Minneapolis Heart Institute® at Abbott Northwestern Hospital

Radial vs Femoral

Or

Really?

Is that still a thing?
Quality Initiatives to Prevent and Manage Major Femoral Access-Site Bleeding

This Tip of the Month summarizes effective strategies for the prevention and management of major femoral bleeding following percutaneous coronary intervention (PCI).

Read the Tip

For more information on quality improvement in the cath lab, check out our QI toolkit, including modules on procedural quality, facility and environmental issues, and care coordination.
SCAI Quality Measures for Prevention of Major Femoral Bleeding:

1st recommendation:
Use radial instead of femoral access for PCI, if possible, especially in patients at high risk of bleeding, including ACS. In the RIVAL trial, transradial PCI was associated with a 64% reduction in access-site bleeding (ACUITY trial definition) compared with transfemoral PCI in patients with both non-STEMI and STEMI.
CHANGE IN RECOMMENDATIONS 2012

- Radial access
  - MATRIX™

- DES over BMS
  - EXAMINATION™, COMFORTABLE AMI™, NORTENT™

- Complete Revascularization
  - PRAH™, DANAMI-3-PRIMULI™, CVL PRIT™, COMPARE-ACUET™

- Thrombus Aspiration
  - TOTAL™, TASTE™

- Bivalirudin
  - MATRIX™, HEAT-PCI™

- Enoxaparin
  - ATOLL™, Meta-analysis™

- Early Hospital Discharge
  - Small trials & observational data

- Oxygen when
  - SaO₂ <95%
  - Avoid™, DETOX™
  - Oxygen when
  - SaO₂ <90%

- Dose i.v. TNK-PA
  - STREAM™
  - Same in all patients
  - Half in pts ≥75 years

2017 NEW RECOMMENDATIONS

- Additional lipid lowering therapy if LDL >1.8 mmol/L (70 mg/dL) despite on maximum tolerated statins
  - IMPROVE-IT™, FOURIER™

- Complete revascularization during index primary PCI in STEMI patients in shock
  - Expert opinion

- Cangrelor if P2Y₁₂ inhibitors have not been given
  - CHAMPION™

- Switch to potent P2Y₁₂ inhibitors 48 hours after fibrinolysis
  - Expert opinion

- Extend Ticagrelor up to 36 months in high-risk patients
  - PEGASUS-TIMI 54™

- Use of polypill to increase adherence
  - FOCUS™

- Routine use of deferred stenting
  - DANAMI 3 DEFER™

2017 NEW / REVISED CONCEPTS

MINOCA AND QUALITY INDICATORS:
- New chapters dedicated to these topics.

STRATEGY SELECTION AND TIME DELAYS:
- Clear definition of first medical contact (FMC).
- Definition of “time 0” to choose referral strategy (i.e., the strategy clock starts at the time of “STEMI diagnosis”).
- Selection of PCI over fibrinolysis when anticipated delay from “STEMI diagnosis” to wire crossing is ≤120 min.
- Maximum delay time from “STEMI diagnosis” to bolus of fibrinolysis agent is set in 10 min.
- “Door-to-Ballon” term eliminated from guidelines.

TIME LIMITS FOR ROUTINE OPENING OF AN IRA:
- 0-12h (Class I), 12-48h (Class IIa), >48h (Class III).

ELECTROCARDIOGRAM AT PRESENTATION:
- Left and right bundle branch block considered equal for recommending urgent angiography if ischemic symptoms.

TIME TO ANGIOGRAPHY AFTER FIBRINOLYSIS:
- Timeframe is set in 2–24h after successful fibrinolysis.

PATIENTS TAKING ANTICOAGULANTS:
- Acute and chronic management presented.
Bleeding complications have decreased but are still bad!

Figure 1. Changing Incidence of Major Femoral Bleeding Complications From 1994 to 2005

The incidence of major femoral bleeding declined significantly from the earliest (8.4%) to the contemporary time period (3.5%).
### Study (A)

<table>
<thead>
<tr>
<th>Study</th>
<th>RADIAL Events Total</th>
<th>FEMORAL Events Total</th>
<th>Mortality – SIHD or ACS OR 95%–CI W(random)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRAFE 1997</td>
<td>0</td>
<td>50</td>
<td>3.01 [0.12; 74.18] 0.0% 7.8%</td>
</tr>
<tr>
<td>ACCESS 1997</td>
<td>1</td>
<td>300</td>
<td>1.30 [0.44; 3.81] 69.0% 15.6%</td>
</tr>
<tr>
<td>OCTOPUS 2004</td>
<td>8</td>
<td>192</td>
<td>3.02 [0.31; 29.18] 0.0% 7.6%</td>
</tr>
<tr>
<td>OUTCLAS 2005</td>
<td>3</td>
<td>322</td>
<td>0.35 [0.01; 8.85] 100% 100%</td>
</tr>
<tr>
<td>Brueck 2009</td>
<td>0</td>
<td>512</td>
<td>1.43 [0.61; 3.40] 100% 100%</td>
</tr>
<tr>
<td>Ziakas 2010</td>
<td>0</td>
<td>27</td>
<td>1.43 [0.58; 3.50] 100% 100%</td>
</tr>
</tbody>
</table>

Fixed effect model

Random effects model

Heterogeneity: I²-squared=0%, tau-squared=0, p=0.7073

### Study (B)

<table>
<thead>
<tr>
<th>Study</th>
<th>RADIAL Events Total</th>
<th>FEMORAL Events Total</th>
<th>Mortality – ACS OR 95%–CI W(random)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mann 1998</td>
<td>0</td>
<td>68</td>
<td>0.51 [0.14; 1.82] 0.0% 2.7%</td>
</tr>
<tr>
<td>TEMPURA 2003</td>
<td>4</td>
<td>77</td>
<td>0.32 [0.01; 8.25] 0.4% 1.6%</td>
</tr>
<tr>
<td>RADIOMI Pilot 2005</td>
<td>3</td>
<td>57</td>
<td>1.00 [0.19; 5.18] 0.0% 0.6%</td>
</tr>
<tr>
<td>Farmi 2007</td>
<td>0</td>
<td>155</td>
<td>1.00 [0.06; 16.44] 0.0% 0.0%</td>
</tr>
<tr>
<td>Achenbach 2008</td>
<td>1</td>
<td>50</td>
<td>0.86 [0.57; 1.29] 26.5%</td>
</tr>
<tr>
<td>RADIOMI 2009</td>
<td>0</td>
<td>50</td>
<td>0.54 [0.33; 0.89] 17.6%</td>
</tr>
<tr>
<td>RADIOMI II 2011</td>
<td>0</td>
<td>59</td>
<td>0.74 [0.30; 1.87] 5.1%</td>
</tr>
<tr>
<td>RIVAL 2011</td>
<td>44</td>
<td>3507</td>
<td>0.77 [0.19; 3.03] 2.3%</td>
</tr>
<tr>
<td>RIFLE–STEAC 2012</td>
<td>26</td>
<td>500</td>
<td>0.72 [0.52; 0.99] 42.7%</td>
</tr>
<tr>
<td>Wang 2012</td>
<td>0</td>
<td>60</td>
<td>0.71 [0.58; 0.88] 100% 100%</td>
</tr>
<tr>
<td>STEMI–RADIAL 2014</td>
<td>8</td>
<td>348</td>
<td>0.72 [0.58; 0.88] 100% 100%</td>
</tr>
<tr>
<td>OCEAN RACE 2014</td>
<td>4</td>
<td>52</td>
<td></td>
</tr>
<tr>
<td>MATRIX 2015</td>
<td>66</td>
<td>4197</td>
<td></td>
</tr>
</tbody>
</table>

Fixed effect model

Random effects model

Heterogeneity: I²-squared=0%, tau-squared=0, p=0.9649
Mortality is lower with radial access in STEMI

**Figure 2: Death In Patients With STEMI and NSTEMI**

For death, there was a significant interaction between access site allocation (radial or femoral) and acute coronary syndrome type (STEMI or NSTEMI) with an interaction p value of 0.001. In patients with STEMI (A), radial artery access reduced the mortality compared with femoral artery access, whereas in patients with NSTEMI (B), there was no significant difference in mortality between radial and femoral artery access. Abbreviations as in Figure 1.
Matrix: improved outcomes with radial
Most common rationalization for using femoral access

“It’s better for high risk or complex interventions”
### Central Illustration: Bleeding Outcomes For LM PCI- Radial versus Femoral access

#### (A) Major Bleeding

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>TRA Events</th>
<th>TFA Events</th>
<th>Total Events</th>
<th>Total Weight</th>
<th>Odds Ratio</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tomassini et al.</td>
<td>0</td>
<td>27</td>
<td>1</td>
<td>22</td>
<td>0.26 [0.01, 0.672]</td>
<td>2013</td>
</tr>
<tr>
<td>Gao et al.</td>
<td>1</td>
<td>508</td>
<td>1</td>
<td>297</td>
<td>0.58 [0.04, 9.37]</td>
<td>2014</td>
</tr>
<tr>
<td>Chung et al.</td>
<td>0</td>
<td>161</td>
<td>5</td>
<td>322</td>
<td>0.18 [0.01, 3.25]</td>
<td>2015</td>
</tr>
<tr>
<td>Kinnard et al.</td>
<td>29</td>
<td>4292</td>
<td>39</td>
<td>2611</td>
<td>0.45 [0.28, 0.73]</td>
<td>2018</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>4988</strong></td>
<td><strong>3252</strong></td>
<td></td>
<td><strong>100.0%</strong></td>
<td><strong>0.44 [0.27, 0.69]</strong></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 30 (TRA) vs 46 (TFA), Heterogeneity: Tau² = 0.00; Chi² = 0.52, df = 3 (P = 0.91); I² = 0%
Test for overall effect: Z = 3.50 (P = 0.0005)

#### (B) Access Site Bleeding

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>TRA Events</th>
<th>TFA Events</th>
<th>Total Events</th>
<th>Total Weight</th>
<th>Odds Ratio</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hsueh et al.</td>
<td>0</td>
<td>116</td>
<td>1</td>
<td>15</td>
<td>0.04 [0.00, 1.07]</td>
<td>2008</td>
</tr>
<tr>
<td>DeMaria et al.</td>
<td>3</td>
<td>244</td>
<td>14</td>
<td>221</td>
<td>0.18 [0.05, 0.65]</td>
<td>2015</td>
</tr>
<tr>
<td>Kinnard et al.</td>
<td>2</td>
<td>4292</td>
<td>20</td>
<td>2611</td>
<td>0.06 [0.01, 0.26]</td>
<td>2018</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>4652</strong></td>
<td><strong>2847</strong></td>
<td></td>
<td><strong>100.0%</strong></td>
<td><strong>0.11 [0.04, 0.26]</strong></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 5 (TRA) vs 35 (TFA), Heterogeneity: Tau² = 0.00; Chi² = 1.64, df = 2 (P = 0.44); I² = 0%
Test for overall effect: Z = 4.83 (P < 0.00001)

#### (C) Any Bleeding

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>TRA Events</th>
<th>TFA Events</th>
<th>Total Events</th>
<th>Total Weight</th>
<th>Odds Ratio</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yang et al.</td>
<td>2</td>
<td>353</td>
<td>13</td>
<td>468</td>
<td>0.20 [0.04, 0.89]</td>
<td>2010</td>
</tr>
<tr>
<td>Gao et al.</td>
<td>29</td>
<td>508</td>
<td>34</td>
<td>297</td>
<td>0.47 [0.26, 0.79]</td>
<td>2014</td>
</tr>
<tr>
<td>Almudarra et al.</td>
<td>5</td>
<td>1602</td>
<td>10</td>
<td>3266</td>
<td>1.02 [0.35, 2.99]</td>
<td>2014</td>
</tr>
<tr>
<td>Chung et al.</td>
<td>4</td>
<td>161</td>
<td>27</td>
<td>322</td>
<td>0.28 [0.10, 0.81]</td>
<td>2015</td>
</tr>
<tr>
<td>Gili et al.</td>
<td>2</td>
<td>177</td>
<td>7</td>
<td>177</td>
<td>0.28 [0.06, 1.36]</td>
<td>2017</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>2801</strong></td>
<td><strong>4530</strong></td>
<td></td>
<td><strong>100.0%</strong></td>
<td><strong>0.43 [0.27, 0.69]</strong></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 42 (TRA) vs 91 (TFA), Heterogeneity: Tau² = 0.04; Chi² = 4.57, df = 4 (P = 0.33); I² = 12%
Test for overall effect: Z = 3.66 (P = 0.0004)
### In-Hospital Outcomes For LM PCI

#### (A) In-Hospital Mortality

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>TRA Events</th>
<th>TFA Events</th>
<th>Total Events</th>
<th>Total Weight</th>
<th>M-H, Random, 95% CI Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ziakas et al.</td>
<td>0</td>
<td>27</td>
<td>23</td>
<td>2.4%</td>
<td>0.37 [0.02, 8.08] 2004</td>
</tr>
<tr>
<td>Hsueh et al.</td>
<td>1</td>
<td>116</td>
<td>22</td>
<td>3.6%</td>
<td>0.06 [0.00, 0.67] 2008</td>
</tr>
<tr>
<td>Tomassini et al.</td>
<td>0</td>
<td>27</td>
<td>43</td>
<td>2.4%</td>
<td>0.10 [0.00, 0.477] 2013</td>
</tr>
<tr>
<td>Gao et al.</td>
<td>1</td>
<td>508</td>
<td>207</td>
<td>2.2%</td>
<td>1.76 [0.07, 43.31] 2014</td>
</tr>
<tr>
<td>DeMaria et al.</td>
<td>5</td>
<td>244</td>
<td>11</td>
<td>16.4%</td>
<td>0.46 [0.14, 1.17] 2016</td>
</tr>
<tr>
<td>Kinnaird et al.</td>
<td>105</td>
<td>4202</td>
<td>107</td>
<td>73.1%</td>
<td>0.69 [0.45, 0.77] 2018</td>
</tr>
</tbody>
</table>

Total (95% CI): 5214 / 3218 = 160.6%

Total events: 112 / 125

Heterogeneity: Tau² = 0.06; Chi² = 5.69, df = 5 (P = 0.35); I² = 11%

Test for overall effect: Z = 2.92 (P = 0.004)

#### (B) In-Hospital MI

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>TRA Events</th>
<th>TFA Events</th>
<th>Total Events</th>
<th>Total Weight</th>
<th>M-H, Random, 95% CI Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ziakas et al.</td>
<td>2</td>
<td>27</td>
<td>5</td>
<td>2.1%</td>
<td>4.10 [0.30, 40.00] 2004</td>
</tr>
<tr>
<td>Hsueh et al.</td>
<td>7</td>
<td>116</td>
<td>44</td>
<td>4.4%</td>
<td>0.42 [0.08, 2.23] 2008</td>
</tr>
<tr>
<td>Yang et al.</td>
<td>10</td>
<td>353</td>
<td>468</td>
<td>13.0%</td>
<td>1.92 [0.72, 5.10] 2010</td>
</tr>
<tr>
<td>Tomassini et al.</td>
<td>1</td>
<td>27</td>
<td>22</td>
<td>1.2%</td>
<td>2.55 [0.10, 65.66] 2013</td>
</tr>
<tr>
<td>Gao et al.</td>
<td>50</td>
<td>508</td>
<td>297</td>
<td>38.1%</td>
<td>1.80 [1.02, 3.18] 2014</td>
</tr>
<tr>
<td>Gili et al.</td>
<td>10</td>
<td>177</td>
<td>177</td>
<td>12.7%</td>
<td>1.45 [0.54, 3.91] 2017</td>
</tr>
<tr>
<td>Kinnaird et al.</td>
<td>22</td>
<td>4292</td>
<td>2611</td>
<td>28.6%</td>
<td>0.89 [0.46, 1.72] 2018</td>
</tr>
</tbody>
</table>

Total (95% CI): 5500 / 3643 = 100.0%

Total events: 102 / 49

Heterogeneity: Tau² = 0.00; Chi² = 5.36, df = 6 (P = 0.44); I² = 0%

Test for overall effect: Z = 1.81 (P = 0.07)

#### (C) In-Hospital TVR

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>TRA Events</th>
<th>TFA Events</th>
<th>Total Events</th>
<th>Total Weight</th>
<th>M-H, Random, 95% CI Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ziakas et al.</td>
<td>0</td>
<td>27</td>
<td>23</td>
<td>12.0%</td>
<td>Not estimable</td>
</tr>
<tr>
<td>Hsueh et al.</td>
<td>1</td>
<td>116</td>
<td>2</td>
<td>15</td>
<td>0.12 [0.01, 2.06] 2008</td>
</tr>
<tr>
<td>Yang et al.</td>
<td>4</td>
<td>353</td>
<td>468</td>
<td>68.4%</td>
<td>0.58 [0.18, 1.91] 2010</td>
</tr>
<tr>
<td>Tomassini et al.</td>
<td>0</td>
<td>27</td>
<td>22</td>
<td>9.1%</td>
<td>0.26 [0.04, 0.72] 2013</td>
</tr>
<tr>
<td>Gao et al.</td>
<td>0</td>
<td>508</td>
<td>267</td>
<td>10.4%</td>
<td>0.12 [0.01, 0.43] 2014</td>
</tr>
</tbody>
</table>

Total (95% CI): 1031 / 855 = 100.0%

Total events: 5 / 13

Heterogeneity: Tau² = 0.00; Chi² = 1.77, df = 3 (P = 0.62); I² = 0%

Test for overall effect: Z = 1.93 (P = 0.05)
Radial vs. Femoral Approach in Chronic Total Occlusion Percutaneous Coronary Intervention

Meta-analysis of 9 observational studies (10,590 patients)

<table>
<thead>
<tr>
<th></th>
<th>Radial approach, 45991 patients</th>
<th>Femoral approach, 5999 patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower complexity</td>
<td>2.3 +/- 1.2</td>
<td>2.5 +/- 1.3</td>
</tr>
<tr>
<td>Similar success</td>
<td>78.7%</td>
<td>78.5%</td>
</tr>
<tr>
<td>J-CTO score</td>
<td>p &lt; 0.001</td>
<td></td>
</tr>
<tr>
<td>Technical success</td>
<td>p = 0.24</td>
<td>p &gt; 0.001</td>
</tr>
<tr>
<td>Lower risk</td>
<td>0.73%</td>
<td>1.79%</td>
</tr>
<tr>
<td>Access-site complications</td>
<td>p &lt; 0.001</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>0.18%</td>
<td>0.9%</td>
</tr>
<tr>
<td>p &lt; 0.001</td>
<td>p &lt; 0.001</td>
<td></td>
</tr>
<tr>
<td>Similar risk</td>
<td></td>
<td>In-hospital mortality p = 0.07</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Q-wave myocardial infarction p = 0.13</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pericardial tamponade p = 0.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Emergency bypass surgery p = 0.63</td>
</tr>
</tbody>
</table>

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In Favor of Femoral Access

Radial Vs Femoral Access for Cath/PCI

Mario Goessl, MD PhD
Director, Transcatheter Valve Therapies
LAAO Program
IC Fellowships
DISCLOSURES

• I HAVE NEVER LOST A DEBATE … EVER
Why Go Radial ... earlier mobilization?
Is It Safe to Mobilize Patients Very Early After Transfemoral Coronary Procedures? (SAMOVAR)

A Randomized Clinical Trial

Marianne Wetendorff Nørgaard, PhD, RN; Jane Færch, MSc, RN; Francis R. Joshi, MD, PhD, FRCP; Dan E. Høfsten, MD, PhD; Thomas Engstrøm, MD, PhD, DMS; Henning Kelbæk, MD, DMS
SAMOVAR

- Immediate vs 2h mobilization
- No difference
- Of 2027 patients (IM, 1010; BR, 1017), 40% underwent PCI. The primary outcome* was recorded in 0.7% patients randomized to IM versus 0.5% in BR (P = .58). There was no difference in the incidence of small hematoma, whereas persistent oozing was seen slightly more often after IM compared with BR (12% vs 9%, P = .04).

*The primary end point was a composite of greater than 5 cm of groin hematoma, retroperitoneal hematoma, pseudoaneurysm, and/or bleeding requiring transfusion.
Why Go Radial ...

how about radiation?
Comparison of operator radiation exposure with optimized radiation protection devices during coronary angiograms and ad hoc percutaneous coronary interventions by radial and femoral routes

Camille Brasselet, Thierry Blanpain, Sophie Tassan-Mangina, Alain Deschildre, Sébastien Duval, Fabien Vitry, Nathalie Gaillot-Petit, Jean Paul Clément, Damien Metz
Radial Radiation

- Radiation exposure was significantly higher using the radial route when compared with the femoral route for both CAs and CAs followed by ad hoc PCIs: 29.0 [1.0-195.0] microSv vs. 13.0 [1.0-164.0] microSv; P < 0.0001 and 69.5 [4.0-531.0] microSv vs. 41.0 [2.0-360.0] microSv; P = 0.018, respectively.

Similarly, radiation exposure of patients was significantly higher using the radial route when compared with the femoral route for both CAs and CAs followed by ad hoc PCIs.
Why Go Radial ...the mortality myth?
Radial Versus Femoral Access for Coronary Interventions Across the Entire Spectrum of Patients With Coronary Artery Disease

A Meta-Analysis of Randomized Trials
RESULTS

Twenty-four studies enrolling 22,843 participants were included. Compared with femoral access, radial access was associated with a significantly lower risk for all-cause mortality (odds ratio [OR]: 0.71; 95% confidence interval [CI]: 0.59 to 0.87; p = 0.001, number needed to treat to benefit [NNTB] = 160), major adverse cardiovascular events (OR: 0.84; 95% CI: 0.75 to 0.94; p = 0.002; NNTB = 99), major bleeding (OR: 0.53; 95% CI: 0.42 to 0.65; p < 0.001; NNTB = 103), and major vascular complications (OR: 0.23; 95% CI: 0.16 to 0.35; p < 0.001; NNTB = 117).

Learning curve … ~ 50 PCI necessary
For RIVAL data needed to be extracted, corresponding author etc
RIVAL (the original)

Radial versus femoral access for coronary angiography and intervention in patients with acute coronary syndromes (RIVAL): a randomised, parallel group, multicentre trial

Sanjit S Jolly, Salim Yusuf, John Cairns, Kari Niemelä, Denis Xavier, Petr Widimsky, Andrzej Budaj, Matti Niemelä, Vicent Valentin, Basil S Lewis, Alvaro Avezum, Philippe Gabriel Steg, Sunil V Rao, Peggy Gao, Rizwan Afzal, Campbell D Joyner, Susan Chrolavicius, Shamir R Mehta, for the RIVAL trial group*

Lancet 2011; 377: 1409–20
Interpretation
Radial and femoral approaches are both safe and effective for PCI. However, the lower rate of local vascular complications may be a reason to use the radial approach.
Effects of Radial Versus Femoral Artery Access in Patients With Acute Coronary Syndromes With or Without ST-Segment Elevation

Shamir R. Mehta, MD, MSc,* Sanjit S. Jolly, MD, MSc,* John Cairns, MD,† Kari Niemela, MD, PhD,‡ Sunil V. Rao, MD,§ Asim N. Cheema, MD, PhD,¶ Philippe Gabriel Steg, MD,¶¶ Warren J. Cantor, MD,# Vladimír Džavík, MD,** Andrzej Budaj, MD, PhD,†† Michael Rokoss, MD,* Vicent Valentin, MD,‡‡ Peggy Gao, MSc,* Salim Yusuf, MBBS, DPHIL,* for the RIVAL Investigators

Hamilton, Toronto, Newmarket, Ontario, Vancouver, British Columbia, Canada; Tampere, Finland; Durham, North Carolina; Paris, France; Warsaw, Poland; and Valencia, Spain
Conclusions
In patients with **STEMI**, radial artery access reduced the primary outcome and mortality. **No such benefit** was observed in patients with **NSTEACS**. The radial approach may be preferred in STEMI patients when the operator has considerable radial experience.

... if a reduction in bleeding-related complications was associated with lower mortality, it might **most likely be detected in the STEMI group of patients**.

... higher rate of PCIs (90%) compared with NSTEACS patients (50% to 60%), exposing them to a higher frequency of access site complications.

... more potent initial and subsequent antiplatelet and antithrombotic therapies (as well as fibrinolytic therapy) ... the risk-adjusted rate of bleeding (particularly access-site bleeding) is higher, making the association between bleeding and mortality more readily detectable in this population

**STEMI subgroup:**
30-day mortality was significantly lower with radial access (1.3% vs 3.2%), **which cannot be explained by the very low rates of bleeding at 0.84% (radial access) vs 0.91% (femoral access)**.
The majority of deaths occurred in patients who had **neither a major bleed nor an access site complication**.

Because randomization did not stratify patients by STEMI and non-STEMI, any comparison in the patients with STEMI is a subgroup analysis and prone to potential differences between access groups that may confound the relationship.
Safety and Efficacy of Femoral Access vs Radial Access in ST-Segment Elevation Myocardial Infarction
The SAFARI-STEMI Randomized Clinical Trial

Michel Le May, MD; George Wells, PhD; Derek So, MD; Aun Yeong Chong, MD; Alexander Dick, MD; Michael Froeschl, MD; Christopher Glover, MD; Benjamin Hibbert, MD; Jean-Francois Marquis, MD; Melissa Blondeau, BSc; Christina Osborne, BSc; Andrea MacDougall, MD; Malek Kass, MD; Vernon Paddock, MD; Ata Quraishi, MBBS; Marino Labinaz, MD

JAMA Cardiol. 2020;5(2):126-134
SAFARI-STEMI

• CONCLUSIONS AND RELEVANCE No significant differences were found for survival or other clinical end points at 30 days after the use of radial access vs femoral access in patients with STEMI referred for primary PCI. However, small absolute differences in end points cannot be definitively refuted given the premature termination of the trial.

• Kapadia: best clinical practice vs real world may be the difference? >> do we need to teach better femoral access?

JAMA Cardiol. 2020;5(2):126-134
The primary outcome of 30-day all-cause mortality was not significant between radial access and femoral access groups. As illustrated, the comparisons between the 2 groups are consistently nonsignificant across all subgroups. Squares represent mean values, with error bars representing 95% CIs. RR indicates relative risk; BMI, body mass index calculated as weight in kilograms divided by height in meters squared. To convert creatinine clearance to milliliters per second, multiply by 0.0167.

JAMA Cardiol. 2020;5(2):126-134
Conclusions

• Stable CAD?
• NSTEMI?

• Radial STEMI appeared to be the one MANTRA
  >> debunked by SAFARI

• PLUS: what if we do ultrasound-guided access? REBIRTH
Burke ... *Time to go home!*
Thank you!
Radial versus femoral access in patients with acute coronary syndromes undergoing invasive management: a randomised multicentre trial

Marco Valgimigli, Andrea Gagnor, Paolo Calabrò, Enrico Frigoli, Sergio Leonardi, Tiziana Zaro, Paolo Rubartelli, Carlo Briguori, Giuseppe Andò, Alessandra Repetto, Ugo Limbruno, Bernardo Cortese, Paolo Sganzerla, Alessandro Lupi, Mario Galli, Salvatore Colangelo, Salvatore Ierna, Ariuro Ausiello, Patrizia Presbitero, Gennaro Sardella, Ferdinando Varbella, Giovanni Esposito, Andrea Santarelli, Simone Tresoldi, Marco Nozzaro, Antonio Zingarelli, Nicoletta de Cesare, Stefano Rigattieri, Paolo Tosi, Cataldo Palmieri, Salvatore Brugaletta, Sunil V Rao, Dik Heg, Martina Rothenbühler, Pascal Vranckx, Peter Juni, for the MATRIX Investigators*
Findings
We randomly assigned 8404 patients with acute coronary syndrome, with or without ST-segment elevation, to radial (4197) or femoral (4207) access for coronary angiography and percutaneous coronary intervention. 369 (8%·8%) patients with radial access had major adverse cardiovascular events, compared with 429 (10%·3%) patients with femoral access (rate ratio [RR] 0·85, 95% CI 0·74–0·99; p=0·0307), non-significant at α of 0·025. 410 (9%·8%) patients with radial access had net adverse clinical events compared with 486 (11%·7%) patients with femoral access (0·83, 95% CI 0·73–0·96; p=0·0092). The difference was driven by BARC major bleeding unrelated to coronary artery bypass graft surgery (1%·6% vs 2%·3%, RR 0·67, 95% CI 0·49–0·92; p=0·013) and all-cause mortality (1%·6% vs 2%·2%, RR 0·72, 95% CI 0·53–0·99; p=0·045).

Interpretation In patients with acute coronary syndrome undergoing invasive management, radial as compared with femoral access reduces net adverse clinical events, through a reduction in major bleeding and all-cause mortality.
How on earth does mortality improve when we go radial?

- Different stents >>> No
- Different procedure time >>> No
- Same proceduralists

- Is it all about the bleeding?

- Is it really true?
The North American COVID-19 STEMI Registry

Santiago Garcia, MD
On Behalf of NACMI Investigators
Outline

1. STEMI and other CV emergencies during COVID-19 pandemic
2. Late Presentations/OHCA data
3. NACMI- Main results and subgroups
Where did the heart attacks go?

Garcia et al. JACC 2020
Where did the heart attacks go?
Expanded analysis 17 STEMI Program, 4 US regions

Garcia et al. CCI 2020
Where did the heart attacks go?

Expanded analysis 17 STEMI Program, 4 US regions

D2B: Increased 20 minutes
STEMI Volume
Comparison by COVID Incidence

AC periods includes only Early phase of the pandemic March –April 2020
STEMI Volume
Comparison by Initiation of stay at home orders

MHIF Cardiovascular Grand Rounds
James B Herrick (1861–1954)
Certain clinical features of sudden obstruction of the coronary arteries.

JAMA 1912; 59:2015-20

“The importance of absolute rest in bed for several days is clear.”
“The prevailing view is that patients with cardiac disease are expected to die in bed. If fatalities occur out of bed, the physician is held culpable”
Myocardial mortality rates in the early era of coronary reperfusion

3 decades of progress in STEMI care lost in 2 months?

Where did the heart attacks go?

To the morgue

Out-of-hospital cardiac arrest during the COVID-19 pandemic in Paris, France: a population-based, observational study

Marijon et al. Lancet 2020
58% Increase in out of hospital cardiac arrest in Italy

- Lombardi Cardiac Arrest Registry (4 provinces)
- Total COVID-19 Cases: 9806
- Total Cases of OHCA: 362 vs. 229 during same period 2019 (58% increase)
- Total Cases of OHCA with confirmed COVID-19: 103
Cardiac Arrest
911 Calls in NYC

Heart-wrenching
New York City

Cardiac-arrest 911 calls
To April 5th

Cardiac-arrest deaths
To April 5th

Confirmed covid-19 deaths *
To April 10th

Sources: New York City Fire Department; New York City Department of Health  *Deaths are reported with a significant lag and may be revised later.

The Economist
Other CV Emergencies: Where did the strokes go?
Late Presentations

- 67 yo female
- Did not present to ED due to fear of contracting COVID
- 14 hours later Q-waves inferiorly
- Failed PCI

Alsidawi S et al. JACC Case reports.
Late Presentations
5-days later
MHI Case #2

Anterior MI, fear of contracting COVID, presented 1 week later in heart failure
Elected palliative care, died from free wall rupture
When COVID and Heart attacks Coexist

• Patients with cardiovascular disease have increased risk of mortality with COVID-19
• 15-28% of COVID+ patients admitted to the hospital have elevated Troponin
• Some advocated for a shift to pharmacological reperfusion
• Dismal prognosis (72% mortality in NYC)
## STEMI Series IN COVID 19 – Literature review

<table>
<thead>
<tr>
<th></th>
<th>New York Series, n = 18</th>
<th>Lombardy Series, n = 28</th>
<th>London Series, n = 39</th>
<th>French series, n=11</th>
<th>International, n=78</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Population</strong></td>
<td>6 Hospitals in New York, USA, n of 18</td>
<td>All PCI capable hospitals (?n) in Lombardy Italy, n of 28</td>
<td>115 Consecutive STEMI patients at Barts Heart centre (39 positive for COVID-19)</td>
<td>83 Consecutive STEMI patients at University of Hospital of Nancy, France, (11 positive for COVID-19)</td>
<td>Lithuania, Italy, Spain and Iraq –</td>
</tr>
<tr>
<td><strong>Time Frame</strong></td>
<td>March 2020</td>
<td>Feb 20\textsuperscript{th} – March 30\textsuperscript{th}, 2020</td>
<td>March 01 to May 20, 2020</td>
<td>Feb 26\textsuperscript{th} – May20, 2020</td>
<td>Feb 1\textsuperscript{st} to April 15\textsuperscript{th}, 2020</td>
</tr>
<tr>
<td><strong>Demographics</strong></td>
<td>Median age 63, 83% Male, 67% intubated</td>
<td>Mean age 68, 71% Male</td>
<td>Mean age of 62, 85% Male, 13% intubated</td>
<td>Mean age of 63.6, 64% male</td>
<td>median age of 65, 63% men</td>
</tr>
<tr>
<td><strong>COVID 19 Diagnosis</strong></td>
<td>N/A</td>
<td>Reverse transcriptase PCR</td>
<td>Reverse transcriptase PCR OR symptoms + chest imaging</td>
<td>Reverse transcriptase PCR OR symptoms + chest imaging</td>
<td>Confirmed - positive result on PCR testing of a nasopharyngeal sample.</td>
</tr>
<tr>
<td><strong>Chest pain as initial symptom</strong></td>
<td>6/18 (33%) had chest pain</td>
<td>22/28 (79%)</td>
<td>11/39 had cardiac arrest as initial presentation</td>
<td>4/11 had cardiac arrest as initial presentation</td>
<td>18% were intubated</td>
</tr>
<tr>
<td><strong>Strength of the study</strong></td>
<td>First paper to describe STEMI</td>
<td>Looked at thrombus grade for Grade 5 thrombus, TIMI flow, Blush score 3 interventionists blinded to study looked at images</td>
<td>2 angiographers scored angiograms for thrombotic MINOCA independently</td>
<td>Multi-center</td>
<td></td>
</tr>
<tr>
<td><strong>LVEF</strong></td>
<td>9/17 (53%) had abnormal LVEF</td>
<td>LVEF Mean of 42%</td>
<td>LVEF median of 43%</td>
<td>8/11 had LVEF of &lt; 45%</td>
<td>Median of 39% in PPCI group Median of 44% in lytic group</td>
</tr>
<tr>
<td><strong>Angiograms</strong></td>
<td>9/18 had angiograms; 6/9 (67%) had Obstructive CAD</td>
<td>28/28 had angiograms 17/28 (61%) had Obstructive CAD</td>
<td>39/39 had angiograms 32/39 had TIMI 0/1 (82.1%)</td>
<td>6 of 11 (54%) had thrombotic MINOCA (non-atherosclerotic), compared to</td>
<td>19/78 (25%) had PCI as primary reperfusion strategy 4/19 had stent thrombosis 18/19 had obstructive CAD</td>
</tr>
<tr>
<td><strong>Hosp Mortality</strong></td>
<td>13/18 (72%)</td>
<td>11/28 (39.3%)</td>
<td>7/39 (18%)</td>
<td>3/11 (27%)</td>
<td>9/78 (12%) - (26% in PCI group, and 7% in fibrinolytic group)</td>
</tr>
</tbody>
</table>
#CardioTwitter: STEMI in COVID with non-obstructive CAD
North American COVID Myocardial Infarction Registry (NACMI): A Unique Collaboration
Pathways for enrollment into NACMI

Patient 1
Suspected COVID-19

Clinical diagnosis of coronary MI

Successful primary PCI; COVID-19 ruled out 24 hours later

Patient 2
Confirmed COVID-19

Clinical diagnosis of non-coronary MI

No fibrinolysis; no coronary angiogram

Patient 3
Confirmed COVID-19

Clinical diagnosis of coronary MI

Fibrinolysis followed by successful angioplasty

May be enrolled in NACMI Registry
**NACMI-Initial Results**

**COVID Positive Patients (n = 230)**

- More than 50% of patients are ethnic minorities

**PUI (n = 495)**

- Presentation: Cardiogenic shock (18%), Pulmonary infiltrates (40%), Dyspnea (54%)

**Age and Gender Matched Control (n = 460)**

- Less likely to receive invasive angiography

**In-Hospital Outcomes**

- In-hospital outcomes: MAE, Death, Stroke

**Initial Findings From the North American COVID-19 Myocardial Infarction Registry**

Santiago Garcia, MD,1 Payam Dehghani, MD,1 Cindy Grines, MD,1,2 Laura Davidson, MD,1,2 Keshov R. Nayak, MD1,2,9 Jacqueline Saw, MD1,2, Ron Waksman, MD1,2 John Blair, MD,1 Bagai Akihuy, MD,1,2,9 Ross Garberich, MS,1,2,9

Christian Schmidt, MS1,2 Hung Q. Ly, MD, SM1,3 Scott Sharkey, MD1,2 Nestor Mercado, MD1,2 Carlos E. Alfonso, MD1,2 Naoki Mimaia, MD1,2 Deepak Acharya, MD1,2 Mina Madan, MD1,2 Abdul Meiz Hafiz, MD1,2,9 Nosheen Javed, MD1,2,9 Jay Shavalia, MD1,2 Jay Stone, MD1,2 M. Chadi Al-Araies, MD1,2 Wah Htin, MD1,2 William Downey, MD1,2 Brian A. Bergmark, MD1,2 Josph Shingger, MD1,2 Tareq Alyassaf, MD1,2,9 Houman Khaili, MD1,2,9 Chao-Wei Hwang, MD, PhD1,2,9,20 Joshua Parow, MD, PhD1,2,9 Alexander Llanos, MD1,2,9 Brent McGrath, MD1,2,9 Mark Tannenbaum, MD,1,2 Jon Rosz, MD,1,2 Rodrigo Bagur, MD1,2 Pedro Cox-Alomar, MD1,2

Adi G. Stefanescu Schmid, MD, MSc1,2,9,20,21 Lindsey A. Cilla, MD1,2 Farouc A. Jaffer, MD, PhD1,2 Michael Gracholonsky, MD1,2 Michael Sallinger, MD1,2 Brian Case, MD1,2 Amrour Rabour, MD,1,2,9,20 Xuming Dai, MD1,2,9,20 Osama ElKhatieeb, MD, PhD1,2,9,20 Taiset Kobayashi, MD1,2,9,20 Habib-Ho Kim, MD1,2,9,20 Mazen Roumia, MD1,2,9,20 Frank V. Agnire, MD1,2,9,20 Jeffrey Rado, MD1,2,9,20 Aun-Young Chong, MD1,2,9,20 Hurst M. Hall, MD1,2,9,20 Shy Amlani, MD, PhD1,2,9,20 Alireza Bagherli, MD1,2,9,20 Rajan A.G. Patel, MD1,2,9,20 David A. Wood, MD1,2,9,20,21 Frederick G. Welt, MD, PhD, MPH1,2,9,20 Jay Gilr, MD, MPH1,2,9,20 Ebstin Mahmud, MD1,2,9,20

Timothy D. Henry, MD,1,2,9,20 on behalf of the Society for Cardiac Angiography and Interventions, the Canadian Association of Interventional Cardiology, and the American College of Cardiology Interventional Council

*Garcia et al. JACC 2021*
Registry Timeline

Steering committee formed

Rationale paper submitted AHJ
Patients enrolled

171 COVID + 423 PUI
TCT LateBreaker

64 Clinical Sites
230 COVID + 495 PUI
JACC paper submitted

331 COVID + 645 PUI
SCAI LateBreaker

GOAL: 500 COVID +

March 26th, 2020
April 27th, 2020
Oct 2020 TCT
Dec 1st, 2020
Feb 8, 2021
Apr 15, 2021
Sept 2021
## Baseline characteristics of COVID Positive and PUI

<table>
<thead>
<tr>
<th></th>
<th>COVID positive (n=331)</th>
<th>PUI (n=645)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt;55</td>
<td>252 (76)</td>
<td>462 (72)</td>
<td>0.114</td>
</tr>
<tr>
<td>History of CAD</td>
<td>76 (26)</td>
<td>168 (27)</td>
<td>0.552</td>
</tr>
<tr>
<td>Non-Caucasian</td>
<td>186 (55)</td>
<td>180(25)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>140 (47)</td>
<td>354 (59)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>135 (44)</td>
<td>302 (33)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI, mean ± SD</td>
<td>29.2±6.3</td>
<td>29.7±7.1</td>
<td>0.31</td>
</tr>
<tr>
<td>Arterial Hypertension</td>
<td>231 (73)</td>
<td>452 (72)</td>
<td>0.73</td>
</tr>
<tr>
<td>History of heart failure</td>
<td>49 (17)</td>
<td>64 (11)</td>
<td>0.009</td>
</tr>
<tr>
<td>Statin on Admission</td>
<td>128 (39)</td>
<td>225 (35)</td>
<td>0.244</td>
</tr>
</tbody>
</table>
## Presentation COVID Positive and PUI

<table>
<thead>
<tr>
<th></th>
<th>COVID positive (n=331)</th>
<th>PUI (n=645)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptoms on presentation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dyspnea</td>
<td>169 (51)</td>
<td>228 (35)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Chest pain</td>
<td>175 (53)</td>
<td>514 (80)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Syncope</td>
<td>10 (3)</td>
<td>33 (5)</td>
<td>0.131</td>
</tr>
<tr>
<td><strong>Abnormal Chest X ray findings</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infiltrates</td>
<td>149 (45)</td>
<td>101 (16)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>30 (9)</td>
<td>43 (7)</td>
<td>0.178</td>
</tr>
<tr>
<td>Cardiomegaly</td>
<td>27 (8)</td>
<td>36 (6)</td>
<td>0.121</td>
</tr>
<tr>
<td><strong>High-Risk Pre-PCI conditions</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac arrest pre-PCI</td>
<td>32 (11)</td>
<td>91 (15)</td>
<td>0.144</td>
</tr>
<tr>
<td>Shock pre-PCI</td>
<td>46 (16)</td>
<td>79 (13)</td>
<td>0.177</td>
</tr>
<tr>
<td>Ejection Fraction mean-SD</td>
<td>45 (33,55)</td>
<td>45 (35,53)</td>
<td>0.638</td>
</tr>
<tr>
<td>In-House presentation of MI</td>
<td>21 (7)</td>
<td>10 (2)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Reperfusion Strategies

- 80% underwent angiography
- PPCI (71% of patients referred for angio, 55% of overall group)

<table>
<thead>
<tr>
<th></th>
<th>COVID+</th>
<th>PUI</th>
<th>P-value</th>
<th>Historical Control</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Angio</td>
<td>22%</td>
<td>4%</td>
<td>&lt;0.001</td>
<td>0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>D2B time, median (IQR)</td>
<td>79 (52,125)</td>
<td>77 (55,119)</td>
<td>0.989</td>
<td>66 (46,93)</td>
<td>0.008</td>
</tr>
<tr>
<td>D2B time &lt; 90 minutes (%)</td>
<td>58%</td>
<td>63%</td>
<td>0.422</td>
<td>73%</td>
<td>0.006</td>
</tr>
</tbody>
</table>
Updated Clinical Outcomes in NACMI

- COVID 19 +
- PUI
- Age and Sex Matched Controls

- Primary Endpoint: 14 COVID 19 +, 5 PUI, 4 Age and Sex Matched Controls
- Mortality: 33 COVID 19 +, 11 PUI, 3 Age and Sex Matched Controls
- Stroke: 2 COVID 19 +, 2 PUI, 3 Age and Sex Matched Controls
- Re-infarction: 2 COVID 19 +, 2 PUI, 3 Age and Sex Matched Controls
- ICU Stay: 3 COVID 19 +, 3 PUI, 2 Age and Sex Matched Controls
- Total Length of Stay: 6 COVID 19 +, 3 PUI, 2 Age and Sex Matched Controls
NACMI Patient (MHI)

73-year-old man had in-hospital STEMI (hospital day 3) while intubated in the ICU with severe COVID infection and ARDS. He is taken to the CV lab and receives PPCI for an occluded RCA. Next day, VA ECMO is started for cardiogenic shock and refractory hypoxemia.

On day 5, a CT scan shows intracranial bleeding. Family withdrew support.
Multi-Variate Predictors of Death in COVID + STEMI (n=331)
NACMI Risk Score

Risk Factors | Integer Score
---|---
Dyspnea on presentation | 3
Infiltrates on Chest X-ray | 4
Shock Pre-PCI | 4
Diabetes | 5
Age > 55 | 8
Any Mechanical Support | 9
Mechanical Ventilation | 13

Calculate Total Risk Score

Proportion In Hospital Mortality

- <9 Low: <1%
- 9-15 Moderate: 16%
- 16-25 High: 38%
- >25 Very High: 65%
MCS in NACMI
13 % of COVID + Patients

All STEMI Patients
n=1043

COVID-19
n=377

MCS
n=51

No MCS
n=326

PUI
n=666

MCS
n=87

No MCS
n=579
MCS Devices in NACMI
13% of COVID+ Patients

- In-hospital Mortality
  - COVID+/MCS+: 59%
  - COVID+/MCS-: 26%
Ongoing Analyses

• 1-year Follow-up of survivors
• Angiographic core lab
• ECG core lab
• Gender and ethnic differences
• Canada vs. USA
• Risk score
• MCS
Acknowledgments

MHIF  
ACC  
SCAI  

Industry sponsors
• Medtronic  
• Abbott Vascular
The North American COVID-19 STEMI Registry

Santiago Garcia, MD
## COVID-19 Hospitalization and Death by Race/Ethnicity

**Updated Nov. 30, 2020**

Race and ethnicity are risk markers for other underlying conditions that affect health including socioeconomic status, access to health care, and exposure to the virus related to occupation, e.g., frontline, essential, and critical infrastructure workers.

<table>
<thead>
<tr>
<th>Rate ratios compared to White, Non-Hispanic persons</th>
<th>American Indian or Alaska Native, Non-Hispanic persons</th>
<th>Asian, Non-Hispanic persons</th>
<th>Black or African American, Non-Hispanic persons</th>
<th>Hispanic or Latino persons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases(^1)</td>
<td>1.8x</td>
<td>0.6x</td>
<td>1.4x</td>
<td>1.7x</td>
</tr>
<tr>
<td>Hospitalization(^2)</td>
<td>4.0x</td>
<td>1.2x</td>
<td>3.7x</td>
<td>4.1x</td>
</tr>
<tr>
<td>Death(^3)</td>
<td>2.6x</td>
<td>1.1x</td>
<td>2.8x</td>
<td>2.8x</td>
</tr>
</tbody>
</table>