

Ischemic cardiomyopathy: Indications for Revascularization



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Ischemic Cardiomyopathy

The term ischemic cardiomyopathy has been used to describe significantly impaired left ventricular function (left ventricular ejection fraction ≤ 35 to 40 percent) that results from coronary artery disease



Ischemic Cardiomyopathy (LVHF)

In USA, an estimated 5.1 million adults are living with heart failure

At least 1/2 of HF with reduced EF (HF-REF)

The most common etiology of HF-REF in the developed world is IHD, >60% of diagnoses

Patients with ischemic causes of (LV) systolic dysfunction have significantly higher mortality rates than those with non ischemic etiologies



Case Presentation

65 year old female presenting with a diagnosis of HF

Progressive SOB and orthopnea

Atypical chest discomfort with variable exertion, emotional stress

Past history

HTN

DM

Initial assessment:

BP 130/82, HR 84 bpm (regular), obvious volume overload

NT-BNP 3800 pg/mL, troponin I negative

ECG: sinus rhythm, ST-T wave changes in different leads



Case Presentation

- **Echocardiogram performed:**
 - LVEF ~25%, global hypokinesis
 - LVIDd 5.8cm; LVIDs 5.1cm, EF 29%
 - 2+MR
 - RVSP ~ 45 mmHg
- **Course in hospital over 7 days**
 - Diuresed 4 kg with IV furosemide, at “dry weight”
 - Started on Lisinopril 10 mg/d, and carvedilol 6.25 mg bid



Case - What would you like to do next?

1. Coronary angiogram
2. Myocardial perfusion imaging (persantine sestamibi)
3. Cardiac MRI
4. Referral to EP for ICD and or CRT



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Case Presentation

- **Angiogram reveals multivessel coronary disease**
 - Mid 90% RCA
 - Proximal 80% LAD lesion
 - 90% proximal Diagonal lesion
 - Proximal to mid Cix 80-90% lesion
- Serum creatinine stable at 120 mmol/L, GFR 51 ml/min



Case - Your recommended course of action ?

1. Discharge w/a plan for titrated medical tx until angina occurs
2. Present the patient to CV surgical colleagues to consider CABG
3. Refer to interventional colleague for multivessel PCI
4. Referral for ICD/CRT

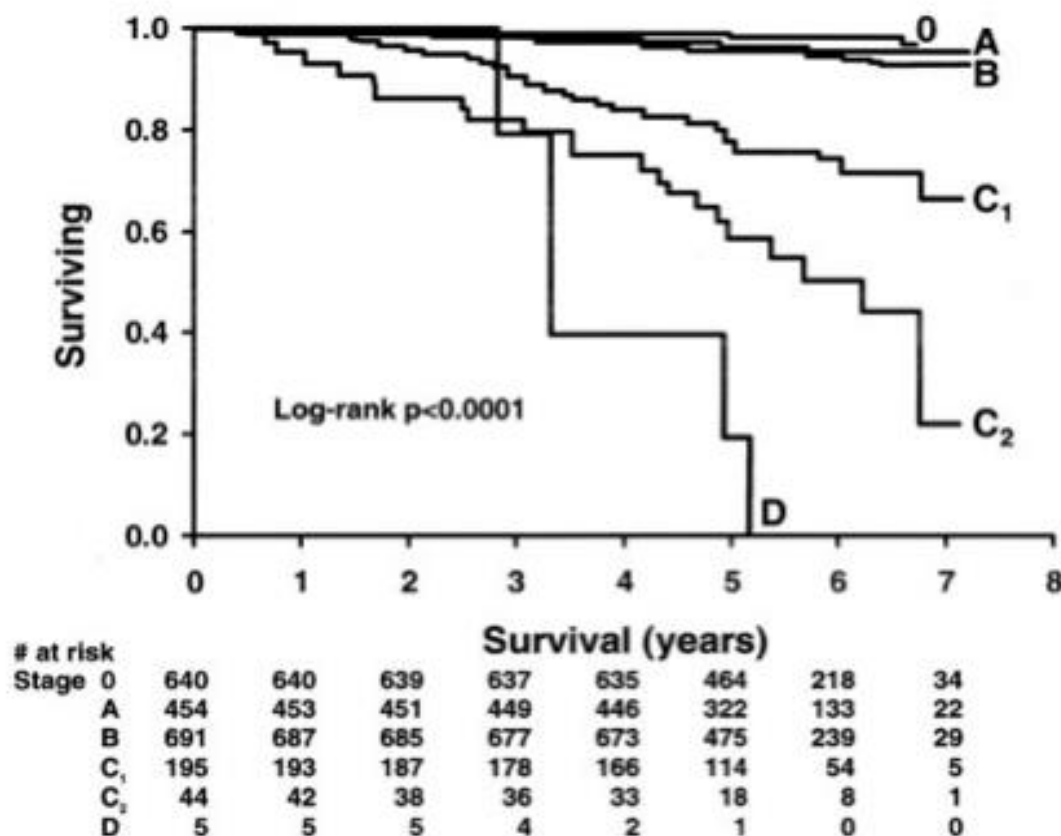


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Progression of Symptomatic HF: Worsening Prognosis



Ischemic heart disease

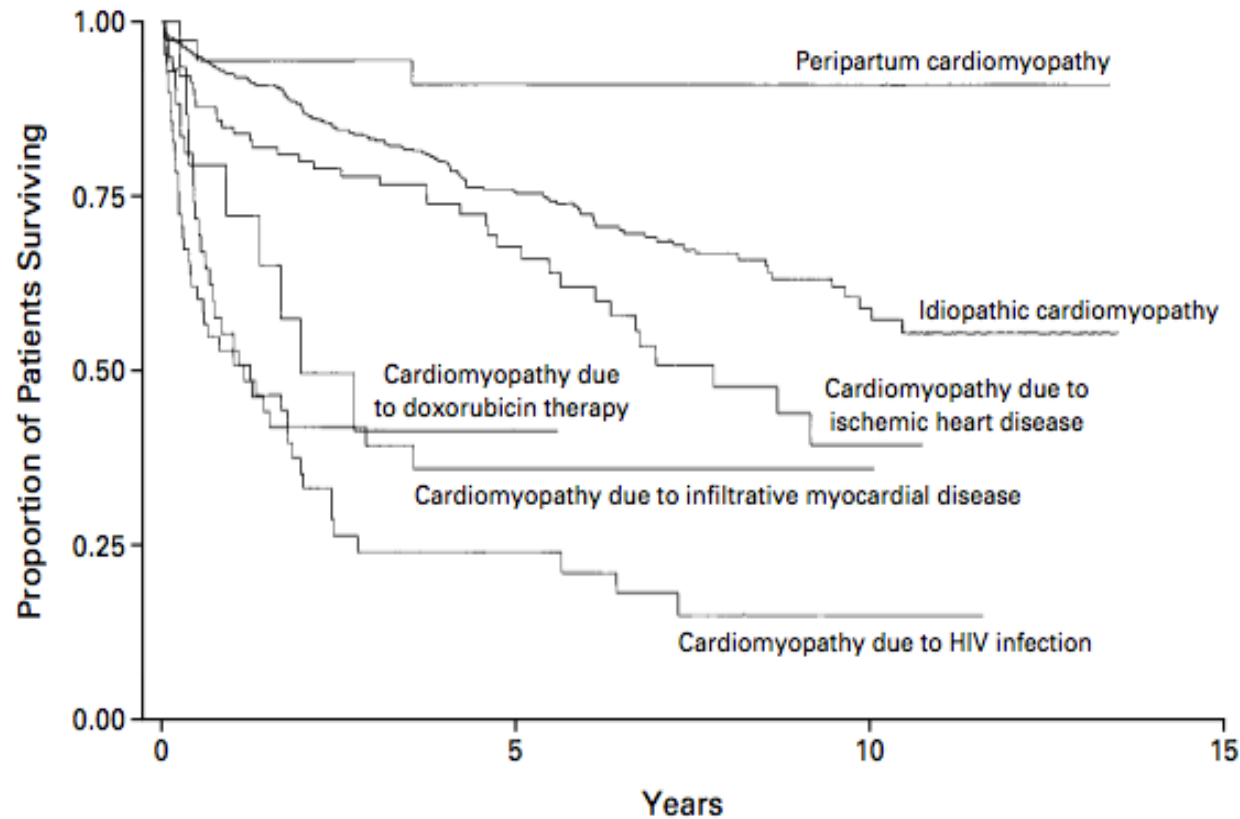
Ischemic heart disease
+ *heart failure*



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Prognostic significance of ischemic cardiomyopathy

>1200 patients with invasive evaluation for cardiomyopathy over 15 years



Ischemic etiology is also an independent predictor of mortality in risk models:

Seattle Heart Failure Model (SHFM)

Heart Failure Survival Score (HFSS)



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Treatment for Ischemic Cardiomyopathy, Evidence ?

- Revascularization
- Surgical
- PCI
- Medical Therapy
- ICD/CRT
- SVR



Surgical Treatment for Ischemic Heart Failure – where's the evidence?

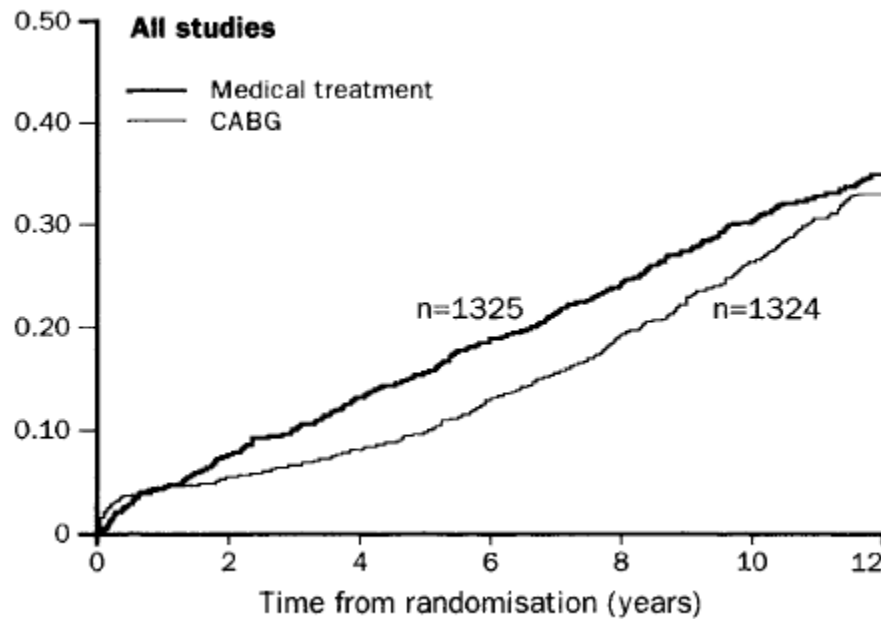


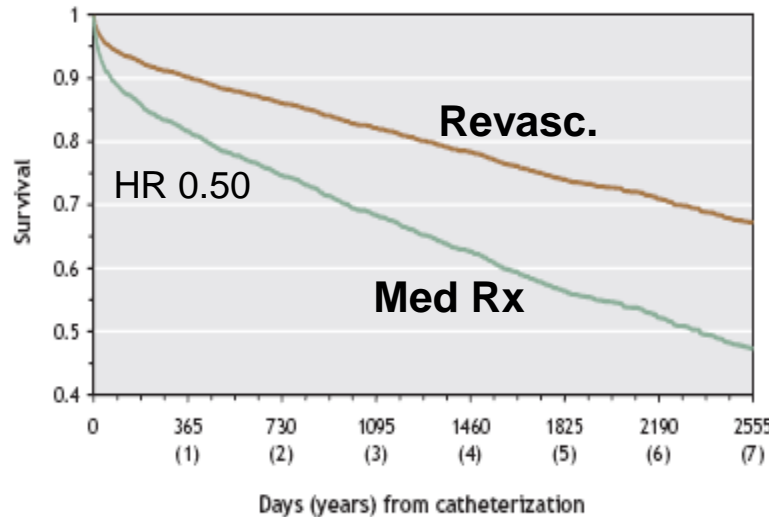
Figure 2: **Survival curve for overall population**

In these early studies:

- 90% had angina
- 80% had normal LVEF
- 10% had arterial conduits
- Medical therapy = digoxin and diuretics



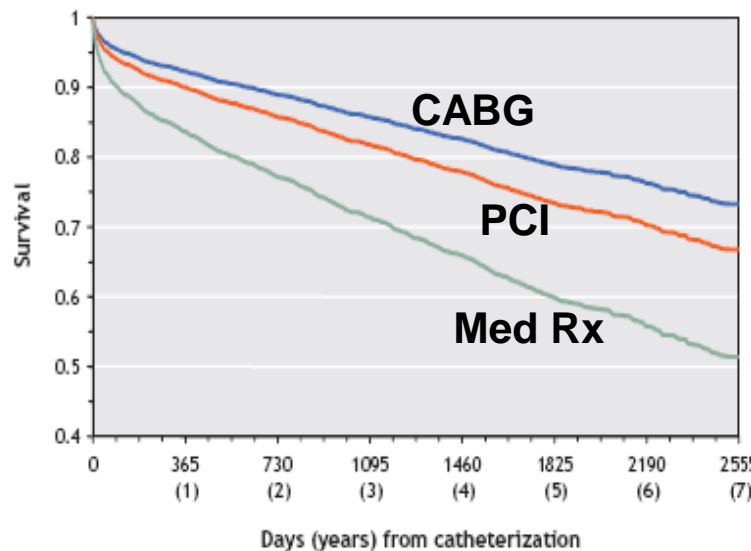
PCI or CABG for ischemic symptoms and heart failure? (Angina included!!)



4200 patients with HF
referred for angiography in Alberta 1995-2001

Adjusted for baseline risk and propensity for
revascularization

2538 underwent revascularization; 1690
managed medically



Majority of patients had ischemic syndromes
Medical management was suboptimal

Revascularization with CABG or PCI associated
with improved survival

Signal for differential outcome, favoring CABG

Tsuyuki et al, CMAJ 2006



TRIALS OF SURGICAL VERSUS PERCUTANEOUS REVASCULARIZATION

- Several trials have compared PCI (balloon angioplasty, bare-metal stents, and drug-eluting stents) and CABG in patients with multivessel CAD.
- Among 27 randomized controlled trials comparing these 2 revascularization strategies
- majority of patients had preserved LV systolic function (EF >50%).



TRIALS OF SURGICAL VERSUS PERCUTANEOUS REVASCULARIZATION

Two relatively large trials

That included patients with LV dysfunction were **BARI** (Bypass Angioplasty Revascularization Investigation) , in which 22% of patients had LVEF <50%, and

AWESOME (Angina With Extremely Serious Operative Mortality Evaluation) , in which 21% had LVEF <35%.

Subgroup analyses in patients with LV dysfunction from these trials suggest no difference in outcome between PCI and CABG ,



TRIALS OF SURGICAL VERSUS PERCUTANEOUS REVASCULARIZATION

The most recent trials comparing PCI with CABG failed to provide more clarity. Only approximately 2% of patients enrolled in the **SYNTAX** (Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery) trial had LVEF <30% More recently, the NHLBI-sponsored

FREEDOM (Future Revascularization Evaluation in Patients With Diabetes Mellitus: Optimal Management of Multivessel Disease) trial reported similar outcomes with PCI with drug-eluting stents and CABG in patients with LVEF <40%, but only 32 patients (2.5%) were in this pre-specified subgroup.

Thus, the available data are insufficient to adequately compare PCI and CABG in patients with severe LV dysfunction.



THE STICH TRIAL

The STICH trial is the only prospective, randomized, controlled trial to specifically investigate the role of CABG in patients with LVEF < 35% who are also receiving GDMT

The surgical revascularization hypothesis evaluated CABG compared with GDMT alone (n = 1,212)

The surgical ventricular reconstruction hypothesis compared CABG with and without SVR (n = 1,000)

GDMT included renin-angiotensin-aldosterone system inhibitors, beta-blockers, statins, and antiplatelet agents titrated to optimal doses; diuretic agents and digitalis were also used



THE STICH TRIAL (Results)

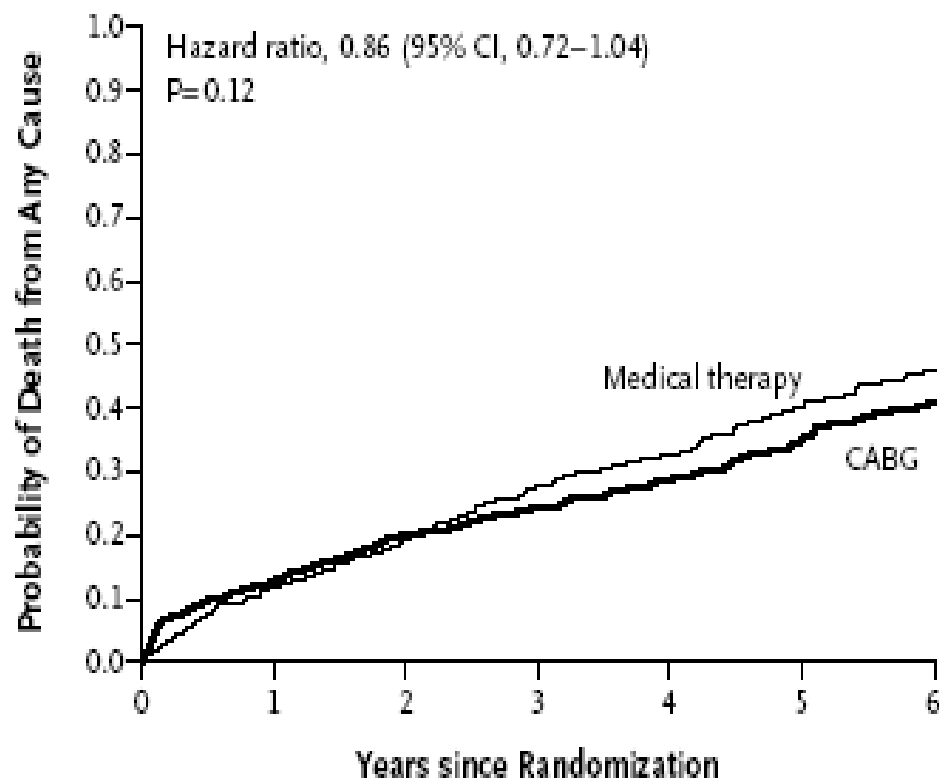
No significant difference was observed in the primary outcome of all-cause mortality between patients randomized to CABG versus GDMT over a median follow-up period of 56months (Figure 1A)

The CABG group had improved rates of death from cardiovascular causes and improved rates of a combined endpoint of death from any cause and hospitalization for heart failure, which were pre-specified secondary endpoints (Figures 1B and C)

In addition, as-treated, perprotocol, and adjusted analyses to account for patient crossovers all suggested an overall favorable effect of CABG on primary and secondary outcomes



STICH Hypothesis 1: Primary outcome



1212 patients randomized to CABG vs medical therapy

Patients with recent MI, major illness, significant L Main disease and severe angina excluded

No difference in all cause mortality seen at median 56 months follow-up

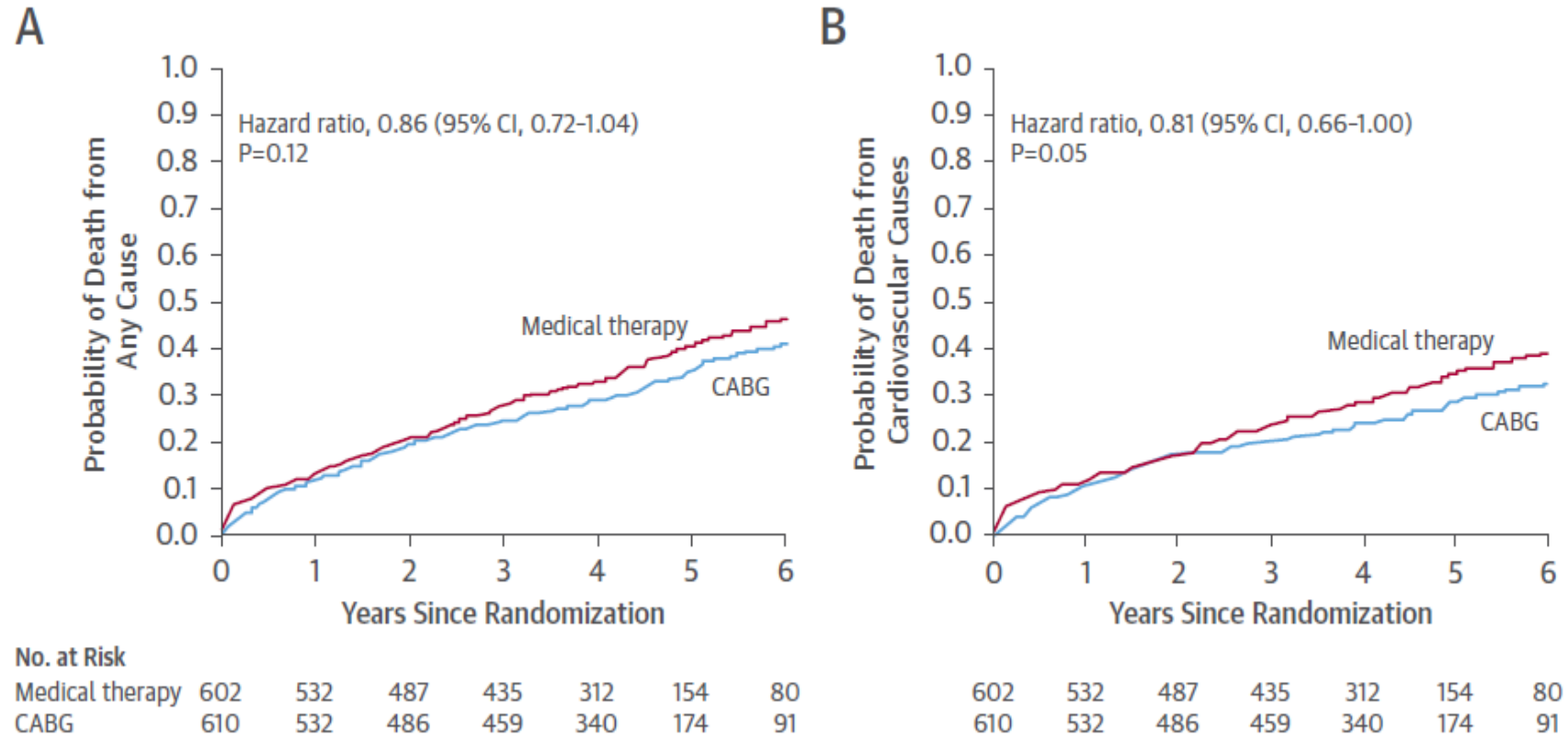
17% of patients in medical therapy arm crossed over to surgical arm

No. at Risk							
Medical therapy	602	532	487	435	312	154	80
CABG	610	532	486	459	340	174	91

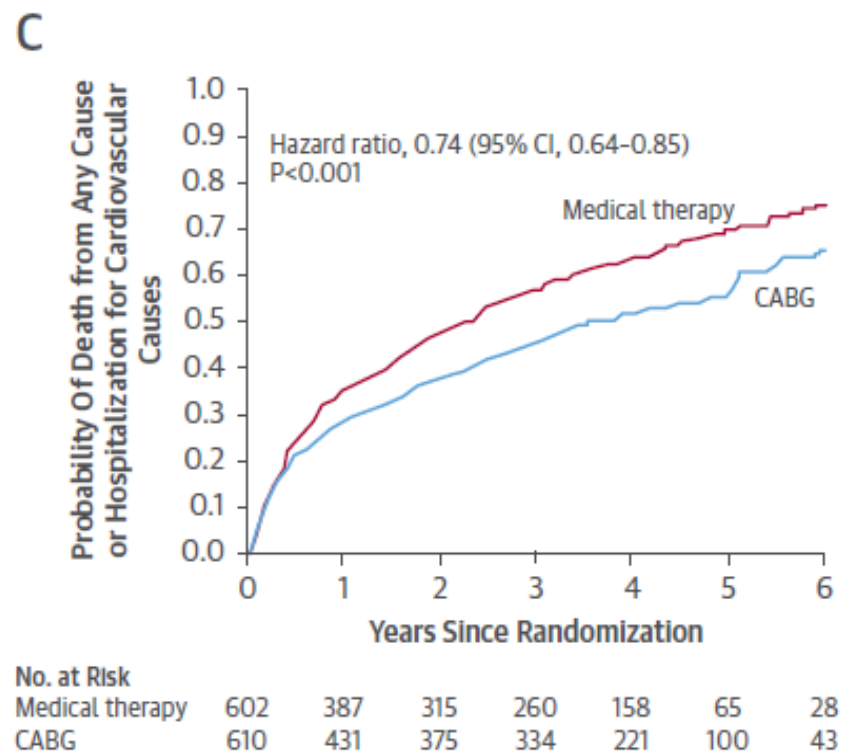


THE STICH TRIAL

FIGURE 1 Survival Analyses in the STICH Trial Using an Intention-to-Treat Analysis

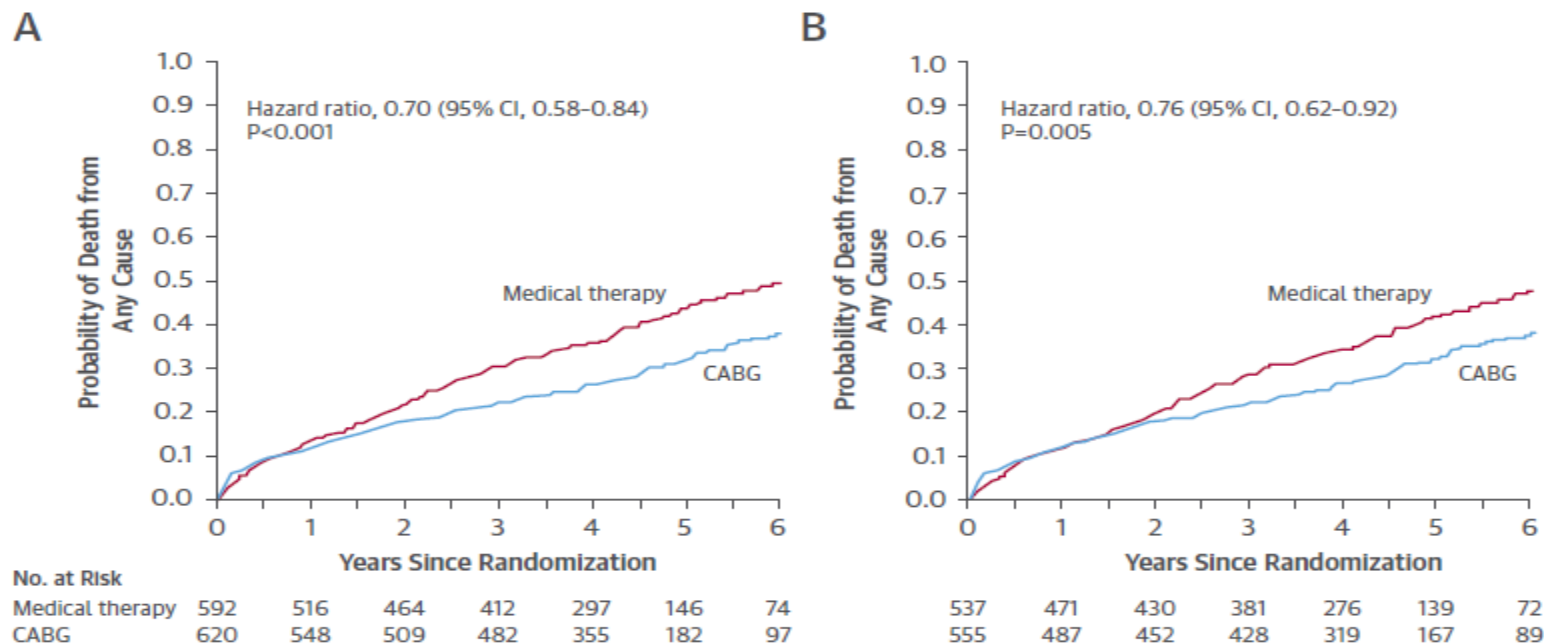


THE STICH TRIAL



THE STICH TRIAL

FIGURE 2 Survival Analyses in the STICH Trial According to Actual Treatment Received



(A) As-treated and **(B)** per-protocol analyses to adjust for early crossovers indicate significant reduction in mortality rates with surgical (CABG) compared with medical therapy. Reproduced with permission from Velazquez et al. (34). Abbreviations as in Figure 1.



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Table 32. Recommendations for Surgical/Percutaneous/Transcatheter Interventional Treatments of HF

Recommendations	COR	LOE	References
CABG or percutaneous intervention is indicated for HF patients on GDMT with angina and suitable coronary anatomy, especially significant left main stenosis or left main equivalent	I	C	10,12,14,848
CABG to improve survival is reasonable in patients with mild to moderate LV systolic dysfunction and significant multivessel CAD or proximal LAD stenosis when viable myocardium is present	IIa	B	848–850
CABG or medical therapy is reasonable to improve morbidity and mortality for patients with severe LV dysfunction (EF <35%), HF, and significant CAD	IIa	B	309,851
Surgical aortic valve replacement is reasonable for patients with critical aortic stenosis and a predicted surgical mortality of no greater than 10%	IIa	B	852
Transcatheter aortic valve replacement is reasonable for patients with critical aortic stenosis who are deemed inoperable	IIa	B	853
CABG may be considered in patients with ischemic heart disease, severe LV systolic dysfunction, and operable coronary anatomy whether or not viable myocardium is present	IIb	B	307–309
Transcatheter mitral valve repair or mitral valve surgery for functional mitral insufficiency is of uncertain benefit	IIb	B	854–857
Surgical reverse remodeling or LV aneurysmectomy may be considered in HF/EF for specific indications, including intractable HF and ventricular arrhythmias	IIb	B	858

CABG indicates coronary artery bypass graft; CAD, coronary artery disease; COR, Class of Recommendation; EF, ejection fraction; GDMT, guideline-directed medical therapy; HF, heart failure; HF/EF, heart failure with reduced ejection fraction; LAD, left anterior descending; LOE, Level of Evidence; and LV, left ventricular.



Surgical/Percutaneous/Transcatheter Interventional Treatments of HF

- **CLASS I**

1. Coronary artery revascularization via CABG or percutaneous intervention (PCI)is indicated for patients (HFpEF and HFrEF) on GDMT with angina and suitable coronary anatomy, especially for a left main stenosis (>50%) or left main equivalent disease (Level of Evidence: C)



Surgical/Percutaneous/Transcatheter Interventional Treatments of HF

- CLASS IIa

1. CABG to improve survival is reasonable in patients with mild to moderate LV systolic dysfunction (EF 35% to 50%) and significant ($\geq 70\%$ diameter stenosis) multivessel CAD or proximal left anterior descending coronary artery stenosis when viable myocardium is present in the region of intended revascularization. (Level of Evidence: B)

2. CABG or medical therapy is reasonable to improve morbidity and cardiovascular mortality for patients with severe LV dysfunction (EF $< 35\%$), HF, and significant CAD
(Level of Evidence: B)



Surgical/Percutaneous/Transcatheter Interventional Treatments of HF

CLASS IIb

1. CABG may be considered with the intent of improving survival in patients with ischemic heart disease with severe LV systolic dysfunction (EF <35%) and operable coronary anatomy whether or not viable myocardium is present (307–309). (Level of Evidence: B)
2. Transcatheter mitral valve repair or mitral valve surgery for functional mitral insufficiency is of uncertain benefit and should only be considered after careful candidate selection and with a background of GDMT (854–857). (Level of Evidence: B)
3. Surgical reverse remodeling or LV aneurysmectomy may be considered in carefully selected patients with HFrEF for specific indications, including intractable HF and ventricular arrhythmias (858). (Level of Evidence: B)



Practical Tips

Revascularization Procedures

Imaging

1. Several non-invasive methods for detection of coronary artery disease are in widespread use

- Dobutamine stress echocardiography (DSE)
- perfusion cardiac magnetic resonance (CMR)
- cardiac positron emission testing (PET)
- nuclear stress imaging

Local factors (availability, price, expertise, practice patterns) will determine the optimal strategy for imaging.

2. Non- invasive imaging modalities may provide critical information such as the degree of ischemic or hibernating myocardium, and may be used to determine the likelihood of regional and global improvement in left ventricular systolic function.



Practical Tips (cont'd)

Revascularization Procedures

Imaging

3. Patients with heart failure, and reduced LV ejection fraction are likely to experience significant improvement in LVEF following successful coronary revascularization if they demonstrate:

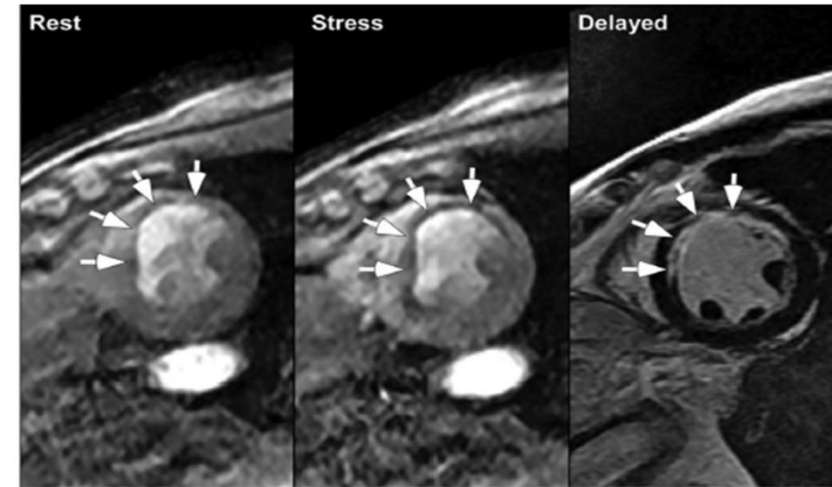
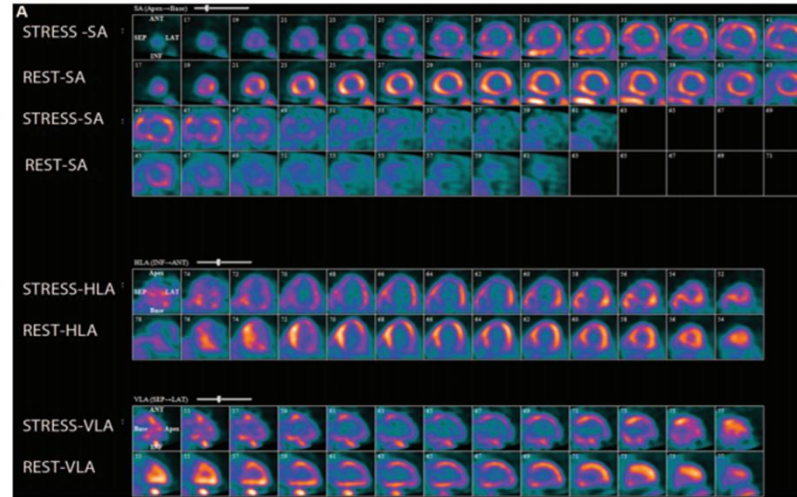
- a) Reversible ischemia or a large segment of viable myocardium ($> 30\%$ of LV) by nuclear stress testing/ viability study;
- b) Reversible ischemia or $>7\%$ hibernating myocardium on PET scanning;
- c) Reversible ischemia or $> 20\%$ of LV shown as viable by DSE;
- d) Less than 50% wall thickness scarring as shown by late gadolinium enhancement by cardiac CMR.



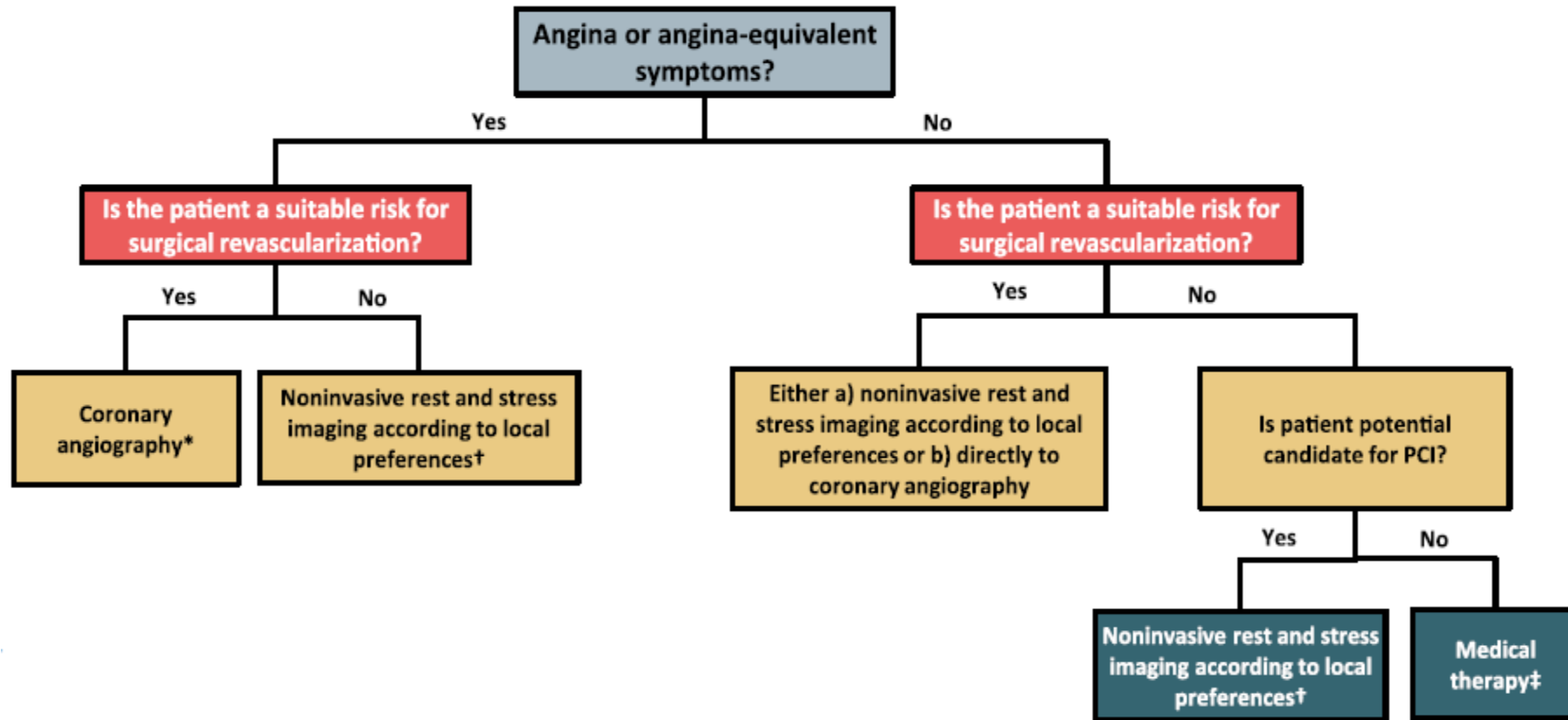
Predicting Benefit From Revascularization in Patients With Ischemic Heart Failure

Imaging of Myocardial Ischemia and Viability

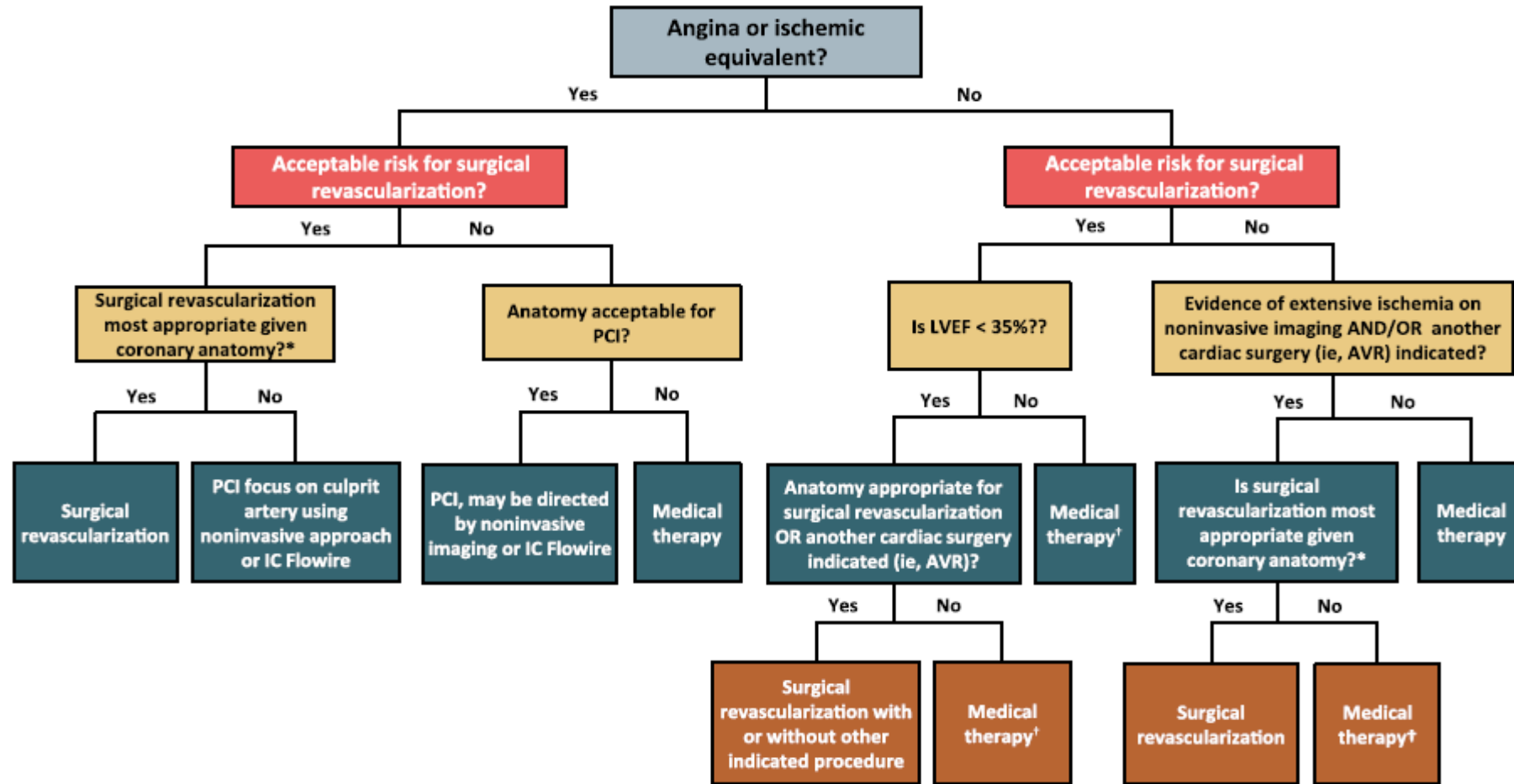
- The prediction of functional, symptomatic, and survival benefit depends on multiple factors
- Including the quality of the target vessels for revascularization
- The magnitude of myocardial ischemia and viability, the degree of LV remodeling after myocardial infarction (MI), and other clinical factors



Approach to Assessment for Coronary Artery Disease in Patients with Heart Failure



Decision Regarding Coronary Revascularization in Heart Failure



Conclusion

- **The highest-risk patients with HF-REF are those with ischemic cardiomyopathy**
- **The cornerstone of treatment is GDMT for all patients and CRT for appropriately selected patients.**
- **According to STICH trial, the surgical revascularization offers improved survival and quality of life, particularly in patients with more extensive multivessel disease and the greatest degree of LV systolic dysfunction and remodeling, who are also at the greatest short-term risk of mortality with CABG**
- **SVR does not appear to add to the clinical benefits of CABG in patients with more severely remodeled ventricles. Concomitant mitral valve surgery is warranted in patients undergoing CABG with severe ischemic MR; clinical trial data have questioned the indications for concomitant mitral valve surgery in those with moderate MR.**



Thank You



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HF With Reduced EF (HFrEF)

- In approximately half of patients with HFrEF, variable degrees of LV enlargement may accompany HFrEF 36 and 37.
- The definition of HFrEF has varied, with guidelines of left ventricular ejection fraction (LVEF) $\leq 35\%$, $< 40\%$, and $\leq 40\%$ 18, 19 and 38. Randomized controlled trials (RCTs) in patients with HF have mainly enrolled patients with HFrEF with an EF $\leq 35\%$ or $\leq 40\%$, and it is only in these patients that efficacious therapies have been demonstrated to date.
- For the present guideline, HFrEF is defined as the clinical diagnosis of HF and EF $\leq 40\%$. Those with LV systolic dysfunction commonly have elements of diastolic dysfunction as well (39). Although coronary artery disease (CAD) with antecedent myocardial infarction (MI) is a major cause of HFrEF, many other risk factors (Section 4.6) may lead to LV enlargement and HFrEF.

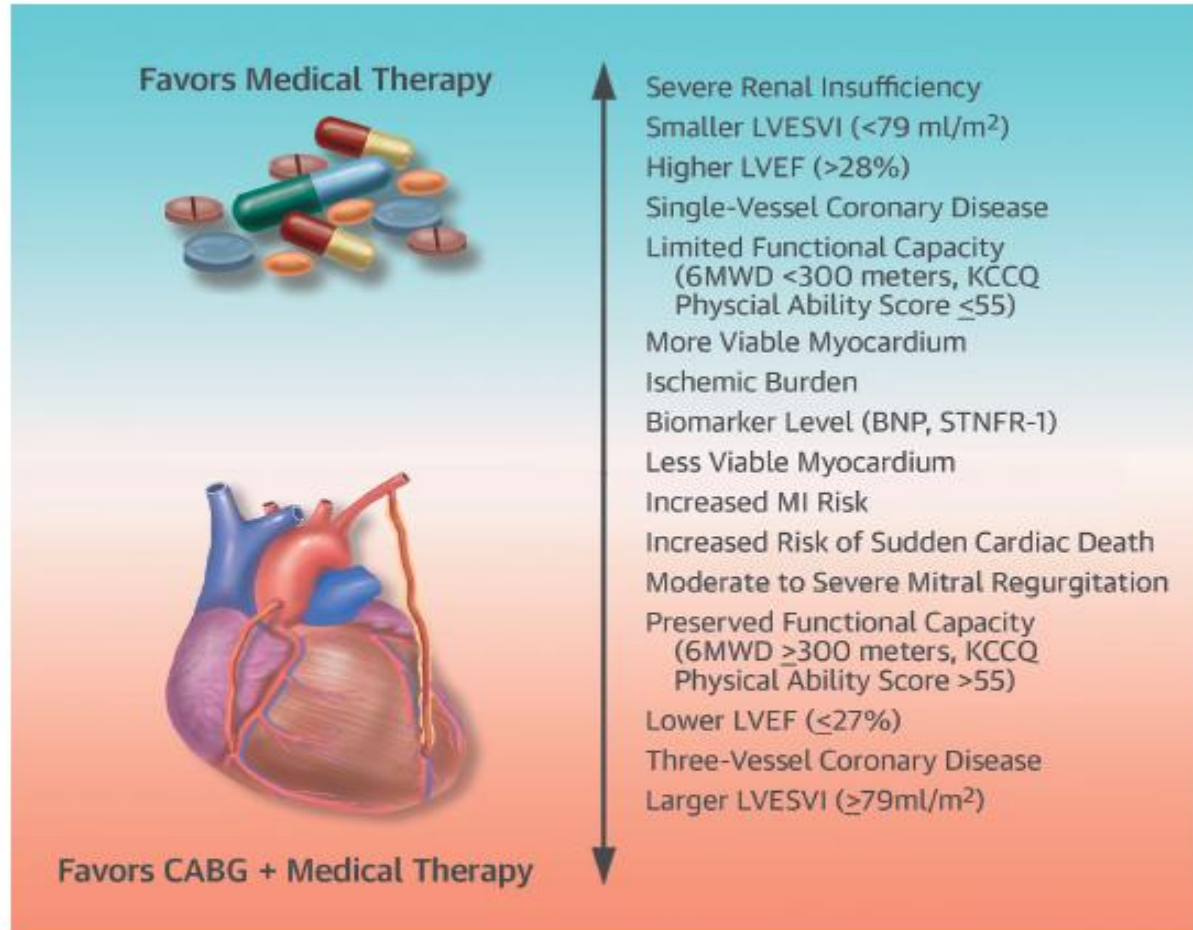


Left-Heart Catheterization

- Left-heart catheterization or coronary angiography is indicated for patients with HF and angina and may be useful for those patients without angina but with LV dysfunction.
- Invasive coronary angiography should be used in accordance with the ACCF/AHA coronary artery bypass graft (CABG) and percutaneous coronary intervention guidelines and should only be performed in patients who are potentially eligible for revascularization and. In patients with known CAD and angina or with significant ischemia diagnosed by ECG or noninvasive testing and impaired ventricular function, coronary angiography is indicated.
- Among those without a prior diagnosis, CAD should be considered as a potential etiology of impaired LV function and should be excluded wherever possible. Coronary angiography may be considered in these circumstances to detect and localize large-vessel coronary obstructions. In patients in whom CAD has been excluded as the cause of LV dysfunction, coronary angiography is generally not indicated unless a change in clinical status suggests interim development of ischemic disease.



CENTRAL ILLUSTRATION Revascularization in Heart Failure: Proposed Contributing Factors Influencing the Decision for Revascularization in Patients With Severe Left Ventricular Dysfunction



Velazquez, E.J. et al. J Am Coll Cardiol. 2015; 65(6):615-24.

Genetics, biomarkers, ischemia, viability assessment, and presence of mitral regurgitation do not have as significant an impact on this decision as risk of sudden death and recurrent infarction, functional capacity, multivessel coronary artery disease, and severity of left ventricular remodeling. BNP = B-type natriuretic peptide; CABG = coronary artery bypass graft surgery; KCCQ = Kansas City Cardiomyopathy Questionnaire; LVEF = left ventricular ejection fraction; LVESVI = left ventricular end systolic volume index; MI = myocardial infarction; 6MWD = 6-min walk distance; STNFR-1 = soluble tumor necrosis factor receptor 1.



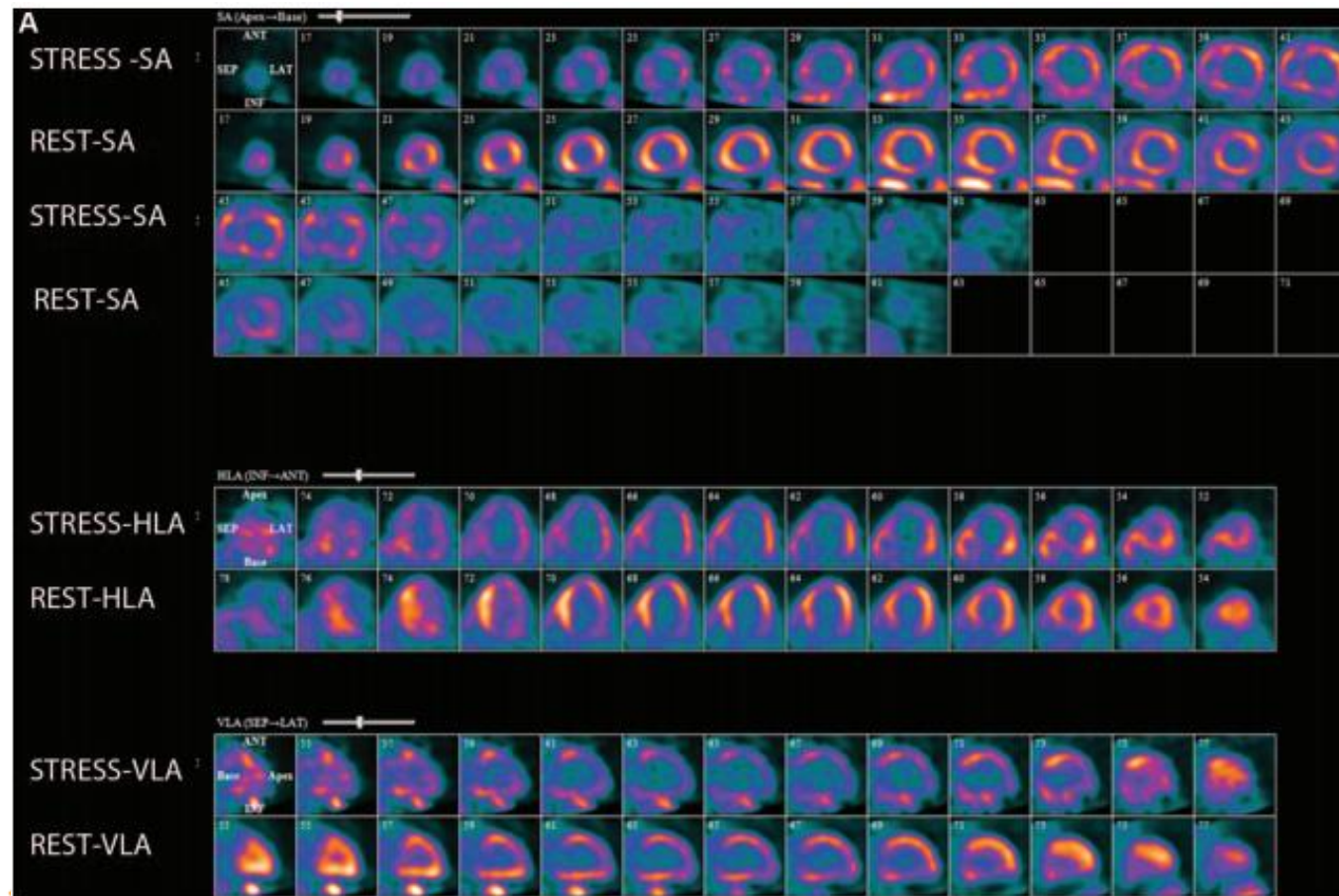
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Ischemic Cardiomyopathy

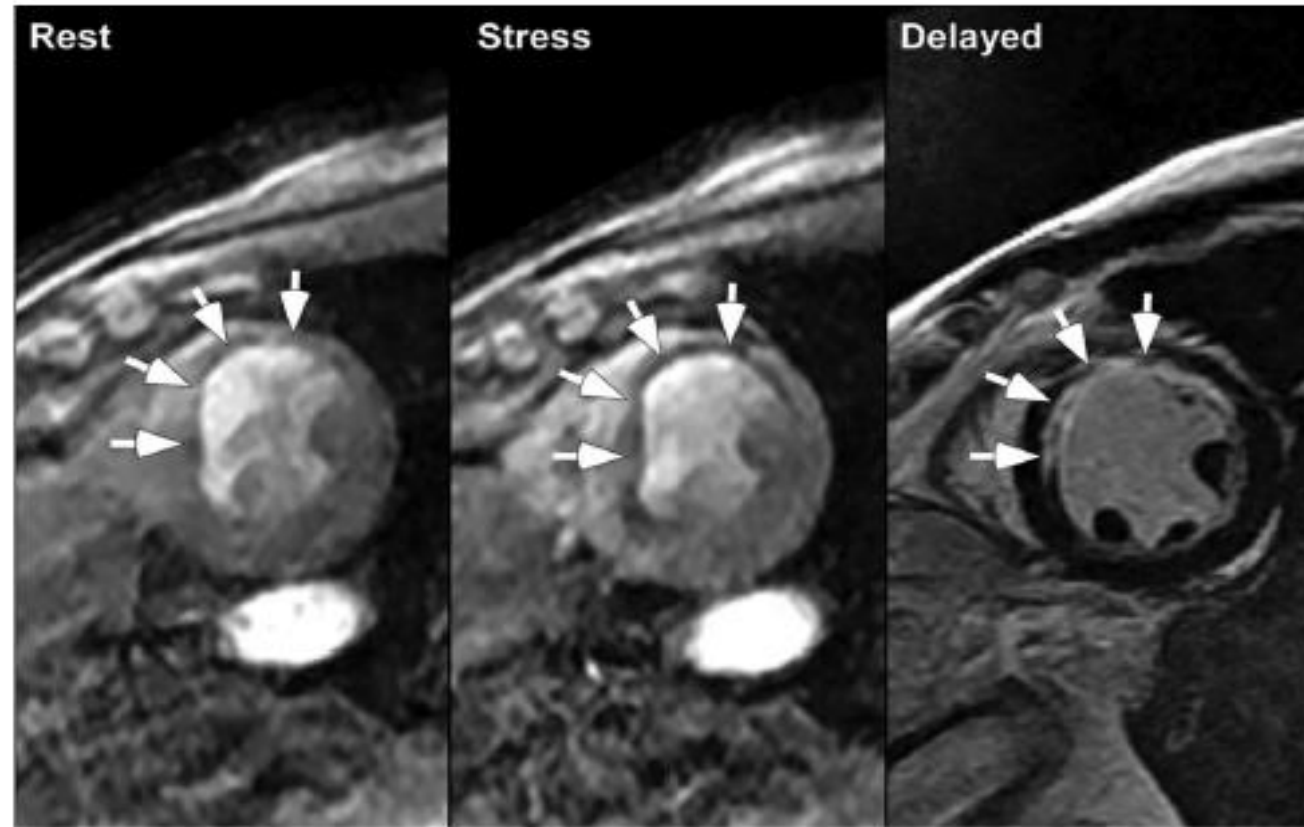
- **Cardiac dysfunction is felt to be caused by coronary artery disease and ischemic injury**
 - Usually implies LV systolic dysfunction
 - May or may not be a prior history of MI
 - Usually due to multivessel disease or significant ischemic damage to large territory of myocardium
- **Most common cause of systolic HF (~50-65% of all cases)**
- **Associated with worse prognosis than other forms of LV systolic dysfunction**



A, Stress-rest rubidium 82 (82Rb) myocardial perfusion PET/computed tomography study in corresponding short-axis (SA; top), horizontal long-axis (HLA; middle), and vertical long-axis (VLA; bottom) slices. The LV is severely dilated (end-diastolic volume of 335 mL), and LV ejection fraction is reduced at 18%. There is a large and severe perfusion defect throughout the anterior and anteroseptal walls and the LV apex, consistent with extensive stress-induced ischemia throughout the left anterior descending coronary artery territory. In addition, there is an associated small area of fixed perfusion deficit that involves the basal inferior and inferolateral walls, consistent with scar in the left circumflex artery territory indicated. B, Three-dimensionally rendered reconstructions of the LV demonstrating the quantitative extent and severity of perfusion deficit (blackout region) and the magnitude of stress-induced ischemia or defect reversibility (pink)



Selecting the Approach for Assessment of Myocardial Viability



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- The occurrence of severe LV systolic dysfunction after MI, especially if associated with heart failure, is associated with very poor survival. Differentiation between LV dysfunction caused by infarction, necrosis, and scar tissue formation versus LV dysfunction due to ischemic but viable myocardium has important implications.
- Identification of the latter group of patients with these potentially reversible causes of heart failure may be associated with substantial survival benefit, symptomatic improvement, and improved LV function with revascularization
- Determination of the risk-versusbenefit ratio from high-risk revascularization in patients with ischemic LV dysfunction is not always clear-cut. Multiple factors are known to influence clinical outcomes.
- The clinical decision to revascularize is generally straightforward in patients with severe LV dysfunction, severe anginal symptoms, mild LV remodeling, adequate target vessels for revascularization, and minimal comorbidities.³



Practical Tips

Revascularization Procedures

Surgical Revascularization for Patients with IHD and HF

1. In the setting of heart failure, angina and single territory coronary artery disease, PCI may be the treatment of first choice.

However, PCI has not been shown to improve outcomes for patients with chronic stable heart failure, irrespective of underlying anatomy.

1. Urgent directed culprit vessel angioplasty continues to be the revascularization modality of choice for patients with heart failure and acute coronary syndrome.



There are two main pathogenetic mechanisms, which are importantly distinguished by the possibility of corrective therapy

- Irreversible loss of myocardium due to prior myocardial infarction with ventricular remodeling. Recovery of myocardial function in such patients cannot be achieved by coronary revascularization since the infarcted tissue is not viable.
- At least partially reversible loss of contractility due to reduced function of ischemic but still viable myocardium, which can be detected on imaging studies. Hibernating myocardium is typically used interchangeably with viable myocardium.
- However, by strict definition, the term hibernating myocardium refers to contractile dysfunction in viable myocardium that improves after revascularization or perhaps medical therapy .
- Stunned myocardium refers to transient postischemic dysfunction and can coexist with hibernating myocardium

