Stent Thrombosis in Bifurcation Stenting

Associate Professor Tan Huay Cheem
MBBS, M Med(Int Med), MRCP, FRCP(UK), FAMS, FACC, FSCAI
Director, National University Heart Centre, Singapore
Senior Consultant Cardiologist and Chief,
Cardiac Department, National University Hospital
Adjunct Associate Professor, Yong Loo Lin School of Medicine
National University of Singapore
National University Hospital
Why Are Bifurcation Lesion More Prone to Thrombosis

Pathological studies suggest that arterial branch points are foci of low shear and low flow velocity and are sites predisposed to the development of atherosclerotic plaque, thrombosis and inflammation.
NHLBI Dynamic Registry

<table>
<thead>
<tr>
<th></th>
<th>Bifurcation (n=321)</th>
<th>Non-bifurcation (n=2,115)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angiographic success</td>
<td>86.0%</td>
<td>93.5%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Side-branch closure</td>
<td>7.3%</td>
<td>2.3%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>In-hospital MACE</td>
<td>7.2%</td>
<td>5.0%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>One-Year MACE</td>
<td>32.1%</td>
<td>25.7%</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>
Predictors of Stent Thrombosis After DES Implantation

Overall stent thrombosis = 1.3% ( \( P = .09, N = 2229 \) )

Holmes DR Rev Cardiovasc Med 2007; 8: S11
Iakovou I et al JAMA 2005; 293: 2126
## J CYPHER: Predictors of Definite and Probable Stent Thrombosis Through 1-Year

<table>
<thead>
<tr>
<th>Factors</th>
<th>OR 95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 stent approach in bifurcation lesions</td>
<td>2.05 (1.22-3.30)</td>
<td>0.0085</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>2.04 (1.22-3.16)</td>
<td>0.009</td>
</tr>
<tr>
<td>Emergency procedure</td>
<td>1.73 (0.97-2.82)</td>
<td>0.006</td>
</tr>
</tbody>
</table>
ARTS II

The clinical outcome of percutaneous treatment of bifurcation lesions in multivessel coronary artery disease with the sirolimus-eluting stent: insights from the Arterial Revascularization Therapies Study part II (ARTS II)

- 5 cases of ST (1.5%) occurred in a total of 465 bifurcations in 324 pts treated with 1 stent. 4 were subacute ST, with 3 bifurcation lesions having had a poor angiographic result at end of procedure.

- The only case of late ST occurred in a nonbifurcation lesion

Tsuchida K et al Euo Heart J 28: 433-442
Multifactorial Causes of Stent Thrombosis

Stent Thrombogenicity
- Material Designs (open vs closed cell)
- Surface coating
- Adjunctive therapies (drug, radiation)

Patient/Lesion Factors
- Vessel size, Lesion length
- ACS / MI
- Plaque characteristics
- Intrinsic platelet/
- Coagulation activity
- Ejection fraction/CHF

Biocompatibility

Multiple stents
- Stent length

Blood Flow

Procedure-Related Factors
- Morphometric and/or morphologic abnormalities
  (under-expansion / Dissection, incomplete apposition, thrombus, tissue protrusion)
- Mechanical vessel injury
- Antithrombotic therapy

Keneiakes DK et al Rex Cardiovasc Med 2004; 5: 9-15
Patient/ Lesion Factor
Diabetes as Predictor of Stent Thrombosis

Kuchulakanti
Circ 2006

Urban
Circ 2006

Machecourt
JACC 2007

lakovou
JAMA 2005

Daemen
Lancet 2007

lijima
Am J Card 2007

De la Torre
JACC 2008

OR=2.0
(0.8-4.9)

OR=2.8
(1.7-4.3)

OR=2.7
(1.4-5.2)

HR=3.7
(1.7-7.9)

HR=2.0
(1.1-3.8)

HR=2.2
(1.1-4.3)

HR=1.75
(1.0-3.0)
Impact of Bifurcation Lesion on Risk of Stent Thrombosis With DES in Pts With STEMI

**Independent Predictors of ST**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hazard Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.6</td>
<td>0.4-0.8</td>
</tr>
<tr>
<td>Index ST</td>
<td>6.2</td>
<td>2.1-18.9</td>
</tr>
<tr>
<td>Bifurcation</td>
<td>4.1</td>
<td>1.6-10.0</td>
</tr>
<tr>
<td>Thrombectomy</td>
<td>0.1</td>
<td>0.01-0.8</td>
</tr>
<tr>
<td>Large thrombus</td>
<td>8.7</td>
<td>3.4-22.5</td>
</tr>
</tbody>
</table>

DES vs BMS In Bifurcation Stenting
**SCANDSTENT: DES vs BMS**

- SCANSTENT: randomised study comparing SES with BMS implantation in patients with complex CAD
- Subgroup analysis of those with a bifurcation (n=126)

![Graph showing late loss comparison between SES and BMS in main and side branches](chart.png)

*Thiesen et al AHJ 2006; 152: 1140-1145*
SCANDSTENT:
Clinical Outcomes in Bifurcation Lesions

<table>
<thead>
<tr>
<th>Event</th>
<th>SES</th>
<th>BMS</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>0</td>
<td>1.8</td>
<td>p=NS</td>
</tr>
<tr>
<td>MI</td>
<td>3.0</td>
<td>5.2</td>
<td>p=NS</td>
</tr>
<tr>
<td>TVR</td>
<td>6.0</td>
<td>21.1</td>
<td>p=0.016</td>
</tr>
<tr>
<td>MACE</td>
<td>9.0</td>
<td>28.1</td>
<td>p=0.009</td>
</tr>
<tr>
<td>Stent thrombosis</td>
<td>0</td>
<td>8.8</td>
<td>p=0.019</td>
</tr>
</tbody>
</table>

Thiesen et al. AHJ 2006; 152: 1140-1145
Cypher vs Taxus In Bifurcation Stenting: Long-term Clinical Follow-up

- N= 78 (CYPHER=24; TAXUS=54)

- 80 bifurcation lesions (CYPHER=24; TAXUS=56)

- Median follow-up period: 32 (range: 21 to 48) months

- The overall long-term MACE rates for the CYPHER & TAXUS gps were 25% & 24% respectively

- Two sudden deaths occurred at 6 & 17 mths in the TAXUS gp (no post-mortem examination performed)

Lee CH, Tan HC et al Int J Cardiol 2007
Risk of Stent Thrombosis When 2 stents versus 1 stent Is Used
## 2-Stent vs 1-Stent
### Bifurcation Stenting

<table>
<thead>
<tr>
<th></th>
<th>2-stent (n=53)</th>
<th>1-stent (n=39)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>SB Residual Stenosis (%)</td>
<td>7.4 ± 10.9</td>
<td>23.4 ± 18.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Immediate Success</td>
<td>87%</td>
<td>92%</td>
<td></td>
</tr>
<tr>
<td>In-hospital MACE</td>
<td>13%</td>
<td>0%</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Restenosis</td>
<td>62%</td>
<td>48%</td>
<td>NS</td>
</tr>
<tr>
<td>Target lesion revascularisation</td>
<td>38%</td>
<td>36%</td>
<td>NS</td>
</tr>
<tr>
<td>6 Mth MACE</td>
<td>51%</td>
<td>38%</td>
<td>NS</td>
</tr>
</tbody>
</table>

Yamashita et al JACC 2000; 35: 1145-51
Safety of DES: Stent Thrombosis

% Stent Thrombosis

- 2 Stents
- 1 stent + PTS

Pan, Lefèvre, Darremont, Nordic I, Ferenc, Cactus, Moussa, Ge 1 vs 2, Colombo, Serruys, J Cypher, Terstein, Ge Crush, Hoye Crush, Bif. Sirius

TCT 2008
**Nordic I Bifurcation Study**

- Multicenter study of the SES in bifurcations
- Randomised to a provisional versus a 2-stent strategy

<table>
<thead>
<tr>
<th>6-months Clinical FU</th>
<th>Single stent n = 207</th>
<th>MB + SB Stent n=206</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>1</td>
<td>1</td>
<td>1.0</td>
</tr>
<tr>
<td>MI (%)</td>
<td>0</td>
<td>0.5</td>
<td>0.3</td>
</tr>
<tr>
<td>TLR (%)</td>
<td>2</td>
<td>1</td>
<td>0.4</td>
</tr>
<tr>
<td>TVR (%)</td>
<td>2</td>
<td>2</td>
<td>1.0</td>
</tr>
<tr>
<td>MACE (%)</td>
<td>3</td>
<td>3</td>
<td>ns</td>
</tr>
<tr>
<td>Stent thrombosis (%)</td>
<td>0.5</td>
<td>0</td>
<td>0.3</td>
</tr>
</tbody>
</table>

Only 1 patient had definite ST, and he was treated with 1 stent

*Steigen TK et al Circulation 2006; 114: 1955-61*
### NORDIC I: Clinical Endpoints After 14 Mths

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>MV</th>
<th>MV + SB</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definite stent thrombosis, n (%)</td>
<td>2/199 (1.0)</td>
<td>1/196 (0.5)</td>
<td>ns</td>
</tr>
<tr>
<td>Probable stent thrombosis, n (%)</td>
<td>2/199 (1.0)</td>
<td>0/196 (0)</td>
<td>ns</td>
</tr>
<tr>
<td>Possible stent thrombosis, n (%)</td>
<td>1/199 (0.5)</td>
<td>0/196 (0)</td>
<td>ns</td>
</tr>
<tr>
<td>Overall stent thrombosis, n (%)</td>
<td>4/19 (2.0)</td>
<td>1/199 (0.5)</td>
<td>ns</td>
</tr>
<tr>
<td>Total death, n (%)</td>
<td>5/207 (2.4)</td>
<td>2/206 (1.0)</td>
<td>ns</td>
</tr>
<tr>
<td>Cardiac death, n (%)</td>
<td>3/207 (1.4)</td>
<td>2/206 (1.0)</td>
<td>ns</td>
</tr>
<tr>
<td>Myocardial infarction, n (%)</td>
<td>4/199 (2.0)</td>
<td>2/196 (1.0)</td>
<td>ns</td>
</tr>
<tr>
<td>TLR, n (%)</td>
<td>13/199 (6.5)</td>
<td>11/196 (5.6)</td>
<td>ns</td>
</tr>
<tr>
<td>TVR, n (%)</td>
<td>15/199 (7.5)</td>
<td>12/196 (6.1)</td>
<td>ns</td>
</tr>
<tr>
<td>MACE, n (%)</td>
<td>19/199 (9.5)</td>
<td>16/196 (8.2)</td>
<td>ns</td>
</tr>
</tbody>
</table>

Jensen JS et al EuroInterv 2008; 4: 229-233
n = 350 patients

de novo TRUE bifurcation lesions of the native coronary arteries

Dual antiplatelet therapy was recommended in all pts for at least 6 months

Colombo A et al Circulation 2009; 119: 71-78
### CACTUS: Stent Thrombosis

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Acute (first day)</th>
<th>Subacute (days 2-30)</th>
<th>Late (days 31-180)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crush (n=177)</td>
<td>3 (1.7%)</td>
<td>1 (0.5%)</td>
<td>2* (1.1%)</td>
<td>0</td>
</tr>
<tr>
<td>Prov. T (n=173)</td>
<td>2 (1.1%)</td>
<td>0</td>
<td>1 (0.5%)</td>
<td>1 (0.5%)</td>
</tr>
</tbody>
</table>

*p = 0.62 for comparisons between crush and prov.-T

*One patient did not take thienopyridine therapy after discharge

Colombo A et al Circulation 2009; 119: 71-78
Pitfalls of 2-Stent Stenting Techniques
Long Term Outcomes After Stenting of Bifurcation Lesions with the “Crush” Technique

- At 9 mths, incidence of post-procedural stent thrombosis was 4.3%
- Only independent predictor of TLR was left main stem therapy (OR 4.97; 95% CI 2.00 to 12.37, p=0.001)

Hoye A et al J Am Coll Cardiol 2006; 47: 1949-58
Kissing Ballooning is Crucial in Crush Technique

6-mo restenosis rate
(Colombo A, Ital Heart J 2005)

6-mo TLR
(Lenox Hill, TCT 2004)
Final Kissing Balloon Inflation by Classic Crush Stenting Did Not Improve the Clinical Outcomes for the Treatment of Unprotected Left Main Bifurcation Lesions: The Importance of Double-Kissing Crush Technique

- Unsatisfactory kissing rate (>20% residual stenosis) in the Classic Group was significantly higher (26.3% vs 5.9%)

- SB restenosis rate (42.1% vs 5.9%, p=0.01) and MACE (42.1% vs 5.8%, p=0.001) higher in Classic Group
Conclusions

• Stenting of bifurcation lesions is associated with an increased risk of stent thrombosis, even in DES era

• Risk is not greater with DES compared with BMS

• Risk is not greater when 2 stents versus 1 stent is used

• Implanting 2 stents always demands more attention and expertise to obtain the best result in both MB and SB

• Selection of appropriate diameter and length of stent to both optimally cover the target lesions and appropriate expansion is crucial in preventing stent thrombosis
Thank You