Multi-Vessel Disease Revascularization: Consensus and Gaps in 2023

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ISCHEMIA Trial: Summary

- 5179 patients randomized to INV vs. CON
 - Largest treatment strategy trial of SIHD
- Enrolled high-risk subset
 - 54% severe ischemia; 76% with multivessel CAD; 47% with proximal LAD disease (CCTA)
- Cath and Revascularization
 - Invasive strategy: 80% revascularized (74% PCI/26% CABG)
 - Conservative strategy: 28% cath; 23% revasc at 4-years
- Medication Therapy
 - 95% statins; 66% high intensity statin; LDL 64 mg/dl; SBP 129 mm Hg

Which Patients were Not Enrolled in ISCHEMIA?

- ACS within 2 months
- EF < 35%
- NYHA Class III-IV HF
- Unacceptable angina despite medical therapy
- PCI or CABG within 1 year
- Severe left main disease

Potential Reasons for Revascularization in SIHD

- To improve survival
- To prevent other cardiovascular events
- To improve quality of life

- Overall cohort
- High risk subgroups
 - Left main disease
 - LV dysfunction
 - 3-vessel disease
 - Proximal LAD disease
 - Extensive ischemia

Contemporary Revascularization vs. Medicine SIHD Trials No difference in mortality

2007



No difference in death

2009



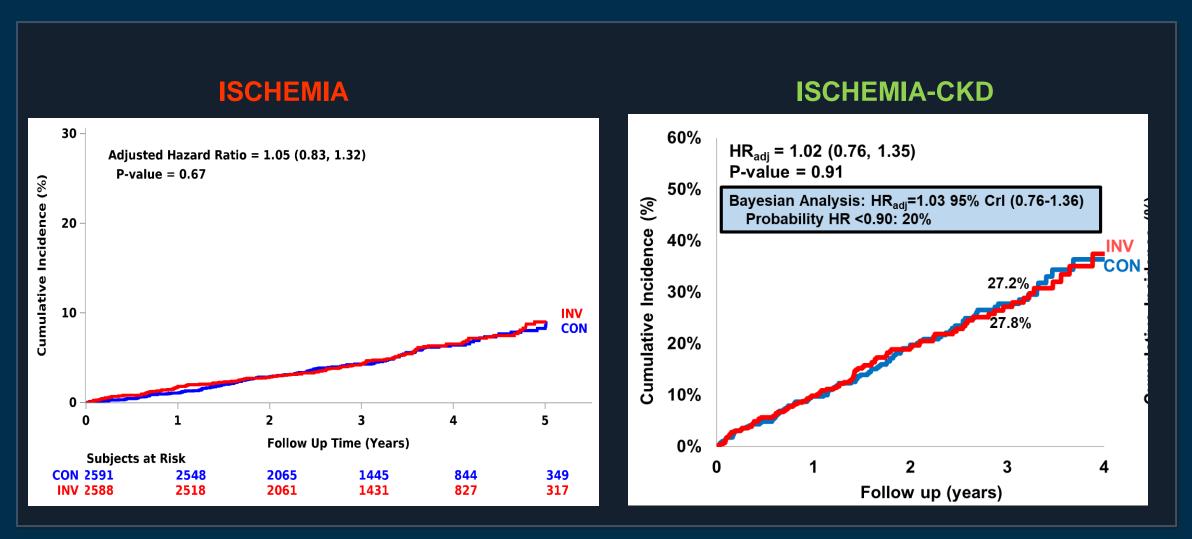
No difference in death

2012

FAME 2
Trial

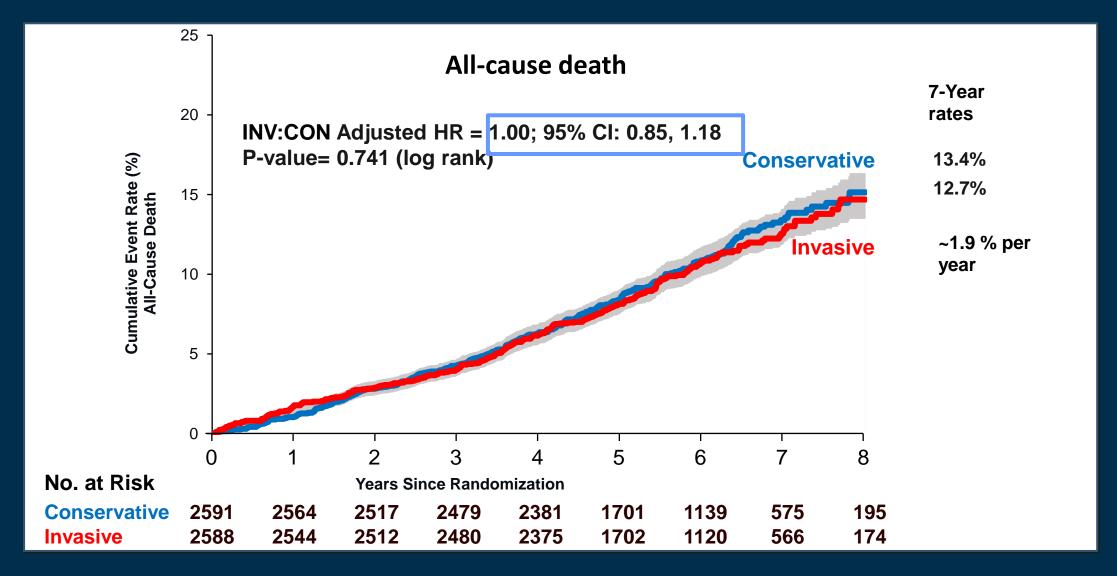
No difference in death

ISCHEMIA and ISCHEMIA-CKD trials No difference in mortality



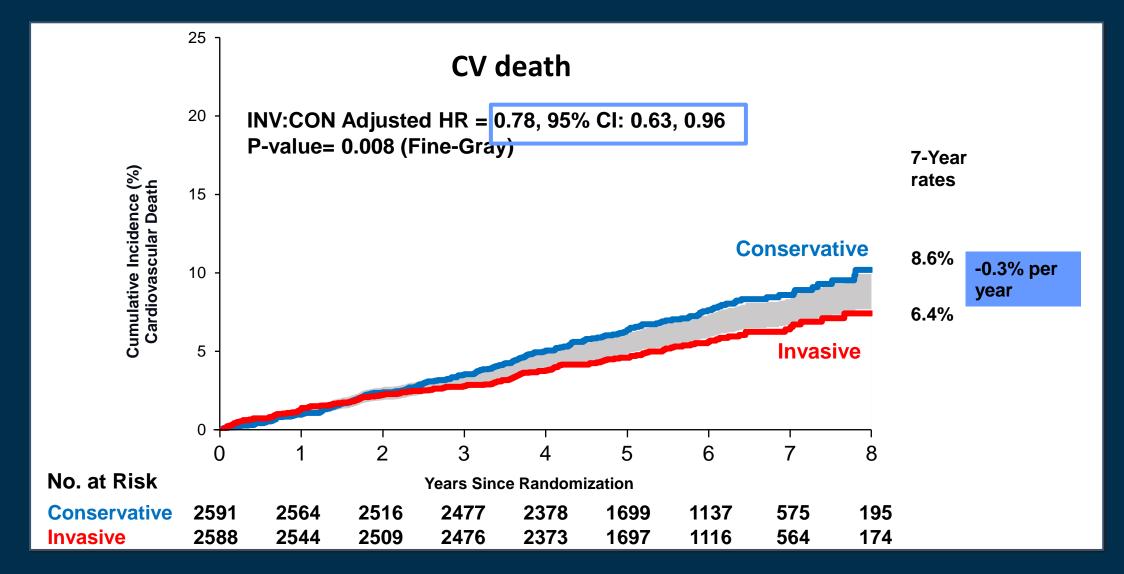


ISCHEMIA EXTEND: All-cause death



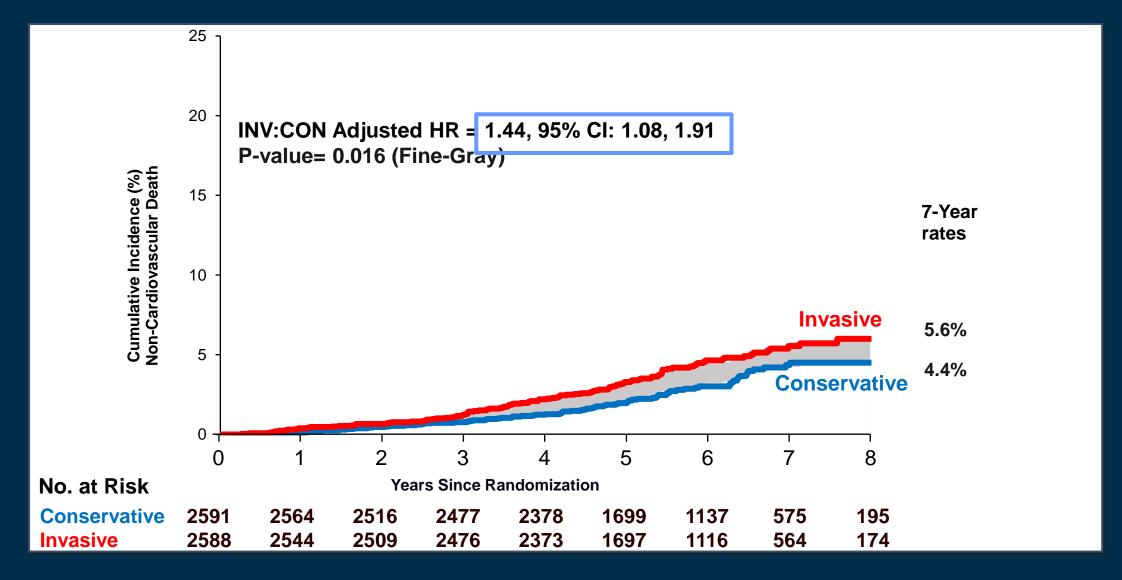


ISCHEMIA EXTEND: CV death





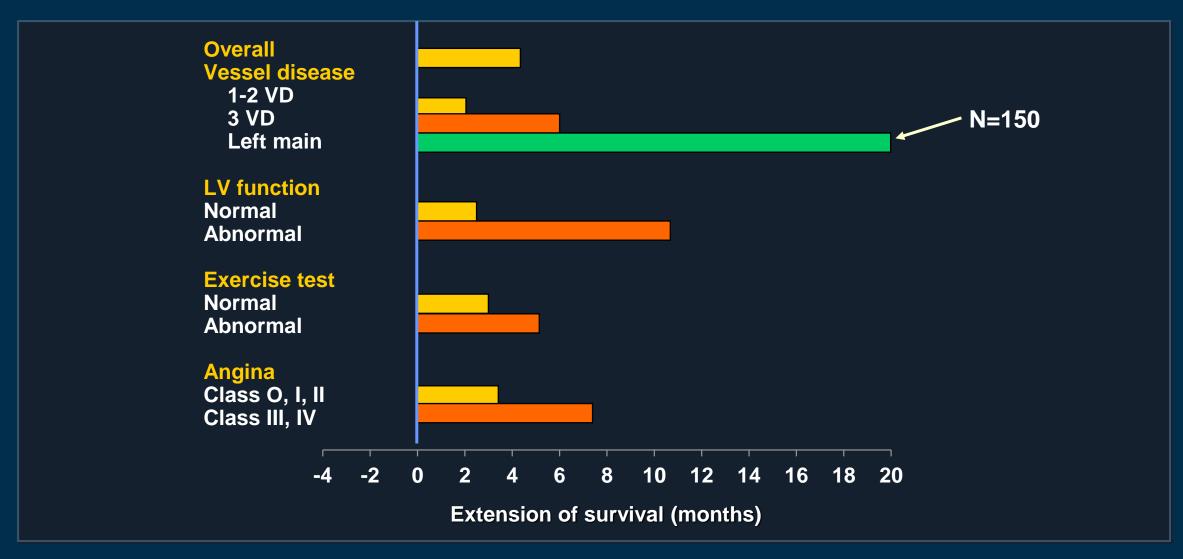
ISCHEMIA EXTEND: Non CV death



- Overall cohort
 - Similar survival compared with MT
 - Small reduction (0.3%/year) in cardiac death
- High risk subgroups
 - Left main disease
 - LV dysfunction
 - 3-vessel disease
 - Proximal LAD disease
 - Extensive ischemia

- Overall cohort
- High risk subgroups
 - Left main disease
 - LV dysfunction
 - 3-vessel disease
 - Proximal LAD disease
 - Extensive ischemia

Extension of Survival in Left Main Disease with Revascularization CABG vs. No CABG trials-1980s



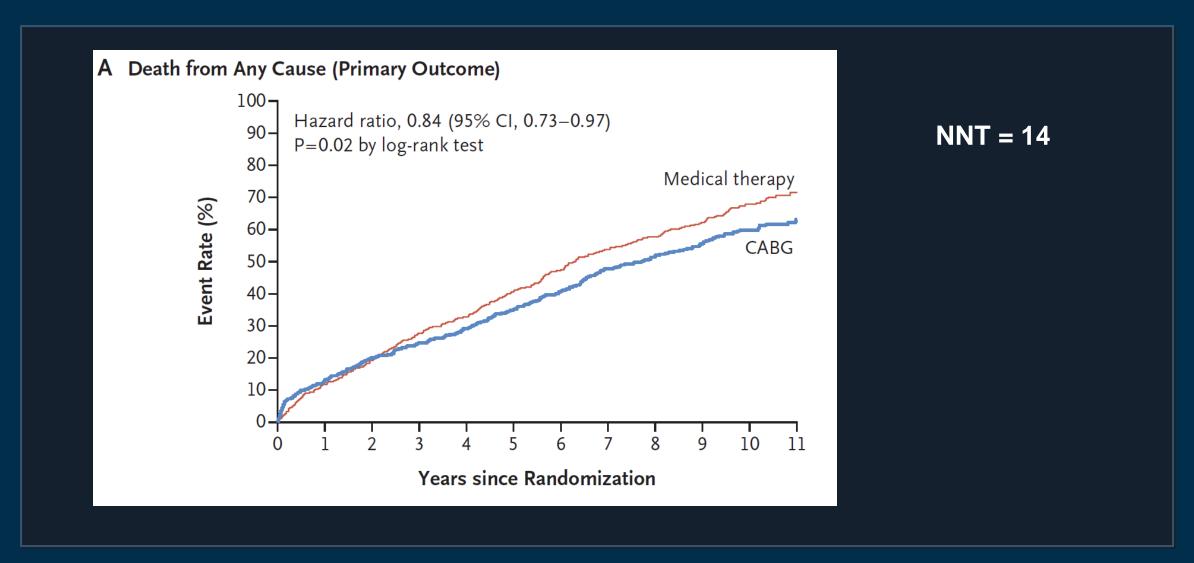
Yusuf et al. Lancet 1994;344:563-570.

Revascularization to Improve Survival in High Risk Subgroups

- Overall cohort
- High risk subgroups
 - Left main disease. Revasc vs. Med: Survival benefit of CABG (older trials-150 patients)
 - LV dysfunction
 - 3-vessel disease
 - Proximal LAD disease
 - Extensive ischemia

- Overall cohort
- High risk subgroups
 - Left main disease
 - LV dysfunction
 - 3-vessel disease
 - Proximal LAD disease
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Extension of Survival in LV Dysfunction with Revascularization STICHES trial





ISCHEMIA: Heart failure/LVSD

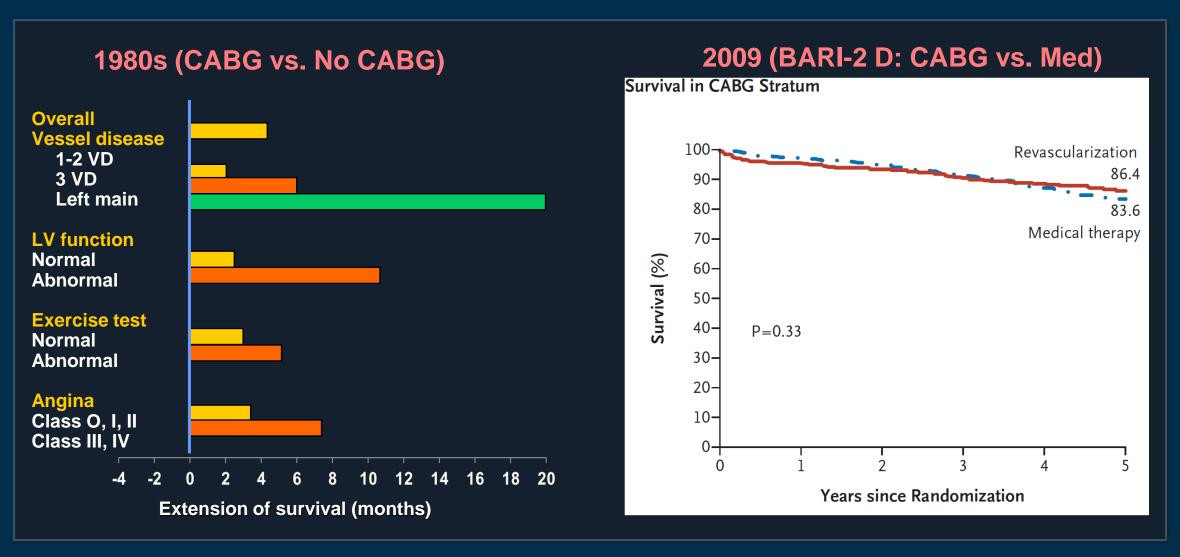
398 (7.7%) participants with HF/LVD

	Event	4-year Cumulative Incidence (95% CI)		Difference in Event Rate, INV - CON (95% CI)		Interaction P-value	
Prir	mary endpoint	INV	CON		I		0.055
	history of HF/LVD	13.0% (11.5%, 14.6%)	14.6% (13.0%, 16.2%)			-1.6% (-3.8%, 0.7%)	0.000
	story of HF/LVD	17.2% (11.6%, 23.8%)	29.3% (21.2%, 38.0%)			-12.1% (-22.6%, -1.6%)	
CV	death or MI	, ,	,			,	0.061
No	o history of HF/LVD	11.4% (10.0%, 12.9%)	13.1% (11.5%, 14.7%)			-1.6% (-3.8%, 0.5%)	
Hi	story of HF/LVD	14.6% (9.4%, 20.9%)	25.9% (18.2%, 34.3%)		-	-11.4% (-21.4%, -1.4%)	
	cause death					/	U.4Ub
	history of HF/LVD	6.2% (5.1%, 7.5%)	5.9% (4.8%, 7.1%)		_ 🕇	0.3% (-1.3%, 2.0%)	
	story of HF/LVD	10.2% (5.8%, 15.9%)	13.3% (7.9%, 20.0%)		-	-3.1% (-11.1%, 4.8%)	
	death	0.004 (0.004 4.004)	. = =			0.004.4.0.004.0.0043	0.154
	history of HF/LVD	3.8% (3.0%, 4.9%)	4.5% (3.5%, 5.5%)		_ 🖶	-0.6% (-2.0%, 0.8%)	
	story of HF/LVD	6.7% (3.4%, 11.6%)	12.7% (7.5%, 19.5%)		•	-6.0% (-13.3%, 1.3%	0.044
	(Primary Definition)	0.004 /7.004 40.004	0.70/ /0.40/ 44.40/			0.00/ (0.00/ 4.00/))	0.244
	o history of HF/LVD	8.8% (7.6%, 10.2%)	9.7% (8.4%, 11.1%)			-0.9% (-2.8%, 1.0%))	
	story of HF/LVD hospitalization	10.5% (6.2%, 16.2%)	16.5% (10.5%, 23.8%)		_	-6.0% (-14.4%, 2.4%)	0.864
	history of HF/LVD	0.6% (0.4%, 1.1%)	1.5% (1.0%, 2.1%)			-0.8% (-1.5%, -0.2%)	0.004
	story of HF/LVD	0.5% (0.0%, 2.4%)	1.1% (0.2%, 3.7%)		1	-0.7% (-2.5%, 1.2%)	
	spitalization for HF	0.570 (0.070, 2.470)	1.170 (0.270, 3.170)			-0.7 70 (-2.070, 1.270)	0.550
	o history of HF/LVD	2.0% (1.4%, 2.8%)	0.6% (0.3%, 1.1%)			1.4% (0.6%, 2.1%)	0.550
	story of HF/LVD	4.4% (1.9%, 8.6%)	4.5% (1.9%, 8.7%)			-0.1% (-4.8%, 4.6%)	
	ath or HF hospitalization	1. 170 (1.576, 5.576)	1.070 (1.070, 0.770)			3.170 (1.070, 1.070)	0.293
	history of HF/LVD	7.5% (6.3%, 8.9%)	6.2% (5.1%, 7.5%)		ļ	1.3% (-0.4%, 3.1%)	0.200
	story of HF/LVD	13.3% (8.3%, 19.6%)	16.8% (10.7%, 24.1%)			-3.5% (-12.3%, 5.3%)	
	death	,	, ,			, ,	0.401
No	o history of HF/LVD	0.3% (0.1%, 0.7%)	0.0% (0.0%, 0.3%)			0.3% (-0.0%, 0.6%)	
	story of HF/LVD	0.7% (0.1%, 3.8%)	1.8% (0.3%, 6.2%)			-1.0% (-4.1%, 2.0%)	
	•	,	,	7 7 7		,	
					10 -5 0 5		
				Favors INV	Favors CON		

- Overall cohort
- High risk subgroups
 - Left main disease
 - LV dysfunction
 - CABG vs. Med: Mortality benefit of CABG (STICHES)
 - CABG vs. PCI: Need RCT
 - 3-vessel disease
 - Proximal LAD disease
 - Extensive ischemia

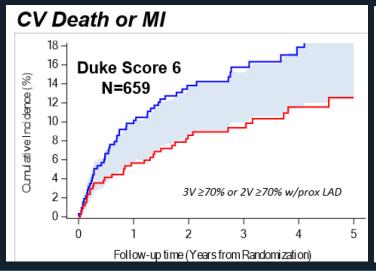
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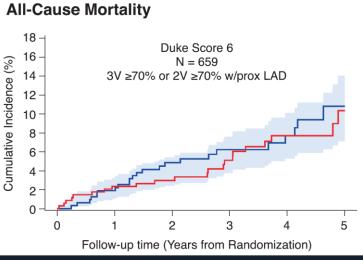
Extension of Survival with 3-vessel disease with Revascularization 1980s to Present

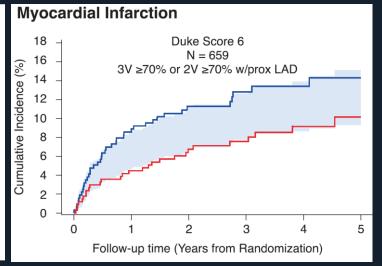


ISCHEMIA: Potential Reduction in CV death/MI in High Anatomic Risk

	Events, n		4-y event rate, %					
	Invasive strategy	Conservative strategy	Invasive strategy	Conservative strategy	Difference (95% CI), %	Interaction <i>P</i> value		
Cardiovascular death or myocardial infarction								
1-Vessel CAD ≥50%	3	4	3.3 (0.9 to 8.6)	8.7 (2.5 to 19.9)	-5.4 (-14.9 to 4.2)			
1-Vessel CAD ≥70% or 2-vessel ≥50%	26	25	8.8 (5.7 to 12.8)	8.7 (5.6 to 12.5)	0.2 (-4.7 to 5.1)			
2-Vessel CAD ≥70% or 3-vessel ≥50% or 70% proximal LAD	38	48	10.2 (7.2 to 13.9)	12.8 (9.5 to 16.7)	-2.6 (-7.5 to 2.3)			
3-Vessel CAD ≥70% or 2-vessel ≥70% in- cluding proximal LAD	34	50	11.6 (8.1 to 15.7)	17.9 (13.4 to 22.8)	-6.3 (-12.4 to -0.2)			



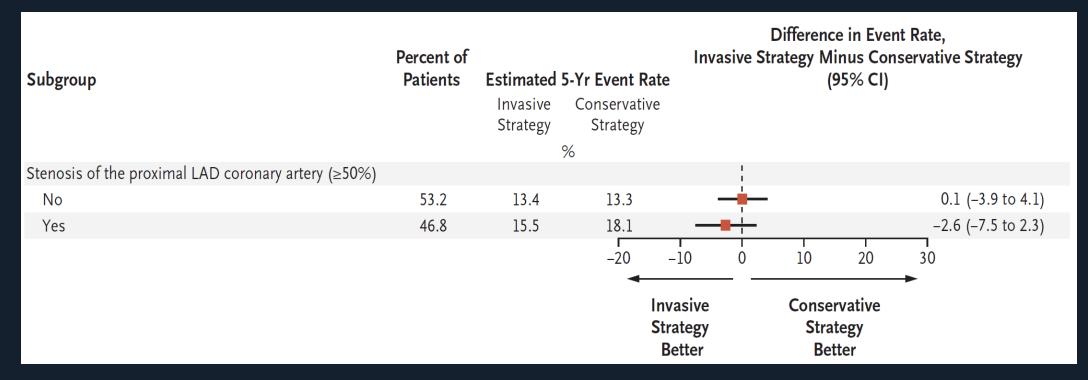




- Overall cohort
- High risk subgroups
 - Left main disease
 - LV dysfunction
 - 3-vessel disease
 - Proximal LAD disease
 - Extensive ischemia

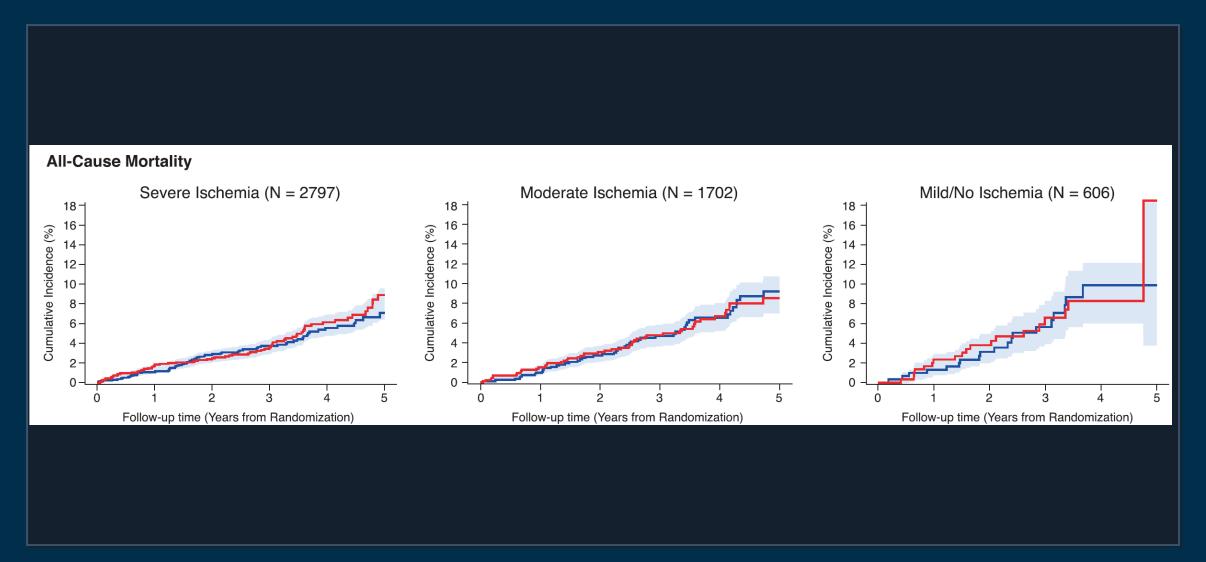
Extension of Survival with Proximal LAD with Revascularization ISCHEMIA: Invasive vs. Conservative

No heterogeneity of treatment effect based on proximal LAD stenosis status for the primary endpoint



- Overall cohort
- High risk subgroups
 - Left main disease
 - LV dysfunction
 - 3-vessel disease
 - Proximal LAD disease
 - Extensive ischemia

Extension of Survival with Revascularization Based on Ischemia Severity ISCHEMIA: Invasive vs. Conservative



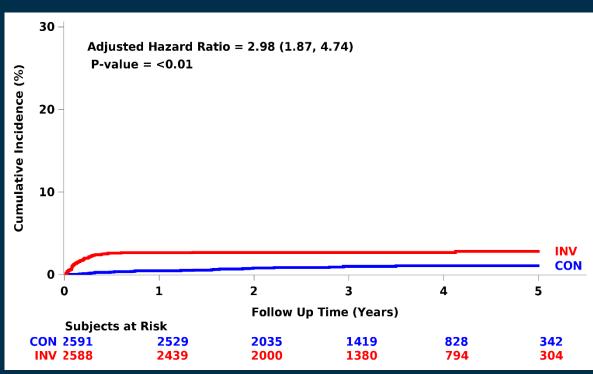
Potential Reasons for Revascularization in SIHD

- To improve survival
- To prevent other cardiovascular events
- To improve quality of life

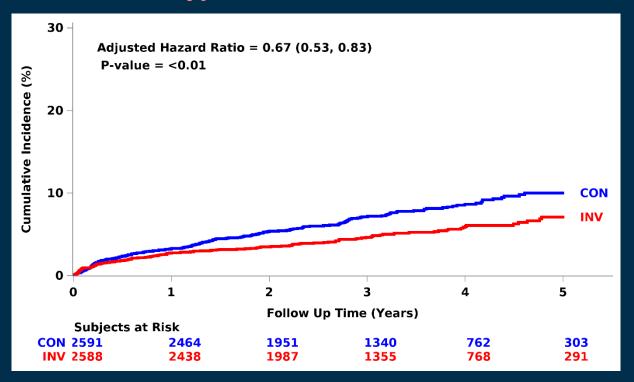
Revascularization Reduces Spontaneous MI

ISCHEMIA: Invasive vs. Conservative

Procedural MI
Type 4a or 5 MI



Spontaneous MI
Types 1, 2, 4b, or 4c MI



Potential Reasons for Revascularization in SIHD

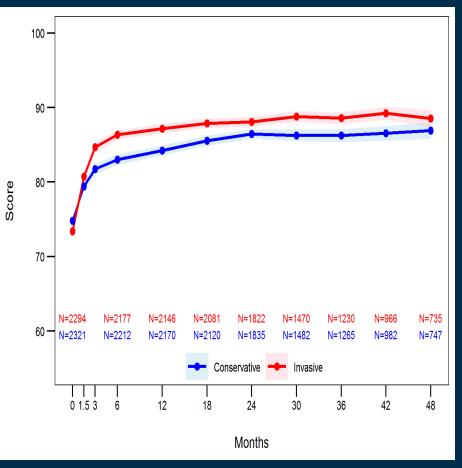
- To improve survival
- To prevent other cardiovascular events
 - Reduces spontaneous MI, unstable angina and lowers CV stays
- To improve quality of life

Potential Reasons for Revascularization in SIHD

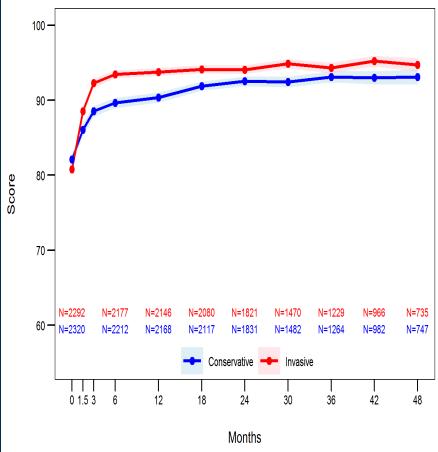
- To improve survival
- To prevent other cardiovascular events
- To improve quality of life

Durable Improvement in Angina Related QoL ISCHEMIA

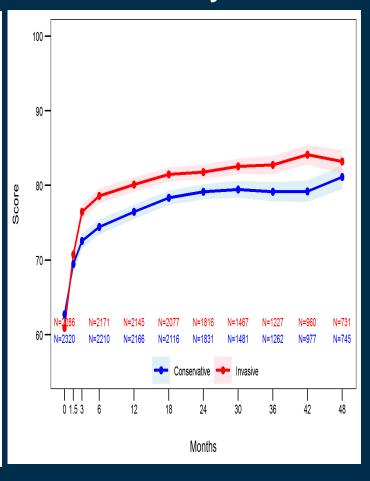
SAQ Summary Score



SAQ Angina Frequency



SAQ Quality of Life



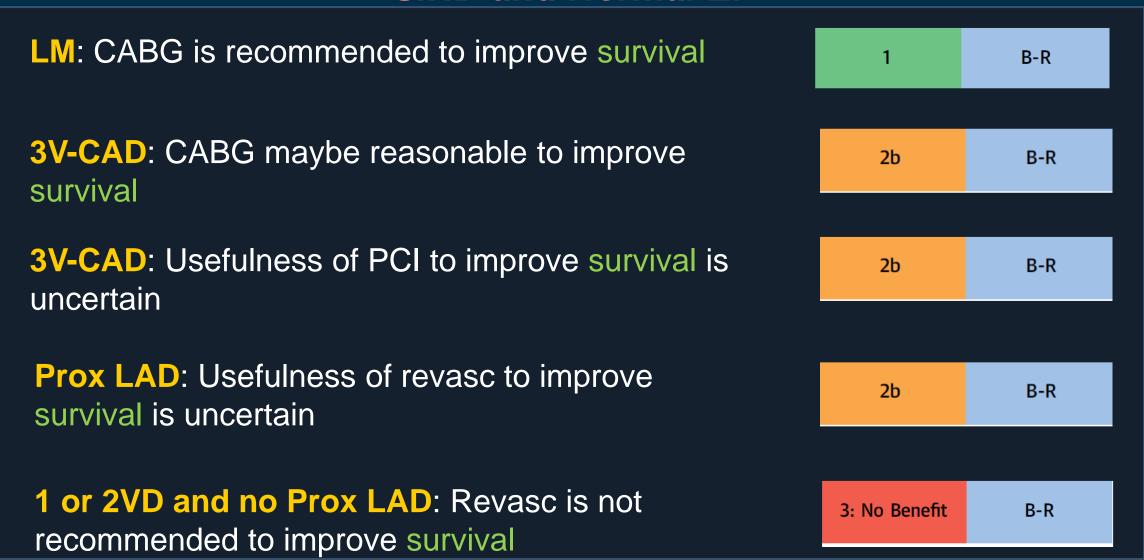
Potential Reasons for Revascularization in SIHD

- To improve survival
- To prevent other cardiovascular events
- To improve quality of life
 - Yes, but not in the asymptomatic patients

Potential Reasons for Revascularization in SIHD Summary

- To improve survival
 - No improvement in survival compared with MT, except in those with LM disease and LV systolic dysfunction
 - Small reduction (0.3%/year) in cardiac death
- To prevent other cardiovascular events
 - Reduces spontaneous MI, unstable angina and lowers CV stays
- To improve quality of life
 - Faster and more durable relief of angina in symptomatic patients

2021 ACC/AHA Revascularization Guidelines SIHD and Normal EF



2021 ACC/AHA Revascularization Guidelines SIHD and Normal EF

Multivessel-CAD: revascularization is reasonable to lower the risk of cardiovascular events such as spontaneous MI, unplanned urgent revascularizations, or cardiac death

