidence and Guidelines

DATE: 04 April 2012

CONTEXT AND POLICY ISSUES

Percutaneous coronary intervention (PCI) or angioplasty is a procedure to treat stenotic (narrowed) coronary arteries. To minimize the risk of thrombotic complications during and shortly after the procedure, patients receive antithrombotic agents. However, antithrombotic agents may increase the risk of bleeding. Peri-procedural bleeding is the most common non-cardiac complication of PCI and is associated with short- and long-term risk of mortality, other ischemic events, prolonged in-hospital stay and higher costs of care.\textsuperscript{1,2} In patients undergoing PCI, approximately half of the bleeding events occur at the arterial access site.\textsuperscript{3} In deciding on the appropriate antithrombotic regimen for patients undergoing PCI, both protection from thrombotic complications and avoidance of peri-procedural bleeding need to be considered.

This review was undertaken to investigate the incidence of procedure site bleeding with pre- or post-operative exposure to antithrombotic agents, specifically clopidogrel, aspirin, tenecteplase, bivalirudin, or heparin, in comparison with no pre- or post-operative exposure to these agents and to examine management strategies for procedure site bleeding complications following PCI.

RESEARCH QUESTIONS

1. What is the clinical evidence regarding the association between pre or post-operative exposure to clopidogrel, aspirin, tenecteplase, bivalirudin, or heparin and procedure site bleeding complications following percutaneous coronary intervention or angioplasty?

2. What are the evidence-based guidelines regarding the management of procedure site bleeding complications following percutaneous coronary intervention or angioplasty?

KEY MESSAGE

One study showed that the incidence of groin bleeding was significantly higher in the patients receiving prolonged post-procedural heparin compared with the patients not receiving post-procedural heparin following PCI. No relevant PCI studies on aspirin, clopidogrel, tenecteplase

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or bivalirudin and no relevant evidence-based guidelines regarding the management of procedure site bleeding complications following PCI were identified.

METHODS:

Literature Search Strategy

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2012, Issue 2), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. To address question 1, methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, randomized controlled trials and non-randomized studies. To address question 2, methodological filters were applied to limit retrieval to guidelines. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2007 and March 7, 2012.

Selection Criteria and Methods

Two reviewers screened articles retrieved from the literature search and selected potentially relevant articles for full-text review based on titles and abstracts. One reviewer selected relevant articles according to the selection criteria in Table 1.

Table 1: Selection Criteria

<table>
<thead>
<tr>
<th>Population</th>
<th>Adult in-patients immediately following percutaneous coronary intervention (PCI) or angioplasty</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
<td>PCI or angioplasty with aspirin, clopidogrel, tenecteplase, bivalirudin, or heparin pre or post-operatively</td>
</tr>
<tr>
<td>Comparator</td>
<td>PCI or angioplasty without pre- or post-operative aspirin, clopidogrel, tenecteplase, bivalirudin, or heparin</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Incidence of procedure site bleeding</td>
</tr>
<tr>
<td>Study Designs</td>
<td>Health technology assessments, systematic reviews and meta-analyses, randomized controlled trials (RCTs), non-randomized studies and evidence-based guidelines</td>
</tr>
</tbody>
</table>

Exclusion Criteria

Studies were excluded if they did not satisfy the selection criteria in Table 1; if they were published prior to 2007, duplicate publications of the same study, or included in a selected health technology assessment or systematic review.
Critical Appraisal of Individual Studies

The quality assessment of the included RCT was based on the Downs and Black checklist. This checklist includes items that determine the quality of studies with respect to study design, potential for biases, and generalizability of findings.

SUMMARY OF EVIDENCE:

Quantity of Research Available

The literature search yielded 662 citations. Upon screening titles and abstracts, 613 articles were excluded and 49 potentially relevant articles were selected for full-text review. Two potentially relevant articles were identified from the grey literature. Of these 51 articles, 50 did not satisfy the inclusion criteria and were excluded. One relevant RCT5 was selected for inclusion. No relevant health technology assessments, systematic reviews, non-randomized studies or evidence-based guidelines were identified. Details of the study selection process are outlined in Appendix 1.

Summary of Study Characteristics

In the RCT5, all patients received aspirin [80 mg/d] and clopidogrel 300-mg bolus before PCI and continued physician prescribed treatment. They also received intra-procedural heparin bolus of 10,000 units. One group received prolonged post procedural heparin and the control group did not. The two groups were comparable with respect to age, gender, dyslipidemia, smoking, opium addiction, family history of cardiovascular heart disease (CHD) prevalence of prior myocardial infarction (MI) or PCI. The prevalence of diabetes and hypertension, however, was significantly higher in the control group compared with the heparin group [P=0.015 and 0.02, respectively (95% confidence interval not reported)]. PCI was performed using the femoral access route. The study characteristics are summarized in Table 2.

Table 2. Study Characteristics

<table>
<thead>
<tr>
<th>First Author, Publication Year, Country</th>
<th>Study Design, Length of Follow-up</th>
<th>Patient Characteristics, Sample Size (N)</th>
<th>Intervention</th>
<th>Comparator</th>
<th>Clinical Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zibaenezhad, 2009, Iran</td>
<td>Randomized, not blinded; follow-up: in-hospital (length of stay not reported)</td>
<td>Patients undergoing PCI; N= 200 Prolonged heparin: N= 100, Age (mean ± SD)= 60.1 ± 11.5 year, F= 52% Control - no post-procedural heparin: N= 100, Age (mean ± SD)= 61.8 ± 10.3 year F= 59%</td>
<td>Prolonged heparin infusion of 10,000 units/h for 12h</td>
<td>No post-procedural heparin</td>
<td>Primary: in-hospital bleeding and vascular events. Secondary: in-hospital ischemic complications</td>
</tr>
</tbody>
</table>

F= female, h= hour, N= number of patients, PCI= percutaneous coronary intervention, SD= standard deviation,
Summary of Critical Appraisal

The study objective and description of the patient characteristics and interventions were explicit. As well, the study appeared to be unblinded and, hence, has the potential of introducing performance and detection biases. The two groups were well matched for most characteristics, except for prevalence of diabetes and hypertension, which could potentially confound the study results. In addition, the power calculation was not mentioned. The single centre study was performed in one country, so the results may not be generalizable.

Summary of Findings

The findings of interest for this review are summarized in Table 3.

Table 3. Summary of Study Findings

<table>
<thead>
<tr>
<th>First Author, Publication Year, Country</th>
<th>Main Study Findings</th>
<th>Authors’ Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zibaenezhad, 2009, Iran</td>
<td>The incidence of groin bleeding was significantly higher in the intervention group (patients receiving prolonged post-procedural heparin) compared with the control group (patients receiving no post-procedural heparin) (20% versus 4%, P&lt;0.001). There was no significant difference in minor vascular events in the intervention group compared with the control group (4% versus 1%, P=0.36). Minor vascular event was defined as a femoral hematoma &gt;6cm, not requiring blood transfusion or vascular repair.</td>
<td>“Heparin infusion after successful PCI could increase the occurrence of bleeding and vascular injury, however, omission of heparin after a successful procedure did not significantly increase incidence of ischemic complications. Thus routine post-procedural heparin is not recommended.” p.69</td>
</tr>
</tbody>
</table>

PCI= percutaneous coronary intervention

Limitations

No relevant studies that compared pre- or post- procedural treatment with aspirin, clopidogrel, tenecteplase or bivalirudin with pre or post- procedural treatment without these drugs, were identified. One relevant RCT which compared post-procedural heparin with no post-procedural heparin was identified. The study results may have been impacted by the fact that the study was not blinded, and the control group had a higher number of patients with hypertension and diabetes. This study was not conducted in Canada. Hence, the applicability of the findings to the Canadian setting is uncertain.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING:

In conclusion, following PCI the incidence of groin bleeding was significantly higher in the patients receiving prolonged post-procedural heparin compared with the patients not receiving post-procedural heparin. These results, however, should be interpreted with caution as the evidence was derived from one single centre RCT. Since the study was not conducted in Canada, the results may not be generalizable to the Canadian health care setting.
REFERENCES


APPENDIX 1: Selection of Included Studies

662 citations identified from electronic literature search and screened

613 citations excluded

49 potentially relevant articles retrieved for scrutiny (full text, if available)

2 potentially relevant reports retrieved from other sources (grey literature)

51 potentially relevant reports

50 reports excluded:
- irrelevant comparator (18)
- irrelevant outcomes (24)
- other (review articles, editorials) (8)

1 report included in review