Diabetic Patients with Multivessel Disease: Stents or Surgery?

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Yoshinobu Onuma
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Coronary artery bypass surgery compared with percutaneous coronary interventions for multivessel disease: a collaborative analysis of individual patient data from ten randomised trials



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Summary

Background Coronary artery bypass graft (CABG) and percutaneous coronary intervention (PCI) are alternative treatments for multivessel coronary disease. Although the procedures have been compared in several randomised trials, their long-term effects on mortality in key clinical subgroups are uncertain. We undertook a collaborative analysis of data from randomised trials to assess whether the effects of the procedures on mortality are modified by patient characteristics.

Lancet 2009; 373:

Stanford University School of Medicine, Stanford, CA, USA (Prof M A Hlatky MD, D B Boothroyd PhD, D M Bravata MD,

Method

We invited the participation of the 13 clinical trials that randomized patients with multivessel coronary disease to either PCI or CABG and that have reported long-term follow-up. Ten trials agreed to provide individual patient data.

For descriptive analyses, we pooled patients from all ten trials and created unadjusted Kaplan-Meier survival curves. For statistical analyses of mortality, we used Cox proportional hazards models stratified by trial that included a gamma frailty term to assess random effects across the ten contributing trials. We tested for interactions of assigned treatment with baseline characteristics using multivariable, stratified Cox models that included treatment assignment, the baseline characteristic of interest, and their interaction. We also tested the significance of these interactions after including other baseline characteristics in the model.

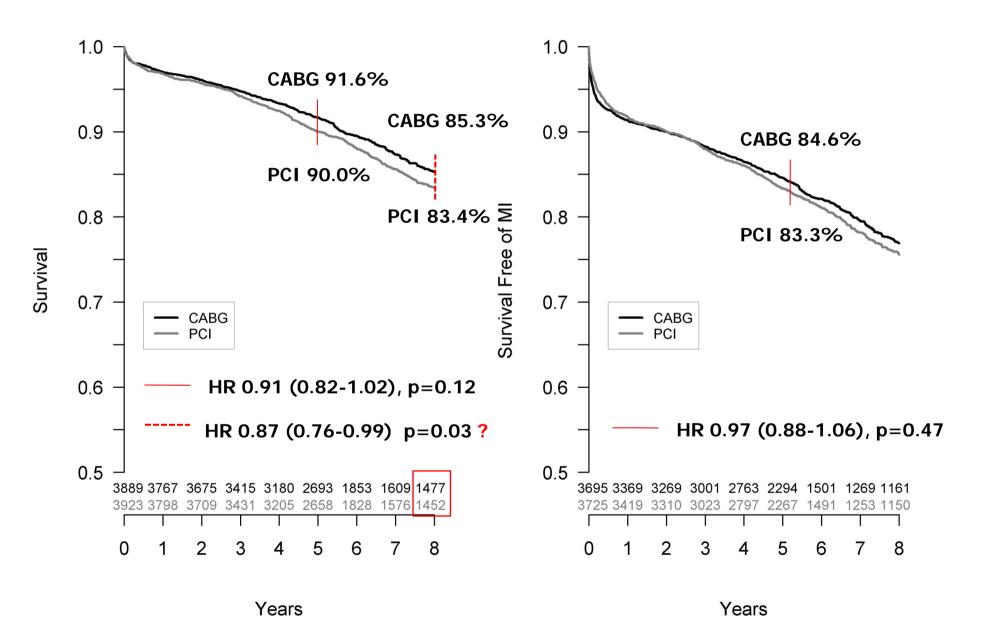
Baseline Characteristics by Study (%)

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Characteristic	Overall	ARTS		CABRI		Ш	GABI	Ш	RITA-1	SoS	Toulouse
Randomized (N)	7812	1205	1829	1054	392	450	323	408	1011	988	152
Age <55	28	28	24	27	24	28	33	32	40	26	9
55-64	37	35	37	42	36	36	40	33	44	34	26
>65	35	38	39	31	40	36	27	35	16	40	66
Female	24	23	27	22	26	21	21	31	19	21	23
Diabetes	16	17	19	12	23	17	13	28	6	14	13
Current Smoking	24	27	25	NA	20	52	11	33	17	15	52
Hypertension	45	45	49	36	53	71	42	62	26	45	42
Hypercholesterolemia	51	58	44	44	40	61	63	79	NA	52	36
Peripheral Vascular											
Disease	10	5	17	7	NA	23	8	0	NA	7	20
Unstable Symptoms	41	37	68	16	NA	92	13	0	NA	20	86
Prior MI	45	43	55	43	41	28	47	47	43	45	38
Heart Failure	3	0	9	0	3	0	0	0	0	6	6
Abnormal LV Function											
Abnormal (of total)	16	16	19	13	16	20	8	3	14	15	9
Data Missing	13	7	3	11	2	1	39	0	45	22	0
Three-Vessel Disease	35	29	41	43	40	49	38	56	12	42	29
Proximal LAD Disease	51	NA	37	61	72	51	28	95	56	46	44
Follow-Up (median)	5.9	5.1	10.4	3	8.2	5	13	5.1	10	6	4.9
Bare Metal Stent use		yes	no	no	no	yes	no	yes	no	yes	no

Comparative Overall 5-Year Clinical Outcomes by Treatment Assigned

Outcome	CABG	PCI	Hazard Ratio	p-value
Survival	91.6 (90.8-92.6)	90.0 (89.1-91.0)	0.91 (0.82-1.02)	0.12
Survival without MI	84.6 (83.4-85.8)	83.3 (82.1-84.6)	0.97 (0.88-1.06)	0.47
Survival without MI, Repeat Revasc	79.9 (78.6-81.3) <u>\</u> <u>\</u> <u>\</u> <u>1</u>	63.6 (62.0-65.2) 6.3	0.52 (0.49-0.57)	<0.001

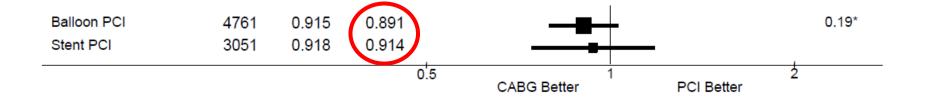
Overall, unadjusted survival and survival free of myocardial infarction after randomization to CABG or PCI



The CABG:PCI hazard ratios within clinical subgroups from a univariate Cox proportional hazards model

Figure 2 Subgroup	5 Year Survival			CABG:PCI Hazard Ratio	Subgroup Interaction p-value
	N	CABG	PCI	1	
No PVD	5713	0.919	0.909		0.33
PVD	665	0.850	0.779		
Stable Symptoms	3740	0.918	0.898		0.30
Unstable Symptoms	2653	0.904	0.889		
No Prior MI	4255	0.926	0.907		0.92
Prior MI	3506	0.905	0.892		

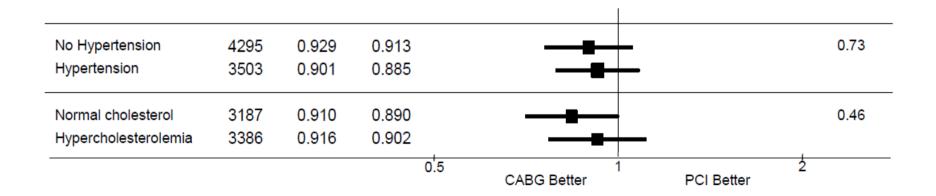
The CABG:PCI hazard ratio in the "balloon-era" trials was 0.91 (CI 0.80 to 1.03) and in the "stent-era" trials was 0.94 (CI 0.74 to 1.18). In a multivariable analysis of pooled data that adjusted for baseline patient characteristics and censored follow-up at five years, there was no significant effect of "stent era" on the treatment comparison of CABG and PCI (p for interaction =0.19).



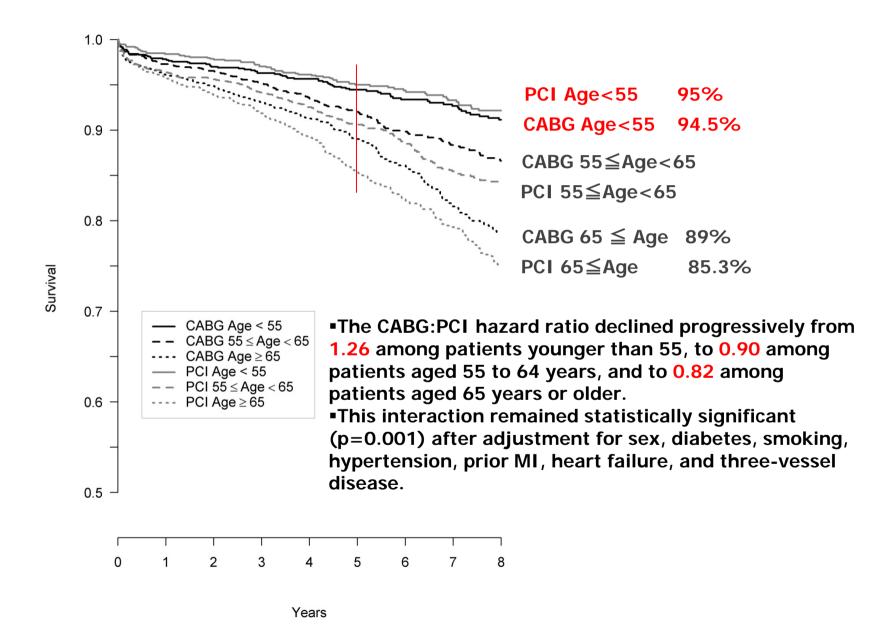
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Figure 2 Subgroup	5 Year Survival			CABG:PCI Hazard Ratio	Subgroup Interaction p-value	
	N	CABG	PCI			
Age < 55	2185	0.945	0.950	+	0.002	
Age 55-64	2933	0.920	0.906			
Age <u>≥</u> 65	2688	0.890	0.853			

•Survival is better after PCI among younger patients and after CABG among older patients.



Overall, unadjusted survival for patients aged 54 years or less, 55 to 64 years, and 65 years or older

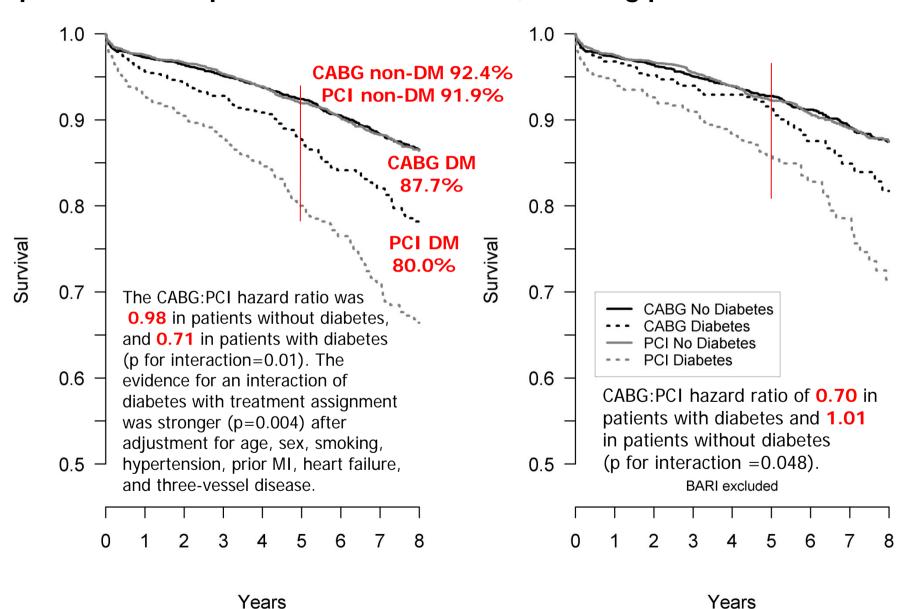


The CABG:PCI hazard ratios within clinical subgroups from a univariate Cox proportional hazards model

<u>Figure 2</u> Subgroup	5 Year Survival			CABG:PCI Hazard Ratio	Subgroup Interaction p-value
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Age 55-64	2933	0.920	0.906		
Age <u>></u> 65	2688	0.890	0.853		
Women	1831	0.904	0.880		0.25
Men	5981	0.920	0.906		
No Diabetes	6561	0.924	0.919		0.014
Diabetes	1233	0.877	0.800	 7	

The CABG:PCI hazard ratio was 0.98 in patients without diabetes, and 0.71 in patients with diabetes (p for interaction=0.01). The evidence for an interaction of diabetes with treatment assignment was stronger (p=0.004) after adjustment for age, sex, smoking, hypertension, prior MI, heart failure, and three-vessel disease. The interaction of diabetes and treatment assignment remained significant after omitting patients enrolled in the BARI trial.

Overall, unadjusted survival for patients with diabetes and without diabetes. The left panel includes patients from all ten trials, and the right panel includes patients from nine trials, omitting patients from the BARI



Meta-analysis of all the trials comparing PCI and CABG

Summary

- The long-term survival (5 years) of patients with multivessel coronary disease randomized to CABG or PCI is not significantly different.
- Patients with diabetes have a significant survival benefit from CABG.
- Survival is better after PCI among younger patients and after CABG among older patients.
- Angina at one year of follow-up was significantly less frequent (p<0.0001) among patients assigned to CABG (13.6%, CI 12.4% to 14.8%) than among patients assigned to PCI (26.4%, CI 24.9% to 28.0%).