Revascularization After FAME 3 How will we decide?

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Recommendations for Revascularization to Improve Survival in SIHD Compared With Medical Therapy
Referenced studies that support the recommendations are summarized in Online Data Supplement 10.

COR	LOE	RECOMMENDATIONS
		Left ventricular dysfunction and multivessel CAD
1	B-R	1. In patients with SIHD and multivessel CAD appropriate for CABG with severe left ventricular systolic dysfunction (left ventricular ejection fraction <35%), CABG is recommended to improve survival (1,2).
2a	B-NR	2. In selected patients with SIHD and multivessel CAD appropriate for CABG and mild-to-moderate left ventricular systolic dysfunction (ejection fraction 35%-50%), CABG (to include a left internal mammary artery [LIMA] graft to the LAD) is reasonable to improve survival (3-8).
		Left main CAD
1	B-R	3. In patients with SIHD and significant left main stenosis, CABG is recommended to improve survival (9-12).
2a	B-NR	4. In selected patients with SIHD and significant left main stenosis for whom PCI can provide equivalent revascularization to that possible with CABG, PCI is reasonable to improve survival (9).
		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).
		Stenosis in the proximal LAD artery
2b	B-R	7. In patients with SIHD, normal left ventricular ejection fraction, and significant stenosis in the proximal LAD, the usefulness of coronary revascularization to improve survival is uncertain (10,14,17,24-27).
		Single- or double-vessel disease not involving the proximal LAD
3: No Benefit	B-R	8. In patients with SIHD, normal left ventricular ejection fraction, and 1- or 2-vessel CAD not involving the proximal LAD, coronary revascularization is not recommended to improve survival (10,14,16,26,28,29).
3: Harm	B-NR	9. In patients with SIHD who have ≥1 coronary arteries that are not anatomically or functionally significant (<70% diameter of non-left main coronary artery stenosis, FFR >0.80), coronary revascularization should not be performed with the primary or sole intent to improve survival (26,30).

Recommendations for Patients With Diabetes
Referenced studies that support the recommendations are summarized in Online Data Supplement 14.

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).

Recommendations for Patients With Complex Disease
Referenced studies that support the recommendations are summarized in Online Data Supplement 13.

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 (e.g., SYNTAX score >33), it is reasonable to choose CABG over PCI to confer a survival advantage (2-5).

The NEW ENGLAND JOURNAL of MEDICINE

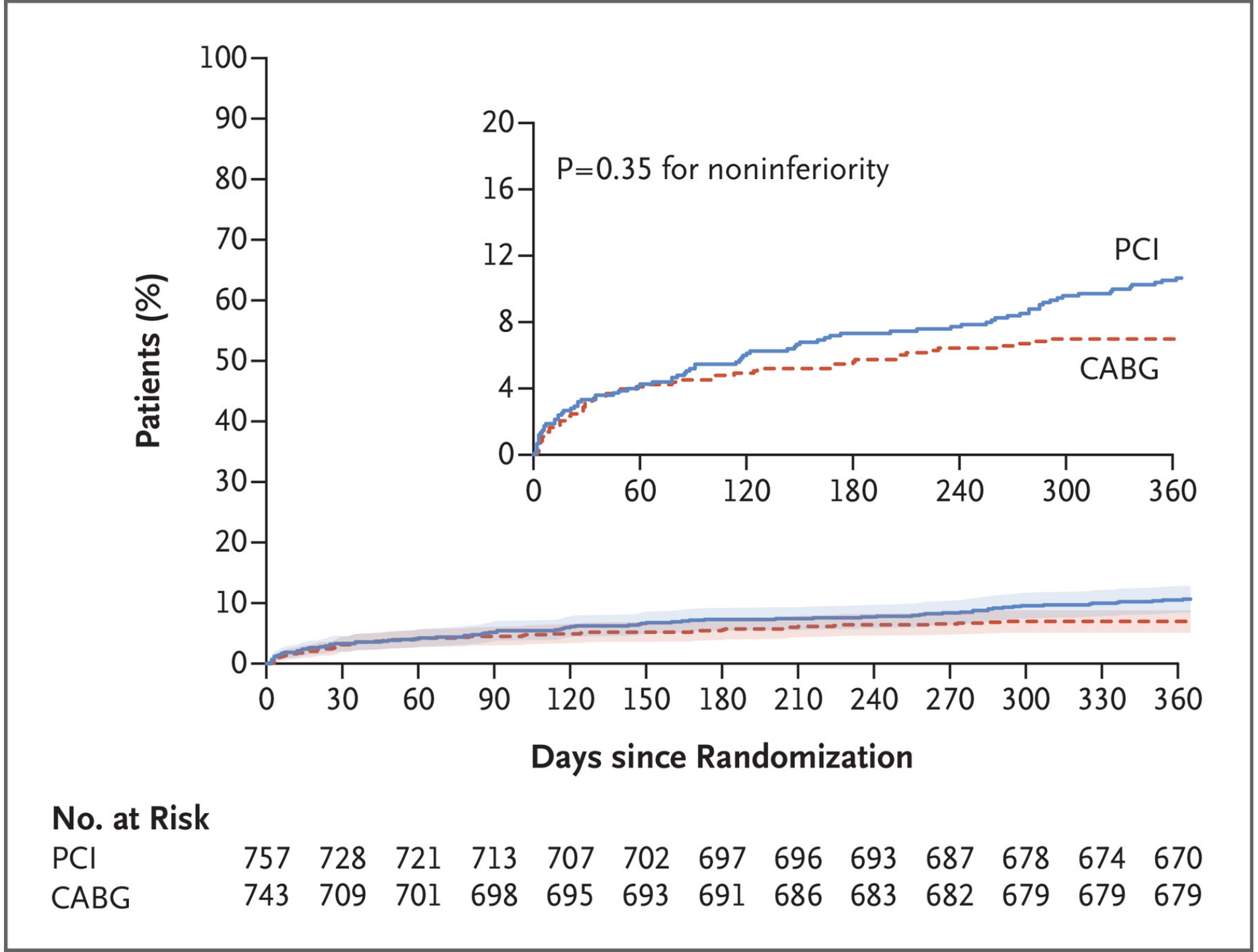
ORIGINAL ARTICLE

Fractional Flow Reserve–Guided PCI as Compared with Coronary Bypass Surgery

W.F. Fearon, F.M. Zimmermann, B. De Bruyne, Z. Piroth, A.H.M. van Straten, L. Szekely, G. Davidavičius, G. Kalinauskas, S. Mansour, R. Kharbanda, N. Östlund-Papadogeorgos, A. Aminian, K.G. Oldroyd, N. Al-Attar, N. Jagic, J.-H.E. Dambrink, P. Kala, O. Angerås, P. MacCarthy, O. Wendler, F. Casselman, N. Witt, K. Mavromatis, S.E.S. Miner, J. Sarma, T. Engstrøm, E.H. Christiansen, P.A.L. Tonino, M.J. Reardon, D. Lu, V.Y. Ding, Y. Kobayashi, M.A. Hlatky, K.W. Mahaffey, M. Desai, Y.J. Woo, A.C. Yeung, and N.H.J. Pijls, for the FAME 3 Investigators*

FAME 3 Trial

Stable 3 vessel CAD randomized to CABG or FFR guided PCI (n=1500)
Primary endpoint: death, MI, stroke or repeat revascularization
Noninferiority design
Diabetes 29%, LVEF<50% 18%, CTO 21%
SYNTAX Score 26
0-22=33%
23-32=49%
>32=18%



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

Figure 1. Kaplan–Meier Curves for the Primary End Point.

The primary end point was the occurrence within 1 year of a major adverse cardiac or cerebrovascular event, defined as death from any cause, myocardial infarction, stroke, or repeat revascularization. The inset shows the same data on an enlarged y axis. CABG denotes coronary-artery bypass grafting, and PCI percutaneous coronary intervention.

FAME 3 MACCE based on SYNTAX Score

SYNTAX	PCI	CABG
0-22	5.5%	8.6%
23-32	13.7%	6.1%
>33	12.1%	6.6%
Total	10.6%	6.9% (HR 1.5; 1.1-2.2)

FAME 3 Endpoints

	PCI	CABG
• Death	1.6%	0.9%
• Death, MI, Stroke	7.3%	5.2%
• Repeat revasc	5.9%	3.9%
• (By PCI)	5.2%	3.5%
• BARK 3-5	1.6%	3.8%
• Re hospitalized	5.5%	10.2%

Subgroup	PCI	CABG	PCI	CABG
	total no.		*1-yr incidence (%)*	
All patients	757	743	10.6	6.9
Age				
≥65 yr	434	409	9.4	8.1
<65 yr	323	334	12.1	5.4
Sex				
Female	141	124	11.3	13.7
Male	616	619	10.4	5.5
Diabetes				
No	543	529	9.4	7.0
Yes	214	214	13.6	6.5
NSTE-ACS				
No	456	454	10.1	5.9
Yes	300	287	11.3	8.4
LVEF				
>50%	616	610	10.4	6.6
30–50%	137	130	10.9	8.5
Previous PCI				
No	658	637	9.3	6.8
Yes	98	104	19.4	7.7
SYNTAX score				
0–22	237	245	5.5	8.6
23–32	365	343	13.7	6.1
≥33	132	122	12.1	6.6

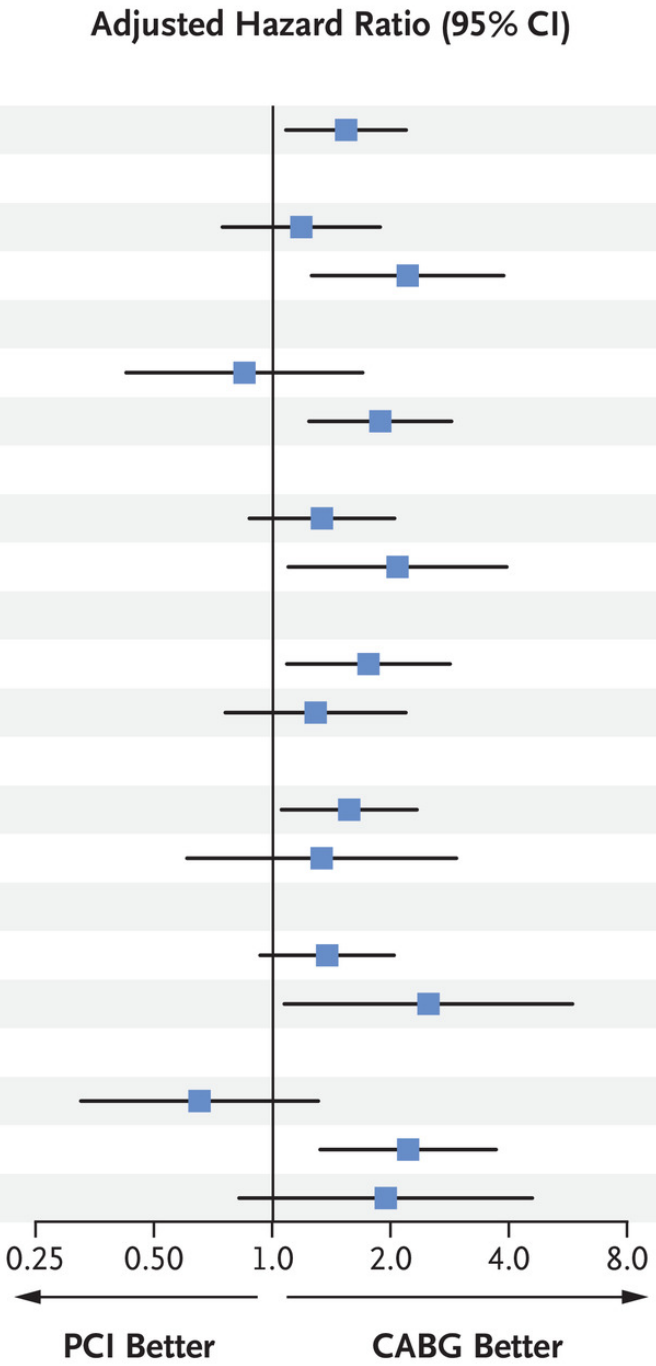


Figure 2. Subgroup Analyses of the Primary End Point.
The Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery (SYNTAX) score is an angiography-based score evaluating the severity of coronary artery disease; lower scores indicate less complexity of coronary artery disease and predict a better outcome with PCI (the lowest score is 0, and there is no upper limit). Scores were calculated by the core laboratory. CI denotes confidence interval, LVEF left ventricular ejection fraction, and NSTE-ACS non–ST-segment elevation acute coronary syndrome.

FLOWER MI Trial

- Patients with STEMI and multivessel CAD (n=1,171)
- Culprit artery PCI followed by angiography guided vs FFR guided non-culprit PCI
- Non-culprit stenting 1/pt in FFR gr and 1.5/pt in angiography gr
- Primary endpoint of death MI or urgent revasc: FFR guided 5.5% and angiography guided 4.2%

- Negative Trial

- NEJM 2021;22:297-308

FUTURE Trial

- FFR vs angiography guided strategy for multivessel CAD (n=927)
- Primary endpoint (Death, stroke, MI revascularization) for FFR gr 14.6% and for angiography group 14.4%.

- **Negative trial**, although stopped early

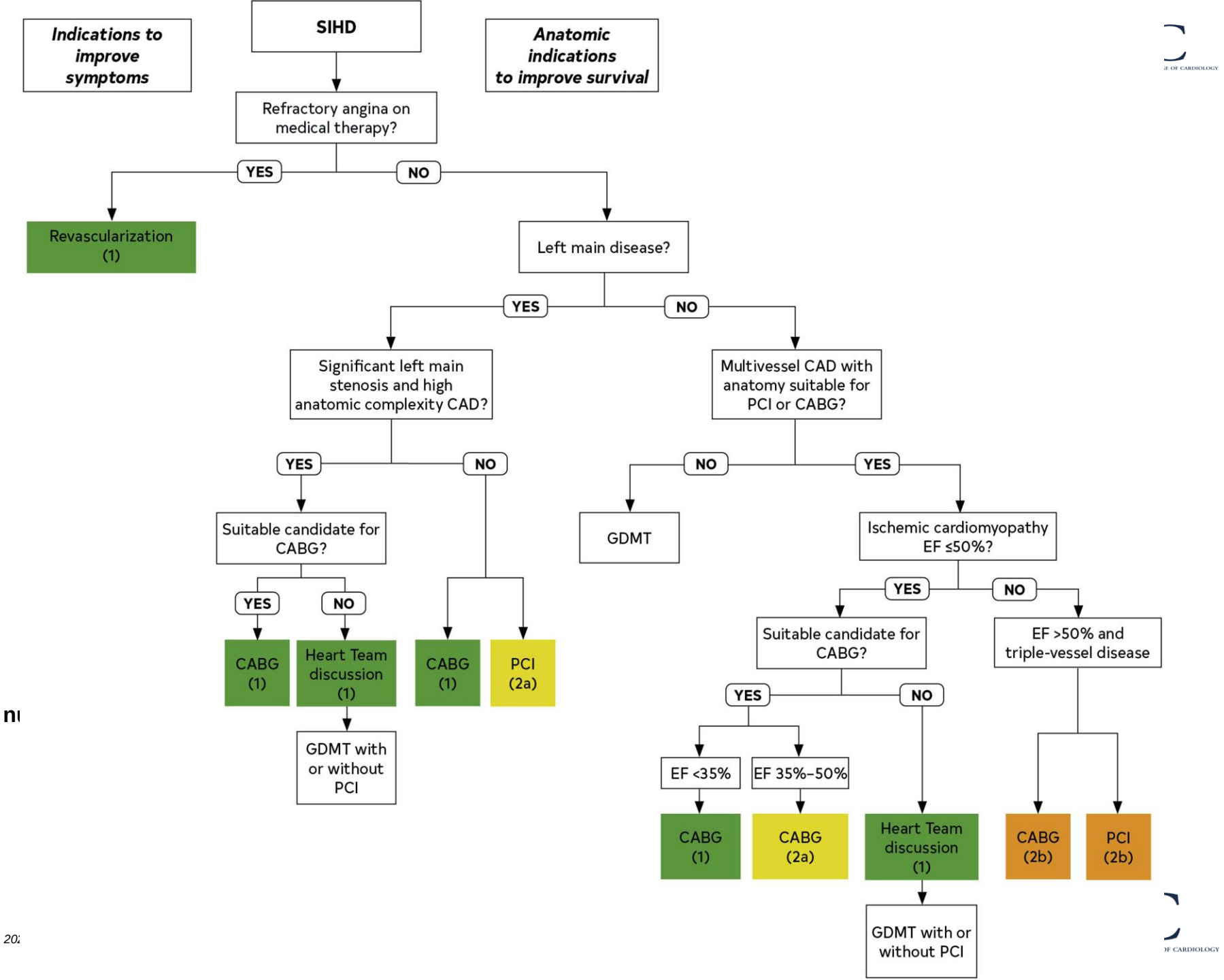
- JACC 2021;78:1875-1885

The good news

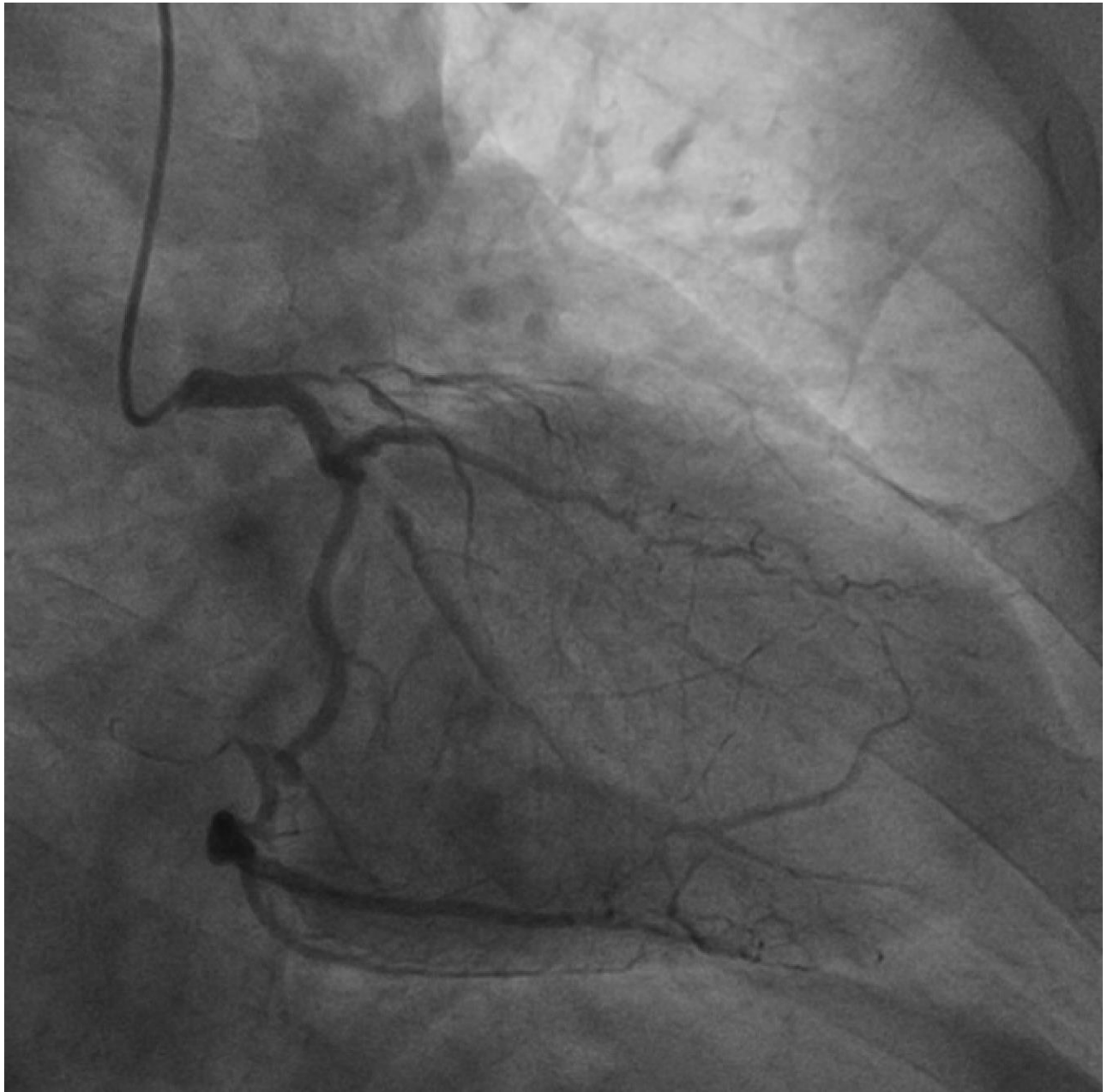
Compared to the SYNTAX trial 10 years ago, FAME 3 had a lower incidence of repeat revascularization (4.9% vs 13.5%) and lower mortality (1.6% vs 4.4%).

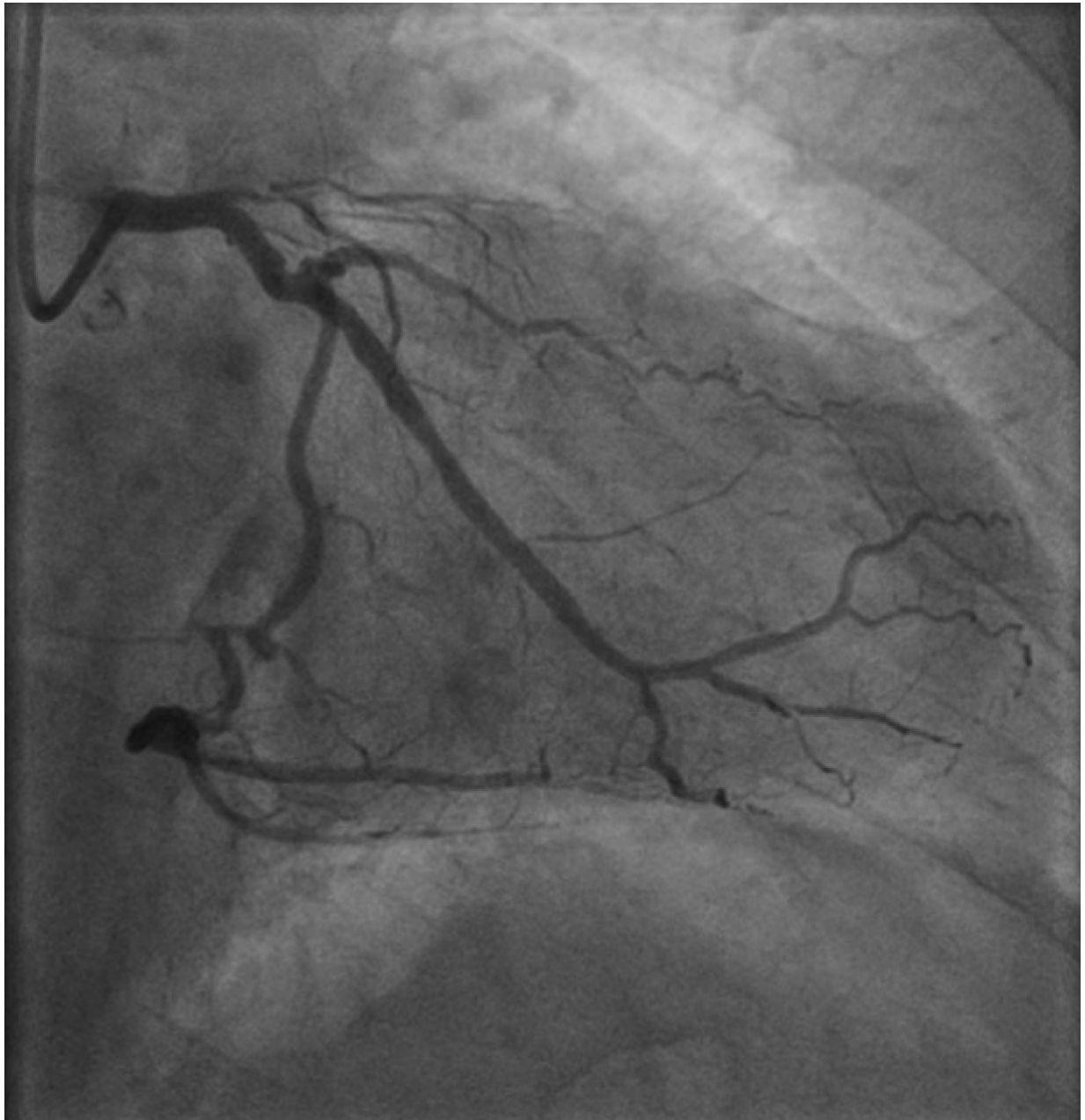
This may be due to improvements in stenting technology but use of more powerful medical therapies must have played a role as well.

How do we select the revascularization method now?

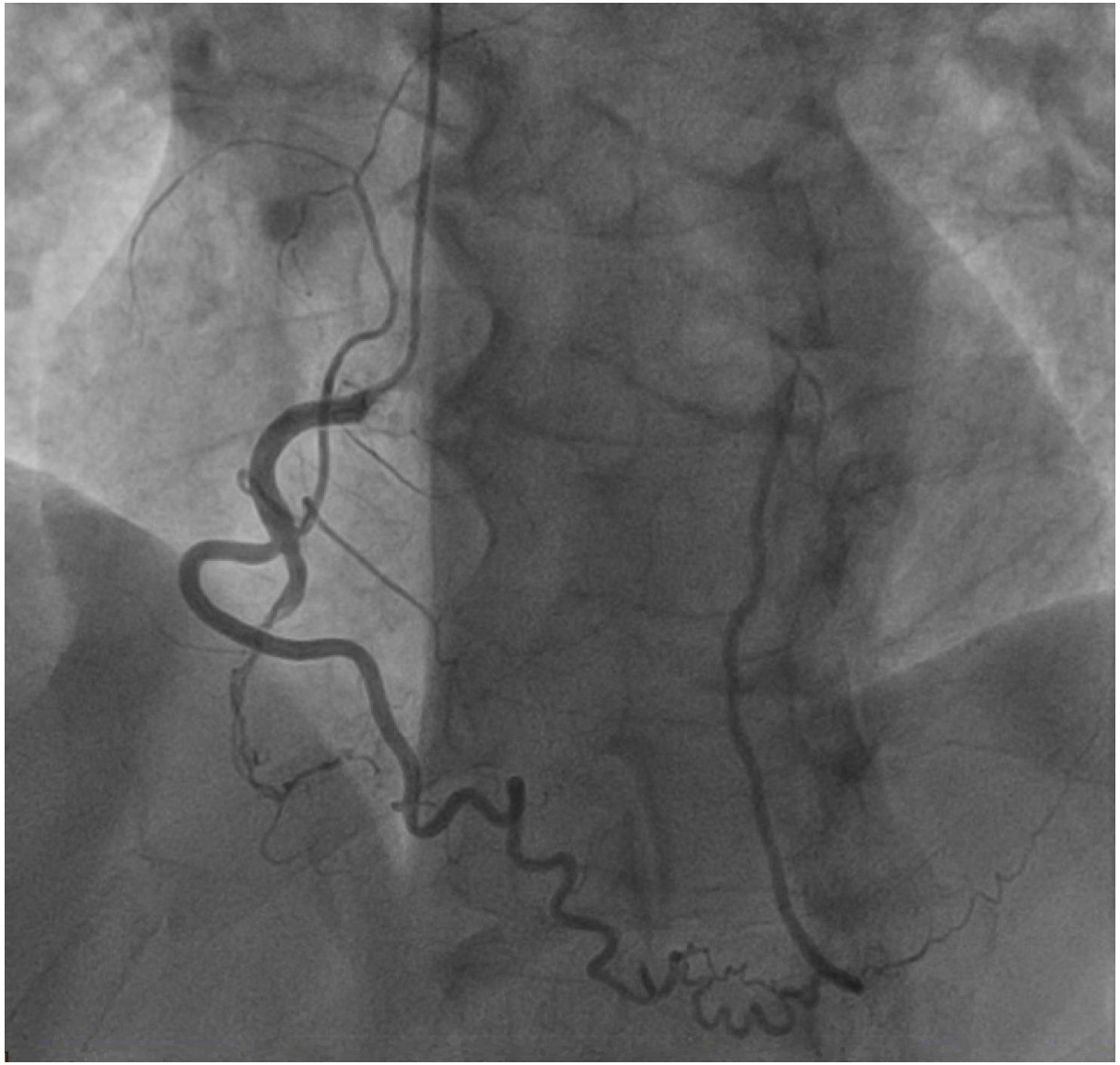

Indications to improve symptoms
SIHD
Anatomic indications to improve survival
Refractory angina on medical therapy?
YES
NO
Revascularization (1)
Left main disease?
YES
NO
Significant left main stenosis and high anatomic complexity CAD?
Multivessel CAD with anatomy suitable for PCI or CABG?
YES
NO
NO
YES
Suitable candidate for CABG?
GDMT
Ischemic cardiomyopathy EF ≤50%?
YES
NO
YES
NO
CABG (1)
Heart Team discussion (1)
CABG (1)
PCI (2a)
GDMT with or without PCI
Suitable candidate for CABG?
EF >50% and triple-vessel disease
YES
NO
EF <35%
EF 35%–50%
CABG (1)
CABG (2a)
Heart Team discussion (1)
CABG (2b)
PCI (2b)
GDMT with or without PCI

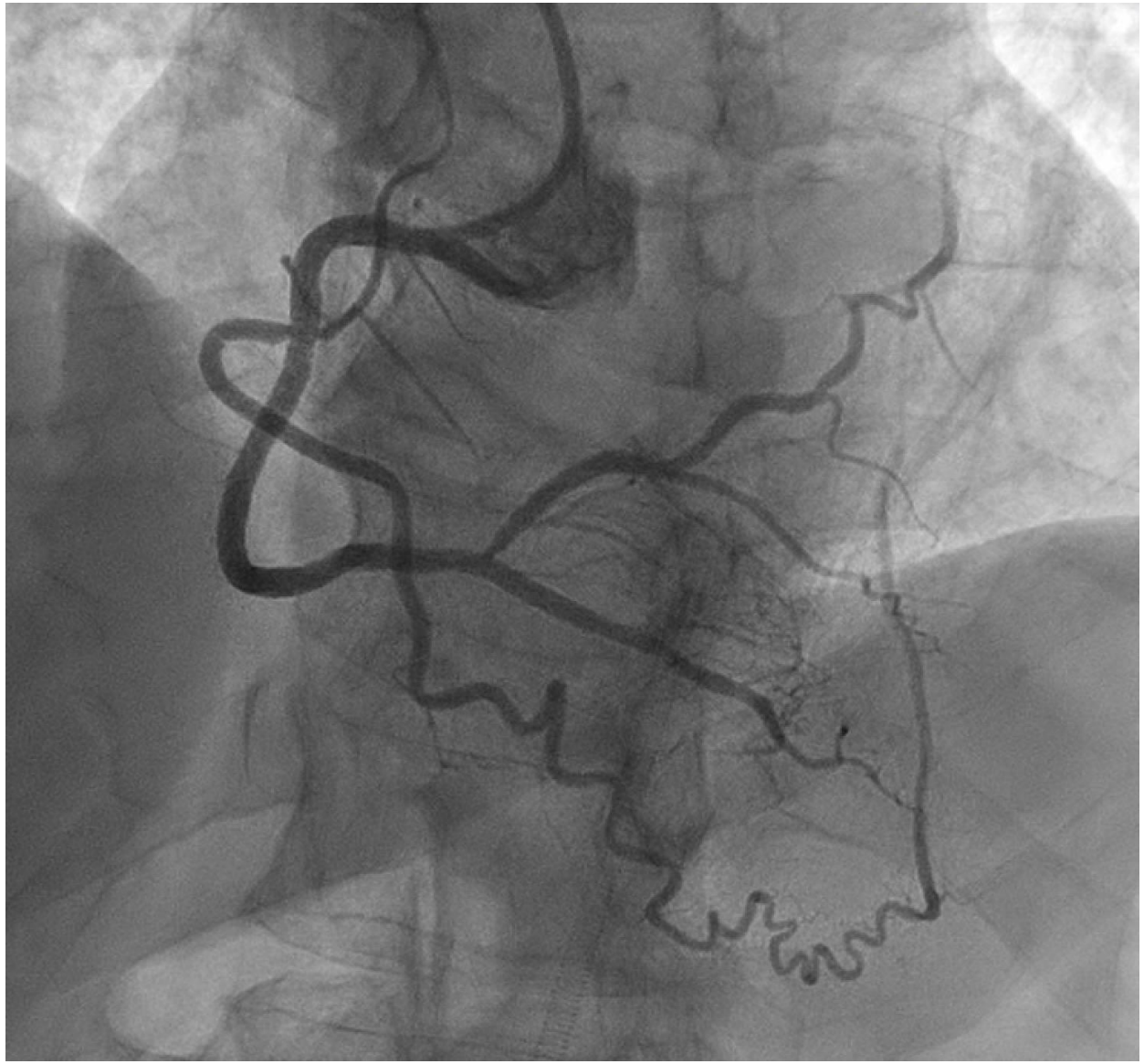
LCX CTO PCI



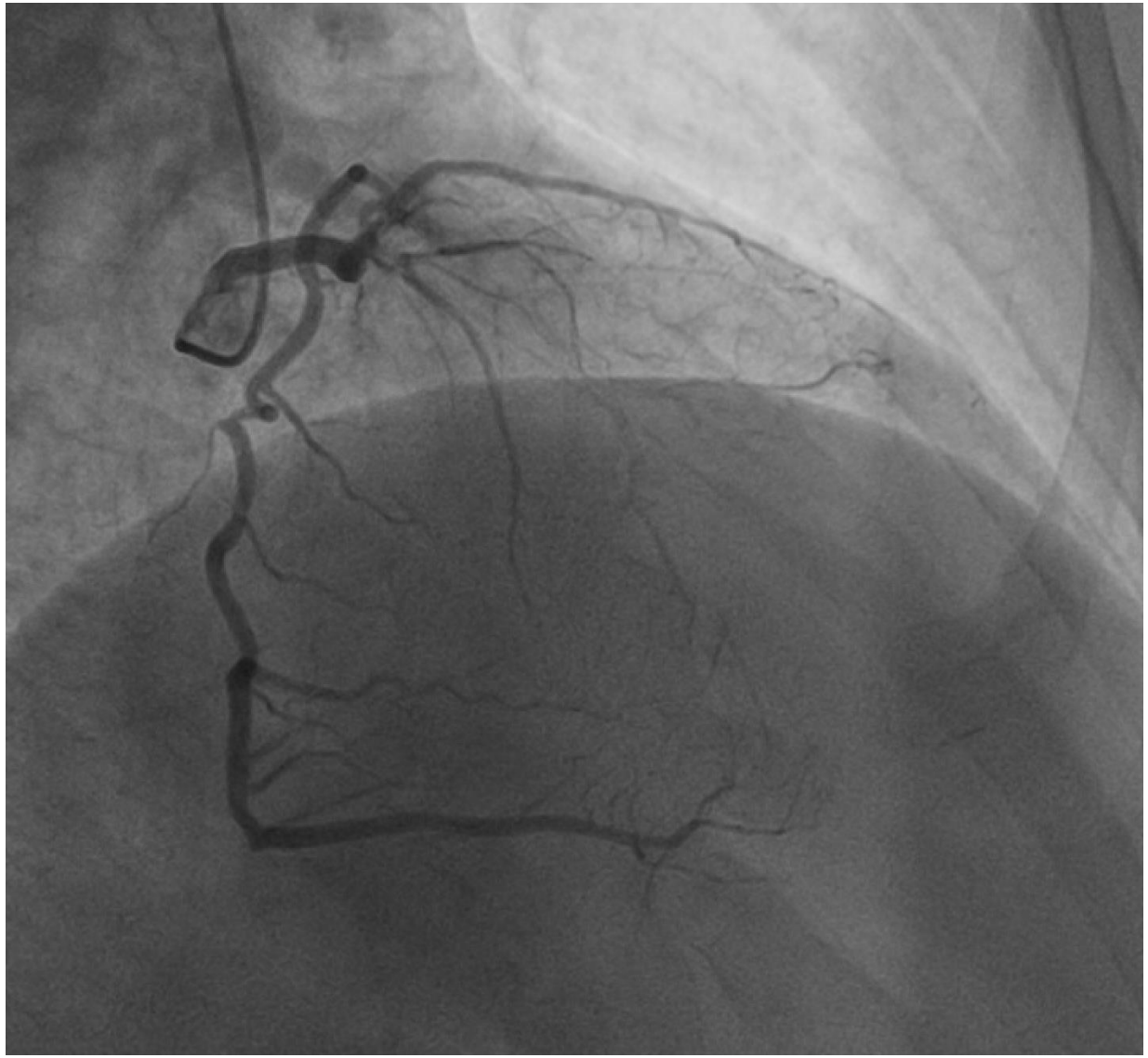


RCA CTO PCI





LAD CTO PCI



Consider the Guidelines and the FAME 3, but also the local expertise and experience.

What may change in the future?

- Diagnostic angiograms will be replaced by coronary CT angiograms
- Noninvasive physiology and plaque characteristics will be collected
- Biomarkers may be added
- With these added technologies will we be better able to predict which patients will suffer cardiac events and which lesions will be responsible?
- ….and therefore be better able to select the best treatment options?

How will revascularization be done after FAME 3?

Pretty much as it was done before FAME 3