INSTITUT JANTUNG NEGARA
National Heart Institute

PCI in Patients with Diabetes Mellitus: Best Treatment Options to Be Considered

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M MED. FACC

Your Heart…Our Passion

OPTIMAL GLUCOSE CONTROL

HbA1C levels and clinical outcomes in diabetic patients following coronary artery stenting

- HbA1C $\leq$ 7% comparable rates of adverse events in optimally-controlled diabetics and non diabetics
- Action to Control Cardiovascular Risk in Diabetes (ACCORD)
- Action in Diabetes and Vascular Disease : Preterax and Diamicron Modified Release Controlled Evaluation (ADVANCE)
- Veterans Affairs Diabetes Trial (VADT)

- Improved glycemic control
- No reduction in rate of cardiovascular events
- In ACCORD trial, increased death from any cause and death from cardiovascular events
- Recommendations of the American Diabetes Association, American Heart Association and American College of Cardiology
    - aim HbA1C of < 7%

- Would CABGS be a better option?

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Strategies for Multivessel Revascularization in Patients with Diabetes

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BACKGROUND

In some randomized trials comparing revascularization strategies for patients with diabetes, coronary-artery bypass grafting (CABG) has had a better outcome than percutaneous coronary intervention (PCI). We sought to discover whether aggressive medical therapy and the use of drug-eluting stents could alter the revascularization approach for patients with diabetes and multivessel coronary artery disease.

METHODS

In this randomized trial, we assigned patients with diabetes and multivessel coronary artery disease to undergo either PCI with drug-eluting stents or CABG. The patients were followed for a minimum of 2 years (median among survivors, 3.8 years). All patients were prescribed currently recommended medical therapies for the control of low-density lipoprotein cholesterol, systolic blood pressure, and glycated hemoglobin. The primary outcome measure was a composite of death from any cause, nonfatal myocardial infarction, or nonfatal stroke.

Table 2. Kaplan–Meier Estimates of Key Outcomes at 2 Years and 5 Years after Randomization.

Outcome	2 Years after Randomization		5 Years after Randomization		Patients with Event		P Value*
	PCI	CABG	PCI	CABG	PCI	CABG	
	number (percent)				*number*		
Primary composite†	121 (13.0)	108 (11.9)	200 (26.6)	146 (18.7)	205	147	0.005‡
Death from any cause	62 (6.7)	57 (6.3)	114 (16.3)	83 (10.9)	118	86	0.049
Myocardial infarction	62 (6.7)	42 (4.7)	98 (13.9)	48 (6.0)	99	48	<0.001
Stroke	14 (1.5)	24 (2.7)	20 (2.4)	37 (5.2)	22	37	0.03§
Cardiovascular death	9 (0.9)	12 (1.3)	73 (10.9)	52 (6.8)	75	55	0.12

* P values were calculated with the use of the log-rank test on the basis of all available follow-up data (i.e., more than 5 years).
† The primary composite outcome was the rate of death from any cause, myocardial infarction, or stroke.
‡ P=0.006 in the as-treated (non–intention-to-treat) analysis.
§ P=0.16 by the Wald test of the Cox regression estimate for study-group assignment in 1712 patients after adjustment for the average glucose level after the procedure.

Table 3. Kaplan–Meier Estimates of Major Adverse Cardiovascular and Cerebrovascular Events at 30 Days and 12 Months after the Procedure.

Event	30 Days after Procedure			12 Months after Procedure		
	PCI	CABG	P Value	PCI	CABG	P Value
	number (percent)			*number (percent)*		
Major adverse cardiovascular and cerebrovascular events	45 (4.8)	47 (5.2)	0.68	157 (16.8)	106 (11.8)	0.004
Death	8 (0.8)	15 (1.7)	0.12	32 (3.4)	38 (4.2)	0.35
Myocardial infarction	17 (1.8)	15 (1.7)	0.82	54 (5.8)	30 (3.4)	0.02
Stroke	3 (0.3)	16 (1.8)	0.002	8 (0.9)	17 (1.9)	0.06
Repeat revascularization	31 (3.3)	10 (1.1)	0.002	117 (12.6)	42 (4.8)	<0.001

Subgroup	No.	5-Yr Rate PCI %	5-Yr Rate CABG %	P Value for Interaction
All patients	1900	27	19	
SYNTAX				0.58
≤22	669	23	17	
23–32	844	27	18	
≥33	374	31	23	
Sex				0.46
Male	1356	27	18	
Female	544	26	21	
Race				0.55
White	1452	27	19	
Black	119	24	16	
Disease type				0.75
2-Vessel disease	314	22	11	
3-Vessel disease	1573	27	20	
LVEF				0.37
<40%	32	62	31	
≥40%	1259	23	18	
LAD involvement				0.83
No	151	23	18	
Yes	1737	27	19	
History of stroke				0.57
Yes	65	59	35	
No	1835	25	18	
Renal insufficiency				0.62
Yes	129	44	37	
No	1771	25	17	
Glycated hemoglobin				0.99
<7%	630	23	16	
≥7%	1119	28	20	
Region				0.05
North America	770	28	16	
Other	1130	25	21	

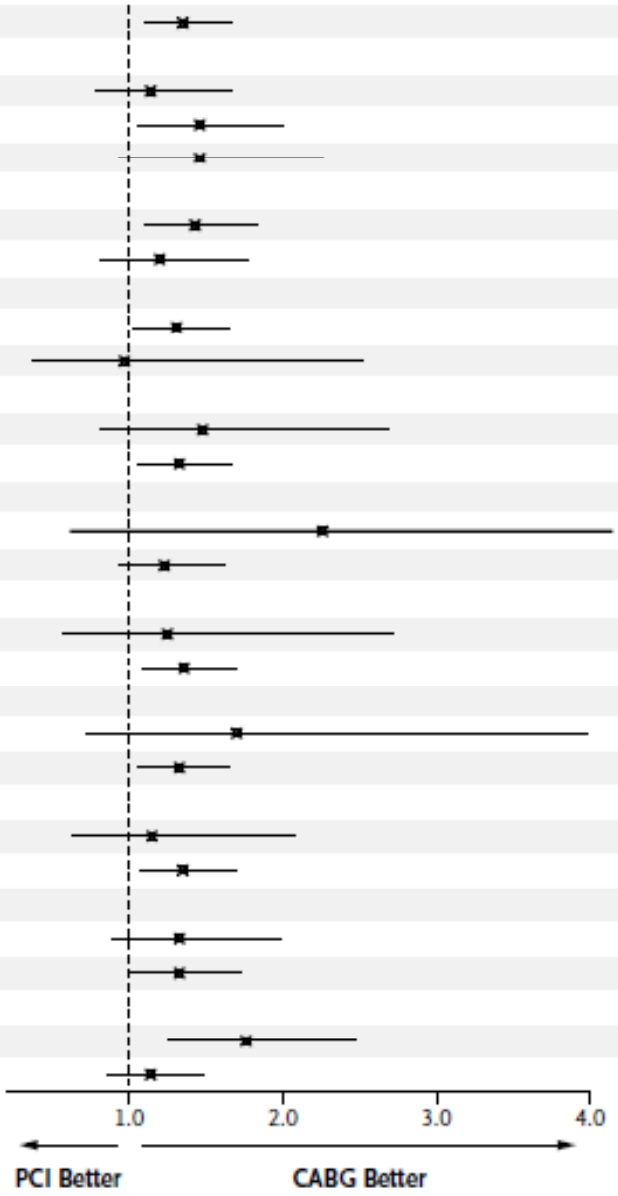
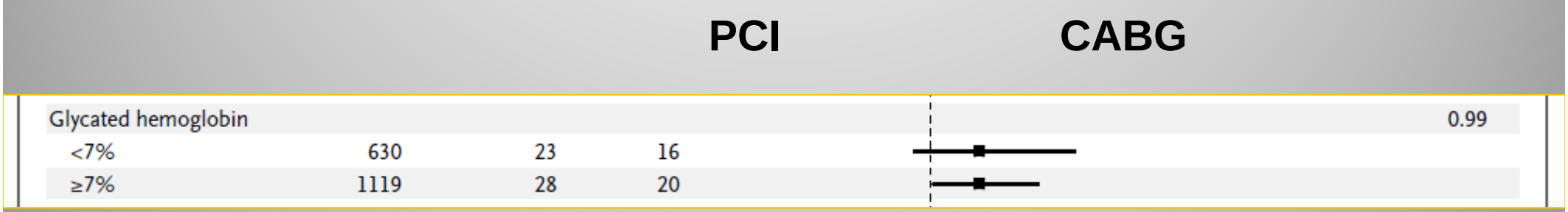


Figure 2. Primary Composite Outcome, According to Subgroup.

Subgroup analyses were performed with the use of Cox proportional-hazards regression. Five-year composite event rates for death, myocardial infarction, or stroke are shown. LAD denotes left anterior descending artery, and LVEF left ventricular ejection fraction.


PCI
CABG
Glycated hemoglobin
0.99
<7%
630
23
16
≥7%
1119
28
20

RESULTS

From 2005 through 2010, we enrolled 1900 patients at 140 international centers. The patients' mean age was 63.1±9.1 years, 29% were women, and 83% had three-vessel disease. The primary outcome occurred more frequently in the PCI group (P=0.005), with 5-year rates of 26.6% in the PCI group and 18.7% in the CABG group. The benefit of CABG was driven by differences in rates of both myocardial infarction (P<0.001) and death from any cause (P=0.049). Stroke was more frequent in the CABG group, with 5-year rates of 2.4% in the PCI group and 5.2% in the CABG group (P=0.03).

CONCLUSIONS

For patients with diabetes and advanced coronary artery disease, CABG was superior to PCI in that it significantly reduced rates of death and myocardial infarction, with a higher rate of stroke. (Funded by the National Heart, Lung, and Blood Institute and others; FREEDOM ClinicalTrials.gov number, NCT00086450.)

CONCLUSION

- CABG superior
- Reduced death and myocardial infarction
- However increased risk of stroke

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CLINICAL RESEARCH **Interventional Cardiology**

Percutaneous Coronary Intervention Versus Coronary Bypass Surgery in United States Veterans With Diabetes

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Methods

In a prospective, multicenter study, 198 eligible patients with diabetes with severe coronary artery disease were randomly assigned to either coronary artery bypass grafting (CABG) (n = 97) or percutaneous coronary intervention (PCI) with drug-eluting stents (n = 101) and followed for at least 2 years. The primary outcome measure was a composite of nonfatal myocardial infarction or death. Secondary outcome measures included all-cause mortality, cardiac mortality, nonfatal myocardial infarction, and stroke.

Results

The study was stopped because of slow recruitment after enrolling only 25% of the intended sample size, leaving it severely underpowered for the primary composite endpoint of death plus nonfatal myocardial infarction (hazard ratio: 0.89; 95% confidence interval: 0.47 to 1.71). However, after a mean follow-up period of 2 years, all-cause mortality was 5.0% for CABG and 21% for PCI (hazard ratio: 0.30; 95% confidence interval: 0.11 to 0.80), while the risk for nonfatal myocardial infarction was 15% for CABG and 6.2% for PCI (hazard ratio: 3.32; 95% confidence interval: 1.07 to 10.30).

Conclusions This study was severely underpowered for its primary endpoint, and therefore no firm conclusions about the comparative effectiveness of CABG and PCI are possible. There were interesting differences in the components of the primary endpoint. However, the confidence intervals are very large, and the findings must be viewed as hypothesis generating only. (Coronary Artery Revascularization in Diabetes; NCT00326196) (J Am Coll Cardiol 2013;61:808–16) © 2013 by the American College of Cardiology Foundation

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ORIGINAL ARTICLE

Treatment of complex coronary artery disease in patients with diabetes: 5-year results comparing outcomes of bypass surgery and percutaneous coronary intervention in the SYNTAX trial†

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Objectives

- DM on LM and 3VD
- in SYNTAX trial

Methods

- 1,800 patients with LM / 3VD
- PCI with TAXUS stent or CABG with DM (n = 452)
- 5 year outcome MACCE, composite safety end-point of all-cause death / stroke / MI and individual MACCE components death, stroke, MI and repeat revascularization

Table 2: Five-year clinical outcomes according to diabetes status

Clinical outcome	Non-diabetic ($n = 1348$)			Diabetic ($n = 452$)			Non-diabetic vs diabetic		
	CABG ($n = 676$)	PCI ($n = 672$)	*P*-value	CABG ($n = 221$)	PCI ($n = 231$)	*P*-value	*P*-value (CABG)	*P*-value (PCI)	Interaction *P*-value[a]
MACCE[b]	26.3% (167)	34.1% (226)	0.002	29.0% (59)	46.5% (105)	<0.001	0.37	<0.001	0.17
All-cause death/stroke/ myocardial infarction	15.9% (101)	19.8% (131)	0.069	19.1% (39)	23.9% (54)	0.26	0.25	0.18	0.76
All-cause death	10.9% (68)	12.0% (79)	0.48	12.9% (26)	19.5% (44)	0.065	0.34	0.003	0.43
Cardiac death	4.9% (30)	7.7% (50)	0.035	6.5% (13)	12.7% (28)	0.034	0.31	0.018	
Stroke	3.5% (22)	2.2% (14)	0.15	4.7% (9)	3.0% (6)	0.34	0.49	0.55	0.97
Myocardial infarction	3.4% (22)	9.9% (64)	<0.001	5.4% (11)	9.0% (19)	0.20	0.22	0.66	0.18
Repeat revascularization	13.4% (82)	22.8% (145)	<0.001	14.6% (28)	35.3% (75)	<0.001	0.60	<0.001	0.081
PCI	12.9% (78)	19.3% (123)	0.001	12.9% (24)	28.5% (60)	<0.001	0.95	0.004	
CABG	1.1% (7)	5.8% (36)	<0.001	1.9% (4)	8.7% (18)	0.004	0.35	0.12	
Graft occlusion/stent thrombosis	3.9% (24)	5.6% (36)	0.14	4.3% (8)	5.3% (11)	0.61	0.84	0.84	0.73

Data are Kaplan–Meier time-to-event estimates expressed as % (*n*); log-rank *P*-value.
CABG: coronary artery bypass grafting; MACCE: major adverse cardiac or cerebrovascular events; PCI: percutaneous coronary intervention.
[a]Binary logistic regression interaction term for diabetes status by treatment arm.
[b]MACCE consists of all-cause death, stroke, myocardial infarction, or repeat revascularization (CABG or PCI) in any vessel.

Diabetes control subgroups

Table 3: Five-year clinical outcomes according to diabetes treatment

Clinical outcome	Oral hypoglycaemic agents (n = 270)			Insulin (n = 452)			Oral vs insulin treatment		Interaction
	CABG (n = 128)	PCI (n = 142)	P-value	CABG (n = 93)	PCI (n = 89)	P-value	P-value (CABG)	P-value (PCI)	P-value[a]
MACCE[b]	26.4% (31)	40.4% (56)	0.022	32.6% (28)	56.2% (49)	0.002	0.37	0.023	0.34
All-cause death/stroke/ myocardial infarction	17.7% (21)	18.8% (26)	0.92	21.0% (18)	32.1% (28)	0.091	0.65	0.018	0.25
All-cause death	12.0% (14)	16.6% (23)	0.32	14.0% (12)	24.1% (21)	0.082	0.70	0.15	0.53
Cardiac death	6.0% (7)	8.9% (12)	0.42	7.1% (6)	18.8% (16)	0.023	0.79	0.030	
Stroke	5.2% (6)	1.6% (2)	0.094	4.0% (3)	5.2% (4)	0.65	0.56	0.13	0.17
Myocardial infarction	5.1% (6)	7.5% (10)	0.49	5.7% (5)	11.6% (9)	0.23	0.83	0.34	0.76
Repeat revascularization	12.0% (13)	29.9% (40)	<0.001	18.1% (15)	44.3% (35)	0.001	0.19	0.063	>0.99
PCI	12.9% (78)	24.8% (33)	0.004	15.0% (12)	34.6% (27)	0.005	0.41	0.21	
CABG	1.1% (7)	7.0% (9)	0.020	3.3% (3)	11.6% (9)	0.064	0.19	0.23	
Graft occlusion/stent thrombosis	5.7% (6)	3.2% (4)	0.35	2.5% (2)	8.6% (7)	0.081	0.30	0.072	0.046

Data are Kaplan–Meier time-to-event estimates expressed as % (n); log-rank P-value.
CABG: coronary artery bypass grafting; MACCE: major adverse cardiac or cerebrovascular events; PCI: percutaneous coronary intervention.
[a]Binary logistic regression interaction term for diabetes status by treatment arm.
[b]MACCE consists of all-cause death, stroke, myocardial infarction or repeat revascularization (CABG or PCI) in any vessel.

RESULTS: In diabetic patients, 5-year rates were significantly higher for PCI vs CABG for MACCE (PCI: 46.5% vs CABG: 29.0%; $P < 0.001$) and repeat revascularization (PCI: 35.3% vs CABG: 14.6%; $P < 0.001$). There was no difference in the composite of all-cause death/stroke/MI (PCI: 23.9% vs CABG: 19.1%; $P = 0.26$) or individual components all-cause death (PCI: 19.5% vs CABG: 12.9%; $P = 0.065$), stroke (PCI: 3.0% vs CABG: 4.7%; $P = 0.34$) or MI (PCI: 9.0% vs CABG: 5.4%; $P = 0.20$). In non-diabetic patients, rates with PCI were also higher for MACCE (PCI: 34.1% vs CABG: 26.3%; $P = 0.002$) and repeat revascularization (PCI: 22.8% vs CABG: 13.4%; $P < 0.001$), but not for the composite end-point of all-cause death/stroke/MI (PCI: 19.8% vs CABG: 15.9%; $P = 0.069$). There were no differences in all-cause death (PCI: 12.0% vs CABG: 10.9%; $P = 0.48$) or stroke (PCI: 2.2% vs CABG: 3.5%; $P = 0.15$), but rates of MI (PCI: 9.9% vs CABG: 3.4%; $P < 0.001$) were significantly increased in the PCI arm in non-diabetic patients.

Conclusions

Both diabetic and non diabetic patients – PCI – higher rate of MACCE and repeat revascularization at 5 years

CABG surgery – choice revascularization for complex anatomy in patients with diabetes mellitus

PCI in Patients with Diabetes Mellitus: Best Treatment Options to be Considered

1. CABG surgery – FREEDOM, SYNTAX
2. PCI – newer generation stents
   - Bioresorbable Vascular Scaffolding (BVS)
   - Moving targets – do we need newer trials?