Νόσος μοσχευμάτων-συσκευές προστασίας

Δημήτριος Στάκος
Αλεξανδρούπολη
SVG: Occlusion Rates

- 1 Year 15%
- 1-6 Years 1-2% / year
- 6-10 Years 4% / year

L. Campeau, NEJM 1984
B. Fitzgibbons, JACC 1996
M. Bourassa, JACC 1991
Scoring of harvested saphenous veins

**Branches.** None (1 point)
- 3 or fewer branches (2 points)
- >3 branches (3 points)

**Varicosity.** Nonvaricose (1 point)
- Semivaricose (2 points)
- Varicose (3 points).

**Diameter.** Internal diameter from 3 mm to 5 mm (1 point)
- Internal diameter >5 mm (2 points)
- Internal diameter <3 mm (3 points)

**Wall Thickness.** Thin (1 point)
- Medium (2 points)
- Thick (3 points)

The best possible score is 4 (indicating a good patency result)
The worst possible score is 12 (indicating a poor result).
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~10% of CABG patients experience SVG-related MACE in 1 year post surgery

Edifoligide for Prevention of SVG Failure Following CABG

PREVENT IV: Randomized controlled trial in 1,920 pts.

Intervention: Treatment of vein grafts with edifoligide, an oligonucleotide decoy that binds to and inhibits E2F transcription factors, potentially preventing neointimal hyperplasia and vein graft failure.

Proportion with Major Adverse Cardiac Events

Placebo

Edifoligide

Log-rank \( P=0.16 \)

JAMA. 2005
Why they fail
1. No reflow prevention

2. DES over BMS

3. Embolic protection

4. Native vs SVG
Microvascular spasm (Platelet degranulation, PMNs, Free radicals)
Distal embolization (thrombi, atheromatous debris, PLT aggregates)

RF for no-reflow: Age of SVG, extent of disease, multiple pre-dilations
Pharmacological Options for No Reflow Treatment

Management of No Reflow

1. IC Adenosine (600 – 2,400 mcg)
   - Mix 6mg Adenosine in 100cc NSS = 60mcg/cc
   - Give 60mcg (1cc) repeatedly q minute (10-40cc)

2. IC Nitroprusside (50 – 250 mcg)
   - Mix 0.25ml (6.25mg – use TB syringe) in 250cc bag D5W – 25mcg/cc

3. IC Verapamil (250 – 500 mcg)
   - Draw 1ml (2.5mg) in syringe and dilute to 10ml = 250mcg/cc
   - Problems with prolonged heart block

4. IC Epinephrine (no reflow with hypotension)
   - Use 1:10,000 dilution. Dilute 1cc in 10cc = 10mcg/cc
   - Give repeated doses of 1cc

5. IC Nicardipine (100 – 500 mcg)
   - Use repeated doses of 300-500mcg

If no preparation (vasodilators), predilatation (no direct stenting), no mechanical protection → No reflow 15-30%
If appropriate prophylaxis → May reduced to 3-5%
1. No reflow prevention

2. DES over BMS

3. Embolic protection

4. Native vs SVG
Drug-Eluting vs. Bare-Metal Stents in Saphenous Vein Graft (SVG) Lesions

ISAR-CABG: Randomized, Superiority Trial in 610 pts.

<table>
<thead>
<tr>
<th>1-Year Follow-up</th>
<th>DES (n = 303)</th>
<th>BMS (n = 307)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death/MI/TLR (Primary Outcome)</td>
<td>15.0%</td>
<td>22.1%</td>
<td>0.02</td>
</tr>
<tr>
<td>TLR</td>
<td>6.8%</td>
<td>13.1%</td>
<td>0.01</td>
</tr>
<tr>
<td>Stent Thrombosis</td>
<td>0.7%</td>
<td>0.7%</td>
<td>0.99</td>
</tr>
</tbody>
</table>

DES reduced angiographic restenosis at 7 months (15% vs. 29%; P < 0.0001).

DES better than BMS (reduce TLR in half in ~ a year follow up)
DES better than BMS (reduce TLR in half in long-term follow up)

High mortality rates anyway
1. No reflow prevention
2. DES over BMS
3. Embolic protection
4. Native vs SVG
<table>
<thead>
<tr>
<th>Device</th>
<th>Manufacturer</th>
<th>Approval date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guardwire</td>
<td>Medtronic</td>
<td>6/2001</td>
</tr>
<tr>
<td>Filterwire</td>
<td>Boston Scientific</td>
<td>6/2003</td>
</tr>
<tr>
<td>Spider</td>
<td>ev3</td>
<td>6/2006</td>
</tr>
</tbody>
</table>

**Embolic protection devices for SVGs**

- Occlusion/aspiration devices
  - Guardwire
- Filters
  - Filterwire
  - Spider
SAFER: Primary Endpoint

30 Day Outcomes

Percent MACE

<table>
<thead>
<tr>
<th>Condition</th>
<th>With Protection n = 406</th>
<th>Without Protection n = 395</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 Day MACE</td>
<td>9.6</td>
<td>16.5</td>
</tr>
<tr>
<td>All MI</td>
<td>8.6</td>
<td>14.7</td>
</tr>
<tr>
<td>Q-wave MI</td>
<td>1.2</td>
<td>1.3</td>
</tr>
<tr>
<td>Non Q-wave MI</td>
<td>7.4</td>
<td>13.7</td>
</tr>
<tr>
<td>No-reflow</td>
<td>3.2</td>
<td>8.3</td>
</tr>
</tbody>
</table>

p = 0.04

p = 0.008

p = 1.0

p = 0.004

p = 0.005

42% relative reduction in MACE

Baim DS. Circulation. 2002
Embolic Protection During SVG Stenting: Pooled Analysis of 6 Trials*

MACE (%)

<table>
<thead>
<tr>
<th>SVG Degeneration Score</th>
<th>0-25%</th>
<th>26-50%</th>
<th>51-75%</th>
<th>76-100%</th>
</tr>
</thead>
<tbody>
<tr>
<td>EPD used</td>
<td>5</td>
<td>10.3</td>
<td>14.4</td>
<td>189</td>
</tr>
<tr>
<td>No EPD used</td>
<td>1269</td>
<td>367</td>
<td>86</td>
<td>31</td>
</tr>
</tbody>
</table>

36% RR
35% RR
39% RR
41% RR
35.5

* SAFER, FIRE, CAPTIVE, PROXIMAL, SPIDER, BLAZE II (n=3,958)
** p<0.0001 for increased MACE with SVG Degeneration Score
30-Day MACE SVG Trials

30-day MACE (%)

- SAFER unprotected: 16.5
- SAFER GuardWire: 9.6
- FIRE Filterwire: 9.9
- FIRE GuardWire: 11.6
- CAPTIVE: 11.4
- SPIDER: 9.2
- PRIDE TriActive: 11.2
- PRIDE Filter/GuardWire: 10.1
- Proximal System: 11.2
- PROXIMAL Proxis System: 7.1
- BLAZE I and II: 5
BCCS – EPD Use and Outcomes

1,359 patients  7.1% Use

TVR free Survival (%)

Adjusted HR=0.70, 95% CI:0.41-1.17, p=0.176
Log-rank test p=0.274

Mortality

Survival (%)

Adjusted HR=0.62, 95% CI:0.33-1.17, p=0.144
Log-rank test p=0.102

Follow-up (days)

Follow-up (days)
## NCDR

49,325 SVG Patients  21% EPD Use

<table>
<thead>
<tr>
<th></th>
<th>EPD</th>
<th>No EPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>No flow</td>
<td>3.9</td>
<td>2.8</td>
</tr>
<tr>
<td>MI</td>
<td>2.8</td>
<td>1.8</td>
</tr>
<tr>
<td>Perf</td>
<td>0.7</td>
<td>0.4</td>
</tr>
</tbody>
</table>

No Difference in 3 year Death, MI, TVR
Total studies identified for Saphenous vein graft intervention utilizing embolic protection device. N=78

Non-relevant and therefore excluded N= 64

Potentially relevant studies identified and screened for retrieval N= 64

Did not meet inclusion criteria N= 8

Total studies comparing desired outcomes N= 6

Two studies identified from additional search of references and related articles N= 8, Total population: 52,893 (Embolic protection device used: 11,506; not used: 41,387)

MACE

all-cause mortality
### Periprocedural MI

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>EPD Events</th>
<th>EPD Total</th>
<th>No EPD Events</th>
<th>No EPD Total</th>
<th>Weight</th>
<th>Odds Ratio M-H, Random, 95% CI</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dixon 2005</td>
<td>4</td>
<td>173</td>
<td>3</td>
<td>185</td>
<td>0.1%</td>
<td>1.44 [0.32, 6.51]</td>
<td>2005</td>
</tr>
<tr>
<td>Matar 2009</td>
<td>1</td>
<td>108</td>
<td>0</td>
<td>94</td>
<td>0.0%</td>
<td>2.64 [0.11, 65.51]</td>
<td>2009</td>
</tr>
<tr>
<td>Golwala 2012</td>
<td>0</td>
<td>71</td>
<td>6</td>
<td>93</td>
<td>0.0%</td>
<td>0.09 [0.01, 1.70]</td>
<td>2012</td>
</tr>
<tr>
<td>Sadr-Ameli 2014</td>
<td>0</td>
<td>22</td>
<td>1</td>
<td>128</td>
<td>0.0%</td>
<td>1.89 [0.07, 47.84]</td>
<td>2014</td>
</tr>
<tr>
<td>Brennan 2015</td>
<td>3129</td>
<td>10432</td>
<td>11668</td>
<td>38893</td>
<td>99.1%</td>
<td>1.00 [0.95, 1.05]</td>
<td>2015</td>
</tr>
<tr>
<td>Iqbal 2016</td>
<td>17</td>
<td>96</td>
<td>265</td>
<td>1263</td>
<td>0.8%</td>
<td>0.81 [0.47, 1.39]</td>
<td>2016</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>10902</strong></td>
<td><strong>40656</strong></td>
<td><strong>100.0%</strong></td>
<td><strong>11943</strong></td>
<td></td>
<td><strong>1.00 [0.95, 1.05]</strong></td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>3151</td>
<td>11943</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 3.86$, df = 5 ($P = 0.57$); $I^2 = 0%$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: $Z = 0.08$ ($P = 0.94$)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
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</table>

### TVR

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>EPD Events</th>
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<th>No EPD Events</th>
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<th>Weight</th>
<th>Odds Ratio M-H, Random, 95% CI</th>
<th>Year</th>
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<tr>
<td>Lavi 2010</td>
<td>4</td>
<td>198</td>
<td>12</td>
<td>336</td>
<td>15.6%</td>
<td>0.56 [0.18, 1.75]</td>
<td>2010</td>
</tr>
<tr>
<td>Golwala 2012</td>
<td>10</td>
<td>71</td>
<td>12</td>
<td>93</td>
<td>21.4%</td>
<td>1.11 [0.45, 2.73]</td>
<td>2012</td>
</tr>
<tr>
<td>Sadr-Ameli 2014</td>
<td>2</td>
<td>22</td>
<td>20</td>
<td>128</td>
<td>10.0%</td>
<td>0.54 [0.12, 2.49]</td>
<td>2014</td>
</tr>
<tr>
<td>Brennan 2015</td>
<td>292</td>
<td>10432</td>
<td>699</td>
<td>38893</td>
<td>53.0%</td>
<td>1.57 [1.37, 1.81]</td>
<td>2015</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>10723</strong></td>
<td><strong>39450</strong></td>
<td><strong>100.0%</strong></td>
<td><strong>743</strong></td>
<td></td>
<td><strong>1.12 [0.65, 1.90]</strong></td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>308</td>
<td>743</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: $\tau^2 = 0.14$; $\chi^2 = 5.44$, df = 3 ($P = 0.14$); $I^2 = 45%$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: $Z = 0.40$ ($P = 0.69$)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>
## Strengths and Weaknesses of Embolic Protection

<table>
<thead>
<tr>
<th></th>
<th>Proximal Occlusion</th>
<th>Distal Occlusion</th>
<th>Distal Filter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maintenance of antegrade blood flow during intervention</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Limited contrast opacification</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Unlimited debris capture</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Capture of debris &lt; 100 μm</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Capture of soluble mediators</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Shunting of debris into proximal side branches</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Ease of use</td>
<td>Complex</td>
<td>Complex</td>
<td>Simple</td>
</tr>
<tr>
<td>Manoeuverability</td>
<td>Good</td>
<td>Good</td>
<td>Reduced</td>
</tr>
<tr>
<td>Crossing profile</td>
<td>NA</td>
<td>Low (2.7 Fr)*</td>
<td>High (3.2 Fr)**</td>
</tr>
</tbody>
</table>
Cost Effectiveness of Embolic Protection During SVG PCI

![Cost Effectiveness Graph]

- Additional Cost: $1,600
- Savings 2° to reduced complications: $1,000
- Net Cost: $582
- Cost per QALY: $3,718

CABG, left main $10,000
Hemodialysis $50,000

J Am Coll Cardiol. 2004
<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distal protection devices should be considered for PCI of SVG lesions.(^{346,350,351})</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>PCI of the bypassed native artery should be considered over PCI of the bypass graft</td>
<td>IIa</td>
<td>C</td>
</tr>
</tbody>
</table>
1. No reflow prevention
2. DES over BMS
3. Embolic protection
4. Native vs SVG
Post-CABG Treatment in VA

Outline of Patient and Lesion Selection for the Present Study

CART

PCI patients (n=60,171)
PCI lesions (n=74,027)

Excluded patients (n=49,075)
- No prior CABG (n=49,053)
- Both SVG and arterial graft (n=22)

Prior CABG (n=11,098)
PCI lesions (n=16,440)

Treated Lesion

Native Coronary Artery
(n=12,073, 73.4%)

SVG
(n=4,114, 25%)

Arterial Graft
(n=253, 1.5%)

CABG = coronary artery bypass grafting; CART = Clinical Assessment, Reporting, and Tracking;
PCI = percutaneous coronary intervention;
SVG = saphenous vein graft.

Brillakis E. JACC Cardiol Intv. 2008
SVG PCI

Native + previous CABG

Native no previous CABG
SVGs as donor vessels for retrograde recanalization
CABG candidate?  
Yes  
LIMA to LAD?  
Yes  
Redo CABG  
No  
Native lesion complex?  
No  
SVG lesion complex?  
Yes  
SVG lesion complex?  
No  
Native lesion PCI  
Yes  
Skills to treat native lesion  
No  
SVG PCI
SVGs and protection devices - Conclusions

1. Poor long-term patency – associated with MACE
2. May turn into complex revascularization
3. Short inflations, vasodilators and direct stenting with DES may be beneficial
4. Use of protection devices and native coronary PCI are encouraged
5. Think SVGs for retrograde recanalisation when severely degenerated or even occluded