1ry PCI large thrombus burden

Hany Ragy MD

EAZI Fellows course

December 2013 Cairo

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Thrombus Presence in STEMI

- Angiographic thrombus is evident in over 70% of STEMI Patients

DeWood et al. NEJM 1986;315:417-23
Simplified Thrombus Classification

- **Small thrombus burden**: from haziness in vessel to a filling defect of less than 2X the vessel diameter
- **Large thrombus burden**: more than 2X the diameter of the reference vessel
- **Massive thrombus burden**: typical of cases frequently treated by AngloJet Thrombectomy

Class 1-2  Class 3-4  Class ???

Thrombus: the Problem

- No reflow
- Distal Embolization
- Stent Thrombosis
**Angiographic Stent Thrombosis After Routine Use of Drug-Eluting Stents in ST-Segment Elevation Myocardial Infarction**

**The Importance of Thrombus Burden**

Georgios Sianos, MD, PhD, Michail I. Papaefthymi, MD, Joost Daemen, MD, Sofia Vaima, MD, Carlos A. van Mieghem, MD, Ron T. van Domburg, PhD, Lampros K. Michalis, MD, MRCP, Patrick W. Serruy, MD, PhD, FACC

**Objectives**

This study sought to investigate the impact of thrombus burden on the clinical outcome and angiographic infarct-related artery stent thrombosis (IRA-ST) in patients routinely treated with drug-eluting stent (DES) implantation for ST-segment elevation myocardial infarction (STEMI).

**Background**

There are limited data for the safety and effectiveness of DES in STEMI.

**Methods**

We retrospectively analyzed 812 consecutive patients treated with DES implantation for STEMI. Intracoronary thrombus burden was angiographically estimated and categorized as large thrombus burden (LTB), defined as thrombus burden =2 vessel diameters, and small thrombus burden (STB) to predict clinical outcomes. Major adverse cardiac events (MACE) were defined as death, repeat myocardial infarction, and IRA reintervention.

**Results**

Mean duration of follow-up was 18.2 ± 7.8 months. Large thrombus burden was an independent predictor of mortality (hazard ratio [HR] 1.75, \( p = 0.022 \)) and MACED (HR 1.68, \( p = 0.001 \)). The cumulative angiographic IRA-ST rate was 3.1% at 30 days and 3.2% at 2 years, and continued to augment beyond 2 years. It was significantly higher in the LTB group compared with the STB group (8.2% vs. 1.3% at 2 years, respectively, \( p < 0.001 \)). Significant independent predictors for IRA-ST were LTB (HR 8.77, \( p = 0.001 \)), stent thrombosis at presentation (HR 6.24, \( p = 0.001 \)), bifurcation stenting (HR 4.00, \( p = 0.002 \)), age (HR 0.95, \( p = 0.003 \)), and rheolytic thrombectomy (HR 0.11, \( p = 0.03 \)).

**Conclusions**

Large thrombus burden is an independent predictor of MACE and IRA-ST in patients treated with DES for STEMI. (J Am Coll Cardiol 2007;50:573-83) © 2007 by the American College of Cardiology Foundation

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**Impact of Thrombus Burden with DES in AMI**

**792 STEMI Patients with DES**

- **Small**
  - Final TIMI 3: 94.9%
  - TMPG-3: 53.2%
  - No-reflow: 0.5%
  - Distal Embol.: 3.5%
  - Total Population: 8.2%

- **Large**
  - Final TIMI 3: 83.6%
  - TMPG-3: 35.4%
  - No-reflow: 4.0%
  - Distal Embol.: 17.3%
  - Total Population: 3.2%

*P<0.001

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Sianos G et al, J Am Coll Cardiol 2007; 50:573-83
**Thrombectomy Devices**

**Manual Aspiration**

**Mechanical**

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**UCR**
Uppsala Clinical Research Center

**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
Conclusions

- This large, prospective, registry-based randomized clinical trial showed:
  - no reduction of mortality at 30 days
  - no significant reduction of hospitalization for MI or of stent thrombosis at 30 days
  - no reduction of other important clinical endpoints during hospitalization
- Our findings leave little role for manual thrombus aspiration as a routine adjunct to PCI in STEMI

1.1. AngioJet Rheolytic Thrombectomy
**AIMI Randomized Trial**
(N=480)

- **AngioJet**
  - STR >70% @ 90 mins: 60%
  - Infarct size (mean): 12.5%
- **Control**
  - STR >70% @ 90 mins: 68%
  - Infarct size (mean): 9.8%

- **P=0.14**
- **P<0.02**

All et al. JACC 2006

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**MACE by 30 Days**
(N=480)

<table>
<thead>
<tr>
<th>Event</th>
<th>AngioJet</th>
<th>Control</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>4.6%</td>
<td>0.8%</td>
<td>P&lt;0.02</td>
</tr>
<tr>
<td>Reinfarction (Q-wave)</td>
<td>0%</td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>1.7%</td>
<td>0.8%</td>
<td></td>
</tr>
<tr>
<td>SAT/TLR</td>
<td>2.1%</td>
<td>0.4%</td>
<td>P&lt;0.01</td>
</tr>
<tr>
<td>MACE</td>
<td>6.7%</td>
<td>1.7%</td>
<td></td>
</tr>
</tbody>
</table>

Columbia University Medical Center
Comparison of AngioJet Rheolytic Thrombectomy Before Direct Infarct Artery Stenting With Direct Stenting Alone in Patients With Acute Myocardial Infarction

The JETSTENT Trial

Angela Migliorini, MD,* Amerigo Stabile, MD,† Alfredo E. Rodriguez, MD, PFI*D,‡ Caterina Gandolfo, MD,† Alfredo M. Rodriguez Granillo, MD,‡ Renato Valenti, MD,* Guido Parodi, MD, PFI*D,‡ Franz-Josef Neumann, MD,§ Antonio Colombo, MD,¶
David Antoniucci, MD,* on behalf of the JETSTENT Trial Investigators

Methods

This is a multicenter, international, randomized, 2-arm, prospective study. Eligible patients were patients with acute myocardial infarction, angiographic evidence of thrombus grade 3 to 6, and a reference vessel diameter $\geq$2.5 mm. Co-primary end points were early SI-segment resolution and 99mTc-sestamibi infarct size. An $\alpha$ value of 0.05 achieved by both co-primary surrogate end points or an $\alpha$ value of 0.025 for a single primary surrogate end point would be considered evidence of statistical significance. Other surrogate end points were Thrombolysis In Myocardial Infarction (TIMI) flow grade 3, corrected TIMI frame count, and TIMI grade 3 blush. Clinical end points were a composite of major adverse cardiovascular events at 1, 6, and 12 months.

JACC Vol. 63, No. 18, 2018
October 16, 2018:325-334

JETSTENT

Trial design: STEMI patients were randomized to AngioJet rheolytic thrombectomy plus stenting ($n=256$) vs. direct stenting alone ($n=245$).

Results

- 50% ST resolution at 30 minutes: 86% with thrombectomy vs. 79% with direct stenting ($p=0.043$)
- MACE at 12 months: 14.9% vs. 22.7% ($p=0.036$)
- Death: 3.2% vs. 6.4%
- MI: 0.9% vs. 1.4%
- Stroke: 0.9% vs. 0.4%

Conclusions

- Among patients with STEMI, rheolytic thrombectomy plus stenting was beneficial
- This strategy was associated with improved ST resolution and 12-month MACE, without an apparent increase in stroke
**INFUSE-AMI Trial**

452 pts with anterior STEMI
Anticipated Sx to PCI <5 hrs, TIMI 0-2 flow in prox or mid LAD
Primary PCI with bivalirudin anticoagulation

- Pre-loaded with aspirin and clopidogrel 600 mg or prasugrel 60 mg
- Stratified by symptoms to angio <3 vs ≥3 hrs, and prox vs mid LAD occlusion

**Manual aspiration**
1:1
- IC Abcx
- No Abcx

**No aspiration**
1:1
- IC Abcx
- No Abcx

**Primary endpoint:** Infarct size at 30 days (cMRI)

2° endpoints: TIMI flow, blush, ST-resolution, MACE (30d, 1 yr)

Stone et al. JAMA 2012

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**INFUSE-AMI: Infarct size at 30 days**
- **Major secondary endpoint**

<table>
<thead>
<tr>
<th></th>
<th>Median [IQR]</th>
<th>Median [IQR]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspiration</td>
<td>17.0% [9.0, 22.8]</td>
<td>17.3% [7.1, 25.5]</td>
</tr>
<tr>
<td>No aspiration</td>
<td>P=0.51</td>
<td></td>
</tr>
</tbody>
</table>

*N=229* and *N=223*

*Core laboratory assessed. No interaction was present between the 2 randomization groups for the primary 30-day infarct size endpoint (p=0.46)*
In Egypt, Salwa Labib et al

Fig.15: Angiographic Thrombus grade at baseline of the two studied groups.

Fig.16: Thrombus grade after eptif. & VD injection
CONCLUSION

Local intracoronary delivery of integrilin by means of a dedicated perfusion catheter reduces thrombus burden with the potential to improve coronary microcirculation.
PROMISE\textsuperscript{1}, EMERALD \textsuperscript{2}, RESCUE \textsuperscript{3}, DEDICATION \textsuperscript{4} Trials

- **Conclusions** The routine use of distal protection by a filterwire system during primary PCI does not seem to improve microvascular perfusion, limit infarct size, or reduce the occurrence of MACCE (Drug Elution and Distal Protection During Percutaneous Coronary Intervention in ST Elevation Myocardial Infarction;

1. Gick M. Circulation 112 2005 1462-1469
2. Stone G.W., JAMA 293 2005 1063-1072
Which are optimal options for embolic protection during coronary PCI?

- **Primary PCI for STEMI: prevention of thrombus embolism**

- No-reflow or slow-flow may occur as a consequence of downstream microvascular embolization of thrombotic or atheromatous (lipid-rich) debris and cause reperfusion injury.

- Reversing no-reflow is associated with a favourable effect on LV remodelling even in the absence of significant improvement in regional contractile function.

- Intracoronary administration of vasodilators such as:
  - adenosine, verapamil, nicorandil, papaverine, and nitroprusside
  - during and after primary PCI improves flow in the infarct-related coronary artery and myocardial perfusion and/or reduces infarct size,
  - High-dose i.v. adenosine infusion was also associated with a reduction in infarct size, but clinical outcomes were not significantly improved.209
• Self-expanding Nitinol stent deployed by retracting a sheath (no balloon)
• Bare or Paclitaxel-eluting with ProTeqtor biostable polymer
• 6 French, single-wire, rapid exchange
• Disconnecting struts for side-branch access


Gentle deployment, less distal embolization

95% of STENTYS patients in APPOSITION III had TIMI III flow post-procedure

• Less aggressive STENTYS stent expansion → less plaque disruption/distal embolisation

Stent opens as a flower: avoids thrombus dislodgement distally
Gentle deployment, less distal embolization

95% of STENTYS patients in APPOSITION III had TIMI III flow post-procedure

- Small cell area → better coverage of ruptured plaque/thrombus, reduces necrotic core prolapse

Small STENTYS cell area: better coverage compared with Vision stent

Comparison of Vision stent cell area (left, 3.86mm²) and STENTYS™ stent cell area (right, 0.95mm²)

1. Data on file at STENTYS Inc.

Dr. Giovanni Amoroso
on behalf of the APPOSITION III Investigators

APPOSITION III

Evaluation of the STENTYS self-apposing bare and drug-eluting stent in 1000 STEMI patients in a real-life setting: in-hospital and 30-day outcomes
Conclusions

• Results from the APPOSITION III show low MACE and death rates at 30 days with the STENTYS self-apposing stent system in an unselected real-life STEMI population.
• These results support the hypothesis that correct stent sizing and elimination of early malapposition improve short-term results of primary PCI.
• Routine post-dilatation is beneficial in order to prevent early stent thrombosis (due to residual stenosis).
• Follow-up to 12 months is required to assess whether early clinical benefit is maintained and to substantiate the impact on TLR.

The MASTER Trial
A Prospective, Randomized, Multicenter Evaluation of a PET Micronet Mesh Covered Stent (MGuard) in STEMI

Gregg W. Stone, MD
Columbia University Medical Center
New York-Presbyterian Hospital
Cardiovascular Research Foundation
**The MGuard and MGuard Prime Embolic Protection Stent (EPS)**

<table>
<thead>
<tr>
<th></th>
<th>MGuard</th>
<th>MGuard Prime</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metallic frame</td>
<td>316L stainless steel</td>
<td>L605 cobalt chromium</td>
</tr>
<tr>
<td>Strut width</td>
<td>100 µm</td>
<td>80 µm</td>
</tr>
<tr>
<td>Crossing profile</td>
<td>1.1 – 1.3 mm</td>
<td>1.0 – 1.2 mm</td>
</tr>
<tr>
<td>Shaft dimensions</td>
<td>0.65 – 0.86 mm</td>
<td>0.65 – 0.86 mm</td>
</tr>
<tr>
<td>Mesh sleeve</td>
<td>PET**</td>
<td>PET**</td>
</tr>
<tr>
<td>- Fiber width</td>
<td>20 µm</td>
<td>20 µm</td>
</tr>
<tr>
<td>- Net aperture size</td>
<td>150 - 180 µm</td>
<td>150 - 180 µm</td>
</tr>
</tbody>
</table>

**Thrombus Entrapment by the MGuard in STEMI**

Post MGuard

Mesh

Thrombus trapped behind mesh

Jain AK and Rothman MT. JACC 2011;58:e39
**MGUARD for Acute ST Elevation Reperfusion**

**The MASTER Trial**

STEMI with symptom onset within 12 hours at 432 pts at 50 sites in 9 countries

Stratified by infarct vessel and thrombus aspiration

PCI with BMS or DES  
PCI with MGuard

Follow-up: 30 days, 6 months, 1 year  
Primary endpoint: ST-segment resolution at 60-90 minutes

Substudies:  
Cardiac MRI: 60 pts (30 pts in each arm) at 3-5 days  
Angio FU: 50 pts in MGuard arm at 13 months

**Primary Endpoint:**  
Complete ST-segment resolution

<table>
<thead>
<tr>
<th></th>
<th>MGuard (n=204)</th>
<th>Control (n=206)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete (≥70%)</td>
<td>16.7%</td>
<td>25.5%</td>
</tr>
<tr>
<td>Partial (&gt;30% - &lt;70%)</td>
<td>57.8%</td>
<td>38.3%</td>
</tr>
<tr>
<td>Absent (≤30%)</td>
<td>17.0%</td>
<td>44.7%</td>
</tr>
</tbody>
</table>

Difference [95%CI] = 13.2% [3.1, 23.3]  
P=0.008
<table>
<thead>
<tr>
<th>Event</th>
<th>MGuard stent (n=217)</th>
<th>Control stent (n=214)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MACE</td>
<td>4 (1.8%)</td>
<td>5 (2.3%)</td>
<td>0.75</td>
</tr>
<tr>
<td>– Cardiac mortality*</td>
<td>0 (0.0%)</td>
<td>4 (1.9%)</td>
<td>0.06</td>
</tr>
<tr>
<td>– Reinfarction</td>
<td>3 (1.4%)</td>
<td>2 (0.9%)</td>
<td>1.00</td>
</tr>
<tr>
<td>– TLR, ischemia-driven</td>
<td>4 (1.8%)</td>
<td>1 (0.5%)</td>
<td>0.37</td>
</tr>
<tr>
<td>TVR, ischemia-driven</td>
<td>6 (2.8%)</td>
<td>1 (0.5%)</td>
<td>0.12</td>
</tr>
<tr>
<td>Stent thrombosis, def/prob</td>
<td>3 (1.4%)</td>
<td>2 (0.9%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Stroke</td>
<td>1 (0.5%)</td>
<td>0 (0.0%)</td>
<td>1.00</td>
</tr>
<tr>
<td>TIMI bleeding, major/minor</td>
<td>4 (1.8%)</td>
<td>4 (1.9%)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Mortality at 30 days occurred in 0/211 pts with complete STR and in 4/198 pts with partial or absent STR (0% vs 2.0%, p=0.05)

* There were no non-cardiac mortalities
Table 3. Potential advantages and disadvantages of delayed PCI

Advantages of delayed PCI
- Decreased rates of angiographic events (distal emboli, no-reflow) with reduced infarct size
- Time to assign the most appropriate treatment strategy (stent vs coronary artery bypass grafting vs medical therapy alone)
- No stent or PTCA needed in 10% of patients
- Allows statin preloading before angioplasty
- Stent selectively implanted during routine duty hours
- Possible reduction in congestive heart failure, reinfarction, and death

Disadvantages of delayed PCI
- Increased bleeding hazard
- Possible acute coronary reocclusion
- Repeated cardiac catheterization required
- Prolonged hospital stay and increased immediate costs (cost-effectiveness unknown)

PCI, percutaneous coronary intervention; PTCA, percutaneous transluminal coronary angioplasty.
CONCLUSION

1. Thrombus management in STEMI remains a problem, manual thrombectomy which is guideline based is unlikely to remain in the guidelines after the taste trial.

2. Mechanical thrombectomy may have a role in selected patients, but non evidence based

3. Local drug infusion has shown promise in small trials

4. New stents designed specifically for this are promising, as the M-Guard and Stentys, with encouraging trial data

5. Deferred stenting may be an option for selected patients