I have nothing to disclose.
Large Thrombus Burden

Olivier Muller MD/PhD
University Hospital of Lausanne
Switzerland
Large thrombus burden

- 60 yo male
- HTA, smoking
- STEMI inferior lead
- 3 hours of chest pain
- Clopidogrel 600 mg
- Aspirin 500 mg
- Heparin 5000 U
Clinical implications

• Predictor of complications?

• Management of large thrombus burden
Clinical implications

- 8 prospective randomized trials
  - 2,752 patients with visible thrombus
  - 5,165 without thrombus
  - 6 trials (1986-1995)
    • CAVEAT
    • CAVEAT-II
    • CADRES
    • PBC
    • EPIC
    • IMPACT-II

- Several adverse outcomes were higher in patients with thrombus:
  - death/MI (8.4 vs. 5.5%, p ≤ 0.001),
  - in-hospital abrupt closure (5.9 vs. 3.9%, p ≤ 0.001)
  - in-hospital composite of death, MI and/or repeat revascularization (15.4 vs. 11.2%, p ≤ 0.001).

Singh et al., JACC vol 38;3, 2001
### Thrombosis grade classification

<table>
<thead>
<tr>
<th>Thrombus Grade</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombus grade 0 (G0)</td>
<td>No angiographic characteristics of thrombus are present</td>
</tr>
</tbody>
</table>
| Thrombus grade 1 (G1) | Possible thrombus is present, with such angiography characteristics as  
- Reduced contrast density, haziness, irregular lesion contour,  
- Or a smooth convex meniscus at the site of total occlusion suggestive but not diagnostic of thrombus; in thrombus |
| Thrombus grade 2 (G2) | There is definite thrombus, with greatest dimensions < 1/2 the vessel diameter |
| Thrombus grade 3 (G3) | There is definite thrombus but with greatest linear dimension >1/2 but < 2 vessel diameters |
| Thrombus grade 4 (G4) | There is definite thrombus with greatest linear dimension > 2 vessel diameters |
| Thrombus grade 5 (G5) | There is total occlusion (unable to assess thrombus burden due to total vessel occlusion). |
Thrombosis grade classification

- Thrombus grade 1
- Thrombus grade 2
- Thrombus grade 3
- Thrombus grade 4
- Thrombus grade 5
Thrombosis grade classification

- Thrombus grade 1
- Thrombus grade 2
- Thrombus grade 3
- Thrombus grade 4

Small Thrombus Burden

Large Thrombus Burden
Thrombus burden: clinical implications

![Graph showing cumulative MACE rate over months of follow-up for LTB and STB](image-url)
Clinical implications

• Predictor of complications? YES
  – Distal embolization
  – Stent thrombosis

• Management of large thrombus burden
Management

Several mechanical and pharmacological management tools have been tested in large randomized clinical trials for the prevention of distal embolization in patients with AMI, and only specific treatments for large thrombus have been reported in small studies.
Management of Thrombus in PCI

**Devices**
- Manual Aspiration catheter
- Mechanical aspiration catheter
- Distal protection

**Pharmacotherapy**
- Antithrombotics
- Antiplatelets
- Thrombolytics

**Treatment of no-reflow**
- Adenosine
- Ca++ blockers
- Nitroprusside
These results were impressive but not conclusive, since this was a single center study and since the study was not powered to detect differences in clinical endpoints, and mortality was not a pre-specified endpoint.
Meta-analysis of manual thrombectomy

9 RT
2417 patients

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Number of studies</th>
<th>Number of patients</th>
<th>30-Day mortality (manual thrombectomy)</th>
<th>30-day Mortality (Control)</th>
<th>30-day mortality [OR (95% CI)]</th>
<th>P-value</th>
<th>P-heterogeneity</th>
<th>P-interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>9</td>
<td>2401</td>
<td>21/1200</td>
<td>37/1201</td>
<td>0.58 (0.34–0.98)</td>
<td>0.04</td>
<td>0.97</td>
<td>0.82</td>
</tr>
<tr>
<td>Published^</td>
<td>5</td>
<td>1629</td>
<td>17/809</td>
<td>31/820</td>
<td>0.55 (0.31–1.00)</td>
<td>0.05</td>
<td>0.79</td>
<td></td>
</tr>
<tr>
<td>Unpublished</td>
<td>4</td>
<td>772</td>
<td>4/391</td>
<td>6/381</td>
<td>0.69 (0.22–2.21)</td>
<td>0.53</td>
<td>0.9</td>
<td></td>
</tr>
<tr>
<td>Large size (&gt;150 patients)</td>
<td>5</td>
<td>2031</td>
<td>18/1016</td>
<td>31/1015</td>
<td>0.58 (0.32–1.04)</td>
<td>0.07</td>
<td>0.95</td>
<td>0.86</td>
</tr>
<tr>
<td>Small size (≤150 patients)</td>
<td>4</td>
<td>370</td>
<td>3/184</td>
<td>6/186</td>
<td>0.56 (0.16–1.99)</td>
<td>0.37</td>
<td>0.6</td>
<td></td>
</tr>
<tr>
<td>High study quality</td>
<td>4</td>
<td>1553</td>
<td>17/771</td>
<td>29/782</td>
<td>0.58 (0.32–1.07)</td>
<td>0.08</td>
<td>0.77</td>
<td>0.78</td>
</tr>
<tr>
<td>Low study quality</td>
<td>5</td>
<td>848</td>
<td>4/429</td>
<td>8/419</td>
<td>0.56 (0.19–1.62)</td>
<td>0.28</td>
<td>0.88</td>
<td></td>
</tr>
</tbody>
</table>
Manual aspiration
Meta-analysis of aspiration

- 30 RT
- 6415 patients
- Comparison
  - Manual aspiration
  - Mechanical aspiration
  - Embolic protection
Mechanical aspiration
Mechanical aspiration
Meta-analysis:

11 RT
5 RT missing
2686 patients
Patient level analysis
Pharmacotherapy
Thrombolytic / GP IIb/IIIa

- Full-dose lytic therapy
- Half-dose lytic therapy with a glycoprotein (GP)IIb/IIIa inhibitor
- GPIIb/IIIa inhibitor alone

There is no evidence of a significant clinical benefit with any of these agents

ASSENT-4, Lancet 2006;367:569–578
Antiplatelets therapy
Guidelines

GP IIb/IIa inhibitors should be considered for bailout therapy if there is angiographic evidence of massive thrombus, slow or no-reflow or a thrombotic complication.

ESC 20102

ACC/AHA 2011
Abciximab: IC vs IV meta-analysis

IC abciximab administration cannot be routinely recommended, but may be considered in high-risk patients.
Intracoronary vs intravenous abciximab

2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention

CLASS IIb
1. In patients undergoing primary PCI with abciximab, it may be reasonable to administer intracoronary abciximab (589,591–604).

(Level of Evidence: B)
Large Thrombus Burden

Intracoronary bolus Abciximab
Large Thrombus Burden

Manual aspiration (2\textsuperscript{nd})
Large Thrombus Burden

Stenting (DES)
Algorithm treatment of no-reflow


No reflow

Exclude another cause

Thrombus, Spasm, Dissection, air embolism
- NTG 100-200 mcg to 4 bolus
- Distal contrast injections

Check ACT

Target 200-250 s
UFH:UFH + 2b/3a

Delivery system
- Guiding catheter
- Over-the-wire catheter
- Micocatheter
- Aspiration catheter

Hemodynamic stabilization

Pressors Agents
IABP
O2 delivery
Pacemaker

Never shown to be effective
1. Nitroglycerin (arteriols > 100 mm)

First line management (each bolus can be given several times)
1. Adenosine up to 60 mcg bolus
2. Verapamil up to 500 mcg bolus or 100 mcg/min up to 1000 mcg total, with temporary pacer on standby
3. Nitroprusside 50 to 200 mcg bolus, up to 1000 mcg total dose
4. Epinephrine 50-200 ug
5. Nicardipine 200 ug
6. Nicorandil 4mg
7. Diltiazem 0.5 – 2.5 mg over 1 min up to 5 mcg

Exclude another cause

Final Results

Adenosine IC bolus
Verapamil bolus
20 minutes
Conclusions Large Thrombus Burden

- Large thrombus burden is associated with worse prognosis

- Large RCT are needed to evaluate the efficacy of thrombectomy device / pharmacotherapy (IC vs IV) according to thrombus grade
Thank you

Centre Hospitalier Universitaire Vaudois
Lausanne, Suisse
<table>
<thead>
<tr>
<th>Grade</th>
<th>Thrombus Definition</th>
<th>Angiographic Examples</th>
<th>Mehta Classification</th>
<th>Technical Tips of Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No cine angiographic characteristics of thrombus present</td>
<td></td>
<td>Aspiration Catheter</td>
<td>• Most effective with fresh clot; organized thrombus is more resistant to debulking.</td>
</tr>
<tr>
<td>1</td>
<td>Possible thrombus present. Angiography demonstrates reduced contrast density, haziness, irregular lesion contour or a smooth convex &quot;meniscus&quot; at the site of total occlusion suggestive but not diagnostic of thrombus</td>
<td></td>
<td>Direct Stent+/Pre dilatation</td>
<td>• Have different profiles, different push-ability, tractability and aspiration rates.</td>
</tr>
<tr>
<td>2</td>
<td>Thrombus present-small size: Definite thrombus with greatest dimensions less than or equal to ½ vessel diameter</td>
<td></td>
<td>Aspiration thrombectomy</td>
<td>• All are 6F-compatible. It is useful to stock and be familiar with the use of at least one.</td>
</tr>
<tr>
<td>3</td>
<td>Thrombus present- moderate size: Definite thrombus but with greatest linear dimension greater than ½ but less than 2 vessel diameters</td>
<td></td>
<td></td>
<td>• Flush catheter lumen well before use as it facilitates better tracking over the wire.</td>
</tr>
<tr>
<td>4</td>
<td>Thrombus present- large size: As in Grade 3 but with the largest dimension greater than or equal to 2 vessel diameters</td>
<td></td>
<td></td>
<td>• Avoid kinking the catheter – advance slowly over the initial, softer portion of the catheter.</td>
</tr>
<tr>
<td>5</td>
<td>Total occlusion</td>
<td></td>
<td>Angio Jet</td>
<td>• Monitor distal tip of the guide wire as the aspiration catheter is advanced – it is not uncommon for the guide wire to advance during this maneuver.</td>
</tr>
</tbody>
</table>

**Technical Tips of Use for Aspiration Catheter and Angio Jet**

- Aspiration Catheter
  - • Most effective with fresh clot; organized thrombus is more resistant to debulking.
  - • Have different profiles, different push-ability, tractability and aspiration rates.
  - • All are 6F-compatible. It is useful to stock and be familiar with the use of at least one.
  - • Flush catheter lumen well before use as it facilitates better tracking over the wire.
  - • Avoid advancing in severe tortuosity and in vessels<2mm.
  - • Since the Angiojet is used for large thrombus burden and high thrombus grade, consider Abciximab as adjunctive therapy.

- Angio Jet
  - • Can be used from the radial route. Although LAD and some LCX may not need a TPM, I place TPM’s in all Angiojet procedures.
  - • Often, multiple passes will be required. Try to pause after every 2-3 passes to enable hemodynamics to be restored, to optimize guide wire and guiding catheter support and to evaluate the results.
  - • Often, just the first passage will restore adequate flow.
  - • Resistant and stubborn thrombus will require more distal advancement that must be done more carefully.
  - • Avoid advancing in severe tortuosity and in vessels<2mm.
• **Limitations of the Mehta Strategy**
  - Several catheterization laboratories are not equipped with mechanical thrombectomy devices (AngioJet, Medrad Interventional/Possis, Minneapolis, Minnesota). Operators are unfamiliar with their use, which can delay D2B. Abciximab via the Atrium Clearway catheter provides a good alternative.
  - The new rheolytic thrombectomy device narrowed our relative contraindications (< 2.0 mm vessel size and severe tortuosity) regarding unfavorable anatomy.
  - We recommend mechanical thrombectomy for large thrombus grade, but in some cases thrombo-aspiration can work (Figure 5). Excellent debulking is observed with aspiration catheters. We suspect this happens in patients who present early, with fresh, red, soft thrombi that are easily and completely aspirated with these catheters. This observation is contrary to our proposed hypothesis, yet this powerful observation is shared for its tremendous practical benefit. Incidentally, this is also a rare situation where we will use a low-profile balloon to verify that the guidewire is in the true lumen. We currently postulate thrombo-aspiration as a default strategy. The rationale is the aspiration catheters are user-friendly, relatively inexpensive and take less than a balloon catheter to prep and deploy. With this methodology, we grade thrombus nevertheless, then quickly make a pass with the aspiration catheter, and either persist with more thrombo-aspiration or advance to using mechanical thrombectomy.
  - In some cases, even with moderate thrombus burden, the dense, organized thrombus cannot be debulked with thrombo-aspiration (Figures 6a and 6b).
  - Several newer trials appear to validate our strategy with the appropriate presently available devices. Founded on extensive experience, we feel confident in our strategy for effective thrombus management for STEMI interventions; nevertheless, this strategy needs endorsement by clinical trials. A single individual experience, irrespective of its expertise, cannot substitute for data from large, randomized, clinical trials and/or established guidelines.
  - We have also explored possibilities of using a time-to-presentation based strategy for applying a thrombectomy device. This idea is akin to use of prehospital lysis, as in the CAPTIM Trial, where the cohorts of very early AMI patients benefit from early lysis. This probably results from effective lysis of a fresh clot. Thrombo-aspiration is effective therapy for early presenters (< 6 hours) and mechanical thrombectomy for late presenters (> 6 hours). Calculating time-to-presentation is challenging. Many variables affect thrombus presentation in STEMI, and the heterogeneity of thrombus and of its over-simplification. Interventional management of soft, red, early thrombus is quite different than that of dense, organized thrombus.
• **Conclusion**
• Dedicated attention to thrombus cannot be underestimated in STEMI interventions. Mechanical adjunct devices are useful tools for PCI, especially in evading distal embolization.
Table 1. Meta-analyses evaluating aspiration thrombectomy with primary PCI

<table>
<thead>
<tr>
<th>Meta-analysis</th>
<th>Number of Trials</th>
<th>Number of Patients</th>
<th>TIMI 3 Flow</th>
<th>MBG</th>
<th>STR</th>
<th>No Re-flow</th>
<th>Distal Emboli</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bavry et al(^5)</td>
<td>13</td>
<td>3,026</td>
<td>positive</td>
<td>positive</td>
<td>positive</td>
<td>positive</td>
<td>positive</td>
<td>positive</td>
</tr>
<tr>
<td>De Luca et al(^7)</td>
<td>9</td>
<td>2,417</td>
<td>positive</td>
<td>positive</td>
<td>positive</td>
<td>positive</td>
<td>positive</td>
<td>positive</td>
</tr>
<tr>
<td>Burgotta et al(^8)</td>
<td>11</td>
<td>2,686</td>
<td>positive</td>
<td>positive</td>
<td>positive</td>
<td>positive</td>
<td>positive</td>
<td>positive</td>
</tr>
<tr>
<td>Mongeon et al(^10)</td>
<td>16</td>
<td>3,365</td>
<td>positive</td>
<td>positive</td>
<td>positive</td>
<td>positive</td>
<td>positive</td>
<td>positive</td>
</tr>
</tbody>
</table>

TIMI-3 Flow = TIMI 3 Flow post-PCI; MBG = myocardial blush grade post-PCI; STR = ST-segment resolution post-PCI
Positive indicates significant benefit with aspiration thrombectomy compared with control.
Neutral indicates no significant difference between aspiration thrombectomy and control.
Guidelines

ACC/AHA revascularization

- Trials of GP IIb/IIIa inhibitors in the setting of STEMI and primary PCI were conducted in the era before routine stenting and DAPT. The results of these and more recent trials, as well as several meta-analyses, have yielded mixed results.

- Therefore these agents might provide more benefit in selective use, such as in patients with large anterior MI and/or large thrombus burden.

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