TCTAP 2023

GREAT DEBATE ON MVD

Surgery is Still Standard

David P Taggart MD PhD FRCS FESC
Professor of Cardiovascular Surgery, University of Oxford

Conflicts of Interest:

(i) Clinical: Cardiac Surgeon (I will try to present All Relevant data in a Balanced way)
(ii) Commercial: Consultant to Medistim, Medtronic, VGS, Farady

CABG vs PCI: 3 Cautions and Key 'Rules' For Interpreting Trials/Data

(i) Are TRIAL patients typical of 'real life' clinical practice (CAD severity) ?

✖ No: usually **HIGHLY SELECTED** patients with less severe CAD (Taggart 2006)

✔ **Underestimates the benefit of CABG in routine practice where MOST patients have more severe CAD than in trial patients**

(ii) Duration of follow-up ?

✖ Must be a **MINIMUM** of 5 years (ideally 10 years as in ART, SYNTAXES, STITCH)

✔ **Increasing length of follow-up = increasing and accelerating benefit of CABG**

(iii) Use of Optimal Medical Therapy (OMT)/Guideline Directed Medical Therapy (GDMT) ?

✖ Frequently **SIGNIFICANTLY INFERIOR** in CABG vs PCI patients

✔ **CABG + GDMT: then even greater benefits over PCI**

General Tip: Examine actual data/results BEFORE READING text

✖ Why ?: text often has pro-PCI bias which can even CONTRADICT the ACTUAL DATA (EXCEL RCT !)

✔ **Data consistently shows superiority of CABG for Survival, MI, Revasc**

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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,

ISCHEMIA
NEJM 2000

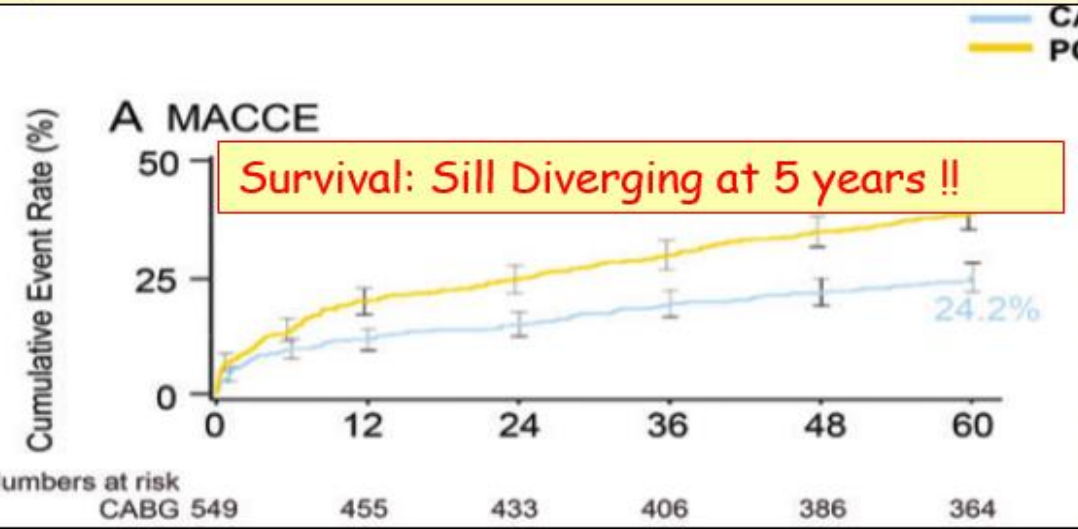
- RCT of Initial Conservative vs Invasive Management OF SIHD (Not OMT vs Revasc) BUT
- >50 authors but a single cardiac surgeon !
- 8518 patients enrolled at 320 sites over 5.5 years ie < 5 patients per site each year ! (after exclusion < 3/year)
- Trial patients were mainly low burden CAD with mean EF of 60% [BUT 2/3 'real-life' CABG patients excluded (LM, ACS, reduced EF, heart failure, symptoms despite OMT)]
- Follow-up too short (Median) 3.2 years
- Large number of X-overs ignored: 20% of Conservative group had revasc and 20% of Invasive group no revasc
- Revasc:75% PCI vs 25% CABG (despite 42% with DM); Lumped Together BUT NOT EQUIVALENT !
- PCI repeatedly shown to have no benefit over OMT (COURAGE, BARI 2-D)
- CABG consistently shown to be superior to PCI and especially over long-term (SYNTAX, FREEDOM,FAME

(i) Construct of Trial Flawed (1 surgeon) and Title highly misleading as it was a very highly selected population
(ii) Results used to downgrade CABG in Guidelines and (Disaster for PATIENTS with severe anatomical CAD)

SYNTAX RCT (5 Years): 3 Vessel Disease [EHJ 2013]

	PCI	CABG	
nos	546	549	
Death	14.6	9.2 (-5.4%)	.006
Cardiac Death	9.2	4.0 (-5.2%)	.001
MI	10.6	3.3 (-7.3%)	<.001
CVA	3.0	3.4 (+0.6%)	.66
D+C+M	22	14 (-8%)	<.001
Revasc	25.4	12.6 (-12.8%)	<.001

(i) Consistent with PM registry data > 10 years
(ii) Similar rate of stroke in PCI/CABG



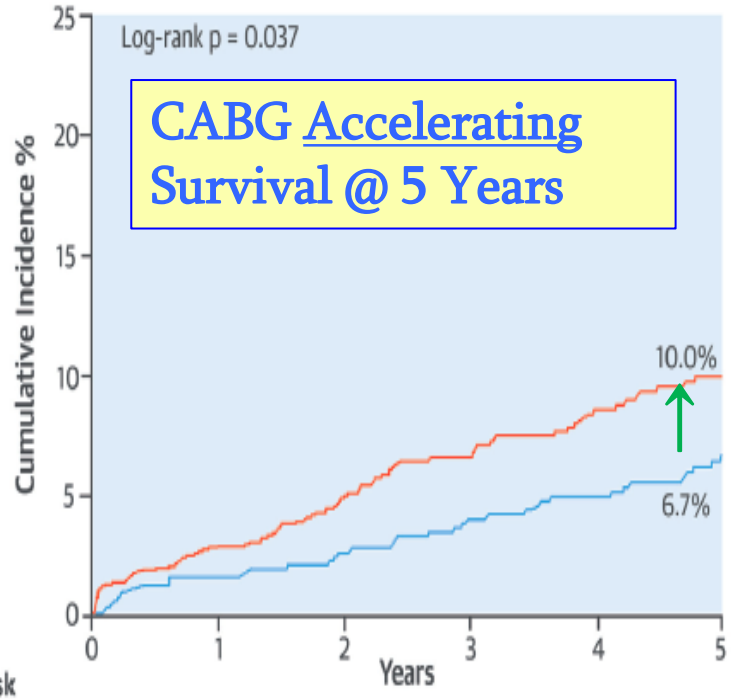
Low <23	nos	181	171	
	DEATH	10.2	9.3	.81
	CVA	1.8	3.9	.24
	MI	8.8	4.9	.20
21%	D+C+M	17.5	14.8	.56
	Revasc	23.	14.6	.04
Int 23-32	nos	207	208	
	DEATH (7%)	16.3	9.6	047
	CVA	2.5	3.6	.53
	MI	13.8	3.1	.00
	D+C+M	23.2	14.7	.04
79%	Revasc	25.1	11.0	000
High >32	nos	155	166	
	DEATH (9%)	17.8	8.8	.02
	CVA	5.1	2.6	.31
	MI	8.7	1.9	.008
	D+C+M	26.2	12.5	.002
	Revasc	28.2	12.6	.000

Long-Term Mortality After Coronary Revascularization in Nondiabetic Patients With Multivessel Disease

[JACC 2016]

Mineok Chang, MD,[a] Jung-Min Ahn, MD,[a] Cheol Whan Lee, MD,[a] Rafael Cavalcante, MD,[b] Yohei Sotomi, MD,[c] Yoshinobu Onuma, MD,[b] Erhan Tenekecioglu, MD,[b] Minkyu Han, PhD,[d] Duk-Woo Park, MD,[a] Soo-Jin Kang, MD,[a] Seung-Whan Lee, MD,[a] Young-Hak Kim, MD,[a] Seong-Wook Park, MD, PhD,[a] Patrick W. Serruys, MD, PhD,[b,e] Seung-Jung Park, MD, PhD[a]

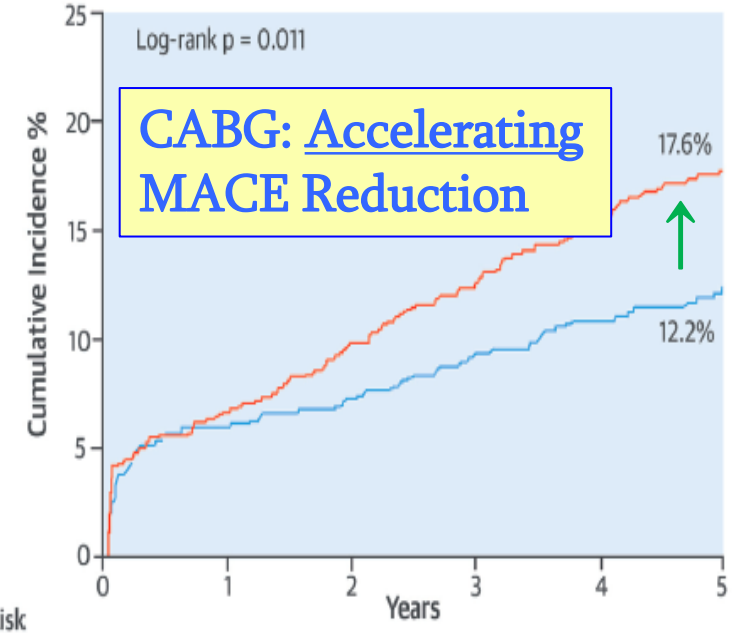
A. Death



Patients at Risk

CABG	638	608	578	540	485	316
PCI	637	616	581	540	487	314

B. Death, Myocardial Infarction, or Stroke



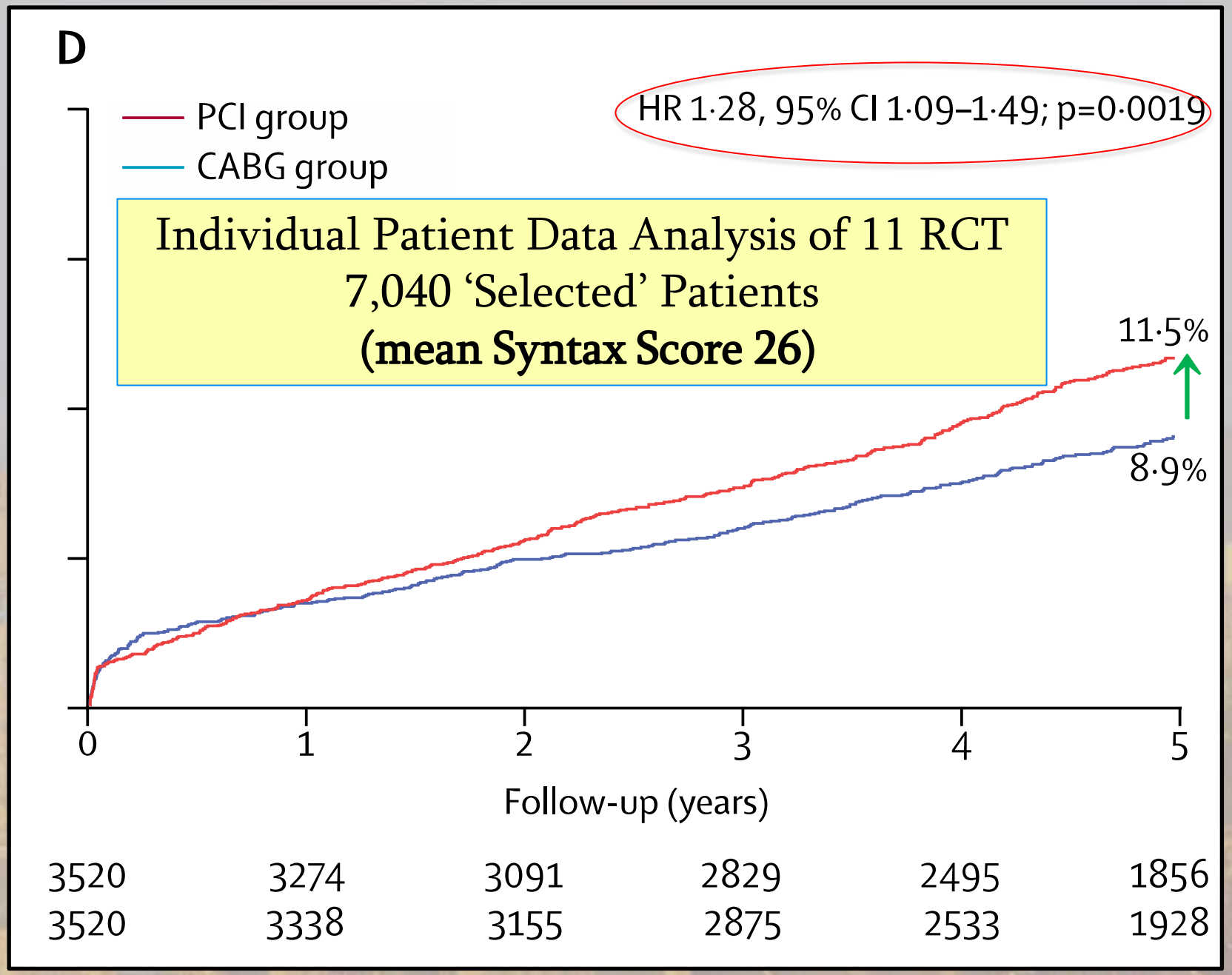
Patients at Risk

CABG	638	582	550	508	455	296
PCI	637	592	551	505	447	285

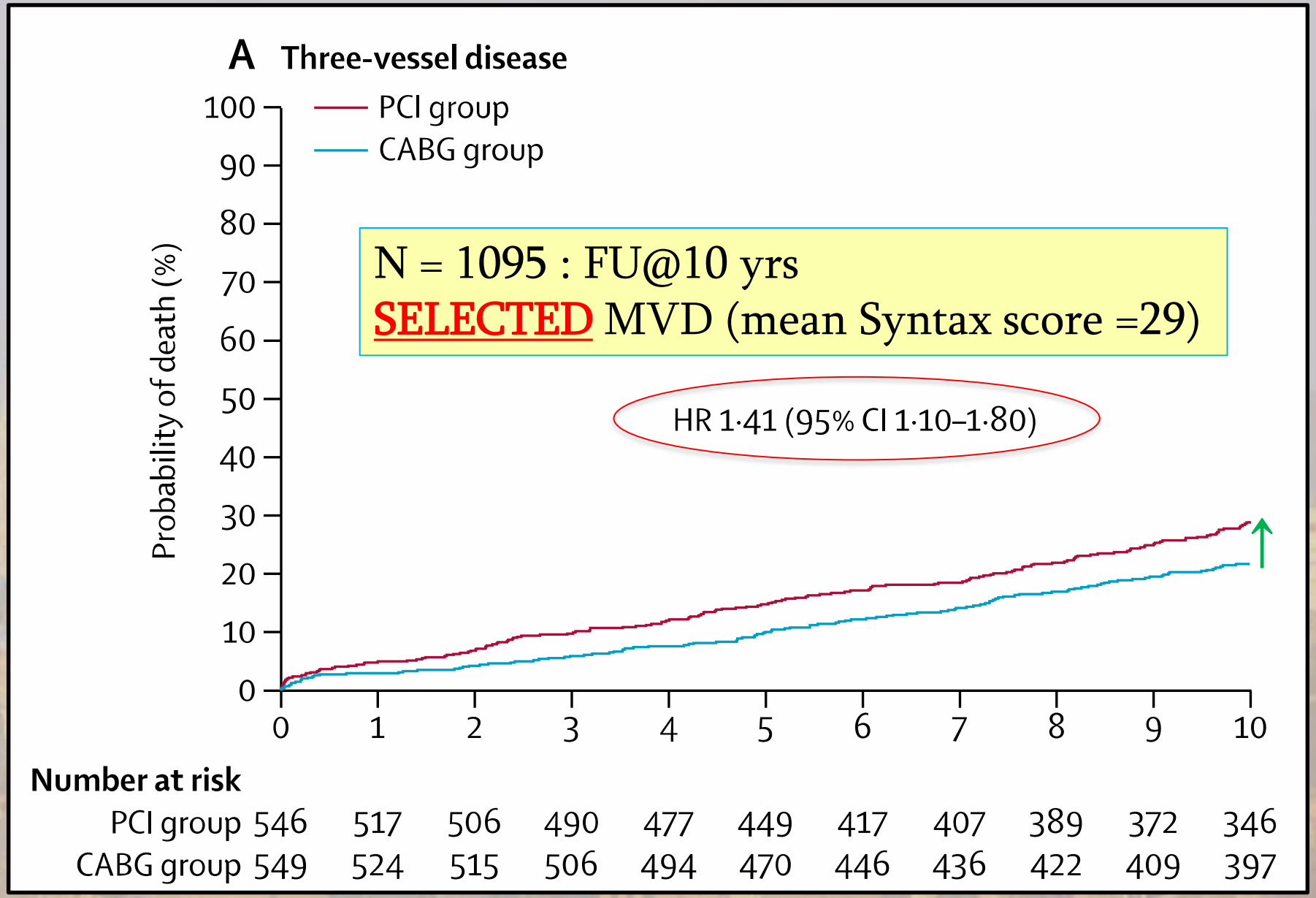
CABG PCI

CONCLUSIONS CABG, as compared with PCI with drug-eluting stents, significantly reduced the long-term risk of mortality in nondiabetic patients with multivessel CAD. (J Am Coll Cardiol 2016;68:29-36)

3 Vessel Disease: CABG Superior Survival (Head et al Lancet 2018)



SYNTAXES at 10 years: 3VD [Thuijs et al Lancet 2019] (N=1095)



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*

ABSTRACT

BACKGROUND
Patients with three-vessel coronary artery disease have been found to have better outcomes with coronary-artery bypass grafting (CABG) than with percutaneous coronary intervention (PCI), but studies in which PCI is guided by measurement of fractional flow reserve (FFR) have been lacking.

METHODS
In this multicenter, international, noninferiority trial, patients with three-vessel coronary artery disease were randomly assigned to undergo CABG or FFR-guided PCI with current-generation zotarolimus-eluting stents. 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. Noninferiority of FFR-guided PCI to CABG was prespecified as an upper boundary of less than 1.65 for the 95% confidence interval of the hazard ratio. Secondary end points included a composite of death, myocardial infarction, or stroke; safety was also assessed.

RESULTS
A total of 1500 patients underwent randomization at 48 centers. Patients assigned to undergo PCI received a mean (±SD) of 3.7±1.9 stents, and those assigned to undergo CABG received 3.4±1.0 distal anastomoses. The 1-year incidence of the composite primary end point was 10.6% among patients randomly assigned to undergo FFR-guided PCI and 6.9% among those assigned to undergo CABG (hazard ratio, 1.5; 95% confidence interval [CI], 1.1 to 2.2), findings that were not consistent with noninferiority of FFR-guided PCI (P=0.35 for noninferiority). The incidence of death, myocardial infarction, or stroke was 7.3% in the FFR-guided PCI group and 5.2% in the CABG group (hazard ratio, 1.4; 95% CI, 0.9 to 2.1). The incidences of major bleeding, arrhythmia, and acute kidney injury were higher in the CABG group than in the FFR-guided PCI group.

CONCLUSIONS
In patients with three-vessel coronary artery disease, FFR-guided PCI was not found to be noninferior to CABG with respect to the incidence of a composite of death, myocardial infarction, stroke, or repeat revascularization at 1 year. (Funded by Medtronic and Abbott Vascular; FAME 3 ClinicalTrials.gov number, NCT02100722.)

- FAME 3 (NEJM January 2022): PCI vs CABG
- Non-inferiority trial of 1500 patients with 3 VD to address 'limitations' of SYNTAX (1st generation DES)
- PCI: FFR Guided + BEST DES (Zotarolimus)
- Median Syntax Score 26 (82% <33)
- Composite MACE Primary End-Point at 1 year
  - MACE (Death, MI, Stroke, Revasc)
  - Wide non-inferiority margins upper limit of 1.65
- RESULTS at 1 year for PCI vs CABG
  - MACE 10.6% PCI vs 6.9% CABG
  - (HR 1.5; 95% CI 1.1-2.2)
  - P=0.35 for non inferiority

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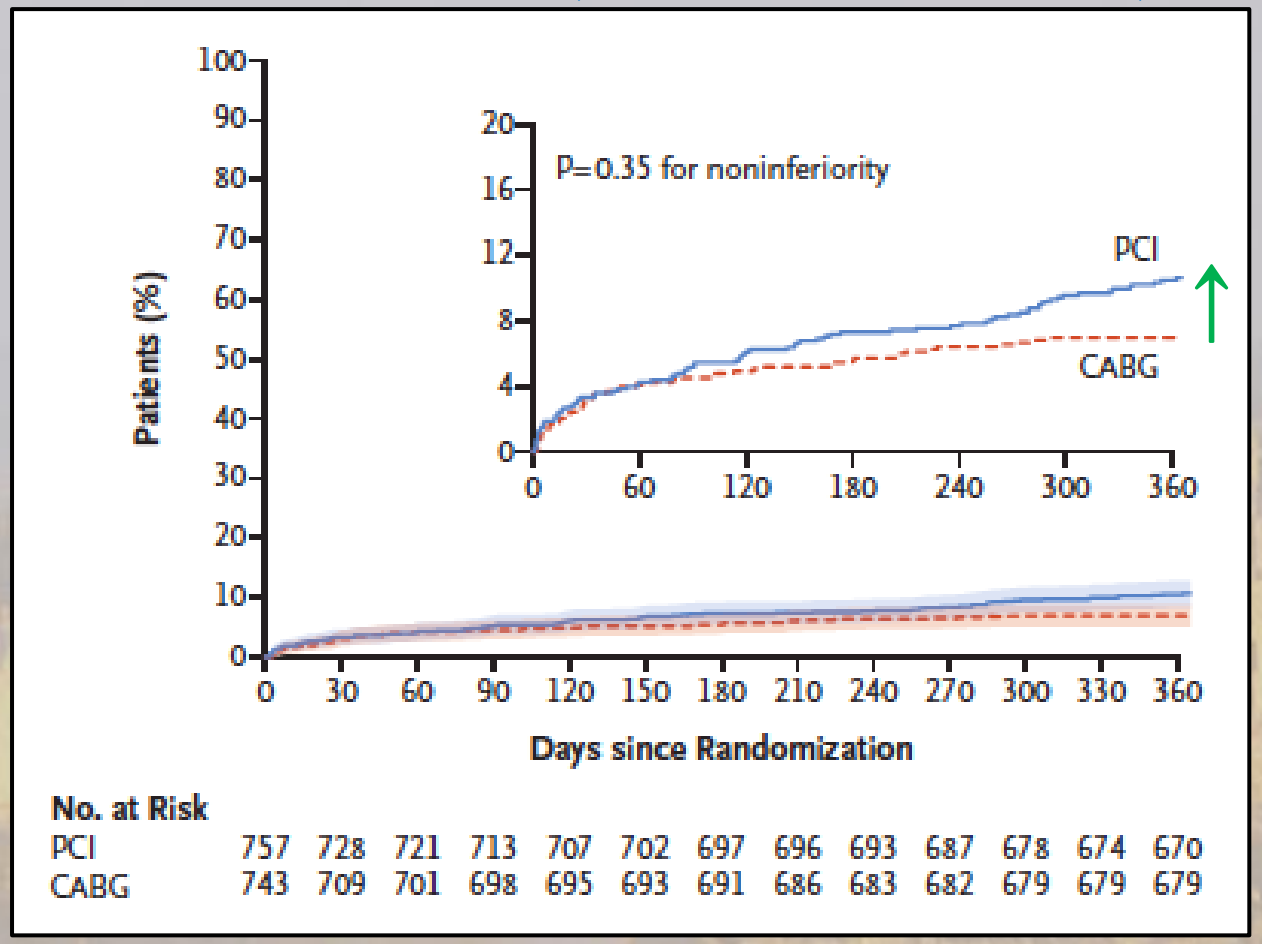
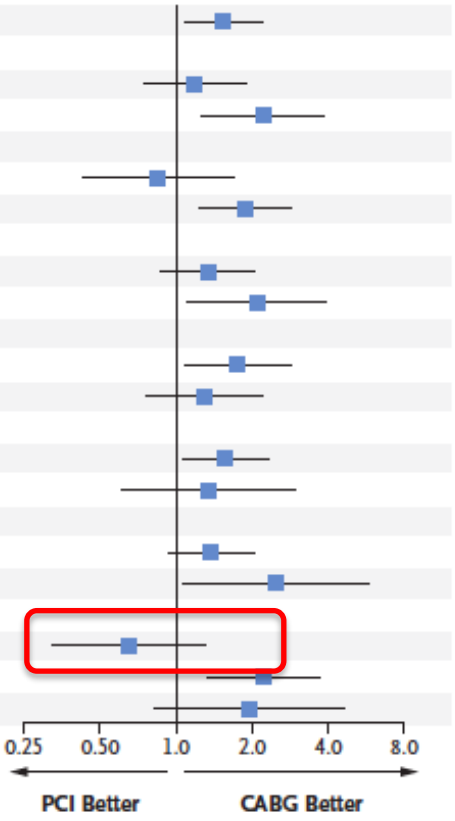
FAME-3: 1-year Primary Outcome

MACE 10.6% vs 6.9 (HR 1.5; 95% CI 1.1-2.2)



Subgroup	PCI (total no.)	CABG (total no.)	PCI (1-yr incidence %)	CABG (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



Long-Term Survival Following Multivessel Revascularization in Patients With Diabetes

The FREEDOM Follow-On Study

[JACC 2019]

Michael E. Farkouh, MD, MSc,[a] Michael Domanski, MD,[b] George D. Dangas, MD, PhD,[c] Lucas C. Godoy, MD,[a,d] Michael J. Mack, MD,[e] Flora S. Siami, MPH,[f] Taye H. Hamza, PhD,[f] Binita Shah, MD, MS,[g] Giulio G. Stefanini, MD,[h] Mandeep S. Sidhu, MD,[i] Jean-François Tanguay, MD,[j] Krishnan Ramanathan, MBChB,[k] Samin K. Sharma, MD,[c] John French, MBChB, PhD,[l] Whady Hueb, MD, PhD,[d] David J. Cohen, MD, MSc,[m] Valentin Fuster, MD, PhD,[c,n] for the FREEDOM Follow-On Study Investigators

FIGURE 2 Kaplan-Meier Estimates of Survival in the 2 Treatment Groups

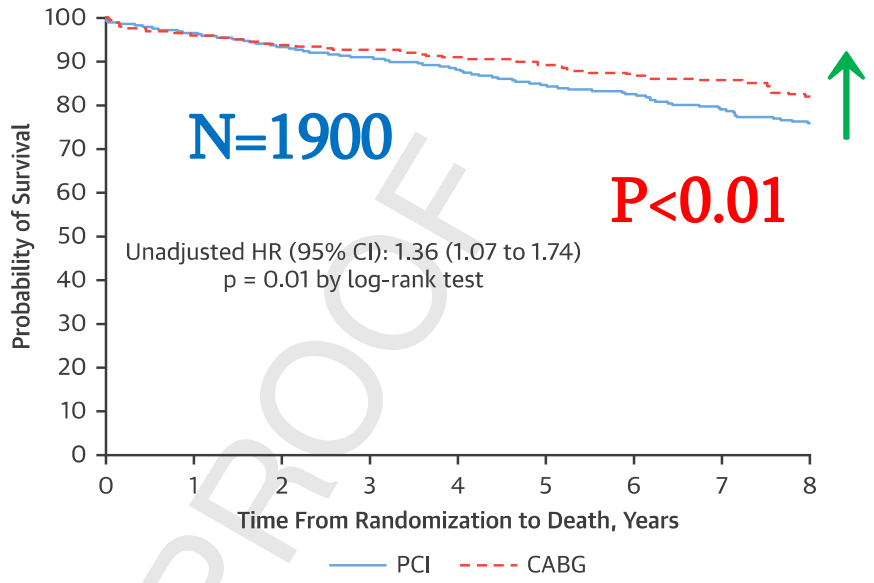
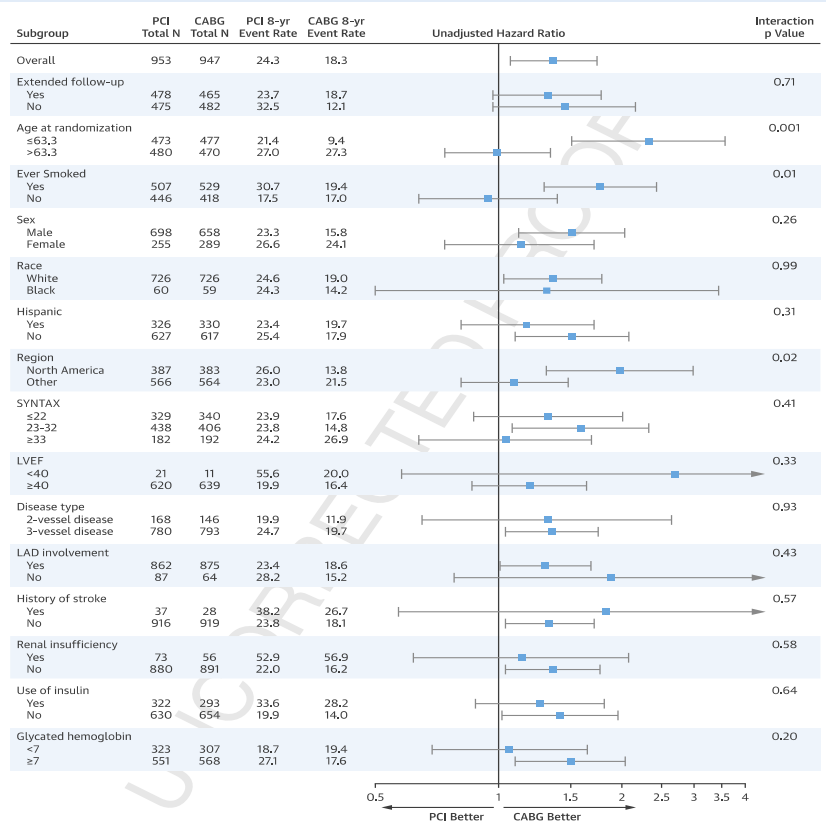


FIGURE 3 Subgroup Analysis of All-Cause Mortality for the Whole Cohort



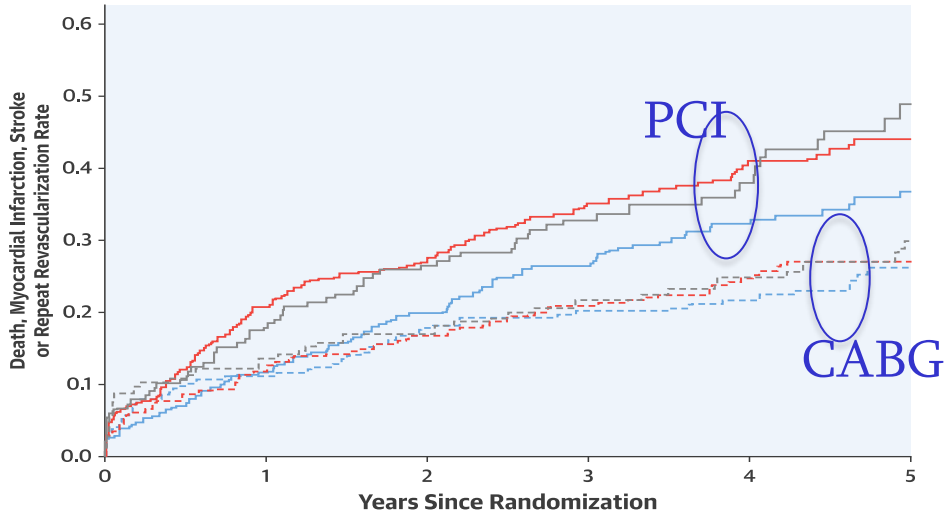
Subgroup	PCI Total N	CABG Total N	PCI 8-yr Event Rate	CABG 8-yr Event Rate	Interaction p Value
Overall	953	947	24.3	18.3	
Extended follow-up					0.71
Yes	478	465	23.7	18.7	
No	475	482	32.5	12.1	
Age at randomization					0.001
≤63.3	473	477	21.4	9.4	
>63.3	480	470	27.0	27.3	
Ever Smoked					0.01
Yes	507	529	30.7	19.4	
No	446	418	17.5	17.0	
Sex					0.26
Male	698	658	23.3	15.8	
Female	255	289	26.6	24.1	
Race					0.99
White	726	726	24.6	19.0	
Black	60	59	24.3	14.2	
Hispanic					0.31
Yes	326	330	23.4	19.7	
No	627	617	25.4	17.9	
Region					0.02
North America	387	383	26.0	13.8	
Other	566	564	23.0	21.5	
SYNTAX					0.41
≤22	329	340	23.9	17.6	
23-32	438	406	23.8	14.8	
≥33	182	192	24.2	26.9	
LVEF					0.33
<40	21	11	55.6	20.0	
≥40	620	639	19.9	16.4	
Disease type					0.93
2-vessel disease	168	146	19.9	11.9	
3-vessel disease	780	793	24.7	19.7	
LAD involvement					0.43
Yes	862	875	23.4	18.6	
No	87	64	28.2	15.2	
History of stroke					0.57
Yes	37	28	38.2	26.7	
No	916	919	23.8	18.1	
Renal insufficiency					0.58
Yes	73	56	52.9	56.9	
No	880	891	22.0	16.2	
Use of insulin					0.64
Yes	322	293	33.6	28.2	
No	630	654	19.9	14.0	
Glycated hemoglobin					0.20
<7	323	307	18.7	19.4	
≥7	551	568	27.1	17.6	

'CONCLUSIONS In patients with DM and MVD, CABG leads to lower all-cause mortality than with PCI-DES in long-term follow-up'. (NB:Selected Patients With Low Severity Disease !)

SYNTAX Score in Patients With Diabetes Undergoing Coronary Revascularization in the FREEDOM Trial [JACC 2019]

Rodrigo B. Esper, MD, PhD,[a,b,*] Michael E. Farkouh, MD, MSc,[c,*] Expedito E. Ribeiro, MD, PhD,[a] Whady Hueb, MD, PhD,[a] Michael Domanski, MD,[d] Taye H. Hamza, PhD,[e] Flora S. Siami, MPH,[e] Lucas Colombo Godoy, MD,[a,c] Verghese Mathew, MD,[f] John French, MBChB, PhD,[g] Valentin Fuster, MD, PhD[h,i]

CENTRAL ILLUSTRATION Major Adverse Cardiac and Cerebrovascular Events in Patients With Diabetes Mellitus With Multivessel Coronary Artery Disease Submitted to CABG or PCI According to SYNTAX Score Categories



SYNTAX Score Category - Revascularization Strategy	No. at Risk
High SYNTAX - PCI	182
Intermediate SYNTAX - PCI	438
Low SYNTAX - PCI	328
High SYNTAX - CABG	192
Intermediate SYNTAX - CABG	406
Low SYNTAX - CABG	339

Esper, R.B. et al. J Am Coll Cardiol. 2018;72(23):2826–37.

In diabetes mellitus (DM) patients with multivessel coronary artery disease (CAD) without left main stenosis and indication for myocardial revascularization, coronary artery bypass grafting (CABG) should be the preferred method of coronary revascularization regardless of the complexity of the coronary disease. In all SYNTAX score categories, CABG had fewer major adverse cardiac and cerebrovascular events (MACCE), defined by death from any cause, nonfatal myocardial infarction, nonfatal stroke, and need for repeat revascularization, versus percutaneous coronary intervention (PCI) with drug-eluting stents in the FREEDOM (Future REvascularization Evaluation in patients with Diabetes mellitus: Optimal management of Multivessel disease) trial.

CONCLUSION

'In diabetes mellitus (DM) patients with multivessel coronary artery disease (CAD) without left main stenosis coronary artery bypass grafting (CABG) should be the preferred method of coronary revascularization regardless of the complexity of the coronary disease. In all SYNTAX score categories, CABG had fewer major adverse cardiac and cerebrovascular events (MACCE), defined by death from any cause, nonfatal myocardial infarction, nonfatal stroke, and need for repeat revascularization, versus percutaneous coronary intervention (PCI) with drug-eluting stents'.

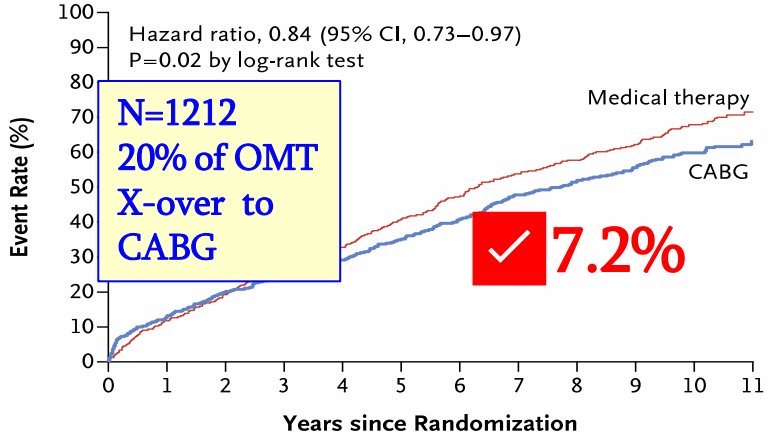
CABG Superior to PCI for every level of SYNTAX score !!

ORIGINAL ARTICLE [NEJM 2016]

Coronary-Artery Bypass Surgery in Patients with Ischemic Cardiomyopathy

Eric J. Velazquez, M.D., Kerry L. Lee, Ph.D., Robert H. Jones, M.D.,

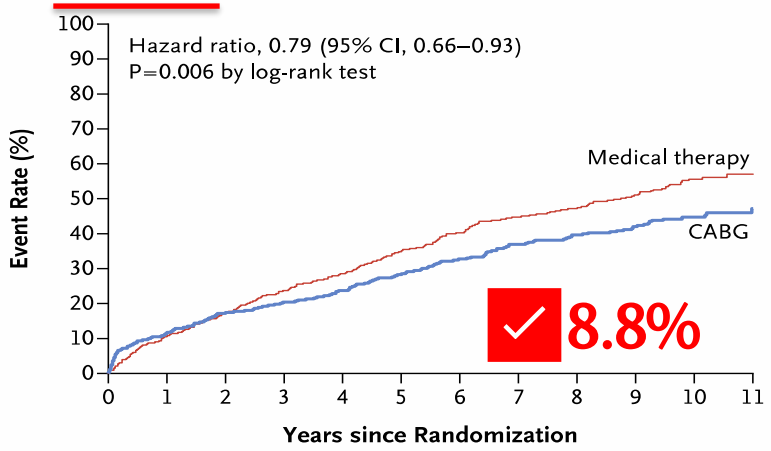
A Death from Any Cause (Primary Outcome)



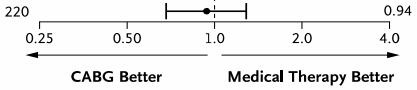
No. at Risk

Medical therapy	602	532	487	435	404	357	315	274	248	164	82	37
CABG	610	532	487	460	432	392	356	312	286	205	103	42

B Death from Cardiovascular Causes



Subgroup	No. of Patients	Hazard Ratio (95% CI)	P Value for Interaction
All patients	1212	0.84 (0.73–0.97)	
Age			0.18
≥60 yr	589	0.91 (0.75–1.10)	
<60 yr	623	0.75 (0.60–0.93)	
Sex			0.50
Male	1064	0.85 (0.73–0.99)	
Female	148	0.73 (0.46–1.16)	
Race or ethnic group			0.02
Hispanic, Latino, or nonwhite	421	0.67 (0.52–0.86)	
White	791	0.95 (0.80–1.12)	
Region or country			0.28
Poland	319	1.01 (0.77–1.33)	
United States	120	0.85 (0.55–1.31)	
Canada	123	0.77 (0.48–1.22)	
Western Europe	112	1.08 (0.68–1.69)	
Other	538	0.72 (0.57–0.89)	
NYHA heart failure class			0.74
I or II	765	0.85 (0.71–1.02)	
III or IV	447	0.81 (0.65–1.01)	
LVEF			0.31
≤28%	653	0.77 (0.64–0.92)	
>28%	559	0.89 (0.71–1.11)	
End-systolic volume index			0.68
≤78 ml/m²	564	0.85 (0.68–1.06)	
>78 ml/m²	551	0.80 (0.65–0.98)	
Stratum			0.03
A	1061	0.89 (0.77–1.04)	
B	151	0.55 (0.36–0.84)	
Diabetes			0.95
Yes	478	0.84 (0.67–1.04)	
No	734	0.84 (0.69–1.01)	
CCS angina class			0.52
No angina or I	629	0.80 (0.65–0.97)	
II, III, or IV	583	0.88 (0.72–1.09)	
No. of diseased vessels with ≥75% stenosis			0.04
0, 1, or 2	769	0.93 (0.77–1.11)	
3	442	0.68 (0.54–0.86)	
LM ≥50% or PLAD ≥75% stenosis			0.81
No	373	0.81 (0.62–1.05)	
Yes	838	0.85 (0.71–1.00)	
Mitral regurgitation			0.34
None or trace	435	0.92 (0.71–1.17)	
Mild (≤2+)	554	0.74 (0.60–0.92)	
Moderate or severe (3+ or 4+)	220	0.94 (0.68–1.29)	



3 REASONS FOR PERSISTING SURVIVAL BENEFIT of CABG OVER PCI

1 **Anatomically, atheroma is mainly located in the proximal coronary arteries**

Placing bypass grafts to the **MID CORONARY VESSEL** has **TWO** effects

(i) Complexity of proximal '**CULPRIT**' lesion is irrelevant

(ii) Over the long term offers prophylaxis against **FUTURE** proximal 'culprit' lesions

In contrast, PCI only treats **'SUITABLE'** localised proximal 'culprit' lesions but has **NO PROPHYLACTIC BENEFIT** against new proximal disease

2

THE NEW ENGLAND JOURNAL OF MEDICINE Aug. 25, 1988

IMA elutes NO into coronary circulation reducing risk of further disease

DIFFERENCE BETWEEN ENDOTHELIUM-DEPENDENT RELAXATION IN ARTERIAL AND IN VENOUS CORONARY BYPASS GRAFTS

THOMAS F. LÜSCHER, M.D., DENNIS DIEDERICH, M.D., ROBERT SIEBENMANN, M.D., KURT LEHMANN, M.D.,

Drug-Eluting Stent and Coronary Thrombosis

Biological Mechanisms and Clinical Implications [CIRC 2007]

Thomas F. Lüscher, MD; Jan Steffel, MD; Franz R. Eberli, MD; Michael Joner, MD;

impairs re-endothelialization, downstream endothelial function and creates pro-thrombotic milieu

3 PCI means incomplete revascularization (Hannan Circ 2006)

Of 22,000 PCI 69% had incomplete revascularization

>2 vessels (+/- CTO) HR for mortality 1.4 (95% CI = 1.1-1.7)

Residual SYNTAX score >8 increases mortality and MACCE (Farooq, Serruys CIRC 2013)

PCI will 'never' match the results of CABG for LM/MVD (POBA;BMS;DES)

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2018 ESC/EACTS Guidelines on myocardial revascularization

Recommendations according to extent of CAD	CABG		PCI	
	Class[a]	Level[b]	Class[a]	Level[b]
One-vessel CAD				
Without proximal LAD stenosis.	IIb	C	I	C
With proximal LAD stenosis.[68,101,139–144]	I	A	I	A
Two-vessel CAD				
Without proximal LAD stenosis.	IIb	C	I	C
With proximal LAD stenosis.[68,70,73]	I	B	I	C
Left main CAD				
Left main disease with low SYNTAX score (0 - 22).[69,121,122,124,145–148]	I	A	I	A
Left main disease with intermediate SYNTAX score (23 - 32).[69,121,122,124,145–148]	I	A	IIa ?	A
Left main disease with high SYNTAX score (≥33).[c 69,121,122,124,146–148] 66%	I	A	III	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] 79%	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

CABG would be better if more arterial grafts and optimization of medical therapy !!

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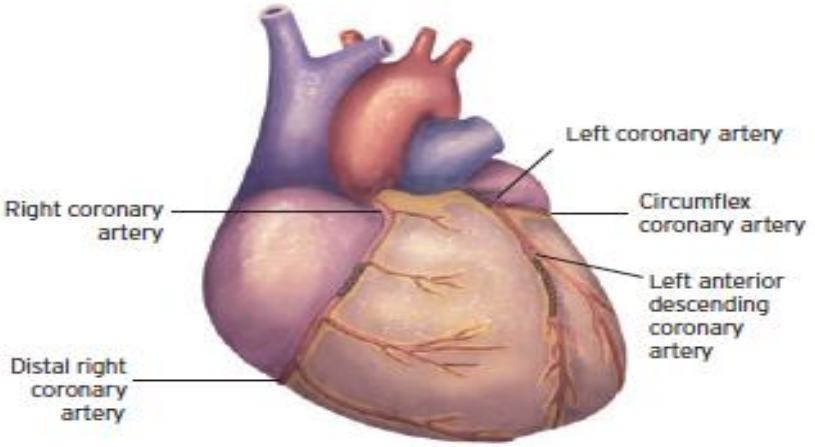
ESC/EACTS Guidelines on Myocardial Revascularization 2018:

PCI



FAVOURS PCI

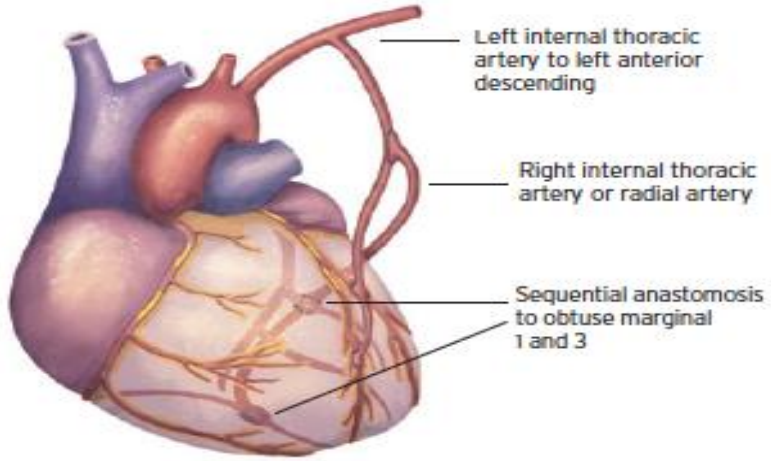
Clinical characteristics

- Presence of severe co-morbidity (not adequately reflected by scores)
- Advanced age/frailty/reduced life expectancy
- Restricted mobility and conditions that affect the rehabilitation process

Anatomical and technical aspects

- MVD with SYNTAX score 0-22
- Anatomy likely resulting in incomplete revascularization with CABG due to poor quality or missing conduits
- Severe chest deformation or scoliosis
- Sequelae of chest radiation
- Porcelain aorta[a]

CABG



FAVOURS CABG

Clinical characteristics

- Diabetes
- Reduced LV function (EF ≤35%)
- Contraindication to DAPT
- Recurrent diffuse in-stent restenosis

Anatomical and technical aspects

- MVD with SYNTAX score ≥23
- Anatomy likely resulting in incomplete revascularization with PCI
- Severely calcified coronary artery lesions limiting lesion expansion

Need for concomitant interventions

- Ascending aortic pathology with indication for surgery
- Concomitant cardiac surgery

Look at the whole clinical picture (use your common sense !)

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