Surgical Treatment in CAD
Beyond the CABG

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Surgical Treatment in CAD
Beyond the CABG

• Introduction
• Let’s make it real: case presentation
• Historical considerations
• Current recommendations
• Enhancing outcomes
Objectives:

- Identify current clinical indicators for surgical intervention in patients with ischemic heart failure
- Discuss options in ischemic heart failure beyond CABG
- Identify best practices and long term outcomes in the management of these patients
Surgery in Ischemic Heart Failure

What are the options?

• High Risk CABG+/- IABP
• Consideration for advanced heart failure therapy
• Transplantation vs mechanical circulatory support
• Innovational therapies
Johns Hopkins Surgery
Dr. Blalock Appointed Hopkins Surgery Chief, Succeeding Dean Lewis

Professor At Vanderbilt University Gets Chair Of Medical School

Famous Selection After Nation-Wide
For Man For Post

Appointment of Dr. Alfred Blalock as professor of surgery in the School of Medicine of the Hopkins University was announced today by Isaiah Bowman, president of the university.

Blalock is now professor of surgery at the Vanderbilt University, Nashville, and is widely known as one of the younger surgeons of the country. He is 41 years old, a native of Ohio, and is an alumnus of the School of Medicine, which he attended.

Replaces Dr. Dean Lewis

Dr. Dean Lewis, who has been chairman of the Hopkins chair of surgery since September 1, 1930.

Not all time, the university has been in a nation-wide search to find a successor. Dr. Blalock's appointment was recommended unanimously by the advisory committee of the medical faculty on December 12.
Birth of Cardiac Surgery
Heart disease is the leading killer of women and men in America.
Coronary advanced fibrolipid plaque. When seen in cross-sections of arteries which have been fixed by perfusion with formalin the lumen is round in shape; the plaque is situated to one side of the artery leaving a segment of normal arterial wall opposite the plaque. The tissue slice has been treated with oil red O to show the lipid in the core. The core is separated from the arterial lumen by the fibrous cap of the plaque which is pearly grey in colour due to its high collagen content.
**Human Regional Myocardial Infarction:**

In this untreated unfixed slice of myocardium there is an infarct which was between 5 and 7 days in duration by clinical history. By this stage, the centre of the infarct is yellow and there is a red rim where vessels are beginning to invade the infarcted tissue to initiate organization. The infarct is full thickness and involves the posteriomedial papillary muscle. The infarct is in the regional supplied by the right coronary artery which was occluded by thrombus.
Death From CHD in the US is Declining

Deaths per 100,000 population*

1st Statin

Year

* Age-adjusted

Pathophysiology of Ischemic Cardiomyopathy
Post-MI Remodeling

- Ventricular dilatation
- Mitral valve/papillary muscle dysfunction
- Mitral regurgitation
- Low cardiac output
- Pulmonary edema
- Peripheral edema/venous congestion

Congestive Heart Failure
Congestive Heart Failure: The Problem

Epidemiology

- 5 million Americans, 10 million worldwide
- 500,000 to 1 million new cases diagnosed yearly
- 70% of men, 79% of women with CHF have history of hypertension
- Huge economic impact in diagnosis, treatment, including AICD
- Bi-ventricular pacing, recurrent hospitalizations, transplant/LVADs
- Requires extraordinary measures to address the problem!

The Changing Environment of Heart Failure Treatments

Adapted From: Kaessmeyer Circulation 1994: 90: 1029-32 and AHA 2001 Statistical Update
The Elderly Population Will Double between 2000 and 2050

Source: U.S. Dept. of Commerce, Bureau of the Census
Impact of Coronary Revascularization

Coronary surgery relieves angina and prolongs life expectancy.
Compared with saphenous-vein coronary bypass grafts, internal-thoracic-artery grafts conferred a survival advantage throughout a 15-year follow-up period.

**Coronary Bypass Surgery with Internal-Thoracic-Artery Grafts — Effects on Survival over a 15-Year Period**


The significant survival advantage of coronary artery bypass surgery with the use of multiple arterial grafting.

LV Dysfunction Secondary to Ischemic Cardiomyopathy

- CABG is cornerstone of revascularization in patients LVEF > 35%
- **STICH Trial**: multicenter, randomized study at 127 clinical sites to evaluate patients with ischemic cardiomyopathy
  - 1212 patients with **LVEF < 35%** and CAD were randomized to medical therapy vs. medical therapy + CABG
Coronary-Artery Bypass Surgery in Patients with Ischemic Cardiomyopathy

Eric J. Velazquez, M.D., Kerry L. Lee, Ph.D., Robert H. Jones, M.D., Hussein R. Al-Khalidi, Ph.D., James A. Hill, M.D., Julio A. Panza, M.D., Robert E. Michler, M.D., Robert O. Bonow, M.D., Torsten Doenst, M.D., Mark C. Petrie, M.D., Jae K. Oh, M.D., Lilin She, Ph.D., Vanessa L. Moore, A.A.S., Patrice Desvigne-Nickens, M.D., George Sopko, M.D., M.P.H., Jean L. Rouleau, M.D., for the STICHES Investigators

N Engl J Med
Volume 374(16):1511-1520
April 21, 2016
Randomization and Follow-up.

1212 Patients underwent randomization

610 Were assigned to undergo CABG plus medical therapy

Intermediate results: median follow-up, 4.9 yr
218 Died
392 Survived

13 Withdrew or were lost to follow-up

610 Were included in long-term follow-up analyses (median follow-up, 9.9 yr; maximum follow-up, 13.3 yr)

602 Were assigned to receive medical therapy alone

Intermediate results: median follow-up, 4.9 yr
244 Died
358 Survived

12 Withdrew or were lost to follow-up

602 Were included in long-term follow-up analyses (median follow-up, 9.8 yr; maximum follow-up, 13.4 yr)

From: The STICH Trial (Surgical Treatment for Ischemic Heart Failure): Mode-of-Death Results


Figure Legend:

Sudden Death Kaplan-Meier Curves
Abbreviations as in Figure 1.
LV Dysfunction Secondary to Ischemic Cardiomyopathy

- **Results:**
  - No significant difference between medical treatment vs. medical treatment + CABG
  - However, at 10 years, death rate from cardiovascular causes were lower by 16% in CABG patients
Clinical Case Presentation

62 year old male presents with angina, SOB, Non-ST segment elevation MI:

- Transferred to JHH on heparin, ASA, Plavix for coronary angiography and possible PCI
- PMH – stable angina
- LV ejection fraction 25% by echo
- Severe triple vessel CAD not amenable to PCI
- Angina at rest requires IABP
- CABG successful x 4
- 18 months later recurrent advanced heart failure

? Next Steps ?
Stratum C Case – Preoperative MRI
Advanced heart failure
Case Considerations for the Multidisciplinary Team

- All CABG Grafts patent
- Maximum Medical Therapy for CHF
- LVEF <20%

Options
? mitral valve repair or replacement
? Mechanical support
? Transplant
Myocardial Infarction & Remodeling

Days → Weeks → Months - Years

Acute Anterior Infarction → Fibrosis & Remodeling → Dilation & Failure

Repair is limited to hypertrophy and scar formation due to inability of cardiomyocytes to proliferate.
Assessment of Myocardial Viability
Current tools

• Myocardial perfusion imaging (SPECT) screening tool for CAD
• Glucose metabolism substitutes free fatty acid metabolism as main energy source in ischemic, but viable myocardium
• F-FDG, glucose analogue + tracer, uptake suggestive of hibernating myocardium
• Gadolinium-enhanced MRI also

*Non Viable myocardium (scar) won’t improve with revascularization*
Mitral valve disease in Ischemic Cardiomyopathy Disease (Should we repair or replace?)

ACC/AHA stages of systolic HF and treatment options

Stage A
High risk with no symptoms

Stage B
Structural heart disease, no symptoms

Stage C
Structural disease, previous or current symptoms

Stage D
Refractory symptoms requiring special intervention

- Hospice
- VAD, transplantation
- Inotropes
- Aldosterone antagonist, nesiritide
- Consider multidisciplinary team
- Revascularization, mitral-valve surgery
- Cardiac resynchronization if bundle-branch block present
- Dietary sodium restriction, diuretics, and digoxin
- ACE inhibitors and β-blockers in all patients
- ACE inhibitors or ARBs in all patients; β-blockers
- Treat hypertension, diabetes, dyslipidemia; ACE inhibitors or ARBs
- Risk-factor reduction, patient and family education

*In appropriate patients

Transplant Signature Program
Henry Ford Hospital (1993-1999)
Adult and Pediatric Heart Transplants
Number of Transplants by Year and Location

NOTE: This figure includes only the heart transplants that are reported to the ISHLT Transplant Registry. As such, the presented data may not mirror the changes in the number of heart transplants performed worldwide.
Indications for Heart Transplantation

• **End-Stage Heart Failure**

  *NYHA class III or IV on maximal medical therapy evidenced by:*
  - Reduced LVEF
  - Severe diastolic dysfunction
  - Reduced functional capacity (VO2 ≤ 12)

• Inoperable coronary artery disease with intractable angina symptoms refractory to medical therapy

• Malignant ventricular arrhythmias unresponsive to medical or surgical therapy
The Prognostic Value of Maximal Oxygen Consumption

VO₂ > 14 ml/Kg/min

VO₂ ≤ 14 ml/Kg/min (listed)*

VO₂ ≤ 14 ml/Kg/min (not listed)*

* p<0.005 for VO₂ ≤ 14 vs > 14

Circulation 1991;83:778-786
Transplant Success

GOOD DONOR

GOOD RECIPIENT

GOOD OUTCOME
Transplant At A Glance: 2018
(as of 1/16/18)

115,267
People needing a lifesaving organ transplant (total waiting list)

>34,772
Transplants performed this year (2017)

16,468
Donors – Organ donation and Transplantation can save lives

• Every 10 minutes, someone is added to the national transplant waiting list
• On average, 22 people die each day while waiting for a transplant
• One organ donor can save eight lives
Primary Goal: Reduce deaths on the waitlist.

The Problem

- Demand > Supply
- Our challenge is to allocate a resource where demand greatly exceeds supply.
- This means we need to make trade-offs based on evidence, values and guiding principles.
Organ Perfusion Systems

OCS Cardiac Resuscitation System
Advanced Heart Failure Options

Cardiac Transplant

Permanent Assist Pump or Artificial Heart

15 years  65 years (Age)
Difficult Decisions of End Stage Heart Failure: Mechanical Circulatory Support

The risks of multi-system organ failure from progressive heart failure (> 50% death in 1 year) vs.

The risks of surgical intervention for MCSD and ongoing MCSD support
Thoratec Heartmate II

- Continuous, axial flow LVAD approved as BTT 2005 (CE Mark)
- FDA approval as BTT/DT 2008
- Clinical experience >700 implants worldwide
- 79% patients survive to transplant, recovery or ongoing support as DT
- Mean support 169 days
- Requires aggressive anticoagulation
Can LVADs Outlive Heart Transplants?

• 52 yo WF with breast cancer diagnosis
• Complete cure after therapy
• Chemotherapy (Adriamycin) induced cardiomyopathy
• Advanced heart failure
• Heartmate II 2005
• **Uneventful postop course: Year 10**
Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS)
Analysis of Pump Thrombosis in the HeartMate II LVAD

James K. Kirklin, MD, David C. Naftel, PhD, Robert L. Kormos, MD, Francis D. Pagani, MD, Susan L. Myers, MPH, Lynne W. Stevenson, MD, Michael A. Acker, MD, Daniel L. Goldstein, MD,
Scott C. Silvestry, MD, Carmelo A. Milano, MD, J. Timothy Baldwin, MD, Sean Pinney, MD, J. Eduardo Rame, MD, Marissa A. Miller, DVM, MPH

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Next Generation LVADs

- Smaller, easier implant
- Bridge to recovery possibility, destination application
- Still requires aggressive anticoagulation
- Pump (Blood) flow estimation based upon pump speed/power
- Pre-load dependent, after-load sensitive
- Variable adaptability to changes in patients physical demands
- The HeartMate 3 LVAS includes a fully magnetically levitated centrifugal blood pump
In the meantime...
waiting for a heart transplant

Left to right:
Mr. J. Everett Logan, Mrs. Launa Logan, Dr. Robert Higgins
The Gift of Life
FIGURE 18.13  ■ Bicaval anastomotic technique.
Complications

• Infection
• Rejection (acute and chronic)
• Cancer
  – solid tumors
  – lymphoma
Median survival = 11 years
Median survival conditional on surviving 1st year = 13 years

N = 103,299

N at risk at 26 years = 117
• World Record Heart Transplant Recipient Dies Of Cancer-13 Aug 2009

Tony Huesman, the world's longest surviving single heart transplant recipient died at age 51 of cancer on Sunday evening, nearly 31 years after receiving a heart from an anonymous donor at a US hospital.
Adult Heart Transplants
Cumulative Incidence of Leading Causes of Death
(Transplants: January 1994 – June 2011)

Incidence of Cause-Specific Deaths

- CAV
- Acute Rejection
- Malignancy (non-Lymph/PTLD)

Years

0% 2% 4% 6% 8% 10% 12% 14%

0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Total Artificial Heart

- Provides bi-ventricular support
- Pneumatically driven
- FDA approved for BTT in 2004
- Ongoing trial for DT designation: approved December 18, 2014
SynCardia Total Artificial Heart
SynCardia Total Artificial Heart
SynCardia Total Artificial Heart
What Does the Patient Think?
Stem Therapy in the Future

Cardiogenic differentiation of pluripotent stem cells (ESC or iPSC)
- Limitations: cellular heterogeneity, immature cardiac phenotype, immunogenic (if allogenic)
  - Growth factors (e.g. activin/Nodal, BMP4, Wnt)
  - Small molecules

Cardiogenic reprogramming of somatic cells
- Limitations: incomplete cardiac phenotype, inefficiency of reprogramming, integrating viral vectors, unknown long-term stability
- In situ
  - Local delivery of reprogramming factors (e.g. GMT or microRNA)
- In vitro (i.e. fibroblasts)
  - Lentiviral/retroviral transduction (e.g. GMT, microRNA or small molecules)

Cardiogenic differentiation of adult stem cells
- Limitations: assessment confounded by cell fusion
- 5-aza, growth factors

Current Opinion in Biotechnology

https://doi.org/10.1016/j.copbio.2017.05.011
Xenotransplantation: The Future of Organ Failure Therapy?
Thank You