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Risk of Mortality Following Surgery in Patients With a Previous Cardiovascular Event

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IMPORTANCE There is a lack of consensus regarding the interval of time-dependent postoperative mortality risk following acute coronary syndrome or stroke.

OBJECTIVE To determine the magnitude and duration of risk associated with the time interval between a preoperative cardiovascular event and 30-day postoperative mortality.

DESIGN, SETTING, AND PARTICIPANTS This is a longitudinal retrospective population-based cohort study. This study linked data from the Hospital Episode Statistics for National Health Service England, Myocardial Ischaemia National Audit Project and the Office for National Statistics mortality registry. All adults undergoing a National Health Service–funded noncardiac, nonneurologic surgery in England between April 1, 2007, and March 31, 2018, registered in Hospital Episode Statistics Admitted Patient Care were included. Data were analyzed from July 2021 to July 2022.

EXPOSURE The time interval between a previous cardiovascular event (acute coronary syndrome or stroke) and surgery.

MAIN OUTCOMES AND MEASURES The primary outcome was 30-day all-cause mortality. Secondary outcomes were postoperative mortality at 60, 90, and 365 days. Multivariable logistic regression models with restricted cubic splines were used to estimate adjusted odds ratios.

RESULTS There were 877 430 patients with and 20 582 717 without a prior cardiovascular event (overall mean [SD] age, 53.4 [19.4] years; 11 577 157 [54%] female). Among patients with a previous cardiovascular event, the time interval associated with increased risk of postoperative mortality was surgery within 11.3 months (95% CI, 10.8-11.7), with subgroup risks of 14.2 months before elective surgery (95% CI, 13.3-15.3) and 7.3 months for emergency surgery (95% CI, 6.8-7.8). Heterogeneity in these timings was noted across many surgical specialties. The time-dependent risk intervals following stroke and myocardial infarction were similar, but the absolute risk was greater following a stroke. Regarding surgical urgency, the risk of 30-day mortality was higher in those with a prior cardiovascular event for emergency surgery (adjusted hazard ratio, 1.35; 95% CI, 1.34-1.37) and an elective procedure (adjusted hazard ratio, 1.83; 95% CI, 1.78-1.89) than those without a prior cardiovascular event.

CONCLUSIONS AND RELEVANCE In this study, surgery within 1 year of an acute coronary syndrome or stroke was associated with increased postoperative mortality before reaching a new baseline, particularly for elective surgery. This information may help clinicians and patients balance deferring the potential benefits of the surgery against the desire to avoid increased mortality from overly expeditious surgery after a recent cardiovascular event.

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Supplemental content

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Ischemic heart disease and stroke are the second and third most common causes of disability-adjusted life-years worldwide, exceeded only by congenital diseases.[1] In the UK, more than 5 million operations are performed each year,[2] and it is recognized that preexisting cardiovascular disease strongly contributes to adverse perioperative outcomes.[3] Despite improved and increased use of preventive and interventional treatments[4,5] the prevalence of cardiovascular disease in the surgical population continues to increase.[6] This results in surgery being offered to patients with comorbidities who were previously considered at serious high risk or for whom surgery would have been precluded completely.[7,8] It is also not well known which characteristics of the preoperative cardiovascular event or which treatments received at the time may predict a future adverse perioperative outcome other than that the very nature of requiring intervention is a risk factor.[9]

Surgery can cause hemodynamic, endocrine, and inflammatory disturbances, which are especially important for perioperative risk among patients with cardiovascular disease.[10] The optimal time for surgery after an event is a complex interplay of the changing relative risks of adverse events associated with cardiovascular events, risks of delaying surgery (eg, disease progression, and functional decline), absolute risks, and patient preferences. Currently, there is limited evidence on the interactions between time, patient and surgical characteristics, and risk of postoperative adverse events.[11-13] Recent large electronic health record studies have demonstrated a lack of consensus concerning the time-dependent risk interval.[12,14] The 2022 European Society of Cardiology guidelines make limited recommendations concerning the timing of noncardiac surgery.[15]

Using individual patient-level data, we aimed to support shared decision-making by describing the time-dependent association between preoperative cardiovascular events and postoperative mortality in an extensive and unselected cohort of patients in the National Health Service (NHS) undergoing noncardiac, nonneurosurgical surgery between 2007 and 2018 in England.

Key Points

Question Is the time elapsed since a cardiovascular event associated with an increased risk of mortality in patients undergoing nonneurologic, noncardiac surgery?

Findings In this study, the increased risk of postoperative mortality after elective surgery decreased with increasing time since the cardiovascular event, with a plateau approximately 14 months after the event. A similar pattern was seen with emergency surgery, but plateaued sooner after the event.

Meaning The findings indicate that clinicians should balance the potential benefits of surgery against the risk of increased mortality from overly expeditious surgery after a recent cardiovascular event.

Methods

Study Design and Population

This is a longitudinal retrospective population-based cohort study of all adult patients (18 years and older) undergoing an NHS-funded surgery between April 1, 2007, and March 31, 2018, registered in Hospital Episode Statistics Admitted Patient Care (HES APC). The first surgery was identified using *Office of Population Censuses and Surveys Classification of Surgical Operations and Procedures* (*OPCS-4*) codes. Patients with cardiovascular events (acute coronary syndrome or stroke) within 10 years prior to surgery were identified using *International Classification of Diseases* (*ICD-10*) codes. Linking HES records to the Myocardial Infarction National Audit Project (MINAP), additional acute coronary syndrome cases were identified. Further details about the study design, cardiovascular events, and surgery codes can be found in the prospectively published protocol.[16] Ethical approval was obtained from East Midlands - Nottingham research ethics committee and Health Research Authority confidential advisory group.

Setting

This study used HES APC for NHS England linked to MINAP and Office for National Statistics (ONS) mortality data. HES APC is a national registry database containing details of all admissions to NHS hospitals in England and has been available since 1989.[17] Data from 1997 to 2018 were extracted. MINAP is a national cardiac clinical audit that collects information to measure the process and care outcomes of every patient diagnosed with myocardial infarction. Data from 2003 (registry inception) to 2018 were extracted.[18] The ONS mortality data were extracted between 2007 and 2019. Data were analyzed from July 2021 to July 2022.

NHS Digital is responsible for collecting, quality assurance, and governance of HES APC and ONS data. The data in HES APC undergo extensive cleaning before linkage. After the linkage of NHS Digital's HES APC and ONS to the MINAP data set, the data were further cleaned to identify duplicates, lack of agreement, and potentially erroneously linked patient episodes. NHS Digital (HES) and the ONS openly publish how their databases are regularly checked to ensure the accuracy of the recorded data and their methods of data cleaning and quality assurance.[19,20] The National Institute for Cardiovascular Outcomes Research (NICOR) is the data processor for MINAP. They are responsible for data collection and quality assurance, and perform annual audits demonstrating high case ascertainment rates.[21] The Healthcare Quality Improvement Partnership is the data controller.

Classification of Surgery

To stratify the effects of increasing operative severity, a classification was used based on *OPCS-4* codes taking a minor, moderate, and major interpretation of the surgical invasiveness.[2] All *OPCS-4* codes were reviewed, and nonoperative codes were excluded (eg, radiotherapy and diagnostic imaging). The minor category comprised all procedures that might be considered surgery, including minor surgery, such as superficial skin procedures, interventional radiology procedures, and diagnostic endoscopies, but excluding noninvasive diagnostic procedures (eg, diagnostic imaging). The moderate category included procedures routinely undertaken in an operating theater or under general or regional anesthesia. The major category included major procedures that may result in severe tissue injury due to duration or complexity. We prespecified common operations by surgical specialty in orthopedic, vascular, gastrointestinal, gynecological, urological, ear, nose, and throat, ophthalmological, and breast surgery. Finally, the surgical urgency was assessed according to the admission method (elective or emergency) recorded in HES.

We excluded cardiac surgery, neurosurgical, carotid endarterectomy, obstetrics, tracheostomy, and percutaneous gastrostomy.[16] Cardiac procedures were excluded based on a preexisting specialty-specific risk prediction tool (EuroSCORE II) and lack of specificity within *ICD-10* coding making it impossible to reliably identify type III to V myocardial infarctions. Neurosurgery and carotid endarterectomy were excluded based on the recognized high stroke risk specific to these procedures. Percutaneous gastrostomy insertion and tracheostomy formation were excluded due to significant confounding with poststroke bulbar dysfunction.

Outcomes

The primary outcome was 30-day all-cause postoperative mortality. Secondary outcomes were postoperative mortality at 60, 90, and 365 days.

Statistical Analysis

The primary exposure was the time interval between the most recent preoperative cardiovascular event and index surgery. Potential confounders in all patients from HES APC that were included as covariates in the modeling were age (continuous), sex, index of multiple deprivation, comorbidities (hypertension, atrial fibrillation, stable angina, peripheral vascular disease, valvular heart disease, congestive heart failure, respiratory failure, diabetes, kidney failure, cancer, liver disease, and dementia). All patients included in the analyses were unique individuals.

Multivariable logistic regression models were constructed for the association between the time interval from the most recent preoperative cardiovascular event to index surgery and postoperative mortality modeling time as a categorical variable to provide clinically interpretable thresholds, using 0 to 2, 3 to 6, 7 to 12, 12 to 24, and 24 or more months. Splines of the association of time elapsed between a cardiovascular event and 30-day mortality were created by restricted cubic spline functions.[22] Knots were placed at the 10th, 25th, 50th, 75th, and 90th percentile, with the 50th (median) as the reference. Because patients without a cardiovascular event did not have a time variable, restricted cubic splines and logistic regression analyses were restricted to patients with previous cardiovascular events. Multivariable logistic regression models were fitted for 30-day mortality among patients with a cardiovascular event with the following factors: cardiac arrest, left ventricle ejection fraction, infarction site, QRS, reperfusion treatment, and Killip class.

Hazard ratio (HR) estimates and 95% CIs were calculated using Cox regression analysis, comparing the mortality risk between those with and without a cardiovascular event before surgery. The Cox model assumption was tested using Schoenfeld residuals.

Subgroup analyses were also performed for common operations by surgical specialty. Sensitivity analysis was also performed by taking the patient's last operation (instead of the first). Missing values for the index of multiple deprivation were retained by assigning a new category for them. Any missing data from the MINAP data set were also assigned to a new category. All statistical analyses were performed using R version 4.1.2 (R Foundation). Two-tailed *P* values less than .05 were considered significant.

Results

Baseline Characteristics

The study population included 21 460 147 patients (overall mean [SD] age, 53.4 [19.4] years; 11 577 157 [54%] female) from 316 hospitals in England undergoing surgery between 2007 and 2018 (**Table 1**) after excluding 186 038 patients younger than 18 years and 10 715 patients with unknown sex (eFigure 1 in Supplement 1). A total of 877 430 (4.1%) procedures were performed in patients with a cardiovascular event history. On average, patients with a prior cardiovascular event were 19.3 years older, more often male, and more frequently had comorbidities. Elective surgery accounted for 17 833 826 patients (83%). Emergency surgery was more frequent in patients with a prior cardiovascular event (251 908 [29%] vs 3 374 413 [16%] ; $P < .001$).

Time Elapsed From Cardiovascular Event to Surgery and Mortality

In patients with a prior cardiovascular event, there was a stepwise decline in the adjusted odds associated with 30-day mortality for longer time periods between the event and operation (eTable 3 in Supplement 1). The time-dependent association between a preoperative cardiovascular event and postoperative mortality more than 30 days is presented in eTables 4 to 6 in Supplement 1. The odds of 30-day all-cause mortality leveled off at 11.3 months (95% CI, 10.8-11.7), irrespective of surgical invasiveness (**Figure**). This plateau was 14.2 months (95% CI, 13.3-15.3) for elective surgery and 7.3 months (95% CI, 6.8-7.8) for emergency surgery (Figure). There were differences in the time to plateau for different surgical specialties (eTables 8-35 and eFigures 2-23 in Supplement 1). Specifically, increased risk was observed for 6, 9, and 12 months in gynecological (eFigure 4 in Supplement 1), gastrointestinal (eFigure 19 in Supplement 1), and urological (eFigure 2 in Supplement 1) surgery, respectively. The time-dependency following stroke and myocardial events were similar, but absolute risks were greater with stroke (Figure). Sensitivity analysis taking patients' last operation between 2007 and 2018 demonstrated similar results (eFigure 36 in Supplement 1). The estimates reported when analyzing only patients from the more specialized MINAP data set were the same as HES APC (eTables 39-42 and eFigures 37-41 in Supplement 1).

Table 1. Baseline Characteristics of All Patients Undergoing Surgery Between 2007 and 2017

	No. (%)			
	Overall (N = 21 460 147)	Without prior event (n = 20 582 717)	With prior event (n = 877 430)	Absolute difference (95% CI)
Age, mean (SD), y	53.4 (19.4)	52.6 (19.2)	71.9 (12.7)	−19.3 (−19.2 to −19.1)
Sex				
Female	11 577 157 (54)	11 220 826 (55)	356 331 (41)	14.0 (13.8 to 14.2)
Male	9 882 990 (46)	9 361 891 (45)	521 099 (59)	−14.0 (−14.1 to −13.9)
Ethnicity[a]				
Asian	3 217 494 (15)	3 150 564 (15)	66 930 (8)	7.4 (7.2 to 7.6)
Black	929 443 (4.3)	891 350 (4)	38 093 (4)	0.0 (−0.2 to 0.2)
White	16 367 832 (76)	15 617 378 (76)	750 454 (86)	−10.0 (−10.1 to −9.9)
Other[b]	475 541 (2.2)	464 016 (2)	11 525 (1)	1 (0.9 to 1.3)
Unknown	469 837 (2.2)	459 409 (2)	10 428 (1)	1.0 (0.8 to 1.2)
Index of multiple deprivation				
Least deprived	4 029 196 (19)	3 877 746 (19)	151 450 (17)	2.0 (1.8 to 2.2)
2nd Quintile	4 202 019 (20)	4 030 286 (20)	171 733 (20)	0.0 (−0.2 to 0.2)
3rd Quintile	4 197 716 (20)	4 016 653 (20)	181 063 (21)	−1.0 (−1.2 to −0.8)
4th Quintile	4 154 682 (19)	3 975 900 (19)	178 782 (20)	−1.0 (−1.2 to −0.8)
Most deprived	4 176 252 (19)	3 988 656 (19)	187 596 (21)	−2.0 (−2.2 to −1.8)
Unknown	700 282 (3)	693 476 (3)	6806 (1)	2.0 (1.8 to 2.2)
Charlson Comorbidity Index				
0	16 401 423 (76)	15 936 777 (77)	464 646 (53)	24.0 (23.8 to 24.2)
1	3 936 433 (18)	3 673 547 (18)	262 886 (30)	−12.0 (−12.2 to −11.8)
2	889 944 (4)	782 878 (4)	107 066 (12)	−8.0 (−8.2 to −7.8)
≥3	232 347 (1)	189 515 (1)	42 832 (5)	−4.0 (−4.2 to −3.8)
Comorbidities				
Hypertension	3 804 608 (18)	3 389 416 (16)	415 192 (47)	−31.0 (−31.1 to −30.8)
Atrial fibrillation	594 199 (3)	480 216 (2)	113 983 (13)	−10.7 (−10.9 to −10.5)
Stable angina	50 786 (0)	4016 (0)	46 770 (5)	−5.2 (−5.4 to −5.0)
Dementia	242 844 (1)	193 834 (1)	49 010 (6)	−4.7 (−4.9 to −4.5)
Peripheral vascular disease	108 255 (1)	89 306 (0)	18 949 (2)	−1.8 (−2.0 to −1.6)
Valvular heart disease	212 441 (1)	151 632 (1)	60 809 (7)	−6.2 (−6.4 to −6.0)
Heart failure	1 920 406 (9)	1 796 263 (9)	124 143 (14)	−5.3 (−5.5 to −5.1)
Respiratory disease	1 455 402 (7)	1 295 413 (6)	159 989 (18)	−11.7 (−11.9 to −11.5)
Diabetes	420 301 (2)	353 673 (2)	66 628 (8)	−5.9 (−6.1 to −5.7)
Chronic kidney disease	1 153 917 (5)	1 091 083 (5)	62 834 (7)	−1.9 (−2.1 to −1.78)
Active malignancy	199 401 (1)	189 443 (1)	9958 (1)	−0.2 (−0.4 to 0.0)
Chronic liver disease	208 294 (1)	174 318 (1)	33 976 (4)	−3.1 (−3.3 to −2.9)
Surgical invasiveness				
Minor	7 493 661 (35)	7 142 867 (35)	350 794 (40)	−5.0 (−5.2 to −4.8)
Moderate	9 413 447 (44)	9 056 811 (44)	356 636 (41)	3.0 (2.8 to 3.2)
Major	4 553 039 (21)	4 383 039 (21)	170 000 (19)	2.0 (1.8 to 2.2)
Surgical urgency				
Elective	17 833 826 (83)	17 208 304 (84)	625 522 (71)	13.0 (12.8 to 13.2)
Emergency	3 626 321 (17)	3 374 413 (16)	251 908 (29)	−13.0 (−13.2 to −12.8)

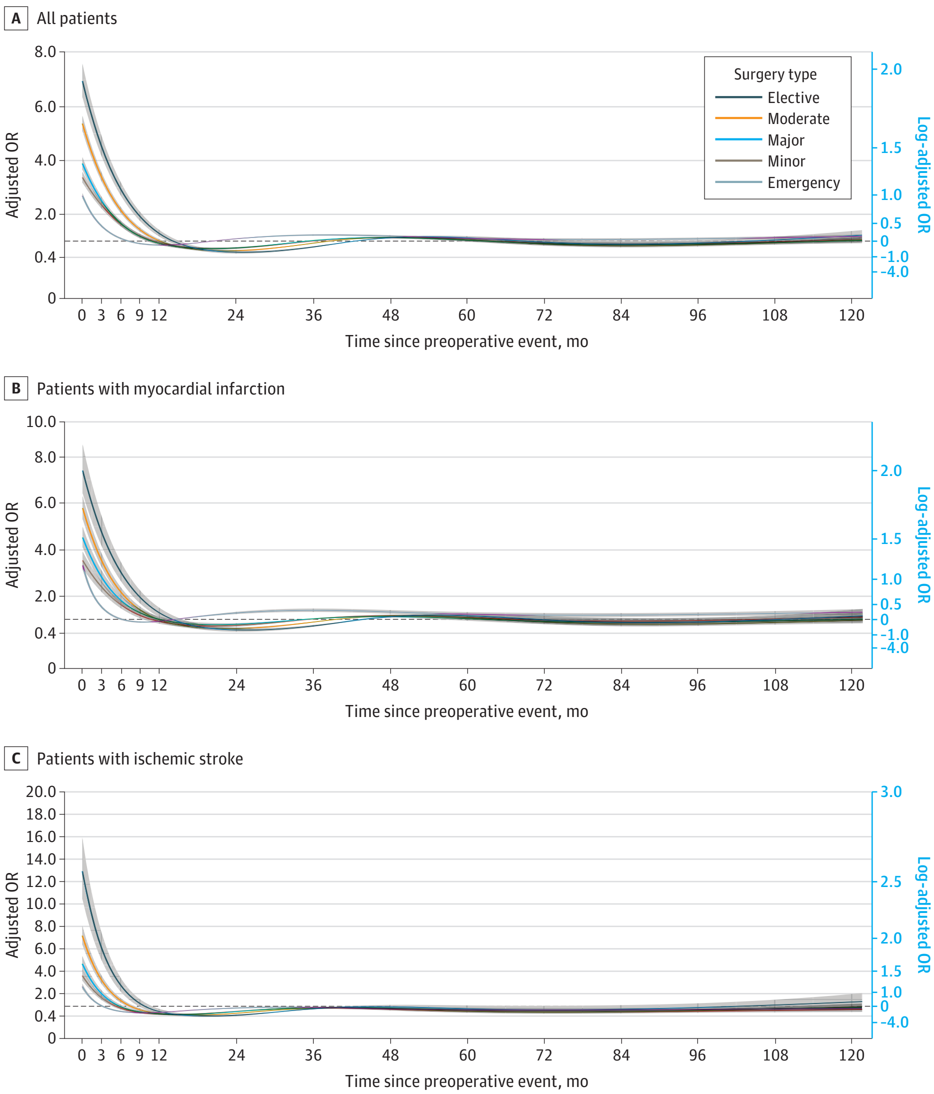
[a] Ethnicity data were recorded based on information in the patient record, extracted by expert coders, and mapped to a defined set of codes.

[b] Other includes Chinese, any other ethnic group, mixed ethnicity, and not stated. These were collapsed due to small numbers.

Mortality Among Those With and Without a Prior Cardiovascular Event

Comparing those with an event at any time point to those with no event, 30-day crude mortality was greater across all types and urgency of surgery (minor, 3.4% vs 0.8%; moderate, 4.8% vs 0.8%; major, 7.2% vs 1.1%; elective, 0.9% vs 0.2%; emergency, 14% vs 4.4%; all $P < .001$) (eTables 1 and 2 in Supplement 1). Mortality rates were higher in patients with a cardiovascular event before surgery than those without (**Table 2**). Following adjustment, the highest risk of 30-day mortality was in those with prior cardiovascular events undergoing major surgery (adjusted hazard ratio [aHR], 1.75; 95% CI, 1.71-1.79). Elec-

Figure. Restricted Cubic Splines for Risk of 30-Day All-Cause Mortality by the Time Between the Most Recent Cardiovascular Event and Myocardial Infarction and Ischemic Stroke by Surgery Invasiveness and Urgency



The spline was adjusted for age, sex, index of multiple deprivation, hypertension, atrial fibrillation, stable angina, peripheral vascular disease, valvular heart disease, congestive heart failure, respiratory diseases, diabetes, kidney failure, cancer, liver disease, and dementia. OR indicates odds ratio.

tive procedures had the greater relative risks (aHR, 1.83; 95% CI, 1.78-1.89) for those cardiovascular diagnoses than emergency surgery (aHR, 1.35; 95% CI, 1.34-1.37).

Perioperative Risk Factors

Deprivation was associated with postoperative mortality, with the greatest risk for the most deprived patients, regardless of surgical severity (eTable 7 in Supplement 1). Patients with previous cardiovascular events had greater levels of socioeconomic deprivation than those without (without cardiovascular events 3 877 746 [19%] least deprived vs with cardiovascular events (151 450 [17%] (absolute difference, 2.0; 95% CI, 1.8 to 2.2); most deprived 3 988 656 (19%) vs 187 596 (21%) (absolute difference, −2.0; 95% CI, −2.2 to −1.8). However, deprivation was less important in emergency surgery (most vs least deprived aOR, 1.04; 95% CI, 0.99-1.0). Liver disease (OR, 4.52; 95% CI, 3.96-5.15), kidney failure (OR, 2.52; 95% CI, 2.41-2.64), and congestive heart failure (OR, 2.40; 95% CI, 2.28-2.52) were the 3 comorbidities associated with the greatest increases in 30-day mortality. Using MINAP-linked data, impaired cardiac contractility (left ventricular ejection fraction) at the time of the cardiac event was associated with increased odds of 30-day postoperative mortality irrespective of surgical invasiveness (**Table 3**). Considering elective surgery, poor left ventricular ejection fraction after myocardial event (aOR, 1.51; 95% CI, 1.15-1.98) but not moderate left ventricular ejection fraction impairment was associated with increased odds of mortality (aOR, 1.23; 95% CI, 1.00-1.53). Moderate and poor left ventricular ejection fraction were associated with increased postoperative mortality following emergency surgery (aOR, 1.17; 95% CI, 1.05-1.30 and aOR, 1.78; 95% CI, 1.57-2.02, respectively). Any infarction site (indeterminate, anterior, or lateral) carried a higher mortality risk than the inferior territory. Of note, those who had primary percutaneous coronary inter-

Table 2. Hazard Ratios (HRs) of Mortality After a Surgical Event Comparing Patients With a Cardiovascular Event Before the Surgery and Those Without Any Cardiovascular Event

	With prior event		Without prior event		HR (95%CI)	
All-cause mortality	Events, No.	Incidence per 1000 person-year	Events, No.	Incidence per 1000 person-year	Unadjusted	Adjusted[a,b]
Minor surgery						
No.	350 794	NA	7 142 867	NA	NA	NA
30 d	11 806	417.5 (410.0-425.1)	59 622	102.1 (101.3-102.9)	4.09 (4.01-4.17)	1.44 (1.41-1.47)
31 to 60 d	7068	127.6 (124.6-7-130.6)	41 447	35.7 (35.3-36.0)	3.59 (3.50-3.68)	1.36 (1.32-1.40)
61 to 90 d	5190	63.6 (61.9-65.4)	32 535	18.8 (18.6-19.0)	3.40 (3.30-3.50)	1.31 (1.27-1.35)
91 d to 1 y	27 108	86.0 (85.0-87.0)	177 463	25.6 (25.5-25.7)	3.38 (3.33-3.42)	1.34 (1.32-1.36)
Within 1 y	51 172	161.1 (159.7-162.5)	311 067	44.8 (44.6-44.9)	3.55 (3.52-3.58)	1.36 (1.35-1.37)
Moderate surgery						
No.	356 636	NA	9 056 811	NA	NA	NA
30 d	17 011	599.7 (590.7-608.7)	71 484	96.6 (95.9-97.3)	6.17 (6.07-6.27)	1.71 (1.68-1.74)
31 to 60 d	5424	97.6 (95.0-100.3)	27 860	18.9 (18.7-19.1)	5.19 (5.04-5.34)	1.59 (1.54-1.64)
61 to 90 d	3672	44.7 (43.3-46.1)	20 589	9.3 (9.2-9.5)	4.80 (4.64-4.97)	1.52 (1.46-1.57)
91 d to 1 y	22 085	68.7 (67.8-69.6)	132 317	14.9 (14.8-15.0)	4.64 (4.57-4.70)	1.53 (1.51-1.56)
Within 1 y	48 192	149.1 (147.7-150.4)	252 250	28.4 (28.3-28.5)	5.16 (5.11-5.21)	1.59 (1.58-1.61)
Major surgery						
No.	NA	170 000	NA	4 383 039	NA	NA
30 d	12 182	914.8 (898.7-931.2)	47 441	132.7 (131.5-133.9)	6.83 (6.70-6.97)	1.75 (1.71-1.79)
31 to 60 d	4684	182.1 (177.0-189.4)	22 963	32.3 (31.9-32.7)	5.67 (5.50-5.86)	1.58 (1.52-1.63)
61 to 90 d	3076	81.8 (79.0-84.7)	16 468	15.5 (15.3-15.7)	5.30 (5.10-5.51)	1.54 (1.48-1.61)
91 d to 1 y	12 373	85.5 (84.0-87.1)	81 295	19.1 (19.0-19.2)	4.51 (4.42-4.59)	1.49 (1.46-1.52)
Within 1 y	32 315	221.0 (218.6-223.4)	168 167	39.4 (39.2-39.6)	5.44 (5.38-5.51)	1.59 (1.57-1.61)
Elective surgery						
No.	NA	625 522	NA	17 208 304	NA	NA
30 d	5462	106.8 (104.0-109.7)	29 407	20.8 (20.6-21.1)	5.13 (4.98-5.28)	1.83 (1.78-1.89)
31 to 60 d	4428	43.5 (42.3-44-9)	33 364	11.8 (11.7-12.0)	3.69 (3.57-3.80)	1.49 (1.44-1.54)
61 to 90 d	4031	26.6 (25.8-27.4)	31 898	7.6 (7.5-7.6)	3.53 (3.41-3.65)	1.42 (1.37-1.47)
91 d to 1 y	30 839	51.5 (50.9-52.0)	239 573	14.1 (14.0-14.1)	3.67 (3.63-3.71)	1.49 (1.47-1.51)
Within 1 y	44 760	74.5 (43.8-75.2)	334 242	19.6 (19.6-19.7)	3.79 (3.75-3.83)	1.52 (1.50-1.53)
Emergency surgery						
No.	NA	251 908	NA	3 374 413	NA	NA
30 d	35 537	1887.2 (1867.7-1906.9)	149 140	553.6 (550.8-556.4)	3.36 (3.32-3.40)	1.35 (1.34-1.37)
31 to 60 d	12 748	364.3 (358.0-370.7)	58 906	111.7 (110.8-112.6)	3.29 (3.23-3.36)	1.30 (1.28-1.33)
61 to 90 d	7907	158.6 (155.2-162.2)	37 694	48.4 (47.9-48.9)	3.31 (3.23-3.39)	1.28 (1.25-1.32)
91 d to 1 y	30 727	168.7 (166.9-170.6)	151 502	49.5 (49.3-49.8)	3.44 (3.40-3.48)	1.29 (1.27-1.30)
Within 1 y	86 919	466.5 (463.4-469.6))	397 242	129.0 (128.6-129.4)	3.37 (3.35-3.40)	1.31 (1.30-1.33)

Abbreviation: NA, not applicable.

[a] Adjusted for age, sex, index of multiple deprivation, hypertension, atrial fibrillation, stable angina, peripheral vascular disease, valvular heart disease, congestive heart failure, respiratory diseases, diabetes, kidney failure, cancer, liver disease, and dementia.

[b] All P values <.001.

vention had lower odds of 30-day postoperative mortality after a minor (aOR, 0.77; 95% CI, 0.65-0.91) or elective (aOR, 0.78; 95% CI, 0.63-0.97) surgery compared with no reperfusion therapy following an acute coronary syndrome.

Discussion

Our cohort study of 21.4 million patients undergoing surgery in England demonstrated a strong time-dependent association between prior cardiovascular events and postoperative mortality, with risk plateauing after 14 months for elective surgery and 7 months for emergency surgery.

Our findings about postoperative mortality in those with a prior stroke or acute coronary syndrome are consistent with other registry analysis. Fowler et al[23] reported that 90-day postoperative mortality in those with previous stroke and myocardial infarction was 10.7% and 5.7%, respectively, similar to our study (eTable 36 in Supplement 1).

Modeling the time after a cardiovascular event until surgery against postoperative mortality, the risk decreased nonlinearly as the time interval increased. Jørgensen et al[12] dem-

Table 3. Preoperative Variable Associated With 30-Day All-Cause Mortality by Surgical Invasiveness and Urgency Using Hospital Episode Statistics–Linked Myocardial Infarction National Audit Project Data

Variable	Surgical invasiveness						Surgical urgency			
	Minor		Moderate		Major		Elective		Emergency	
	aOR (95% CI)[a]	*P* value	aOR (95% CI)[a]	*P* value	aOR (95% CI)[a]	*P* value	aOR (95% CI)[a]	*P* value	aOR (95% CI)[a]	*P* value
30-d All-cause mortality										
Cardiac arrest	3.17 (2.66-3.78)	<.001	3.15 (2.76-3.59)	<.001	2.96 (2.46-3.57)	<.001	2.28 (1.80-2.90)	<.001	3.35 (3.02-3.7)	<.001
Left ventricle ejection fraction										
Good	1 [Reference]	NA	1 [Reference]	NA	1 [Reference]	NA	1 [Reference]	NA	1 [Reference]	NA
Moderate	1.07 (0.90-1.28)	.46	1.26 (1.09-1.45)	0.002	1.21 (1.01-1.47)	0.04	1.23 (1.00-1.53)	.05	1.17 (1.05-1.30)	.003
Poor	1.85 (1.50-2.27)	<.001	1.67 (1.42-1.97)	<.001	1.62 (1.27-2.05)	<.001	1.51 (1.15-1.98)	.003	1.78 (1.57-2.02)	<.001
Unassessed	1.42 (1.22-1.65)	<.001	1.61 (1.42-1.83)	<.001	1.48 (1.26-1.73)	<.001	1.21 (1.00-1.47)	.045	1.60 (1.46-1.75)	<.001
Unknown	1.32 (1.15-1.52)	<.001	1.42 (1.26-1.59)	<.001	1.41 (1.22-1.63)	<.001	1.24 (1.05-1.48)	.01	1.44 (1.33-1.57)	<.001
Infarction site										
Inferior	1 [Reference]	NA	1 [Reference]	NA	1 [Reference]	NA	1 [Reference]	NA	1 [Reference]	NA
Indeterminate	1.44 (1.15-1.81)	.002	1.27 (1.07-1.44)	.007	1.36 (1.09-1.70)	.007	1.44 (1.10-1.87)	.008	1.24 (1.08-1.41)	.002
Anterior	1.40 (1.14-1.73)	.001	1.23 (1.05-1.51)	.01	1.10 (0.89-1.37)	.38	1.30 (1.02-1.66)	.04	1.17 (1.03-1.32)	.02
Lateral	1.51 (1.11-2.05)	.009	1.27 (1.00-1.60)	.048	1.54 (1.15-2.06)	.004	1.31 (0.91-1.90)	.15	1.37 (1.15-1.63)	. <001
Posterior	1.36 (0.79-2.32)	.27	0.99 (0.61-1.62)	.98	0.87 (0.46-1.66)	.68	0.80 (0.37-1.77)	.59	1.07 (0.75-1.52)	.71
Unknown	1.23 (1.04-1.46)	.01	0.99 (0.87-1.13)	.92	1.07 (0.91-1.27)	.41	0.97 (0.80-1.18)	.77	1.09 (0.98-1.20)	.10
QRS complex										
Normal	1 [Reference]	NA	1 [Reference]	NA	1 [Reference]	NA	1 [Reference]	NA	1 [Reference]	NA
Prolonged	0.97 (0.80-1.18)	.80	1.16 (1.00-1.34)	.04	0.98 (0.81-1.20)	.86	1.05 (0.82-1.34)	.70	1.09 (0.98-1.22)	0.11
Unknown	1.18 (1.06-1.31)	.002	1.10 (1.01-1.20)	.03	1.22 (1.09-1.36)	<.001	1.22 (1.06-1.39)	.004	1.11 (1.05-1.19)	<.001
Reperfusion treatment										
None	1 [Reference]	NA	1 [Reference]	NA	1 [Reference]	NA	1 [Reference]	NA	1 [Reference]	NA
PPCI	0.77 (0.65-0.91)	.002	1.04 (0.91-1.18)	.60	0.94 (0.78-1.14)	.55	0.78 (0.63-0.97)	.02	0.92 (0.83-1.02)	.12
Thrombolysis	1.05 (0.84-1.31)	.67	0.93 (0.76-1.12)	.44	1.27 (1.01-1.61)	.04	1.05 (0.80-1.38)	.74	1.03 (0.90-1.19)	.66
Unknown	0.88 (0.77-0.99)	.04	0.98 (0.88-1.08)	.64	1.11 (0.98-1.26)	.10	0.78 (0.67-0.92)	.003	1.02 (0.94-1.10)	.65
Killip class										
I	1 [Reference]	NA	1 [Reference]	NA	1 [Reference]	NA	1 [Reference]	NA	1 [Reference]	NA
II	1.14 (0.89-1.45)	.31	1.24 (1.02-1.51)	.03	1.32 (1.02-1.70)	.03	1.74 (1.27-2.38)	<.001	1.19 (1.03-1.37)	.02
III	1.48 (1.09-2.00)	.01	1.01 (0.79-1.29)	.94	0.80 (0.54-1.19)	.28	1.51 (0.97-2.36)	.07	1.10 (0.92-1.32)	.29
IV	2.71 (1.41-5.19)	.003	3.04 (2.12-4.37)	<.001	3.44 (1.57-7.52)	.002	4.23 (2.14-8.34)	<.001	3.05 (2.25-4.13)	<.001
Unknown	1.33 (1.16-1.53)	<.001	1.54 (1.37-1.73)	<.001	1.46 (1.27-1.69)	<.001	1.65 (1.37-1.98)	<.001	1.42 (1.30-1.54)	<.001

Abbreviations: aOR, adjusted odds ratio; NA, not applicable; PPCI, primary percutaneous coronary intervention.

[a] Adjusted for age, sex, index of multiple deprivation, hypertension, atrial fibrillation, unstable angina, peripheral vascular disease, valvular heart disease, congestive heart failure, respiratory diseases, diabetes, kidney failure, cancer, liver disease, and dementia.

onstrated elective surgery within 2 months after stroke carried the highest risk. This agrees with our findings, where the odds of death were more than 9-fold greater for patients with surgery within 2 months. Regarding previous stroke, they identified 9 months as a cutoff for elective surgery compared to our 14-month time frame. Sanders et al[13] examined the association between time elapsed before surgery following acute coronary syndrome or stroke and postoperative mortality. Although their focus was only elective arthroplasty and abdominal aortic aneurism repair, surgery within 1 year of acute coronary syndrome was associated with increased postoperative mortality. In contrast, while they did not find an association between the timing of previous stroke and mortality after elective joint replacement, the authors acknowledged that their study lacked sufficient power to detect this.

The existing recommendation in patients with a preoperative cardiovascular event is a 6-month deferment of surgery where possible,[24] preferably 12 months.[11,25-27] In our study, 225 944 patients had surgery within this 12-month window of their preoperative cardiovascular event, and 9.8% died within 30 days of surgery. Our data strongly support the recommendation that perioperative mortality risk is high during the first year after a cardiovascular event.[28] This is at variance with previous registry research, which suggested the shorter 6-month interval before elective surgery[24] and European Society of Cardiology guidelines, which suggest a minimum of 3 months.[15]

While postoperative mortality risk reached a plateau at 12 months across most surgical specialties, several exceptions were seen in subgroup analyses. Cardiovascular events were only associated with increased mortality risk for emergency vascular surgery within 3 months. This is most likely due to other predominating risk factors, such as the underlying reason for surgery. In contrast, for elective orthopedic surgery, such as hip arthroplasty, the risk was elevated for 18 months, wherein the relative contribution to risk from cardiovascular disease can be reasonably expected to be large compared to the surgery itself.

It is well recognized that emergency surgery is associated with increased perioperative risk due to the unplanned nature, out-of-hours operating, limited time for optimization, and emergent underlying pathology. The magnitude of the deleterious effect of operating shortly after a cardiovascular event is therefore likely largely lost compared with these other drivers of postoperative mortality. In other words, the circumstances and underlying reason for surgery in the emergency setting are such that no matter what the baseline patient condition at presentation, the risks are predominantly from the former, which may be why the risk associated with a previous cardiovascular event did not manifest for very long.

Postoperative mortality rates were similar between ischemic stroke, hemorrhagic stroke, and myocardial infarction (non–ST-segment elevation myocardial infarction and ST-segment elevation myocardial infarction), although we found that preoperative transient ischemic attack and unstable angina were associated with lower postoperative mortality rates (eTable 36 in Supplement 1). This would support placing comparable emphasis on understanding the time-dependent risk of preoperative stroke and myocardial infarction, justifying our aggregate reporting. It is important to emphasize that the risk curves for stroke and myocardial infarction indicated that similar plateaus were reached at 12 months. Linking the MINAP data, we could show that patients with a history of acute coronary syndrome had favorable postoperative mortality rates when the acute coronary syndrome had been treated with a primary percutaneous coronary intervention revascularization strategy (Table 3).

The demographic findings that a history of previous cardiovascular events is more common in older male individuals with multiple other comorbidities are already well established.[29] Importantly, we were also able to demonstrate that in this surgical population, increasing levels of socioeconomic deprivation were more common in those with a previous cardiovascular event, in agreement with existing findings in the general population.[30,31] In accordance with previous population-level mortality data from the UK, we found liver disease, kidney failure, and congestive heart failure were the 3 comorbidities associated with the greatest fold increase in 30-day mortality, followed by peripheral vascular disease, dementia, and cardiac arrhythmias.[13,23]

This is the largest and most detailed study of the time-dependent nature of postoperative mortality in patients with a prior cardiovascular event. The next largest study of the time-dependent nature of a preoperative cardiovascular risk factor was by Jorgensen et al,[12] who studied 7137 people undergoing surgery after a previous stroke, with 145 postoperative deaths within 30 days of surgery. In contrast, we report on 877 430 people undergoing surgery after stroke or acute coronary syndrome, with 40 999 deaths within 30 days of surgery. While the primary outcome assessed 30-day mortality and allowed comparability with existing surgical literature,[32] we were also able to model 60-day, 90-day, and 1-year mortality against time since the preoperative event. This allows future comparison as surgical research and clinical practice moving beyond 30-day mortality.[33-35] The demographic characteristics in our study are comparable with those of large North American[36] and other Western European surgical populations[12] with broad inclusion criteria, maximizing the generalizability of our findings in these populations. Due to the magnitude of our study population and the event rate, we provided reliable estimates for subgroup analysis, allowing clinicians to refer to their specific surgical specialty.

Limitations

This is an observational study, and caution must be exercised in drawing inferences about causality between the timing of surgery and postoperative outcome. Some time-dependent changes in mortality will be unrelated to surgery—mortality hazards decay with time after stroke and myocardial infarction. This may lead to unavoidable survivor bias; that is, those who are fit enough to have surgery more than 1 year after an event may represent a different cohort than those having surgery earlier. However, the data are specifically presented to inform patients and their perioperative care team about the temporal nature of preoperative cardiovascular risk factors as part of a shared decision-making process, not to dictate when nor whether an individual patient is offered surgery. Coding inaccuracies risk underrepresentation of comorbidity diagnoses. However, by linking data between HES and MINAP, we corroborated our findings across different registries and indicated the association between the time interval and mortality remains present. Some patients undergo unavoidable high-risk surgery irrespective of a recent cardiovascular event with the potential to skew mortality findings; however, we present the data by surgical severity and urgency to minimize this effect. Some patients may have undergone surgery without knowing their history of the cardiovascular event. However, this is unlikely to be in large numbers and reflects clinical practice where patient medical histories are sometimes incomplete. As these are routinely collected inpatient data, we did not have information on lifestyle factors (eg, smoking) more commonly recorded in primary care data sets.

Conclusions

Clinicians must balance deferring the benefits of the surgery (eg, relief of pain and avoidance of disease progression) against the increased mortality from overly expeditious surgery after a recent cardiovascular event. As part of shared decision-making, this requires integrating patients' values about competing aspects of their health.

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Invited Commentary

Managing Competing Risks for Surgical Patients With Complex Medical Problems—Considering Confounding

Laura A. Graham, PhD, MPH; Mary T. Hawn, MD, MPH

The timing of surgery following a myocardial infarction or stroke is a critical consideration, as it can significantly impact the risk of death and complications that diminish the potential benefit of the surgical procedure. The most recent guidelines recommend delaying nonurgent surgery until dual antiplatelet therapy (DAPT) can be completed.[1] For patients with a percutaneous coronary intervention (PCI), this means delaying surgery for 6 months. However, for patients with acute coronary syndrome and no PCI, DAPT is continued for up to 12 months after the event.[2]

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Leveraging an administrative data source of 21 million procedures, Chalitsios et al[3] found an increased risk of mortality after surgery that persisted for up to 14 months after an event with elective surgery (odds ratio = 1.22 [95% CI, 1.06-1.39] for procedures within 6-12 months) and 7 months with emergent surgery.

Their findings should be interpreted with caution. The large sample size gives the study power to detect differences regardless of significance. And the combination of severe confounding, selection bias (only patients deemed healthy enough to have surgery will have surgery), and immortal time bias (some patients will die before they have the opportunity to have surgery) substantially blurs the results of this nonexperimental retrospective population-based cohort study. Further, there is evidence of a difference in effect by procedure types that, with the exception of stratification, is unaccounted for in their models.

As demonstrated in Table 1 in the Chalitsios et al article,[3] surgical procedures among patients with a prior cardiovascular event are markedly different from the typical surgical procedure. Patients with a prior cardio- or cerebrovascular event are already at an increased risk of mortality, regardless of whether they have surgery or not.[4,5] We also have concerns about misattribution and confounding in this analysis. For example, when looking at the elective vs emergent classification, which is the biggest predictor of mortality, only 27% of their patients underwent elective abdominal aortic aneurysm repair. This proportion is markedly different from our practice in the United States, as reported in a recent publica-