Clinical Lessons from BMC2-PCI

The Blue Cross Blue Shield of Michigan Cardiovascular Consortium

Hitinder Gurm, M.D.
University of Michigan
Overview

- 32 papers since inception
- 10 papers published this year
- Our mission
  - Improve quality
  - Advance science
Topics for Today

• Anticoagulation
  – Aspirin - old but not usually forgotten
  – Bivalirudin and renal dysfunction
  – Dosing of Eptifibatide
  – Predicting transfusion and some clinical lessons
Aspirin Non-Use Prior to Percutaneous Coronary Intervention: Prevalence and Implications

Mohamad Kenaan, Milan Seth, Herbert D. Aronow, David Wohns, et al for BMC2
Background

• ASA is cornerstone of procedural and post-procedural PCI therapy.

• Antiplatelet and anti-inflammatory.

• Well tolerated, inexpensive and safe therapy.
Objective

- To examine frequency and implications of pre-procedural aspirin non-use.
- Pre-procedure ASA defined as receiving aspirin within 24 hours prior to procedure.
- Population
  - 65,175 PCI’s performed between 01/2010 and 12/2011 at 44 institutions.
Results

- 4,640 (7.1%) did not receive ASA.
- 495 (10.7%) with documented contraindication.
Unadjusted Outcomes

<table>
<thead>
<tr>
<th>In-Hospital Outcome</th>
<th>ASA non-receivers</th>
<th>ASA receivers</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>3.9%</td>
<td>1.2%</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Transfusion</td>
<td>5.3%</td>
<td>3.3%</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Post-procedure Myocardial Infarction</td>
<td>0.7%</td>
<td>0.5%</td>
<td>0.18</td>
</tr>
<tr>
<td>Coronary artery bypass grafting (CABG)</td>
<td>1.5%</td>
<td>0.9%</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Emergent CABG</td>
<td>0.2%</td>
<td>0.2%</td>
<td>1.00</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.5%</td>
<td>0.2%</td>
<td>0.02</td>
</tr>
<tr>
<td>Repeat PCI to the same lesion</td>
<td>0.5%</td>
<td>0.6%</td>
<td>0.41</td>
</tr>
<tr>
<td>Vascular Complications</td>
<td>3.4%</td>
<td>2.9%</td>
<td>0.06</td>
</tr>
<tr>
<td>Contrast Induced Nephropathy (CIN)</td>
<td>4.0%</td>
<td>2.5%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Nephropathy Requiring Dialysis</td>
<td>0.5%</td>
<td>0.2%</td>
<td>0.005</td>
</tr>
</tbody>
</table>
Adjusted Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>No ASA Incidence</th>
<th>ASA Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>1.89 (1.32, 2.71)</td>
<td>3.87% 2.79%</td>
</tr>
<tr>
<td>Transfusion</td>
<td>1.08 (0.84, 1.39)</td>
<td>5.71% 5.54%</td>
</tr>
<tr>
<td>Nephropathy requiring dialysis</td>
<td>0.79 (0.38, 1.64)</td>
<td>0.47% 0.60%</td>
</tr>
<tr>
<td>CABG</td>
<td>1.52 (0.97, 2.40)</td>
<td>1.65% 1.00%</td>
</tr>
<tr>
<td>Contrast induced nephropathy</td>
<td>1.17 (0.89, 1.54)</td>
<td>4.37% 4.14%</td>
</tr>
<tr>
<td>Vascular complication</td>
<td>0.89 (0.68, 1.17)</td>
<td>3.47% 4.07%</td>
</tr>
<tr>
<td>Stroke/CVA</td>
<td>4.24 (1.49, 12.11)</td>
<td>0.52% 0.15%</td>
</tr>
<tr>
<td>Repeat PCI (same lesion)</td>
<td>1.13 (0.55, 2.34)</td>
<td>0.50% 0.47%</td>
</tr>
<tr>
<td>Emergent CABG</td>
<td>0.94 (0.26, 3.43)</td>
<td>0.20% 0.20%</td>
</tr>
<tr>
<td>Post procedural MI</td>
<td>1.54 (0.77, 3.05)</td>
<td>0.70% 0.50%</td>
</tr>
</tbody>
</table>

<< favors No ASA >> favors ASA
*Adjusted analysis was not performed for the stable angina population due to an exceedingly low event rate.
Despite ACC/AHA and ESC class I recommendations, a significant number of patients do not receive ASA prior to PCI.

- Aspirin non-use is associated with higher in-hospital all-cause mortality and stroke.
- Our study results should motivate quality efforts focused on optimizing ASA use prior to PCI.
The Impact of Worsening Renal Dysfunction on the Comparative Efficacy of Bivalirudin and Platelet Glycoprotein IIbIIIa Inhibitors: Insights from the Blue Cross Blue Shield of Michigan Cardiovascular Consortium (BMC2)

Emily Perdoncin MD, Min Zhang PhD, Arthur Riba MD, Thomas Lalonde MD, Cindy Grines MD, Hitinder Gurm MD

ACC 2013
Renal insufficiency is highly prevalent among patients with coronary artery disease (CAD).

Patients with CKD and CAD are known to have reduced survival and increased incidence of bleeding complications following PCI.

Despite their increased risk, patients with more severe degrees of renal dysfunction are often excluded or underrepresented in clinical trials.
• Several RCTs and observational studies have demonstrated that the use of bivalirudin is non-inferior to heparin plus GPI, with the added benefit of significant reduction in the incidence of bleeding.

• Post hoc analyses suggest that the benefits of bivalirudin are preserved in patients with CKD, but have excluded patients with more advanced CKD (stage III-IV).
Objective

• What is the impact of worsening renal function on the comparative bleeding risk associated with use of bivalirudin versus GPI?
Study Population

- 64,052 consecutive patients undergoing PCI from 2007 to 2009 at 33 hospitals participating in the BMC2.

- 32,880 patients had some amount of renal dysfunction broken down as follows:
  - 19,618 with stage II CKD (GFR 60-89)
  - 12,087 with stage III CKD (GFR 30-59)
  - 1,092 with stage IV CKD (GFR 15-29)

- **Exclusion criteria**: dialysis prior to undergoing PCI, PCI for cardiogenic shock or cardiac arrest, fibrinolytic therapy, death in the cath lab.
## Results

<table>
<thead>
<tr>
<th></th>
<th>Unadjusted Outcome</th>
<th>Propensity – Matched Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Heparin + GPI</td>
<td>Bivalirudin</td>
</tr>
<tr>
<td>Transfusion</td>
<td>5.1%</td>
<td>2.3%</td>
</tr>
<tr>
<td>GI bleed</td>
<td>1.5%</td>
<td>0.4%</td>
</tr>
<tr>
<td>Vascular complications</td>
<td>2.7%</td>
<td>1.0%</td>
</tr>
<tr>
<td>Subacute stent thrombosis</td>
<td>0.3%</td>
<td>0.2%</td>
</tr>
<tr>
<td>CABG</td>
<td>1.1%</td>
<td>0.2%</td>
</tr>
<tr>
<td>Stroke and TIA</td>
<td>0.4%</td>
<td>0.2%</td>
</tr>
<tr>
<td>Death</td>
<td>0.7%</td>
<td>0.3%</td>
</tr>
<tr>
<td>Nephropathy requiring dialysis</td>
<td>0.3%</td>
<td>0.1%</td>
</tr>
</tbody>
</table>
Odds of GI Bleeding by CKD Stage.

- GFR (mL/min/1.73m²):
  - >90: Event Rate 0.2 vs. 0.5, p=0.0027
  - 60-89: Event Rate 0.5 vs. 1.2, p=0.0003
  - 30-59: Event Rate 1.0 vs. 3.0, p<0.0001
  - 15-29: Event Rate 1.9 vs. 4.0, p=0.1786

Odds Ratio for Gastro Intestinal Bleeding
Conclusions

• The risk of bleeding complications was higher in patients with more severe CKD, but the bleeding avoidance benefit of bivalirudin was evident across the entire spectrum of renal dysfunction.

• These findings further support that bivalirudin monotherapy is an acceptable, if not more appropriate alternative, to GPI in patients with CKD.
If GP IIb/IIIa Has to be Used

**Abbreviated Infusion of Eptifibatide After Successful Coronary Intervention**

The BRIEF-PCI (Brief Infusion of Eptifibatide Following Percutaneous Coronary Intervention) Randomized Trial

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Vancouver, British Columbia, Canada

The incidence of periprocedural myonecrosis was 30.1% in the <2-h group versus 28.3% in the ≥2-h group (mean difference: 1.8%; upper bound of 95% confidence interval: 7.8%; p < 0.012 for noninferiority). The 30-day incidence of myocardial infarction, death, and target vessel revascularization was similar (p = NS). Major bleeding was less frequent in the <2-h group (1.0% vs. 4.2%, p = 0.02).

**Objective**

**Background**

**Methods**

Included death, myocardial infarction, urgent target vessel revascularization at 30 days, and in-hospital major bleeding using the REPLACE-2 (Randomized Evaluation in PCI Linking Angioplasty to Reduced Clinical Events) trial criteria.

**Results**

The incidence of periprocedural myonecrosis was 30.1% in the <2-h group versus 28.3% in the ≥2-h group (mean difference: 1.8%; upper bound of 95% confidence interval: 7.8%; p < 0.012 for noninferiority). The 30-day incidence of myocardial infarction, death, and target vessel revascularization was similar in both groups (p = NS). Major bleeding was less frequent in the <2-h group (1.0% vs. 4.2%, p = 0.02).

**Conclusions**

After uncomplicated PCI, eptifibatide infusion can be abbreviated safely to <2 h. It is not inferior to the standard 18-h infusion in preventing ischemic outcome, and it may be associated with less major bleeding. (Brief Infusion of Eptifibatide Following Percutaneous Coronary Intervention [BRIEF PCI]; NCT00111566) (J Am Coll Cardiol 2009;53:837-45) © 2009 by the American College of Cardiology Foundation
The Argument Against Infusion

- **Bivalirudin**: Lower bleeding, higher ischemic complications
- **Eptifibatide bolus**: Higher bleeding, lower ischemic complications
- **Eptifibatide bolus and infusion**: ? Optimal Outcome

Anti-ischemic

Bleeding
How Does This Work in Real Life?

- **Population**
  - All patients treated with eptifibatide (2010-2011)
    - 4511 in lab only versus 16,785 got bolus + infusion

- **Exclusions**
  - Aspirin contraindicated, emergent CABG, in lab death, lytics, cardiogenic shock, patients treated with bivalirudin (pre/during/post), recent surgery (within 1 week), GI bleed, Salvage PCI, significant dissection, perforation, IABP used, other mechanical ventricular support used, cardiac arrest within 24 hours, cardiogenic shock (within 24 hours and during procedure)
Exact and Optimal Matching

<table>
<thead>
<tr>
<th>Event</th>
<th># of events</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vasc Comp during or post</td>
<td>124</td>
<td>0.249</td>
</tr>
<tr>
<td>Transfusion during or post</td>
<td>558</td>
<td>0.012</td>
</tr>
<tr>
<td>Bleeding event within 72 hrs</td>
<td>764</td>
<td>0.014</td>
</tr>
<tr>
<td>Death post PCI</td>
<td>87</td>
<td>0.508</td>
</tr>
<tr>
<td>Stent Thrombosis</td>
<td>35</td>
<td>0.312</td>
</tr>
<tr>
<td>Redo PCI</td>
<td>88</td>
<td>0.132</td>
</tr>
<tr>
<td>MI during or post PCI</td>
<td>398</td>
<td>0.097</td>
</tr>
</tbody>
</table>
Conclusions

• Using bolus only Eptifibatide dosing and foregoing the infusion appears to be associated with a reduction in bleeding and transfusion without an excess of ischemic events.

• Potential to reduce direct cost and reduce complications
One Institution’s Experience

University of Michigan - post procedural eptifibatide

Post-Proc GPI (%)
A Better Model for CIN Detection

A Novel Tool for Reliable and Accurate Prediction of Renal Complications in Patients Undergoing Percutaneous Coronary Intervention

Hitinder S. Gurm, MD,* Milan Seth, MS,* Judith Kooiman, MSc,† David Share, MD†
Ann Arbor and Detroit, Michigan; and Leiden, the Netherlands

Objectives
The aim of the study was to develop and validate a tool for predicting risk of contrast-induced nephropathy (CIN) in patients undergoing contemporary percutaneous coronary intervention (PCI).

Background
CIN is a common complication of PCI and is associated with adverse short- and long-term outcomes. Previously described risk scores for predicting CIN either have modest discrimination or include procedural variables and thus cannot be applied for pre-procedural risk stratification.

Methods
Random forest models were developed using 46 pre-procedural clinical and laboratory variables to estimate the risk of CIN in patients undergoing PCI. The 15 most influential variables were selected for inclusion in a reduced model. Model performance estimating risk of CIN and new requirement for dialysis (NRD) was evaluated in an independent validation data set using area under the receiver-operating characteristic curve (AUC), with net reclassification improvement used to compare full and reduced model CIN prediction after grouping in low-, intermediate-, and high-risk categories.

Results
Our study cohort comprised 68,573 PCI procedures performed at 46 hospitals between January 2010 and June 2012 in Michigan, of which 48,001 (70%) were randomly selected for training the models and 20,572 (30%) for validation. The models demonstrated excellent calibration and discrimination for both endpoints (CIN AUC for full model 0.85 and for reduced model 0.84, p for difference < 0.01; NRD AUC for both models 0.88, p for difference = 0.82; net reclassification improvement 2.92%, p = 0.006).

Conclusions
The risk of CIN and NRD among patients undergoing PCI can be reliably calculated using a novel easy-to-use computational tool. This risk prediction algorithm may prove useful for both bedside clinical decision making and risk adjustment for assessment of quality. (J Am Coll Cardiol 2013;61:6–10) © 2013 by the American College of Cardiology Foundation

https://bmc2.org/calculators/cin
Similar Novel Tool to Predict Transfusion

• Random forest based approach, 1000 models
• High accuracy and discrimination (c statistic = 0.88)
• Most patients (70%) are at low risk of transfusion and efforts to reduce bleeding can be focused on those at higher risk.

https://bmc2.org/calculators/transfusion
A Better Model for Transfusion

Figure 2. The observed transfusion rates across the three predicted risk categories in patients treated with heparin only, bivalirudin and platelet glycoprotein IIb/IIIa inhibitor (GPI) (Panel A). Panel B depicts the total number of patients treated with each anticoagulation strategy across the three transfusion risk groups. The use of anticoagulation does not appear to be influenced by transfusion risk.

Figure 3. The observed transfusion rates across the three predicted risk categories in patients treated with femoral versus radial access (Panel A). Panel B depicts the total number of patients treated with the two access routes across the three transfusion risk groups suggesting that there is an inverse association between predicted transfusion risk and access route with radial access being more commonly used in the low risk patients.

https://bmc2.org/calculators/transfusion
• Make sure every patient gets ASA prior to PCI.
• Consider Bivalirudin in patients with renal dysfunction.
• If using GP IIbIIIa inhibitors, bolus only may significantly reduce bleeding and transfusion.
• A novel BMC2 transfusion model can help guide strategies to reduce bleeding.
Acknowledgment
STEMI- Door to Balloon Time, Mortality

D2B time

Flynn et al, Archives Int Med 2010
STEMI- Door to Balloon Time, Mortality

Flynn et al, Archives Int Med 2010
Door to Balloon Time in the US

The NEW ENGLAND JOURNAL of MEDICINE

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Door-to-Balloon Time and Mortality among Patients Undergoing Primary PCI

Daniel S. Meneses, M.D., Eric D. Peterson, M.D., Yongfei Wang, M.S., Jeptha P. Curtis, M.D., John C. Messenger, M.D., John S. Rumsfeld, M.D., Ph.D., and Hitinder S. Gurm, M.B., B.S.

Abstract

Background: Current guidelines for the treatment of ST-segment elevation myocardial infarction recommend a door-to-balloon time of 90 minutes or less for patients undergoing primary percutaneous coronary intervention (PCI). Door-to-balloon time has become a performance measure and is the focus of regional and national quality improvement initiatives. However, it is not known whether national improvements in door-to-balloon times have been accompanied by a decline in mortality.

Methods: We analyzed annual trends in door-to-balloon times and in-hospital mortality using data from 96,738 admissions for patients undergoing primary PCI for ST-segment elevation myocardial infarction from July 2005 through June 2009 at 515 hospitals participating in the CathPCI Registry. In a subgroup analysis using a linked Medicare data set, we assessed 30-day mortality.

Results: Median door-to-balloon times declined significantly, from 83 minutes in the 12 months from July 2005 through June 2006 to 67 minutes in the 12 months from July 2008 through June 2009 (P<0.001). Similarly, the percentage of patients for whom the door-to-balloon time was 90 minutes or less increased from 59.7% in the first year to 83.1% in the last year (P<0.001). Despite improvements in door-to-balloon times, there was no significant overall change in unadjusted in-hospital mortality (4.8% in 2005–2006 and 4.7% in 2006–2009, P=0.43 for trend) or in risk-adjusted in-hospital mortality (5.0% in 2005–2006 and 4.7% in 2008–2009, P=0.34), nor was a significant difference observed in unadjusted 30-day mortality (P=0.54).

Conclusions: Although national door-to-balloon times have improved significantly for patients undergoing primary PCI for ST-segment elevation myocardial infarction, in-hospital mortality has remained virtually unchanged. These data suggest that additional strategies are needed to reduce in-hospital mortality in this population. (Funded by the National Cardiovascular Data Registry of the American College of Cardiology Foundation.)
Propensity matched odds of vascular complications and transfusion in the overall cohort and different subgroups of patients at varying risk of access site complications. * This P value reflects the test for significance for the overall comparison while all the other p values reflect test for interaction for each of the subgroups.