Bare Metal Stents vs. Drug-Eluting Stents for STEMI: Is it Settled?

Ajay J. Kirtane, MD, SM

Columbia University Medical Center / New York Presbyterian Hospital
Conflict of Interest Disclosure

• Ajay J. Kirtane
  – In the last 12 months, I have received honoraria/consultancy fees from Abbott Vascular, Boston Scientific, and Medtronic CardioVascular
  – Off-label use will be discussed
DES vs. BMS in STEMI: Why the Debate?

- STEMI patients have the highest thrombotic risk (potential for worse safety)
  - Worsened healing response after stenting?
  - Greater potential for malapposition and/or underexpansion
  - Highest ST rates, meeting patient “under the gun”
- STEMI lesions have lower restenosis rates (potential for less DES efficacy)
  - Less plaque, ISR less manifest
Distinction between AMI and Non-AMI Lesions

- **AMI lesion**
  - Neointima
  - Culprit site
  - Post stent

- **Stable lesion**
  - Neointima
  - Fibroatheroma culprit site (control)
  - Post stent

**Columbia University Medical Center**
Persistent fibrin deposition and uncovered struts in AMI compared to stable lesions treated with DES

Nakazawa and Virmani et al. Circulation 2008
Pathologic Assessment at Culprit Site (AMI vs. Stable patients)

<table>
<thead>
<tr>
<th></th>
<th>AMI with rupture (n=17)</th>
<th>Stable with FA (n=18)</th>
<th>p value AMI vs. Stable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neointimal thickness, mm</td>
<td>0.04 (0.02, 0.09)</td>
<td>0.11 (0.07, 0.21)</td>
<td>0.008</td>
</tr>
<tr>
<td>Strut with fibrin deposition, %</td>
<td>63 ± 28</td>
<td>36 ± 27</td>
<td>0.008</td>
</tr>
<tr>
<td>Strut with inflammation, %</td>
<td>35 (27, 49)</td>
<td>17 (7, 25)</td>
<td>0.003</td>
</tr>
<tr>
<td>Uncovered strut, %</td>
<td>49 (16, 96)</td>
<td>9 (0, 39)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Nakazawa and Virmani et al., Circulation 2008
HORIZONS-AMI IVUS Substudy

402 patients, 446 lesions with serial IVUS data

- PES reduced net volume obstruction compared to BMS

- PES was associated with more late malapposition compared to BMS (29.6% vs. 7.9%, p<0.001)

Maehara A et al, Circulation 2009
Stent Thrombosis

Patient, Procedure, Device

Patient Factors
- Higher Risk (Syndrome, Comorbidities)
- Adjunctive therapies
- AP Adherence and/or Responsiveness

Procedure
- Lesion pre/post
- Stent Expansion
- Flow/Runoff

Device
- Polymer
- Drug
- Surface
The Spanish ESTROFA Registry
23,500 pts treated w/DES at 20 Spanish hospitals from 2002–06; 63% PES, 37% SES. Dual antiplatelet Rx for 8 ± 3 months.
1.3% ST rate at median FU 22 (11, 32) mos ; 2.0% ST at 3 yrs

Multivariate Predictors of Stent Thrombosis (n=14,120)

<table>
<thead>
<tr>
<th></th>
<th>HR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Late</td>
<td></td>
<td></td>
</tr>
<tr>
<td>STEMI</td>
<td>5.5 (3.5–7.6)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LAD</td>
<td>3.0 (2.0–4.4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Stent length (per mm↑)</td>
<td>1.07 (1.05–1.09)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

de la Torre Hernandez JM et al. JACC 2008;51:986-90
Impact of Thrombus Burden with DES in AMI

792 STEMI Patients with DES

<table>
<thead>
<tr>
<th></th>
<th>Small</th>
<th>Large</th>
</tr>
</thead>
<tbody>
<tr>
<td>Final TIMI 3</td>
<td>94.9%</td>
<td>83.6%*</td>
</tr>
<tr>
<td>TMPG-3</td>
<td>53.2%</td>
<td>35.4%*</td>
</tr>
<tr>
<td>No-reflow</td>
<td>0.5%</td>
<td>4.0%*</td>
</tr>
<tr>
<td>Distal Embol.</td>
<td>3.5%</td>
<td>17.3%*</td>
</tr>
</tbody>
</table>

*P<0.001

Rate of IRA-ST

- Large Thrombus Burden: 8.2%
- Total Population: 3.2%
- Small Thrombus Burden: 1.3%

Sianos G et al, J Am Coll Cardiol 2007; 50:573-83
Stent Thrombosis at 5 years
ARC definite, probable, possible

Hazard Ratio 1.13
[95% CI: 0.44-2.9]; p=0.78

J Am Coll Cardiol in press
Two-Year Stent Thrombosis (ARC Definite or Probable)

- TAXUS DES (n=2257)
- EXPRESS BMS (n=749)

Stent Thrombosis (%) vs Months

Number at risk:
- TAXUS DES: 2238, 2108, 2061, 1998, 1661
- EXPRESS BMS: 744, 696, 681, 661, 547

HR [95%CI] = 1.00 [0.66, 1.51]
p = 0.99

4.1%
TYPHOON: ARC Definite/Probable Stent Thrombosis at 4 Years

- **Early (0 to 30 days)**
  - BMS (n=250): 9 (3.6%) Stent Thrombosis
  - CYPHER (n=251): 6 (2.4%)

- **Very Late (> 1yr)**
  - BMS (n=250): 3 (1.2%)
  - CYPHER (n=251): 5 (2.0%)

Total Thrombosis: BMS = 12 (4.8%), CYPHER = 11 (4.4%)

P = 0.83
## 5-Year LST and VLST

<table>
<thead>
<tr>
<th></th>
<th>PES N=310</th>
<th>BMS N=309</th>
<th>HR (95% CI)</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Definite ST</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30 days – 1 year</td>
<td>1 (0.3%)</td>
<td>0 (0.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 year – 5 years</td>
<td>7 (2.5%)</td>
<td>2 (0.7%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>8 (2.9%)</td>
<td>2 (0.8%)</td>
<td>3.95 (0.81 – 18.61)</td>
<td>0.06</td>
</tr>
<tr>
<td><strong>Definite or Probable ST</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30 days – 1 year</td>
<td>2 (0.7%)</td>
<td>0 (0.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 year – 5 years</td>
<td>7 (2.5%)</td>
<td>3 (1.1%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>9 (3.2%)</td>
<td>3 (1.1%)</td>
<td>2.97 (0.80 – 12.97)</td>
<td>0.09</td>
</tr>
</tbody>
</table>

Incidences were estimated from the Kaplan-Meier curves

Vink, ACC/I2 2010
Impact of premature thienopyridine discontinuation: The PREMIER registry

500 pts with AMI undergoing primary PCI with DES at 19 U.S. medical centers, alive and well at 30 days

68 (13.6%) were no longer taking prescribed thienopyridines at 30 days

![Graph showing 1 Year Mortality (%): D/C thienopyridine at 30 days (7.5), Taking thienopyridine at 30 days (0.7), P<0.0001. Propensity adjusted for reasons to d/c thien: HR = 9.02 (1.3-60.6), P=0.02.]

Death/MI Related to Delays in Filling Clopidogrel Prescription after DES

Of 7,402 patients, 16% did not fill a clopidogrel prescription on day of discharge (median delay of 3 days)

Ho et al, Circ Cardiovasc Qual Outcomes 2010
DES in AMI Meta-Analysis

Study Flow

Dates: 2000 to 2008
FDA approved DES
Number of patients: 33,873

Search of Multiple Data Sources

DES vs. BMS in AMI

13 RCTs
N=7,352

18 Registries
N=26,521

DES
N=4,515

BMS
N=2,837

Brar et al. JACC 2009; 53(18)
DES in AMI Meta-Analysis

Mortality (RCTs)

Relative Risk (95% CI)
0.89
(0.70 - 1.14)

I² = 0%

Brar et al. JACC 2009; 53(18)
Di Lorenzo et al.
STRATEGY
BASKET-AMI
PASSION
TYPHOON
DEDICATION Stent
HAAMU-STENT
MISSION
SELECTION
Diaz de la Llera et al.
HORIZONS-AMI Stent
MULTISTRATEGY

Relative Risk (95% CI)
0.97
(0.73 - 1.28)

I² = 0%

Brar et al. JACC 2009; 53(18)
2-year mortality (propensity adjusted) in 1298 matched pairs (2596 pts) with STEMI at 21 hospitals between 4/03–9/04

1% mortality difference at 2 days
2.1% mortality difference at 30 days

Days after Initial Procedure

Death (adjusted) (%)

BMS (n=1298)
11.6%

DES (n=1298)
8.5%

Drug-Eluting Stent
No. at risk 1298 1298 1250 1227 1213
Cum. incidence (%) 0.7 3.7 5.5 6.5 8.5

Bare-Metal Stent
No. at risk 1298 1292 1223 1194 1173
Cum. incidence (%) 0.5 5.8 8.0 9.6 11.6

Mauri L et al. *NEJM* 2008;359:1330-42
DES vs. BMS in STEMI: Case Closed?

• Despite higher theoretical risks of delayed healing, malapposition, and other potential risks…
  • Overall rates of ST and other clinical safety outcomes have been similar for BMS and DES

• So what about efficacy?
DES in AMI Meta-Analysis

Target Vessel Revascularization (RCTs)

Favors DES  Favors BMS

Di Lorenzo et al.
STRATEGY
BASKET-AMI
PASSION
TYPHOON
SELECTION
SESAMI
Diaz de la Llera et al.
DEDICATION Stent
HAAMU-STENT
MISSION
HORIZONS-AMI Stent
MULTISTRATEGY
Overall

REDUCTION
56%

Relative Risk (95% CI)
0.44
(0.35 - 0.55)

p < 0.001

I² = 26%

Brar et al. JACC 2009; 53(18)
**TYPHOON**

4-Year Follow-Up of SES vs. BMS for AMI

<table>
<thead>
<tr>
<th>4-Year Outcomes</th>
<th>Cypher n = 251</th>
<th>BMS n = 250</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TLR (%)</td>
<td>7.2</td>
<td>15.2</td>
<td>0.005</td>
</tr>
<tr>
<td>MI (%)</td>
<td>4.8</td>
<td>4.0</td>
<td>0.83</td>
</tr>
<tr>
<td>Death (%)</td>
<td>4.0</td>
<td>6.4</td>
<td>0.23</td>
</tr>
</tbody>
</table>

**Conclusion:** At 4 years, SES still maintain their initial advantage in terms of revascularization rates over BMS.

Primary Efficacy Endpoint: Ischemic TLR

**Number at risk**
- TAXUS DES (n=2257)
- EXPRESS BMS (n=749)

**Ischemic TLR (%)**

- **Diff = -3.0%**
- **HR = 0.59**
- **P=0.002**

Which is more impressive?
1. 41% reduction in ischemic TLR
2. Need to treat 33 patients with DES vs. BMS to prevent one TLR event
Primary Efficacy Endpoint: Ischemic TLR

**Ischemic TLR (%)**

- **TAXUS DES (n=2257)**: HR [95%CI] = 0.58 [0.44, 0.76], P<0.001
- **EXPRESS BMS (n=749)**: 11.6%

**Number at risk**

<table>
<thead>
<tr>
<th></th>
<th>TAXUS DES</th>
<th>EXPRESS BMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Months</td>
<td>2257</td>
<td>749</td>
</tr>
<tr>
<td>0</td>
<td>2257</td>
<td>749</td>
</tr>
<tr>
<td>3</td>
<td>2105</td>
<td>677</td>
</tr>
<tr>
<td>6</td>
<td>2041</td>
<td>654</td>
</tr>
<tr>
<td>9</td>
<td>1949</td>
<td>611</td>
</tr>
<tr>
<td>12</td>
<td>1618</td>
<td>507</td>
</tr>
<tr>
<td>15</td>
<td>1618</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>1618</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>1618</td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>1618</td>
<td></td>
</tr>
</tbody>
</table>
Primary Efficacy Endpoint: Ischemic TLR

Ischemic TLR (%)

TAXUS DES (n=2257)
EXPRESS BMS (n=749)

13 mo angio FU

11.6%
6.8%

HR [95%CI] = 0.58 [0.44, 0.76]
P<0.001

Number at risk
TAXUS DES  EXPRESS BMS
2257  2105
2105  2041
2041  1949
1949  1618
1618  1618
1618  507
507

1-yr HR [95%CI] = 0.60 [0.43, 0.84]
p = 0.002
1-Year TLR According to BMS Risk Score (N=2915)

<table>
<thead>
<tr>
<th>Express BMS TLR Risk Score</th>
<th>Ischemic TLR at 1-Year (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>N=946 (32.5%)</td>
</tr>
<tr>
<td></td>
<td>3.2</td>
</tr>
<tr>
<td>1</td>
<td>N=1520 (52.1%)</td>
</tr>
<tr>
<td></td>
<td>7.3</td>
</tr>
<tr>
<td>≥2</td>
<td>N=449 (15.4%)</td>
</tr>
<tr>
<td></td>
<td>16.3</td>
</tr>
<tr>
<td></td>
<td>6.6</td>
</tr>
</tbody>
</table>
Safety of DES vs. BMS in STEMI: Case Closed?

- Despite higher theoretical risks of delayed healing, malapposition, and other potential safety risks...
  - Overall ST and other safety outcomes (mortality, MI) have been similar for BMS and DES
  - Continued long-term FU and investigation of newer DES systems is needed
  - Issues of DAPT adherence are critical in the clinical setting
Efficacy of DES vs. BMS in STEMI: Case Closed?

• Because of lower absolute event rates of TLR, careful attention to absolute risk reductions (and number needed to treat) rather than relative risk reductions is needed.

• An estimation of baseline restenotic risk should be performed in order to determine the potential benefit of DES in an individual patient!!