Heparin versus bivalirudin in patients with non ST-elevation acute coronary syndrome undergoing percutaneous coronary intervention - a report from the Swedish Coronary Angiography and Angioplasty Registry (SCAAR)

Angerås O¹, Koul S², Söderbom M³, Albertsson P¹, Råmunddal T¹, Matejka G¹, Scherstén F², Oldgren J⁴, James S⁴, Lagerqvist B⁴, Fröbert F⁵, Wedel H⁶, Erlinge D², Omerovic E¹

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³Department of Economics, University of Gothenburg, Gothenburg, Sweden
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⁵Department of Cardiology, Örebro University Hospital, Örebro, Sweden
⁶Nordic School of Public Health, Gothenburg, Sweden
Potential conflicts of interests

• Advisory board: AstraZeneca, Bayer
• Institutional research grant: AstraZeneca, Medtronic, Abbott, Merit Medical
Bivalirudin treatment of choice in NSTE-ACS

– ESC NSTE-ACS guidelines 2011

Bivalirudin plus provisional GP IIb/IIIa receptor inhibitors are recommended as an alternative to UFH plus GP IIb/IIIa receptor inhibitors in patients with an intended urgent or early invasive strategy, particularly in patients with a high risk of bleeding.

– ACC/AHA NSTE-ACS guidelines

Class IIa

2. For UA/NSTEMI patients in whom an initial invasive strategy is selected, it is reasonable to omit administration of an IV GP IIb/IIIa inhibitor if bivalirudin is selected as the anticoagulant and at least 300 mg of clopidogrel was administered at least 6 hours earlier than planned catheterization or PCI (57,76,77). (Level of Evidence: B)
Bivalirudin treatment of choice in NSTE-ACS?

- Bivalirudin vs GPIIb/IIIa inhibitors
- < 60% biomarker positive
- < 60% PCI
- 60% pretreated with clopidogrel
- 6.2% radial access
Anti-thrombotic treatment in NSTE-ACS PCI in Sweden 2006-2013

GPIIb/IIIa inhibitors
Bivalirudin
Heparin alone
Bivalirudin vs Heparin in NSTE-ACS
randomised trials

• **BAT trial** (Bittl et al NEJM 1995;333:764-9)
  – 4098 patients randomised 1993-1994
  – Composite endpoint NS
  – Bivalirudin reduced major bleeding
  – Trend for higher mortality in the bivalirudin group (p=0.08)!

• **ISAR-REACT 3** (Kastrati et al NEJM 2008;359:688-96.)
  – 4570 biomarker negative patients randomised 2005-2008
  – Composite endpoint NS including major bleeding
  – Bivalirudin reduced major bleeding

• All randomised patients had femoral access
• Majority of randomized patients were biomarker negative
Purpose

• Purpose: To compare the outcome of heparin alone versus bivalirudin in patients with NSTE-ACS undergoing PCI between 2005-2013 and registered in SCAAR

• Endpoint: 30-day mortality
30 hospitals performing PCI and angiography. Financed by Swedish government. No support from the industry.
Undvik att skapa Vårdkedja där det inte ska skapas en RIKS-HIA del
Från mitten av april har en ökad mängd Startsidor fått en ägare (dvs en specifik sjukhusenhet har fått ansvaret att registrera denna sida).
Läs mer...

Syrgas eller inte vid hjärtinfarkt?
Anmäl ert sjukhus nu!
Läs mer

http://www.ucr.uu.se/swedeheart/
• 100% coverage
• All coronary angiogram and PCI procedures are registered immediately after procedure
• 200 variables
• Linked to the national cause specific death registry
RANDOMISED REGISTRY CLINICAL TRIAL

RRCT
Thrombus Aspiration in ST-Elevation myocardial infarction in Scandinavia (TASTE trial)

Main results at 30 days

Ole Fröbert, MD, PhD - on behalf of the TASTE investigators
Departement of Cardiology
Örebro University Hospital
Sweden
Thrombus Aspiration during ST-Segment Elevation Myocardial Infarction

Ole Fröbert, M.D., Ph.D., Bo Lagerqvist, M.D., Ph.D., Göran K. Olivecrona, M.D., Ph.D., Elmir Omerovic, M.D., Ph.D., Thorarinn Gudnason, M.D., Ph.D., Michael Maeng, M.D., Ph.D., Mikael Aasa, M.D., Ph.D., Oskar Angerås, M.D., Fredrik Calais, M.D., Mikael Danielewicz, M.D., David Erlinge, M.D., Ph.D., Lars Hellsten, M.D., Ulf Jensen, M.D., Ph.D., Agneta C. Johansson, M.D., Amra Kåregren, M.D., Johan Nilsson, M.D., Ph.D., Lotta Robertson, M.D., Lennart Sandhall, M.D., Ivar Sjögren, M.D., Ollie Östlund, Ph.D., Jan Harnek, M.D., Ph.D., and Stefan K. James, M.D., Ph.D.

This article was published on September 1, 2013, at NEJM.org.
All-cause mortality at 30 days

TASTE trial

HR 0.94 (0.72 - 1.22), P=0.63
Study design

heparin vs. bivalirudin

51,549 consecutive patients with NSTE-ACS in SCAAR not receiving GPIIb/IIIa inhibitors

5,395 patients with missing data

Complete case analysis

Heparin alone 35,167 patients  Bivalirudin 10,985 patients

Multiple imputation

Imputed data set

Heparin alone 39,296 patients  Bivalirudin 12,253 patients
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<td>0.59</td>
<td>0</td>
</tr>
<tr>
<td>Use of DES (%)</td>
<td>48</td>
<td>41</td>
<td>&lt;0.001</td>
<td>0.43</td>
<td>0</td>
</tr>
</tbody>
</table>
Statistical models
(adjustement for confounders)

1. **Complete case analysis** adjusted for propensity score
   Multilevel logistic regression

2. **Imputed data** set adjusted for propensity score
   Missing data imputed by multiple imputation model
   Multilevel logistic regression

3. **Instrumental variable analysis**
   To adjust for unknown/unmeasured confounders!

Adjusted for: age, biomarkers, procedural success, hypertension, hyperlipidemia, gender, antiplatelet therapy, warfarin therapy, UFH/LMWH treatment, prior CABG, prior MI, prior PCI, diabetes, smoking, year, angiographic findings, access site, usage of DES, CTO procedure, completeness of revascularization)
Results

Adjusted odds ratio
30-day mortality

Complete case

Imputed dataset

Instrumental variable

Favours bivalirudin  Favours heparin

1.08
1.40
1.56
Conclusion

• Our large observational study questions the superiority of bivalirudin over heparin in the absence of GP IIb/IIIa blockade in patients with NSTE-ACS undergoing PCI.

• A prospective randomized trial evaluating bivalirudin vs heparin is highly warranted.

• The register-based randomized clinical trial VALIDATE-SWEDEHEART comparing bivalirudin to heparin in patients pretreated with novel ADP-receptor blockers (n=6000) is under way.
Planned RRCTs in SCAAR

**REAL-SWEDEHEART**

- **STEMI**
  - N=3450
- Radial
  - N=1725
- Femoral
  - N=1725
- Primary outcome: death at 180 days

**VALIDATE-SWEDEHEART**

- **STEMI**
  - N=3000
- NSTEMI
  - N=3000
- Heparin alone
  - N=3000
- Bivalirudin
  - N=3000
- Primary outcome: death, MI or major bleeding at 180 days