Outcomes Following Primary Percutaneous Coronary Intervention in patients with previous Coronary Artery Bypass Surgery

Short title: PPCI in patients with CABG

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Abbreviations and Acronyms

CAD = coronary artery disease

CABG = coronary artery bypass grafting

IRA = infarct related artery

PCI = percutaneous coronary intervention

PPCI = primary percutaneous coronary intervention

STEMI = ST-segment elevation myocardial infarction

SVG = saphenous vein graft

What is Known:

- There is limited data on outcomes of patients with previous coronary artery bypass grafting (CABG) presenting with ST-segment elevation myocardial infarction (STEMI) and undergoing primary percutaneous coronary intervention.
- Many of the existing studies are limited because of small sample size.

What the Study Adds:

- This largest study to date found that patients with previous CABG are older, have more co-morbid conditions and adverse procedural variables.
- Once differences are adjusted for, patients with previous CABG are not at increase risk of 30-day or longer term mortality.

Abstract

Background: There are limited data on outcomes of patients with previous coronary artery bypass grafting (CABG) presenting with ST-segment elevation myocardial infarction (STEMI) and undergoing primary percutaneous coronary intervention (PPCI). We report outcomes in STEMI patients undergoing PPCI with or without previous CABG surgery in a large real-world, all-comer population.

Methods and Results: Clinical, demographic, procedural and outcomes data were collected for all patients undergoing PPCI in ~~the UK~~England and Wales from January 2007 to December 2012. All-cause mortality at 30-days and 1-year ~~follow-up~~ were evaluated in the whole and a propensity-matched cohort. Of 79,295 STEMI patients studied, 2,658 (3.4%) patients had prior CABG, of whom 44% (n=1,168) underwent PPCI to native vessels and 56% (n=1,490) to bypass grafts. There were significant differences in the demographic, clinical and procedural characteristics of these groups. Patients with prior CABG (with primary PCI to native artery or graft) had higher mortality at 30-days (6.2% with PPCI to native artery, 6.1% with PPCI to bypass graft) than patients with no prior CABG (4.5%, $p<0.001$). However after risk factor adjustments there was no significant difference in outcomes. There were also no significant differences in 30-day mortality, in-hospital MACE, in-hospital stroke and in-hospital bleeding in the propensity-matched population.

Conclusion: A prior history of CABG in patients presenting with STEMI and undergoing PPCI does not independently confer additional risk of mortality, although it is a marker of other high-risk features.

Keywords: Coronary artery bypass graft, Saphenous vein graft, Percutaneous coronary intervention, Mortality, Cardiovascular disease

Introduction

Primary percutaneous coronary intervention (PPCI) is the gold standard of care for patients presenting with acute ST-elevation myocardial infarction (STEMI).[1,2] However, in patients with previous coronary artery bypass grafts (CABG) undergoing PPCI there is limited outcome data with many studies derived from small-scale registries or *post-hoc* analysis of selected small groups of patients with previous CABG from randomized trials.[3-5]

Patients with CABG tend to be older, have a higher incidence of co-morbidities, poorer LV function and multi-vessel disease,[6,7] that may contribute to poorer outcomes reported in the setting of PPCI in these patients.[3,5,8] Even after adjustment for such differences adverse clinical characteristics, some studies report adverse outcomes in patients with previous CABG persist[3,5,9] although others show either a modest[10] or no difference in outcomes.[8] Many of these studies in patients with prior CABG do not differentiate between outcomes if PPCI is performed on native vessel or in the saphenous vein graft (SVG)[4,5,11] that may limit interpretation of outcomes.

Current STEMI guidelines do not specifically address the management of this complex group of patients in the PPCI setting, on account of the limited available evidence and limited outcome data in this cohort of patients, particularly from RCTs. This paucity of evidence may lead to delay or denial of PPCI therapy in patients with prior CABG presenting with STEMI.[5,11] For example, in HORIZONS AMI only 84% of patients with previous CABG presenting with STEMI underwent PPCI whilst this was significantly higher at 93% in those patients with no prior CABG (P=0.0002).[5] Many of the previous studies have reported on outcomes in only a small number of patients, often with cohort sizes of around 100[3-5,9] or have been derived from cohorts

in which contemporary pharmacotherapy was not used and PCI was undertaken using mainly bare metal stents or balloon angioplasty[3,9] hence the applicability of outcomes reported to contemporary practice is unclear. We therefore study early (30-day) and late (1-year) outcomes of PPCI in patients with previous CABG in a large contemporary unselected national cohort from the database of the British Cardiovascular Intervention Society (BCIS) to define whether there are differences in outcomes between native vessel IRA and bypass graft IRA interventions in patients with previous CABG.

Methods

Study design and data collection

This is a retrospective analysis of prospectively collected national data for all patients undergoing PPCI for STEMI in England and Wales from January 2007 to December 2012 in the BCIS database. BCIS records information on PCI practices in UK with data collection managed by the National Institute of Cardiovascular Outcomes Research (NICOR).[12-14] The BCIS database contains 113 clinical, procedural and outcome variables with approximately 80,000 new records added each year. Using data from the Office of National Statistics, mortality was tracked for all patients in England and Wales using the patient's unique NHS number. Patients from Scotland and Northern Ireland were excluded due to the absence of the Office of National Statistics linked mortality data. Institutional review board approval was not sought for this study as all data was anonymized and routinely collected as a part of a national audit.

Variables and outcomes collected

We collected data on participants' demographics, risk factors and comorbidities. In addition, data were also collected on the clinical state at the time of the intervention, left ventricular ejection fraction (LVEF), and all aspects of the interventional treatment and adjunctive pharmacology.

We evaluated all-cause mortality at 30-days and 1-year follow up. We also examined in-hospital major adverse cardiovascular events (MACE, defined as a composite of in-hospital mortality, in-hospital myocardial re-infarction and target vessel revascularization) and in-hospital major bleeding (defined as gastrointestinal bleed, intracerebral bleed, retroperitoneal hematoma, blood or platelet transfusion, or

an arterial access site complication requiring surgery). In-hospital stroke included ischemic stroke, hemorrhagic stroke or transient ischemic attack (TIA).

Statistical methods

The study population was divided into three groups: i) no previous CABG, ii) prior CABG with PPCI to native coronary arteries, iii) Prior CABG with PPCI to bypass grafts. Patients with missing values for follow up time, sex and age were also excluded. The characteristics of patients were compared across the three groups of interest (pairwise) and also across inclusion and exclusion due to missing data. These comparisons were performed using Fisher's exact tests~~chi-square tests~~ for binary/categorical and ANOVA (ANalysis Of Variance) for continuous variables.

To be more inclusive with the data to analyze, account for data missing data and better protect against biases due to informative missing data mechanisms, we used multiple imputation with chained equations to impute data for all variables with missing information. Age, sex, group of participant and study outcomes were registered as complete variables in the imputation models which were used to generate 10 datasets on which we ran the analyses (incomplete and imputed variables were: smoking status, diabetes, hypertension, hyperlipidemia, previous MI, previous stroke, peripheral vascular disease, renal disease, family history, radial access site, glycoprotein IIb/IIIa, shock, circulatory support, number of stents, thrombus aspiration, mechanical ventilation, femoral closure device and LVEF). The STATA code and output of the imputations is shown in Supplementary Data 1.

The risk of adverse outcomes by comparison group was estimated with univariable and multivariable logistic regressions. The former were not controlled for any covariates, while the latter were controlled (adjusted) for various patient characteristics. Covariates in the models included age, sex, smoking status, diabetes, hypertension, hyperlipidemia, previous MI, previous stroke, peripheral vascular disease, renal disease, family history, radial access site, glycoprotein IIb/IIIa, multi-vessel PCI, shock, circulatory support, number of stents, thrombus aspiration, mechanical ventilation, femoral closure device, LVEF, PCI to left main stem, PCI to left anterior descending artery, and distal protection device.

We used multiple imputations with propensity score matching (mi estimate:teffects psmatch) to estimate the average treatment effect (ATE) to account for baseline difference across the groups of participants. We used two separate multiple imputation logistic regression models for which we calculated propensity scores for each group member: a) PCI to native vessel no graft (group 0) vs PCI to native vessel in patient with graft (group 1); and b) PCI to native vessel no graft (group 0) vs PCI to graft (group 2). The scores were then used to perform the matching and simple logistic regression were run (the only predictor being group membership) to obtain the ATE.

We performed additional Kaplan Meier survival analysis and Cox proportional hazards regression analysis for 30-day mortality and 1-year mortality by participant group. Statistical analyses were performed using Stata version 13.1 (Stata Corp., Texas, USA).

RESULTS

Study cohort

The study cohort consisted of 79,295 participants who had PPCI for STEMI in England and Wales and did not have missing values for death, follow-up, sex and age. The process of participant inclusion is shown in Figure 1. A total of 76,637 (96.6%) ~~of~~ patients had no previous CABG whereas 2,658 (3.4%) patients had prior CABG. Among patients with prior CABG, 44% (n=1,168) patients received PPCI to native vessels and 56% (n=1,490) underwent PPCI to bypass grafts. The mean follow up for these participants was 2.4±1.6 years and 86.5% of patients were followed-up for a minimum of one year (or until death if occurring within a year).

Characteristics of participants

There were significant differences in the demographic, clinical and procedural characteristics of the three groups (Table 1). Patients with previous CABG were significantly older, and had a higher prevalence of diabetes, hypertension, peripheral vascular disease and previous MI or a stroke. The characteristics of those included in the study and those excluded are shown in Supplementary Table 1.

Unadjusted outcomes

There was a significant difference in unadjusted mortality and in-hospital MACE among the three groups (Table 2). Figures 2a and b show the unadjusted Kaplan Meier survival curves for the 3 groups at 30 days (Figure 2a) and 1 year (Figure 2b) with significant differences in survival between the 3 groups noted (log-rank test; P<0.001 and P<0.0001 for 30-day and 1-year mortality respectively).

Patients with prior CABG (with primary PCI to native artery or graft) had higher mortality at 30-days (6.2% with PPCI to native artery, 6.1% with PPCI to bypass graft) than patients with no prior CABG (4.5%, p<0.001). Similar

observations were recorded for 1-year mortality with the lowest rates observed in patients with no previous history of CABG (9.1%) with similar rates in patients with previous CABG and PCI to native vessels and bypass grafts (14.5% vs 11.9%; P<0.001).

In-hospital MACE rates, were higher in patients with prior CABG undergoing native vessel PCI (6.0%) compared with prior CABG undergoing PCI to a bypass graft (4.7%) or no prior CABG (4.2%). In contrast, in-hospital stroke rates and in-hospital bleeding rates were similar across all three groups: 0.3% vs. 0.2% vs. 0.2%, respectively for stroke and 0.8% vs. 0.9% vs. 0.7%, respectively for in-hospital bleeding.

Outcomes after risk-adjustment and imputations

The unadjusted, adjusted and imputed risk of mortality, in-hospital MACE, in-hospital major bleeding and stroke outcomes are shown in Table 3**.** In unadjusted univariate analysis the risk of 30-day mortality was significantly higher in PPCI undertaken in native coronary arteries in patients with previous CABG (OR 1.39 95% CI 1.10-1.77, p=0.007) and PPCI in bypass grafts (OR 1.38 95% CI 1.11-1.71, p=0.003) compared to PPCI in native coronary arteries (n=79,295). However following adjustments for baseline co-variates (in both the presence and absence of multiple imputations) there was no significant differences in outcomes for PPCI in native vessels in patients with CABG (OR 1.02 95% CI 0.77-1.34, p=0.89) but significant increase in 30-day mortality among patients with primary PCI to bypass grafts (OR 1.33 95% CI 1.03-1.71, p=0.026).

Similarly, for in-hospital MACE, there were no significant differences in outcomes between PPCI undertaken in native coronary arteries in patients with previous CABG and PPCI in bypass grafts compared to PPCI in native coronary

arteries once differences in baseline co-variates were adjusted for PPCI to native arteries in patients with CABG (OR 0.95 95% CI 0.71-1.26, p=0.72) and PPCI to bypass grafts (OR 0.93 95% CI 0.70-1.22, p=0.58). There were no significant differences after adjustments with and without imputations and for all evaluations for risk of in-hospital stroke (OR 0.56 95% CI 0.14-2.30, p=0.42 and OR 0.69 95% CI 0.22-2.21, p=0.53, respectively) and in-hospital bleeding (OR 0.95 95% CI 0.50-1.81, p=0.88 and OR 0.74 95% CI 0.39-1.43, p=0.38, respectively).

Cox proportional hazards regression yielded similar results to those of unadjusted and adjusted logistic regressions for 30-day and 1 year mortality (Supplementary Table 2)

Outcomes with propensity score matching

We performed a propensity-matching to correct for baseline characteristics (balance diagnostics for propensity model presented in Supplementary Table 3) and there were no differences in outcomes between patients with or without previous CABG or in patients with previous CABG where PCI was performed in either the native vessel or the graft (Table 4).

Discussion

This study from a national unselected cohort represents the largest analysis of patients with prior CABG undergoing PPCI in the literature. We show that patients with prior CABG are older, have more co-morbidities and adverse procedural characteristics but once these differences are adjusted for, patients with prior CABG have similar clinical outcomes following PPCI to patients without prior CABG.

Our unadjusted analysis shows that patients with a history of CABG have the highest mortality and MACE following PPCI when compared to patients with no CABG irrespective of whether the PCI is undertaken in the native coronary vessel or the bypass graft. Patients with a prior CABG have higher co-morbid burden and an overall higher adverse risk profile, which may contribute to poor outcomes observed. Indeed patients with previous CABG undergoing PCI to native vessels had significantly higher rates of cardiogenic shock presentation, mechanical ventilator support and circulatory support. Once adjustment is undertaken for such confounding risk factors, no statistically significant differences in clinical outcomes are seen between patients with or without prior CABG undergoing PPCI, irrespective of whether the PCI is performed in the native vessel or graft.

Previous studies have suggested that patients with prior CABG may have adverse outcomes when presenting with STEMI and treated with PPCI. These studies were either small-scale single center registries or *post-hoc* analysis of small numbers of patients derived from RCT. In the APEX-AMI (Assessment of Pexelizumab in Acute Myocardial Infarction) trial, patients with previous CABG (n=128) had increased 90-day mortality that remained significant after multivariable adjustment (HR 1.9, 95% CI 1.08 to 3.33, p = 0.025).[3] In HORIZONS-AMI (Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction) trial,

previous CABG (n=105) was associated with a higher incidence of MACE (36.4% vs 21.4%, p <0.001) and mortality (11.2% vs 6.7%, p=0.08) at 3 years.[5] In PAMI-2 (Second Primary Angioplasty in Myocardial Infarction) trial, patients with previous CABG (n=58) were reported to have higher in-hospital (9.4% vs. 2.6%, p=0.02) and 6-month (14.3% vs. 4.1%, p=0.001) mortality.[9] A small registry from New York hospitals reported that patients with previous CABG presenting with STEMI (n=93) had higher unadjusted in-hospital mortality and MACE and on multivariate analysis, prior CABG (HR 3.40; 95% CI 1.15-10.00) was independently associated with in-hospital mortality.[4] In another study of 192 patients undergoing PPCI with a SVG culprit were shown to have higher unadjusted rates of mortality at 30 days and MACE at 1 year; although these effects were only modest after multivariable adjustment.[10] A more recent analysis, from Kohl and colleagues, of 249 patients with prior CABG undergoing PPCI has suggested no significant differences in unadjusted rates of in-hospital death (4.8% vs 5.9%, p=0.49), MACE at 30 days (6.8% vs 7.4%, p=0.76) (including stroke, recurrent infarction, recurrent ischemia, or death) or rates of hospital readmission at 30 days (1.7% vs 2.3%, p=0.82) between PPCI in patients with previous CABG compared to those with no history of CABG although no adjustments were made for differences in baseline co-variates.[8] Furthermore, no significant differences in mortality or MACE outcomes where observed in those patients with previous CABG who underwent PCI to either the graft or the native vessel.[8] An overview of these studies is presented in Supplementary Table 4.

Our data suggests differences in the unadjusted clinical outcomes in patients with previous history of CABG, although once differences in baseline co-morbid conditions and procedural characteristics were adjusted for, outcomes were similar to those observed in patients without prior CABG. It has been well documented that

patients with prior CABG presenting with STEMI are less likely to be offered PPCI than patients without prior CABG with similar observations recorded in patients with NSTEMI.[15] In APEX-AMI, PCI was performed less frequently in patients with prior CABG compared with those with no history of CABG (78.9% vs. 93.9%, p<0.001) [3] with similar findings reported by the HORIZON-AMI investigators and the PAMI-2 study.[9] Similarly, in older studies such as reports derived from the National Registry of Myocardial Infarction (NRMI)-3, patients presenting with STEMI with prior CABG were significantly less likely to receive PCI or thrombolysis than those without prior CABG.[16] This practice may be influenced by the paucity of data in patients with prior CABG undergoing PPCI and the perceived lack of efficacy of PPCI in these patients.

Previous reports have debated whether the outcomes are different if PPCI is performed on native vessel or SVG in patients with previous CABG.[3,5,17-19] Although PPCI to vein grafts is often more technically challenging and complex, our data show no significant difference in adjusted outcomes in patients with prior CABG undergoing native or bypass graft PPCI.

Our analysis has several strengths. The BCIS dataset includes an almost complete collection of all PCI procedures performed in the United Kingdom representing unselected real-world experience including high-risk patient often excluded from RCTs and represents the largest analysis of primary PCI for STEMI patients with previous CABG to be reported.

We recognize that this study has several potential limitations. Firstly, whilst mortality tracking within the United Kingdom is very robust, all other outcomes and complications are self-reported without formal adjudication. Therefore, the analysis is potentially vulnerable to reporting biases, and complications may be under-reported.

Second, whilst this analysis reports on outcomes in patients undergoing PPCI, previous studies have suggested that PPCI is less likely to be performed when the infarct-related vessel was a bypass graft rather than a native coronary artery[9] which may contribute to selection/referral biases in our cohort. The BCIS dataset does not record information regarding patients who presented with STEMI but were medically managed and so cannot exclude significant referral or selection bias particularly for those patients with previous CABG similar to other studies.[3, 5, 16] Third, our analysis report outcomes derived from grafts as the BCIS dataset does not differentiate between venous and arterial grafts. Previous data derived from the National Cardiovascular Data Registry (NCDR) CathPCI registry suggests that arterial grafts represented 2.5% of all PCI procedures undertaken to bypass grafts in the United States although this did not report practice or outcomes in a primary PCI cohort specifically.[17]

In conclusion, our data demonstrate that after adjusting for co-morbidities, PPCI for STEMI results in similar outcomes for patients who have had previous CABG (either in a native vessel or a bypass graft) when compared to those who have not had previous CABG. PPCI for STEMI should be the primary treatment strategy for patients who have had previous CABG.

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Table 1: Baseline characteristics of patients

Variable	Group 1 (n=76,637)	Group 2 (n=1,168)	Group 3 (n=1,490)
Age	63.3 (±13.1)	67.1 (±11.5)	67.3 (±11.5)
Female sex	19,846/76,637 (25.9%)	216/1,168 (18.5%)	301/1,490 (20.2%)
Smoking	46,429/68,505 (67.8%)	708/999 (70.9%)	855/1,285 (66.5%)
Diabetes	9,733/73,562 (13.2%)	269/1,081 (24.9%)	279/1,430 (19.5%)
Hypertension	29,757/75,483 (39.4%)	661/1,154 (57.3%)	750/1,470 (51.0%)
Hyperlipidemia	29,368/75,483 (38.9%)	698/1,154 (60.5%)	727/1,470 (49.5%)
Previous MI	8,202/70,196 (11.7%)	555/1,050 (52.9%)	638/1,370 (46.6%)
Previous CVA	2,670/75,483 (3.5%)	71/1,154 (6.2%)	85/1,470 (5.8%)
Peripheral vascular disease	2,329/75,483 (3.1%)	78/1,154 (6.8%)	93/1,470 (6.3%)
Previous renal disease	1,121/70,583 (1.6%)	43/1,023 (4.2%)	48/1,382 (3.5%)
LVEF Good Moderate Poor	 12,535 (53.0%) 8,701 (36.8%) 2,401 (10.2%)	 176 (48.4%) 127 (34.9%) 61 (16.8%)	 206 (46.6%) 187 (42.3%) 49 (11.1%)
Family history of heart disease	24,220/65,018 (37.3%)	426/959 (44.4%)	489/1,238 (39.5%)
Access site Femoral Radial	 36,849 (50.4%) 36,272 (49.6%)	 846 (76.9%) 254 (23.1%)	 968 (69.3%) 428 (30.7%)
Glycoprotein IIb/IIIa inhibitor	36,831/67,562 (54.5%)	478/1,041 (45.9%)	716/1,341 (53.4%)
Target vessel LAD Left main Circumflex Right coronary artery Graft	 34,262 (44.7%) 1,221 (1.6%) 12,094 (15.8%) 33,222 (43.4%) 0 (0%)	 280 (24.0%) 119 (10.2%) 264 (22.6%) 515 (44.1%) 0 (0%)	 37 (2.5%) 10 (0.7%) 44 (3.0%) 70 (4.7%) 1,490 (100%)
Multivessel PCI	8,084/76,637 (10.6%)	101/1,168 (8.7%)	150/1,490 (10.1%)
Cardiogenic shock	4,396/76,126 (5.8%)	93/1,164 (8.0%)	79/1,478 (5.4%)
Circulatory support	3,426/71,346 (4.8%)	81/1,101 (7.4%)	80/1,417 (5.7%)
DES use	42,236/73,837 (57.2%)	618/1,127 (54.8%)	709/1,418 (50.0%)
Number of stents 0 1 2 ≥3	 31,601 (42.8%) 26,290 (35.6%) 11,561 (15.7%) 4,385 (5.9%)	 509 (45.1%) 368 (32.7%) 171 (15.2%) 79 (7.0%)	 709 (50.0%) 396 (27.9%) 213 (15.0%) 100 (7.1%)
Thrombus aspiration	35,550/72,525 (49.0%)	394/1,113 (35.4%)	648/1,443 (44.9%)
Mechanical ventilator support	2,166/67,023 (3.2%)	48/1,028 (4.7%)	51/1,274 (4.0%)
Femoral closure device	24,893/71,187 (35.0%)	500/1,090 (45.9%)	564/1,428 (39.5%)
Use of distal protection device	278/70,259 (0.4%)	17/1,076 (1.6%)	132/1,398 (9.4%)

Symptom to balloon time (hrs)	2.3±2.0	2.6±2.2	2.4±1.8

Group 1: Primary PCI in native coronary arteries
Group 2: Primary PCI in native coronary arteries in patient with CABG
Group 3: Primary PCI in bypass grafts
MI = myocardial infarction, CVA = cerebrovascular accident, LVEF = left ventricular ejection fraction, LAD = left anterior descending, DES = drug eluting stent

Table 2: Unadjusted outcomes

Outcome	Group 1 (n=76,637)	Group 2 (n=1,168)	Group 3 (n=1,490)	p-value Group 1 vs Group 2*	p-value Group 1 vs Group 3*	p-value Group 2 vs Group 3*
In-hospital mortality	2,465/73,677 (3.4%)	55/1,080 (5.1%)	53/1,442 (3.7%)	0.003	0.46	0.091
30-day mortality	3,447/76,637 (4.5%)	72/1,168 (6.2%)	91/1,490 (6.1%)	0.009	0.005	1.00
1-year mortality	6,026/66,217 (9.1%)	147/1,014 (14.5%)	158/1,329 (11.9%)	<0.001	0.001	0.072
In-hospital MACE	3,108/74,369 (4.2%)	65/1,089 (6.0%)	69/1,455 (4.7%)	0.006	0.29	0.18
In-hospital re-infarction	264/74,319 (0.4%)	4/1,084 (0.4%)	12/1,454 (0.8%)	0.80	0.012	-
In-hospital re-intervention	447/74,319 (0.6%)	6/1,084 (0.6%)	8/1,454 (0.6%)	1.00	1.00	-
In-hospital emergency CABG	69/74,319 (0.1%)	2/1,084 (0.2%)	1/1,454 (0.1%)	0.27	1.00	-
In-hospital stroke	215/74,319 (0.3%)	2/1,084 (0.2%)	3/1,454 (0.2%)	0.78	0.80	-
In-hospital embolic stroke	129/74,319 (0.2%)	2/1,084 (0.2%)	3/1,454 (0.2%)	0.71	0.74	-
In-hospital TIA	53/74,319 (0.1%)	0/1,084 (0%)	0/1,454 (0%)	1.00	0.63	-
In-hospital hemorrhagic stroke	34/74,319 (0.1%)	0/1,084 (0%)	0/1,454 (0%)	1.00	1.00	-
In-hospital bleeding	578/74,320 (0.8%)	10/1,084 (0.9%)	10/1,454 (0.7%)	0.60	0.88	0.51

Group 1: Primary PCI in native coronary arteries
Group 2: Primary PCI in native coronary arteries in patient with CABG
Group 3: Primary PCI in bypass grafts
MACE = major adverse cardiovascular events, CABG = coronary artery bypass graft, TIA = transient ischemic attack
*P-value determined by Fisher's exact test

Table 3: Risk of adverse outcomes with unadjusted and adjusted results

Variable	Group 1: Primary PCI in native coronary arteries	Group 2: Primary PCI in native coronary arteries in patient with CABG	Group 3: Primary PCI in bypass grafts
In-hospital mortality			
Unadjusted (n=76,199)	Reference	1.55 (1.18-2.04), p=0.002	1.10 (0.84-1.45), p=0.49
Adjusted† (n=76,199)	Reference	1.07 (0.78-1.48), p=0.66	0.99 (0.72-1.37), p=0.96
30 day mortality			
Unadjusted (n=79,295)	Reference	1.39 (1.10-1.77), p=0.007	1.38 (1.11-1.71), p=0.003
Adjusted† (n=79,295)	Reference	1.02 (0.77-1.34), p=0.89	1.33 (1.03-1.71), p=0.028
1 year mortality			
Unadjusted (n=68,560)	Reference	1.69 (1.42-2.02), p<0.001	1.35 (1.14-1.59), p=0.001
Adjusted† (n=68,560)	Reference	1.17 (0.95-1.43), p=0.15	1.16 (0.95-1.41), p=0.14
In-hospital MACE			
Unadjusted (n=76,913)	Reference	1.46 (1.13-1.87), p=0.004	1.14 (0.89-1.46), p=0.29
Adjusted† (n=76,913)	Reference	0.95 (0.71-1.26), p=0.72	0.93 (0.70-1.22), p=0.58
In-hospital Stroke			
Unadjusted (n=76,857)	Reference	0.64 (0.16-2.57), p=0.53	0.71 (0.23-2.23), p=0.56
Adjusted† (n=76,857)	Reference	0.56 (0.14-2.30), p=0.42	0.69 (0.22-2.21), p=0.53
In-hospital Bleeding			
Unadjusted (n=76,858)	Reference	1.19 (0.63-2.23), p=0.59	0.88 (0.47-1.65), p=0.70
Adjusted† (n=76,858)	Reference	0.95 (0.50-1.81), p=0.88	0.74 (0.39-1.43), p=0.38

†Adjusted for age, sex, smoking status, diabetes, hypertension, hyperlipidemia, previous myocardial infarction, previous stroke, peripheral vascular disease, renal disease, family history, radial access site, glycoprotein IIb/IIIa inhibitor, multivessel, PCI to left anterior descending artery, PCI to left main artery, shock, circulatory support, no of stents, thrombus aspiration, ventilation, femoral closure device, distal protection device, symptom to balloon with 10 imputations for all variables.

Table 4: Propensity score matched analysis with average treatment effects

Analysis	Group	Coefficient	95% CI		p-value
In-hospital mortality	Group 1: Primary PCI in native coronary arteries	Reference			
	Group 2: Primary PCI in native coronary arteries in patient with CABG (n=72,068)	0.0143	-0.0163	0.0448	0.36
	Group 3: Primary PCI in bypass grafts (n=72,407)	0.1505	-0.2237	0.5247	0.42
30 day mortality	Group 1: Primary PCI in native coronary arteries	Reference			
	Group 2: Primary PCI in native coronary arteries in patient with CABG (n=74,964)	0.0121	-0.0212	0.0454	0.47
	Group 3: Primary PCI in bypass grafts (n=75,255)	0.1524	-0.2252	0.5300	0.42
1 year Mortality	Group 1: Primary PCI in native coronary arteries	Reference			
	Group 2: Primary PCI in native coronary arteries in patient with CABG (n=64,756)	0.2689	-0.0129	0.0666	0.19
	Group 3: Primary PCI in bypass grafts (n=65,039)	0.1450	-0.2877	0.5778	0.50
In-hospital MACE	Group 1: Primary PCI in native coronary arteries	Reference			
	Group 2: Primary PCI in native coronary arteries in patient with CABG (n=72,735)	0.0135	-0.0176	0.0445	0.39
	Group 3: Primary PCI in bypass grafts (n=73,078)	0.1494	-0.2371	0.5359	0.44
In-hospital stroke	Group 1: Primary PCI in native coronary arteries	Reference			
	Group 2: Primary PCI in native coronary arteries in patient with CABG (n=72,683)	-0.0011	-0.0057	0.0035	0.63
	Group 3: Primary PCI in bypass grafts (n=73,030)	-0.0014	-0.0043	0.0015	0.33
In-hospital bleeding	Group 1: Primary PCI in native coronary arteries	Reference			
	Group 2: Primary PCI in native coronary arteries in patient with CABG (n=72,684)	-0.0025	-0.0117	0.0067	0.59
	Group 3: Primary PCI in bypass grafts (n=73,031)	-0.0061	-0.0084	-0.0038	<0.001

Figure 1: Flow chart of participant inclusion

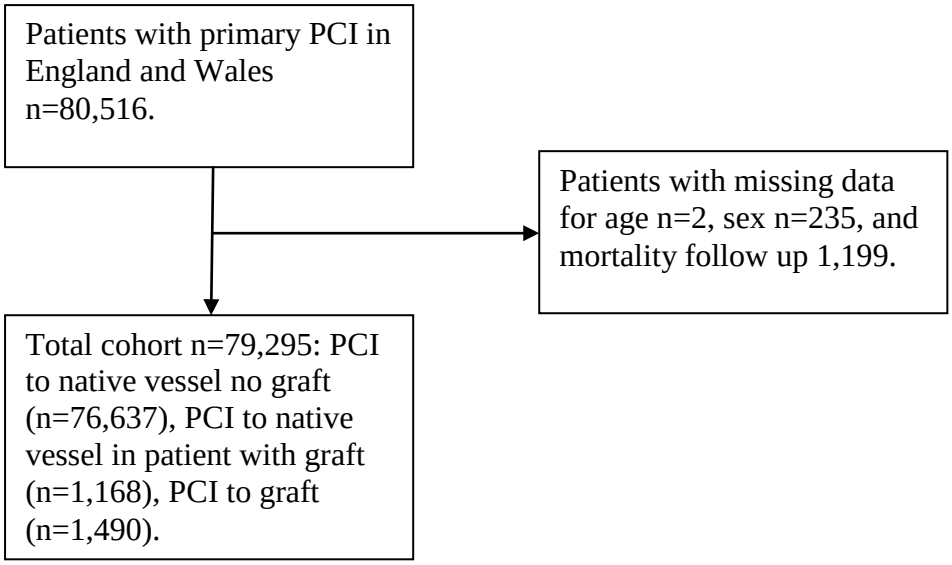
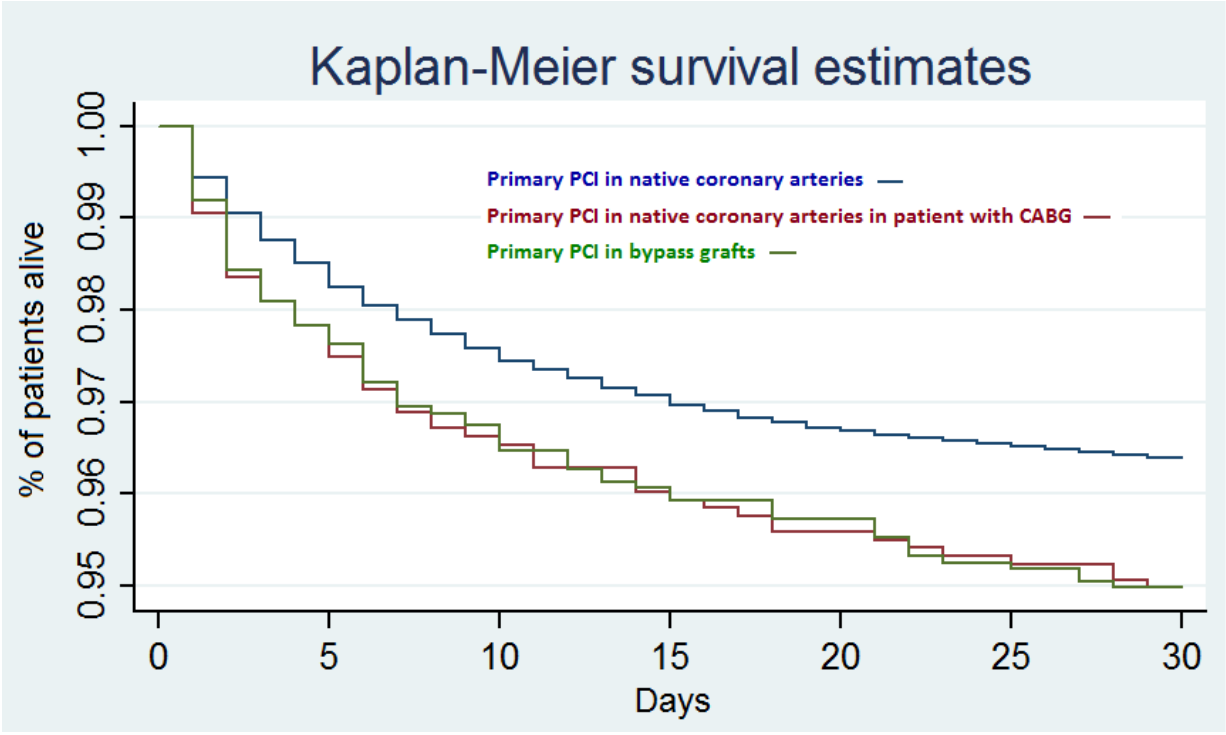


Figure 2: Kaplan-Meier survival curves at 30 days and 1 year

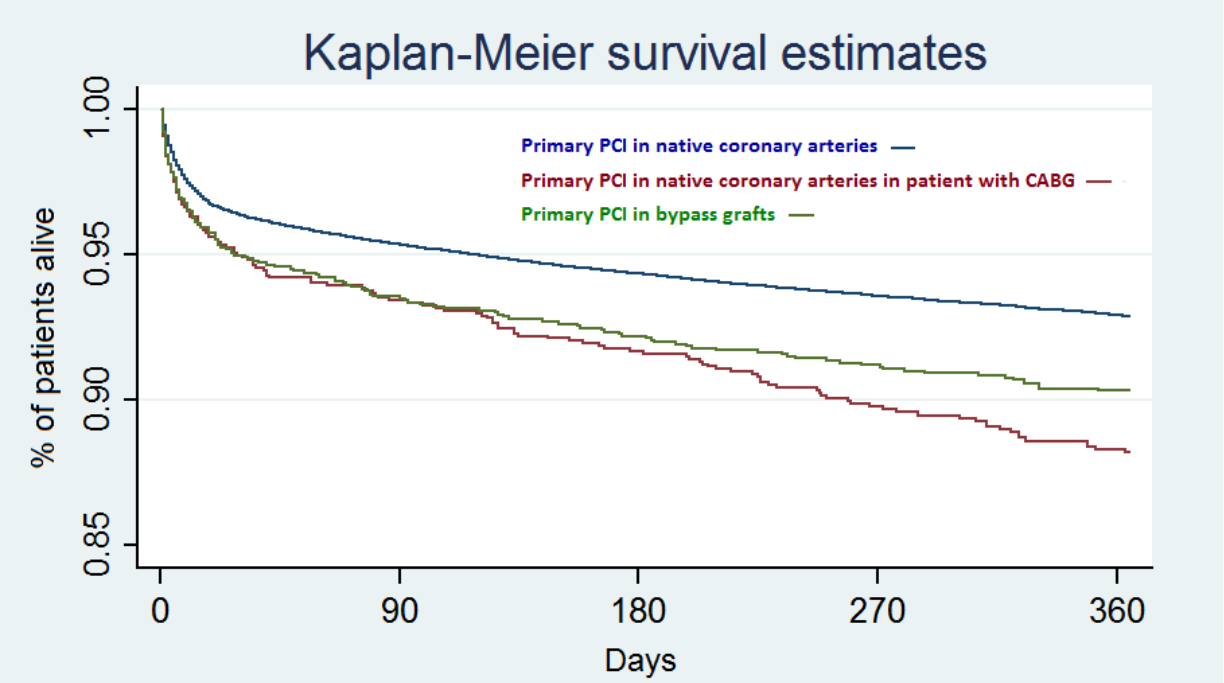
A)



Follow up	Day 0	Day 10	Day 20	Day 30
Number at risk in PCI to native coronary arteries	75,932	74,097	73,440	73,190
Number at risk in PCI to native coronary arteries in patient with CABG	1,154	1,115	1,103	1,096
Number at risk in PCI to bypass graft	1,473	1,425	1,410	1,399

Log-rank test $p<0.001$

B)



Log-rank test p<0.001

Follow up	Day 0	Day 90	Day 180	Day 270	Day 365
Number at risk in PCI to native coronary arteries	75,932	72,373	70,513	65,259	60,456
Number at risk in PCI to native coronary arteries in patient with CABG	1,154	1,078	1,041	953	871
Number at risk in PCI to bypass graft	1,473	1,378	1,341	1,258	1,177

Supplementary Table 1: Missing data table

Variable	Data available for imputations	Missing data or excluded
Age	79,295	1,221
Female	79,295	1,221
Smoking	70,789	9,727
Diabetes	76,073	4,443
Hypertension	78,107	2,409
Hyperlipidemia	78,107	2,409
Previous MI	72,616	7,900
Previous CVA	78,107	2,409
Peripheral vascular disease	78,107	2,409
Previous renal disease	72,988	7,528
LVEF	24,443	56,073
Family history of heart disease	67,215	13,301
Access site	75,617	4,899
Glycoprotein IIb/IIIa inhibitor	69,944	10,572
Target vessel		
LAD	79,205	1,311
Left main	79,205	1,311
Circumflex	79,205	1,311
Right coronary artery	79,205	1,311
Graft	79,205	1,311
Multivessel	79,295	1,221
Thrombectomy device	72,599	7,917
Cardiogenic shock	78,768	1,748
Circulatory support	73,864	6,652
DES use	76,382	4,134
Number of stents	76,382	4,134
Thrombus aspiration	75,081	5,435
Ventilatory support	69,325	11,191
Femoral closure device	73,705	6,811
Use of distal protection device	72,733	7,783

Supplementary Table 2: Logistic regression and Cox proportional hazards analysis for 30-day mortality and 1-year mortality

Outcome	Logistic regression odds ratio for outcome (95% CI), p-value	Cox proportional hazard ratio for outcome (95% CI), p-value
Unadjusted 30 day mortality		
Group 1	1.00 (ref)	1.00 (ref)
Group 2	1.39 (1.10-1.77), p=0.007	1.40 (1.08-1.82), p=0.011
Group 3	1.38 (1.11-1.71), p=0.003	1.40 (1.11-1.76), p=0.004
Adjusted 30 day mortality*		
Group 1	1.00 (ref)	1.00 (ref)
Group 2	1.02 (0.77-1.34), p=0.89	1.07 (0.81-1.40), p=0.65
Group 3	1.33 (1.03-1.70), p=0.028	1.41 (1.10-1.79), p=0.006
Unadjusted 1-year mortality		
Group 1	1.00 (ref)	1.00 (ref)
Group 2	1.69 (1.42-2.02), p<0.001	1.67 (1.41-1.98), p<0.001
Group 3	1.35 (1.14-1.59), p=0.001	1.34 (1.14-1.59), p=0.001
Adjusted 1-year mortality*		
Group 1	1.00 (ref)	1.00 (ref)
Group 2	1.17 (0.95-1.43), p=0.15	1.11 (0.92-1.33), p=0.28
Group 3	1.16 (0.95-1.41), p=0.14	1.21 (1.01-1.44), p=0.035

Group 1: Primary PCI in native coronary arteries, Group 2: Primary PCI in native coronary arteries in patient with CABG, Group 3: Primary PCI in bypass grafts
*Adjusted for age, sex, smoking status, hypertension, hyperlipidemia, diabetes mellitus, previous stroke, peripheral vascular disease, renal disease, family history, access site, use of glycoprotein IIb/IIIa inhibitor, multivessel PCI, femoral closure device, cardiogenic shock, use of circulatory support, number of stents, use of thrombectomy device, receipt of ventilation, LV ejection fraction, embolic protection device, left main stem disease, left anterior descending disease, balloon time.

Supplementary Table 3: Balance diagnostics for propensity model

Groups		Mean (SD)	Median (IQR)
Group 1: Primary PCI in native coronary arteries vs Group 2: Primary PCI in native coronary arteries in patient with CABG	Case	0.9850 (0.0314)	0.9939 (0.9865, 0.9969)
	Control	0.9850 (0.0.314)	0.9939 (0.9865, 0.9969)
	Abs(Case-Control)	0.00005 (0.00036)	0.00002 ($7*10^{-6}$, 0.00004)
Group 1: Primary PCI in native coronary arteries vs Group 3: Primary PCI in bypass grafts	Case	0.9811 (0.0440)	0.9907 (0.9812, 0.9995)
	Control	0.9811 (0.0439)	0.9907 (0.9811, 0.9994)
	Abs(Case-Control)	0.0001 (0.0007)	0.00004 (0.00001, 0.00013)

Supplementary Table 4: Summary of the studies evaluating mortality and major adverse cardiovascular events in patient with and without prior coronary artery bypass graft who present with STEMI or acute myocardial infarction.

Study ID	No. of participants	Unadjusted results	Adjusted results
Bench 2013	1,649 PPCI in patient with STEMI. 93 with prior CABG.	Prior CABG vs no revascularization: MACCE 6.5% vs 2.7%, in-hospital death 6.5% vs 2.2%.	Prior CABG was not associated with increased MACE (OR 1.77 95%CI 0.67-4.70) but was associated with increased in-hospital mortality (OR 3.40 95%CI 1.15-10.00).
Gaglia 2011	4,192 PCI in patient with acute myocardial infarction. 192 with prior CABG.	Saphenous vein graft versus native vessel: in-hospital cardiac mortality 6.6% vs 3.3% and overall mortality at 30 days 14.3% vs 8.4%. 1 year MACE 36.8% vs 24.5%, 1 year mortality 29.8% vs 16.4%.	Prior CABG and 30 day mortality HR 2.13 95% CI 1.06-4.26. 1 year MACE HR 1.87 95% CI 1.22-2.87.
Kohl 2014	3,542 patients with STEMI. 249 had prior CABG.	Previous CABG vs no previous CABG and outcomes at 30 days: death 4.8% vs 5.9%, p=0.49, MACE 6.8% vs 7.4%, p=0.76. Outcomes at 1 year: death 10.8% vs 9.1%, p=0.36, MACE 15.7% vs 14.2%, p=0.12.	No adjusted results.
Nikolsky 2013	3,599 patients with STEMI. 105 had prior CABG.	Previous CABG and no previous CABG at outcomes at 30 days: death 3.8% vs 2.6%, MACE 8.6% vs 5.4%.	Prior CABG was not a predictor of 3 year mortality HR 0.37 95% CI 0.10-1.34, 3 year MACE HR 0.81 95% CI 0.42-1.55.
Stone 2000	1,100 patients with acute myocardial infarction. 58 had prior CABG.	Previous CABG and no previous CABG and in-hospital outcomes: death 6.9% vs 2.6%, MACE 15.5% vs 19.4%.	No adjusted results.
Welsh 2010	5,745 patients with STEMI. 128 had prior CABG.	Previous CABG vs no previous CABG and 90 day outcomes: death 11.9% vs 4.6%, death/congestive heart failure/shock 16.4% vs 10.1%.	Prior CABG was associated with 90-day death HR 1.90 95% CI 1.08-3.33 but not death/congestive heart failure/shock HR 1.06 95% CI 0.66-1.70.

Supplementary Data 1: Stata code for multiple imputations

```
mi set mlong

mi register imputed balloontime shock mi dm gpi circsupp femclose smoking fh hchol htn pvd
cva ventilate fem0rad1 lvef /*device*/ renal stents des emboli thromb
(66636 m=0 obs. now marked as incomplete)

 mi register regular group age sex multivessel mfu inhospdeath dead30 dead365 dead mace
cvableed cvaembolic tia emergcabg reintervention reinfarction bleed stroke lmain lad cx rca
graft

mi impute chained (truncreg) balloontime (logit) shock mi dm gpi circsupp femclose smoking
fh hchol htn pvd cva ventilate fem0rad1 /*device*/ renal emboli thromb (mlogit) stents (ologit)
lvef = age i.sex i.group i.multivessel mfu, add(10) /*noisily*/ augment report chaindots

Checking equations:
 -- above applies to specification (logit ) shock = age i.sex i.group i.multivessel mfu
 -- above applies to specification (logit ) hchol = age i.sex i.group i.multivessel mfu
 -- above applies to specification (logit ) htn = age i.sex i.group i.multivessel mfu
 -- above applies to specification (logit ) pvd = age i.sex i.group i.multivessel mfu
 -- above applies to specification (logit ) cva = age i.sex i.group i.multivessel mfu
 -- above applies to specification (mlogit ) stents = age i.sex i.group i.multivessel mfu
 -- above applies to specification (logit ) dm = age i.sex i.group i.multivessel mfu
 -- above applies to specification (logit ) fem0rad1 = age i.sex i.group i.multivessel mfu
 -- above applies to specification (logit ) thromb = age i.sex i.group i.multivessel mfu
 -- above applies to specification (logit ) circsupp = age i.sex i.group i.multivessel mfu
 -- above applies to specification (logit ) femclose = age i.sex i.group i.multivessel mfu
 -- above applies to specification (logit ) renal = age i.sex i.group i.multivessel mfu
 -- above applies to specification (logit ) emboli = age i.sex i.group i.multivessel mfu
 -- above applies to specification (logit ) mi = age i.sex i.group i.multivessel mfu
 -- above applies to specification (logit ) smoking = age i.sex i.group i.multivessel mfu
 -- above applies to specification (logit ) gpi = age i.sex i.group i.multivessel mfu
 -- above applies to specification (logit ) ventilate = age i.sex i.group i.multivessel mfu
 -- above applies to specification (logit ) fh = age i.sex i.group i.multivessel mfu
 -- above applies to specification (truncreg ) balloontime = age i.sex i.group i.multivessel mfu
 -- above applies to specification (ologit ) lvef = age i.sex i.group i.multivessel mfu

Conditional models:

shock: logit shock i.hchol i.htn i.pvd i.cva i.stents i.dm i.fem0rad1 i.thromb i.circsupp
i.femclose i.renal i.emboli i.mi i.smoking i.gpi i.ventilate i.fh balloontime i.lvef age i.sex
i.group i.multivessel mfu, augment

 hchol: logit hchol i.shock i.htn i.pvd i.cva i.stents i.dm i.fem0rad1 i.thromb i.circsupp
i.femclose i.renal i.emboli i.mi i.smoking i.gpi i.ventilate i.fh balloontime i.lvef age i.sex
i.group i.multivessel mfu , augment

htn: logit htn i.shock i.hchol i.pvd i.cva i.stents i.dm i.fem0rad1 i.thromb i.circsupp i.femclose
i.renal i.emboli i.mi i.smoking i.gpi i.ventilate i.fh balloontime i.lvef age i.sex i.group
i.multivessel mfu , augment
```

pvd: logit pvd i.shock i.hchol i.htn i.cva i.stents i.dm i.fem0rad1 i.thromb i.circsupp i.femclose i.renal i.emboli i.mi i.smoking i.gpi i.ventilate i.fh balloontime i.lvef age i.sex i.group i.multivessel mfu , augment

cva: logit cva i.shock i.hchol i.htn i.pvd i.stents i.dm i.fem0rad1 i.thromb i.circsupp i.femclose i.renal i.emboli i.mi i.smoking i.gpi i.ventilate i.fh balloontime i.lvef age i.sex i.group i.multivessel mfu , augment

stents: mlogit stents i.shock i.hchol i.htn i.pvd i.cva i.dm i.fem0rad1 i.thromb i.circsupp i.femclose i.renal i.emboli i.mi i.smoking i.gpi i.ventilate i.fh balloontime i.lvef age i.sex i.group i.multivessel mfu , augment

dm: logit dm i.shock i.hchol i.htn i.pvd i.cva i.stents i.fem0rad1 i.thromb i.circsupp i.femclose i.renal i.emboli i.mi i.smoking i.gpi i.ventilate i.fh balloontime i.lvef age i.sex i.group i.multivessel mfu , augment

fem0rad1: logit fem0rad1 i.shock i.hchol i.htn i.pvd i.cva i.stents i.dm i.thromb i.circsupp i.femclose i.renal i.emboli i.mi i.smoking i.gpi i.ventilate i.fh balloontime i.lvef age i.sex i.group i.multivessel mfu , augment

thromb: logit thromb i.shock i.hchol i.htn i.pvd i.cva i.stents i.dm i.fem0rad1 i.circsupp i.femclose i.renal i.emboli i.mi i.smoking i.gpi i.ventilate i.fh balloontime i.lvef age i.sex i.group i.multivessel mfu , augment

circsupp: logit circsupp i.shock i.hchol i.htn i.pvd i.cva i.stents i.dm i.fem0rad1 i.thromb i.femclose i.renal i.emboli i.mi i.smoking i.gpi i.ventilate i.fh balloontime i.lvef age i.sex i.group i.multivessel mfu , augment

femclose: logit femclose i.shock i.hchol i.htn i.pvd i.cva i.stents i.dm i.fem0rad1 i.thromb i.circsupp i.renal i.emboli i.mi i.smoking i.gpi i.ventilate i.fh balloontime i.lvef age i.sex i.group i.multivessel mfu , augment

renal: logit renal i.shock i.hchol i.htn i.pvd i.cva i.stents i.dm i.fem0rad1 i.thromb i.circsupp i.femclose i.emboli i.mi i.smoking i.gpi i.ventilate i.fh balloontime i.lvef age i.sex i.group i.multivessel mfu , augment

emboli: logit emboli i.shock i.hchol i.htn i.pvd i.cva i.stents i.dm i.fem0rad1 i.thromb i.circsupp i.femclose i.renal i.mi i.smoking i.gpi i.ventilate i.fh balloontime i.lvef age i.sex i.group i.multivessel mfu , augment

mi: logit mi i.shock i.hchol i.htn i.pvd i.cva i.stents i.dm i.fem0rad1 i.thromb i.circsupp i.femclose i.renal i.emboli i.smoking i.gpi i.ventilate i.fh balloontime i.lvef age i.sex i.group i.multivessel mfu , augment

smoking: logit smoking i.shock i.hchol i.htn i.pvd i.cva i.stents i.dm i.fem0rad1 i.thromb i.circsupp i.femclose i.renal i.emboli i.mi i.gpi i.ventilate i.fh balloontime i.lvef age i.sex i.group i.multivessel mfu , augment

gpi: logit gpi i.shock i.hchol i.htn i.pvd i.cva i.stents i.dm i.fem0rad1 i.thromb i.circsupp i.femclose i.renal i.emboli i.mi i.smoking i.ventilate i.fh balloontime i.lvef age i.sex i.group i.multivessel mfu , augment

```
ventilate: logit ventilate i.shock i.hchol i.htn i.pvd i.cva i.stents i.dm i.fem0rad1 i.thromb
i.circsupp i.femclose i.renal i.emboli i.mi i.smoking i.gpi i.fh balloontime i.lvef age i.sex
i.group i.multivessel mfu , augment

fh: logit fh i.shock i.hchol i.htn i.pvd i.cva i.stents i.dm i.fem0rad1 i.thromb i.circsupp
i.femclose i.renal i.emboli i.mi i.smoking i.gpi i.ventilate balloontime i.lvef age i.sex i.group
i.multivessel mfu , augment

balloontime: truncreg balloontime i.shock i.hchol i.htn i.pvd i.cva i.stents i.dm i.fem0rad1
i.thromb i.circsupp i.femclose i.renal i.emboli i.mi i.smoking i.gpi i.ventilate i.fh i.lvef age
i.sex i.group i.multivessel mfu

lvef: ologit lvef i.shock i.hchol i.htn i.pvd i.cva i.stents i.dm i.fem0rad1 i.thromb i.circsupp
i.femclose i.renal i.emboli i.mi i.smoking i.gpi i.ventilate i.fh balloontime age i.sex i.group
i.multivessel mfu , augment

Performing chained iterations:
  imputing m=1: burn-in 10 ..... done
  imputing m=2: burn-in 10 ..... done
  imputing m=3: burn-in 10 ..... done
  imputing m=4: burn-in 10 ..... done
  imputing m=5: burn-in 10 ..... done
  imputing m=6: burn-in 10 ..... done
  imputing m=7: burn-in 10 ..... done
  imputing m=8: burn-in 10 ..... done
  imputing m=9: burn-in 10 ..... done
  imputing m=10: burn-in 10 ..... done

Multivariate imputation                 Imputations = 10
Chained equations                               added =  10
Imputed: m=1 through m=10                       updated = 0

Initialization: monotone                Iterations =  100
                                                burn-in =       10

      balloontime: truncated regression
            shock: logistic regression
               mi: logistic regression
               dm: logistic regression
              gpi: logistic regression
         circsupp: logistic regression
         femclose: logistic regression
          smoking: logistic regression
               fh: logistic regression
            hchol: logistic regression
              htn: logistic regression
              pvd: logistic regression
              cva: logistic regression
        ventilate: logistic regression
         fem0rad1: logistic regression
```

renal: logistic regression
emboli: logistic regression
thromb: logistic regression
stents: multinomial logistic regression
lvef: ordered logistic regression

Variable	Complete	Incomplete	Imputed	Total
	Observations per m			
balloontime	65492	13803	13803	79295
shock	78768	527	527	79295
mi	72616	6679	6679	79295
dm	76073	3222	3222	79295
gpi	69944	9351	9351	79295
circsupp	73864	5431	5431	79295
femclose	73705	5590	5590	79295
smoking	70789	8506	8506	79295
fh	67215	12080	12080	79295
hchol	78107	1188	1188	79295
htn	78107	1188	1188	79295
pvd	78107	1188	1188	79295
cva	78107	1188	1188	79295
ventilate	69325	9970	9970	79295
fem0rad1	75617	3678	3678	79295
renal	72988	6307	6307	79295
emboli	72733	6562	6562	79295
thromb	75081	4214	4214	79295
stents	76382	2913	2913	79295
lvef	24443	54852	54852	79295

(complete + incomplete = total; imputed is the minimum across m
of the number of filled-in observations.)