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ORIGINAL ARTICLE

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Prognostic factors of 10-year mortality after coronary artery bypass graft surgery: a secondary analysis of the arterial revascularization trial

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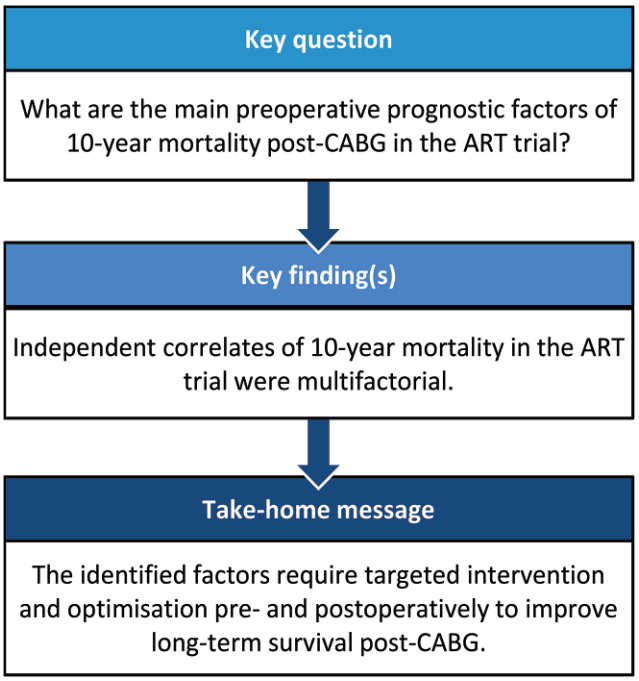

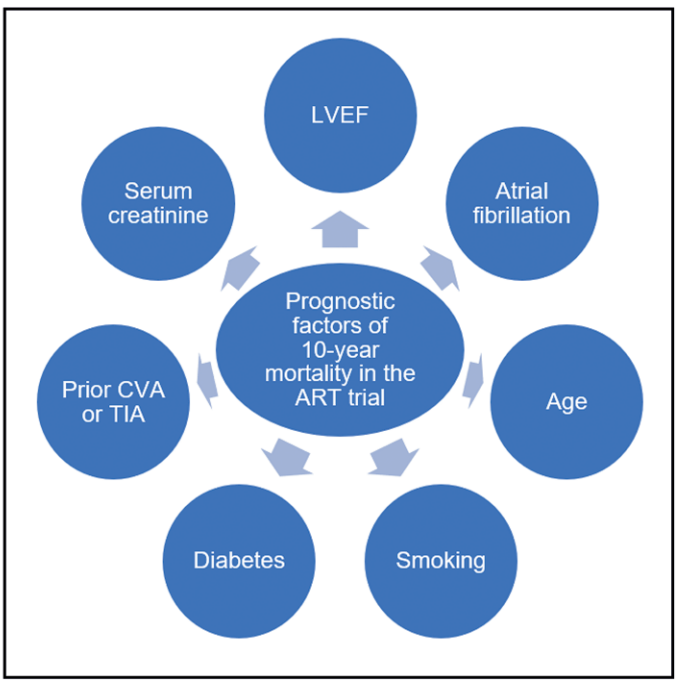

Abstract

OBJECTIVES: The objective of this investigation was to determine the preoperative prognostic factors of long-term (10-year) mortality in patients treated with isolated coronary artery bypass graft surgery in the arterial revascularization trial (ART).

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METHODS: A *post hoc* analysis of the ART was conducted. Cumulative 10-year mortality was estimated using the Kaplan–Meier method. Prospectively collected preoperative data were used to determine the prognostic factors of 10-year all-cause mortality in patients who participated in the ART (Cox proportional hazards model).

RESULTS: A total of 3102 patients who participated in the ART were included in the analysis. Ten-year follow-up was completed in 3040 patients (98%). A total of 644 patients (20.8%) had died by 10 years. Preoperative factors that were identified as statistically significant predictors of 10-year mortality in the multivariable analysis (all $P \leq 0.01$) were: left ventricular ejection fraction, atrial fibrillation, age, diabetes, prior cerebrovascular event (stroke or transient ischaemic attack), serum creatinine and smoking status. The following variables were significantly associated in univariable models but did not retain significance in the multivariable model for mortality: non-Caucasian ethnicity, hypertension, peripheral vascular disease, chronic obstructive pulmonary disease and prior myocardial infarction.

CONCLUSIONS: Independent predictors of 10-year mortality in the ART were multifactorial. Several key independent predictors of 10-year mortality in the ART were identified including: heart function, renal function, cerebrovascular disease, age, atrial fibrillation, smoking status and diabetes. Understanding which preoperative variables influence long-term outcome after coronary artery bypass grafting may help to target treatments to those at higher risk to reduce mortality.

Keywords: ART • Prognostic factors • Mortality

ABBREVIATIONS

AF	Atrial fibrillation
ART	Arterial revascularization trial
CABG	Coronary artery bypass graft
CAD	Coronary artery disease
CCS	Canadian Cardiovascular Society
COPD	Chronic obstructive pulmonary disease
Hb	Haemoglobin
MI	Myocardial infarction
NYHA	New York Heart Association
PVD	Peripheral vascular disease
TIA	Transient ischaemic attack

INTRODUCTION

Coronary artery bypass graft (CABG) surgery is a well-established and effective treatment for coronary artery disease (CAD) [1]. Fortunately, short-term mortality post-CABG occurs infrequently (<2%) and multiple models have been established to predict short-term mortality risk after CABG, such as The European System for Cardiac Operative Risk Evaluation (EuroSCORE) II [2, 3]. The effects of specific risk factors on short-term outcomes of CABG are well established. Previous studies have demonstrated that cardiac factors, e.g. prior myocardial infarction (MI), poor left ventricular function and urgency of operation, are critical with regard to short-term mortality risk post-CABG as they contribute to cardiovascular mortality, which is often seen within the first year post-CABG. There is a shift towards noncardiac-related variables, e.g. diabetes with regard to long-term mortality post-CABG [4]. As expected, patients undergoing CABG have a higher long-term mortality rate than the general population and less is known about the long-term effects of preoperative characteristics, such as comorbidities, for patients undergoing this surgery and prevention factors are not yet optimal [5]. An informed decision about the best therapeutic option for a patient can be made when the impact of risk factors of mortality can be reliably estimated. Understanding factors influencing long-term mortality post-CABG may help to better stratify patients' risk and therefore organize a tailored, patient-centred plan of care. The aim of this study was to determine the prognostic factors of all-cause mortality at 10 years following isolated CABG in the randomized arterial revascularization trial (ART).

PATIENTS AND METHODS

Ethical statement

The ART complied with the Medical Research Council Guidelines for Good Clinical Practice in Clinical Trials and the Declaration of Helsinki guidelines. The trial commenced following ethical approval from participating hospitals (Northern and Yorkshire research ethics committee approval MREC 04//3/006) and informed consent was obtained from each participant.

Study population

The ART was a two-arm, prospective, randomized multicentre trial of patients with multivessel CAD who were scheduled to undergo urgent or elective CABG (Current Controlled Trials number, ISRCTN46552265). Patients were randomized to receive either single or bilateral internal thoracic artery grafts in a 1:1 ratio, with supplemental vein or radial artery grafts as required. Patients excluded from the trial included those requiring a single graft, evolving MI, concomitant procedures and those with prior CABG. Isolated CABG is defined as patients undergoing only CABG, not involving other concurrent surgery. The primary outcome was all-cause mortality at 10 years of follow-up. All-cause mortality is defined as death from any cause as reported by the centre. Analysis of the primary outcome was carried out on the intention-to-treat population and time from randomization to death was calculated. For patients who were alive and for whom their status was not known, the time from randomization until they were last recorded as alive was calculated. Patients with incomplete follow-up were censored at the date of last follow-up. The protocol and 1-, 5- and 10-year results have been published previously [6–9].

Prognostic factors

Potential prognostic factors were chosen based on prior literature (published CABG short-term and long-term models) and clinical experience. Those examined were demographics (age,

female gender and ethnicity); body mass index; creatinine; New York Heart Association (NYHA) 3 and 4; Canadian Cardiovascular Society (CCS) 3 and 4; the presence of comorbidities, including treated hypertension, treated hyperlipidaemia, diabetes mellitus, preoperative atrial fibrillation (AF), peripheral vascular disease (PVD), chronic obstructive pulmonary disease (COPD), asthma; history of cerebrovascular accident or transient ischaemic attack (TIA); history of MI; left ventricular ejection fraction (LVEF); smoking status (former or current smoker categories); history of percutaneous coronary intervention; and number of grafts. Age, serum creatinine and body mass index were modelled as continuous variables and a linear relationship was assumed between these variables and mortality. The other variables (except for LVEF, CCS angina class, NYHA classification and smoking) were dichotomous, representing presence or absence of the characteristic. The absence of the condition served as a reference group. LVEF was categorized as >50%, 31–49% and ≤30%; both CCS anginal class and NYHA classification were subdivided into class <3 and ≥3. Smoking was categorized as never smoker, current smoker and former smoker.

Statistical methods

A *post hoc* analysis of the ART was conducted. Cumulative 10-year mortality was estimated using the Kaplan–Meier method. In this article, categorical variables are presented as percentages and counts and continuous variables are presented as mean and standard deviation. For the outcome (all-cause mortality at 10 years), Cox proportional hazard regression analyses were performed to estimate for each variable a hazard ratio (HR). Univariable Cox regression models were applied to all candidate variables. All candidate variables were then included in 1 multivariable model, without any variable selection. This approach to development of the final model is called the full model approach, where all predictors are included in the model irrespective of their association with the outcome. A full model approach, unlike conventional automatic variable selection strategies, avoids excluding important variables that can contribute significantly when they are combined and reduces the probability of selection bias [10]. Missing data were accounted for by multiple imputation with multivariate imputation by chained equations. The number of datasets imputed was 10. The individual coefficients from the regression model from each imputed dataset were pooled using Rubin's rule [11]. Statistical analyses were performed in R software version 3.6.2.

RESULTS

The ART enrolled 3102 patients between 2004 and 2007 at 28 hospitals in 7 countries. Within the randomized ART, baseline demographics and clinical characteristics have previously been described [9]. The baseline characteristics are shown in Table 1. Ten-year follow-up was complete in 3040 patients (98%). Patients were censored at the end of the follow-up period, with the remainder of censoring due to lost to follow-up. A total of 644 patients (20.8% of the overall trial population) had died by 10 years; information about death classification is available (see Supplementary Material). There were significant differences in preoperative comorbidities between patients who survived and did not survive by the end of 10-year follow-up and this analysis provides a basis to identify potential prognostic variables (see Supplementary Material).

Table 1: Preoperative clinical profiles of ART population ($n = 3102$)

Characteristic	Value
Age (years), mean (SD)	63.63 (8.93)
Gender, % (*n*)	
Male	85.6 (2656)
Female	14.4 (446)
Ethnicity, % (*n*)	
Caucasian	91.9 (2849)
East Asian	0.2 (6)
South Asian	4.8 (150)
Afro-Caribbean	0.1 (2)
African	0.2 (5)
Other	2.9 (89)
Height (cm), mean (SD)	170.24 (8.46)
Weight (kg), mean (SD)	81.93 (13.90)
BMI (kg/m^2), mean (SD)	28.22 (4.03)
Creatinine (μmol/l), mean (SD)	96.82 (22.29)
CrCl (ml/min), mean (SD)	92.39 (29.09)
NYHA functional class, % (*n*)	
1–2	78.4 (2431)
3–4	21.6 (669)
CCS anginal class, % (*n*)	
No angina, 1–2	92.3 (2862)
3–4	7.7 (240)
Hypertension treated with drugs, % (*n*)	77.7 (2410)
Hyperlipidaemia treated with drugs, % (*n*)	93.7 (2905)
Diabetes, % (*n*)	23.7 (734)
Atrial fibrillation, % (*n*)	1.5 (45)
Smoking, % (*n*)	
Current smoking	14.5 (451)
Former smoking	55.8 (1732)
Never smoked	29.6 (919)
COPD, % (*n*)	2.5 (77)
Asthma, % (*n*)	4.4 (135)
PVD, % (*n*)	7.1 (221)
Prior CVA or TIA, % (*n*)	6.4 (200)
LMSD, % (*n*)[a]	16.9 (225)
Number of vessels grafted	
1	19
2	545
3	1520
4+	992
Radial artery graft	639
Saphenous vein graft	2402
Previous PCI, with or without stent, % (*n*)	15.8 (490)
LVEF, % (*n*)	
≥50%	75.5 (2276)
31–49%	22.4 (674)
≤30%	2.2(65)
Previous MI, % (*n*)	41.9 (1300)

[a]LMSD data were incomplete (53% missing data).

BMI: body mass index; CCS: Canadian Cardiovascular Society; COPD: chronic obstructive pulmonary disease; CrCl: creatinine clearance; CVA: cerebrovascular accident; LMSD: left main stem disease; LVEF: left ventricular ejection fraction; MI: myocardial infarction; NYHA: New York Heart Association; PCI: percutaneous coronary intervention; PVD: peripheral vascular disease; SD: standard deviation; TIA: transient ischaemic attack.

Table 2 shows the univariable relationships between the candidate prognostic factors and 10-year mortality. Among the 28 variables evaluated, 13 were significantly associated with mortality ($P \leq 0.01$): non-Caucasian ethnicity, hypertension, diabetes mellitus, AF, PVD, prior cerebrovascular accident or TIA, current smoker, COPD, prior MI, LVEF 31–49%, LVEF ≤30%, age and serum

Table 2: Univariable associations of candidate prognostic factors with 10-year mortality in the entire population of the randomized arterial revascularization trial ($n = 3102$)

CABG ($n = 3102$) univariable correlates of 10-year mortality	Incidence of mortality, no./total (%)	Hazard ratio (95% CI)	*P*-Value
Categorical variables			
Gender			
Male	535/2656 (20.1)	Ref	
Female	109/446 (24.4)	1.28 (1.04–1.57)	0.019
Ethnicity			
Caucasian	612/2849 (21.5)	Ref	
Non-Caucasian	*32/252 (12.7)*	*0.56 (0.39–0.80)*	*0.002*
NYHA class			
NYHA 1 and 2	486/2431 (20.0)	Ref	
NYHA 3 and 4	158/669 (23.6)	1.23 (1.03–1.47)	0.025
CCS class			
CCS 1 and 2	587/2862 (20.5)	Ref	
CCS 3 and 4	57/240 (23.8)	1.16 (0.89–1.53)	0.271
Hypertension	*534/2410 (22.2)*	*1.41 (1.15–1.74)*	*0.001*
Hyperlipidaemia	598/2905 (20.6)	0.85 (0.63–1.15)	0.290
Diabetes mellitus	*186/734 (25.3)*	*1.36 (1.15–1.61)*	*<0.001*
AF	*24/45 (53.3)*	*3.76 (2.50–5.65)*	*<0.001*
PVD	*68/221 (30.8)*	*1.66 (1.29–2.13)*	*<0.001*
Prior CVA or TIA	*75/185 (40.5)*	*2.30 (1.81–2.93)*	*<0.001*
Smoking			
Never smoker	171/919 (18.6)	Ref	
Former smoker	362/1732 (20.9)	1.16 (0.97–1.39)	0.110
Current smoker	*111/451 (24.6)*	*1.48 (1.17–1.88)*	*0.001*
COPD	*29/77 (37.7)*	*2.01 (1.38–2.91)*	*<0.001*
Asthma	35/135 (25.9)	1.36 (0.97–1.92)	0.075
Prior MI	*296/1300 (22.8)*	*1.24 (1.06–1.45)*	*0.007*
Prior PCI	107/490 (21.8)	1.08 (0.88–1.33)	0.461
LVEF			
≥50%	396/2276	Ref	
31–49%	*199/674 (29.5)*	*1.82 (1.53–2.16)*	*<0.001*
≤30%	*28/65 (43.1)*	*3.36 (2.29–4.93)*	*<0.001*
Continuous variables[a]			
Age per increase in 1 year	*68.61 (SD: 8.4)*	*1.08 (1.07–1.09)*	*<0.001*
BMI per increase in 1 kg/m^2	27.99 (SD: 4.02)	0.98 (0.97–1.00)	0.127
Serum creatinine per increase in 1 μmol/l	*104.15 (SD: 29.12)*	*1.01 (1.01–1.01)*	*<0.001*
Number of grafts	3.18 (SD: 0.8)	0.99 (0.90–1.09)	0.782

The variables significantly associated with mortality are in italics.

[a]Continuous variables are presented as mean (SD) in patients who died within 10 years.

AF: atrial fibrillation; BMI: body mass index; CABG: coronary artery bypass graft surgery; CCS: Canadian Cardiovascular Society; CI: confidence interval; COPD: chronic obstructive pulmonary disease; CVA: cerebrovascular accident; LVEF: left ventricular ejection fraction; MI: myocardial infarction; NYHA: New York Heart Association; PCI: percutaneous coronary intervention; PVD: peripheral vascular disease; Ref: reference; SD: standard deviation; TIA: transient ischaemic attack.

creatinine. Table 3 shows the multivariable relationships. In all, 7 factors emerged as independent predictors of death over 10-year follow-up in the multivariable analysis (all $P \leq 0.01$): age, creatinine, diabetes, AF, prior cerebrovascular event (stroke or TIA), smoking status and LVEF (see figure 1). Figure 2 is a forest plot showing the hazard ratios of the significant multivariable correlates for mortality at 10 years in patients undergoing CABG in the ART. The inclusion of the as-treated groups of single or multiple arterial grafts as a risk factor for the analysis demonstrated no change to the multivariable model (see Supplementary Material). The following variables were significantly associated in the univariable models but did not retain significance in the multivariable model for mortality: non-Caucasian ethnicity, hypertension, PVD, COPD and prior MI.

DISCUSSION

In this study, we identified the key preoperative predictors of long-term mortality within the ART and estimated the associations of these variables with all-cause mortality over 10 years after CABG. The multivariable model shows that there are several independent prognostic factors on long-term survival after CABG: age, creatinine, diabetes, AF, cerebrovascular disease, LVEF and smoking status.

Our study demonstrates that diabetes increases the risk of 10-year mortality by 1.28-fold. Diabetes contributes to accelerated atherosclerosis and the development of extensive multivessel atherosclerosis [12]. A study demonstrated that elevated preoperative haemoglobin (Hb) A1c levels (HbA1c >8%) led to increased long-term mortality post-CABG [13]. This supports the importance of the clinician in becoming engaged in improving the care of the high-risk population of patients with diabetes undergoing CABG by optimizing glucose and risk factor control at all stages of care for CABG patients. We suggest the need to improve and standardize the quality of glycaemic control in patients with diabetes undergoing CABG; pre-procedure HbA1c measurement in all patients to identify the growing number of nondiagnosed diabetes; preoperative and postoperative patient education of all

Table 3: Multivariable correlates of 10-year mortality in the entire population of the randomized arterial revascularization trial ($n = 3102$)

Multivariable correlates of 10-year mortality	Hazard ratio (95% CI)	*P*-Value
Female	1.20 (0.97–1.49)	0.10
BMI per increase in 1 kg/m^2	0.99 (0.97–1.01)	0.369
Ethnicity		
Non-Caucasian	0.97 (0.66–1.41)	0.861
COPD	1.27 (0.86–1.88)	0.225
Asthma	1.20 (0.84–1.71)	0.311
Hypertension	1.18 (0.96–1.47)	0.12
Hyperlipidaemia	0.90 (0.66–1.23)	0.505
Diabetes mellitus	1.28 (1.08–1.53)	0.006
Atrial fibrillation	2.13 (1.40–3.25)	<0.001
Peripheral vascular disease	1.07 (0.83–1.40)	0.594
Prior CVA or TIA	1.60 (1.25–2.04)	<0.001
Smoking		
Former smoker	1.21 (1.00–1.46)	0.052
Current smoker	2.65 (2.05–3.43)	<0.001
NYHA 3 and 4	1.10 (0.90–1.34)	0.363
CCS 3 and 4	1.10 (0.82–1.47)	0.525
Prior MI	1.06 (0.90–1.25)	0.470
Prior PCI	1.23 (0.99–1.52)	0.063
LVEF		
31–49%	1.66 (1.39–1.98)	<0.001
≤30%	2.31 (1.54–3.47)	<0.001
Age per increase in 1 year	1.08 (1.07–1.09)	<0.001
Serum creatinine per increase in 1 μmol/l	1.01 (1.01–1.01)	<0.001
Number of grafts	1.02 (0.92–1.12)	0.768

BMI: body mass index; CCS: Canadian Cardiovascular Society; CI: confidence interval; COPD: chronic obstructive pulmonary disease; CVA: cerebrovascular accident; LVEF: left ventricular ejection fraction; MI: myocardial infarction; NYHA: New York Heart Association; PCI: percutaneous coronary intervention; TIA: transient ischaemic attack.

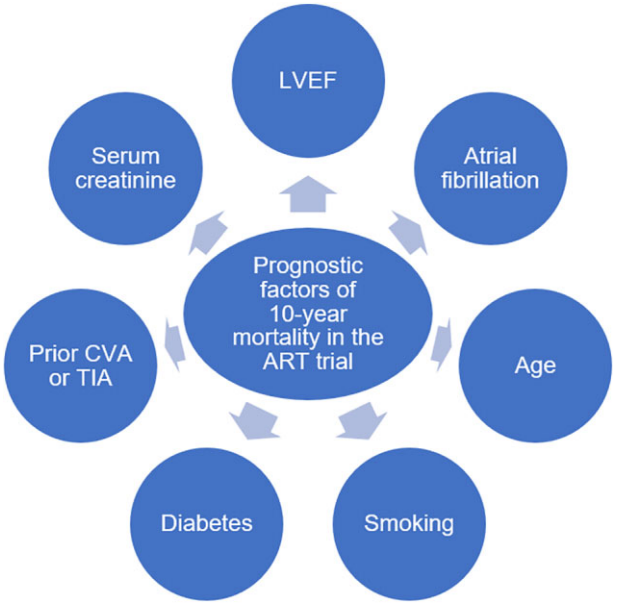

Figure 1: The prognostic factors of 10-year mortality in the arterial revascularization trial trial. ART: arterial revascularization trial; CVA: cerebrovascular accident; LVEF: left ventricular ejection fraction; TIA: transient ischaemic attack.

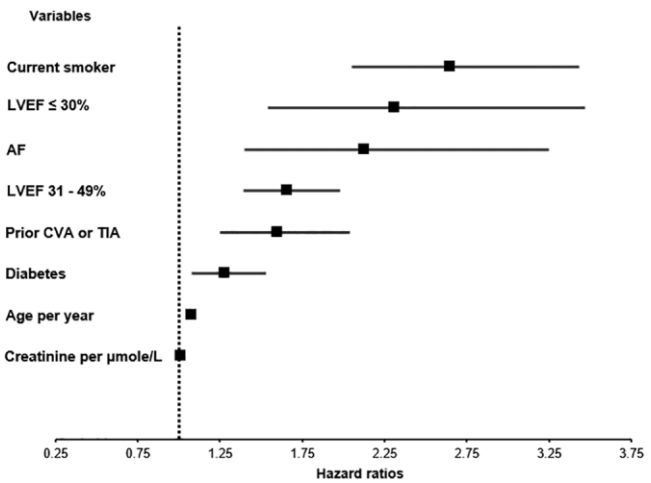

Figure 2: Forest plot of the significant predictors of mortality at 10 years in the arterial revascularization trial. AF: atrial fibrillation; CVA: cerebrovascular accident; LVEF: left ventricular ejection fraction; TIA: transient ischaemic attack.

patients with diabetes; and appropriate follow-up with patients' general practitioner. In patients with high cardiovascular risk and diabetes, future studies could examine whether novel interventions such as sodium-glucose co-transporter 2 inhibitors and glucagon-like peptide-1 receptor agonists and tighter glucose control would improve the long-term survival in these patients [14]. Glucagon-like peptide-1 receptor agonists work by improving glycaemic control in patients with severe diabetes and leads to improved insulin sensitivity and decreased HbA1c.

In our study, LVEF ≤30% was associated with poor long-term survival. Mortality in these patients may be attributed to ventricular arrythmias, progression of heart failure and recurrent ischaemia. Prophylactic implantation with an automatic internal cardioverter defibrillator (e.g. during or immediately after CABG) may reduce long-term mortality risk in patients with a prior MI and advanced left ventricular dysfunction, but this strategy would need to be tested in future research studies [15]. Biventricular pacing was shown to be effective in improving outcomes and clinical symptoms in patients with heart failure and left bundle branch block and may be considered as a potential approach in CABG patients with similar clinical syndromes [16].

Unlike diabetes, preoperative AF and history of cerebrovascular disease are factors that occur infrequently in populations and was found in only 2% and 3% of patients in the ART, respectively, yet were found to be strongly associated with long-term mortality in patients post-CABG. Because of their rare occurrence, they may not be identified as important for large populations and not contributing to overall mortality risk, but they represent important variables expressing risk when present in an individual patient. AF has previously been described as a risk factor for long-term mortality with hazard ratios ranging from 1.39–1.67 [17–20]. A reduction in long-term survival in patients with AF may be due to further thromboembolic events, bleeding risk from anticoagulation therapy, tachycardia-mediated cardiomyopathy and low cardiac output. High incidence of mortality in CABG patients with preoperative and/or postoperative AF is attributed to ischaemic stroke. An underuse of anticoagulation in AF patients undergoing CABG has been found; therefore, the number of these patients receiving anticoagulation may need to be increased [21]. This may

also contribute to discussions about the role of ablative surgery during CABG in improving long-term survival [22].

Benedetto *et al.* [23] found that postoperative AF was independently associated with all-cause mortality at 10 years (HR 1.34; 95% confidence interval, 1.13–1.59) in patients who participated in the ART. Operative and postoperative variables have been previously shown to be predictive of long-term mortality post-CABG; however, the focus of our study was the assessment of preoperative variables as potential predictors. As operative data are not available prior surgery, surgeons can only rely on preoperative patient characteristics for informed consent, counselling and surgical decision-making. Further research is needed to identify whether operative and postoperative variables need to be considered in predictive models. Possible contenders include mean number and type of grafts (multiple/total arterial grafting), postoperative AF and hospital length of stay. Biomarkers such as postoperative creatinine-kinase myocardial band and troponin have previously been shown to be independent predictors of long-term mortality post-CABG [24].

Current smoking was associated with the highest hazard ratio. We must find even better ways of preventing patients from smoking and involve the general practitioner and smoking cessation services prior to CABG to improve long-term prognosis in current smokers undergoing CABG.

The Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery (SYNTAX) trial was a multicentre, randomized trial in which 1800 patients with left main or three-vessel CAD were randomized to undergo CABG or percutaneous coronary intervention surgery and were followed up for 10 years [25]. The following variables were identified as multivariable correlates of 4-year mortality: age, PVD, chronic lung disease, serum creatinine and lack of discharge aspirin [26]. Our study extends those results to a larger sample and longer follow-up. We were able to demonstrate that although COPD and PVD are associated with late mortality in univariable analysis, they were not retained in the multivariable model. In the SYNTAX CABG model, there may not have been enough events (78 deaths) to include all significant variables in the multivariable model. This may result in imprecise and biased estimates in the direction of more extreme values when the event per variable is low. The ART is one of the largest CABG trials with about 30 000 patient-years of follow-up and there were enough events (644 deaths) to provide reasonable power in all of the univariable correlates evaluated, although we still had several groups with low numbers of events, such as ethnicity, which could lead to errors. While not all variables in the model were significantly associated with all-cause mortality, they can be identified as variables to be used for adjustment in future analyses.

Although previous studies have shown that COPD is predictive of long-term mortality after CABG [27, 28], our study did not show this, possibly due to the small sample size (2.5%) of patients with chronic lung disease in the ART. The impact of gender on long-term mortality post-CABG is debateable. Studies have shown that being female increases the risk of operative mortality after CABG and is not an independent predictor of long-term mortality [29, 30]. Preoperative assessment of renal dysfunction can improve postoperative long-term survival through lifestyle and medication management. Informing the postoperative inpatient team about nephrotoxic medications and medications that are renally cleared may be needed. In patients with severe renal impairment, a nephrology referral prior to operation may be warranted to enable more informed decision-making regarding long-term mortality risk. Longer-term efforts to manage renal disease should focus on management of risk factors like hypertension and diabetes and provision of protective agents such as angiotensin receptor blockers and SGLT-2 inhibitors in appropriate patients. We have shown that long-term outcomes are less affected by predictors of early mortality, such as angina class III/IV and previous MI but are more strongly associated with chronic conditions and comorbidities, such as renal impairment, diabetes and heart function.

Limitations

In the analysis we did not include factors related to operative techniques other than number of grafts. We did not examine factors associated with long-term cardiovascular mortality. We were unable to investigate the association of left main stem disease with long-term mortality as this variable was not included in the analysis due to having 53% missing data (see Supplementary Material). However, by excluding left main stem disease we enabled a full dataset where missingness is <3%. The category 'former smoker' was crude and did not include details on how long it had been after the former smokers quite their smoking behaviour and number of cigarettes they had consumed. Hence, the hazard ratio estimates for smoking status in this analysis may not be reliable. Patients with prognostic factors identified in this study, such as diabetes, may have disparities in care received, raising the possibility of unmeasured confounding, though this may be subtle and difficult to quantify. Our study considered a wide range of candidate variables (demographic, cardiac and non-cardiac-related factors), thus reducing the possibility of important unknown confounders. There was a high rate of guideline-directed medical therapy in ART; therefore, the possible confounding influence of medical therapy on mortality is reduced due to optimal drug compliance in the ART. The statistical models have inherent limitations including small sample sizes for certain variables, which can lead to errors in estimating the strength of associations.

CONCLUSIONS

Independent predictors of 10-year mortality in the ART were multifactorial. Optimizing characteristics such as diabetes and atherosclerosis are essential for the prevention of poor outcomes and the improvement of long-term survival. Future studies are needed to evaluate whether specific interventions for key prognostic factors in post-CABG patients can improve long-term survival and if more specific risk stratification models can help to identify those CABG patients who need more intensive management of co-morbidities.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *EJCTS* online.

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Conflict of interest: None declared except for Umberto Benedetto who was supported by the National Institute for Health Research Bristol Biomedical Research Centre Cardiovascular Theme.

Data Availability Statement

The authors declare that all data are available to other researchers on reasonable request.

Author contributions

Suprateeka Talukder: Writing—original draft. **Arnaldo Dimagli:** Formal analysis; Methodology; Software; Writing—review & editing. **Umberto Benedetto:** Writing—review & editing. **Alastair Gray:** Writing—review & editing. **Stephen Gerry:** Writing—review & editing. **Belinda Lees:** Writing—review & editing. **Łukasz Krzych:** Writing—review & editing. **Mario Gaudino:** Writing—review & editing. **David P. Taggart:** Writing—review & editing. **Marcus Flather:** Conceptualization; Supervision; Writing—review & editing.

Reviewer information

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