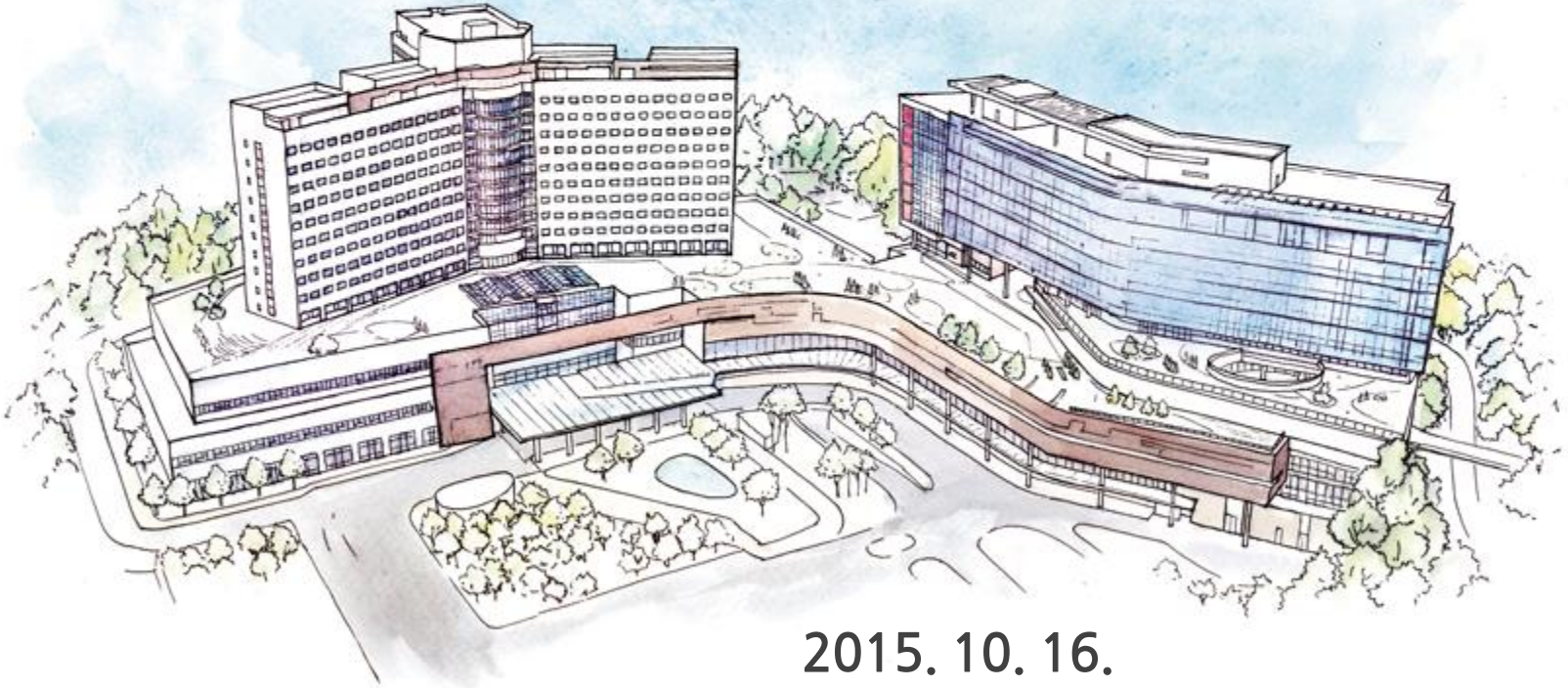
Update in Ischemic Cardiomyopathy: PCI vs CABG vs Medical Treatment



2015. 10. 16.

분당서울대학교병원
윤창환

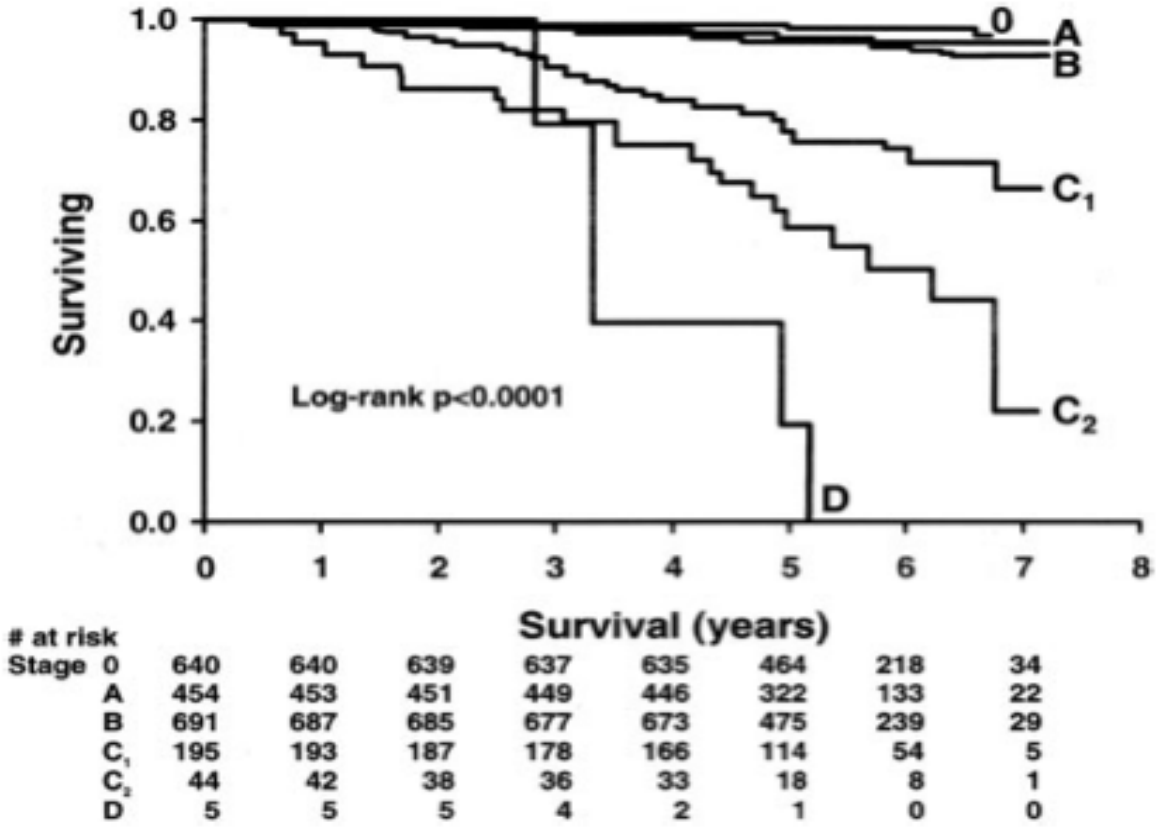
Update in ischemic cardiomyopathy

1. **Ischemic cardiomyopathy**
   Definition, epidemiology and medical treatment
2. **Medical treatment vs Surgical revascularization**
3. **PCI vs CABG**
4. **Conclusions**

Ischemic Cardiomyopathy

- Distinct condition in which cardiac dysfunction is felt to be caused by coronary artery disease and ischemic injury
  - Usually implies LV systolic dysfunction (LV EF < 35-40%)
  - May or may not be a prior history of MI
    - Irreversible loss of myocardium due to prior myocardial infarction
    - Reversible loss of contractility due to hibernating viable myocardium
  - 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

Progression of Symptomatic HF: Worsening Prognosis



# at risk								
Stage 0	640	640	639	637	635	464	218	34
A	454	453	451	449	446	322	133	22
B	691	687	685	677	673	475	239	29
C_1	195	193	187	178	166	114	54	5
C_2	44	42	38	36	33	18	8	1
D	5	5	5	4	2	1	0	0

Ischemic heart disease

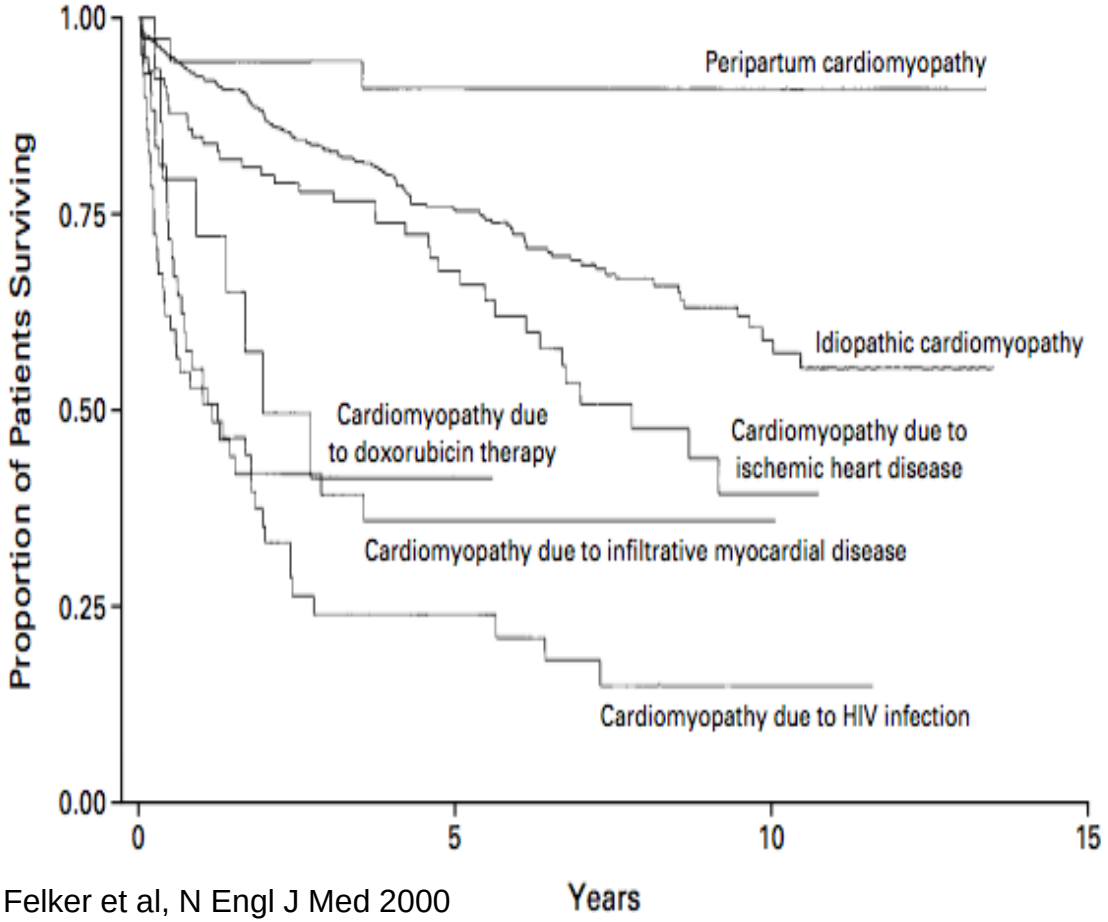
Ischemic heart disease
+ heart failure

- Progression to overt HF associated with > 5-fold mortality risk

Wang et al, Circulation 2003, Ammar et al, Circulation 2007

Prognostic significance of ischemic cardiomyopathy

>1200 patients with invasive evaluation for cardiomyopathy over 15 years



Felker et al, N Engl J Med 2000

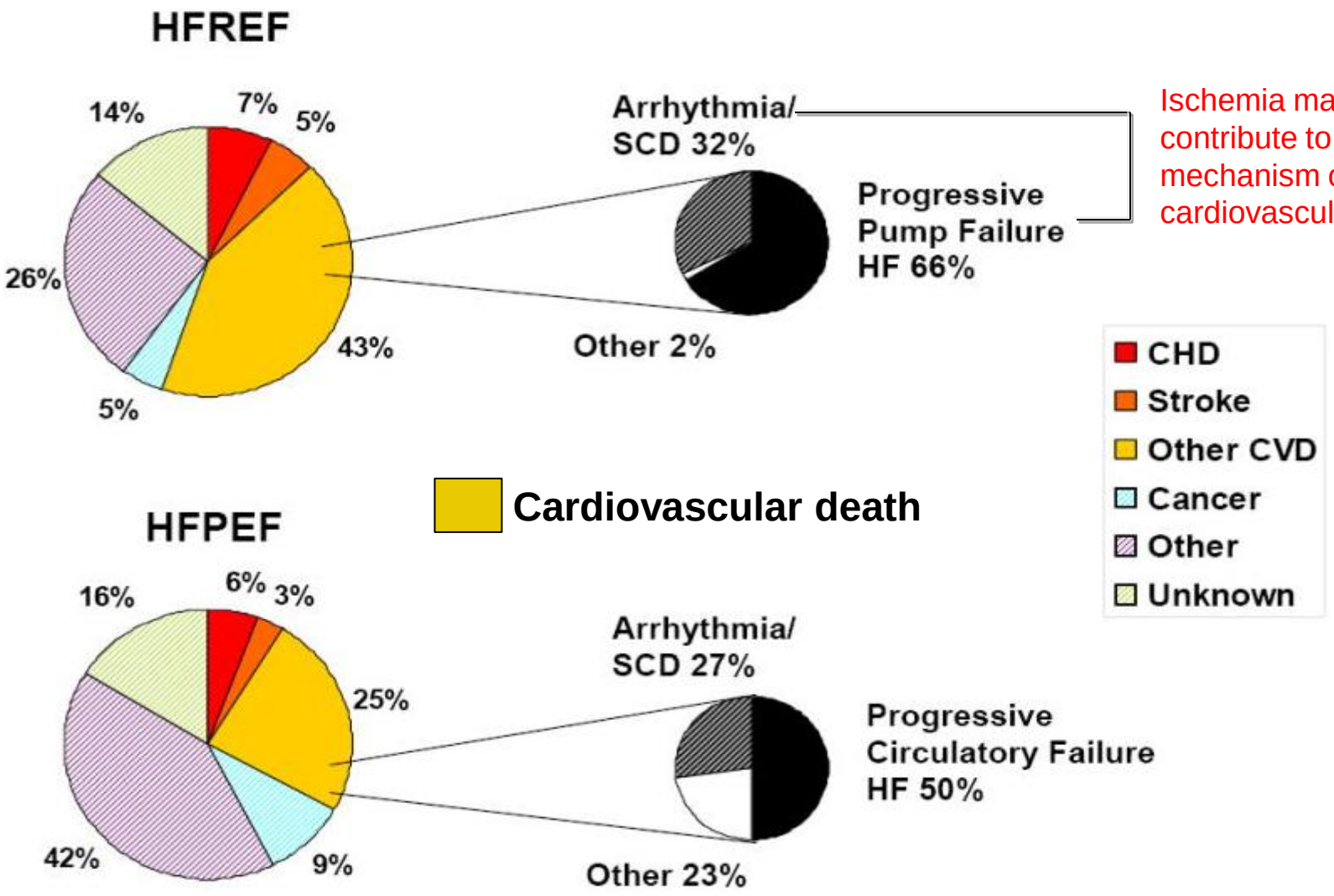
Ischemic etiology is also an independent predictor of m ortality in risk models:

Seattle Heart Failure Model (SHFM)

Heart Failure Survival Score (HFSS)

Levy et al, Circulation 2006
Aaronson et al, Circulation 1997

Cardiac Death in Heart Failure



Lee et al Circ Heart Failure 2011

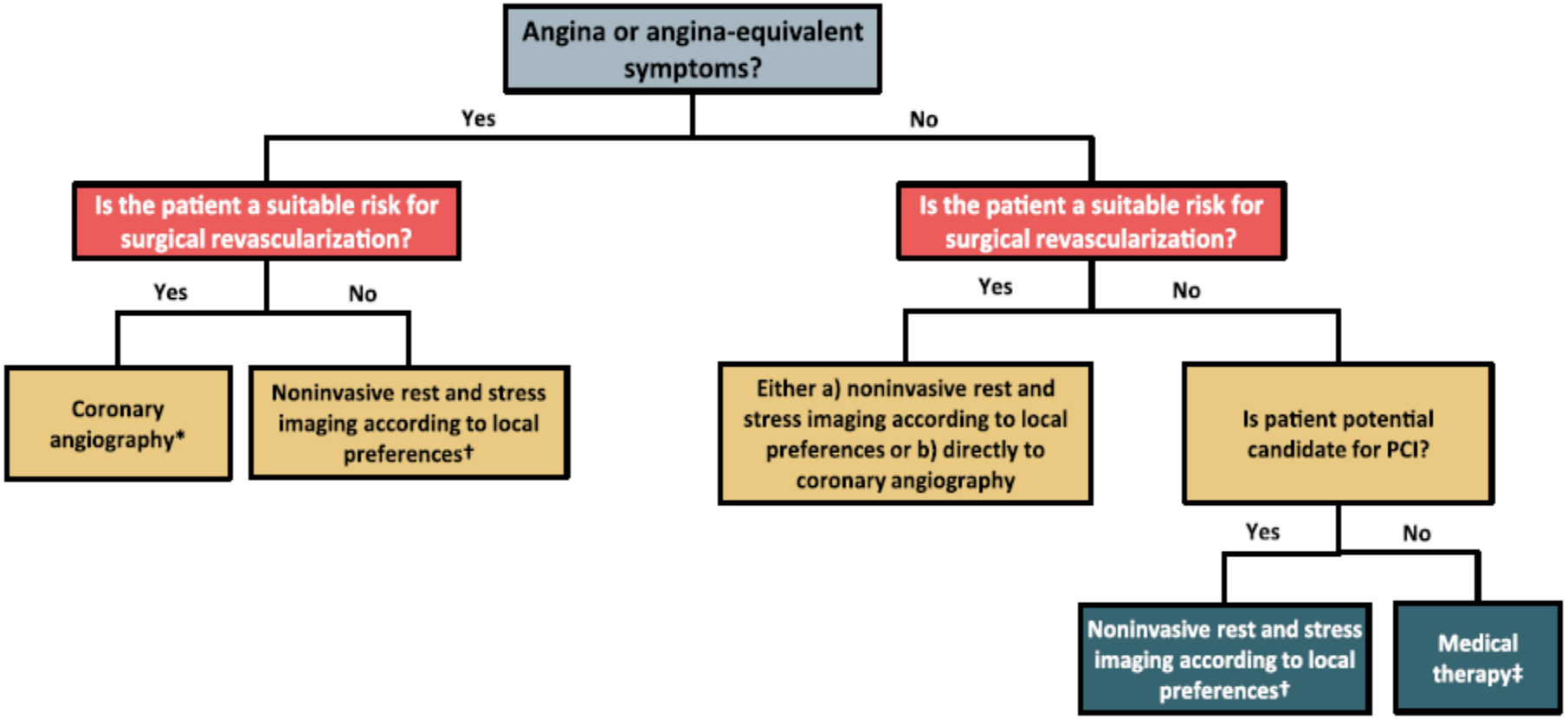
Epidemiology of ICMP

- 44% of HF in a Korean acute HF registry
- 28% increased risk compared to non-ischemic HF
  - Yoon CH, et al. 2012. J Card F.
- Ischemic cause of HF: 68% in men, 56% in women in US
  - He J, et al. 2001. Arch Intern Med.
- LV EF <40% at AMI admission in KAMIR & KorMI database: 16.2% in NSTEMI, 19.3% in STEMI
  - Park HW, Yoon CH et al. 2013. Int J Cardiol
- HF Readmission after AMI
  - 10.7% at a median follow-up of 23 months
    - Suleiman M, et al. 2006. JACC
  - 1.7% (7 patients out of 411) at 9 months after AMI
    - AMI readmission monitoring at SNUBH in 2013

Diagnosis

- Two steps
  - The detection of clinically significant coronary artery disease
  - The detection of potentially reversible hibernating (viable) myocardium

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



Comorbidities of the patients with heart failure

Age	**75 years**
Hypertension	**72%**
Diabetes	**44%**
Atrial fibrillation	**31%**
COPD	**31%**
Chronic kidney disease	**30%**

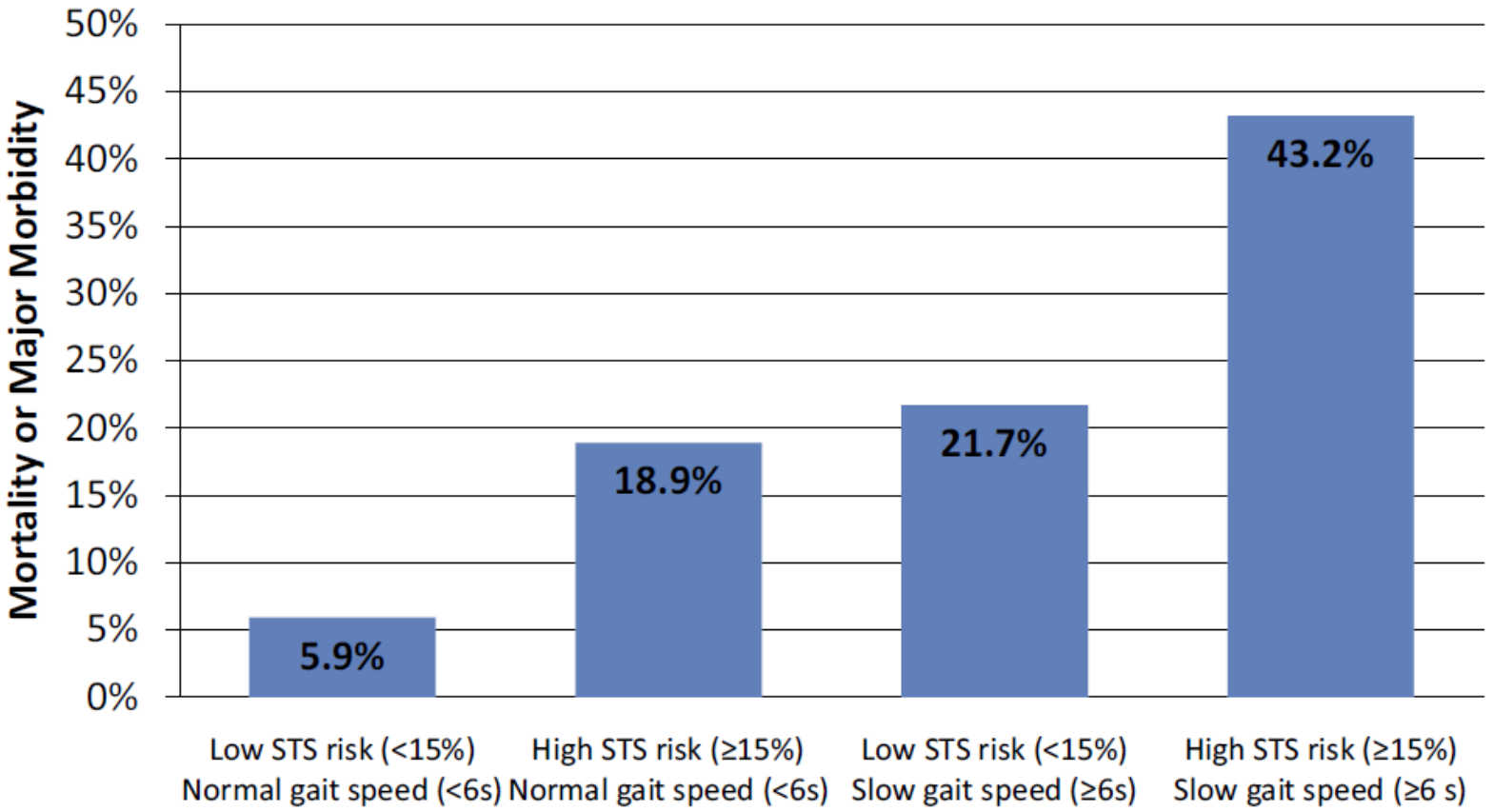
Gheorghiade, Eur Heart J, 2005

Frailty and cardiac surgery

- Prospective cohort, 4 sites, ≥ 70 yrs, for CABG ± valve
  - Non-emergent / urgent; no major psychiatric Dx
- 5 meter walk: if ≥6 seconds, classified as frail
- 131 pts, 75.8±4.4 yrs old
  - 46% frail (usually diabetic, IADL problems)
  - No correlation with STS risk score (i.e. different domains)
- Outcome: mortality, renal failure, stroke, reoperation, prolonged ventilation, deep sternal infection

Afilalo et al J Am Coll Cardiol 2010

Frailty and cardiac surgery



Gait speed predicts mortality/major morbidity (OR 3.05, 95%CI 1.23–7.54)

Afilalo et al J Am Coll Cardiol 2010

The detection of potentially reversible hibernating (viable) myocardium

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.

The detection of potentially reversible hibernating (viable) myocardium

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:

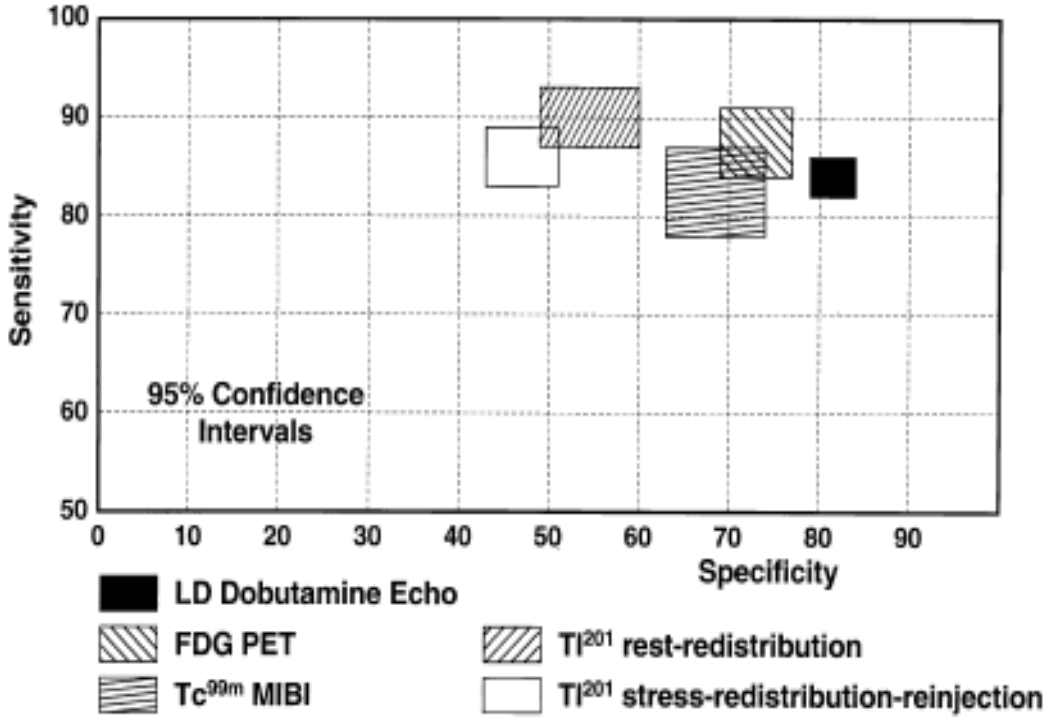
a) Reversible ischemia or a large segment of viable myocardium (> 30% of LV) by nuclear stress testing/ viability study;

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.

Viability and LV functional recovery after revascularization



Systematic review of non-invasive Imaging techniques in predicting Regional myocardial recovery

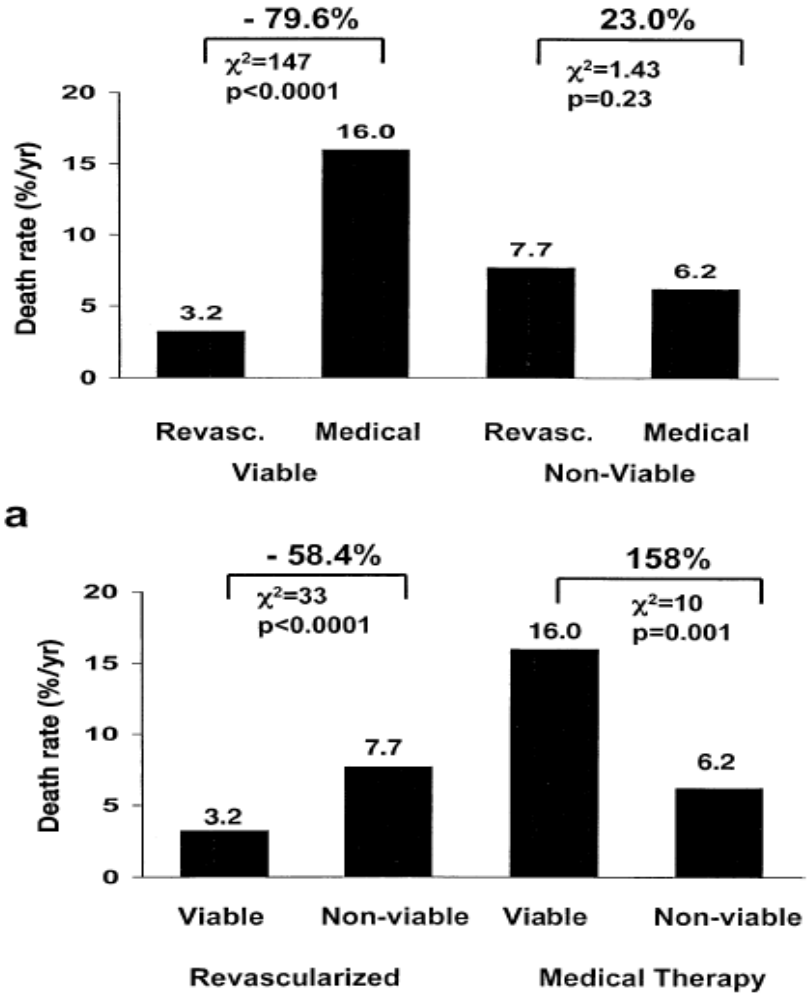
37 observational studies

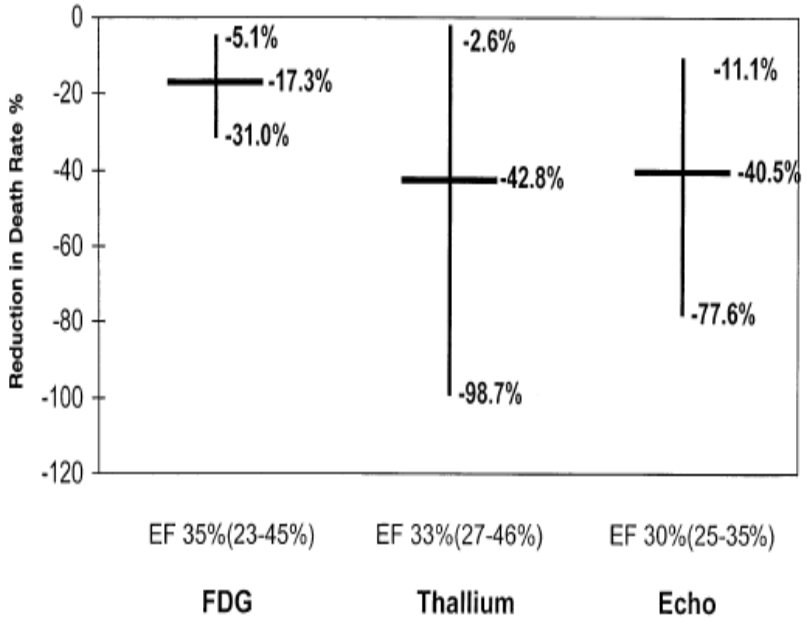
Thallium, FDG PET and DSE show high degree of sensitivity

DSE and FDG PET show greatest specificity

Bax et al J Am Coll Cardiol 1997

Viability and survival after revascularization





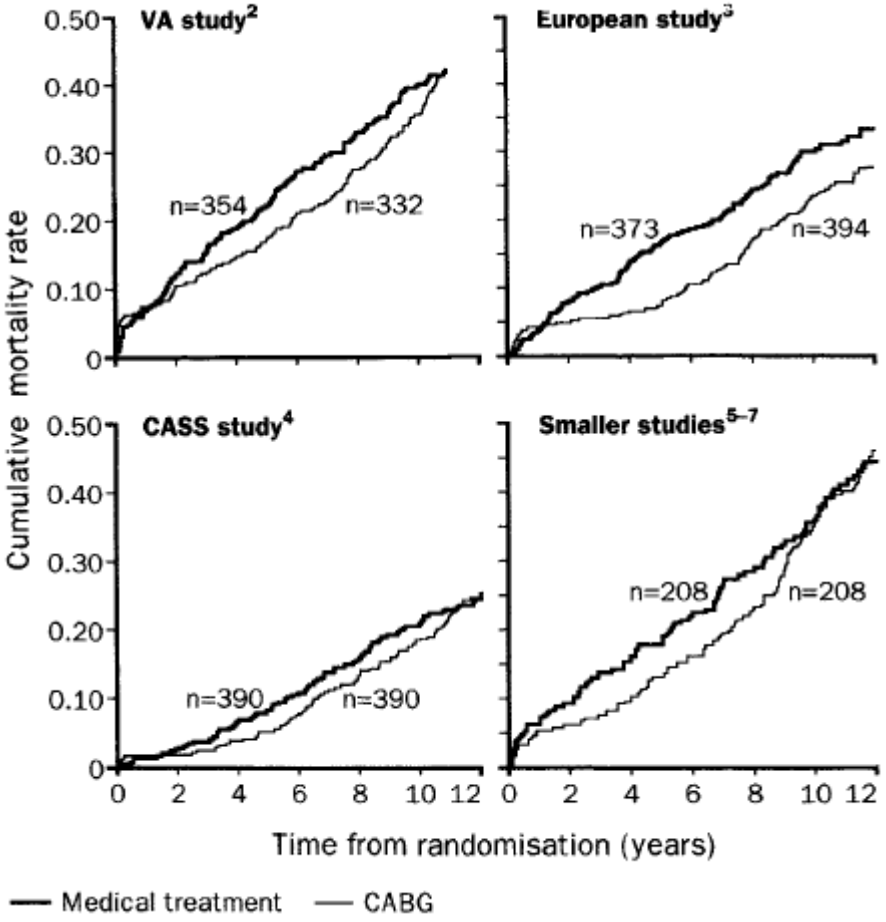
Systematic review of 24 observational studies Evaluating relationship between death, viability and revascularization

Allman et al, J Am Coll Cardiol 2002

Medical treatment

- An ACE inhibitor
- An beta blocker
- A statin as part of the secondary prevention of established CAD
- A loop diuretics and dietary salt restriction with evidence of fluid overload (Adequate maintenance of dry weight in patients with ESRD on HD)
- The combination of hydralazine and a nitrate
- Aldosterone antagonist with monitoring of renal function and potassium
- Angiotensin receptor blockers as an alternative to ACEI
- Risk factor reduction (aspirin, control of hypertension, diabetes, cessation of smoking)
- Exercise, cardiac rehabilitation

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



Individual patient level meta-analysis of 7 trials

- 2600 patients enrolled 1972-84
- CABG associated with mortality reduction
- 39% at 5 years, 17% at 10 years
- No interaction with LV dysfunction and mortality reduction but higher absolute benefits seen in high risk subgroups

Yusuf et al, Lancet 2004

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

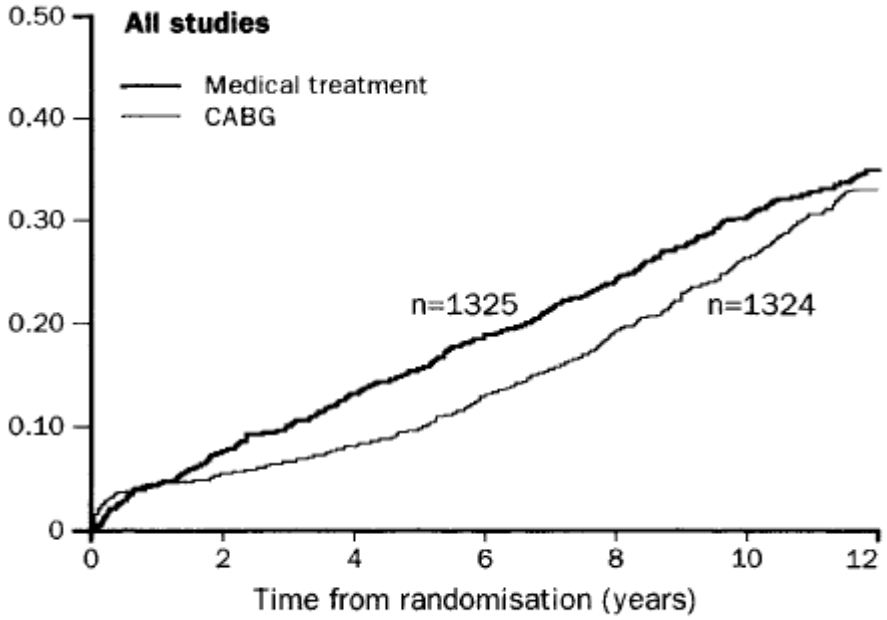


Figure 2: **Survival curve for overall population**

- In these early studies:
  - 90% had angina
  - 80% had normal LVEF
  - 10% had arterial conduits
  - Medical therapy = digoxin and diuretics
  - Non-randomized trials, observational studies
    - Selection bias
    - A lesser likelihood of publication of negative studies

Need to assess the benefits of revascularization in contemporary patients with ischemic cardiomypathy

Yusuf et al, Lancet 2004

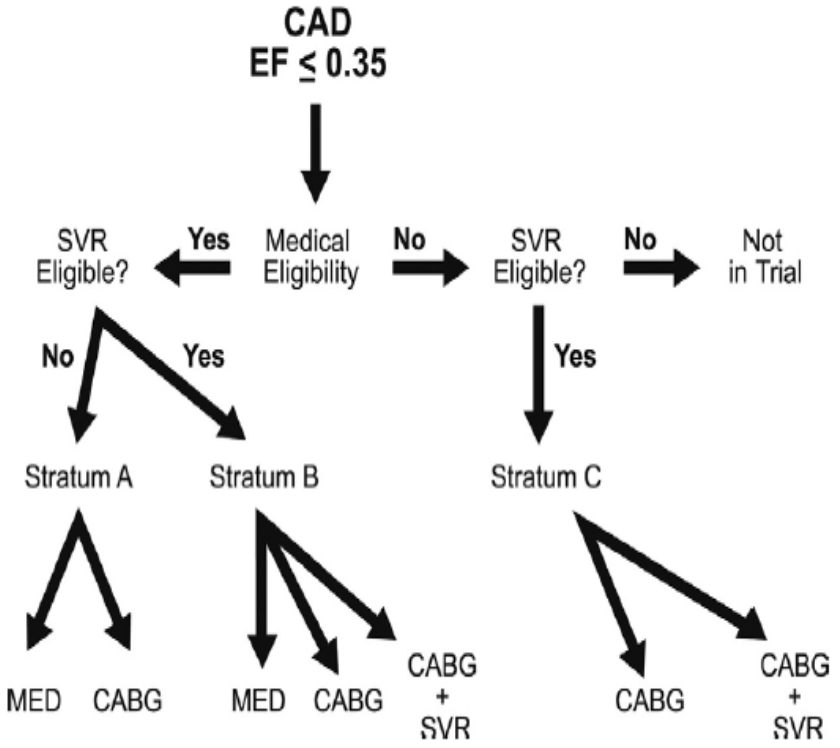
Surgical Treatment for Ischemic Heart failure (STICH) trial

Randomized non-blinded study of surgical revascularization:

Included patients with LVEF <35% and CAD suitable for revascularization

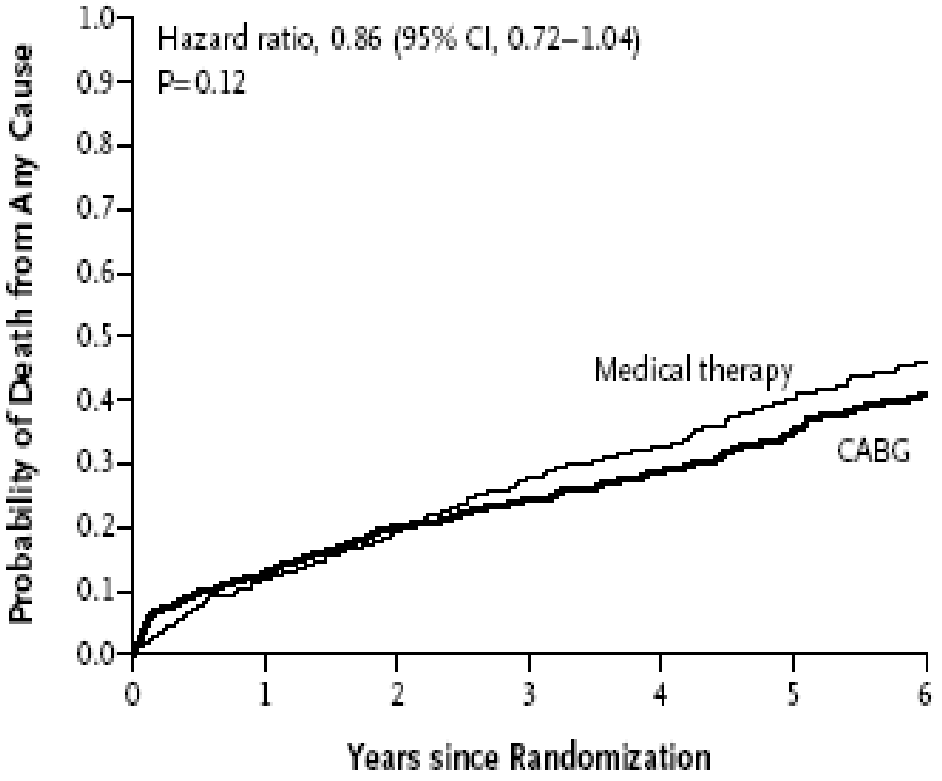
Hypothesis 1:
CABG + medical rx superior to medical rx alone

Hypothesis 2:
CABG + SVR superior to CABG alone in patients undergoing revascularization with anterior wall akinesis/dyskinesis



Velazquez et al, J Thorac and Cardiovasc Surg

STICH Hypothesis 1: Primary outcome



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

1212 patients randomized to CABG vs medical therapy

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

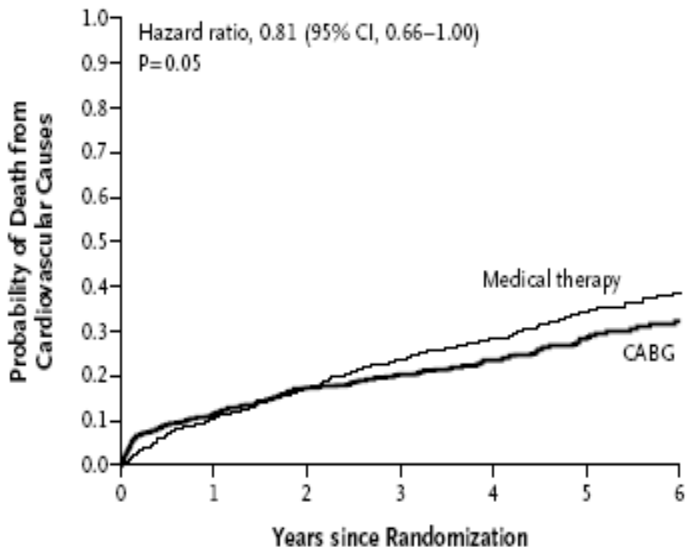
No difference in all cause mortality seen at median 56 months follow-up

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

Velazquez et al, 2011. NEJM

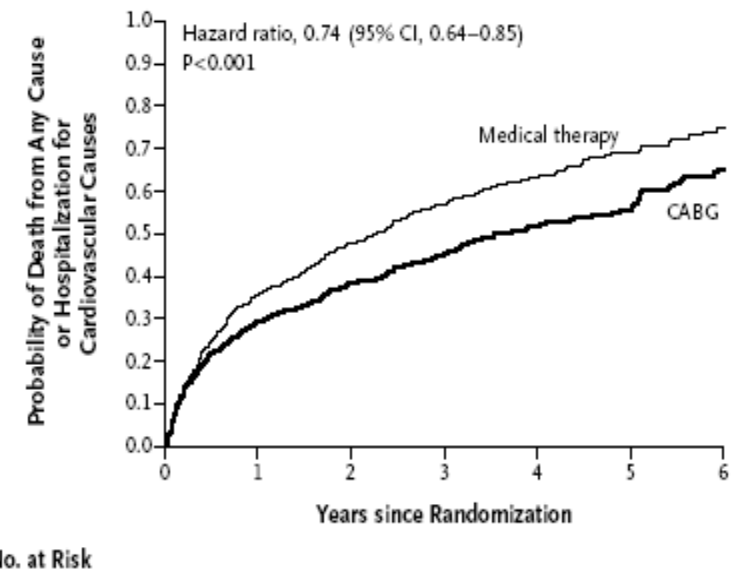
STICH Hypothesis 1: secondary outcomes

A



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

B

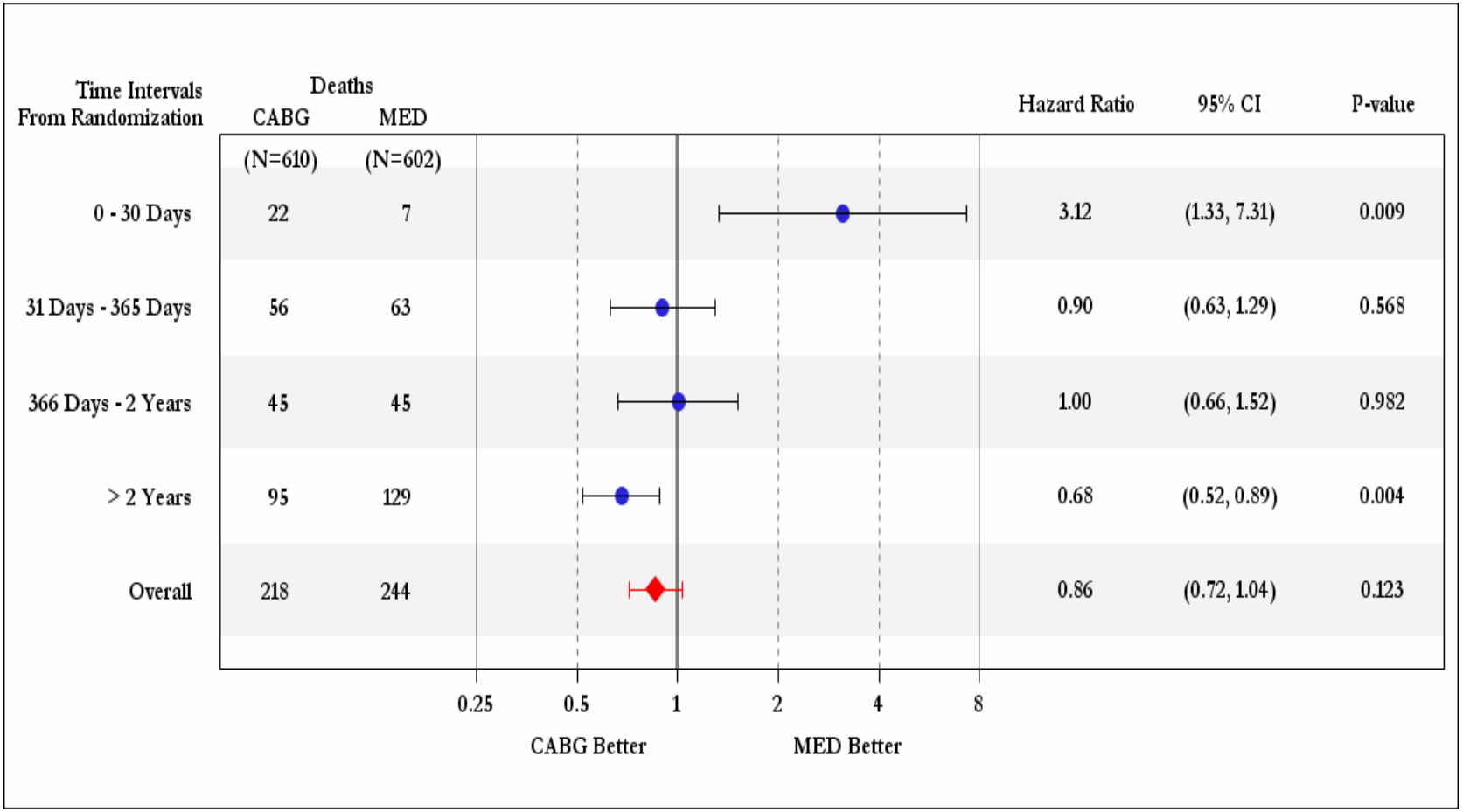


No. at Risk							
Medical therapy	602	387	315	260	158	65	28
CABG	610	431	375	334	221	100	43

CABG associated with reduction in cardiovascular death and combined outcome of death or cardiovascular hospitalization

CABG also associated with 30% relative reduction in mortality in “on-treatment” analysis (accounting for patients crossing over within 1st year of study)

Time-varying hazard ratios for all-cause mortality in patients randomized to CABG or MED.

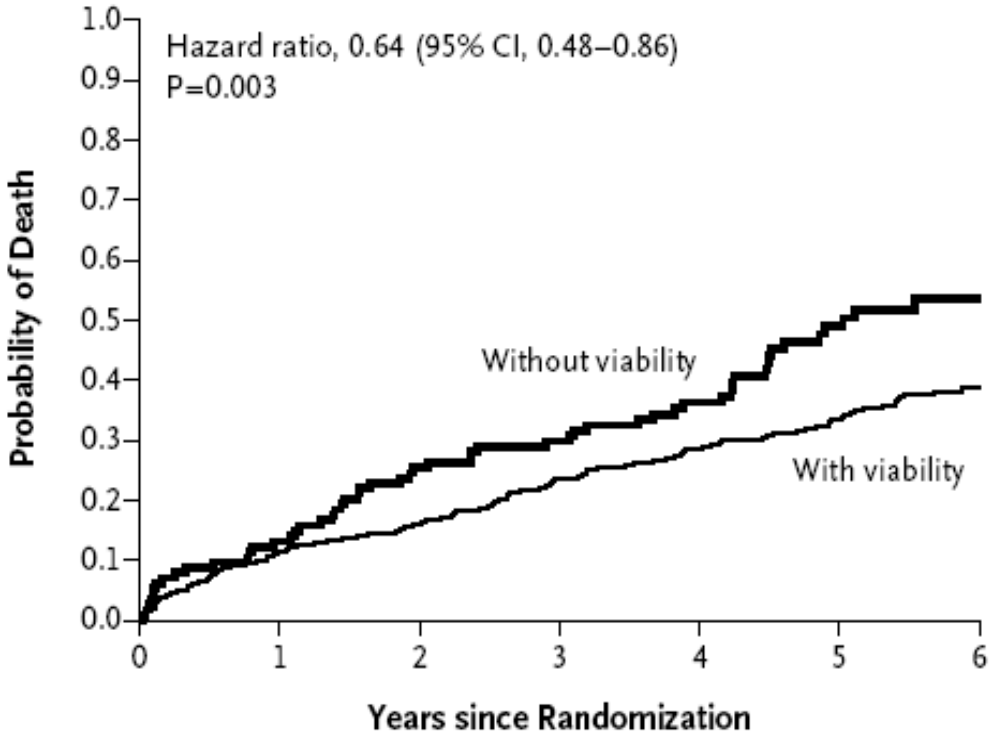


Quality-of-life outcome of STICH trial

- The Kansas City Cardiomyopathy Questionnaire overall summary score was consistently higher (more favorable) in the CABG group than in the medical therapy group
- 4.4 points (95% CI, 1.8 to 7.0 points) at 4 months
- 5.8 points (CI, 3.1 to 8.6 points) at 12 months
- 4.1 points (CI, 1.2 to 7.1 points) at 24 months
- 3.2 points (CI, 0.2 to 6.3 points) at 36 months.

Mark DB, Ann Intern Med 2014

STICH Analysis
Improved prognosis with viability



No. at Risk

Without viability	114	99	85	80	63	36	16
With viability	487	432	409	371	294	188	102

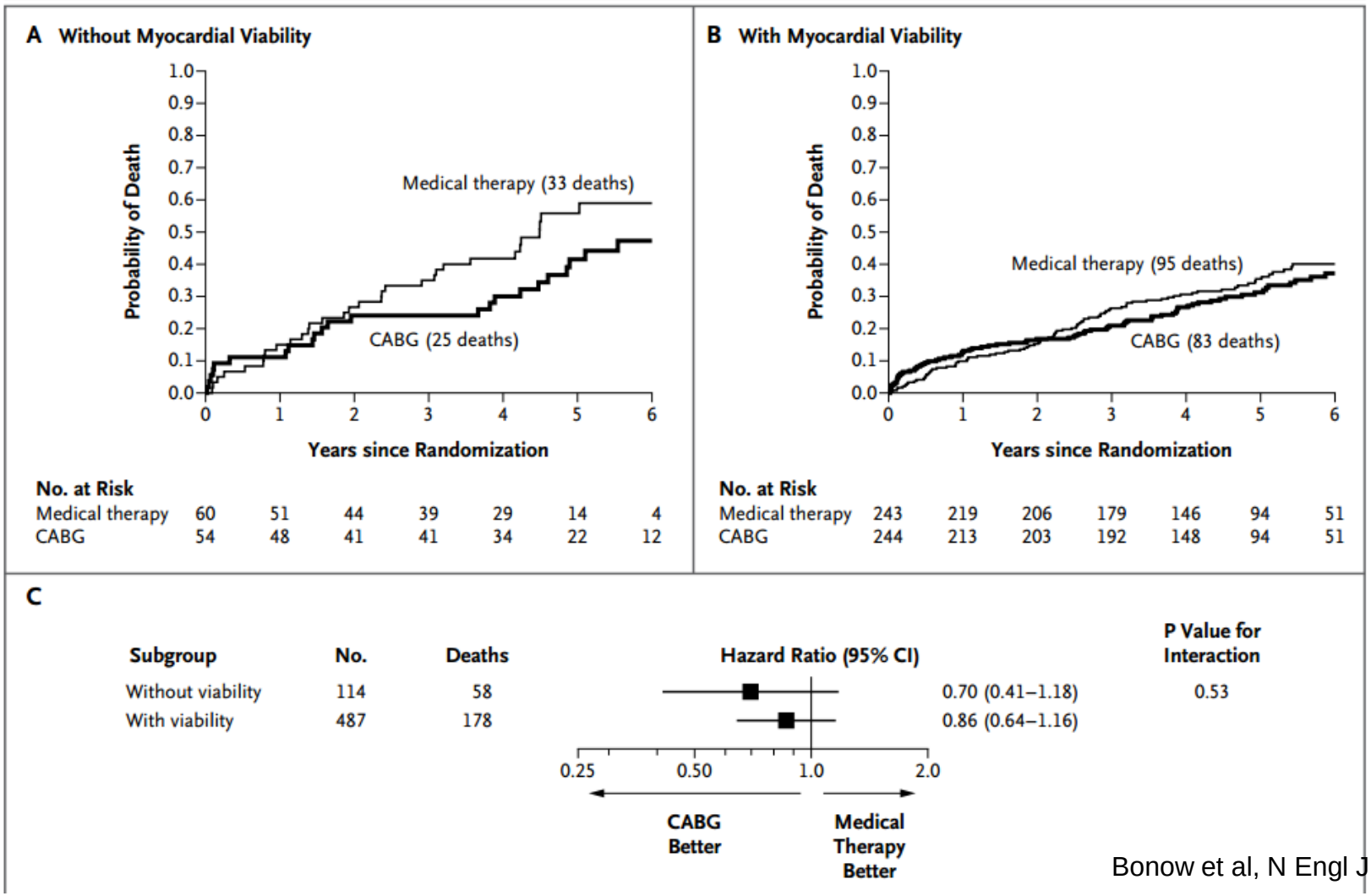
Analysis of 601 patients with viability testing data available

Viability defined as ≥ 11 segments on SPECT or ≥ 5 segments on DSE imaging

Bonow et al, N Engl J Med 2011

STICH Analysis

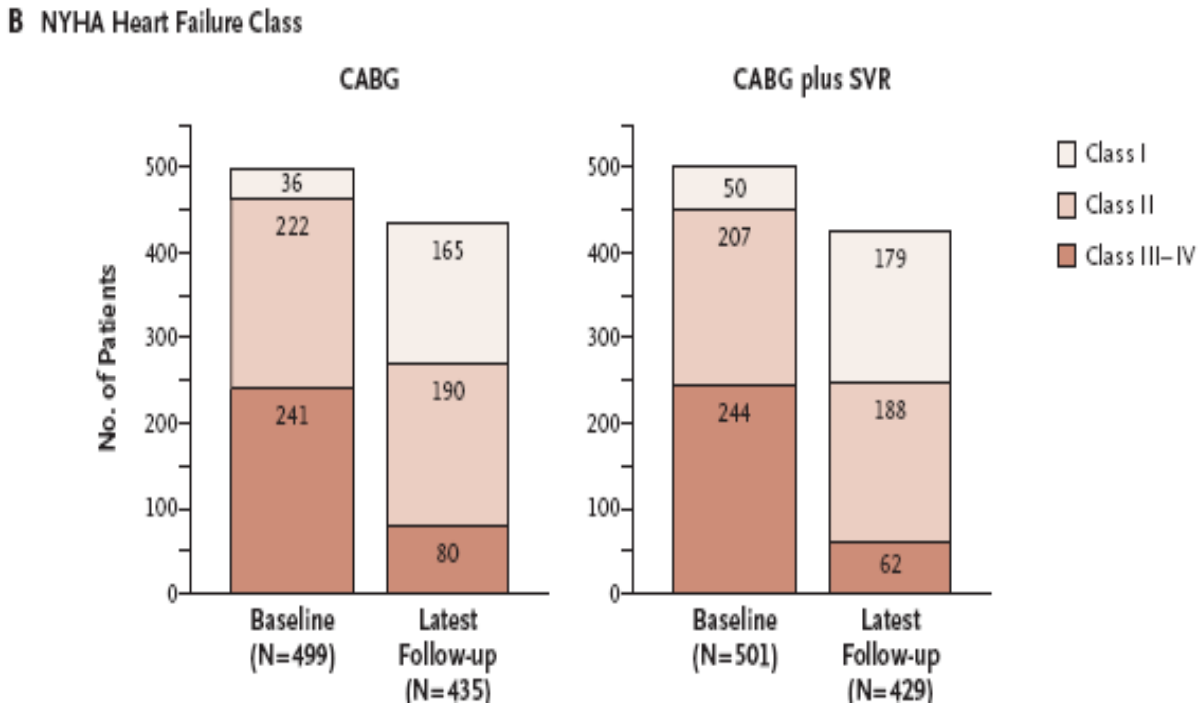
Viability doesn't necessarily predict improved outcomes with surgery vs medical therapy



Bonow et al, N Engl J Med 2011

STICH Hypothesis 2:

CABG and CABG +SVR improved HF symptoms



1000 patients undergoing CA BG in STICH trial further randomized to CABG alone vs CABG + SVR

Dominant anterior wall motion abnormality required for inclusion

Median f/u 48 months

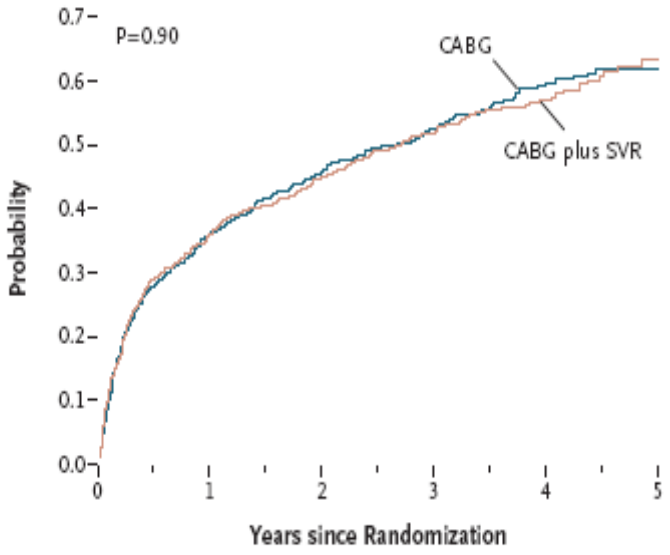
CABG + SVR achieved a reduction in LV end-systolic index by 19% vs 6% for CABG alone

Jones et al, N Engl J Med 2009

STICH Hypothesis 2:

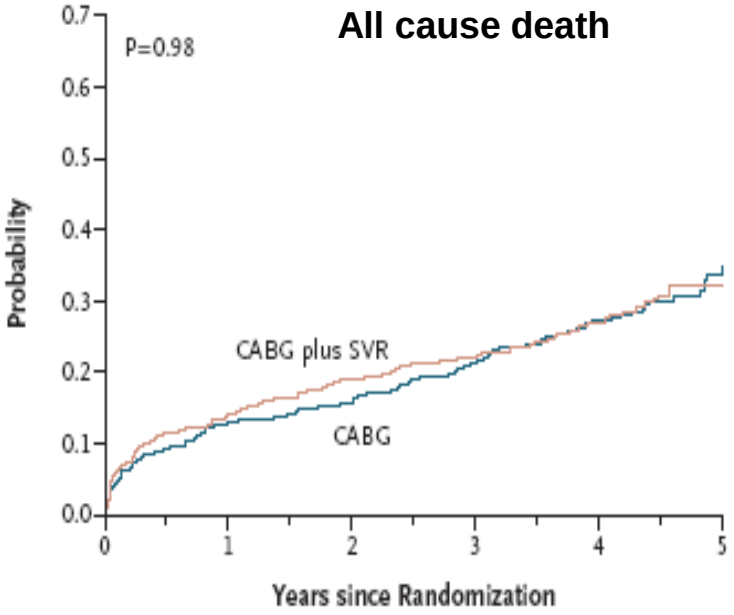
No difference in primary or secondary outcomes between CABG vs CABG + SVR

All cause death or cardiovascular hospitalization



No. at Risk						
CABG	499	319	270	220	99	23
CABG plus SVR	501	319	275	216	111	23

All cause death



No. at Risk						
CABG	499	434	417	363	201	59
CABG plus SVR	501	429	404	352	193	53

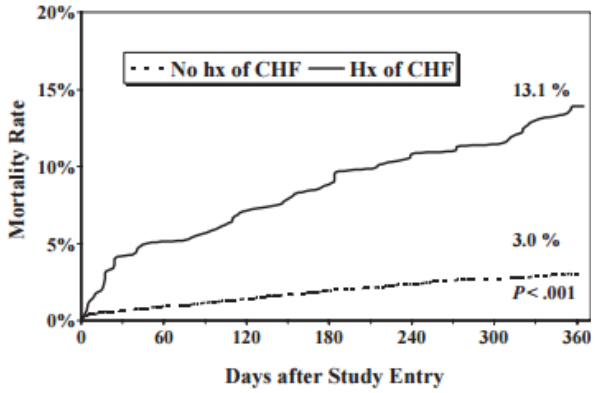
Jones et al, N Engl J Med 2009

Summary (Medical Tx vs Surgery)

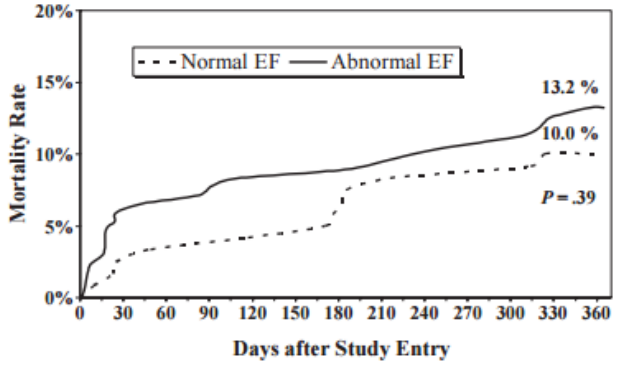
- Initial course of optimal medical therapy
- Re-evaluation for any changes in clinical status or symptoms
- CABG as initial therapy may be considered in patients who are willing to accept the increased risk of morbidity related to surgery in exchange for a potential mortality benefit and likelihood of greater improvement in quality of life.
- Revascularization should be also considered in patient with angina symptoms despite of optimal medical therapy.

PCI as a revascularization method in patients with ischemic CMP

- Presence of heart failure is an adverse predictor of outcome after PCI.
- However, outcomes after PCI in patients with heart failure continue to improve with enhancements in care (stents, antiplatelet therapy, …)



Kaplan-Meier rates of 1-year mortality: CHF versus no CHF.



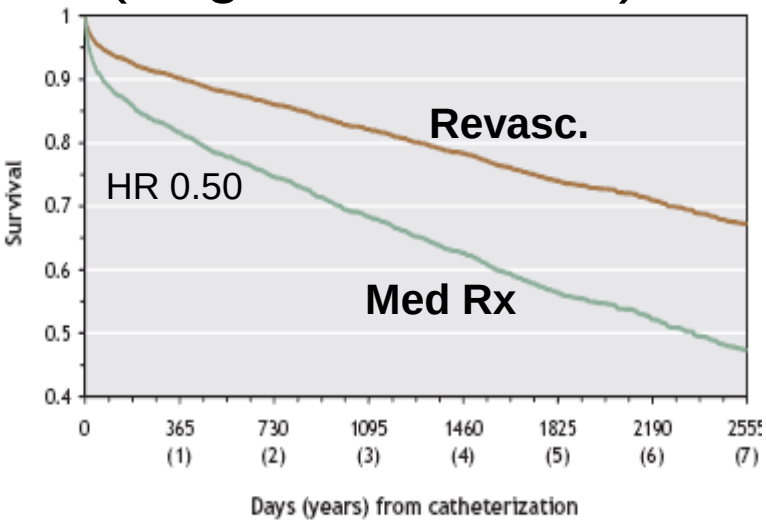
Kaplan-Meier rates of 1-year mortality: abnormal versus normal EF in patients with CHF.

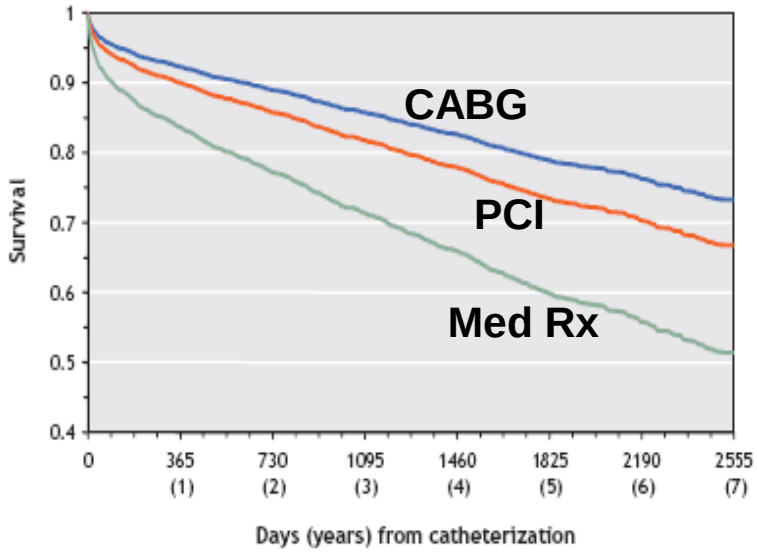
Table V. Adjusted inhospital and 1-year outcomes for Dynamic Registry versus 1985-1986 PTCA Registry

	Adjusted OR	
Inhospital events	**OR (95% CI)**	***P***
Death	0.39 (0.15-1.02)	NS
CABG	0.12 (0.03-0.42)	≤.001
Death/MI/CABG	0.19 (0.09-0.42)	≤.001
	Adjusted RR	
1-y events	**RR (95% CI)**	***P***
Death	0.58 (0.33-1.02)	NS
CABG	0.31 (0.15-0.61)	≤.001
Death/MI/CABG	0.54 (0.36-0.82)	<.01
PCI after discharge/CABG	0.43 (0.27-0.69)	≤.001

Holper EM, 2006. Am Heart J : data from 1997-2001 registry

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

PCI vs CABG in patients with ischemic CMP

- BARI (Bypass Angioplasty Revascularization Investigation) (BARI investigators, 1996, NEJM),
  - In which 22% of patients had LVEF <50%
- AWESOME (Angina With Extremely Serious Operative Mortality
  - Evaluation) (Morrison, 2001, JACC), 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
- Limitation
  - involve <500 patients
  - PCI with both balloon angioplasty and bare-metal stents.

PCI vs CABG in patients with ischemic CMP

- 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% (Serruys, 2009, NEJM)
- FREEDOM (Future Revascularization Evaluation in Patients With Diabetes Mellitus: Optimal Management of Multivessel Disease) trial (Farkouh, 2012, NEJM)
- 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.

AWESOME trial

- Patients were enrolled only if they had ≥1 of 5 risk factors for adverse outcomes with CABG (prior CABG; myocardial infarction within 7 days; left ventricular ejection fraction [LVEF] < 35%; age >70 years; or intra-aortic balloon required to stabilize).
- Eligible patients who were deemed by their physicians and by study investigators to be suitable for CABG and PCI were asked to participate in the randomized trial.

Table 3. Coronary Artery Bypass Graft Surgery and PCI 36-Month Survival, Survival Free of Unstable Angina and Survival Free of Unstable Angina or Repeat Revascularizations

Outcome	CABG	PCI	PCI-CABG (Difference)	SE (Difference)	
Survival	79%	80%	1%	3.7%	p=0.46
Survival free of unstable angina	65%	59%	−4%	5.5%	p=0.16
Survival free of unstable angina or repeat revascularization	61%	48%	−13%	5.0%	p=0.001

CABG = coronary artery bypass graft surgery; PCI = percutaneous coronary intervention; SE = standard error.

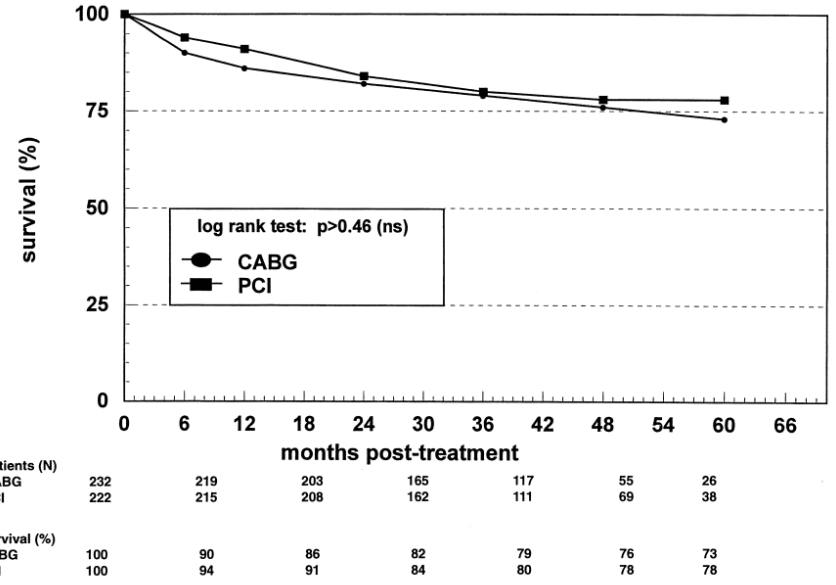
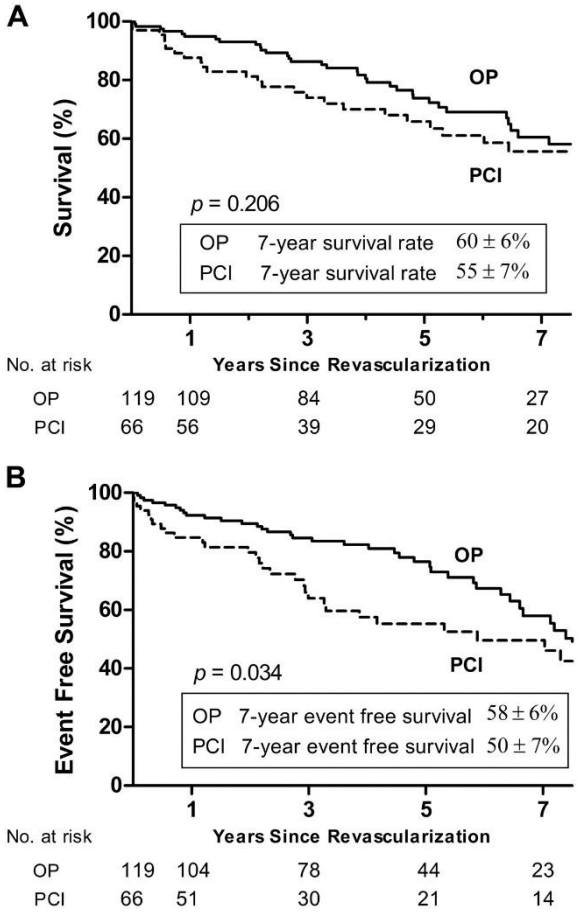


Figure 1. Kaplan-Meier survival plot of coronary artery bypass graft surgery (CABG) **(circles)** versus percutaneous coronary intervention (PCI) **(squares)**. The CABG and PCI number of patients (N) and the percentage surviving for each time period are shown at the bottom of the plot.

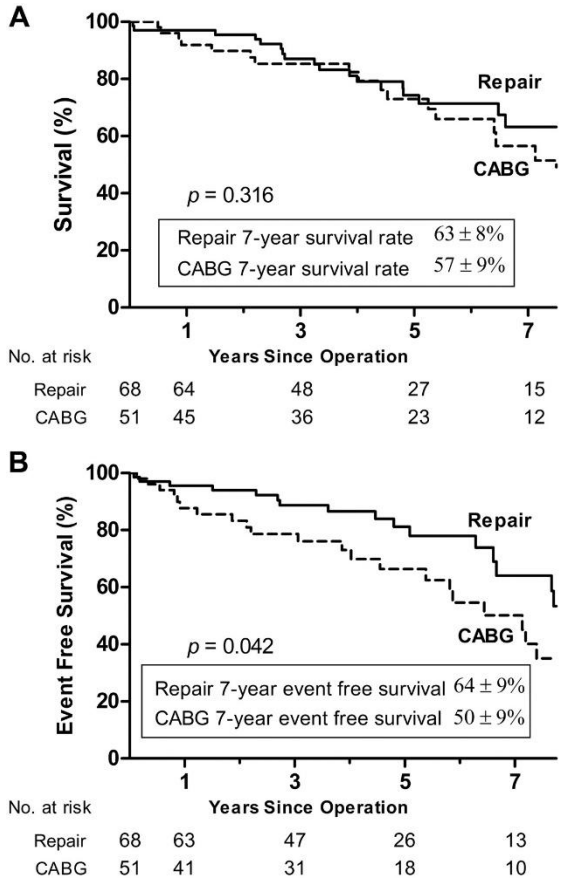
Morrison, 2001, JACC

Percutaneous Versus Surgical Revascularization in Patients With Ischemic Mitral Regurgitation

Survival (A) and event-free survival (B)



Survival (A) and event-free survival (B)



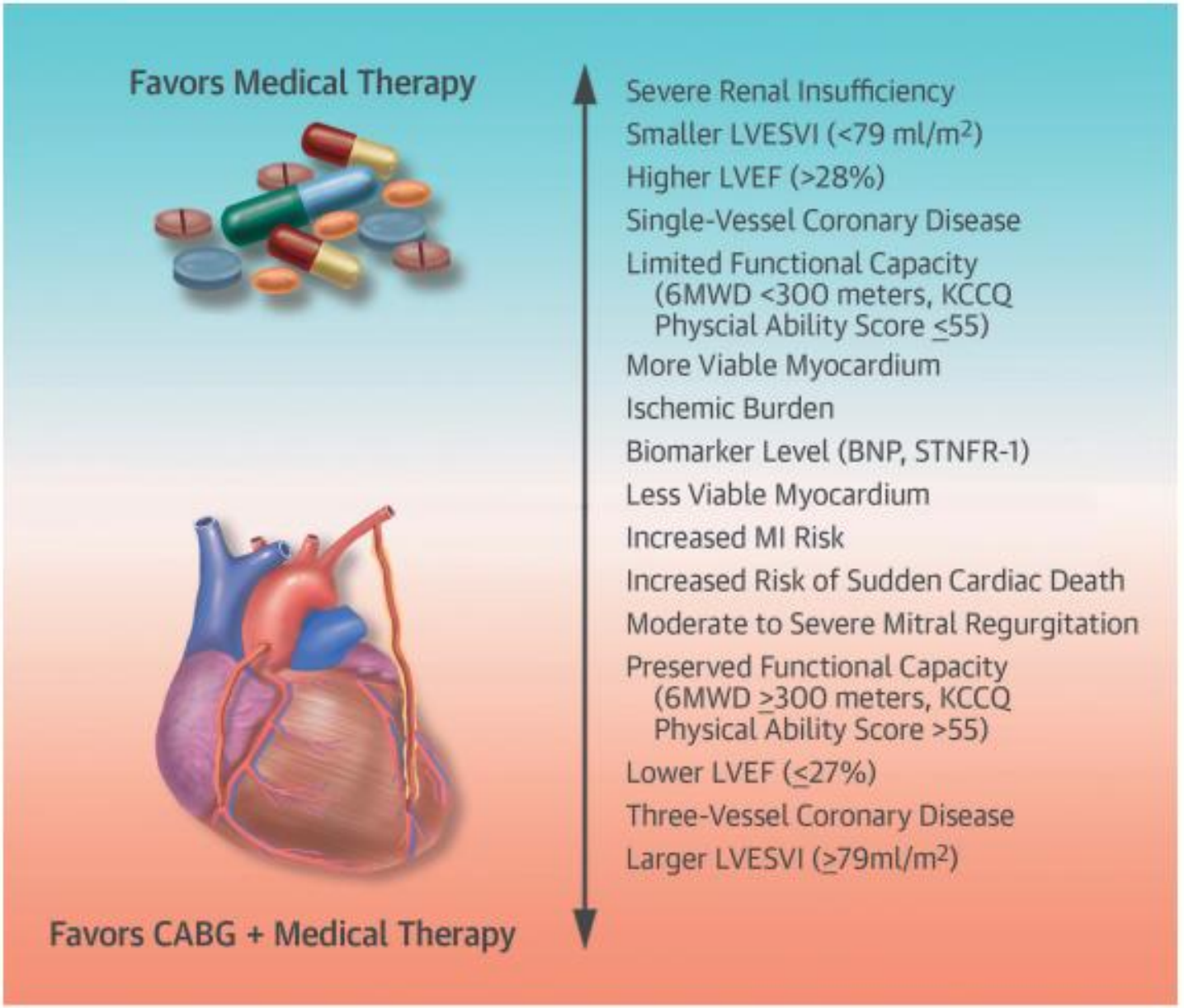
Kang DH, Circulation, 2011. Volume 124

PCI in patients with ischemic CMP

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.

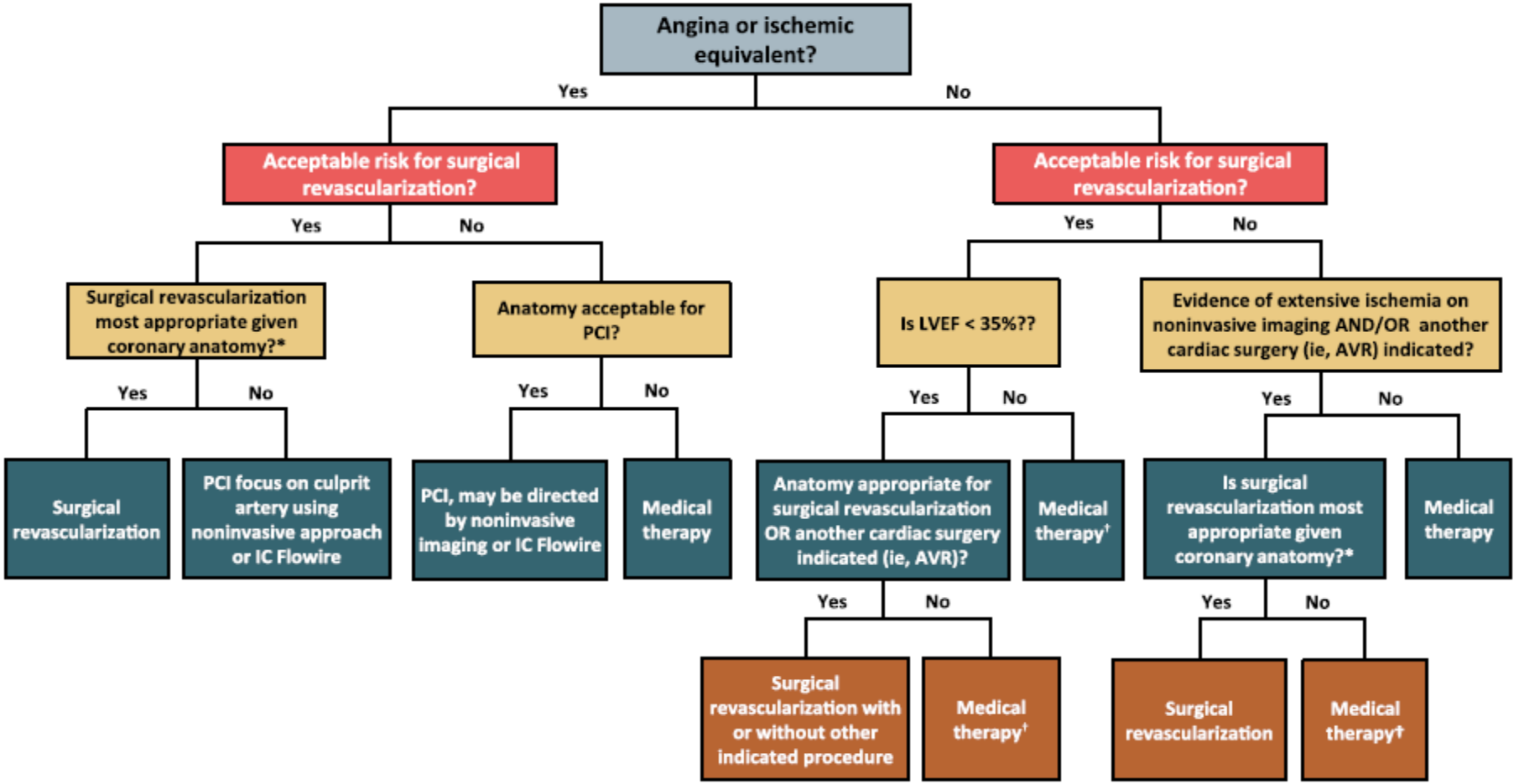
2.Urgent directed culprit vessel angioplasty continues to be the revascularization modality of choice for patients with heart failure and acute coronary syndrome.

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.

Decision Regarding Coronary Revascularization in Heart Failure



경청해 주셔서 감사합니다 !