

ACC/AHA Guidelines on Revascularization: The Controversy – The CV Surgical Perspective

Joseph F. Sabik, III, MD

**Oliver H. Payne Professor and Chairman
Surgeon-In-Chief**

Department of Surgery

**University Hospitals Cleveland Medical Center
Case Western Reserve University School of Medicine**



Indications for Revascularization

- Prolong Survival
 - Decreasing Cardiovascular Death
- Decrease Future Ischemic Events
 - Angina
 - Myocardial Infarction
 - Repeat Revascularization

2018 ESC/EACTS Guidelines

Indications for revascularization in patients with stable angina or silent ischaemia

Extent of CAD (anatomical and/or functional)		Class ^a	Level ^b
For prognosis	Left main disease with stenosis >50%. ^{c 68-71}	I	A
	Proximal LAD stenosis >50%. ^{c 62,68,70,72}	I	A
	Two- or three-vessel disease with stenosis >50% with impaired LV function (LVEF ≤35%). ^{c 61,62,68,70,73-83}	I	A
	Large area of ischaemia detected by functional testing (>10% LV) or abnormal invasive FFR. ^{d 24,59,84-90}	I	B
	Single remaining patent coronary artery with stenosis >50%. ^c	I	C
For symptoms	Haemodynamically significant coronary stenosis ^c in the presence of limiting angina or angina equivalent, with insufficient response to optimized medical therapy. ^{e 24,63,91-97}	I	A

2018 ESC/EACTS Guidelines : MVD

Recommendations according to extent of CAD	CABG		PCI	
	Class ^a	Level ^b	Class ^a	Level ^b
Three-vessel CAD without diabetes mellitus				
Three-vessel disease with low SYNTAX score (0 - 22). ^{102,105,121,123,124,135,149}	I	A	I	A
Three-vessel disease with intermediate or high SYNTAX score (>22). ^{c 102,105,121,123,124,135,149}	I	A	III	A
Three-vessel CAD with diabetes mellitus				
Three-vessel disease with low SYNTAX score 0–22. ^{102,105,121,123,124,135,150–157}	I	A	IIb	A
Three-vessel disease with intermediate or high SYNTAX score (>22). ^{c 102,105,121,123,124,135,150–157}	I	A	III	A

2021 ACC/AHA/SCAI CAD Revascularization Guidelines : MVD

Multivessel CAD		
2b	B-R	5. In patients with SIHD, normal ejection fraction, significant stenosis in 3 major coronary arteries (with or without proximal LAD), and anatomy suitable for CABG, CABG may be reasonable to improve survival. ^{10,13-15}
2b	B-R	6. In patients with SIHD, normal ejection fraction, significant stenosis in 3 major coronary arteries (with or without proximal LAD), and anatomy suitable for PCI, the usefulness of PCI to improve survival is uncertain. ¹⁴⁻²⁴

2012 Guideline on Management of SIHD

3-vessel disease with or without proximal LAD artery disease*		
CABG	I	B
	IIa—It is reasonable to choose CABG over PCI in patients with complex 3-vessel CAD (e.g., SYNTAX score >22) who are good candidates for CABG.	B
PCI	IIb—Of uncertain benefit	B

2021 ACC/AHA/SCAI CAD Revascularization Guidelines : Complex Disease

COR	LOE	Recommendations
1	B-R	1. In patients who require revascularization for significant left main CAD with high-complexity CAD, it is recommended to choose CABG over PCI to improve survival. ^{1,2}
2a	B-R	2. In patients who require revascularization for multivessel CAD with complex or diffuse CAD (eg, SYNTAX score >33), it is reasonable to choose CABG over PCI to confer a survival advantage. ²⁻⁵

2021 ACC/AHA/SCAI CAD Revascularization Guidelines : Diabetes

COR	LOE	Recommendations
1	A	1. In patients with diabetes and multivessel CAD with the involvement of the LAD, who are appropriate candidates for CABG, CABG (with a LIMA to the LAD) is recommended in preference to PCI to reduce mortality and repeat revascularizations. ¹⁻⁸
2a	B-NR	2. In patients with diabetes who have multivessel CAD amenable to PCI and an indication for revascularization and are poor candidates for surgery, PCI can be useful to reduce long-term ischemic outcomes. ^{9,10}
2b	B-R	3. In patients with diabetes who have left main stenosis and low- or intermediate-complexity CAD in the rest of the coronary anatomy, PCI may be considered an alternative to CABG to reduce major adverse cardiovascular outcomes. ^{5,11}

Revascularization in MVD

- ESC/EACTS European Guidelines
 - Revascularization > OMT
 - CABG > PCI
 - Intermediate/Complex CAD
 - Diabetes
- ACC/AHA/SCAI Guidelines
 - Revascularization = OMT
 - CABG = PCI
 - CABG > PCI
 - Complex CAD
 - Diabetes

Who Is Right ?

Survival

Revascularization versus OMT

Randomized Trials : CABG vs. Medical Therapy

Trial	CABG	Medical Treatment
VA	332	354
European	394	373
CASS	390	390
Texas	56	60
Oregon	51	49
New Zealand	51	49
New Zealand	50	50
Total	1324	1325

CABG Prolongs Survival

Risk Stratification

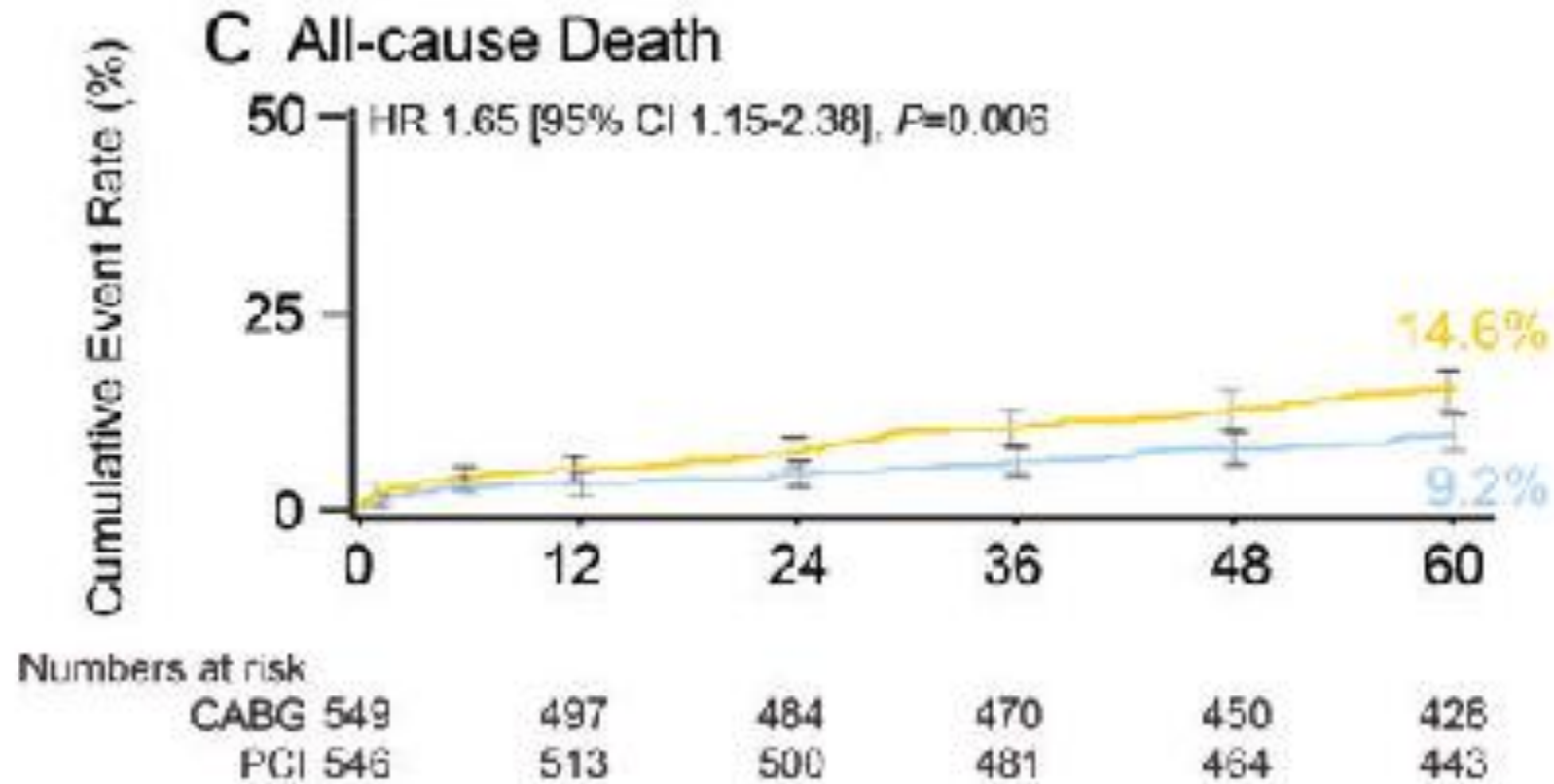
Angiographic Subgroups	MR (%)
• LMT stenosis (> 50%)	68%
• 3V CAD (> 50%)	42%
• 1/2V CAD and proximal LAD	32%
• No proximal LAD	-5%

Randomized Trials

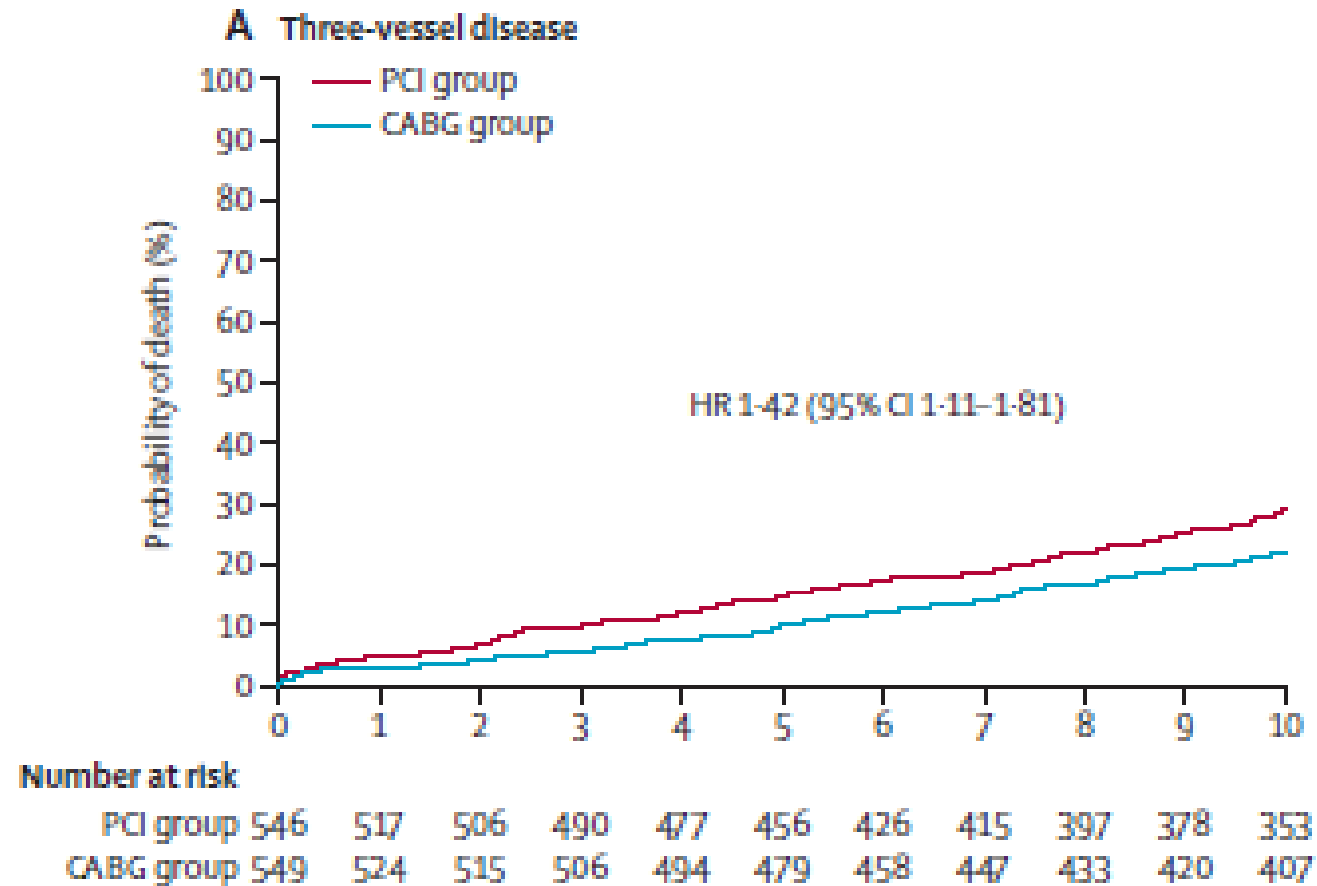
- ITA Grafting (10%)
- Myocardial Protection
- Aspirin (1/5 medical, 1/4 surgical)
- B-Blockers (2/3 medical, 1/5 surgical)
- Ace Inhibitors
- Statins

**No Randomized Trial has demonstrated PCI
better than OMT in SIHD in improving
Survival**

SYNTAX 3V CAD 5 Year Survival



SYNTAX 3V CAD 10 Year Survival



Percutaneous coronary intervention versus coronary artery bypass grafting in patients with three-vessel or left main coronary artery disease: 10-year follow-up of the multicentre randomised controlled SYNTAX trial

Daniel J F M Thuijs, A Pieter Kappetein, Patrick W Serruys, Friedrich-Wilhelm Mohr, Marie-Claude Morice, Michael J Mack, David R Holmes Jr, Nick Curzen, Piroze Davierwala, Thilo Noack, Milan Milojevic, Keith D Dawkins, Bruno R da Costa, Peter Jüni, Stuart J Head, for the SYNTAX Extended Survival Investigators*

Summary

Background The Synergy between PCI with Taxus and Cardiac Surgery (SYNTAX) trial was a non-inferiority trial that compared percutaneous coronary intervention (PCI) using first-generation paclitaxel-eluting stents with coronary artery bypass grafting (CABG) in patients with de-novo three-vessel and left main coronary artery disease, and reported results up to 5 years. We now report 10-year all-cause death results.

Methods The SYNTAX Extended Survival (SYNTAXES) study is an investigator-driven extension of follow-up of a multicentre, randomised controlled trial done in 85 hospitals across 18 North American and European countries. Patients with de-novo three-vessel and left main coronary artery disease were randomly assigned (1:1) to the PCI group or CABG group. Patients with a history of PCI or CABG, acute myocardial infarction, or an indication for concomitant cardiac surgery were excluded. The primary endpoint of the SYNTAXES study was 10-year all-cause death, which was assessed according to the intention-to-treat principle. Prespecified subgroup analyses were performed according to the presence or absence of left main coronary artery disease and diabetes, and according to coronary complexity defined by core laboratory SYNTAX score tertiles. This study is registered with ClinicalTrials.gov, NCT03417050.

Findings From March, 2005, to April, 2007, 1800 patients were randomly assigned to the PCI (n=903) or CABG (n=897) group. Vital status information at 10 years was complete for 841 (93%) patients in the PCI group and 848 (95%) patients in the CABG group. At 10 years, 248 (28%) patients had died after PCI and 212 (24%) after CABG (hazard ratio 1.19 [95% CI 0.99–1.43], $p=0.066$). Among patients with three-vessel disease, 153 (28%) of 546 had died after PCI versus 114 (21%) of 549 after CABG (hazard ratio 1.42 [95% CI 1.11–1.81]), and among patients with left main coronary artery disease, 95 (27%) of 357 had died after PCI versus 98 (28%) of 348 after CABG (0.92 [0.69–1.22], $p_{\text{interaction}}=0.023$). There was no treatment-by-subgroup interaction with diabetes ($p_{\text{interaction}}=0.60$) and no linear trend across SYNTAX score tertiles ($p_{\text{trend}}=0.20$).

Interpretation At 10 years, no significant difference existed in all-cause death between PCI using first-generation paclitaxel-eluting stents and CABG. However, CABG provided a significant survival benefit in patients with three-vessel disease, but not in patients with left main coronary artery disease.

Percutaneous coronary intervention versus coronary artery bypass grafting in patients with three-vessel or left main coronary artery disease: 10-year follow-up of the multicentre randomised controlled SYNTAX trial

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High School Mathematics

- If
 - $PCI = OMT$
- And
 - $CABG > PCI$
- Then
 - $CABG > OMT$

Initial Invasive or Conservative Strategy for Stable Coronary Disease

D.J. Maron, J.S. Hochman, H.R. Reynolds, S. Bangalore, S.M. O'Brien, W.E. Boden, B.R. Chaitman, R. Senior, J. López-Sendón, K.P. Alexander, R.D. Lopes, L.J. Shaw, J.S. Berger, J.D. Newman, M.S. Sidhu, S.G. Goodman, W. Ruzyllo, G. Gosselin, A.P. Maggioni, H.D. White, B. Bhargava, J.K. Min, G.B.J. Mancini, D.S. Berman, M.H. Picard, R.Y. Kwong, Z.A. Ali, D.B. Mark, J.A. Spertus, M.N. Krishnan, A. Elghamraz, N. Moorthy, W.A. Hueb, M. Demkow, K. Mavromatis, O. Bockeria, J. Peteiro, T.D. Miller, H. Szwed, R. Doerr, M. Keltai, J.B. Selvanayagam, P.G. Steg, C. Held, S. Kohsaka, S. Mavromichalis, R. Kirby, N.O. Jeffries, F.E. Harrell, Jr., F.W. Rockhold, S. Broderick, T.B. Ferguson, Jr., D.O. Williams, R.A. Harrington, G.W. Stone, and Y. Rosenberg, for the ISCHEMIA Research Group*

ABSTRACT

BACKGROUND

Among patients with stable coronary disease and moderate or severe ischemia, whether clinical outcomes are better in those who receive an invasive intervention plus medical therapy than in those who receive medical therapy alone is uncertain.

METHODS

We randomly assigned 5179 patients with moderate or severe ischemia to an initial invasive strategy (angiography and revascularization when feasible) and medical therapy or to an initial conservative strategy of medical therapy alone and angiography if medical therapy failed. The primary outcome was a composite of death from cardiovascular causes, myocardial infarction, or hospitalization for unstable angina, heart failure, or resuscitated cardiac arrest. A key secondary outcome was death from cardiovascular causes or myocardial infarction.

RESULTS

Over a median of 3.2 years, 318 primary outcome events occurred in the invasive-strategy group and 352 occurred in the conservative-strategy group. At 6 months, the cumulative event rate was 5.3% in the invasive-strategy group and 3.4% in the conservative-strategy group (difference, 1.9 percentage points; 95% confidence interval [CI], 0.8 to 3.0); at 5 years, the cumulative event rate was 16.4% and 18.2%, respectively (difference, -1.8 percentage points; 95% CI, -4.7 to 1.0). Results were similar with respect to the key secondary outcome. The incidence of the primary outcome was sensitive to the definition of myocardial infarction; a secondary analysis yielded more procedural myocardial infarctions of uncertain clinical importance. There were 145 deaths in the invasive-strategy group and 144 deaths in the conservative-strategy group (hazard ratio, 1.05; 95% CI, 0.83 to 1.32).

CONCLUSIONS

Among patients with stable coronary disease and moderate or severe ischemia, we did not find evidence that an initial invasive strategy, as compared with an initial conservative strategy, reduced the risk of ischemic cardiovascular events or death from any cause over a median of 3.2 years. The trial findings were sensitive to the definition of myocardial infarction that was used. (Funded by the National Heart, Lung, and Blood Institute and others; ISCHEMIA ClinicalTrials.gov number, NCT01471522.)

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Maron at the Department of Medicine, Stanford University School of Medicine, 1265 Welch Rd., Medical School Office Bldg. x314, Stanford, CA 94305, or at david.maron@stanford.edu; or to Dr. Hochman at the New York University Grossman School of Medicine—New York University Langone Health, 530 First Ave., Skirball 9R, New York, NY 10016, or at judith.hochman@nyumc.org.

*A full list of ISCHEMIA Research Group members is provided in the Supplementary Appendix, available at NEJM.org.

Drs. Maron and Hochman contributed equally to this article.

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ISCHEMIA

- Compared Initial Conservative Strategy vs. Initial Invasive Strategy (angiography +/- revascularization)
- No Difference in composite endpoint (death from CV causes, MI, hospitalization for unstable angina, heart failure, or cardiac arrest)
- Not designed to determine if CABG improved survival
 - CABG only 26% of all revascularizations
 - CABG performed in only 20% of all pts in initial invasive strategy group
 - More pts in initial invasive strategy received MT alone (21%) than received CABG (20%)
 - More pts in initial conservative strategy received revascularization (N=544) than pts in initial invasive strategy that received CABG (N=530)

CABG Underutilized in ISCHEMIA

Choice of Revascularization left to Local Heart Teams

- Those that underwent angiography and intervention (79%)
 - 71% had multi-vessel CAD
 - 2V CAD in 32%
 - 3V CAD in 40%
 - 42% had diabetes
 - CABG in 26% (CABG in 20% of entire initial invasive strategy group)

The impact of CABG on survival cannot be ascertained from trials in which the majority of revascularization procedures performed were PCI and not CABG, such as ISCHEMIA.

Coronary Artery Disease and Ischemia Severity

Harmony R. Reynolds¹, MD; Leslee J. Shaw², PhD; James K. Min, MD; Courtney B. Page, MA; Daniel S. Berman, MD; Bernard R. Chaitman³, MD; Michael H. Picard⁴, MD; Raymond Y. Kwong⁵, MD, MPH; Sean M. O'Brien, PhD; Zhen Huang, MS; Daniel B. Mark⁶, MD, MPH; Ranjit K. Nath⁷, MD, DM; Sudhanshu K. Dwivedi, MD; Paola E.P. Smanio, MD, PhD; Peter H. Stone, MD; Claes Held, MD, PhD; Matyas Keltai, MD, PhD, DSc; Sripal Bangalore⁸, MD, MHA; Jonathan D. Newman⁹, MD, MPH; John A. Spertus¹⁰, MD, MPH; Gregg W. Stone, MD; David J. Maron, MD; Judith S. Hochman¹¹, MD

BACKGROUND: The ISCHEMIA trial (International Study of Comparative Health Effectiveness With Medical and Invasive Approaches) postulated that patients with stable coronary artery disease (CAD) and moderate or severe ischemia would benefit from revascularization. We investigated the relationship between severity of CAD and ischemia and trial outcomes, overall and by management strategy.

METHODS: In total, 5179 patients with moderate or severe ischemia were randomized to an initial invasive or conservative management strategy. Blinded, core laboratory–interpreted coronary computed tomographic angiography was used to assess anatomic eligibility for randomization. Extent and severity of CAD were classified with the modified Duke Prognostic Index ($n=2475$, 48%). Ischemia severity was interpreted by independent core laboratories (nuclear, echocardiography, magnetic resonance imaging, exercise tolerance testing, $n=5105$, 99%). We compared 4-year event rates across subgroups defined by severity of ischemia and CAD. The primary end point for this analysis was all-cause mortality. Secondary end points were myocardial infarction (MI), cardiovascular death or MI, and the trial primary end point (cardiovascular death, MI, or hospitalization for unstable angina, heart failure, or resuscitated cardiac arrest).

RESULTS: Relative to mild/no ischemia, neither moderate ischemia nor severe ischemia was associated with increased mortality (moderate ischemia hazard ratio [HR], 0.89 [95% CI, 0.61–1.30]; severe ischemia HR, 0.83 [95% CI, 0.57–1.21]; $P=0.33$). Nonfatal MI rates increased with worsening ischemia severity (HR for moderate ischemia, 1.20 [95% CI, 0.86–1.69] versus mild/no ischemia; HR for severe ischemia, 1.37 [95% CI, 0.98–1.91]; $P=0.04$ for trend, $P=NS$ after adjustment for CAD). Increasing CAD severity was associated with death (HR, 2.72 [95% CI, 1.06–6.98]) and MI (HR, 3.78 [95% CI, 1.63–8.78]) for the most versus least severe CAD subgroup. Ischemia severity did not identify a subgroup with treatment benefit on mortality, MI, the trial primary end point, or cardiovascular death or MI. In the most severe CAD subgroup ($n=659$), the 4-year rate of cardiovascular death or MI was lower in the invasive strategy group (difference, 6.3% [95% CI, 0.2%–12.4%]), but 4-year all-cause mortality was similar.

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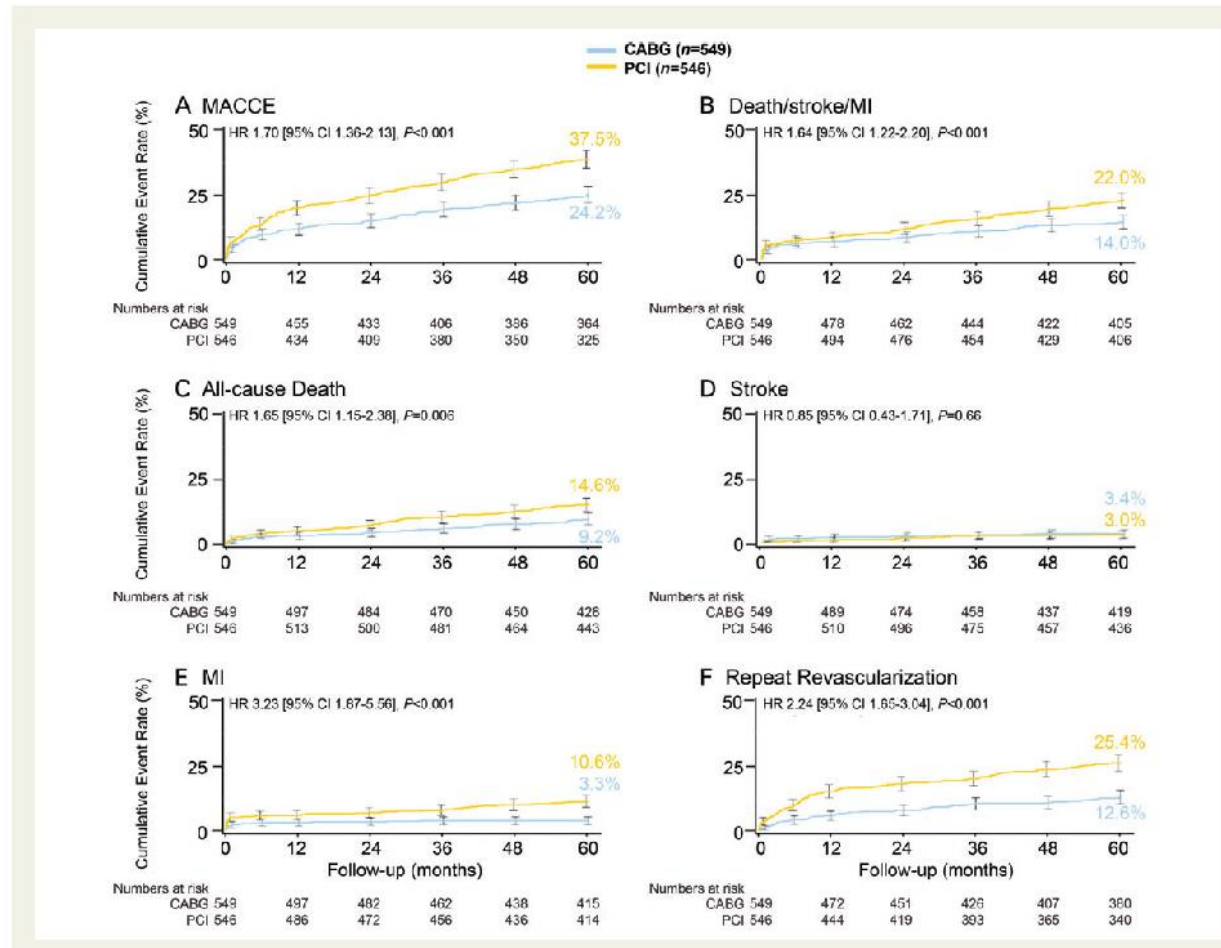
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Future Ischemic Events

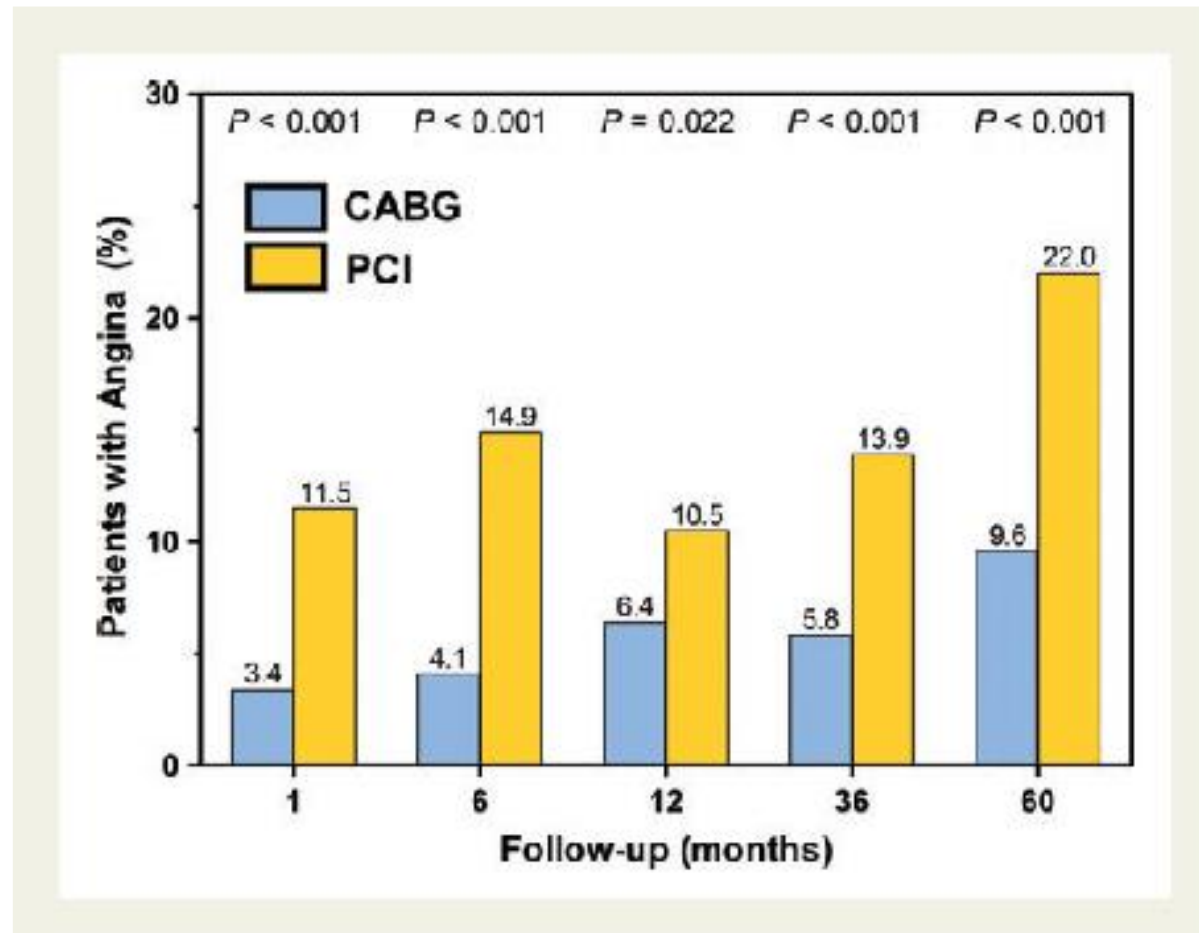
2021 ACC/AHA/SCAI CAD Revascularization Guidelines : Future Events

COR	LOE	Recommendation
2a	B-R	1. In patients with SIHD and multivessel CAD appropriate for either CABG or PCI, revascularization is reasonable to lower the risk of cardiovascular events such as spontaneous MI, unplanned urgent revascularizations, or cardiac death. ¹⁻⁸

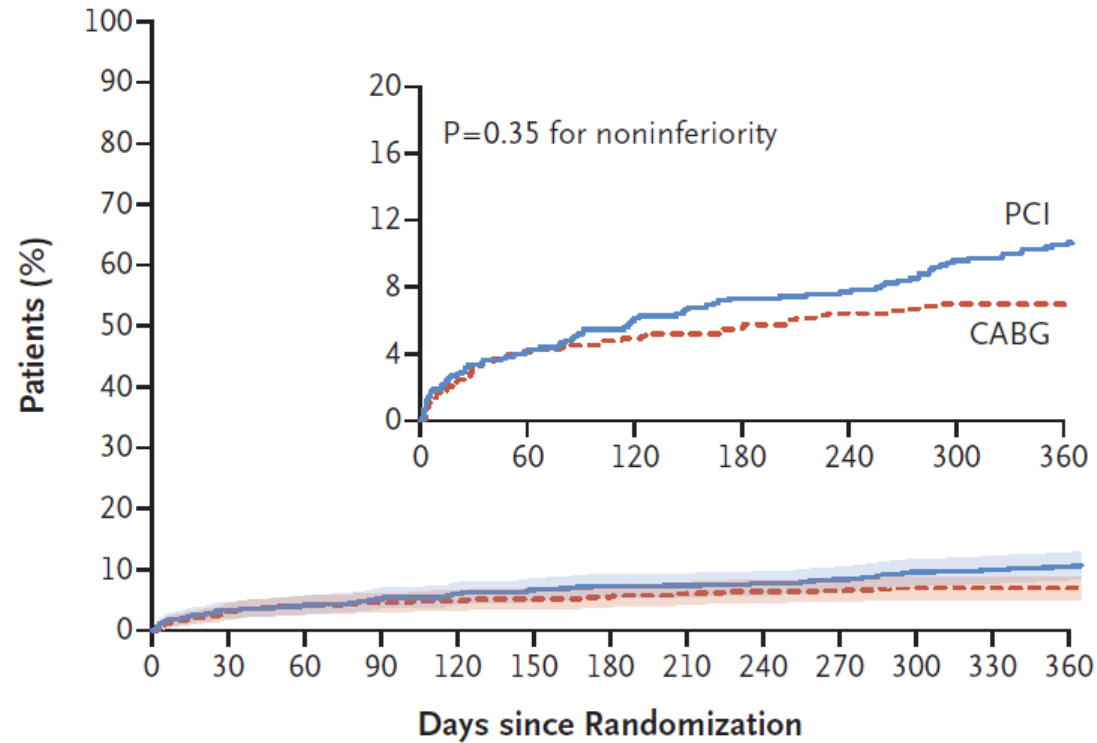
SYNTAX 5 Years – 3V CAD



SYNTAX 5 Years – 3V CAD with Angina



FAME 3 – 1 Year



No. at Risk

PCI	757	728	721	713	707	702	697	696	693	687	678	674	670
CABG	743	709	701	698	695	693	691	686	683	682	679	679	679

Summary

- CABG prolongs survival in patients with MVD
 - CABG does not equal PCI
 - CABG should have a higher COR than PCI

- CABG decreases future ischemic events in patients with MVD
 - CABG does not equal PCI
 - CABG should have a higher COR than PCI

Summary

- CABG should not have been downgraded to equal PCI in ACC/AHA/SCAI Guidelines
 - Survival vs. OMT
 - Reduction of Future Ischemic Events
- ESC/EACTS Guidelines aligned with evidence