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State of the art in coronary revascularization: Everolimus eluting stents versus multiple arterial grafting☆

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ABSTRACT

Background: Contemporary comparisons on coronary revascularization should take into account the state of the art percutaneous coronary intervention (PCI) with new generation everolimus-eluting stents (EESs) and coronary artery bypass grafting (CABG) with multiple arterial grafts (MAGs). We aimed to compare early outcomes and late survival after EES versus MAG in patients with multivessel coronary artery disease using a single centre institutional database.

Methods: In an observational registry study, we identified 3787 patients with multivessel coronary disease. Of these 696 (18.3%) underwent PCI with EES and 3091 (81.7%) CABG with MAG. With the use of propensity-score matching, we identified 483 pairs for final comparison (C-statistic: 0.91).

Results: The two groups were comparable for 30-day mortality (1.6% versus 0.8% in the EES and MAG group respectively, P = 0.38). Stroke was not observed in the EES group and it was 0.8% in the MAG group (P = 0.13). After a mean follow-up of 3.1 years, PCI with EES was associated with a higher risk of late death (HR 2.2; 95% CI 1.18–4.16; P = 0.01).

Conclusions: In patients with multivessel coronary disease, CABG with multiple arterial grafts when compared with PCI with new generation drug eluting stent, was associated with significantly improved long-term survival. Further randomized studies are warranted to identify the best revascularization strategies in the current era.

1. Introduction

Coronary-artery bypass grafting (CABG) and percutaneous coronary intervention (PCI) are treatment options for patients with multivessel coronary artery disease as they have been shown to provide similar survival rate [1]. Despite studies showing a trend toward a lower mortality after CABG, compared with PCI [2], the routine use of drug-eluting stents has improved outcomes [1,3]. Furthermore, the newer-generation drug-eluting stents, in particular the everolimus-eluting stent (EES), have been shown to reduce the risks of death, myocardial infarction, and stent thrombosis, compared with bare-metal stents or first-generation drug-eluting stents [4]. In contrast, despite compelling evidence supporting a survival advantage from the use of multiple arterial grafting (MAG) over the conventional strategy with single internal thoracic artery [5–7], CABG has changed little over the years. Only 10% of patients undergoing CABG currently receive a second arterial graft in the United States, approximately 4% with bilateral internal thoracic artery (BITA) and 6% with radial artery (RA) grafts [8]. Contemporary comparisons between PCI and CABG, therefore, should include state of the art strategies: PCI with new generation EES and CABG with MAG. In an observational registry study, we compared the outcomes in patients with multivessel disease who underwent elective CABG with MAG or PCI with the EES.

2. Methods

2.1. Study design

The study was conducted in accordance with the principles of the Declaration of Helsinki. The local audit committee approved the study, and the requirement for individual patient consent was waived. This study was a registry-based analysis involving patients with multivessel coronary artery disease who underwent elective isolated CABG using at least two arterial conduits and patients who underwent PCI with EES between January 2007 and April 2015, at Bristol Heart Institute, United Kingdom. We retrospectively analysed prospectively collected data from the National Institute for Cardiovascular Outcomes Research (NICOR) registry and the British Cardiovascular Intervention Society (BCIS) registry for audit and quality assessment of PCI in the United Kingdom. Reproducible cleaning algorithms were applied to the

☆ These authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation

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database, which are regularly updated as required. Briefly, duplicate records and non-adult cardiac surgery entries were removed; transcriptional discrepancies harmonized; and clinical conflicts and extreme values corrected or removed. The data are returned regularly to the local units for validation. Further details and definition of variables are available at http://www.ucl.ac.uk/nicor/audits/adultcardiac/datasets.

2.2. Study population

Patients were eligible for inclusion in the study if they had multivessel coronary disease, which was defined as severe stenosis (≥70%) in at least two major epicardial arteries including the proximal-mid LAD artery with or without left main coronary disease (≥50%), and if they had undergone either PCI with implantation of an EES cobalt–chromium everolimus eluting stents (CoCr-EES, XIENCE V Boston Scientific and Abbott Vascular, Santa Clara, California) or platinum–chromium everolimus-eluting stents (PtCr-EES, PROMUS Element; Boston Scientific, Natick, Massachusetts) or isolated CABG using at least two arterial conduits in the following configuration: bilateral internal thoracic arteries (BITA), left internal thoracic artery and radial artery (RA) and their combination with or without additional saphenous vein grafts (SVG). Exclusion criteria were the following: revascularization within 1 year before the index procedure; previous cardiac surgery (CABG or valve surgery), PCI with a stent other than an EES or with a combination of stents; myocardial infarction within 24 h before the index procedure including primary PCI; and cardiogenic shock.

2.3. Outcomes

The primary outcome of the study was all-cause mortality. All-cause mortality is the most robust and unbiased index because no adjudication is required; thus, inaccurate or biased documentation or clinical assessments are avoided [9]. Information about post-discharge mortality tracking was available for all patients (100%) and was obtained by linking the institutional database with the National General Register Office. Secondary outcomes investigated included procedural complications as postoperative stroke, postoperative low output syndrome requiring intra-aortic balloon pump, postoperative dialysis, procedural access complication including arterial bleeding and/or pseudoaneurysm and/or dissection for PCI group and re-exploration for bleeding and/or sternal wound reconstruction for CABG group.

2.4. Statistical analysis

Multiple imputation was used to address missing data (http://www.jstatsoft.org/v45/i07/). To control for measured potential confounders in the data set, a propensity score (PS) was generated for each patient from a multivariable logistic regression model based on pre-treatment covariates as independent variables with treatment type (MAG versus EES) as a binary dependent variable [10]. Pairs of patients receiving EES and MAG were derived using greedy 1:1 matching with a calliper of width of 0.2 standard deviation of the logit of the PS (http://CRAN.Rproject.org/package=nonrandom). The quality of the match was assessed by comparing selected pre-treatment variables in propensity score — matched patients using the standardized mean difference (SMD), by which an absolute standardized difference of greater than 20% is suggested to represent meaningful covariate imbalance [10]. Analytic methods for the estimation of the treatment effect in the matched samples included McNemar's to compare proportions [10]. Time-segmented Cox regression models (within 30 days and beyond 30 days) [11] that stratified on the matched pairs [12] were used to investigate the effect of treatment (MAG versus EES) on early and late mortality. This approach accounts for the within-pair homogeneity by allowing the baseline hazard function to vary across matched sets(http://CRAN.R-project.org/package=survival).

Subgroup PS matching analyses were conducted to compare the effect of EES versus BITA and RA separately. Additional subgroup PS matching was also conducted to compare CoCrEES and PtCrEES separately versus MAG. Finally, the comparison between EES and MAG was repeated in a subgroup PS matching analysis including patients with complete revascularization only to exclude the potential bias related to higher rate of incomplete revascularization in the EES group. As sensitivity analysis, for all the comparisons, we performed Cox analysis on early (within 30 days) and late mortality (beyond 30 days) by regressing the outcome on the treatment assignment and the estimated propensity score [10]. All p-values <0.05 were considered to indicate statistical significance. All statistical analysis was performed using R Statistical Software (version 3.2.3; R Foundation for Statistical Computing, Vienna, Austria).

3. Results

3.1. Study population

We identified 3787 patients with multivessel coronary disease who met our inclusion criteria, of these 696 (18.3%) underwent PCI with EES and 3091 (81.7%) CABG with MAG (Table 1).

3.2. Procedural data

In the EES group, arterial access was the radial artery in 512 (73%) cases and the femoral artery in the remaining 184 (27%). CoCr-EESs were used in 496 (71%) patients, PtCr-EESs were used in 171 (25%) patients and a combination of both was used in the remaining 29 (4%). Pressure wire for fractional flow reserve was used in 58 (8.3%) cases and intravascular ultrasound (IVUS) in 43 (6.1%) cases. Rotational atherectomy was performed in 29 (4.1%) cases. A total of 60 chronic total occlusions and 20 in-stent restenosis were attempted. A total of 2.3 ± 1.1 stents per patient were used. Mean number of lesions treated per patient was 2.4 ± 0.9. The average longest stented segment was 27 mm ± 9 mm and the average largest stent used was 3.5 ± 2.8 mm. Coronary dissection/perforation occurred in 27 (3.8%) patients, no flow phenomena in 6 (0.8%) patients and side branch occlusion in 7 (1%) patients. Incomplete revascularization defined as at least one diseased primary arterial territory not stented, occurred in 258 (37%) of

Table 1
Everolimus-eluting stent (EES) and multiple arterial grafting (MAG) groups characteristics before matching.

	u-EES (n = 696)		u-MAG (n = 3091)		SMD	P
	n	%	n	%		
Age, years (mean, ds)	69 ± 12		60 ± 9		0.85	<0.001
Female	209	30.0	344	11.1	0.48	<0.001
Body mass index ≥ 30	235	33.8	923	29.9	0.08	0.07
Angina	291	41.8	1392	45.0	0.06	0.13
Congestive heart failure	185	26.6	689	22.3	0.1	0.02
Prior MI	232	33.3	1361	44.0	0.22	<0.001
Prior PCI	169	24.3	159	5.1	0.56	<0.001
Diabetes: no	552	79.3	2672	86.4	0.15	<0.001
Orally treated	96	13.8	246	8.0		
On insulin	48	6.9	173	5.6		
Hypertension	492	70.7	2026	65.5	0.11	0.01
Smoking	149	21.4	507	16.4	0.13	0.002
Creatinine ≥ 200 mmol/l	32	4.6	29	0.9	0.22	<0.001
Previous stroke	19	2.7	71	2.3	0.03	0.58
Peripheral vascular disease	71	10.2	209	6.8	0.12	0.002
LVEF ≥50%	441	63.4	2528	81.8	0.48	<0.001
30–49%	179	25.7	505	16.3		
≤30%	76	10.9	58	1.9		
Non-elective admission	433	62.2	1289	41.7	0.42	<0.001
3-Vessel disease	128	18.4	2109	68.2	1.16	<0.001
Left main disease	88	12.6	735	23.8	0.29	<0.001
Trainee as operator	327	47.0	1020	33.0	0.28	<0.001

SMD: standardized mean difference; MI: myocardial infarction; PCI: percutaneous coronary intervention; LVEF: left ventricular ejection fraction.