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.

Methods We pooled individual patient data from ten randomised trials to compare the effectiveness of CABG with PCI according to patients' baseline clinical characteristics. We used stratified, random effects Cox proportional hazards models to test the effect on all-cause mortality of randomised treatment assignment and its interaction with clinical characteristics. All analyses were by intention to treat.

Findings Ten participating trials provided data on 7812 patients. PCI was done with balloon angioplasty in six trials and with bare-metal stents in four trials. Over a median follow-up of 5·9 years (IQR 5·0–10·0), 575 (15%) of 3889 patients assigned to CABG died compared with 628 (16%) of 3923 patients assigned to PCI (hazard ratio [HR] 0·91, 95% CI 0·82–1·02; p=0·12). In patients with diabetes (CABG, n=615; PCI, n=618), mortality was substantially lower in the CABG group than in the PCI group (HR 0·70, 0·56–0·87); however, mortality was similar between groups in patients without diabetes (HR 0·98, 0·86–1·12; p=0·014 for interaction). Patient age modified the effect of treatment on mortality, with hazard ratios of 1·25 (0·94–1·66) in patients younger than 55 years, 0·90 (0·75–1·09) in patients aged 55–64 years, and 0·82 (0·70–0·97) in patients 65 years and older (p=0·002 for interaction). Treatment effect was not modified by the number of diseased vessels or other baseline characteristics.

Interpretation Long-term mortality is similar after CABG and PCI in most patient subgroups with multivessel coronary artery disease, so choice of treatment should depend on patient preferences for other outcomes. CABG might be a better option for patients with diabetes and patients aged 65 years or older because we found mortality to be lower in these subgroups.

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Introduction

Coronary artery bypass graft (CABG) and percutaneous coronary intervention (PCI) are alternative revascularisation procedures for patients with multivessel coronary artery disease. The effects of these two procedures on patient outcomes (mortality, myocardial infarction, angina symptoms, repeat procedures) over long-term follow-up have been compared in several randomised clinical trials,[1–12] in analyses of large clinical registries,[13–17] and in meta-analyses of the published trial results.[18–20] However, the outcomes of the procedures might vary according to patient characteristics, such as the presence of diabetes or the number of diseased vessels. This possibility has been difficult to assess because no randomised trial has been large enough to provide adequate statistical power, meta-analyses in patient subgroups have been limited by inconsistent reporting in published trials,[20] and observational studies have been confounded by treatment selection biases.

Pooling of individual patient data from randomised trials substantially increases the number of patients within clinical subgroups of interest and provides a more precise assessment of the effects of treatment.[21–24] Previous collaborations among clinical trial groups have provided information about variation in the efficacy of other cardiovascular treatments according to baseline clinical characteristics.[25,26] We undertook a collaborative analysis of data from randomised trials of patients with multivessel coronary artery disease to assess whether the effects of CABG and PCI on mortality are modified by patient characteristics.

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Methods

Patients and procedures

Details of the search strategy that was used to identify relevant trials for inclusion in this collaborative analysis have been reported elsewhere.[20] Briefly, we searched Medline, Embase, and Cochrane databases for studies published between January, 1966, and August, 2006, by use of terms including "angioplasty", "coronary", and "coronary artery bypass surgery". We also reviewed the reference lists of retrieved articles, conference abstracts, and the bibliographies of expert advisers. We did not limit the searches to the English language. Clinical trials that randomly assigned patients with multivessel coronary artery disease to either CABG or PCI and that reported at least 3 years of follow-up were eligible for inclusion. We excluded trials that compared either method alone with medical therapy, those that compared two forms of PCI, and those that compared two forms of CABG. All included trials were reviewed and approved by ethics committees.

We identified 12 eligible trials; the principal investigators of these studies were invited to participate in this collaborative analysis.[1–12] Investigators from ten of the trials[1–10] provided individual patient data on a set of core clinical variables consisting of demographics (age, sex, and ethnicity), cardiac risk factors (diabetes, smoking, hypertension, and hypercholesterolaemia), clinical manifestations (stable or unstable symptoms, history of myocardial infarction, heart failure, previous PCI, previous CABG, and peripheral vascular disease), angiographic factors (abnormal left ventricular function, number of diseased vessels, and disease of the proximal left anterior descending coronary artery), randomised treatment assignment, and outcomes in follow-up (death, myocardial infarction, stroke, repeat revascularisation, last follow-up contact, and angina). We recoded data from each trial in a uniform format after resolution of data queries and checked data summaries from individual trials against the associated publications for accuracy.

The primary outcome measure of this study was all-cause mortality over all available follow-up, and the principal research question was whether survival after random assignment to CABG or PCI was modified by patients' baseline clinical characteristics.

Statistical analysis

All analyses followed the intention-to-treat principle. For descriptive analyses, we pooled individual patient data 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[24] that included a gamma frailty term to assess random effects across the ten contributing trials.[27] We tested for interactions of assigned treatment with baseline characteristics by use of 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.

We undertook several analyses to test the sensitivity of results to various assumptions and model specifications. Since length of follow-up varied among the trials, we tested for any differences in the hazard ratio (HR) for CABG versus PCI as a function of follow-up time (0–3 years, 3–6 years, 6–9 years, and >9 years) in a stratified Cox model. Additionally, we checked for any violation of the proportional hazards assumption by testing for a correlation with follow-up time of scaled Schoenfeld residuals. We tested the effect of diabetes on mortality with and without inclusion of the trial that had previously shown an effect of diabetes on survival in patients randomised to CABG and PCI.[28] We also assessed whether the method of PCI used in the trial (ie, balloon angioplasty or bare-metal coronary stents) had an effect on treatment outcome. Statistical analyses were done with SAS version 9.1 and R version 2.4.0.

Role of the funding source

The sponsor of the study had no role in the study design, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit the manuscript for publication.

Results

The ten participating trials provided data on 7812 patients. The median age of the study population was 61 years (IQR 53–67), with 389 (5%) patients aged 75 years or older (only 19 patients were aged 80 years or older). Table 1 shows the baseline characteristics of patients included in the trials. Median follow-up time in surviving patients was 5·9 years, and varied among trials from 3·0 years to 13·0 years (table 1).

Most patients received the assigned treatment within 60 days of randomisation. Within 90 days of randomisation, 75 (2%) of 3889 patients assigned to CABG died, compared with 74 (2%) of 3923 patients assigned to PCI (p=0·89). The composite endpoint of death or myocardial infarction within 90 days, which could be assessed in nine trials,[1–3,5–10] occurred in 240 (6%) of 3695 patients in the CABG group and 201 (5%) of 3725 patients in the PCI group (p=0·045). Data on stroke within 90 days of randomisation were available from seven trials:[1,5–10] 26 (1%) of 2268 patients assigned to CABG had a stroke compared with 12 (0·5%) of 2269 patients assigned to PCI (p=0·02).

Overall mortality was similar between treatment groups (figure 1); 575 (15%) of 3889 patients died in the CABG group compared with 628 (16%) of 3923 patients in the PCI group (HR for mortality 0·91, 95% CI 0·82–1·02; p=0·12; table 2). There was no evidence of a treatment–time interaction—ie, the proportional hazards assumption was not violated.

	Overall (N=7812)	ARTS[1] (N=1205)	BARI[2] (N=1829)	CABRI[3] (N=1054)	EAST[4] (N=392)	ERACI-II[5] (N=450)	GABI[6] (N=323)	MASS-II[7] (N=408)	RITA-1[8] (N=1011)	SoS[9] (N=988)	Toulouse[10] (N=152)
Age											
<55 years	2185 (28%)	332 (28%)	442 (24%)	286 (27%)	94 (24%)	124 (28%)	107 (33%)	131 (32%)	403 (40%)	253 (26%)	13 (9%)
55–64 years	2933 (38%)	420 (35%)	678 (37%)	443 (42%)	143 (36%)	163 (36%)	130 (40%)	135 (33%)	442 (44%)	340 (34%)	39 (26%)
≥65 years	2688 (34%)	453 (38%)	709 (39%)	320 (31%)	155 (40%)	162 (36%)	86 (27%)	142 (35%)	166 (16%)	395 (40%)	100 (66%)
Female	1831 (23%)	283 (23%)	489 (27%)	234 (22%)	103 (26%)	93 (21%)	67 (21%)	125 (31%)	196 (19%)	206 (21%)	35 (23%)
Diabetes	1233 (16%)	208 (17%)	353 (19%)	124 (12%)	90 (23%)	78 (17%)	41 (13%)	115 (28%)	62 (6%)	142 (14%)	20 (13%)
Current smoker	1665 (25%)	323 (27%)	463 (25%)	NA	79 (20%)	233 (52%)	36 (11%)	134 (33%)	169 (17%)	149 (15%)	79 (52%)
Hypertension	3503 (45%)	540 (45%)	896 (49%)	378 (36%)	206 (53%)	318 (71%)	136 (42%)	253 (62%)	265 (26%)	447 (45%)	64 (42%)
Hypercholesterolaemia	3386 (52%)	694 (58%)	725 (44%)	460 (44%)	146 (40%)	275 (61%)	201 (63%)	322 (79%)	NA	509 (52%)	54 (36%)
Peripheral vascular disease	665 (10%)	64 (5%)	303 (17%)	72 (7%)	NA	103 (23%)	26 (8%)	0 (0%)	NA	66 (7%)	31 (20%)
Unstable symptoms	2653 (41%)	451 (37%)	1250 (68%)	166 (16%)	NA	412 (92%)	41 (13%)	0 (0%)	NA	202 (20%)	131 (86%)
Previous myocardial infarction	3506 (45%)	520 (43%)	987 (55%)	439 (43%)	160 (41%)	126 (28%)	150 (47%)	191 (47%)	428 (43%)	448 (45%)	57 (38%)
Heart failure	245 (3%)	0 (0%)	161 (9%)	0 (0%)	13 (3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	62 (6%)	9 (6%)
Abnormal left ventricular function	1166 (17%)	189 (17%)	341 (19%)	138 (15%)	63 (16%)	88 (20%)	25 (13%)	13 (3%)	142 (26%)	153 (20%)	14 (9%)
Three-vessel disease	2853 (37%)	338 (29%)	754 (41%)	449 (43%)	156 (40%)	219 (49%)	119 (38%)	230 (56%)	125 (12%)	419 (42%)	44 (29%)
Proximal LAD disease	3391 (51%)	NA	668 (37%)	638 (61%)	283 (72%)	230 (51%)	92 (28%)	389 (95%)	567 (56%)	457 (46%)	67 (44%)
Follow-up (years)	5·9 (5·0–10·0)	5·1 (5·0–5·3)	10·4 (10·0–11·0)	3·0 (2·4–3·7)	8·2 (8·2–8·2)	5·0 (5·0–5·0)	13·0 (12·1–14·5)	5·1 (5·1–5·2)	10·0 (10·0–10·0)	6·0 (5·5–6·7)	4·9 (4·0–5·7)
Stent use in PCI*	1432 (37%)	580 (98%)	9 (1%)	0 (0%)	0 (0%)	221 (100%)	0 (0%)	157 (82%)	0 (0%)	465 (97%)	0 (0%)
IMA use in CABG†	2573 (83%)	539 (93%)	729 (82%)	NA	NA	198 (96%)	62 (39%)	188 (95%)	364 (74%)	451 (93%)	42 (55%)

ARTS=Arterial Revascularization Therapies Study. BARI=Bypass Angioplasty Revascularization Investigation. CABRI=Coronary Angioplasty versus Bypass Revascularisation Investigation. CABG=coronary artery bypass graft. EAST=Emory Angioplasty versus Surgery Trial. ERACI=Argentine Randomised Trial of Coronary Angioplasty Versus Bypass Surgery in Multivessel Disease. GABI=German Angioplasty Bypass Surgery Investigation. IMA=internal mammary artery. LAD=left anterior descending artery. MASS=Medicine, Angioplasty, or Surgery Study. NA=not available. RITA=Randomised Intervention Treatment of Angina trial. SoS=Stent or Surgery trial. Data are n (%) or median (IQR). The number of randomised patients in each trial (N) is shown. Patients with missing data were omitted from the calculation of percentages for baseline characteristics. For trials from which data were available, between 0 and 51 (0·7%) patients had missing values on baseline characteristics, apart from hypercholesterolaemia (228 missing values) and left ventricular function (1066 missing values). Definitons for hypertension and hypercholesterolaemia differed among the trials. *Stent use in 3841 patients assigned to PCI who received this treatment. †Eight trials provided individual patient data on IMA use, in which 3087 patients assigned to CABG received this treatment. The CABRI trial[3] previously reported 81% use of IMA grafts.

Table 1: **Baseline characteristics by study**

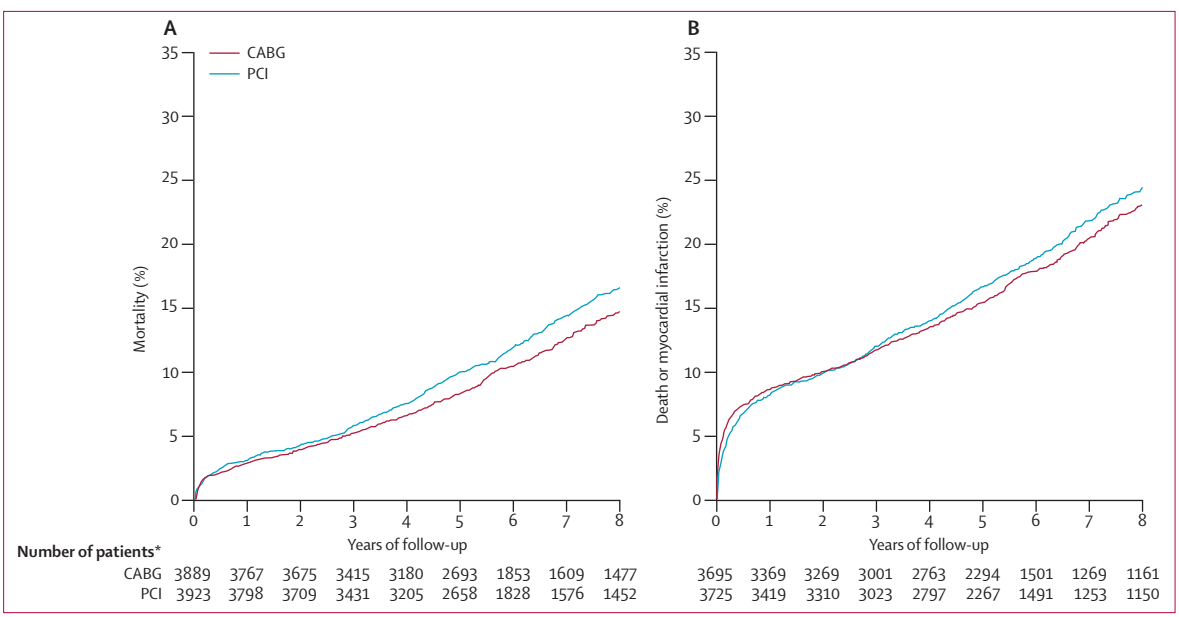

Figure 1: **Outcomes of treatment with coronary artery bypass graft or percutaneous coronary intervention**
CABG=coronary artery bypass graft. PCI=percutaneous coronary intervention. *Number of patients available for follow-up. Data show overall unadjusted mortality (A) and composite endpoint of death or myocardial infarction (B) after randomisation to CABG or PCI. Data on death with myocardial infarction were not available from the Emory Angioplasty versus Surgery Trial.[4]

Several secondary endpoints could be assessed in most, but not all, trials (table 2). The composite endpoint of death or myocardial infarction was not significantly different between treatment groups (figure 1). The composite outcome of death or repeat revascularisation was significantly lower (p<0·0001) in patients assigned to CABG than in patients assigned to PCI (table 2). Angina at 1 year of follow-up was significantly less frequent (p<0·0001) in the CABG group (439 [14%] of 3228 patients) than in the PCI group (856 [26%] of 3240 patients; difference 13%, 95% CI 11–15).

Treatment effect was not modified by clinical characteristics, apart from diabetes and age (figure 2). Of the 1233 patients with diabetes, 143 (23%) of 615 patients assigned to CABG died, compared with 179 (29%) of 618 patients assigned to PCI (figure 3). By contrast, of the 6561 patients without diabetes, 432 (13%) of 3263 patients and 448 (14%) of 3298 patients died, respectively (p=0·014 for interaction). The interaction of diabetes with treatment remained after adjustment for age, sex, smoking, hypertension, history of myocardial infarction, heart failure, and three-vessel disease (p=0·008), and also after exclusion of patients enrolled in the Bypass Angioplasty Revascularization Investigation (BARI) trial[28] (HR 0·68, 0·47–0·95, in

	5-year event rate (% [95% CI])		Hazard ratio (95% CI)*	p value
	CABG	PCI		
Death	8·4% (7·4–9·2)	10·0% (9·0–10·9)	0·91 (0·82–1·02)	0·12
Death or myocardial infarction†	15·4% (14·2–16·6)	16·7% (15·4–17·9)	0·97 (0·88–1·06)	0·47
Death or repeat revascularisation‡	9·9% (8·9–10·9)	24·5% (23·0–26·0)	0·41 (0·37–0·45)	<0·0001
Death, myocardial infarction, or repeat revascularisation§	20·1% (18·7–21·4)	36·4% (34·8–38·0)	0·52 (0·49–0·57)	<0·0001

Event rates are unadjusted, 5-year Kaplan-Meier estimates. *Hazard ratios for coronary artery bypass graft (CABG) versus percutaneous coronary intervention (PCI) are based on the full duration of follow-up from all trials. †No data were available on myocardial infarction from the Emory Angioplasty versus Surgery Trial (EAST).[4] ‡No data were available on repeat revascularisation from the Toulouse trial.[10] §No data were available from the EAST[4] and Toulouse[10] trials.

Table 2: **Overall clinical outcomes by treatment assignment**

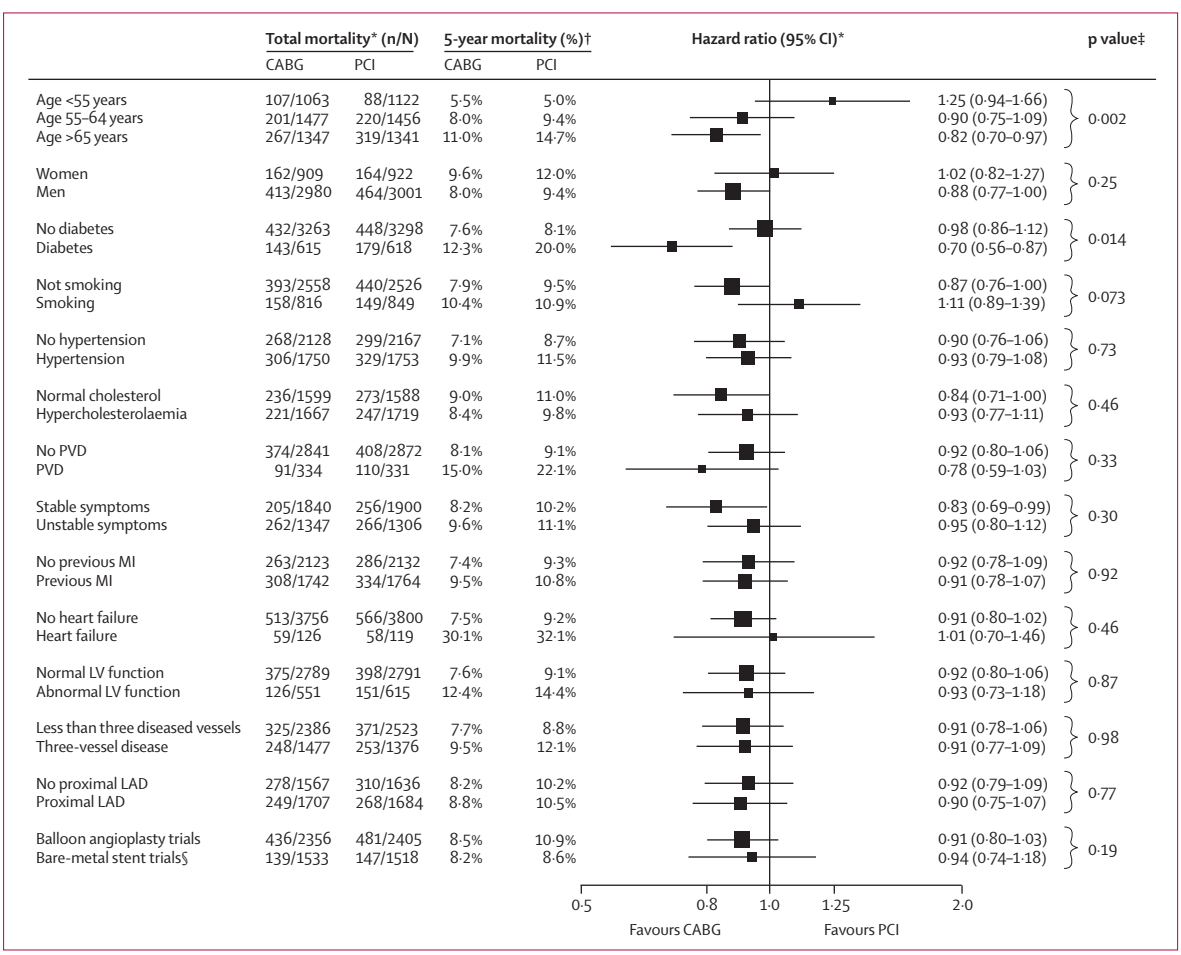

Figure 2: **Subgroup analyses for mortality after treatment with coronary artery bypass graft or percutaneous coronary intervention**
CABG=coronary artery bypass graft. LAD=left anterior descending artery. LV=left ventricular. MI=myocardial infarction. PCI=percutaneous coronary intervention. PVD=peripheral vascular disease. The vertical line indicates a hazard ratio of 1·0, equivalent to no difference between treatment groups. *Based on on the full duration of follow-up in all trials. †Pooled unadjusted 5-year Kaplan-Meier survival rates. ‡p value for the treatment by covariate interaction. §The analysis that compares patients enrolled in balloon angioplasty trials[2–4,6,8,10] and bare-metal stent trials[1,5,7,9] is pooled and not stratified by study.

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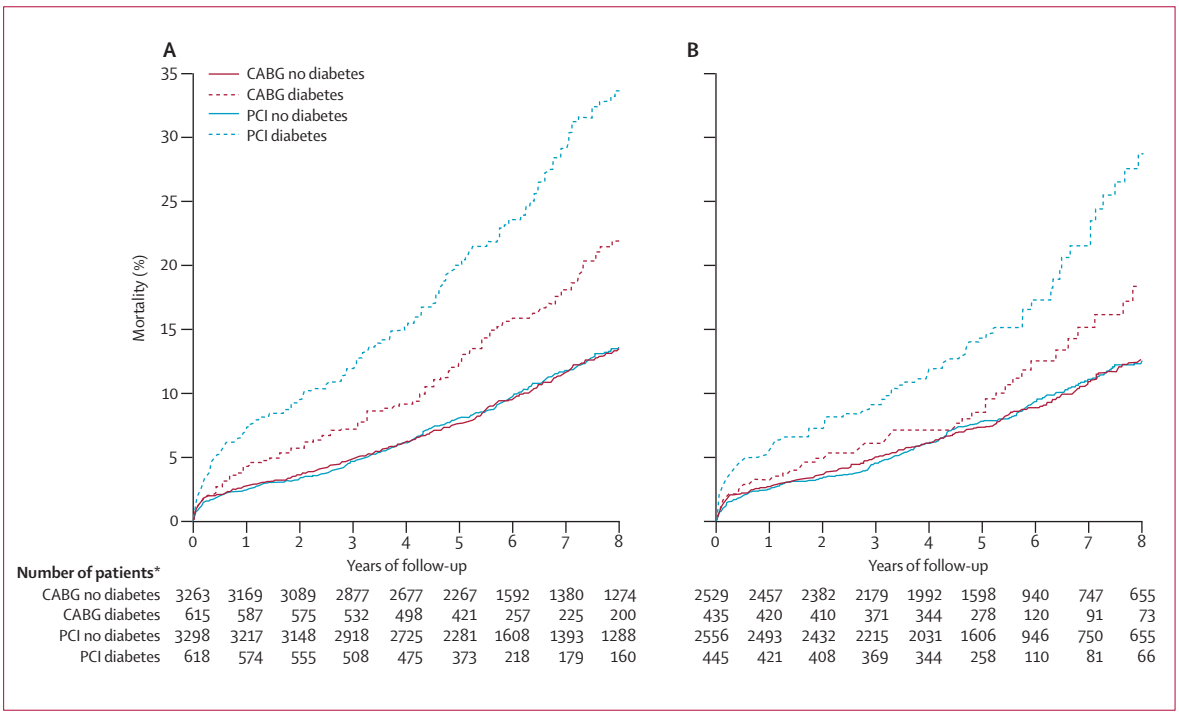

***Figure 3*: Mortality in patients assigned to coronary artery bypass graft or percutaneous coronary intervention by diabetes status**
CABG=coronary artery bypass graft. PCI=percutaneous coronary intervention. *Number of patients available for follow-up. Data show overall unadjusted mortality rates for patients with diabetes and without diabetes. Panel A includes patients from all ten trials. Panel B excludes patients from the Bypass Angioplasty Revascularization Investigation trial.[2]

patients with diabetes; HR 1·01, 0·85–1·20, in patients without diabetes; p=0·048 for interaction; figure 3).

Patient age had a graded effect on mortality after CABG or PCI (p=0·002 for interaction with age as a continuous variable; figure 2 and figure 4). 107 (10%) of 1063 patients younger than 55 years who were assigned to CABG died compared with 88 (8%) of 1122 patients assigned to PCI. 201 (14%) of 1477 patients aged 55–64 years in the CABG group died compared with 220 (15%) of 1456 patients in the PCI group. In patients aged 65 years and older, mortality was 20% (267 of 1347 patients) for CABG and 24% (319 of 1341 patients) for PCI. The interaction between age and treatment effect remained after adjustment for sex, diabetes, smoking, hypertension, history of myocardial infarction, heart failure, and three-vessel disease (p=0·002).

In the six earliest trials,[2–4,6,8,10] PCI was done with balloon angioplasty, whereas in the four more recent trials, the procedure was done with bare-metal stents.[1,5,7,9] Most baseline clinical characteristics differed significantly (p<0·0001) between patients in the two types of trial (table 3). There was no significant difference in survival between CABG and PCI groups when assessed by bare-metal stent or balloon angioplasty (figure 2). In the six balloon angioplasty trials, 436 (19%) of 2356 patients died in the CABG group compared with 481 (20%) of 2405 patients in the PCI group, whereas in the bare-metal stent trials 139 (9%) of 1533 patients and 147 (10%) of 1518 patients died,

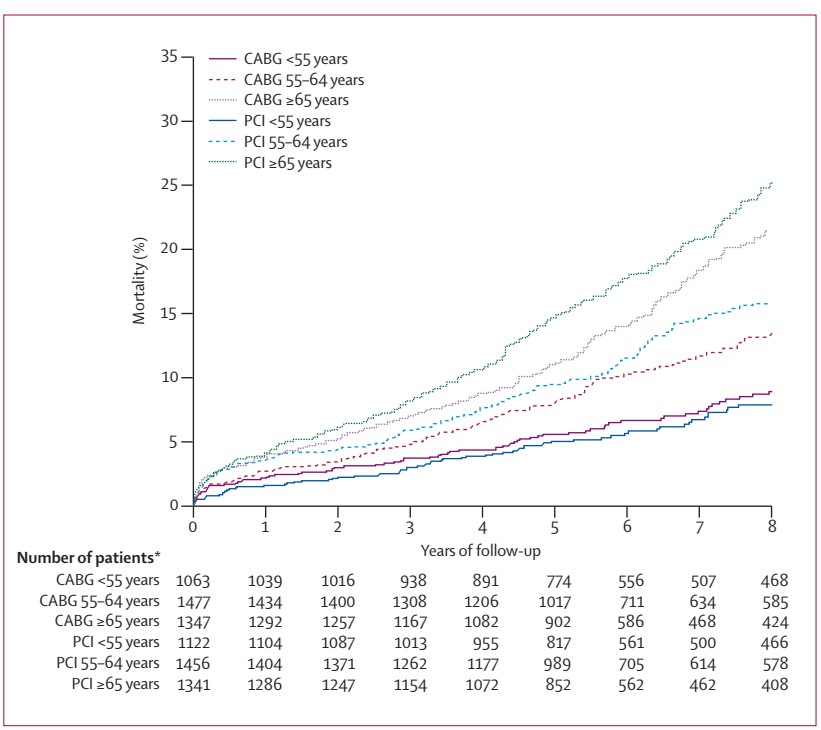

***Figure 4*: Mortality in patients assigned to coronary artery bypass graft or percutaneous coronary intervention by age**
CABG=coronary artery bypass graft. PCI=percutaneous coronary intervention. *Number of patients available for follow-up. Data show overall unadjusted mortality rates for patients aged less than 55 years, 55–64 years, and 65 years or older.

	Balloon angioplasty trials[2–4,6,8,10] (N=4761)	Bare-metal stent trials[1,5,7,9] (N=3051)	p value
Age			
<55 years	1345 (28%)	840 (28%)	<0·0001
55–64 years	1875 (39%)	1058 (35%)	..
≥65 years	1536 (32%)	1152 (38%)	..
Female	1124 (24%)	707 (23%)	0·66
Diabetes	690 (15%)	543 (18%)	0·0001
Current smoker	826 (22%)	839 (28%)	<0·0001
Hypertension	1945 (41%)	1558 (51%)	<0·0001
Hypercholesterolaemia	1586 (45%)	1800 (59%)	<0·0001
Peripheral vascular disease	432 (13%)	233 (8%)	<0·0001
Unstable symptoms	1588 (48%)	1065 (35%)	<0·0001
Previous myocardial infarction	2221 (47%)	1285 (42%)	<0·0001
Heart failure	183 (4%)	62 (2%)	<0·0001
Abnormal left ventricular function	723 (18%)	443 (16%)	0·04
Three-vessel disease	1647 (35%)	1206 (40%)	<0·0001
Proximal LAD disease	2315 (49%)	1076 (58%)	<0·0001

LAD=left anterior descending artery. Data are n (%). Patients with missing data were omitted from the calculations of percentages for baseline characteristics.

Table 3: **Clinical characteristics before randomisation to treatment by percutaneous coronary intervention method used in the trial**

respectively (figure 2). In a multivariable analysis of pooled data that adjusted for baseline patient characteristics and restricted length of follow-up to a maximum of 5 years, there was no significant effect of trial use of bare-metal stents on the treatment comparison of CABG and PCI (p=0·19 for interaction). The interactions of diabetes and age with treatment assignment that were present in the overall population were evident in both balloon angioplasty and bare-metal stent trials (data not shown).

Discussion

Randomised clinical trials provide the reference standard for comparing the effectiveness of treatments for a given clinical condition. The effectiveness of treatments might vary among patients included in randomised trials, but this possibility cannot be tested adequately in a single study because of limited statistical power. Combining individual patient data from several randomised trials helps to overcome this limitation by increasing the number of patients available for analysis in clinical subgroups, thus enhancing statistical power.

Our combined analysis of individual patient data from ten randomised trials suggests that diabetes and age modify the effect of CABG compared with PCI on the survival of patients with multivessel coronary disease. Treatment effect was not altered by other patient characteristics, including the number of diseased coronary vessels, despite observational data strongly suggesting that this factor would modify the effectiveness of coronary revascularisation.[13,14,16] The pooled data provide more precise estimates of the overall effect of CABG and PCI on long-term survival, both overall and within clinical subgroups.

The BARI trial[28] was the first to report that patients with diabetes had substantially better survival after CABG than after PCI. This result was not universally accepted, since analyses of large clinical registries did not confirm this effect;[29,30] similarly, other, smaller randomised clinical trials were unable to replicate the BARI trial findings.[4,6,8,31] Our analysis is based on pooled data from 1233 randomised patients with diabetes and provides strong evidence that survival is substantially higher after CABG than PCI for the treatment of multivessel disease. This finding is not a result of the inclusion of the BARI trial,[2] since a significant interaction of diabetes with treatment assignment remained after exclusion of that trial. Nor is our result explained by the adverse clinical risk profile of patients with diabetes, because it remained significant after adjustment for other baseline clinical characteristics. Despite the strength of our finding, it is important to note that coronary revascularisation and background medical treatment have continued to advance since the trials in this study were done. Further evidence in this long-running debate will be provided by the results of current trials of the procedures in patients with diabetes.[32,33]

Our finding that patient age modifies the relative effectiveness of CABG and PCI on survival has not previously been reported by individual randomised trials. The interaction of age with assigned treatment might be mediated by the more favourable clinical characteristics in younger patients; however, we found that the effect persisted after multivariable adjustment for such characteristics. One potential interpretation of this finding is that younger patients might benefit more from initial PCI than from CABG because the latter treatment could be done at a more appropriate time in the course of their disease. Another potential interpretation is that older age might be a marker for more severe disease that was otherwise unmeasured and that might respond better to CABG. It is important to emphasise that few patients in this study were 75 years or older, and the older patients randomised in these trials might have been more highly selected.

Observational comparisons of CABG with PCI suggest a strong relation between the extent of coronary disease and the relative effectiveness of these procedures on survival.[13,14,16] In particular, clinical registry studies have reported that patients with the least extensive coronary disease have better survival after PCI, whereas patients with the most extensive disease have better survival after CABG.[13] Contrary to these observational data and to our previous hypothesis, we found no significant interaction between the number of diseased vessels and treatment effect. An association might have been found if we had been able to analyse a more detailed measure of extent of disease, such as the Duke[13] or SYNTAX[34] scores. However, a count of diseased vessels was the only measure available from all ten trials. The extent of disease in patients

eligible for randomisation might also have fallen into a narrow range in which CABG and PCI yield equivalent results.[13] Additionally, the results of observational studies might represent the residual effects of selection bias rather than a true variation in clinical effectiveness, since the extent of coronary disease is the strongest clinical factor affecting the choice between CABG and PCI for coronary revascularisation.[17]

The techniques of the procedures investigated here continue to be refined over time, and coronary stents in particular have been widely adopted for PCI. Six of the trials included in this analysis were done before the introduction of coronary stents,[2–4,6,8,10] whereas the remaining four studies[1,5,7,9] were done after bare-metal stents became available. We attempted to assess whether the results of the earlier trials differed from those of the subsequent trials. This analysis was difficult because stent use was completely confounded with patient enrolment in specific trials. There were also many other differences between these trials, including important differences in baseline clinical characteristics (table 3). We found that the effect of CABG compared with PCI on survival did not differ between balloon angioplasty and bare-metal stent trials. This result is consistent with the findings from meta-analyses of randomised trials that showed no significant difference in survival, despite significant reductions in the rate of repeat revascularisation procedures, between balloon angioplasty PCI and bare-metal stents,[35] or between bare-metal stents and drug-eluting stents.[36]

Our study shows that the pooling of individual patient data from randomised trials to assess treatment has advantages over the more common technique of meta-analysis of published aggregate data. Most clinical trials do not publish results in key subgroups of interest,[20] and even when they do, the data are typically presented in different ways and are difficult to combine in a meta-analysis. Pooling of individual patient data overcomes these limitations, and also allows use of more sensitive statistical methods, including analysis of survival times, use of multivariable models, and tests for treatment-by-covariate interactions. However, this technique poses logistical challenges and requires collaboration among trial groups and support from funding agencies; thus, it has not been used as often as meta-analysis of published data. Our experience suggests that collaborative analysis could be used more often, especially to assess subgroup effects that are difficult to address in one trial.

Our study has several limitations. We were not able to obtain data from two smaller trials of CABG and PCI that enrolled 359 patients with multivessel disease,[11,12] but we did analyse data from 95% of all randomised patients, and believe our results would be unlikely to change if these smaller trials were included. We have no data on concomitant drug treatment or on control of coronary risk factors during follow-up.

Our analysis shares the underlying limitations of the ten participating trials, which excluded some patients of interest (eg, those with previous CABG or PCI), and did not have adequate representation of others (eg, patients aged 75 years and older or patients with reduced left ventricular function). The participating studies selected patients in whom either treatment would be technically feasible and for whom either would be a reasonable clinical option. Consequently, patients with extensive three-vessel disease or left main coronary artery disease were generally excluded because CABG would be the most appropriate treatment, and patients with limited single-vessel disease were excluded because PCI would be most appropriate. Therefore, our findings should not be extrapolated to all patients with coronary disease; they apply only to patients for whom either CABG or PCI is a reasonable therapeutic option and to patients similar to those enrolled in the contributing trials.

None of the ten trials included in this study used drug-eluting stents for PCI. Although clinical trials have shown equivalent rates of mortality and myocardial infarction after randomisation to either bare-metal stents or drug-eluting stents,[36] trials that compare CABG with PCI by use of drug-eluting stents are still in progress.[33,37] The recently reported 1-year follow-up from the SYNTAX trial,[37] which showed no significant difference in the combined endpoint of death, myocardial infarction, or stroke between patients randomly assigned to CABG or to PCI with drug-eluting stents, are generally consistent with the results of our combined analysis.

Thus, pooled data from ten long-term randomised trials of patients with multivessel coronary disease suitable for either CABG or PCI suggest that patients with diabetes, and older patients, might have a significant survival advantage if treated with CABG.

Contributors

MAH, DBB, DMB, KMM, and DKO designed the collaborative analysis. The individual patient data were collected and prepared for analysis by the investigators representing the ten participating trials: EB, PS (ARTS);[1] MMB, SFK (BARI);[2] ND (CABRI);[3] SBK, ASK (EAST);[4] AR (ERACI-II);[5] CWH, JK (GABI);[6] WAH, NL (MASS-II);[7] TCC, SJP (RITA-I);[8] JB, TCC, MF, US, RHS (SoS);[9] and DC (Toulouse).[10] DBB and MAH participated in data analysis. MAH drafted the manuscript. All authors reviewed and revised the manuscript, and approved the final version.

Conflict of interest statement

The authors declare research support from Boston Scientific (SJP, RHS, TCC), Cordis (RHS, MF), Eli Lilly (MF), Medtronic (RHS, MF), Boehringer Ingleheim (RHS), Pfizer (ND), Sanofi-Aventis (MF), and Servier (ND); serving as consultants or on advisory boards to Boston Scientific (RHS), Medtronic (RHS), Cordis (RHS), Abbot (RHS), Eli Lilly (RHS), and Sanofi-Aventis (RHS); and receiving speaking fees from AstraZeneca (ND), Boston Scientific (RHS), Medtronic (RHS), Cordis (RHS, ND), Eli-Lilly (RHS, ND), Sanofi-Aventis (RHS, ND), Bristol Myers Squibb (RHS, ND), Boehringer Ingleheim (RHS, ND), GlaxoSmithKline (ND), Novartis (ND), Pfizer (ND), Servier (ND), MSD (ND), and Takeda (ND). All other authors declare that they have no conflict of interest.

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