PCI in Patients with Transplant Coronary Artery Disease

Michael S. Lee, MD, FACC, FSCAI
Assistant Professor
UCLA School of Medicine
Faculty Disclosure

- Honararia for Boston Scientific, BMS, Daiichi Sankyo, Novartis, and Merck
Orthotopic heart transplantation (OHT) is a well-established therapeutic option for patients with severe congestive heart failure.

Approximately 2000 OHT are performed every year.¹

Within the first year post-op, rejection and infection are the most common causes of death.

Transplant coronary artery disease (TCAD) remains the most significant cause of morbidity and mortality after orthotopic heart transplantation. Transplant coronary artery disease is largely an immunologic phenomenon, driven by an inflammatory milieu consisting of multiple cell types that contribute to fibromuscular and smooth muscle cell proliferation with subsequent coronary obstruction. Multiple clinical factors contribute to the development of TCAD. Coronary angiography is the gold standard for the diagnosis of TCAD. Current treatments for TCAD include pharmacotherapy, percutaneous coronary intervention, and repeat transplantation, although other novel therapies are emerging. Although percutaneous coronary intervention has generally demonstrated high procedural success rates, it has been plagued by a high incidence of in-stent restenosis. Drug-eluting stents reduce in-stent restenosis compared with bare metal stents. Repeat transplantation is the only definitive treatment. Prospective randomized trials comparing different pharmacotherapies as well as revascularization strategies are needed to identify the optimal therapy for patients who develop TCAD. (J Am Coll Cardiol Intv 2010; 3:367–77) © 2010 by the American College of Cardiology Foundation
Transplant Coronary Artery Disease (TCAD) is a rapidly progressive form of diffuse arterial narrowing.

TCAD is characterized by:
1. Endothelial dysfunction
2. Luminal narrowing
3. Intimal hyperplasia
Transplant Coronary Artery Disease

• TCAD is the major cause of late death in transplant patients and is the primary cause of allograft loss.¹

• At 5 years after OHT, 50% of patients have angiographic evidence of TCAD.²

• When the diagnosis of TCAD is made, long-term prognosis is poor, and the 5-year life expectancy of the allograft is approximately 17%.³

Histology of Transplant Coronary Artery Disease

- Subendothelial accumulation of T lymphocytes (arrow) characteristic of endothelitis, which is a manifestation of chronic rejection

Histology of Transplant Coronary Artery Disease

- Progressive arterial occlusion with lipid-laden foam cell macrophages
- This intense inflammatory response is believed to play a key role in TCAD and may be responsible for the increased risk of restenosis after PCI

Positive remodeling is a compensatory mechanism in patients with TCAD that prevents luminal narrowing despite intimal hyperplasia.
• Statins may decrease the incidence of TCAD, graft rejection, and increase long-term survival.¹

• However, there currently is no medical therapy to reverse CAV.

PCI for the Treatment of Transplant Coronary Artery Disease

- Used as a palliative treatment option for TCAD
- When compared with native coronary artery lesions it is associated with
  - Higher procedural complications
  - Long-term morbidity and mortality
  - Higher restenosis rates
CABG for the Treatment of Transplant Coronary Artery Disease

- **Distal arteriopathy** (diffuse, predominantly distal vessel disease) is prevalent in OHT patients and therefore makes CABG technically difficult and a poor treatment option.

- Repeat sternotomy and the associated mediastinal scarring and risk of infection in these immunocompromised patients may increase the risk of complications.

- The perioperative mortality rate is high (40%-80%), and the long-term patency rates of bypass grafts are unknown.

- CABG in patients with left main disease is also associated with a higher incidence of stroke, pneumonia, and a longer length of stay compared with PCI.

- In addition, 7% of patients required repeat operation for significant bleeding.

Repeat OHT for the Treatment of Transplant Coronary Artery Disease

- Repeat OHT is associated with high perioperative mortality and poor long-term survival.¹
- 1-year mortality rate of 25%.²
- 50% develop recurrent TCAD in the second graft.³
- Shortage of organs.
- Ethical dilemma

Comparison of Percutaneous Coronary Intervention With Bare-Metal and Drug-Eluting Stents for Cardiac Allograft Vasculopathy

Michael S. Lee, MD, Jon Kobashigawa, MD, Jonathan Tobis, MD

Los Angeles, California

Objectives We sought to compare percutaneous coronary intervention (PCI) with bare-metal stents (BMS) and drug-eluting stents (DES) for cardiac allograft vasculopathy (CAV).

Background Cardiac allograft vasculopathy is a rapidly progressive form of atherosclerosis and is one of the main limitations to long-term survival after orthotopic heart transplantation. Percutaneous coronary intervention has been used as a palliative treatment option for CAV but is associated with worse clinical outcomes and greater rate of restenosis compared with PCI of native coronary arteries.

Methods Between 1995 and 2007, data on 82 consecutive heart transplant patients who underwent PCI with BMS and DES at the University of California at Los Angeles Medical Center were retrospectively analyzed.

Results A total of 82 lesions were treated with 98 BMS and 76 lesions were treated with 80 DES. Follow-up angiography was performed on 57 of 82 lesions (70%) treated with BMS and 58 of 76 (76%) treated with DES (p = 0.7) at a mean follow-up of 9.5 ± 5.5 months for BMS and 12.6 ± 8.2 months for DES (p = 0.02). Compared with BMS, DES was associated with a lower binary restenosis rate (12% vs. 30%, p = 0.02), lower percent diameter stenosis (24 ± 20 vs. 34 ± 36, p = 0.06), and less late lumen loss (0.24 ± 0.75 mm vs. 0.82 ± 1.03 mm, p = 0.01). No angiographic stent thrombosis was observed with DES.

Conclusions When compared with BMS, PCI with DES was safe and reduced the rate of angiographic restenosis in patients with CAV. A randomized clinical trial comparing BMS versus DES with longer follow-up is needed to identify the optimal long-term revascularization strategy in patients with CAV. (J Am Coll Cardiol Intv 2008;1:710–5) © 2008 by the American College of Cardiology Foundation.
Lee MS et al., J Am Coll Cardiol: Cardiovasc Interv 2008

Binary Restenosis at Follow-Up

P < 0.001

DES (76 lesions) BMS (82 lesions)
Mean f/u 12.6 mo Mean f/u 9.5 mo

% of Patients

0 5 10 15 20 25 30 35 40
Late lumen loss (mm)

Late Lumen Loss at Follow-Up

P = 0.01

- DES (76 lesions)
  Mean f/u 12.6 mo
  Late lumen loss = 0.24 mm

- BMS (82 lesions)
  Mean f/u 9.5 mo
  Late lumen loss = 0.82 mm

Lee MS et al., J Am Coll Cardiol: Cardiovasc Interv 2008
Stent Thrombosis in Cardiac Transplant Patients

- **Bare metal stents**
  - N=98
  - 2 lesions were totally occluded on follow-up angiography

- **Cypher**
  - N=58
  - No angiographic stent thrombosis

- **TAXUS**
  - N=22

Lee MS et al., *J Am Coll Cardiol: Cardiovasc Interv* 2008
Sirolimus- Versus Paclitaxel-Eluting Stents for the Treatment of Cardiac Allograft Vasculopathy

Michael S. Lee, MD,* Giuseppe Tarantini, MD,† Jola Xhaxho, MD,† Tae Yang, MD,* Ashkan Ebdaie, MD,* Ravi Bhatia, MD,* Enrico Favaretto, MD,† Jonathan Tobis, MD*

Los Angeles, California; and Padua, Italy

Objectives The aim of this study was to compare outcomes after percutaneous coronary intervention (PCI) with sirolimus-eluting stents (SES) and paclitaxel-eluting stents (PES) in the treatment of cardiac allograft vasculopathy (CAV).

Background PCI in patients with CAV is associated with increased rates of restenosis compared with PCI in patients without CAV. There are no dedicated studies on the influence of different drug-eluting stents (DES) on the outcomes of patients with CAV.

Methods This is a retrospective observational study of 108 consecutive patients with CAV who underwent PCI with SES and PES at UCLA Medical Center and University of Padova Medical Center between 2002 and 2008.

Results Baseline characteristics were similar among SES (n = 68) and PES (n = 40) patients with the exception of older patients, larger minimal lumen diameter, and smaller diameter stenosis in the SES-treated patients. Angiographic follow-up at 1 year was high in the SES and PES groups (74% vs. 76%, p = 0.8). The SES and PES groups had similar binary restenosis rates (10% vs. 9%, p = 0.7), percent diameter stenosis (24 ± 24% vs. 24 ± 18%, p = 0.94), and late lumen loss (0.67 ± 1.03 mm vs. 0.68 ± 1.11 mm, p > 0.9). One-year clinical outcomes were not significantly different among CAV patients treated with either SES or PES (major adverse cardiac events: 10% vs. 15%, p = 0.5; death: 3% vs. 5%, p = 0.4; myocardial infarction: 3% vs. 5%, p = 0.4; target vessel revascularization: 4% vs. 8%, p = 0.3).

Conclusions In patients who underwent PCI for CAV, both SES and PES were safe and effective with no significant differences in clinical and angiographic outcomes. Randomized clinical trials comparing different DES with longer follow-up are necessary to identify the optimal treatment strategy for patients with CAV.
# Table 3. 1-Year Angiographic Outcomes

<table>
<thead>
<tr>
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<th>SES (n = 68)</th>
<th>PES (n = 40)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow-up angiography</td>
<td>50 (74)</td>
<td>30 (76)</td>
<td>0.8</td>
</tr>
<tr>
<td>Binary restenosis</td>
<td>7 (10)</td>
<td>4 (9)</td>
<td>0.7</td>
</tr>
<tr>
<td>Percent diameter stenosis</td>
<td>24 ± 24</td>
<td>24 ± 18</td>
<td>0.9</td>
</tr>
<tr>
<td>Late lumen loss (mm)</td>
<td>0.67 ± 1.03</td>
<td>0.68 ± 1.11</td>
<td>&gt;0.9</td>
</tr>
<tr>
<td>MLD (mm)</td>
<td>2.25 ± 0.78</td>
<td>2.31 ± 0.70</td>
<td>0.8</td>
</tr>
</tbody>
</table>
## Table 4. 1-Year Clinical Outcomes

<table>
<thead>
<tr>
<th>Event</th>
<th>SES (n = 68)</th>
<th>PES (n = 40)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major adverse cardiac events</td>
<td>7 (10)</td>
<td>6 (15)</td>
<td>0.5</td>
</tr>
<tr>
<td>Cardiac death</td>
<td>2 (3)</td>
<td>2 (5)</td>
<td>0.4</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>2 (3)</td>
<td>2 (5)</td>
<td>0.4</td>
</tr>
<tr>
<td>Target vessel revascularization</td>
<td>3 (4)</td>
<td>3 (8)</td>
<td>0.3</td>
</tr>
<tr>
<td>Target lesion revascularization</td>
<td>2 (3)</td>
<td>1 (3)</td>
<td>0.9</td>
</tr>
<tr>
<td>Stent thrombosis</td>
<td>1 (1.5)</td>
<td>2 (5)</td>
<td>0.3</td>
</tr>
<tr>
<td>Repeat transplantation</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>&gt;0.9</td>
</tr>
</tbody>
</table>
Treatment Options for Cardiac Transplant Patients With Left Main Disease

• Medical therapy is probably not an option, as the only clinical manifestation of left main disease may be sudden death.

• Medical therapy for left main disease in non-transplant patients has been associated with a 3-year mortality rate of approximately 50%.¹

Drug-Eluting Stenting of Unprotected Left Main Coronary Artery Stenosis in Patients With Orthotopic Heart Transplantation: Initial Clinical Experience

Michael S. Lee,* MD, Kook-Jin Chun, MD, and Jonathan M. Tobis, MD

- 8 out of 82 transplant patients who underwent PCI had left main disease
- 5 of the 8 transplant patients underwent PCI with DES
PCI with DES for Unprotected Left Main Disease in Cardiac Transplant Patients

- 23 year-old male with a past medical history of cardiac transplantation 5 years ago and LV dysfunction (EF = 40%) underwent annual surveillance angiography
Left Main PCI in Cardiac Transplant Patients

Multicenter, international registry
22 patients

Time (years)
Probability
Survival
MACE-free survival

Lee MS, et al. Am J Cardiol (submitted)
Conclusions

• In transplant patients, PCI is safe, technically feasible, with excellent technical results and may serve as a bridge to repeat OHT.

• Although improvements in DES and pharmacotherapy may decrease the risk of restenosis and stent thrombosis, randomized trials with long-term f/u are needed to determine the ideal treatment for this difficult patient population.

• However, because ULMCA disease in transplant patients is uncommon, such a clinical trial may not be practical.
Thank you!