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Adverse events following percutaneous and surgical coronary revascularisation: Analysis of non-MACE outcomes in the Stent or Surgery (SoS) Trial☆

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ABSTRACT

Objectives: To analyse adverse events requiring or prolonging hospitalisation in the Stent or Surgery (SoS) trial.
Background: Many adverse events following coronary revascularisation are non-major adverse cardiovascular events (non-MACE). Trials comparing percutaneous coronary intervention (PCI) and coronary artery bypass surgery (CABG) have reported rates of mortality and MACE only.
Material and methods: Comparisons between PCI and CABG groups in the SOS trial were by intention to treat. For patients with non-fatal/non-MACE, number of events per 100 patient years follow-up and duration of hospital stay were assessed. Competing risk analysis was used to illustrate temporal pattern of adverse outcomes.
Results: During 2y median follow up, 1 one or more adverse event occurred in 47.3% (231) of the PCI group and 53% (265) of the CABG group ($p = 0.086$). Non-fatal/non-MACE occurred in 11.9% of the PCI group and 38.6% of the CABG group ($p < 0.001$). Non-fatal/non-MACE per 100 patient years follow-up was 17.49 (PCI) and 35.04 (CABG), rate ratio 2.0, 95% CI 1.7 to 2.4, $p < 0.001$. Cumulative non-fatal/non-MACE associated hospital stays were 1387 and 3287 days in PCI and CABG groups respectively. Median duration of hospitalisation per non-fatal/non-MACE was 5 days (interquartile range 2 to 11.75 days) in the PCI group and 6 days (interquartile range 2 to 12 days) in the CABG group, $p = 0.245$.
Conclusions: CABG had lower cumulative incidence of fatal or MACE outcomes, higher cumulative incidence of non-fatal/non-MACE outcomes, and longer cumulative hospitalisation periods compared to the PCI group.

1. Introduction

The optimum revascularisation strategy in patients with multivessel coronary artery disease remains a subject of debate [1–5]. Studies comparing percutaneous coronary intervention (PCI) and coronary artery bypass surgery (CABG) have reported major adverse cardiovascular event (MACE) rates as principal outcome measures [5–10]. This selective focus does not allow a full appreciation of the impact of different treatments on patients and healthcare systems. Randomised trial based exploration and quantification of the full range of clinical outcomes following different revascularisation strategies have been limited. No trial has reported a specific evaluation of the full range of non-MACE outcomes.

We present an analysis of non-fatal/non-MACE adverse events occurring during follow-up of patients enrolled in the SoS trial to provide a more complete and evidence-based appreciation of the morbidity associated with percutaneous and surgical revascularisation.

2. Material and methods

2.1. Trial design

The design and principal results of the SoS trial have been published [6,11–14]. In summary, this was a multinational randomised controlled trial comparing PCI and CABG. Symptomatic patients with documented multivessel coronary artery stenosis were eligible if the cardiologist and surgeon agreed that revascularisation by either technique was both clinically indicated and feasible. Coexisting disease of the valves or great vessels requiring interventional treatment were grounds for exclusion. The primary outcome was the rate of repeat revascularisation and secondary outcomes were death and myocardial infarction, all-cause mortality, symptoms of angina, cardiac medication requirements, and left ventricular function. The trial recruited patients between 1996 and 1999, with follow up from randomization of between 1 and 4 years. Bare metal stents were used for percutaneous interventions and standard surgical techniques of the time were employed for CABG. Surgical revascularisation was almost exclusively on-pump.

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Ethical approval was granted in all recruiting centres, and all patients gave written informed consent.

2.2. Adverse events

Clinical events requiring or prolonging hospitalisation were recorded from randomisation onwards, with routine follow-up at 6 and 12 months, and then annual follow-up until trial closure. A clinical events committee adjudicated all outcomes, blinded to the treatment centre and randomisation allocation. For the present analysis, which was not pre-specified in the trial outline, adverse events in the CABG and PCI groups were compared on a number of levels. Firstly, a simple count of all adverse events was made, followed by generation of cumulative incidence curves using competing risks analysis to illustrate temporal occurrence of first adverse event per patient in each group. Secondly, non-fatal/non-MACE adverse events were selectively analysed. These included new or prolonged hospitalisations for any adverse event except death, myocardial infarction, ventricular tachycardia/ventricular fibrillation/cardiac arrest, coronary revascularisation, cardiac failure, stroke or transient cerebral ischaemia. Simple comparisons were made on the basis of the number of patients in each group suffering non-fatal/non-MACE and the number of such events per 100 patient years of follow-up in each group.

2.3. Hospitalisation for adverse events

Hospitalisations associated with adverse event occurrence were evaluated with respect to the number of occurrences per group and associated duration of hospital stay. Cases where more than one adverse event occurred during the same hospitalisation were identified in order to ensure that hospital stay duration was not duplicated. Median and cumulative duration of hospital stay associated with non-fatal/non-MACE was calculated for each randomisation group.

2.4. Statistical analysis

Parametric data are expressed as means with standard deviations. Non-parametric data are expressed as medians with inter-quartile ranges. Simple proportions are compared with Chi square testing. Cumulative incidence rates are compared using rate ratios with associated 95% confidence intervals. Non-parametric data are compared using the Mann Whitney *U* test. Cumulative incidence curves were generated using competing risks analysis and Gray's test. All p values are 2-tailed with a significance threshold of 0.05. Analysis is by intention to treat.

3. Results

3.1. Trial population

Four hundred and eighty-eight patients were randomised to PCI and 500 to CABG. Of those randomised to PCI, 1 patient died before treatment and 7 crossed over to surgical revascularisation. Of the 500 patients randomised to CABG, 2 subsequently declined revascularisation and 11 went on to undergo PCI as crossovers. Follow-up ranged from 1 to 4 years. Over the entire population, mean age was 61 years, 79% were men, 46% had Canadian Cardiovascular Society classification 3 or 4 Angina, and 24% presented with an acute coronary syndrome. Other baseline characteristics are detailed in Table 1. For trial profile, see Fig. 1. For average number of days use of cardiac medication in the first year, see Table 2.

3.2. All adverse events

Among the 488 patients allocated to PCI, 231 (47.3%) had at least one adverse event during follow-up. There were 207 further adverse events among this set of patients. Among the 500 patients allocated to CABG, 265 (53%) had at least one adverse event (compared with PCI group, Chi sq 2.95, p = 0.086). There were a further 170 adverse events among this cohort of 265 patients.

The cumulative incidence function curves for first adverse event show early separation of PCI and CABG groups, with a statistically significant difference across the range (PCI: 0.54, 95% CI 0.48–0.6. CABG: 0.59, 95% CI 0.53–0.64, Chi sq 5.2, p 0.022) (Fig. 2).

Table 1
Baseline characteristics.
Data are number of patients (%) unless otherwise indicated.

	PCI (n = 488)	CABG (n = 500)
Male	390 (80%)	392 (78%)
Age (yrs, mean, ST deviation)	61 (9.2)	62 (9.5)
Previous MI	214 (44%)	234 (47%)
Previous cerebro-vascular accident	5 (1%)	14 (3%)
Previous transient ischaemic attack	7 (1%)	11 (2%)
Previous peripheral arterial disease	31 (6%)	35 (7%)
Family history of cardiovascular disease	235/487 (48%)	240/499 (48%)
Type I diabetes	19 (4%)	9 (2%)
Type II non insulin dependent diabetes	49 (10%)	65 (13%)
Hypertension	212 (43%)	235 (47%)
Hyperlipidaemia	258 (53%)	251 (50%)
Current smoker	77 (16%)	72 (14%)
Ex smoker	259 (53%)	286 (57%)
CCS class III	116 (24%)	133 (27%)
CCS class IV	94 (19%)	108 (22%)
Mean left ventricular ejection fraction	57%[a]	57%[b]
Number of segments with significant stenosis	3.2	3.2
Two-vessel disease	303 (62%)	262 (52%)
Three-vessel disease	183 (38%)	236 (47%)
Diseased vessel territory	4 (1%)	3 (1%)
Left anterior descending: proximal	235 (48%)	222 (44%)
Left anterior descending: other	214 (44%)	241 (48%)
Circumflex	342 (70%)	374 (75%)
Right coronary artery	361 (74%)	395 (79%)
One occluded vessel	77 (16%)	70 (14%)
Two occluded vessels	4 (1%)	12 (2%)

[a] n = 398 at baseline.
[b] n = 373 at baseline.

3.3. Fatal and MACE

Cumulative incidence function curves for death and MACE are shown in Fig. 3, CABG having the better outcome. Cardiac and non-cardiac deaths are shown in Table 3.

3.4. Non-fatal/non-MACE

Non-fatal/non-MACE events occurred in 58 PCI patients and 193 CABG patients (Chi sq. 91.6, p < 0.001). Cumulative incidence function curves for non-fatal/non-MACE are shown in Fig. 4. A greater proportion of the CABG group required prolonged inpatient rehabilitation (transfer to another hospital for further treatment or rehabilitation) (p < 0.001), or developed atrial arrhythmia (supraventricular tachycardia, atrial fibrillation, atrial flutter) (p = 0.002), pleural effusion (0.029), or major bleeding (0.028). The total non-fatal/non-MACE adverse event rate was twice as high for CABG compared to PCI, at 35.04 (95% CI 33.88 to 36.2) compared to 17.49 (16.67 to 18.31) events per 100 patient years of follow-up respectively (rate ratio 2.0, 95% CI 1.7 to 2.4, p < 0.001). Specific adverse events are given in Table 4.

3.5. Hospital stay

Hospitalisation data are available for 426 out of 438 adverse events (MACE and non-MACE) occurring in 227 PCI patients and for 428 out of 435 adverse events occurring in 261 CABG patients. Duration of hospital stay ranged from 0 to 122 days in the PCI group and 0 to 182 days in the CABG group. The cumulative sum of all hospital stays was 2935 days for the PCI group and 4028 days for the CABG group. Median cumulative duration of stay per patient experiencing an adverse event was 7 days (inter-quartile range 2 to 15) for the PCI group and 9 days (inter-quartile range 4 to 19) for the CABG group (p = 0.019).

Cumulative non-MACE associated hospital stay was 1387 in the PCI group and 3287 in the CABG group. Hospital stay per adverse event was similar for both groups (see Table 5).