Preoperative Stroke and Outcomes after Coronary Artery Bypass Graft Surgery

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ABSTRACT

Background: Data are lacking on the optimal scheduling of coronary artery bypass grafting (CABG) surgery after stroke. The authors investigated the preoperative predictors of adverse outcomes in patients undergoing CABG, with a focus on the importance of the time interval between prior stroke and CABG.

Methods: The Hospital Episode Statistics database (April 2006–March 2010) was analyzed for elective admissions for CABG. Independent preoperative patient factors influencing length of stay, postoperative stroke, and mortality, were identified by logistic regression and presented as adjusted odds ratios (OR).

What We Already Know about This Topic

- Determining the appropriateness and timing of surgery is dependent on the balance of perioperative risk *versus* effectiveness of therapy. However, data are lacking on perioperative risk in potentially vulnerable subgroups, such as patients with stroke.
- This study investigated the impact of prior stroke on perioperative outcomes after coronary artery bypass graft surgery.

What This Article Tells Us That Is New

- Preoperative stroke was associated with increased mortality, risk of postoperative stroke, and length of stay. However, the greater the time interval between the time of the preoperative stroke and surgery, the greater the increased risk of postoperative stroke. Therefore, these data do not support delaying elective coronary artery bypass graft surgery in the presence of a recent stroke.

Results: In all, 62,104 patients underwent CABG (1.8% mortality). Prior stroke influenced mortality (OR 2.20 [95% CI 1.47–3.29]), postoperative stroke (OR 1.99 [1.39–2.85]), and prolonged length of stay (OR 1.31 [1.11–1.56]). The time interval between stroke and CABG did not influence mortality or prolonged length of stay. However, a longer time interval between stroke and CABG surgery was associated with a small increase in risk of postoperative stroke (OR per month elapsed 1.02 [1.00–1.04]; P = 0.047). An interaction was evident between prior stroke and myocardial infarction for death (OR 5.50 [2.84–10.8], indicating the importance of the combination of comorbidities. Prominent effects on mortality were also exerted by liver disease (OR 20.8 [15.18–28.51]) and renal failure (OR 4.59 [3.85–5.46]).

Conclusions: The authors found no evidence that more recent preoperative stroke predisposed patients undergoing CABG surgery to suffer postoperative stroke, death, or prolonged length of stay. The combination of prior stroke and myocardial infarction substantially increased perioperative risk.

CORONARY artery bypass grafting (CABG) remains an important therapeutic option in patients with coronary artery disease not suitable for percutaneous coronary intervention (PCI). Indeed, CABG continues to be

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the treatment of choice in patients with left main and/or multivessel coronary artery disease with intermediate to high synergy between PCI with Taxus and cardiac surgery scores.[1,2] Other relative indications for CABG include the presence of diabetes mellitus, low left ventricular ejection fraction, and requirement of rescue therapy after failed PCI.[3] Determination of the appropriateness and timing of surgery is dependent on the balance of perioperative risk *versus* effectiveness of therapy. Although randomized controlled trials continue to define efficacy issues (especially in comparison with PCI),[2,3] further data are required on the evaluation of perioperative risk, especially in potentially vulnerable subgroups such as patients with stroke.

Excellent scoring systems such as the European System for Cardiac Operative Risk Evaluation[4] and the Society of Thoracic Surgeons risk score[5] aid judgment of perioperative risk. However, despite the information they provide on the impact of various comorbidities such as stroke, they are lacking in quantifying the impact of the timing of prior stroke with subsequent surgery. In this study, we were interested in quantifying the impact of a wide range of comorbid diseases on outcomes after cardiac surgery, with a particular interest in the impact of prior stoke. In particular, we wished to identify whether there was a time interval after stroke during which CABG surgery should be considered higher risk. We have recently studied this in elective noncardiac surgery and were unable to find an association between the time interval between stroke and surgery and perioperative outcomes.[6]

Given the potential of preoperative stroke to predict perioperative outcomes after CABG surgery, we were of the opinion that specific evaluation of this population was warranted.[7] *A priori* we were interested in (1) quantifying the impact of prior stroke on perioperative outcomes from CABG surgery and (2) investigating whether the time interval between stroke and CABG surgery influenced outcomes. During the analysis we developed a third hypothesis that there may be an interaction between stroke and myocardial infarction (MI).

Materials and Methods

Local research ethics committee (Imperial College London, London, United Kingdom) and Section 251 (formerly Section 60) National Information Governance Board for Health and Social Care approval were obtained. We then extracted all nonduplicate elective admissions for CABG in England for the financial years April 1, 2006–March 31, 2010, with patient identification and valid age, sex, and length of stay (LOS) from the Hospital Episode Statistics database. Hospital Episode Statistics is an administrative database covering all admissions to National Health Services (public) hospitals in England, including private patients treated in these hospitals. Diagnostic information is coded using the International Classification of Diseases system version 10; the 13 secondary diagnoses record comorbidities and complications. Its 12 procedure fields use the classification of interventions and procedures of the Office of Population Censuses and Surveys, unique to the United Kingdom. Admissions (defined as "spells" in the database) ending in transfer to another hospital were linked together to form "superspells" (we will refer to the continuous inpatient period, including any transfers, as 1 admission). The principal procedure of interest in this study was CABG (Office of Population Census and Surveys codes K40-K46). We conducted the initial analysis including valve surgery, PCI, or revisions (Office of Population Census and Surveys codes K25-K38, K49, K50, K75, K442, K456, K465) that we refer to as the "full dataset." We also conducted the analysis without valve surgery, PCI, or revisions, referred to as "uncomplicated" CABG. "Complicated" CABG referred to procedures with valve surgery, prior failed PCI, or revision operations. We excluded 732 procedures (1.2% of the total) due to invalid age, sex, or postal code.

Preoperative "vascular events," including stroke, MI, and unstable angina, were defined as conditions that necessitated hospital admission. This provided a primary diagnosis code with known timing as we have used previously for noncardiac surgery.[6] We looked retrospectively in the data set for admissions within the 10 yr before the CABG date with the primary diagnosis of stroke (I61-I64 or I66), MI (I21, I22), and unstable angina (I200). We looked throughout the preoperative admissions in case the stroke, MI, or unstable angina occurred after transfer. The time (in days) from the stroke, to the index operation was noted. If a patient had more than one "vascular event" then the date of the most recent was used.

The other comorbidities not meeting the criteria for a "vascular event," such as diabetes mellitus, liver disease, or renal failure, were identified from the secondary diagnosis codes on admission for CABG (as in our previous study).[6] Age was analyzed as a continuous variable ("risk per additional single year") though in table 1 a threshold is displayed for illustrative purposes. The reference sex was male. We derived a set of comorbidity variables representing risk factors for postoperative death, using an International Classification of Diseases system version 10 version of the Charlson comorbidity index[8] and other risk indices[9–11] as a starting point and augmenting their components where necessary.[6] However, rather than using the Charlson comorbidity index to adjust for perioperative risk, we adjusted for the impact of each preoperative factor individually as we have done previously.[6] We also adjusted for area-level socioeconomic status using the population weighted Carstairs Deprivation quintiles.[12] All comorbidities, age, sex, and socioeconomic status were included in our final regression model and adjusted odds ratios (ORs) for each variable are reported. Our primary endpoint was the adjusted OR of perioperative mortality (defined as inpatient death within 30 days of surgery); secondary endpoints were two surrogates of perioperative morbidity: prolonged LOS (above the upper quartile) and postoperative stroke. Postoperative stroke was identified in secondary diagnosis fields for

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Table 1. Patient Demographics and Crude Outcomes from Bivariate Analysis for Patients Undergoing CABG Surgery

Factor	N (% of Total)	Deaths if Factor Present (Rate as %)	Deaths if Factor Absent (Rate as %)	*P* Value for Factor Present *vs.* Absent	Postop Stroke If Factor Present (Rate as %)	Postop Stroke If Factor Absent (Rate As %)	*P* Value for Factor Present *vs.* Absent
Male sex	49,838 (80.2%)	725 (1.5%)	366 (3.0%)	<0.001	323 (0.6%)	100 (0.8%)	0.044
Age >70 yr	25,055 (40.3%)	739 (2.9%)	352 (1.0%)	<0.001	272 (1.1%)	151 (0.4%)	<0.001
"Complicated" procedure*	12,608 (20.3%)	576 (4.6%)	515 (1.0%)	<0.001	190 (1.5%)	233 (0.5%)	<0.001
Lowest socioeconomic quintile	10,339 (16.6%)	189 (1.8%)	902 (1.7%)	0.546	74 (0.7%)	349 (0.7%)	0.639
Hypertension	39,903 (64.3%)	636 (1.6%)	455 (2.0%)	<0.001	276 (0.7%)	147 (0.7%)	0.668
Atrial fibrillation	15,275 (24.6%)	407 (2.7%)	684 (1.5%)	<0.001	198 (1.3%)	225 (0.5%)	<0.001
Other arrhythmia	2,211 (3.6%)	140 (6.3%)	951 (1.6%)	<0.001	30 (1.4%)	393 (0.7%)	<0.001
Stable angina	5,224 (8.4%)	81 (1.6%)	1,010 (1.8%)	0.236	27 (0.5%)	396 (0.7%)	0.131
Valvular disease	9639 (15.5%)	344 (3.6%)	747 (1.4%)	<0.001	112 (1.2%)	311 (0.6%)	<0.001
Congestive heart failure	4,697 (7.6%)	301 (6.4%)	790 (1.4%)	<0.001	50 (1.1%)	373 (0.6%)	0.001
Lower respiratory disease	6,055 (9.7%)	123 (2.0%)	968 (1.7%)	0.087	42 (0.7%)	381 (0.7%)	0.901
Diabetes	13857 (22.3%)	237 (1.7%)	854 (1.8%)	0.637	82 (0.6%)	341 (0.7%)	0.147
Chronic renal failure	2,008 (3.2%)	214 (10.7%)	877 (1.5%)	<0.001	42 (2.1%)	381 (0.6%)	<0.001
Cancer	709 (1.1%)	18 (2.5%)	1,073 (1.7%)	0.111	7 (1.0%)	416 (0.7%)	0.319
Liver disease	248 (0.4%)	83 (33.5%)	1,008 (1.6%)	<0.001	4 (1.6%)	419 (0.7%)	0.074
Peripheral vascular disease	4,943 (8.0%)	162 (3.3%)	929 (1.6%)	<0.001	54 (1.1%)	369 (0.6%)	<0.001
Stroke in prior 10 yr	695 (1.1%)	28 (4.0%)	1,063 (1.7%)	<0.001	11 (1.6%)	412 (0.7%)	0.004
MI in prior 10 yr	10,418 (16.8%)	190 (1.8%)	901 (1.7%)	0.568	72 (0.7%)	351 (0.7%)	0.892
UA in prior 10 yr	5,241 (8.4%)	114 (2.2%)	977 (1.7%)	0.016	34 (0.6%)	389 (0.7%)	0.766
Stroke in prior 3 mo	28 (0%)	0 (0%)	1,091 (1.8%)	0.479	0 (0%)	423 (0.7%)	0.661
Stroke in prior 6 mo	84 (0.1%)	3 (3.6%)	1,088 (1.8%)	0.205	1 (1.2%)	422 (0.7%)	0.57

* CABG with valve procedure after failed percutaneous coronary intervention or revision procedure.
CABG = coronary artery bypass grafting; MI = myocardial infarction; UA = unstable angina.

the admission using the codes I61-I64 or I66. Code I69 ("old stroke") was excluded. However, the date and time of the stroke are not recorded so the exact timing of the stroke is not known. We also investigated whether the time interval between stroke and surgery affected a composite outcome of "mortality or postoperative stroke."

Details of patients with a defined stroke were extracted and then analyzed, using the aforementioned outcomes, to define the adjusted risk imposed by the timing of the condition preoperatively. In further analyses, we reanalyzed our data set to probe for any interaction between MI and stroke to understand whether this population was of higher risk again than those who had a prior MI or stroke alone. We also analyzed for an interaction between heart failure and stroke.

Statistical Analysis

Logistic regression models were fitted for mortality, prolonged LOS, and postoperative stroke with the following patient factors: age, sex, area-level deprivation score using Carstairs deprivation population-weighted quintiles,[12,13] and comorbidities. In further analyses, the date of the previous stroke was incorporated into the analysis to discern whether the time interval between stroke and CABG affected postoperative outcomes. This was conducted using time as a continuous variable (odds per month) and also with thresholds at 3 months (acute stroke less than 3 months old *vs.* older stroke), 6 months and 5 yr (stroke less than 5 yr old *vs.* older than 5 yr). Other comorbidities were included as indicator variables if they were recorded in at least 30 patients but sometimes had to be dropped even with more than 30 patients, to enable the model to converge. To avoid the problems of stepwise model selection procedures, we retained all candidate variables even if not significant and only removed those that prevented model convergence. We tried fitting two-level models to account for the clustering of patients within hospitals but found minimal clustering, and therefore present the results from the single-level regression models. All analyses were performed using SAS v9.2 (Cary, NC). Data are tabulated and reported as adjusted OR. Statistical significance was defined as $P < 0.05$. No attempts were made to adjust for multiple comparisons but that exact *P* values are reported so further adjustments can be made by the reader. The data are presented in accordance with Strengthening the Reporting of Observational Studies in Epidemiology guidance.

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Results

Cohort Demographics

In the full data set, 62,104 patients underwent CABG surgery between 2006 and 2010 (table 1). Of these, 49,496 (79.7%) had "uncomplicated" CABG procedures. "Complicated" procedures were less common, including valve surgery (12,120; 19.5%), after PCI (78; 0.1%) and revisions (567; 0.9%). Of the total patients 81.5% underwent CABG within 90 days of being listed for the operation (median wait, 57 days; interquartile range, 27–84 days). When considering the full data set, 1.1% (695 patients) had a prior admission for stroke in the previous 10 yr (table 1). Overall mortality was 1.8% (1,091 deaths) though it was lower in the cohort of "uncomplicated" operations that excluded valve surgery, patients with prior failed PCI, and revision operations (1.0%; 515 deaths). In the full data set, prolonged LOS occurred for 13,594 patients (21.9%) and postoperative stroke occurred in 423 patients (0.7%). A composite endpoint of postoperative stroke or death occurred in 1,446 patients (2.3%).

Effect of Preoperative Variables on Perioperative Outcomes

Prior stroke was associated with an increase in mortality (OR 2.20 [1.47–3.29]), postoperative stroke (OR 1.99 [1.39–2.85]) and prolonged LOS (OR 1.31 [1.11–1.56]). In addition, age, female sex, nonatrial fibrillation arrhythmia, valvular heart disease, heart failure, renal failure, peripheral vascular disease, unstable angina, and liver disease all increased perioperative mortality whereas prior MI did not (table 2). Despite occurring in only 0.4% of the population (248 patients), liver disease exerted the most pronounced effect on mortality with 33.5% of liver disease patients (83) dying. In contrast, a prior diagnosis of hypertension was shown to be protective (table 2).

When uncomplicated CABG surgery was considered separately, these risk factors were largely unchanged, though valvular heart disease was dropped as a risk factor in favor of lung disease (table 3). For prior stroke, the odds of mortality was 2.97 (95% CI 1.78–4.96) and postoperative stroke was 3.05 (1.55–6.01) in these patients.

Perioperative Risk Factors in Patients with Prior Stroke

In our subgroup of 695 patients with prior stroke undergoing CABG, surgery was frequently conducted within the first year of stroke; however, only 28 patients underwent CABG surgery within 3 months of their stroke (with no deaths). Mortality rate was 4% (28 patients), postoperative stroke rate was 1.6% (11 patients), and "postoperative stroke or death" occurred in 5% (35 patients) of the cohort with prior stroke. Contrary to our hypothesis, we did not find a relationship between a short time interval between the stroke and subsequent surgery and perioperative outcomes when analyzed as a continuous

Table 2. Association between Preoperative Variables and Outcomes after CABG Surgery (Full Data Set)

	Mortality		Long LOS		Postoperative Stroke	
Variables	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
Age (per yr)	1.06 (1.05–1.07)	<0.001	1.05 (1.04–1.05)	<0.001	1.05 (1.03 – 1.06)	<0.001
Sex (F *vs.* M)	1.82 (1.59–2.09)	<0.001	1.36 (1.3–1.43)	<0.001	0.95 (0.76–1.2)	0.688
Socioeconomic quintile 2 *vs.* 1	1.12 (0.92–1.36)	0.269	1.06 (1–1.13)	0.068	1.14 (0.84–1.55)	0.405
Socioeconomic quintile 3 *vs.* 1	1.09 (0.9–1.33)	0.379	1.15 (1.08–1.23)	<0.001	1.21 (0.89–1.64)	0.233
Socioeconomic quintile 4 *vs.* 1	1.04 (0.84–1.28)	0.740	1.28 (1.2–1.37)	<0.001	1.31 (0.95–1.8)	0.096
Socioeconomic quintile 5 *vs.* 1	1.26 (1.02–1.56)	0.036	1.48 (1.38–1.58)	<0.001	1.47 (1.06–2.05)	0.023
Hypertension	0.78 (0.68–0.89)	<0.001	0.98 (0.94–1.02)	0.301	1.1 (0.89–1.35)	0.378
Atrial fibrillation	1.01 (0.88–1.15)	0.916	2.21 (2.11–2.3)	<0.001	1.84 (1.5–2.25)	<0.001
Other arrhythmia	2.84 (2.33–3.47)	<0.001	1.91 (1.74–2.1)	<0.001	1.4 (0.96–2.05)	0.084
Stable angina	1.1 (0.87–1.4)	0.417	0.99 (0.91–1.06)	0.714	0.86 (0.58–1.28)	0.464
Valvular disease	1.65 (1.43–1.9)	<0.001	1.87 (1.78–1.97)	<0.001	0.69 (0.52–0.9)	0.007
Congestive heart failure	3.34 (2.88–3.88)	<0.001	1.67 (1.56–1.78)	<0.001	1.13 (0.83–1.53)	0.449
Lower respiratory disease	1.09 (0.9–1.33)	0.389	1.37 (1.28–1.46)	<0.001	0.93 (0.67–1.28)	0.656
Diabetes	0.97 (0.83–1.13)	0.700	1.27 (1.21–1.34)	<0.001	0.89 (0.7–1.14)	0.375
Chronic renal failure	4.59 (3.85–5.46)	<0.001	3.62 (3.29–4)	<0.001	2.12 (1.52–2.97)	<0.001
Cancer	1.11 (0.67–1.82)	0.693	1.17 (0.98–1.39)	0.079	1.11 (0.52–2.36)	0.791
Liver disease	20.8 (15.18–28.51)	<0.001	1.38 (1.03–1.84)	0.030	1.3 (0.47–3.6)	0.608
Peripheral vascular disease	1.85 (1.55–2.21)	<0.001	1.31 (1.22–1.4)	<0.001	1.47 (1.1–1.97)	0.009
Prior stroke	2.2 (1.47–3.29)	<0.001	1.31 (1.11–1.56)	0.002	1.88 (1.02–3.46)	0.041
Prior unstable angina	1.23 (1–1.52)	0.048	1.13 (1.05–1.21)	0.001	1 (0.7–1.42)	0.987
Prior myocardial infarction	1.11 (0.94–1.31)	0.220	1.03 (0.97–1.08)	0.357	1.23 (0.95–1.59)	0.123

Socioeconomic quintile 5 is the most deprived (lowest fifth).

CABG = coronary artery bypass grafting; F = female; LOS = length of stay; M = male; OR = odds ratio.

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Table 3. Association between Preoperative Variables and Outcomes after "Uncomplicated" CABG Surgery

	Mortality		Long Length of Stay		Postoperative Stroke	
Factor	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value	OR (95% CI)	*P* value
Age (per yr)	1.07 (1.06–1.08)	<0.001	1.05 (1.04–1.05)	<0.001	1.05 (1.03–1.07)	<0.001
Sex (F *vs.* M)	1.71 (1.39–2.09)	<0.001	1.26 (1.19–1.34)	<0.001	0.89 (0.63–1.26)	0.519
Socioeconomic quintile 2 *vs.* 1	1.24 (0.92–1.66)	0.163	1.05 (0.98–1.13)	0.163	1.08 (0.72–1.63)	0.700
Socioeconomic quintile 3 *vs.* 1	1.25 (0.93–1.69)	0.139	1.13 (1.05–1.22)	0.001	1.09 (0.72–1.65)	0.689
Socioeconomic quintile 4 *vs.* 1	1.30 (0.96–1.77)	0.093	1.27 (1.18–1.37)	<0.001	1.24 (0.82–1.89)	0.311
Socioeconomic quintile 5 *vs.* 1	1.55 (1.14–2.11)	0.006	1.49 (1.38–1.61)	<0.001	1.22 (0.78–1.89)	0.389
Hypertension	0.74 (0.61–0.90)	0.002	1.04 (0.99–1.10)	0.087	1.17 (0.88–1.55)	0.295
Atrial fibrillation	1.18 (0.96–1.43)	0.111	2.21 (2.10–2.32)	<0.001	2.26 (1.72–2.95)	<0.001
Other arrhythmia	3.09 (2.34–4.08)	<0.001	2.00 (1.79–2.23)	<0.001	1.08 (0.60–1.95)	0.803
Stable angina	1.14 (0.83–1.56)	0.432	1.05 (0.97–1.14)	0.200	0.81 (0.49–1.33)	0.399
Valvular disease	1.23 (0.84–1.79)	0.288	1.58 (1.40–1.78)	<0.001	0.83 (0.41–1.69)	0.606
Congestive heart failure	3.48 (2.80–4.33)	<0.001	1.55 (1.43–1.68)	<0.001	1.23 (0.80–1.89)	0.354
Lower respiratory disease	1.34 (1.03–1.75)	0.030	1.49 (1.39–1.60)	<0.001	0.81 (0.51–1.29)	0.375
Diabetes	1.05 (0.85–1.30)	0.641	1.39 (1.32–1.46)	<0.001	1.00 (0.74–1.36)	0.980
Chronic renal failure	5.75 (4.50–7.36)	<0.001	3.89 (3.46–4.37)	<0.001	2.97 (1.90–4.63)	<0.001
Cancer	1.45 (0.75–2.80)	0.274	1.11 (0.90–1.37)	0.320	1.28 (0.47–3.47)	0.628
Liver disease	23.1 (14.7–36.2)	<0.001	0.93 (0.63–1.38)	0.710	0.94 (0.13–6.85)	0.949
Peripheral vascular disease	1.74 (1.35–2.25)	<0.001	1.31 (1.21–1.42)	<0.001	1.35 (0.90–2.03)	0.150
Prior stroke	2.97 (1.78–4.96)	<0.001	1.37 (1.12–1.67)	0.002	3.05 (1.55–6.01)	0.001
Prior unstable angina	1.21 (0.92–1.60)	0.180	1.11 (1.03–1.20)	0.007	1.05 (0.69–1.61)	0.811
Prior myocardial infarction	1.15 (0.93–1.43)	0.195	1.10 (1.04–1.17)	0.001	1.27 (0.93–1.72)	0.131

Socioeconomic quintile 5 is the most deprived (lowest fifth).
F = female; M = male; OR = odds ratio.

variable (table 4) or a dichotomous variable at 3 months[14] (table 4) and 6 months (data not shown). An increased risk of postoperative stroke with *increased* time interval between the stroke and surgery was noted (OR per month elapsed 1.02 [1.00–1.04]; P = 0.047). We therefore performed an analysis (not planned *a priori*) to ascertain whether strokes that were less than 5 yr old were less likely to predispose to postoperative stroke than older strokes. This was confirmed (OR 0.27 [CI 0.07–0.98], P = 0.040). However, the number of postoperative strokes in the cohort of patients with prior stroke undergoing CABG surgery was only 11; the low numbers limit confidence in these findings. Therefore, we also looked at a composite outcome of "postoperative death or stroke" but did not find a relationship between the timing of preoperative stroke and the composite outcome when the time interval was measured as a continuous variable (OR 1.00 [0.99–1.01]; P = 0.699) or using the 5-yr threshold (OR = 0.84; CI 0.39–1.81; P = 0.653). Other important variables in patients with prior stroke included age, heart failure, liver disease, and prior MI increased mortality. Age, atrial fibrillation, valvular heart disease, renal failure, and prior MI all increased the odds of prolonged LOS.

Interaction in Perioperative Risk in Patients with Prior MI or Heart Failure and Stroke

Because MI increased perioperative risk in patients with stroke, we added an interaction term to our analysis of all 62,104 CABG patients (table 2) to understand how important the combination of stroke and MI was. After adjusting for all comorbidities, patients with MI and stroke had a fivefold increased odds of mortality (5.54 [2.84–10.8]) and postoperative stroke (5.02 [1.82–13.82]). After adjustment for the combination of MI and stroke, neither prior stroke nor MI alone increased mortality or postoperative stroke (table 5). We found no interaction between heart failure and stroke for mortality (P = 0.94), prolonged LOS (P = 0.55), and postoperative stroke (P = 0.66).

Discussion

The time interval between stroke and surgery did not increase the odds of mortality, prolonged LOS, or a composite of death or postoperative stroke. However, an increased time interval was weakly associated with an increased likelihood of postoperative stroke. An interaction was evident between preoperative stroke and MI for increasing perioperative risk. Overall, preoperative stroke was associated with a doubling of perioperative mortality, though in the selected subgroup of patients undergoing isolated CABG a nearly threefold increase in mortality was noted. Preoperative stroke also increased the risk of postoperative stroke and prolonged LOS. Consistent with scoring systems for risk associated with CABG,[4,5] several important variables associated with poor postoperative outcomes were also identified in this study.

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Table 4. Association between Preoperative Variables, Including the Time Interval between Stroke and CABG, and Perioperative Outcomes in Patients with Prior Stroke

Factor	Mortality OR (95% CI)	*P* Value	Long Length of Stay OR (95% CI)	*P* Value	Postoperative Stroke OR (95% CI)	*P* Value
Timing relation: linear (per month)*	1.00 (0.98–1.01)	0.492	1.00 (0.99–1.00)	0.733	1.02 (1.00–1.04)	0.047
Timing relation: 3/12 *vs.* longer*	N/A	N/A	1.45 (0.87–2.41)	0.156	N/A	N/A
Age (per yr)	1.10 (1.03–1.17)	0.005	1.04 (1.02–1.06)	<0.001	0.98 (0.91–1.05)	0.554
Sex (F *vs.* M)	1.87 (0.71–4.91)	0.202	1.28 (0.82–1.98)	0.277	2.90 (0.77–10.88)	0.115
Socioeconomic quintile 2 *vs.* 1	0.71 (0.19–2.57)	0.596	1.64 (0.91–2.95)	0.099	N/A†	N/A†
Socioeconomic quintile 3 *vs.* 1	1.17 (0.37–3.69)	0.794	1.69 (0.94–3.01)	0.077	N/A†	N/A†
Socioeconomic quintile 4 *vs.* 1	0.44 (0.10–2.07)	0.301	1.64 (0.89–3.00)	0.109	N/A†	N/A†
Socioeconomic quintile 5 *vs.* 1	0.35 (0.06–2.10)	0.252	1.39 (0.73–2.66)	0.313	N/A†	N/A†
Hypertension	0.50 (0.22–1.15)	0.101	0.88 (0.60–1.29)	0.506	0.49 (0.13–1.75)	0.271
Atrial fibrillation	0.68 (0.28–1.62)	0.381	1.68 (1.18–2.40)	0.004	3.29 (0.87–12.4)	0.079
Other arrhythmia	1.37 (0.31–6.07)	0.683	1.53 (0.74–3.16)	0.250	3.21 (0.55–18.8)	0.200
Stable angina	0.56 (0.07–4.40)	0.580	0.80 (0.41–1.57)	0.519	N/A†	N/A†
Valvular disease	0.88 (0.32–2.45)	0.810	2.08 (1.37–3.16)	<0.001	1.05 (0.20–5.57)	0.957
Congestive heart failure	3.27 (1.22–8.80)	0.019	1.74 (0.99–3.04)	0.053	0.46 (0.04–5.30)	0.537
Lower respiratory disease	1.57 (0.42–5.85)	0.500	1.41 (0.81–2.47)	0.226	N/A†	N/A†
Diabetes	3.15 (0.68–14.6)	0.143	4.70 (1.84–12.05)	0.001	1.70 (0.43–6.66)	0.449
Chronic renal failure	1.02 (0.37–2.80)	0.967	1.19 (0.81–1.77)	0.377	1.78 (0.16–20.27)	0.644
Cancer	1.58 (0.43–5.77)	0.491	1.14 (0.67–1.94)	0.628	N/A†	N/A†
Liver disease	3.44 (1.44–8.22)	0.006	1.19 (0.76–1.85)	0.455	N/A†	N/A†
Peripheral vascular disease	1.09 (0.33–3.62)	0.883	0.98 (0.59–1.65)	0.951	N/A†	N/A†
Prior myocardial infarction	1.10 (1.03–1.17)	0.005	1.04 (1.02–1.06)	<0.001	3.23 (0.82–12.66)	0.092
Prior unstable angina	1.87 (0.71–4.91)	0.202	1.28 (0.82–1.98)	0.277	0.33 (0.03–3.5)	0.358

Socioeconomic quintile 5 is the most deprived (lowest fifth).

* Only one of these terms fitted in the same model. As there were no deaths in patients with a 3-month lag, only a linear relation with mortality was fitted. † Variable dropped from the model to allow convergence.

CABG = coronary artery bypass grafting; F = female; M = male; OR = odds ratio.

Effect of Preoperative Stroke

Our cohort of stroke patients undergoing CABG was smaller than anticipated and relatively smaller than other large studies (*e.g.*, 7%).[5] It may be that our definition of stroke ("necessitating admission") is more stringent than other definitions used. Nonetheless, we did not find a relationship between the time interval between stroke and CABG and perioperative outcomes. Rather, our study emphasizes the importance of age and heart failure in stroke patients as further determining mortality risk, though the limited sample size means we should be cautious about ruling out other factors.

We initially hypothesized that there would be a window of vulnerability after stroke during which CABG should be considered high risk. However, our data do not support a higher risk period within 3 or 6 months of a stroke. The reader should note that we were limited by the few operations being conducted in patients with a recent stroke, possibly due to the clinical perception of increased risk. Therefore, we cannot definitively conclude that CABG is safe in the first few months after stroke.

We did note a weak increased risk of postoperative stroke with increased time interval between the index stroke and surgery. In an analysis that was not planned *a priori*, we found

Table 5. Effect of Prior MI, Stroke, or Both on Post-CABG Outcomes after Adjusting for Other Covariates

Factor	Mortality OR (95% CI)	Mortality *P* Value	Long Length of Stay OR (95% CI)	Long Length of Stay *P* Value	Postoperative Stroke OR (95% CI)	Postoperative Stroke *P* Value
No prior MI or stroke	1		1		1	
Prior MI and no prior stroke	1.07 (0.90–1.26)	0.460	1.02 (0.97–1.08)	0.399	1.18 (0.91–1.54)	0.215
Prior stroke and no prior MI	1.58 (0.95–2.65)	0.079	1.28 (1.06–1.55)	0.011	1.43 (0.67–3.05)	0.357
Prior MI and prior stroke	5.54 (2.84–10.8)	<0.001	1.50 (1.01–2.24)	0.046	5.02 (1.82–13.8)	0.002

MI = myocardial infarction; OR = odds ratio.

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that strokes that were more than 5 yr old were more likely to be associated with a new postoperative stroke. Future studies should examine this association in larger cohorts of stroke patients. Indeed, only 11 of our 695 patients with prior stroke incurred a postoperative stroke and the CIs of the finding are wide. In a retrospective analysis of CABG surgery records, Rorick and Furlan[14] noted that patients with recent prior stroke were more likely to exacerbate existing lesions whereas patients with older prior strokes were more likely to incur new lesions. It is possible that the new lesions are easier to diagnose in patients with an older stroke, and thus the putative increase in postoperative stroke we observe with older prior stroke is attributable to recording bias. Alternatively, it may be that other areas of the brain are vulnerable in these patients. Prospective cohort studies, including brain imaging, are required to further identify the risk factors for postoperative stroke and brain injury. These studies should include other stroke-related factors that may affect perioperative outcomes such as the pathogenesis of the prior stroke (thromboembolic or hemorrhagic), severity, and location of stroke. Furthermore, it is important to recognize that other perioperative factors may be modified to improve outcomes in patients with prior stroke such as inflammation,[15] cerebral blood flow,[16,17] or off- *versus* on-pump CABG[18]; these variables should be studied in future cohorts.

Effect of Preoperative Stroke and MI or Heart Failure

As prior MI proved an important risk factor for perioperative mortality in patients with stroke we hypothesized that there may be an interaction between stroke and MI. Indeed, the combination far outweighed the risk of either condition individually (table 5). This may be due to an interaction between hemodynamic compromise and embolic injury of the brain.[19–21] It has been proposed that emboli may lodge in areas of low cerebral blood flow and not be washed out;[22] certainly there is evidence that hemodynamic compromise exacerbates embolic brain injury from animal work.[23] However, we cannot probe this proposed pathogenic explanation because we do not have data on either hemodynamic variables or embolic load. Furthermore, we did not find an interaction between prior stroke and heart failure; therefore, we must be conservative in our conclusions about the cause of the interaction and merely suggest more work is required to validate this finding.

Nonetheless, interactions are important to recognize; most perioperative risk scoring systems assume that comorbidities are additive in risk and thus may not adequately stratify individual patients who have different combinations of comorbidities. Studies are required to identify whether the combination of comorbidities exceeds the sum of each comorbidity's individual effect.

Impact of Other Perioperative Variables

Our finding of a protective effect of hypertension on perioperative outcomes was unexpected but not implausible. These patients may well have been on more aggressive primary and secondary prevention regimes. Alternatively, these patients may have been perceived as being at higher risk and therefore given better perioperative care (*e.g.,* hemodynamic control).[17,24–26] Unfortunately, our database does not contain further pharmaceutical or perioperative data to corroborate these explanations.

Renal failure was the second biggest risk factor for perioperative mortality but increased the odds of a prolonged LOS the most (table 2). The magnitude of this effect is in line with previous data and supports the importance of renal failure in determining perioperative outcomes.[27] We have recently shown that chronic obstructive pulmonary disease is an important risk factor for perioperative mortality in orthopedic, but not vascular, surgical patients.[6] However, given previous evidence,[5] we were surprised that it only emerged as a risk factor for mortality for uncomplicated CABG surgery (table 3).[3] Nonetheless, similar to diabetes mellitus, respiratory disease increased the risk of prolonged LOS even with inclusion of complicated surgery (table 2) and so should be considered an important factor in judging perioperative risk.

Strengths and Limitations

Data from Hospital Episode Statistics have been shown to provide good prediction of perioperative risk from CABG surgery, compared with clinical audit data, despite lacking some clinical information.[28] Our intention was not to replace the excellent risk-prediction systems available, but rather to highlight other factors including the time interval between stroke and subsequent events. The relatively large overall sample size gives us statistical power to survey a range of comorbidities on the robust measures of 30-day mortality and surrogates of morbidity (LOS and postoperative stroke). However, our stroke cohort was smaller than anticipated and the number of patients having CABG surgery within 3 months of their stroke was small. Although we are confident that the majority of patients with stroke are referred to hospitals for treatment, we may not have captured all strokes in the population. Larger cohorts may be required to more fully evaluate our hypothesis. Nonetheless, even when using a composite outcome of stroke or death we could not identify a meaningful impact of a short time interval between stroke and surgery and perioperative outcomes. Indeed, our data suggest that a longer time interval might be detrimental, though any association is weak. Our focus on short-term endpoints is driven by our interest in perioperative risk. However, we acknowledge that further analyses of longer-term outcomes (such as 12-month mortality) are also indicated.

The accuracy of Hospital Episode Statistics administrative data was found to approximate 84 and 97% for diagnostic and operation codes respectively in a 2001 systematic review of coding accuracy.[29] The coding is inspected annually and a data assurance framework ensures continual improvement. Although comorbidity under recording is common in such

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databases, we have no reason to suspect that data inaccuracies are more likely to affect records for patients with prior vascular events than those without. Our endpoint of postoperative stroke was identified in the secondary diagnosis codes, hence we excluded code I69 ("old stroke"). Although we have no reason to presume that an old stroke may be miscoded as a postoperative complication (especially as our postoperative stroke rate was not high), it is possible that some preoperative strokes may be miscoded. However, this is unlikely to be a prevalent or systematic error as there is clear guidance about coding stroke.

Our data set also lacks some potentially important clinical variables like ejection fraction, pulmonary hypertension, and coronary disease pattern, which may influence the results. However, we have previously validated Hospital Episode Statistics administrative data against the National Cardiac Surgical Database in the United Kingdom,[28] showing that risk prediction models devised from administrative data perform as well as the European System for Cardiac Operative Risk Evaluation clinical risk scoring systems based on clinical data.[28] Nonetheless, our data should be viewed as hypothesis generating and require validation in prospective cohort studies.

Conclusions

We have found that increased time interval between stroke and surgery was associated with increased odds of perioperative stroke. Therefore, our data do not support delaying elective CABG surgery in the presence of a recent stroke. Nonetheless, our data are limited by the few operations being conducted in patients with a recent stroke, presumably due to the clinical perception of increased risk. Our data cannot definitively support or refute this view, and further investigations are required. Finally we have observed an interaction between prior MI and stroke for increasing perioperative mortality. This interaction may be overlooked, both clinically and by current scoring systems, and highlights the potential risk of the combination of cardiac and cerebral infarction.

References

1. Capodanno D, Capranzano P, Di Salvo ME, Caggegi A, Tomasello D, Cincotta G, Miano M, Patané M, Tamburino C, Tolaro S, Patané L, Calafiore AM, Tamburino C: Usefulness of SYNTAX score to select patients with left main coronary artery disease to be treated with coronary artery bypass graft. JACC Cardiovasc Interv 2009; 2:731–8
2. Serruys PW, Morice MC, Kappetein AP, Colombo A, Holmes DR, Mack MJ, Ståhle E, Feldman TE, van den Brand M, Bass EJ, Van Dyck N, Leadley K, Dawkins KD, Mohr FW; SYNTAX Investigators: Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. N Engl J Med 2009; 360:961–72
3. Hillis LD, Smith PK, Anderson JL, Bittl JA, Bridges CR, Byrne JG, Cigarroa JE, Disesa VJ, Hiratzka LF, Hutter AM Jr, Jessen ME, Keeley EC, Lahey SJ, Lange RA, London MJ, Mack MJ, Patel MR, Puskas JD, Sabik JF, Selnes O, Shahian DM, Trost JC, Winniford MD: 2011 ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery: executive summary: A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation 2011; 124:2610–42
4. Nashef SA, Roques F, Michel P, Gauducheau E, Lemeshow S, Salamon R: European system for cardiac operative risk evaluation (EuroSCORE). Eur J Cardiothorac Surg 1999; 16:9–13
5. Shahian DM, O'Brien SM, Filardo G, Ferraris VA, Haan CK, Rich JB, Normand SL, DeLong ER, Shewan CM, Dokholyan RS, Peterson ED, Edwards FH, Anderson RP; Society of Thoracic Surgeons Quality Measurement Task Force: The Society of Thoracic Surgeons 2008 cardiac surgery risk models: Part 1–coronary artery bypass grafting surgery. Ann Thorac Surg 2009; 88(1 Suppl):S2–22
6. Sanders RD, Bottle A, Jameson SS, Mozid A, Aylin P, Edger L, Ma D, Reed MR, Walters M, Lees KR, Maze M: Independent preoperative predictors of outcomes in orthopedic and vascular surgery: The influence of time interval between an acute coronary syndrome or stroke and the operation. Ann Surg 2012; 255:901–7
7. Sanders RD, Grocott HP: Perioperative stroke: time to redefine the impact of age? Stroke 2012; 43:3–5
8. Sundararajan V, Henderson T, Perry C, Muggivan A, Quan H, Ghali WA: New ICD-10 version of the Charlson comorbidity index predicted in-hospital mortality. J Clin Epidemiol 2004; 57:1288–94
9. Lee TH, Marcantonio ER, Mangione CM, Thomas EJ, Polanczyk CA, Cook EF, Sugarbaker DJ, Donaldson MC, Poss R, Ho KK, Ludwig LE, Pedan A, Goldman L: Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. Circulation 1999; 100:1043–9
10. Kertai MD, Boersma E, Klein J, van Sambeek M, Schouten O, van Urk H, Poldermans D: Optimizing the prediction of perioperative mortality in vascular surgery by using a customized probability model. Arch Intern Med 2005; 165:898–904
11. Friedman LS: The risk of surgery in patients with liver disease. Hepatology 1999; 29:1617–23
12. Morgan O, Baker A: Measuring deprivation in England and Wales using 2001 Carstairs scores. Health Stat Q 2006: 28–33
13. Carstairs V, Morris R: Deprivation: Explaining differences in mortality between Scotland and England and Wales. BMJ 1989; 299:886–9
14. Rorick MB, Furlan AJ: Risk of cardiac surgery in patients with prior stroke. Neurology 1990; 40:835–7
15. Grocott HP, White WD, Morris RW, Podgoreanu MV, Mathew JP, Nielsen DM, Schwinn DA, Newman MF; Perioperative Genetics and Safety Outcomes Study (PEGASUS) Investigative Team: Genetic polymorphisms and the risk of stroke after cardiac surgery. Stroke 2005; 36:1854–8
16. Ono M, Joshi B, Brady K, Easley RB, Zheng Y, Brown C, Baumgartner W, Hogue CW: Risks for impaired cerebral autoregulation during cardiopulmonary bypass and postoperative stroke. Br J Anaesth 2012; 109:391–8
17. Sanders RD, Degos V, Young WL: Cerebral perfusion under pressure: is the autoregulatory 'plateau' a level playing field for all? Anaesthesia 2011; 66:968–72
18. Afilalo J, Rasti M, Ohayon SM, Shimony A, Eisenberg MJ: Off-pump vs. on-pump coronary artery bypass surgery: an updated meta-analysis and meta-regression of randomized trials. Eur Heart J 2012; 33:1257–67
19. Floyd TF, Harris F, McGarvey M, Detre JA: Recurrence of stroke after cardiac surgery: Insight into pathogenesis via diffusion-weighted and continuous arterial spin labeling perfusion magnetic resonance imaging. J Cardiothorac Vasc Anesth 2007; 21:106–9
20. Derdeyn CP: Hemodynamic impairment and stroke risk: prove it. AJNR Am J Neuroradiol 2001; 22:233–4
21. Derdeyn CP, Grubb RL Jr, Powers WJ: Indications for cerebral revascularization for patients with atherosclerotic carotid occlusion. Skull Base 2005; 15:7–14

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22. Caplan LR, Hennerici M: Impaired clearance of emboli (washout) is an important link between hypoperfusion, embolism, and ischemic stroke. Arch Neurol 1998; 55:1475–82
23. Omae T, Mayzel-Oreg O, Li F, Sotak CH, Fisher M: Inapparent hemodynamic insufficiency exacerbates ischemic damage in a rat microembolic stroke model. Stroke 2000; 31:2494–9
24. Aronson S, Dyke CM, Levy JH, Cheung AT, Lumb PD, Avery EG, Hu MY, Newman MF: Does perioperative systolic blood pressure variability predict mortality after cardiac surgery? An exploratory analysis of the ECLIPSE trials. Anesth Analg 2011; 113:19–30
25. Aronson S, Stafford-Smith M, Phillips-Bute B, Shaw A, Gaca J, Newman M; Cardiothoracic Anesthesiology Research Endeavors: Intraoperative systolic blood pressure variability predicts 30-day mortality in aortocoronary bypass surgery patients. ANESTHESIOLOGY 2010; 113:305–12
26. Aronson S, Varon J: Hemodynamic control and clinical outcomes in the perioperative setting. J Cardiothorac Vasc Anesth 2011; 25:509–25
27. Eagle KA, Guyton RA, Davidoff R, Edwards FH, Ewy GA, Gardner TJ, Hart JC, Herrmann HC, Hillis LD, Hutter AM Jr, Lytle BW, Marlow RA, Nugent WC, Orszulak TA, Antman EM, Smith SC Jr, Alpert JS, Anderson JL, Faxon DP, Fuster V, Gibbons RJ, Gregoratos G, Halperin JL, Hiratzka LF, Hunt SA, Jacobs AK, Ornato JP; American College of Cardiology; American Heart Association Task Force on Practice Guidelines; American Society for Thoracic Surgery and the Society of Thoracic Surgeons: ACC/AHA 2004 guideline update for coronary artery bypass graft surgery: summary article: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1999 Guidelines for Coronary Artery Bypass Graft Surgery). Circulation 2004; 110:1168–76
28. Aylin P, Bottle A, Majeed A: Use of administrative data or clinical databases as predictors of risk of death in hospital: Comparison of models. BMJ 2007; 334:1044
29. Campbell SE, Campbell MK, Grimshaw JM, Walker AE: A systematic review of discharge coding accuracy. J Public Health Med 2001; 23:205–11

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