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Revascularization in HFrEF: Revived or Dead?

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RESEARCH SUMMARY

Percutaneous Revascularization for Ischemic Left Ventricular Dysfunction

Perera D et al. DOI: 10.1056/NEJMoa2206606

CLINICAL PROBLEM

Coronary-artery bypass grafting (CABG) has shown a long-term survival benefit in patients with severe ischemic left ventricular systolic dysfunction, but the short-term risks associated with the procedure are substantial. Percutaneous coronary intervention (PCI) is an alternative revascularization strategy, but whether it can improve event-free survival and left ventricular function in patients with left ventricular dysfunction is unknown.

CLINICAL TRIAL

Design: A prospective, multicenter, randomized, open-label trial examined whether PCI, when added to optimal medical therapy, would improve outcomes in patients with severe ischemic left ventricular systolic dysfunction.

Intervention: 700 patients with a left ventricular ejection fraction (LVEF) of 35% or less, extensive coronary artery disease, and viability in at least four dysfunctional myocardial segments were assigned to a strategy of either PCI plus optimal medical therapy or optimal medical therapy alone. The primary composite outcome was death from any cause or hospitalization for heart failure during at least 24 months of follow-up.

RESULTS

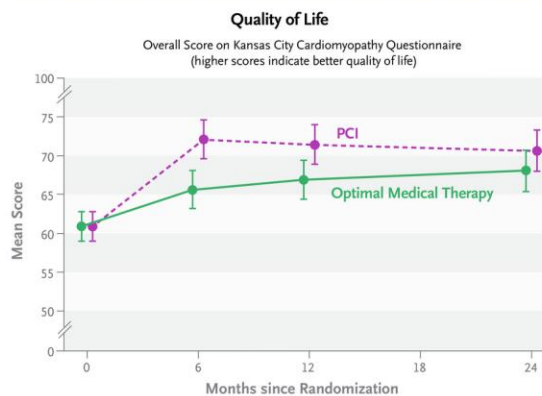
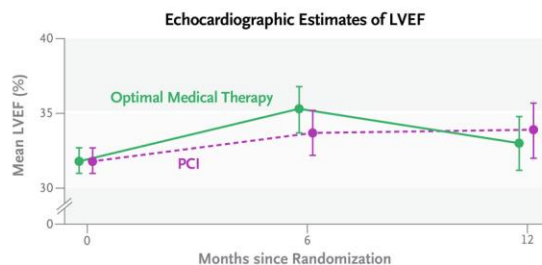
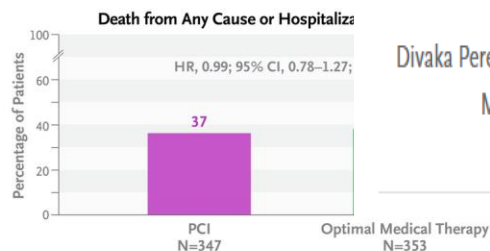
Primary Outcome: During a median follow-up of 41 months, the incidence of a primary-outcome event did not differ significantly between the two groups.

Secondary Outcomes: The mean LVEF at 6 and 12 months did not differ significantly between the two groups. PCI offered an early benefit with respect to quality-of-life measures, but the scores improved over time among those assigned to receive optimal medical therapy alone, thereby diminishing the between-group differences by 24 months.

LIMITATIONS

- The open-label design could have affected any patient-reported outcomes.
- The findings cannot be extrapolated to patients with exercise-limiting angina or acute coronary syndromes, because most participants had little to no angina at enrollment.
- Fewer outcome events occurred than the number originally estimated for the assessment of the primary outcome.

Links: [Full Article](#) | [NEJM Quick Take](#) | [Editorial](#)



CONCLUSIONS

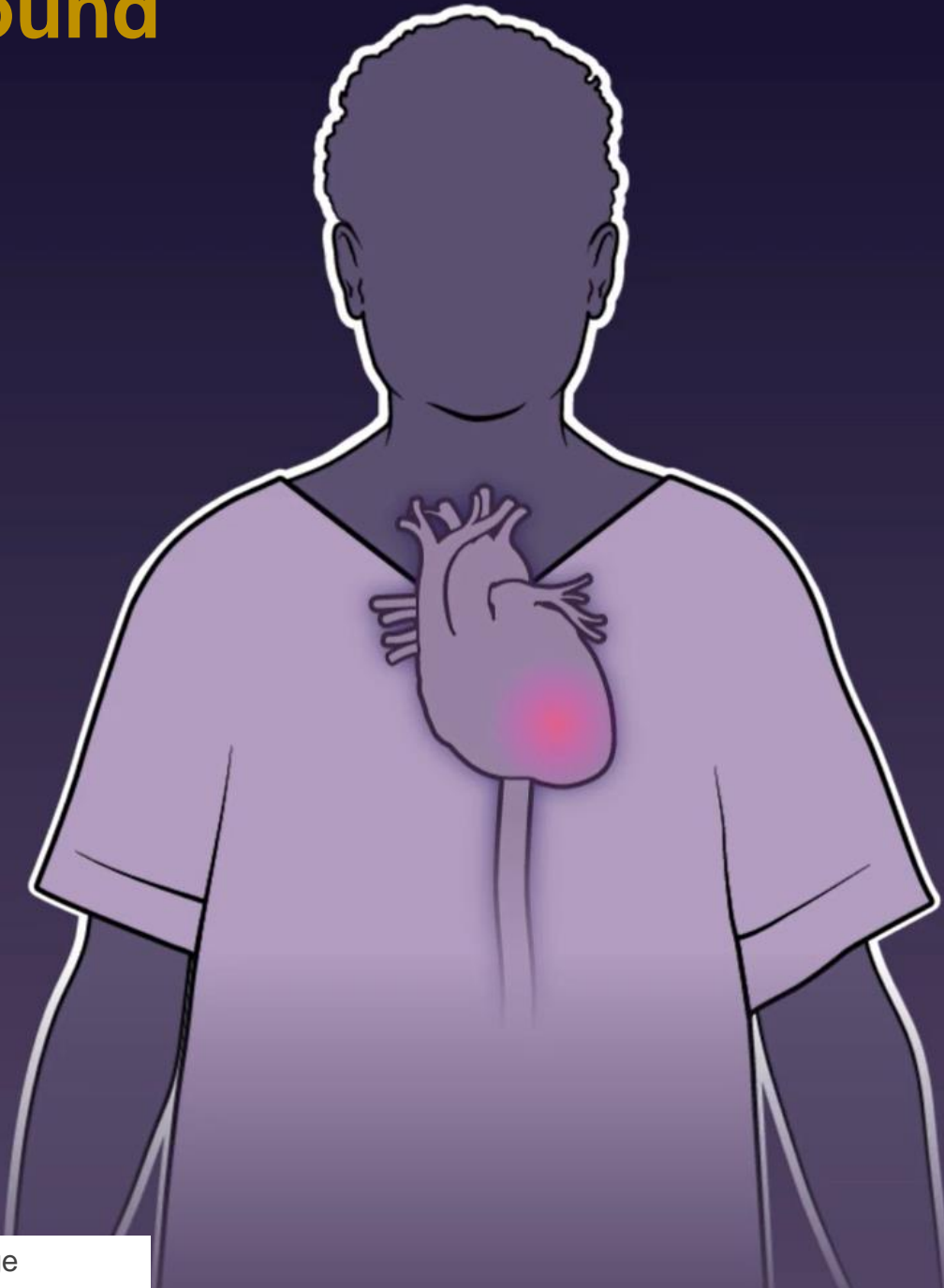
Among patients with severe ischemic left ventricular systolic dysfunction, the risk of death from any cause or hospitalization for heart failure was not lower with PCI plus optimal medical therapy than with optimal medical therapy alone during at least 24 months of follow-up.

Percutaneous Revascularization for Ischemic Left Ventricular Dysfunction

Divaka Perera, M.D., Tim Clayton, M.Sc., Peter D. O'Kane, M.D., John P. Greenwood, Ph.D., Roshan Weerackody, Ph.D., Matthew Ryan, Ph.D., Holly P. Morgan, M.B., B.Ch., Matthew Dodd, M.Sc., Richard Evans, B.A., Ruth Canter, M.Sc., Sophie Arnold, M.Sc., Lana J. Dixon, Ph.D., *et al.*, for the REVIVED-BCIS2 Investigators*

- [October 13, 2022](#)
N Engl J Med 2022; 387:1351-1360
DOI: 10.1056/NEJMoa2206606

Background



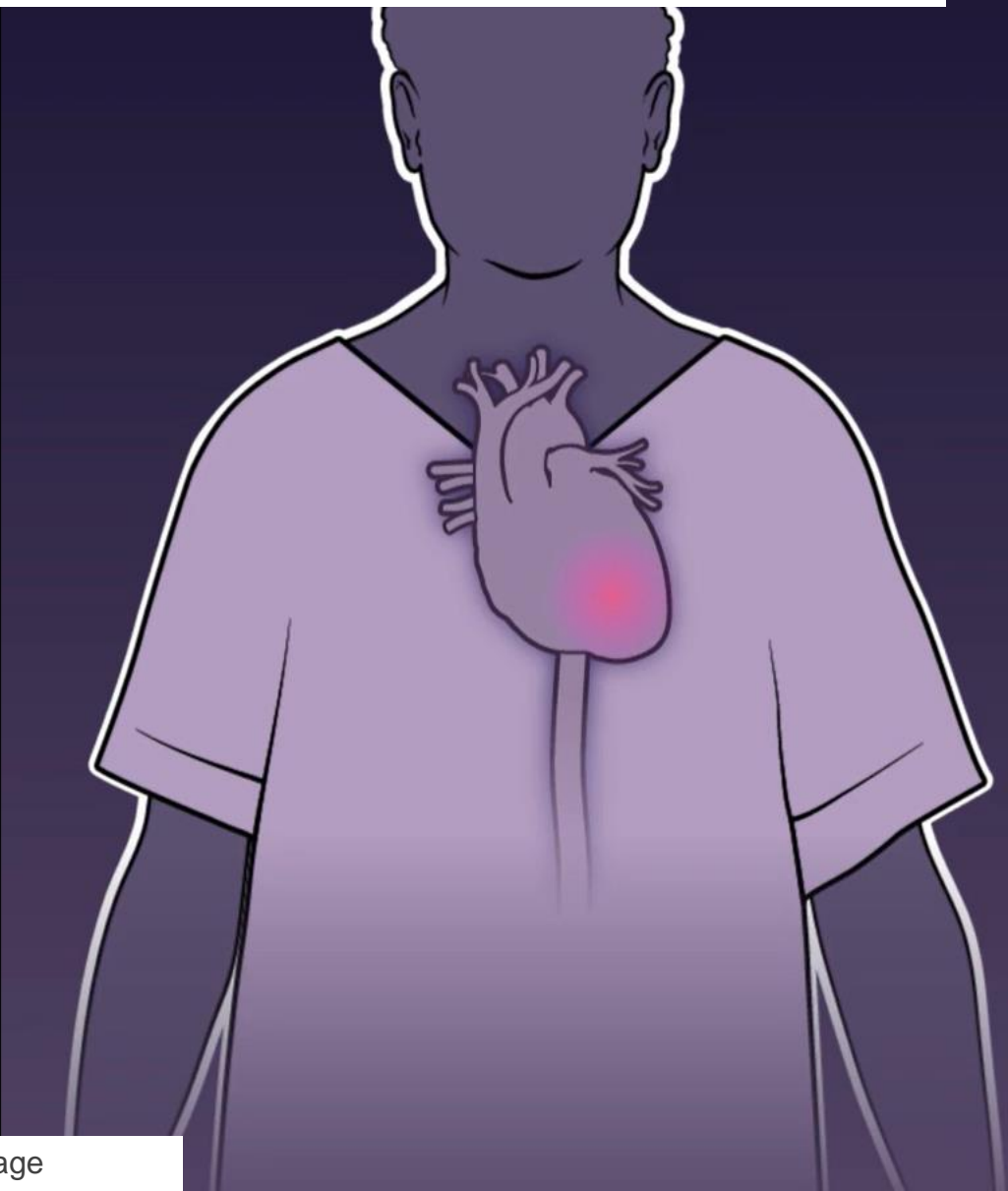
Severe LVSD



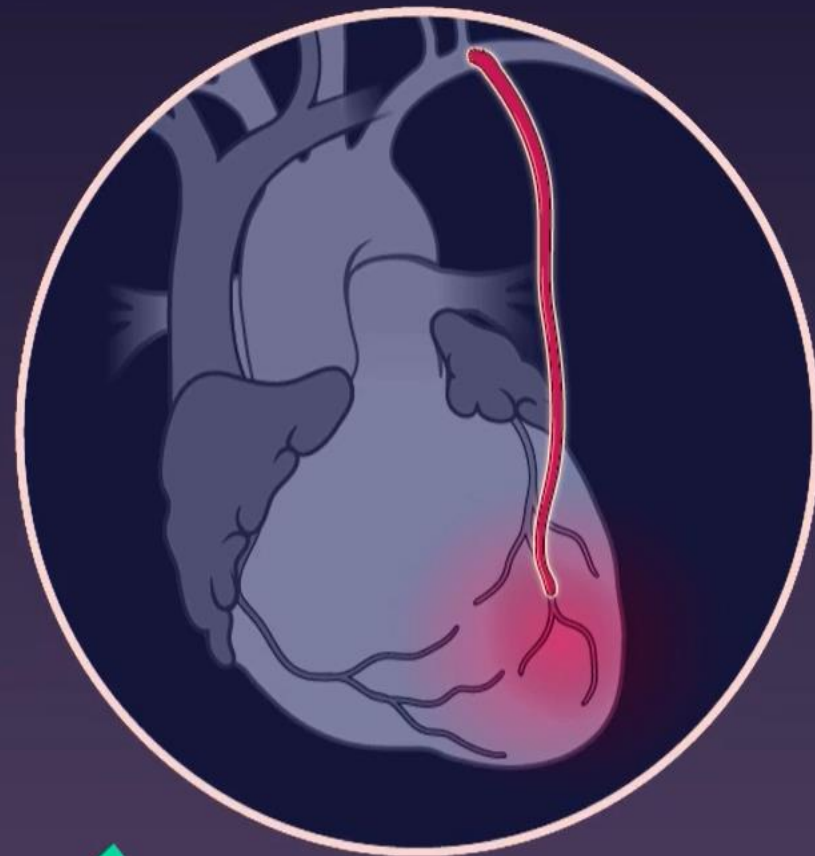
Coronary Artery Disease



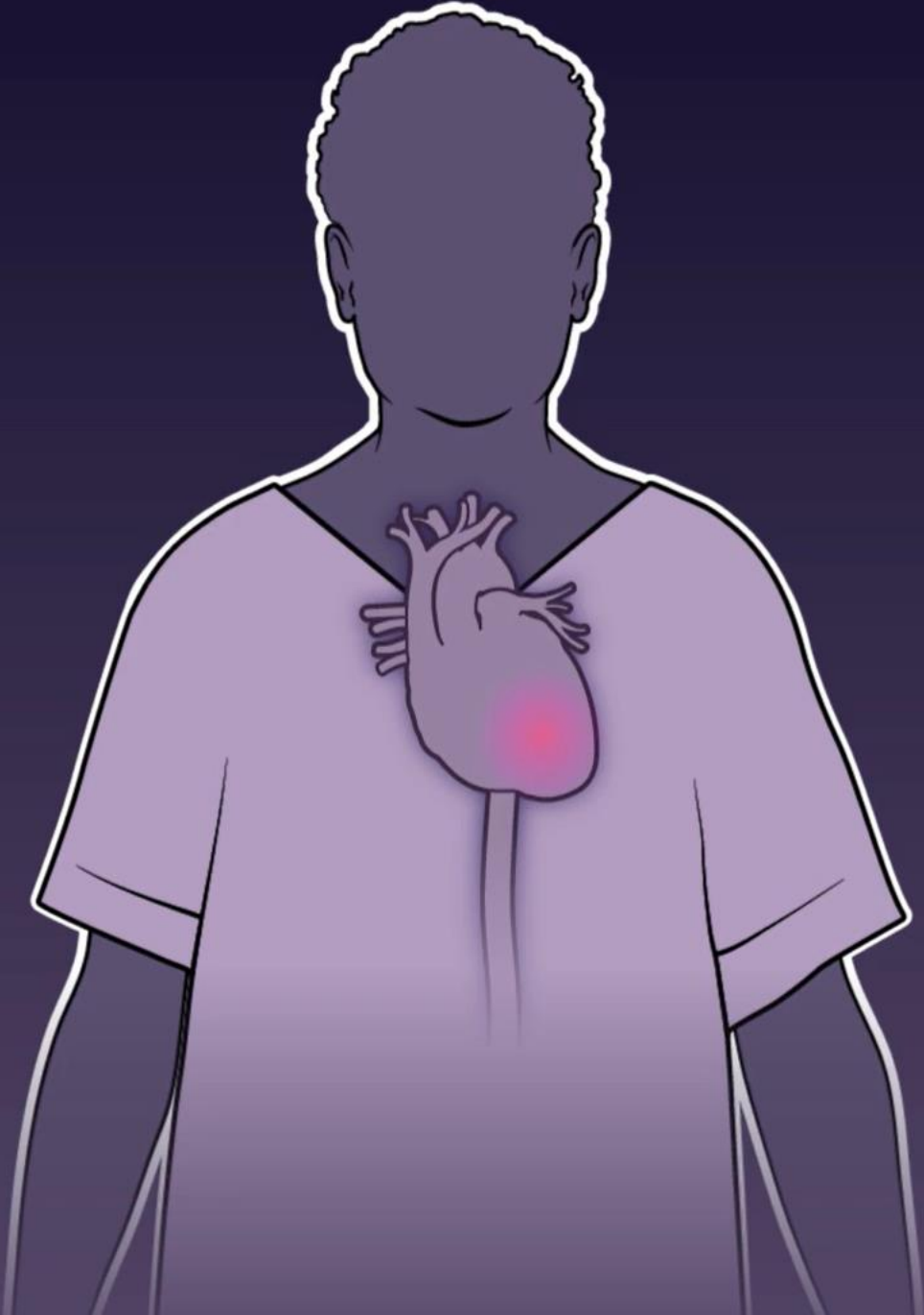
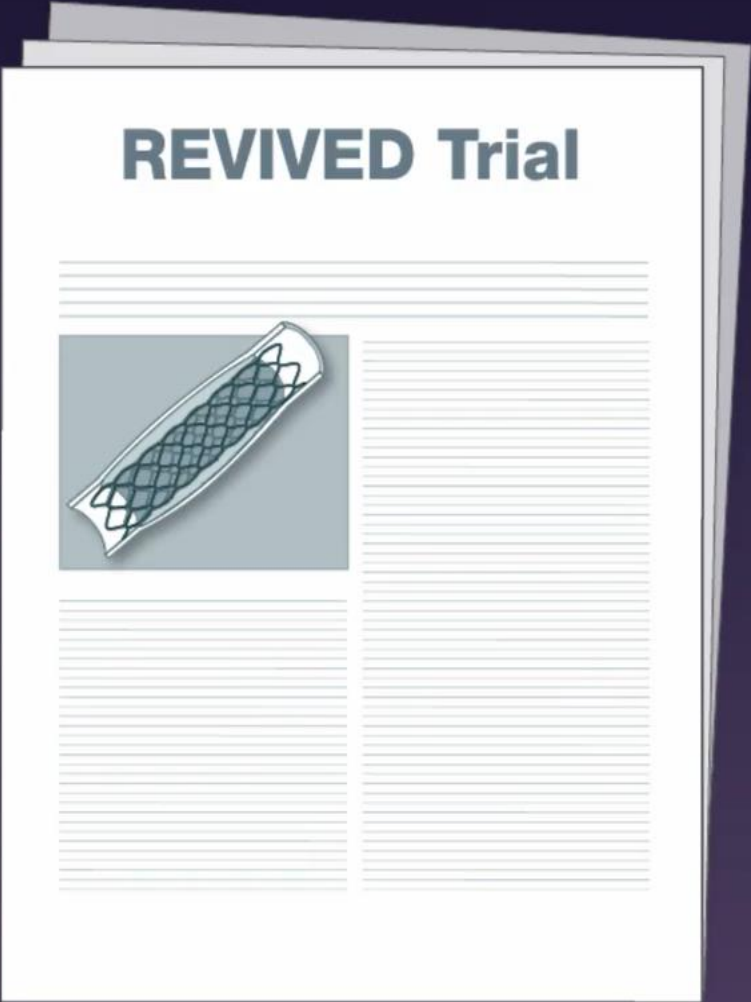
In the Surgical Treatment for Ischemic Heart Failure (STICH) trial, CABG group more likely to be alive after 10 years than those receiving medical therapy alone



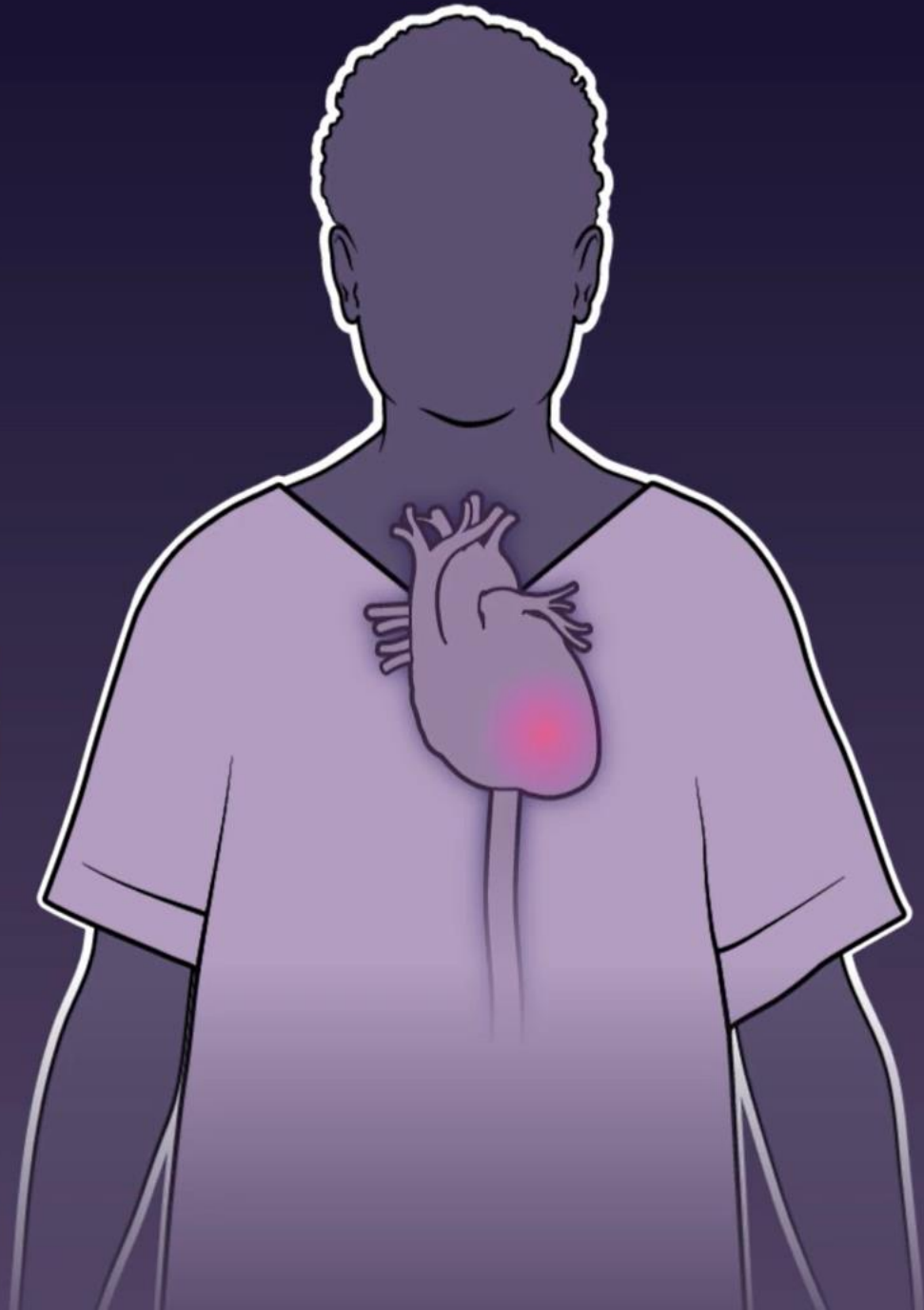
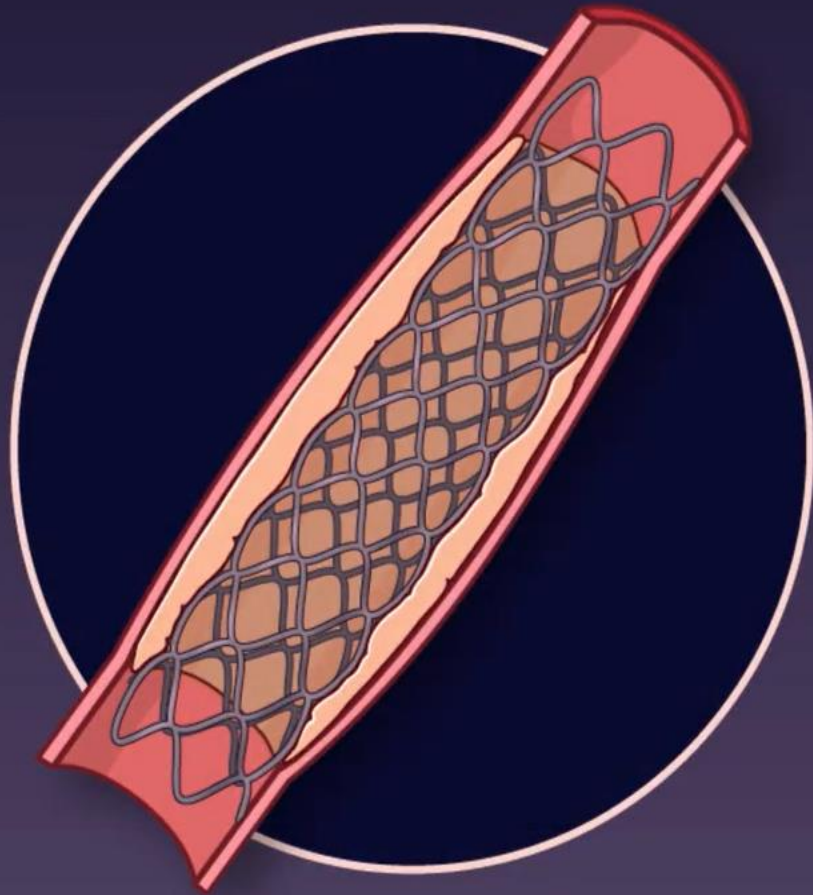
Coronary-Artery Bypass Grafting



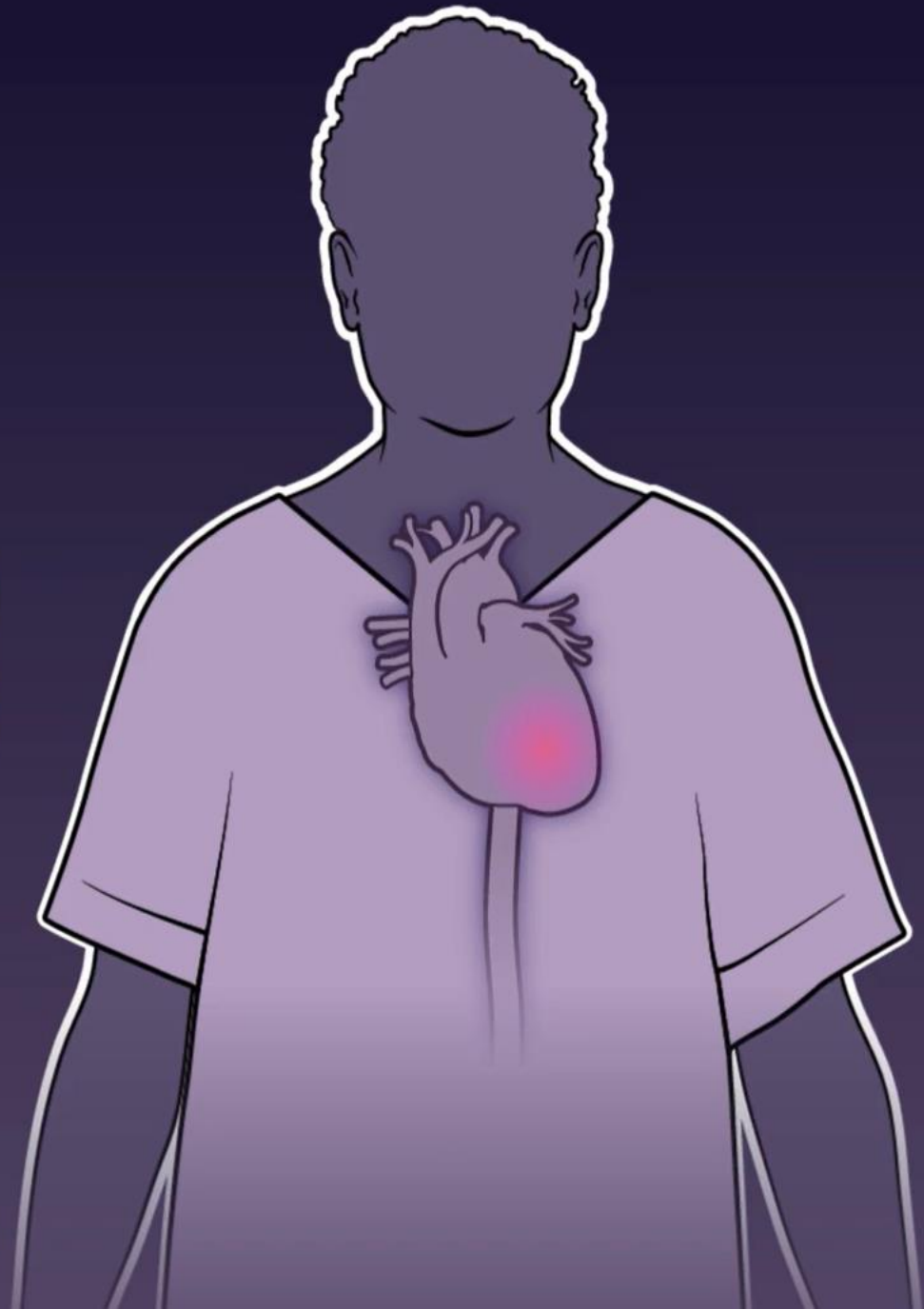
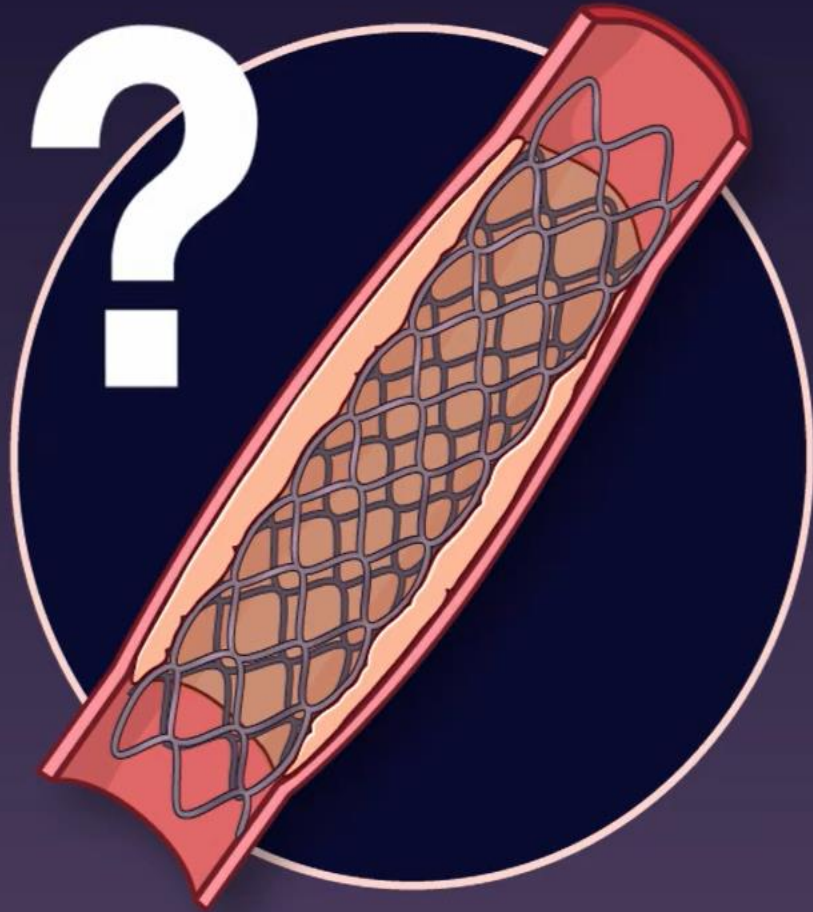
- ✓ Long-term survival benefit
- ✗ Substantial short-term risks



Percutaneous Coronary Intervention

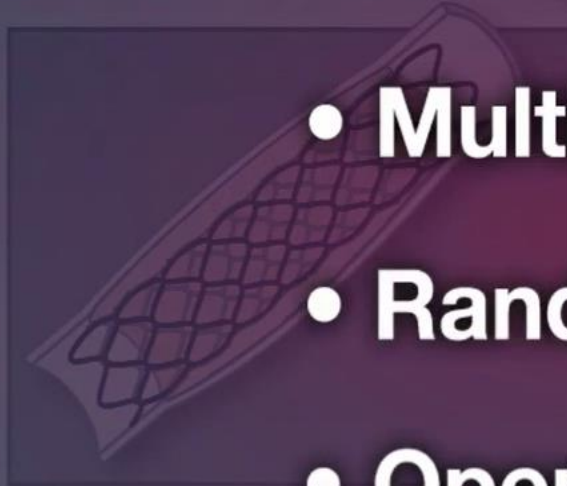


PCI



REVIVED Trial

- **Prospective**
- **Multicenter**
- **Randomized**
- **Open-label**



700 Patients

- **Left ventricular ejection fraction of $\leq 35\%$**
- **Extensive coronary artery disease**
- **Viability in ≥ 4 dysfunctional myocardial segments**

Exclusion

1. Patients were excluded if they had an acute myocardial infarction in the 4 weeks before randomization
2. Acute decompensated heart failure or sustained ventricular arrhythmias within 72 hours before randomization.

PCI + Optimal Medical Therapy

N=347

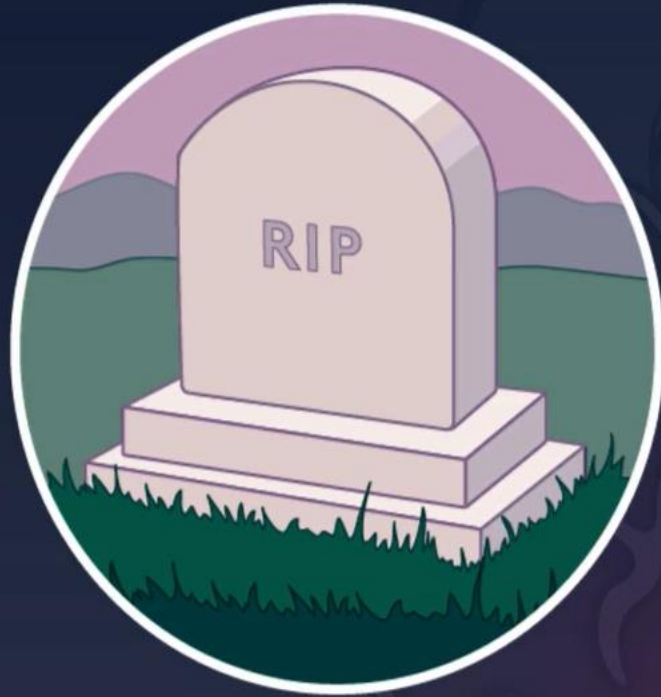


Optimal Medical Therapy

N=353



Primary Composite Outcome



**Death from
any cause**



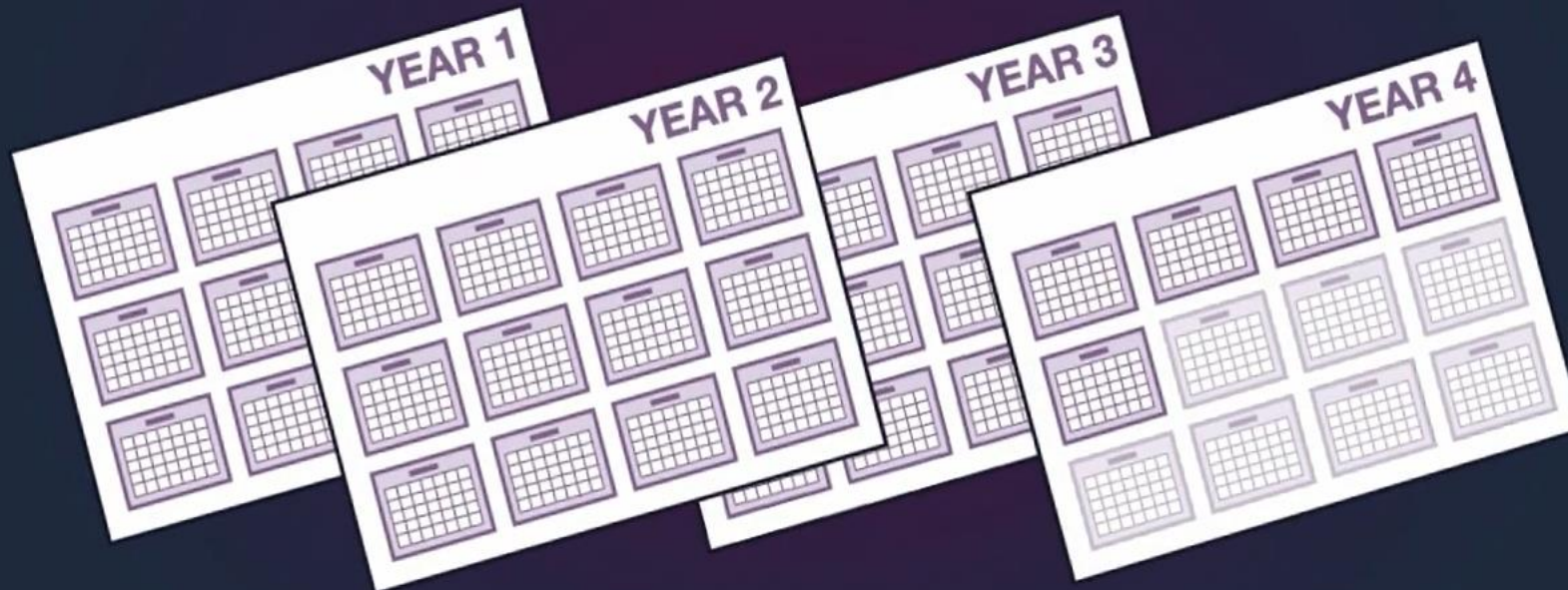
**Hospitalization
for heart failure**

Primary Composite Outcome

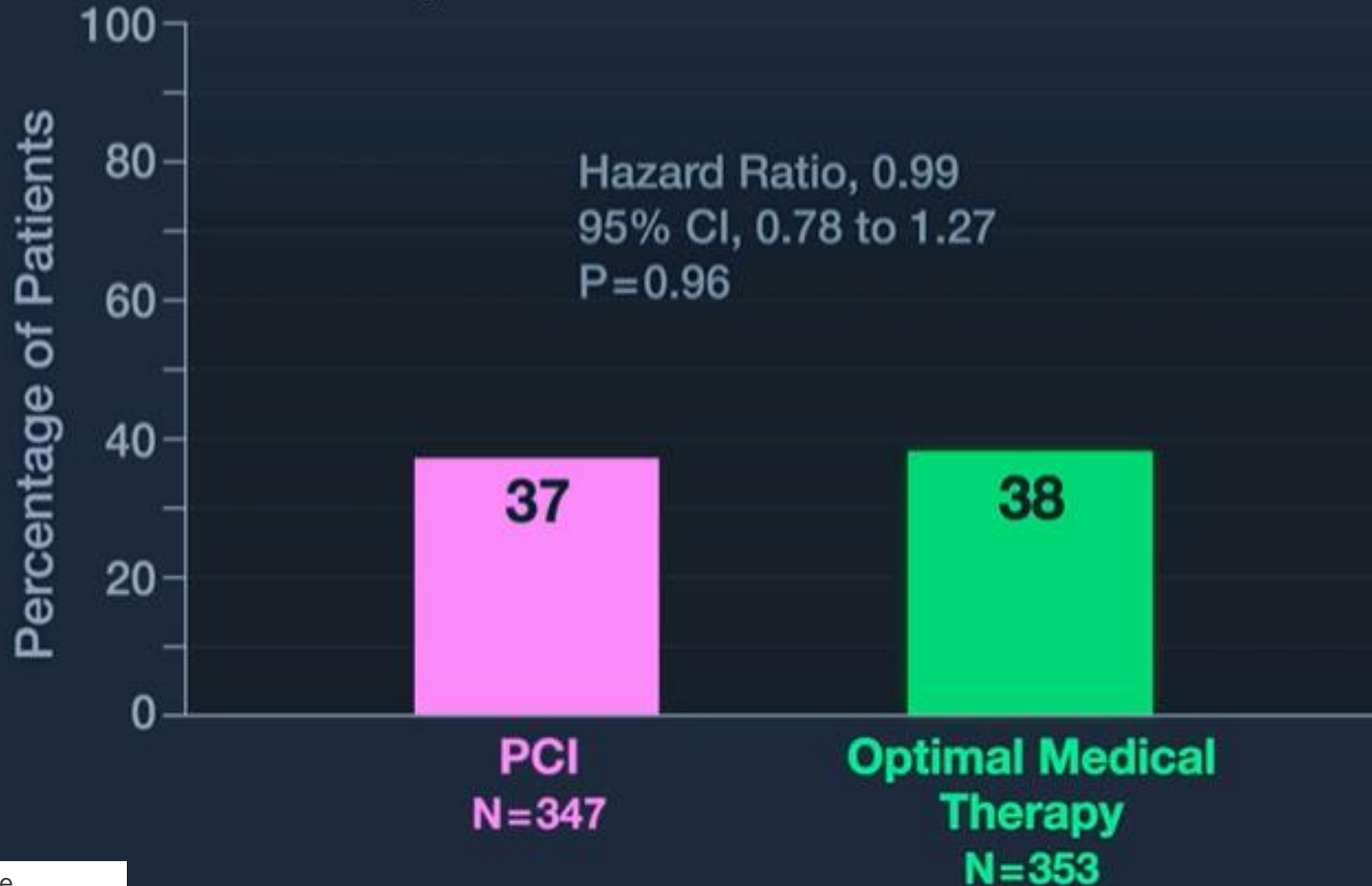


**≥ 24 Mo of
follow-up**

Median follow-up of 41 months

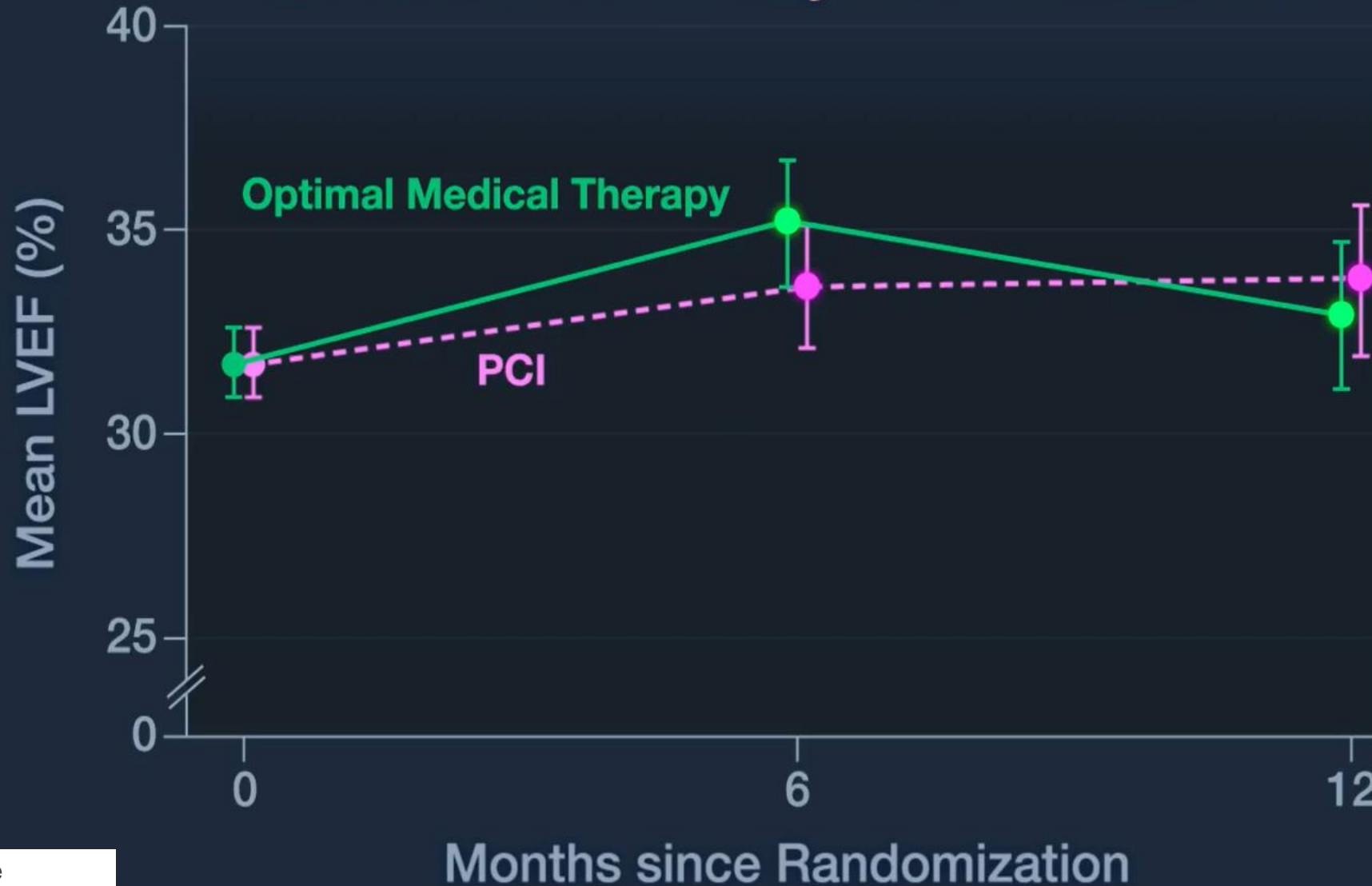


Death from Any Cause or Hospitalization for Heart Failure



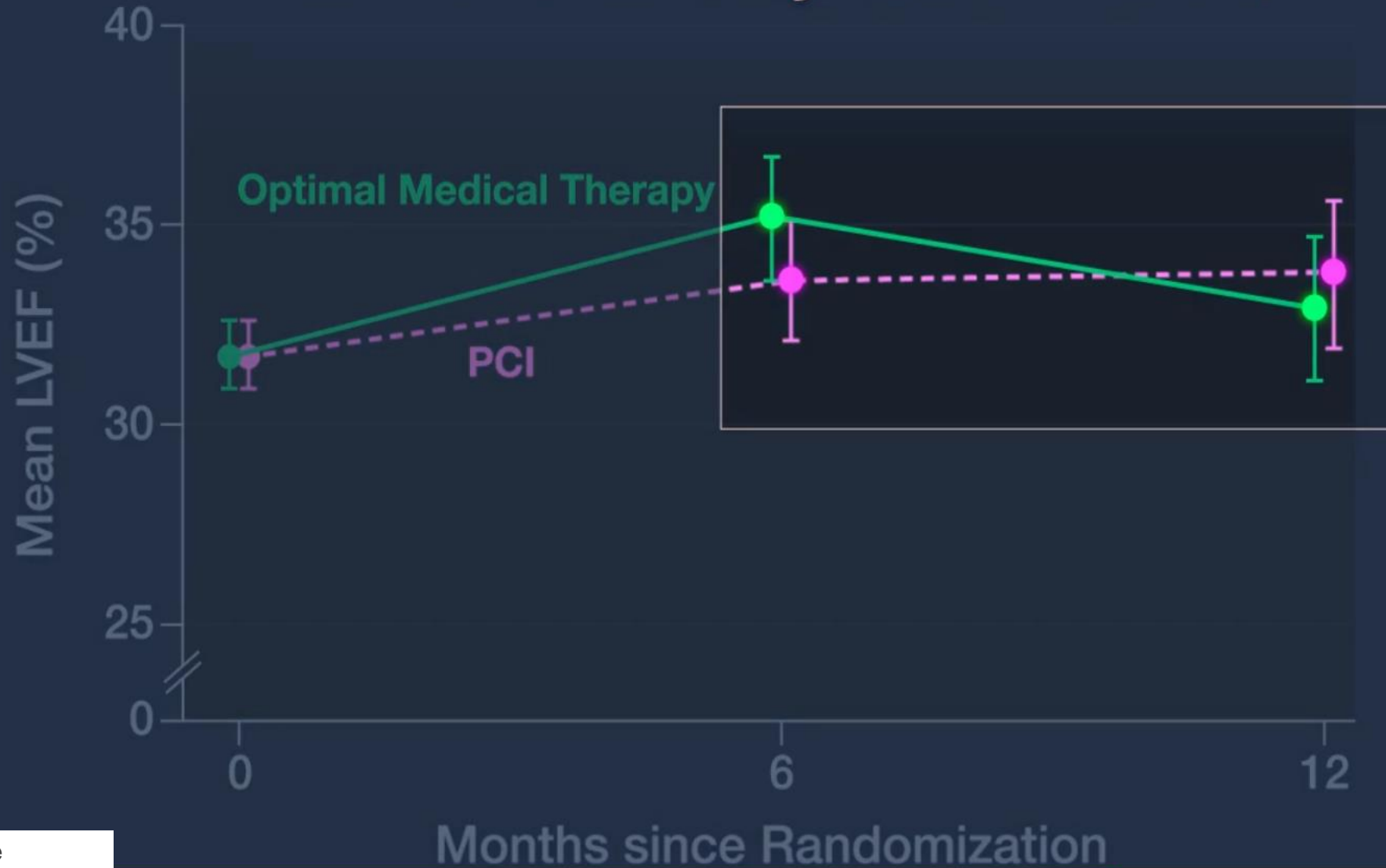
SECONDARY OUTCOMES

Echocardiographic Estimates of Left Ventricular Ejection Fraction



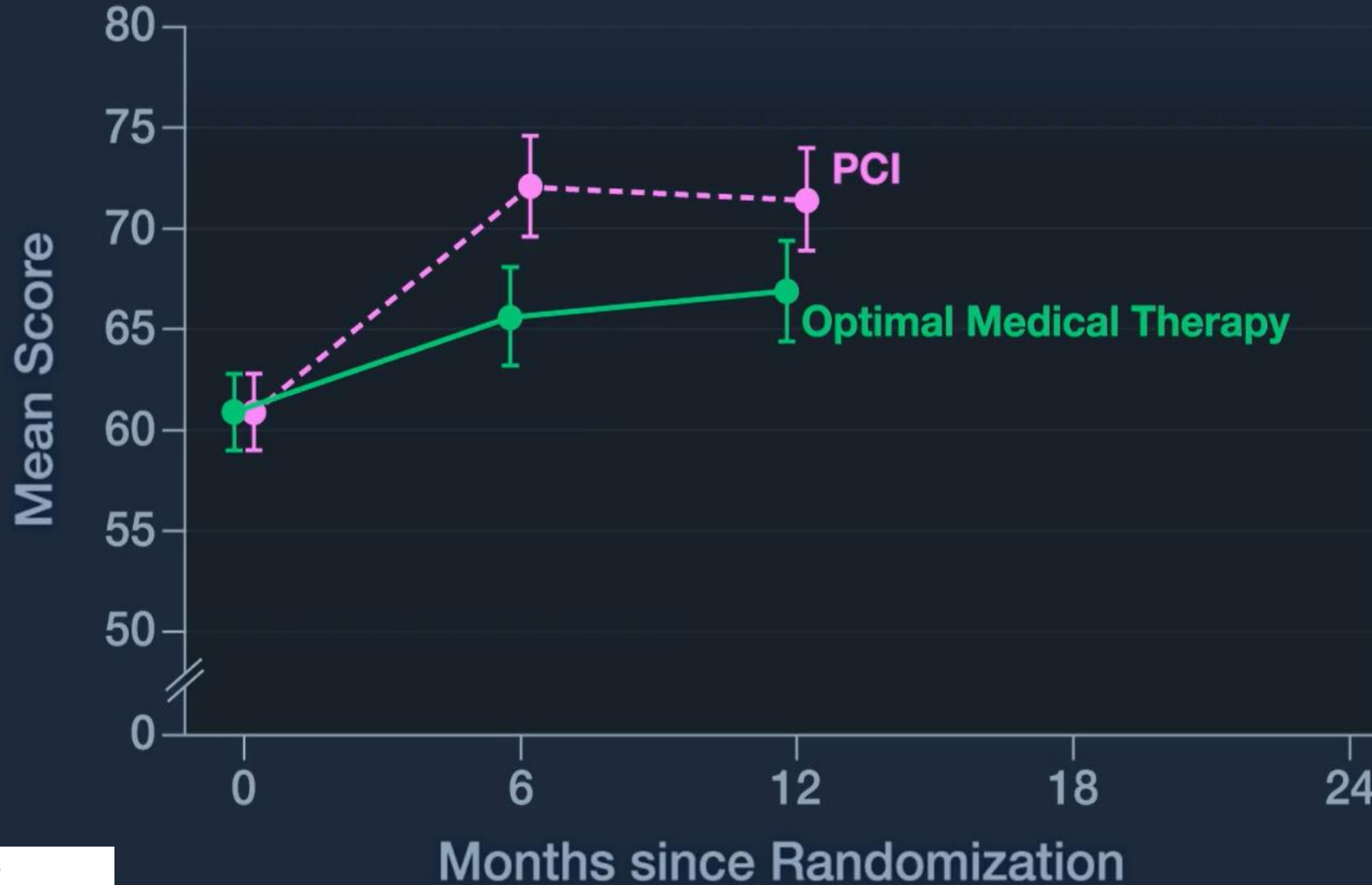
SECONDARY OUTCOMES

Echocardiographic Estimates of Left Ventricular Ejection Fraction



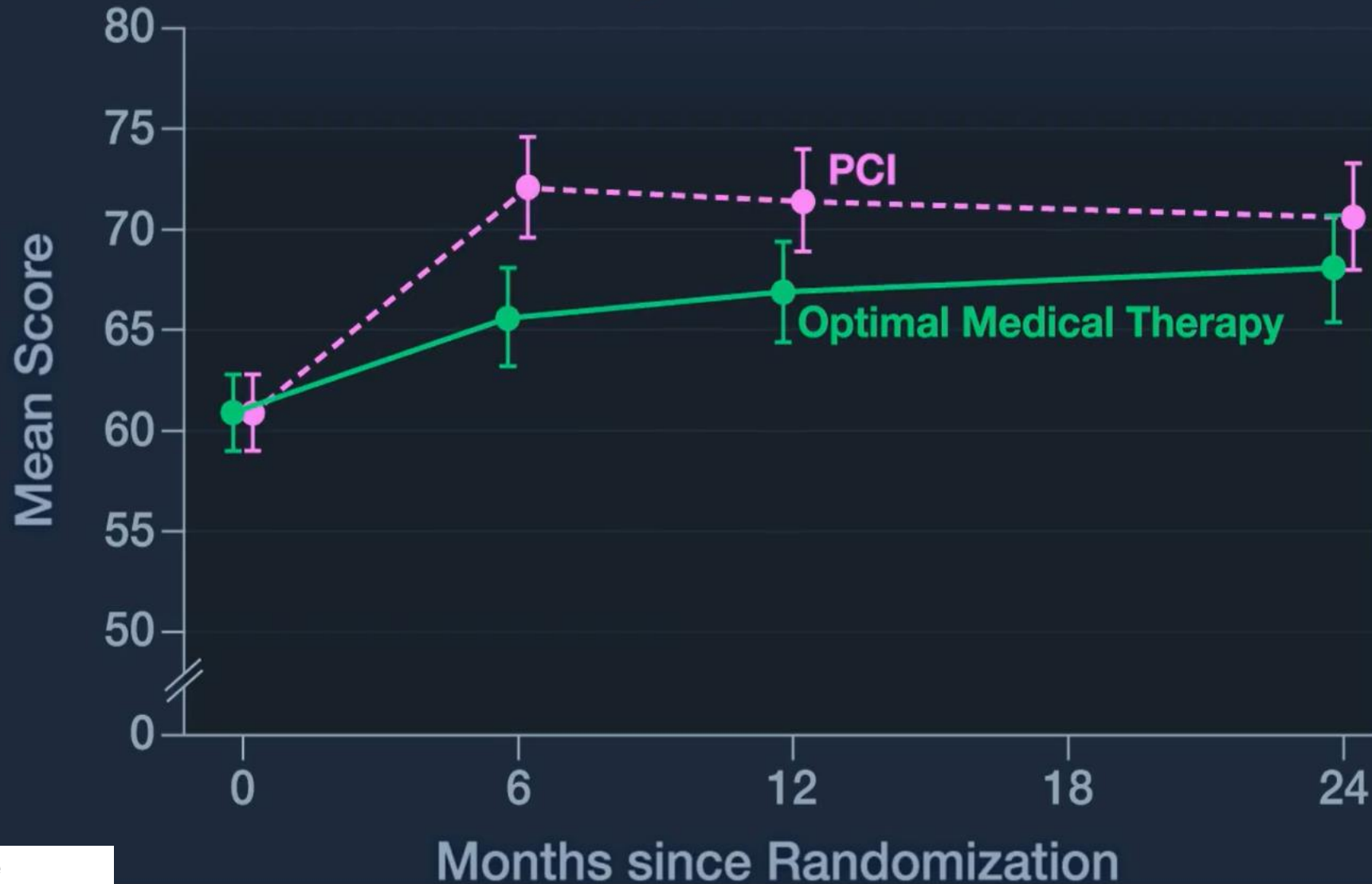
SECONDARY OUTCOMES

Kansas City Cardiomyopathy Questionnaire Quality-of-Life Score

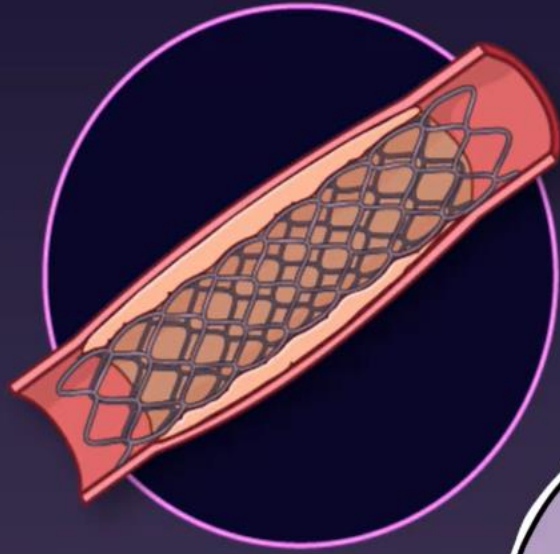


SECONDARY OUTCOMES

Kansas City Cardiomyopathy Questionnaire Quality-of-Life Score



PCI + Optimal Medical Therapy



Optimal Medical Therapy



No improved outcomes during ≥ 24 mo of follow-up



We have a question ...

It is still worth to consider offering PCI to patients with HFrEF ?



In daily practice, we usually consider to offer invasive or OMT

Based on general condition:

Age

LVEF

Risk of CABG

Benefit/Risk of PCI

Symptom of patient



And lets take a close look on the study



Characteristic	PCI (N = 347)	Optimal Medical Therapy (N = 353)
Age — yr	70.0±9.0	68.8±9.1
Male sex — no. (%)	302 (87)	312 (88)
Race — no. (%)†		
White	306 (88)	328 (93)
Asian	32 (9)	17 (5)
Black	3 (1)	3 (1)
Mixed, other, or not reported	6 (2)	5 (1)
Body-mass index‡	28.4±5.5	28.7±5.4
Hypertension — no./total no. (%)	184/347 (53)	207/352 (59)
Diabetes — no. (%)	136 (39)	153 (43)
Current or previous smoker — no. (%)	243 (70)	267 (76)
Previous myocardial infarction — no. (%)	175 (50)	197 (56)
Previous PCI — no. (%)	66 (19)	76 (22)
Previous CABG — no. (%)	12 (3)	22 (6)
NYHA functional class — no./total no. (%)§		
I or II	265/345 (77)	248/350 (71)
III or IV	80/345 (23)	102/350 (29)
CCS angina class — no./total no. (%)¶		
No angina	228/346 (66)	236/351 (67)
I or II	111/346 (32)	107/351 (30)
III	7/346 (2)	8/351 (2)
Left ventricular ejection fraction — %	27.0±6.6	27.0±6.9
Coronary artery disease characteristic		
Median BCIS jeopardy score (IQR)**	10 (8–12)	10 (8–12)
Left main coronary artery disease — no./total no. (%)	50/346 (14)	45/352 (13)
Three-vessel coronary artery disease — no./total no. (%)	133/346 (38)	148/352 (42)
Two-vessel coronary artery disease — no. (%)	178 (51)	166 (47)
Median NT-proBNP — pg/ml (IQR)	1376 (697–3426)	1461 (712–3365)

Demographic and Clinical Characteristics of the patients at baseline

IN summary,

Mean age = 70 y.o.

Male dominance

Caucasian

Not much heart failure symptoms

No angina symptoms

EF poor ~ 27%



- The Revived trial enrolled older patients (mean age, 70 years old)
 - with a greater burden of coronary disease and included patients with left main coronary artery disease
 - Usually asymptomatic

Would those patients be too young or too old?

- Majority of patients are
 - CCS class 0 (about 66% and 67%)
 - NYHF class I to II (77% and 71%)

Most are asymptomatic patients



And lets take a close look on the study

- IN summary,
- Medium age = 70 y.o.
- Male dominance
- Caucasian
- Not much heart failure symptoms
- No angina symptoms
- EF poor ~ 27%
- Median follow up 41 months



Median follow up time is 41 months

The 2nd question is ... is it long enough to make a conclusion?

Table 2. Primary and Secondary Outcomes.

Outcome	PCI (N = 347)	Optimal Medical Therapy (N = 353)	Treatment Effect (95% CI)*
Primary outcome			
Death from any cause or hospitalization for heart failure — no. (%)†	129 (37.2)	134 (38.0)	0.99 (0.78–1.27)
Secondary outcomes‡			
Components of the primary outcome			
Death from any cause	110 (31.7)	115 (32.6)	0.98 (0.75–1.27)
Hospitalization for heart failure§	51 (14.7)	54 (15.3)	0.97 (0.66–1.43)
Death from cardiovascular causes — no. (%)¶	76 (21.9)	88 (24.9)	0.88 (0.65–1.20)
Acute myocardial infarction — no. (%)	37 (10.7)	38 (10.8)	1.01 (0.64–1.60)
Periprocedural — no. (%)**	14 (37.8)	0	
Spontaneous — no. (%)**	18 (48.7)	33 (86.8)	
Sudden death — no. (%)***††	5 (13.5)	5 (13.2)	
Unplanned revascularization — no. (%)‡‡	10 (2.9)	37 (10.5)	0.27 (0.13–0.53)
PCI — no. (%)§§	9 (90.0)	29 (78.4)	
CABG — no. (%)§§	1 (10.0)	8 (21.6)	
Major bleeding — no. (%)			
At 1 yr	10/319 (3.1)	2/316 (0.6)	4.95 (1.09–22.43)
At 2 yr	10/292 (3.4)	7/290 (2.4)	1.42 (0.55–3.68)



Insight from STICH trial

Randomized Controlled Trial > N Engl J Med. 2016 Apr 21;374(16):1511-20.

doi: 10.1056/NEJMoa1602001. Epub 2016 Apr 3.

Coronary-Artery Bypass Surgery in Patients with Ischemic Cardiomyopathy

Eric J Velazquez¹, Kerry L Lee¹, Robert H Jones¹, Hussein R Al-Khalidi¹, James A Hill¹, Julio A Panza¹, Robert E Michler¹, Robert O Bonow¹, Torsten Doenst¹, Mark C Petrie¹, Jae K Oh¹, Lilin She¹, Vanessa L Moore¹, Patrice Desvigne-Nickens¹, George Sopko¹, Jean L Rouleau¹; STICHES Investigators

Collaborators, Affiliations + expand

PMID: 27040723 PMID: PMC4938005 DOI: 10.1056/NEJMoa1602001

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- Cohort
- N = 1212 EF <35%
- Ischemic cardiomyopathy
- Primary end-point: all cause mortality

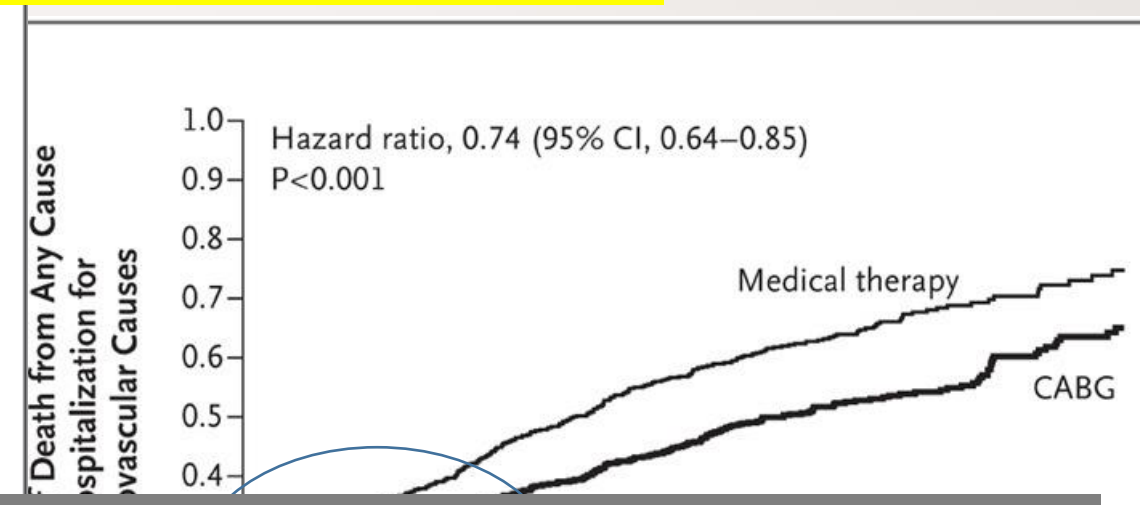
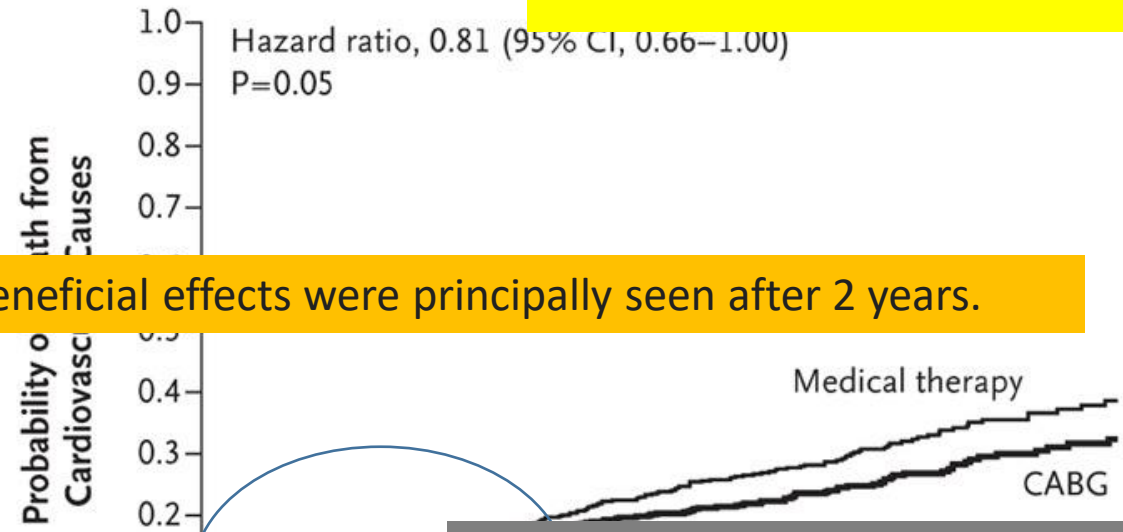
The rates of death from any cause, death from cardiovascular causes, and death from any cause or hospitalization for cardiovascular causes were significantly lower over 10 years among patients who underwent CABG in addition to receiving medical therapy than among those who received medical therapy alone



Insight from

However, a survival benefit emerged over time, with the patients who underwent revascularization with CABG more likely to be alive after 10 years than those receiving medical therapy alone

A



The beneficial effects were principally seen after 2 years.

In the Surgical Treatment for Ischemic Heart Failure (STICH) trial, the incidence of death at 5 years was similar in medical vs CABG treatment group ; a finding that was partly due to the early hazard of CABG among these patients

No. at Risk

Medical therapy	602	532
CABG	610	532

	486	459	340	174	91
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No. at Risk

medical therapy	602	387	315	260	158	65	28
CABG	610	431	375	334	221	100	43





Insight from ISCHEMIA trial

Vol. 147, No. 1 > Survival After Invasive or Conservative Management of Stab...

Survival After Invasive or Conservative Management of Stable Coronary Disease



Judith S. Hochman , Rebecca Anthopolos, Harmony R. Reynolds, Sripal Bangalore, Yifan Xu, Sean M. O'Brien, Stavroula Mavromichalis, Michelle Chang, Aira Contreras, Yves Rosenberg, ... [See all authors](#) 

and on behalf of the ISCHEMIA-EXTEND Research Group

Originally published 6 Nov 2022 | <https://doi.org/10.1161/CIRCULATION>

This article is commented on by t

AIM: Compared

an initial invasive vs an initial conservative management strategy for patients with CAD and moderate or severe ischemia.

Conclusion:

No major difference in most outcomes during a median of **3.2 years**.

There was no difference in all-cause mortality with an initial invasive strategy compared with an initial conservative strategy, but there was **lower risk of cardiovascular mortality** and higher risk of noncardiovascular mortality with an initial invasive strategy during a **median follow-up of 5.7 years.**



Insight from STICH Trial and ISCHEMIA Trial

- We may need to take **longer time** to draw conclusion from the longer term of beneficial effect of PCI ? Need to observe >10 years
- **Complete revascularization** seems to be the game player for survival



Complete revascularization is the key game player

- **Incomplete revascularization** by PCI has historically been a confounder in comparisons between PCI , medical treatment and CABG among patients with stable coronary disease.

Functional completeness of revascularization was not assessed

- Measured by **coronary anatomical index**

It is difficult to know the exact % of functional recovery by revascularization in the study



Insight from FAME 2

FAME2 is Functional study

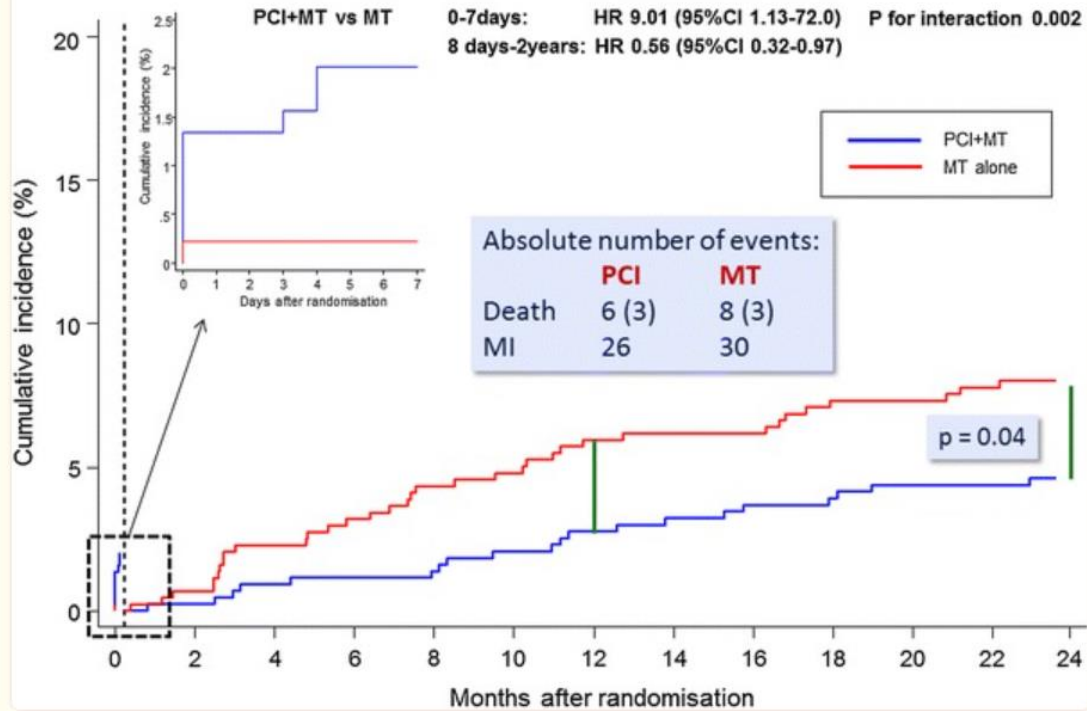
REVIVED based on Anatomical study



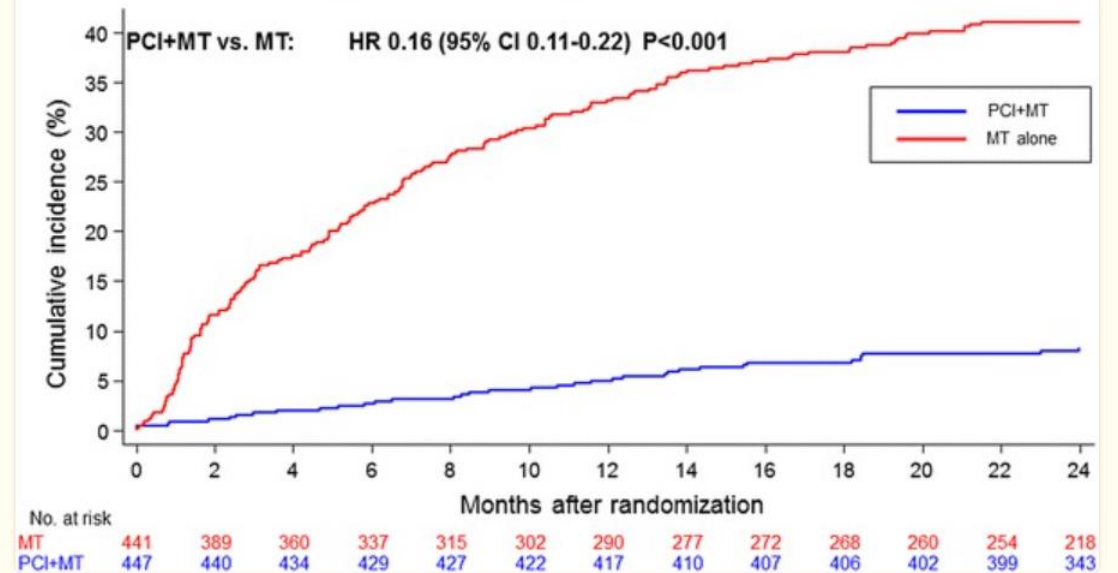
FAME 2 Trial

- N = 888
- FFR-PCI + OMT vs OMT in stable CAD

FAME 2 (at 2 years) Landmark Analysis for Death or Myoc. Infarction



FAME 2 Urgent AND Non-Urgent Revascularizations





3rd Question: severity of lesion in REVIVED trial

Coronary artery disease characteristic

Median BCIS jeopardy score (IQR)**	10 (8–12)	10 (8–12)
Left main coronary artery disease — no./total no. (%)	50/346 (14)	45/352 (13)
Three vessel coronary artery disease — no./total no. (%)	122/346 (38)	148/352 (42)

Despite considerable ventricular dysfunction and Median BCIS score 10, ~ 50% patients had only two-vessel disease, and a median of two lesions and vessels were treated per patient.

This relatively modest degree of coronary artery disease seems unusual for patients selected to undergo revascularization with the hope of restoring or normalizing ventricular function



The 4th question is

- Left ventricular ejection fraction was only 27% in study
 - ?Any other valvular heart disease
 - E.g. functional MR
 - Any Scar in the myocardial tissue

For every patient with impaired EF and CAD, we should ask if the extent and degree of cardiomyopathy are explained by the observed coronary artery disease

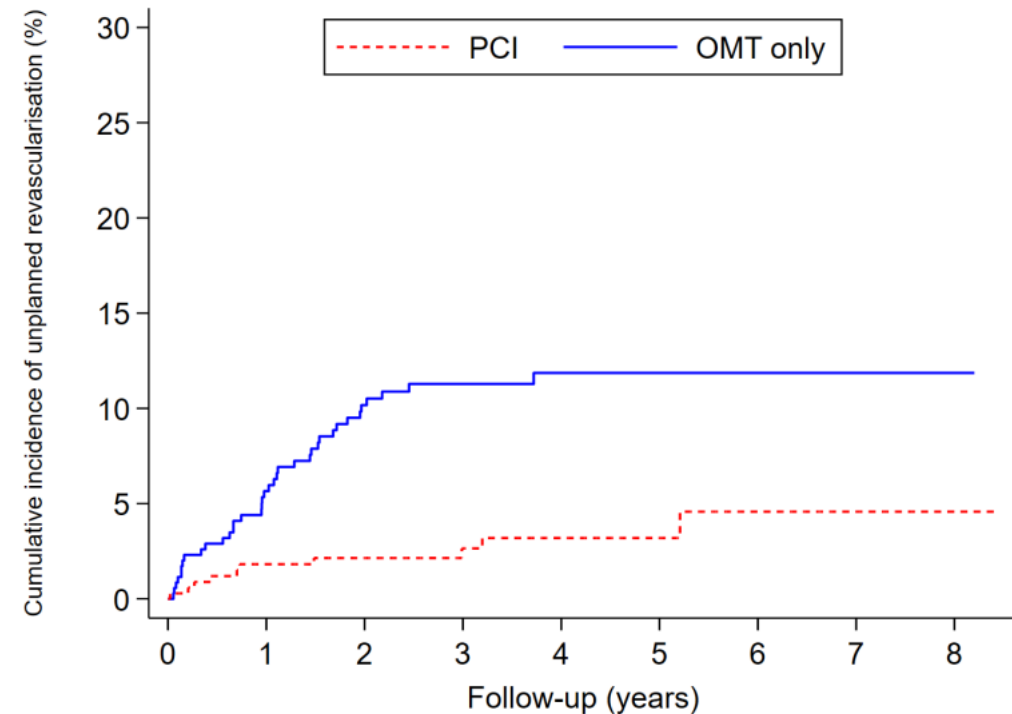
It would be difficult to know if there is any other non-ischemic component causing poor EF by the design of REVIVED Trial



With time, more patient in OMT arm received revascularization

A narrowed survival difference between the treatment groups over time is expected, since subsequent revascularization was performed to a greater extent among the patients who were initially randomly assigned to receive optimal medical therapy alone

Figure S7: Kaplan-Meier Plot for Unplanned Revascularization



Number at risk

PCI	347	311	280	194	139	84	35	14	3
OMT only	353	300	264	184	143	84	31	10	2

OMT – optimal medical therapy, PCI – percutaneous coronary intervention

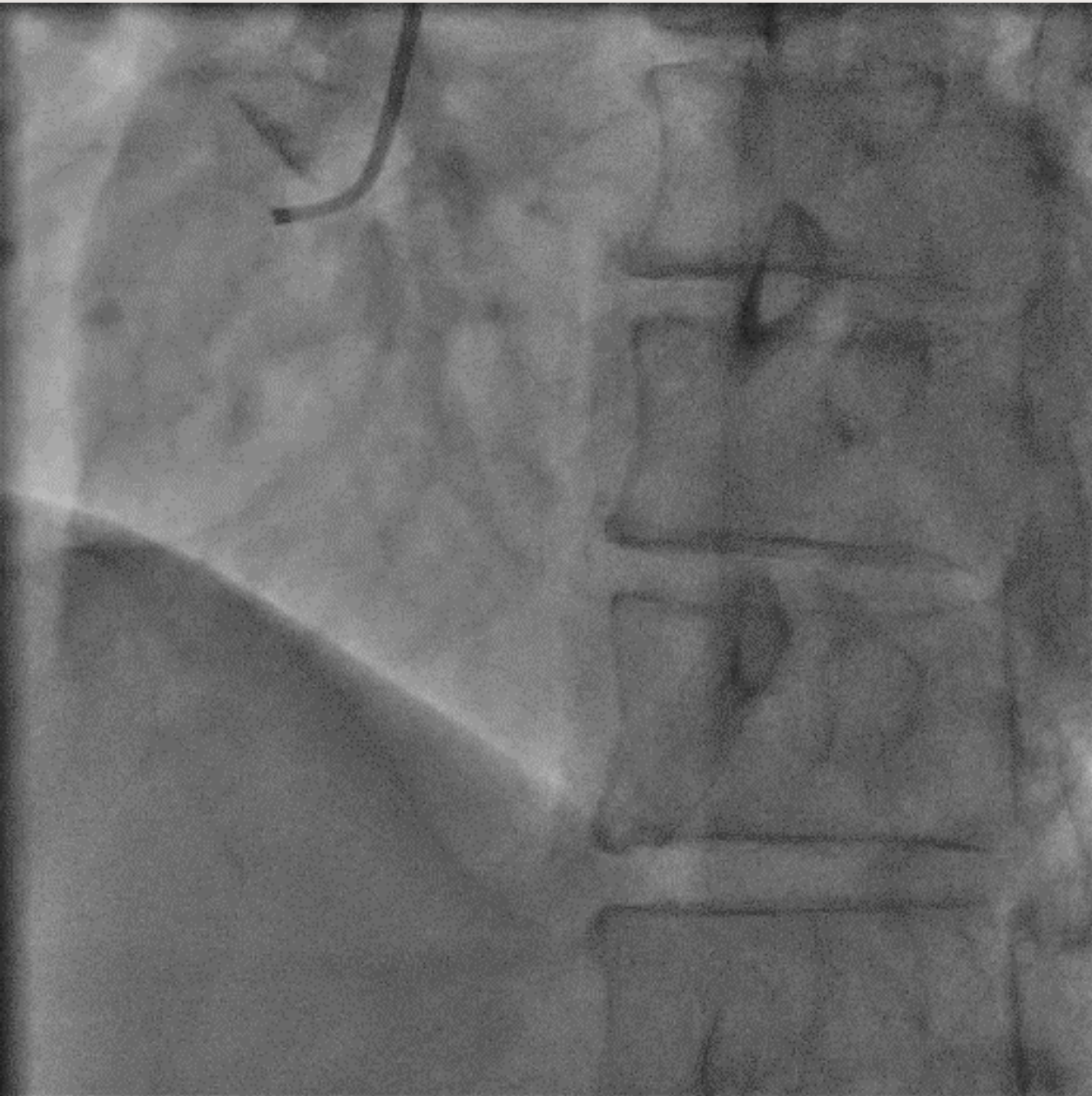


A real life example

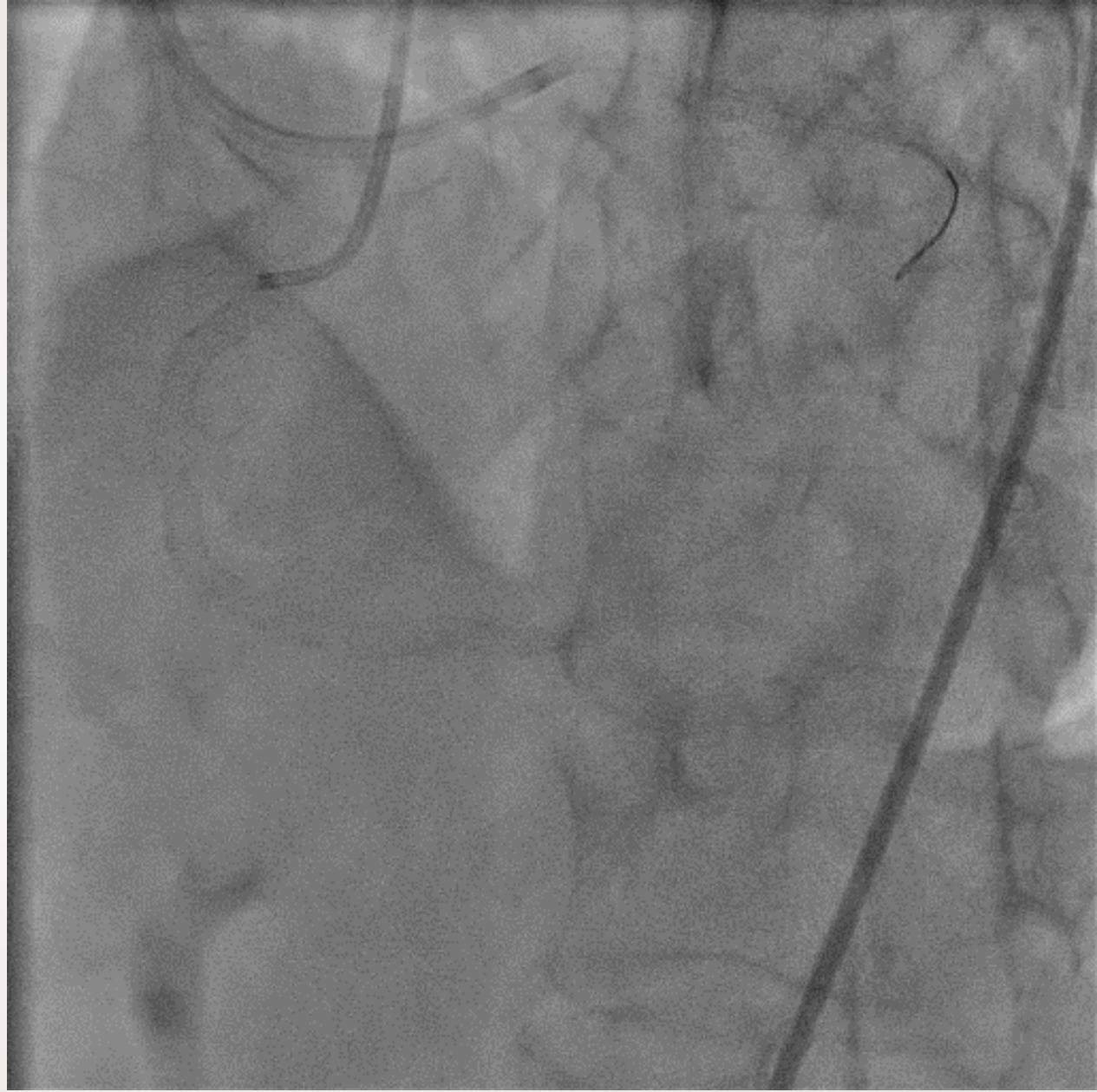
- 67M years old
- Recently admitted to public regional hospital because of ACS with heart failure
- Coro : LM + TVD (RCA CTO, mid LAD CTO, pLCx 80-90%)
- Echo done in public regional hospital : 30-35%
- MRI heart : LVEF 25% ; Extensive LGE with non-viable tissue 75-100% at the sept mid –cavity , lateral free wall about 50% viable



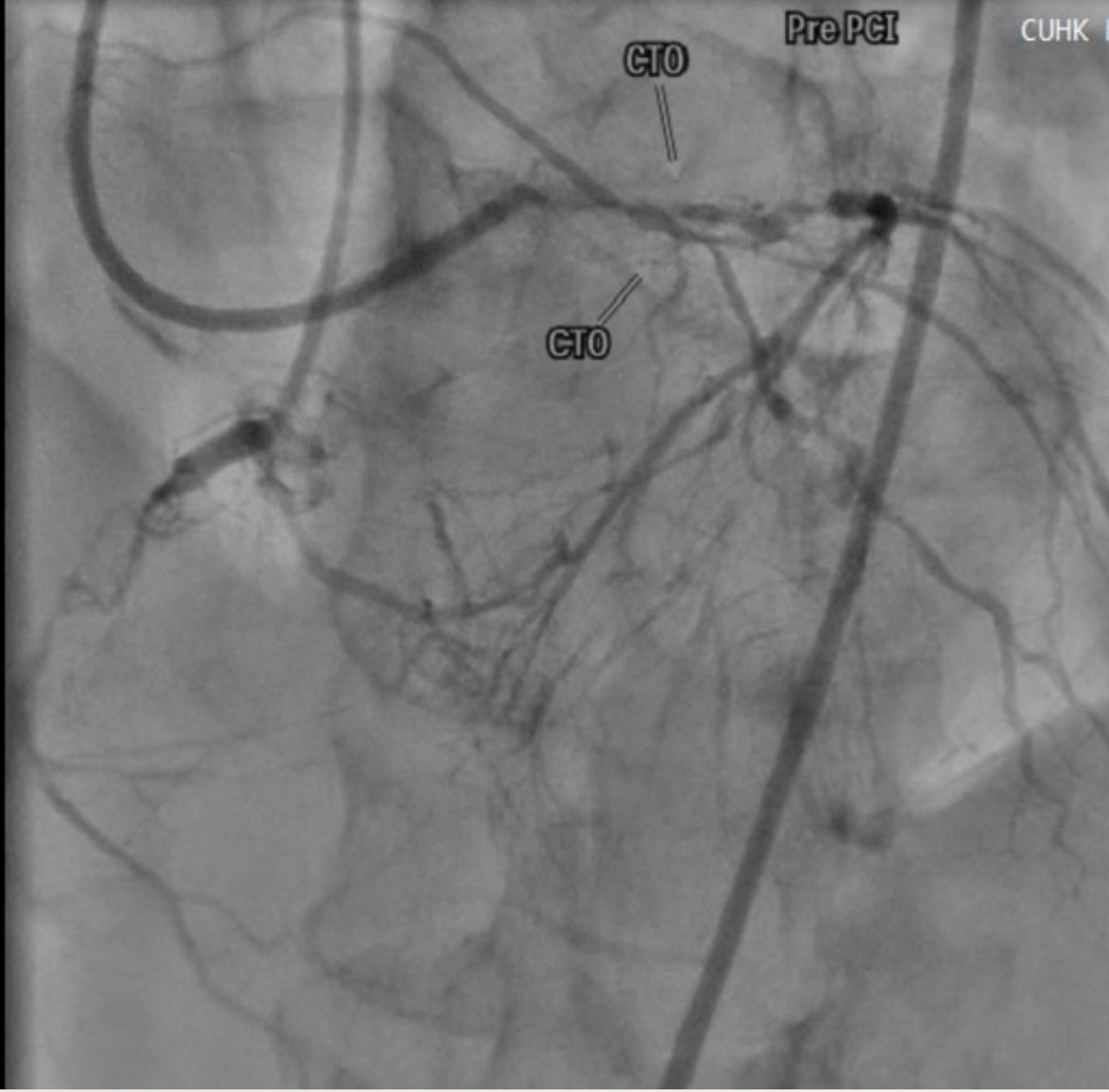
- After discharge, attended to our hospital because of persistently impairment of exercise capacity despite on OMT
- PCI was done to RCA CTO + LM bifurcation + pLAD + Lcx



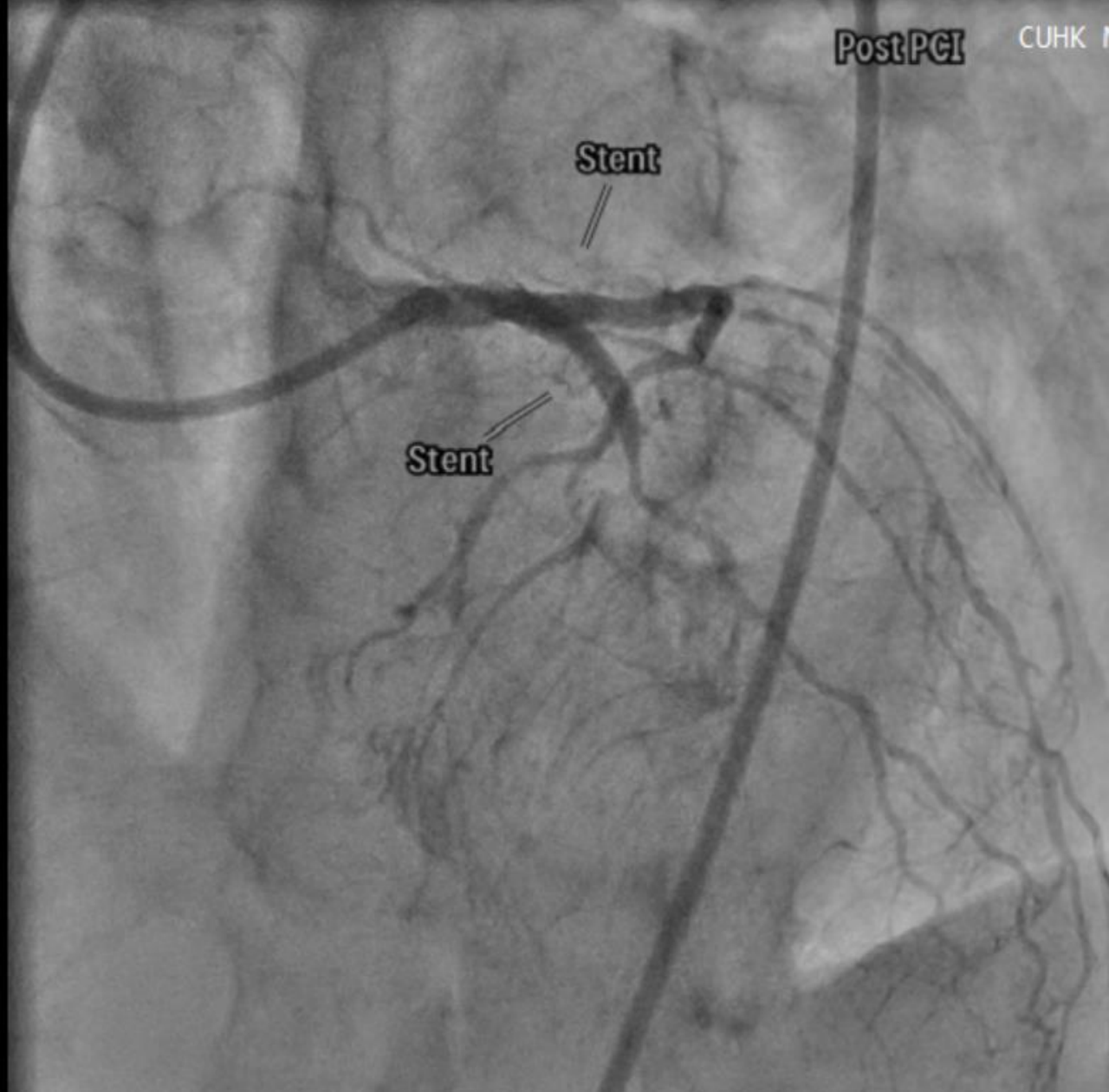
Baseline



Post-PCI



Baseline



Post-PCI



A real life example ...

EF improved to 50%





Therefore, in this real life example ...

We could produce “REVIVED” effect if we chose the right patients to receive percutaneous revascularization



When there is doubt about how to offer the best treatment to patient...

I was taught when I was a first year internal medicine trainee...

You could imagine the patient is your grandmother, then you would know how to manage better



If we want to manage our patient ...

- Study the current guideline and study ---- Evidence based treatment
- Discuss with colleagues ---- HEART TEAM APPROACH
- Discuss with family
 - based on consideration of co-morbidity, life expectancy, expected treatment outcome, risk of procedure, complication rate ...
 - Individualized approach with open discussion and joint decision with patient/family



In conclusion

- Individualized treatment plan, heart team discussion, open discussion with patients are the corner stone of strategy to offer the best treatment to our patients
- Based on REVIVED Trial , STICH Trial , Ischemia Trial, FAME2 ...
Coronary intervention in addition of OMT is still an important strategy of management for patient with stable effort angina
- We would need longer time to observe the beneficial effect of PCI in REVIVED Trial

Revascularization in HFrEF: Revived or Dead?



Choose the right patients to receive the right treatment

We could “Revive” the heart

Thank you







FAME 2

N = 888

FFR-PCI + OMT vs OMT in stable CAD

Randomized Controlled Trial > N Engl J Med. 2018 Jul 19;379(3):250-259.

doi: 10.1056/NEJMoa1803538. Epub 2018 May 22.

Five-Year Outcomes with PCI Guided by Fractional Flow Reserve

Panagiotis Xaplanteris¹, Stephane Fournier¹, Nico H J Pijls¹, William F Fearon¹, Emanuele Barbato¹, Pim A L Tonino¹, Thomas Engstrøm¹, Stefan Käåb¹, Jan-Henk Dambrink¹, Gilles Rioufol¹, Gabor G Toth¹, Zsolt Piroth¹, Nils Witt¹, Ole Frøbert¹, Petr Kala¹, Axel Linke¹, Nicola Jagic¹, Martin Mates¹, Kreton Mavromatis¹, Habib Samady¹, Anand Irimpen¹, Keith Oldroyd¹, Gianluca Campo¹, Martina Rothenbühler¹, Peter Jüni¹, Bernard De Bruyne¹; FAME 2 Investigators

Collaborators, Affiliations + expand

PMID: 29785878 DOI: 10.1056/NEJMoa1803538

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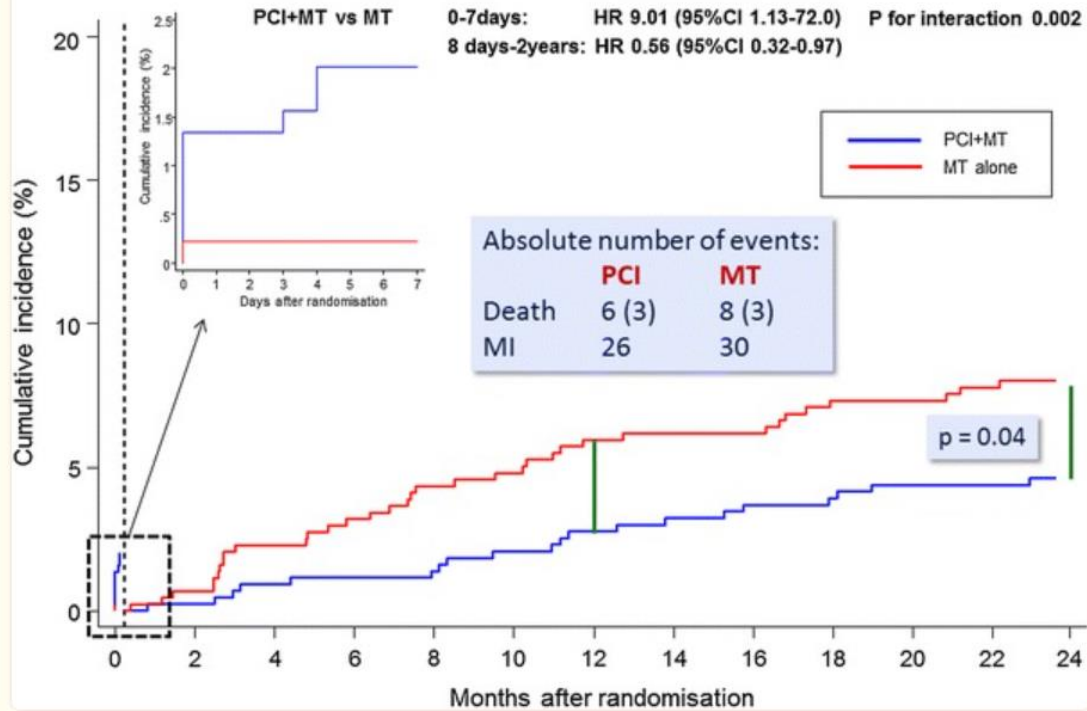
Conclusions: In patients with stable coronary artery disease, an initial FFR-guided PCI strategy was associated with a significantly lower rate of the primary composite end point of death, myocardial infarction, or urgent revascularization at 5 years than medical therapy alone. Patients without hemodynamically significant stenoses had a favorable long-term outcome with medical therapy alone.



FAME 2 Trial

- N = 888
- FFR-PCI + OMT vs OMT in stable CAD

FAME 2 (at 2 years) Landmark Analysis for Death or Myoc. Infarction



FAME 2 Urgent AND Non-Urgent Revascularizations

