TMR Patient Selection

Physician Training
The Clinical Need

Mukherjee et al. Prognosis for untreated medically refractory patients. (JACC, 1999, Cleveland Clinical Review)

• Clinical Outcome for Eligible Cohort:
  o 500 consecutive patients referred for coronary artery disease (CAD) treatment
  o 3 cardiologists reviewed medical history/angiograms

• Findings:
  o 12% had inoperable CAD
  o > 6% are potential TMR candidates
The Clinical Need

Mukherjee et al. Prognosis for untreated medically refractory patients – Clinical outcome follow-up for eligible cohort. (AHJ, 2001)

One year follow-up on the 59 patients ineligible for traditional methods of revascularization...

<table>
<thead>
<tr>
<th>Event</th>
<th>No. of Events</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>10</td>
<td>17%</td>
</tr>
<tr>
<td>MI</td>
<td>15</td>
<td>26%</td>
</tr>
<tr>
<td>Rehospitalizations</td>
<td>76</td>
<td>128%</td>
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</tbody>
</table>
The Clinical Need

Graham et al. Diffuse Coronary Artery Disease (CAD) Impacts Surgical Mortality

- Diffuse CAD can be angiographically quantified
- Diffuse CAD is not a variable in current models of operative risk
- Diffuse CAD is an independent predictor of operative mortality

The Clinical Need

Diffuse Coronary Artery Disease

Operative mortality risk:
- Independently predicted by incomplete revascularization\(^1,2\)
- Current models and national databases do not consider incomplete revascularization in predicting risk
- Case-matched comparisons can be inaccurate

*In the subset of patients with diffuse CAD, current risk models underestimate predicted mortality.*\(^2\)

The Clinical Need

INCOMPLETE REVASCULARIZATION!!!

Occurs in 10% to 25% of CABG patients

- Diffusely diseased targets
- Older, sicker patients being referred

Incomplete Revascularization!!!

- As reported by Prendergast, 19% of patients undergoing CABG had an anticipated graft that could not be bypassed.\(^1\)
- Osswald, et al., Determined: Incomplete revascularization occurred in 16% of elderly patients undergoing a CABG procedure.\(^2\)
- Osswald, et al., Increased mortality was found with incomplete revascularization in patients ≥ 75 years of age and was identified as an independent risk factor for death.
- Bjork, et al., Determined: Early patency was decreased when perioperative graft blood flow was ≤ 20 ml/min. or diameter of recipient coronary artery was smaller than 1.5 mm.\(^3\)
- Higginbotham, et al., Determined: Patency rates of < 1.0 mm vessels was 50%, patency rates of < 2.0 mm vessels was 78%, and patency rates of ≥ 2.0 mm vessels was 100%.\(^4\)
- Corbineau, et al., Determined: The quality of distal runoff of the most frequently grafted vessels is a significant risk factor for CABG operative mortality.\(^5\)

The Clinical Need

- STS registry reports 80% of current TMR procedures are performed as an adjunct to CABG.
- As reported by Mukherjee, 2% to 7% of cardiac catheterization patients may be candidates for sole therapy TMR.
- The availability of laser TMR may allow the cardiac surgeon to accept cases that would otherwise be considered inoperable and to respond better to intraoperative findings.

TMR Candidate – Typical Angiogram

- 64 year old Obese Woman
- Class IV Angina at Baseline
- TMR, 36 channels

33 Month Follow-up: NO ANGINA

Image courtesy of Keith Allen, MD, St. Vincent Hospital, Indianapolis, Indiana
• Stable patient with severe angina CCS Class IV, refractory to medical management
• Regions of the myocardium demonstrating reversible ischemia which are not amenable to direct coronary revascularization (either PCI or CABG)
  o Patients with one or more vessels or branches that are not bypassable (small vessels 1.0 – 1.5 mm diameter or less may be indicators)
• Diffuse Distal Coronary Artery Disease (diffuse atherosclerotic end-stage disease)
• Left ventricular ejection fraction > 30%
• Area of ischemia located in lower ²/₃ of left ventricle (≥ 10% reversibility of perfusion defect)
• Incomplete revascularization
• Profound physical limitations due to severe angina that produces patient/physician sense of hopelessness
• Diabetes
Patient Exclusion Criteria

- Not a treatment for congestive heart failure
- Does not improve shortness of breath (dyspnea) unrelated to angina
- Will not improve a failing pump
- Q-wave MI within past 3 weeks
- Non Q-wave MI within past 2 weeks
- Severely unstable patients (unweanable from I.V. anti-anginal medication)
- Uncontrolled ventricular tachy-arrhythmia
- Cardiac failure, decompensated
Patient History:
- 60 year old Male, Diabetic, Hypertensive, Overweight
- MI – No History
- NYHA Class 3 Angina; Insulin Therapy, Peripheral Artery Disease with Claudication

Treatment Strategy:
- Cardiac Cath: Severe 3 Vessel Disease, EF = 50%, no Graftable Vessels in Posterior-Inferior Wall
- CABG X 5
- TMR to Inferior-Posterior Wall (21 Channels)

2 Year Follow-up, NYHA Class 1, No Cardiac Events, No Cardiac Meds
Patient History:
- 62 year old Male
- History of Hypertension
- NYHA Class 3 Angina

Treatment Strategy:
- Cardiac Cath: Severe 3 Vessel Disease, EF = 60%, Poor LAD and Diagonal Targets
- CABG X 4
- TMR to Anterior Wall as well as Inferior Wall (18 Channels)

3 Year Follow-up, NYHA Class 1, No Cardiac Events
Patient History:
• 55 year old Male, Diabetic
• MI – 1989; Angioplasty x 2 Since to Open Marginal Vessel
• NYHA Class 3 Angina; Positive Stress Test with Ischemia in all Regions; Mild Renal Insufficiency (Creatinine = 1.9)

Treatment Strategy:
• Cardiac Cath: 3 Vessel Disease, EF = 50%, Occluded 2nd Marginal with No Target in that Area Bypassable
• CABG X 3
• TMR to Lateral Wall (11 Channels)

1 Year Follow-up, NYHA Class 1, Normal Stress Exam, Normal Echocardiogram
Patient History:
- 54 year old Male, Hypertensive, Hyperlipidemic, Overweight
- MI – 09/1997; Hospitalized with Unstable Angina and Treated Medically
- NYHA Class 4 Angina

Cardiovascular Interventions:
- Cardiac Cath: Severe 3 Vessel Disease, Only One Vessel Bypassable (OMI), EF = 32%
- CABG X 1
- TMR to All Areas of the Myocardium (39 Channels)

2 Year Follow-up, NYHA Class 1, No Further Cardiac Events, Stable EF
Patient History:
- 54 year old male, increasing symptoms of angina
- Seen by numerous CTS who felt grafting was not an option, nor was attempt to unroof the myocardial bridging
- NYHA class 3 angina; stress test demonstrated severe anterior wall ischemia with limited exercise

Cardiovascular Interventions:
- Cardiac Cath: Revealed extensive bridging of the left anteriodescending coronary artery with near occlusion in systole, and diminished blood supply in diastole as well
- Sole therapy TMR to anterior wall (13 channels)

1.5 Year Follow-up, NYHA Class 1, No Cardiac Events, Normal Stress Exam
Careful Patient Selection Optimizes TMR and TMR+CABG Outcomes – Low Mortality and Sustained Angina Relief

Study Facts:

- 157 patients underwent TMR alone or combined with CABG
- 43% had TMR as a sole therapy and 57% had TMR as an adjunct to CABG. Of the 90 combined (TMR+CABG) procedures, 46 were performed entirely off-pump
- Follow-up range was 0.1–3.2 years with a mean of 1.2 years
- Total TMR hospital experience from 1998-2002
- Utilized the Holmium:YAG TMR Laser with fiber optic Sologrip® Delivery System

Source: Michael Grosso, MD, St. Francis Heart Center, Wilmington, DE
From Hospital Experience Case Study, 2002
Careful Patient Selection Optimizes TMR and TMR+CABG Outcomes – Low Mortality and Sustained Angina Relief

Summary of Results:
• Angina relief was profound and sustained – 82% of patients with no angina or class 1 symptoms at follow-up.
• Improved patient selection over time has significantly reduced mortality rates. Current in-hospital mortality is low (4%). Off-pump adjunctive therapy mortality is only 2%.
• Follow-up reveals low late mortality (1.3%).

Source: Michael Grosso, MD, St. Francis Heart Center, Wilmington, DE
From Hospital Experience Case Study, 2002
Careful Patient Selection Optimizes TMR and TMR+CABG Outcomes – Low Mortality and Sustained Angina Relief

Conclusions:

• These results indicate that TMR, performed as a sole therapy or as an adjunct to CABG, is safe
• These results suggest better outcomes with an off-pump approach
• Careful patient selection maximizes outcomes

Source: Michael Grosso, MD, St. Francis Heart Center, Wilmington, DE
From Hospital Experience Case Study, 2002
FDA Labeling (IFU)

Transmyocardial revascularization with the CardioGenesis® Laser System is indicated for the treatment of stable patients with angina (Canadian Cardiovascular Society Class 4) refractory to medical treatment and secondary to objectively demonstrated coronary artery atherosclerosis and with a region of the myocardium with reversible ischemia not amendable to direct coronary revascularization.
FDA Label
Precautions and Warnings

• Patients who were unstable (defined as unweanable from intravenous anti-anginal medications) experienced 11% (16/150) peri-operative mortality (surgery + 30 days) compared to 5% (7/132) in patients who did not require intravenous anti-anginal medications.

• Do not treat the myocardium in the area of a left ventricular mural thrombus because of potential for the creation of emboli.

1. CardioGenesis IFU
What should we be thinking?

Good Targets
- PCI
- CABG
- Repeat PCI
- Repeat CABG

Bad Targets
- CAD
- Medical Therapy
- Failure?
  - Transplant
  - Endarterectomy
  - TMR
  - Gene Therapy
What should we be thinking?

• The time to schedule a TMR procedure is not only when analyzing the angiogram but intra-operatively as well... the laser should always be ready and scheduled for use
• More knowledge will be available intra-operatively than from the angiogram alone
• TMR can be used for ungraftable vessels with areas of reversible ischemia

Proven Clinical Benefit

Clinical Trials Have Shown a Clinical Benefit with the Use of TMR

• Primary Outcomes:
  - Relief of Angina by Two or More Classes
  - Increased Exercise Tolerance

• Secondary Outcomes:
  - Reduction in Re-Hospitalizations
  - Reduction in Medication Usage
  - Increased Event Free Survival
  - Increased Perfusion
  - Improved Quality of Life

• Long-Term Efficacy
Proven Clinical Benefit

✓ Proven Symptomatic Relief
✓ Dramatic Improvement in Quality of Life
✓ Significant TMR Reimbursement for Hospital and Physician

• The Blue Cross/Blue Shield TEC States:
  o In 1999: TMR Sole Therapy “Improves Net Health Outcomes”
  o In 2001: TMR+CABG “Improves Net Health Outcomes”

• Advantageous for All Stakeholders
  o Patient, Physician, and Healthcare System
References

10. Allen KB, et al. 24-month patient follow-up presentation not yet presented or published. January 2001, St. Vincent Hospital, Indianapolis, IN.