Biomarker prediction of major coronary events and complex revascularization procedures in patients with stable atherosclerosis

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A biomarker-based strategy identified a gradient of risk for cardiovascular (CV) death, myocardial infarction (MI) and stroke among patients post acute coronary syndrome (ACS).
Objective

- Explore the associations of an established biomarker score with major coronary events (MCE) and coronary revascularization procedures in stable patients with ASCVD

- **Biomarker score**: hsTnI (myocardial injury), NT-proBNP (ventricular strain), GDF-15 (inflammation/fibrosis), hsCRP (inflammation)
Methods

• FOURIER was a randomized trial of the PCSK9 inhibitor evolocumab vs placebo in 27,564 patients with stable ASCVD.

• Analyzed associations between baseline biomarker concentrations and MCE (coronary heart disease [CHD] death, MI, or coronary revascularization) using an established biomarker score.
Methods

- **Complex revascularization:**
  - Coronary artery bypass graft surgery (CABG); or
  - Complex percutaneous coronary intervention (PCI)*

- Cox proportional hazards multivariable model with 18 covariates

*GLOBAL LEADERS complex PCI: 1) Multivessel PCI; 2) ≥3 stents implanted; 3) ≥3 lesions treated; 4) bifurcation PCI with ≥2 stents; 5) or total stent length >60 mm
Results

Q4 vs Q1: HR_{adj} 1.41
95% CI (1.22-1.62)
p-trend < 0.0001

HR_{adj} 2.25
(1.94-2.61)
p-trend < 0.0001

HR_{adj} 2.22
(1.91-2.58)
p-trend < 0.0001

HR_{adj} 1.66
(1.42-1.95)
p-trend < 0.0001

Major coronary events at 3 years

hsCRP

NT-proBNP

hsTnI

GDF-15

ACC.21
<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>hsTnI ≥ 6 ng/L</td>
<td>1</td>
</tr>
<tr>
<td>NT-proBNP ≥ 450 pg/mL</td>
<td>1</td>
</tr>
<tr>
<td>GDF-15 ≥ 1800 pg/mL</td>
<td>1</td>
</tr>
<tr>
<td>hsCRP ≥ 2 mg/L</td>
<td>1</td>
</tr>
<tr>
<td>Maximum possible score</td>
<td>4</td>
</tr>
</tbody>
</table>

**Biomarker Score**

- Low score (0 points): 6444 patients (30%)
- Intermediate score (1-2 points): 12439 patients (57%)
- High score (3-4 points): 2761 patients (13%)
Major Coronary Events

<table>
<thead>
<tr>
<th>Score Level</th>
<th>HR adj (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High score (N=2761)</td>
<td>3.04 (2.59-3.57)</td>
</tr>
<tr>
<td>Intermediate score (N=12439)</td>
<td>1.58 (1.40-1.80)</td>
</tr>
<tr>
<td>Low score (N=6444)</td>
<td>Ref</td>
</tr>
</tbody>
</table>

Cumulative Incidence (%)

High score: HR\textsubscript{adj} 3.04 (2.59-3.57)
Intermediate score: HR\textsubscript{adj} 1.58 (1.40-1.80)
Low score: Ref

<table>
<thead>
<tr>
<th>Days</th>
<th>No. At Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>6,444</td>
</tr>
<tr>
<td>180</td>
<td>6,330</td>
</tr>
<tr>
<td>360</td>
<td>6,214</td>
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<tr>
<td>540</td>
<td>6,079</td>
</tr>
<tr>
<td>720</td>
<td>4,116</td>
</tr>
<tr>
<td>900</td>
<td>2,035</td>
</tr>
<tr>
<td>1080</td>
<td>357</td>
</tr>
</tbody>
</table>

P\textsubscript{trend}≤0.0001
Biomarker Score and Coronary Events

- **CHD death**
  - Low score: Ref. 0.5%
  - Int. score: 1.6%
  - High score: 5.1%
  - HR_{adj} 2.52
    - Ref. 3.3%
    - Int. score 5.1%
    - High score 12.7%
  - P_{trend} < 0.0001

- **Myocardial Infarction**
  - Low score: Ref. 2.3%
  - Int. score: 3.1%
  - High score: 4.4%
  - HR_{adj} 3.62
    - Ref. 6.2%
    - Int. score 8.5%
    - High score 12.0%
  - P_{trend} < 0.0001

- **Coronary Revascularization**
  - Low score: Ref. 2.3%
  - Int. score: 3.1%
  - High score: 4.4%
  - HR_{adj} 1.33
    - Ref. 2.3%
    - Int. score 3.1%
    - High score 4.4%
  - P_{trend} < 0.0001

- **Complex Revascularization**
  - Low score: Ref. 2.3%
  - Int. score: 3.1%
  - High score: 4.4%
  - HR_{adj} 2.12
    - Ref. 2.3%
    - Int. score 3.1%
    - High score 4.4%
  - P_{trend} < 0.0001
Revascularization | HR_{adj} (95% CI) (High vs Low score) | P-trend for HR_{adj}
--- | --- | ---
Complex PCI | 1.95 (1.30-2.94) | <0.001
CABG | 2.43 (1.53-3.84) | <0.001
ISR revascularization | 1.98 (1.33-2.93) | <0.001

Model included: age, sex, weight, region, hypertension, current smoking, diabetes, history of CAD, prior MI, prior PCI, high-intensity statin, heart failure, prior stroke, peripheral artery disease (PAD), LDL-C, estimated glomerular filtration rate (eGFR) <60 mL/min/1.73m², microalbuminuria
Biomarker Score and Coronary Anatomy

Event rate at 3 years

- **Ref.** 0.9%
  - Low score n=43
  - Int. score n=93
  - High score n=52
- **HR** 1.07 (0.72-1.59)
- **P** trend for **HR** adj: <0.0001

- **Ref.** 2.3%
  - Low score n=162
  - Int. score n=406
  - High score n=145
- **HR** 2.59 (1.60-4.19)
- **P** trend <0.0001

- **Ref.** 2.8%
  - Low score n=108
  - Int. score n=286
  - High score n=124
- **HR** 2.87 (2.12-3.88)
- **P** trend <0.0001

- **HR** adj 1.37 (1.08-1.74)

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**LMCA ≥ 50%**

**Multivessel Disease**

**CTO**
Conclusion

- In patients with stable atherosclerosis, a biomarker score incorporating indicators of myocardial injury (hsTnI), ventricular strain (NT-proBNP), fibrosis (GDF-15) and inflammation (hsCRP) identifies a significant gradient of risk for:
  - Clinical coronary events, including MI and complex revascularization procedures
  - High-risk coronary anatomy at the time of revascularization
  - Revascularization for in-stent restenosis

- These findings provide new insight into the relationship between biomarker levels, coronary anatomy, and clinical events in patients with stable ASCVD.