CARDIAC TRANSPLANT VASCULOPATHY


Take home points:
1. Coronary allograft vasculopathy is the most common cause of death in heart transplant patients.
2. Dx is difficult because heart tx pts. have denervated hearts and rarely present with CP (though over time, 10-30% of pts. develop some degree of re-innervation); many patients present late, with heart failure.
3. Management includes periodic cardiac catheterization, risk factor modification, and statins (which may play a primary anti-inflammatory role). Because of the diffuse nature of this disease, the benefit of revascularization is limited. Severe disease is an indication for a second heart transplant.
4. Because of the diffuse nature of the disease, angiography may give false negatives; therefore, intravascular ultrasound (IVUS) can play an important role in the management of these patients.

Is this disease common in heart transplant patients?
• Yes. Approximately 40% of heart transplant patients die of this disease (most common cause of death in these patients).

What is the pathophysiology behind this disease?
• Different from traditional coronary artery disease.
• Diffuse process, starts with small, distal vessels and spreads to all coronary arteries (endocardial → epicardial).
• Pathology: concentric (not eccentric, like traditional CAD) hyperplasia with intimal proliferation of the vessels.
• Pathogenesis: immune-mediated endothelial injury (rejection, reperfusion injury, viral (?CMV)) → diffuse intimal hyperplasia → exacerbation of vascular disease with hyperlipidemia, hypertension, diabetes, and steroid use → coronary allograft vasculopathy.

What are the clinical features of the disease?
• Coronary allograft vasculopathy (CAV) vs. coronary artery disease (CAD):

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<thead>
<tr>
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<th>CAV</th>
<th>CAD</th>
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<tbody>
<tr>
<td>Symptoms</td>
<td>Lack of angina; presents with heart failure</td>
<td>Angina or anginal equivalent present</td>
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<tr>
<td>Angiography</td>
<td>Diffuse, distal disease</td>
<td>Focal, proximal disease</td>
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<tr>
<td>Intimal proliferation</td>
<td>Concentric</td>
<td>Eccentric</td>
</tr>
<tr>
<td>Calcium deposition</td>
<td>Absent</td>
<td>Frequently present</td>
</tr>
<tr>
<td>Internal elastic lamina</td>
<td>Intact</td>
<td>Disrupted</td>
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• Diagnosis is difficult because heart transplant patients have denervated hearts and rarely present with chest pain.
  – Although rare, 10-30% of patients develop some degree of re-innervation over time and therefore can present with angina.
  – Most patients, however, present late with signs and symptoms of congestive heart failure (including complications of systolic dysfunction such as ventricular arrhythmias).
• Given the lack of symptoms, most transplant cardiologists will perform cardiac catheterization on an annual basis to look for coronary allograft vasculopathy.
• Unfortunately, angiography can underestimate disease because of the diffuse nature of the vasculopathy. Therefore, intravascular ultrasound (IVUS) can play an important role in the diagnosis of these patients.

What about stress testing?
• Clinical trials with exercise ECG and myocardial perfusion imaging (nuclear studies) have demonstrated low sensitivity and specificity.
• Dobutamine echocardiography has performed the best in clinical trials.

Treatment options?
• Statins have been shown to improve mortality in randomized controlled trials
• Revascularization options are limited given the diffuse nature of the disease
• Aggressive control of risk factors and risk factor modification.
• Treat rejection which prolongs survival (though trials haven’t shown a reduction in transplant vasculopathy).
• Re-transplantation may be necessary.