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Original Article

Impact of postoperative cardiovascular complications on 30-day mortality after major abdominal surgery: an international prospective cohort study

STARSurg Collaborative[†] and **the EuroSurg Collaborative**[†]

Academic Department of Surgery, Institute of Applied Health Research, University of Birmingham

Summary

Cardiovascular complications after major surgery are associated with increases in morbidity and mortality. There is confusion over definitions of cardiac injury or complications, and variability in the assessment and management of patients. This international prospective cohort study aimed to define the incidence and timing of these complications and to investigate their impact on 30-day all-cause mortality. We performed a prospective, international cohort study between January 2022 and May 2022. Data were collected on consecutive patients undergoing major abdominal surgery in 446 hospitals from 28 countries across Europe. The primary outcome measure was cardiovascular complications as defined by the Standardised Endpoints for Perioperative Medicine-Core Outcome Measures for Perioperative and Anaesthetic Care initiative up to 30 days after surgery. The secondary outcome was 30-day postoperative mortality. This study included 24,203 patients, of whom 611 (2.5%) developed cardiovascular complications. In total, 458 (1.9%) patients died within 30 days of surgery, of which 123 (26.9%) deaths were judged to be cardiac-related. Mortality rates were higher in patients who developed postoperative cardiovascular complications than in those who did not (19.8% vs. 1.4%), which persisted after risk adjustment (hazard ratio (95%CI) 4.15 (3.14–5.48)). We estimated an absolute risk reduction (95%CI) of 0.4 (0.3–0.5) in mortality in the absence of all cardiovascular complications. This would confer a relative risk reduction in mortality of 21.1% if all cardiovascular complications were prevented. Postoperative cardiovascular complications are relatively common and occur early after major abdominal surgery. However, over 1 in 5 postoperative deaths were attributable to these complications, highlighting an important area for future randomised trials.

Correspondence to: S. K. Kamarajah
Email: s.k.kamarajah@bham.ac.uk
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[†]Collaborators are detailed in online Supporting Information Appendix S1.
Twitter/X:
@Sivesh93; @STARSurgUK; @EuroSurg

Introduction

Globally each year, 313 million patients undergo surgical procedures to improve quality of life and survival [1]. However, this can entail significant risk for patients due to postoperative complications associated with increased duration of hospital stay, healthcare utilisation and mortality. Recent estimates suggest that 4.2 million (7.7%) of all deaths globally occur within 30 days of surgery [2], making postoperative mortality the third most common cause of death. Centralisation of care for complex surgery

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and advances in peri-operative care have led to substantial reductions in postoperative complications and mortality rates over the last decade [3]. However, patients undergoing major abdominal surgery continue to be at the highest risk of a 30-day complication and death rate for procedures [4, 5].

Postoperative cardiac complications are recognised as being among the most clinically significant and are associated with morbidity and mortality [6, 7]. Peri-operative myocardial injury occurs commonly among asymptomatic patients undergoing non-cardiac surgery and its strong prognostic significance has increased the focus on cardiovascular outcomes in research regarding peri-operative outcomes [8]. Unfortunately, variability in how cardiovascular outcomes are reported have made it difficult to ascertain their incidence and associated mortality. This is important given the growing proportion of older patients with associated frailty and multiple long-term health conditions who have surgery [9–11]. The risk of postoperative cardiovascular complications is known to be higher in patients who have pre-existing cardiovascular disease, as well as in those undergoing high-risk surgery [3].

There have been few large-scale, prospective cohort studies focusing on postoperative cardiovascular complications and their impact on postoperative mortality [7, 12]. Utilising the recently developed Standardised Endpoints for Perioperative Medicine-Core Outcome Measures for Perioperative and Anaesthetic Care (StEP-CoMPAC) initiative [13], we aimed to determine the incidence of postoperative cardiovascular complications after major abdominal surgery across Europe and the impact of these complications on postoperative death.

Methods

CArdiovaSCulAr outcomes after major abDominal surgery (CASCADE) was an international, observational, multicentre, prospective cohort study across Europe, conducted according to a prespecified published protocol [6]. Any centre conducting eligible surgery in Europe was invited to participate, with prospective identification of patients by local collaborators across a pre-defined, two-week data collection window between 23 January and 1 May 2022. Consecutive adult patients (aged ≥ 18 y) undergoing a broad range of major abdominal surgical procedures were eligible (abdominal and/or pelvic visceral resection; formation or reversal of stoma; open vascular surgery; anterior abdominal wall hernia repair; or transplant surgery through any operative approach). Planned day-case procedures and those performed for traumatic indications or without visceral resection were not studied. This process collected routine anonymised data with no changes to clinical care pathways, and local principal investigators were responsible for obtaining required ethical approvals in line with local and national regulations. In the UK, this study was registered at each site as a service evaluation since no changes to clinical pathways were made and Caldicott guardian approvals were obtained before recruitment [14, 15].

Data relating to patient characteristics, peri-operative care and 30-day outcomes for each patient were collected using pre-specified case report forms. Clinically relevant covariables were selected for the purpose of adjustment for case mix. Patient characteristics recorded included: age; sex; BMI; ASA physical status; and smoking status. Other variables of interest were factors known to be associated with cardiac recovery after surgery including: comorbidities (atrial fibrillation, ischaemic heart disease, congestive heart failure, cerebrovascular disease, diabetes mellitus and chronic kidney disease); surgical urgency (elective or emergency); operative indication (benign or malignant); operative approach (open or minimally-invasive); operative contamination (clean, clean-contaminated, contaminated/dirty); operative speciality; peri-operative SARS-CoV-2 status; critical care admission; critical care duration of stay; duration of hospital stay; and 30-day readmissions. Data were submitted and stored on secure Research Electronic Data Capture (REDCap) [16] servers hosted by the Birmingham Surgical Trials Consortium (University of Birmingham, UK), and only data collection periods with > 95% data completeness were accepted for pooled analysis.

All patients were followed up for 30 days postoperatively for cardiovascular complications and all-cause death using available medical record data. Postoperative cardiac complications were defined according to the StEP-COMPAC definition, a globally accepted benchmark established by interdisciplinary leaders in the field [13]. This standardised, composite outcome included diagnoses of the following: new-onset atrial fibrillation; myocardial events (myocardial injury, myocardial infarction, coronary revascularisation and non-fatal cardiac arrest); and thromboembolic events (deep vein thrombosis, pulmonary embolism and thromboembolic stroke) according to standard criteria (online Supporting Information Table S1).

Testing using appropriate parametric or non-parametric tests was done based on visual and statistical evaluation for normality. Categorical data were cross-tabulated, and differences in proportions were tested using χ^2 and Fisher's exact tests, as appropriate. Inter-centre variation in adjusted and unadjusted postoperative cardiovascular complications rates were visualised using funnel plots, with meta-analysis using a random-effects model applied to derive the overall median centre postoperative cardiovascular complications rate and inter-

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centre heterogeneity (I^2 statistic). Mixed-effects multivariable logistic regression was performed to derive risk-adjusted postoperative cardiovascular complication rates, with patients clustered within their hospital (random effect).

We explored the relationship between postoperative cardiovascular complications and subsequent 30-day postoperative mortality using two approaches. First, we used mixed-effects Cox proportional hazards regression to describe the association between these outcomes, accounting for other known risk factors. Clinically plausible pre-operative and surgical variables were incorporated as fixed effects and hospital as a random effect. We included postoperative cardiovascular complications as a time-dependent covariate, and the proportionality assumption was evaluated using the Schoenfeld residuals. Final model selection performed through minimisation of the Akaike Information Criterion and maximising c-statistic. Effect estimates are presented as hazard ratios (95%CI) for time-to-event data. Second, causal inference methods were used to best negate for confounding as much as possible using counterfactual analyses [17]. This allowed simulation of a scenario where these postoperative cardiovascular complications did not occur with a resultant reduction in postoperative deaths. Inverse probability weight estimation was used to account for baseline confounding factors in terms of who did, or did not, experience a postoperative cardiovascular complication. Subsequent doubly robust estimation [18] was performed through risk adjustment of 30-day mortality using multivariable regression, incorporating weights from inverse probability weight estimation. The average treatment effect was calculated to determine the difference in 30-day mortality if postoperative cardiovascular complications were prevented [19], with 95%CIs computed from non-parametric bootstrap procedure (25,000 bootstrap samples). To explore the effect of postoperative cardiovascular complications on 30-day mortality, we conducted further analyses to examine these sub-outcomes (new-onset atrial fibrillation; myocardial damage; and thromboembolic events). The threshold for statistical significance was $p < 0.05$. All analyses were undertaken using R version 4.1.1 (R Foundation for Statistical Computing, Vienna, Austria) with the tidyverse, finalfit, survival and WeightIt packages.

Results

In total, 445 hospitals from 29 countries across Europe participated. Of 24,246 eligible patients in the dataset

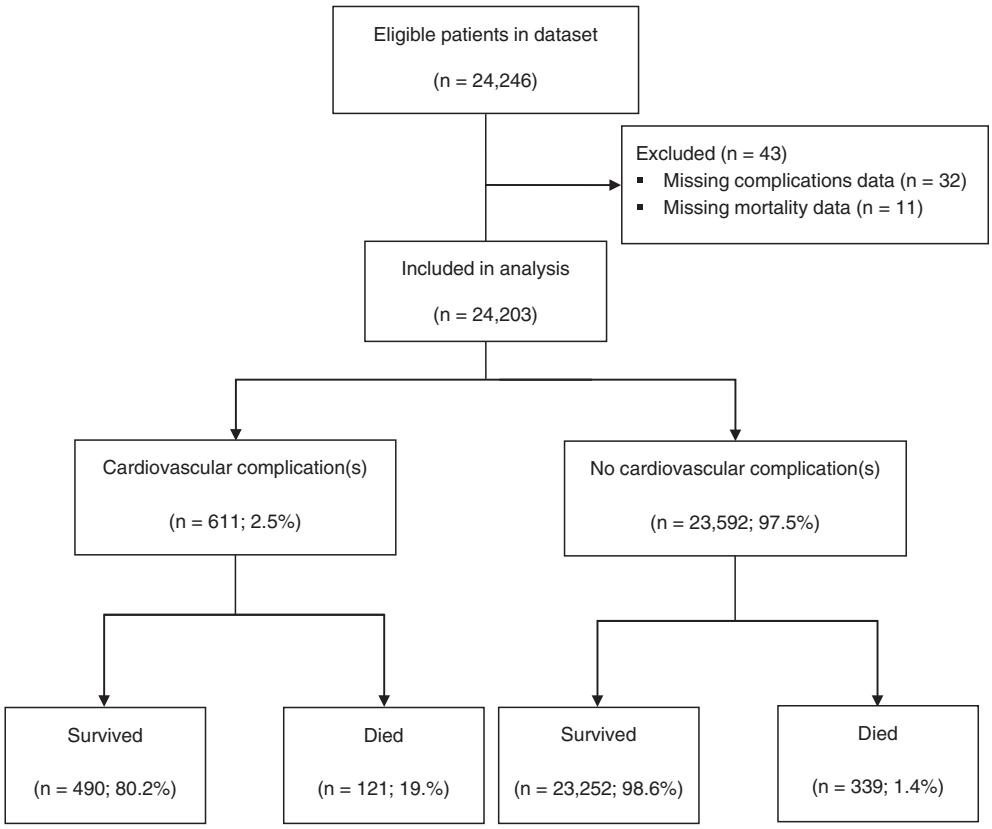


Figure 1 Study flow diagram of included patients in the CASCADE cohort study.

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undergoing major abdominal surgery, 24,203 had complete 30-day follow-up data (Fig. 1, online Supporting Information Table S2). Median (IQR [range]) age was 61 (24 [48–71]) y, with a third of patients classed as ASA physical status 3–4 (n = 7640, 31.6%). The most common cardiovascular comorbidities were atrial fibrillation (n = 1292, 5.3%); ischaemic heart disease (n = 1081, 4.5%); cerebrovascular disease (n = 696, 2.9%); and congestive heart failure (n = 560, 2.3%). Only 1185 (4.9%) patients were SARS-CoV-2 positive peri-operatively (Table 1). Surgical case-mix varied, with most common specialities being colorectal (n = 10,288, 42.5%), hepato-pancreato-biliary (n = 5865, 24.2%) and gynaecology (n = 3421, 14.1%). Overall, most patients underwent elective surgery (n = 17,355, 71.7%) and had minimally invasive procedures (n = 13,895, 57.4%).

Of the 24,203 patients, 611 (2.5%) developed at least one postoperative cardiovascular complication (Fig. 2a), with the most common being new-onset atrial fibrillation (n = 273, 41.9%); pulmonary embolism (n = 121, 18.6%); and myocardial infarction (n = 76, 11.7%). Median (IQR [range]) time to developing a postoperative cardiovascular complication was 4 (8 [2–10]) days. This was consistent among individual postoperative cardiovascular complications with new-onset atrial fibrillation occurring the earliest at a median (IQR [range]) of 3 (4 [1–5]) days and deep vein thrombosis occurring the latest at 7 (13 [3–16]) days (Fig. 2b and c).

Patients who experienced postoperative cardiovascular complications were significantly older and comorbid, with higher rates of emergency surgery and open surgical approach (Table 1). Across all 445 centres, median (95%CI) postoperative cardiovascular complication rate was 2.5 (2.3–2.7)%, with no significant inter-centre heterogeneity (I^2 (95% CI) 0.0% (0.0–12.3)) (online Supporting Information Figure S1a). This remained consistent following adjustment for case-mix using a mixed-effects logistic regression model at 2.4% (2.2–2.6) (I^2 0.0% (0.0–12.3) (online Supporting Information Figure S1b and Table S3)).

Overall 30-day postoperative mortality was 1.9% (n = 460) and this was significantly higher in patients who developed postoperative cardiovascular complications (19.8% vs. 1.4%; p < 0.001). Median (IQR [range]) time from onset of postoperative cardiovascular complications to death was lowest in patients suffering from myocardial infarction at 0 (0 [0–0]) days and highest in patients with atrial fibrillation and deep vein thrombosis (6 (15 [2–17]) days and 11 (4 [10–15]) days, respectively (Fig. 2d)).

The development of postoperative cardiovascular complications was associated with a higher adjusted mortality risk (hazard ratio (HR) (95%CI) 4.15 (3.14–5.48) (Fig. 3a and online Supporting Information Table S4)). On further analyses by aetiology (Fig. 3b and online Supporting Information Table S5), there was a similar risk of death for both atrial fibrillation (HR (95%CI) 3.09 (2.12–4.49)) and thromboembolic events (HR (95%CI) 3.56 (2.32–5.45)). However, this was significantly higher for patients who experienced a myocardial event (HR (95%CI) 11.86 (8.70–16.18)) with a 30-day mortality rate of nearly 50% (Fig. 3c and d).

The proposed causal model is reported in online Supporting Information Figure S2 and counterfactual analysis estimated that in the absence of all postoperative cardiovascular complications, an absolute risk reduction (95%CI) of 0.42% (0.32–0.52) (p < 0.001) in mortality would be observed (relative risk reduction 21.6%, Table 2). On sensitivity analysis by postoperative cardiovascular complications subgroup, the absence of atrial fibrillation and thromboembolic events conferred a non-significant absolute risk reduction (95%CI) in mortality (0.10% (0.00–0.25); p = 0.08 and 0.08% (0.02–0.33); p = 0.35, respectively). However, in the absence of all myocardial events, an absolute risk reduction (95%CI) in mortality of 0.25% (0.17–0.33) (p < 0.01) was observed (relative risk reduction 14.4%) (Table 2).

Discussion

Over the past two decades, understanding of postoperative cardiovascular complications has been compounded by confusion over definitions of cardiac injury or complications and variability in assessment and management of patients. This international prospective cohort study including > 24,000 patients undergoing major abdominal surgery across Europe highlighted that postoperative cardiovascular complications occur infrequently, but when they do occur this happens principally in the early postoperative period. They may have a causal role in postoperative death, with up to 1 in 5 deaths estimated to be avoidable if these can be prevented. Although atrial fibrillation and thromboembolic events are significant contributors to mortality, myocardial events pose the greatest risk of postoperative death.

Previous studies have reported postoperative cardiovascular complications rates ranging from 2% to 35% [7, 8, 13, 20, 21]. This wide range reflects heterogeneity in definitions of these complications used in previous cohort studies and randomised trials, making interpretation of the true incidence challenging. This includes different definitions for postoperative myocardial injury since there is a lack of an acceptable universal definition. For instance, previous cohort studies have used myocardial injury after non-cardiac surgery

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Table 1 Baseline patient- and operative-level characteristics according to postoperative cardiovascular complication status. Values are median (IQR [range]) or number (proportion).

		All patients	Postoperative cardiovascular complications		p value
		Total n = 24,203	No n = 23,592	Yes n = 611	
Patient factors					
Age; y		61 (23 [48–71])	60 (24 [47–71])	72 (16 [63–79])	< 0.001
Sex	Male	11,431 (47.2%)	11,080 (47.0%)	351 (57.4%)	< 0.001
	Female	12,772 (52.8%)	12,512 (53.0%)	260 (42.6%)	
ASA physical status	1–2	15,945 (65.9%)	15,717 (66.6%)	228 (37.3%)	< 0.001
	3–4	7640 (31.6%)	7271 (30.8%)	369 (60.4%)	
	Missing	618 (2.6%)	604 (2.6%)	14 (2.3%)	
BMI; $kg.m^{-2}$	< 18.5	564 (2.3%)	542 (2.3%)	22 (3.6%)	0.295
	18.5–24.9	8151 (33.7%)	7954 (33.7%)	197 (32.2%)	
	25–29.9	7968 (32.9%)	7760 (32.9%)	208 (34.0%)	
	30–39.9	5034 (20.8%)	4908 (20.8%)	126 (20.6%)	
	≥ 40	671 (2.8%)	653 (2.8%)	18 (2.9%)	
	Missing	1815 (7.5%)	1775 (7.5%)	40 (6.5%)	
Smoking status	Not current	16,189 (66.9%)	15,768 (66.8%)	421 (68.9%)	0.348
	Current	4493 (18.6%)	4388 (18.6%)	105 (17.2%)	
	Missing	3521 (14.5%)	3436 (14.6%)	85 (13.9%)	
Ischaemic heart disease	No	23,122 (95.5%)	22,572 (95.7%)	550 (90.0%)	< 0.001
	Yes	1081 (4.5%)	1020 (4.3%)	61 (10.0%)	
Congestive heart failure	No	23,643 (97.7%)	23,072 (97.8%)	571 (93.5%)	< 0.001
	Yes	560 (2.3%)	520 (2.2%)	40 (6.5%)	
Cerebrovascular disease	No	23,507 (97.1%)	22,927 (97.2%)	580 (94.9%)	0.002
	Yes	696 (2.9%)	665 (2.8%)	31 (5.1%)	
Atrial fibrillation	No	22,911 (94.7%)	22,374 (94.8%)	537 (87.9%)	< 0.001
	Yes	1292 (5.3%)	1218 (5.2%)	74 (12.1%)	
Chronic kidney disease	None	19,983 (82.6%)	19,535 (82.8%)	448 (73.3%)	< 0.001
	Stage 1–2	2680 (11.1%)	2593 (11.0%)	87 (14.2%)	
	Stage 3–5	1536 (6.3%)	1460 (6.2%)	76 (12.4%)	
	Missing	4 (<0.1%)	4 (<0.1%)	0	
Respiratory disease	No	21,805 (90.1%)	21,335 (90.4%)	470 (76.9%)	< 0.001
	Yes	2398 (9.9%)	2257 (9.6%)	141 (23.1%)	
Diabetes mellitus	None	20,477 (84.6%)	20,004 (84.8%)	473 (77.4%)	< 0.001
	NIDDM	2902 (12.0%)	2800 (11.9%)	102 (16.7%)	
	IDDM	819 (3.4%)	783 (3.3%)	36 (5.9%)	
	Missing	5 (<0.1%)	5 (<0.1%)	0	
SARS-COV-2 status	Negative	22,946 (94.8%)	22,388 (94.9%)	558 (91.3%)	< 0.001
	Positive	1185 (4.9%)	1133 (4.8%)	52 (8.5%)	
	Missing	72 (0.3%)	71 (0.3%)	1 (0.2%)	
Surgical factors					
Surgical urgency	Elective	17,355 (71.7%)	17,017 (72.1%)	338 (55.3%)	< 0.001
	Emergency	6841 (28.3%)	6568 (27.8%)	273 (44.7%)	
	Missing	7 (<0.1%)	7 (<0.1%)	0	

(continued)

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Table 1 (*continued*)

		All patients	Postoperative cardiovascular complications		p value
		Total n = 24,203	No n = 23,592	Yes n = 611	
Surgical indication	Benign	14,391 (59.5%)	14,095 (59.7%)	296 (48.4%)	< 0.001
	Malignant	9794 (40.5%)	9479 (40.2%)	315 (51.6%)	
	Missing	18 (0.1%)	18 (0.1%)	0	
Surgical approach	Minimally invasive	13,895 (57.4%)	13,693 (58.0%)	202 (33.1%)	< 0.001
	Open	10,305 (42.6%)	9896 (41.9%)	409 (66.9%)	
	Missing	3 (<0.1%)	3 (<0.1%)	0	
Surgical contamination	Clean	10,004 (41.3%)	9816 (41.6%)	188 (30.8%)	< 0.001
	Clean – contaminated	12,264 (50.7%)	11,950 (50.7%)	314 (51.4%)	
	Contaminated – dirty	1904 (7.9%)	1795 (7.6%)	109 (17.8%)	
	Missing	31 (0.1%)	31 (0.1%)	0	
Surgical speciality	Gynaecology	3421 (14.1%)	3395 (14.4%)	26 (4.3%)	< 0.001
	Urology	1796 (7.4%)	1770 (7.5%)	26 (4.3%)	
	Upper GI	1687 (7.0%)	1597 (6.8%)	90 (14.7%)	
	Lower GI	10,288 (42.5%)	9999 (42.4%)	289 (47.3%)	
	Hepatobiliary	5865 (24.2%)	5750 (24.4%)	115 (18.8%)	
	Transplant	524 (2.2%)	501 (2.1%)	23 (3.8%)	
	Vascular	307 (1.3%)	278 (1.2%)	29 (4.7%)	
	Other	315 (1.3%)	302 (1.3%)	13 (2.1%)	

NIDDM, non-insulin-dependent diabetes mellitus; IDDM, insulin-dependent diabetes mellitus; GI, gastrointestinal.

(MINS), with a postoperative peak troponin T (TnT) ≥ 0.04 ng.ml^{-1} with evidence of ischaemia [22]. This contrasts with the definition used in the present study, defined according to the StEP-COMPAC definitions of detection of an elevated TnT value above the 99th percentile of upper range limit. In addition, there is limited guidance regarding sampling frequency and inconsistencies, which can further precipitate variations in the incidence of MINS captured by studies. For example, a shorter duration of monitoring and troponin sampling could lead to events being missed.

In our patient cohort, postoperative cardiovascular complications had a significant causal role in postoperative death, with up to 1 in 5 deaths estimated to be avoidable if these could be prevented; this potential causal relationship has not been reported to date. Studies have only reported associations of postoperative cardiovascular complications with a 30-day mortality rate of up to 17% [7, 23, 24]. The VISION study, including > 40,000 patients across 28 centres in 14 countries, showed MINS was attributed to 17% of postoperative deaths [7]. The differences between the VISION study and our data may reflect changes in the profile of patients undergoing surgery, where those in the present study had higher rates of multiple long-term conditions and were older. The impact of postoperative cardiovascular complications persists with follow-up studies showing recurrent myocardial injury/infarction, congestive heart failure, serious arrhythmia (e.g. cardiac arrest) and increased mortality risk 1 year after surgery [8, 21, 22, 25].

The role those postoperative cardiovascular complications have in the causal pathway of deaths remains unclear. Cardiovascular complications may be a marker of physiological frailty or have a direct influence on risk of death (for example through chronic heart failure or cardiovascular events). Irrespective of the associative role, early postoperative cardiovascular complications are a key predictor of poor short-term postoperative outcomes. This relationship persisted even in patients undergoing elective or emergency surgery, further supporting the significance of postoperative cardiovascular complications. This warrants investigation in future clinical trials on peri-operative cardioprotective interventions, and consideration of routine implementation of risk stratification for postoperative cardiovascular complications prevention bundles and enhanced peri-operative surveillance [20].

A major strength of this study is the prospective, international cohort which represents one of the largest cohort studies on postoperative cardiovascular complications to date. This is the first study to provide a causal estimation of the contribution of postoperative cardiovascular complications

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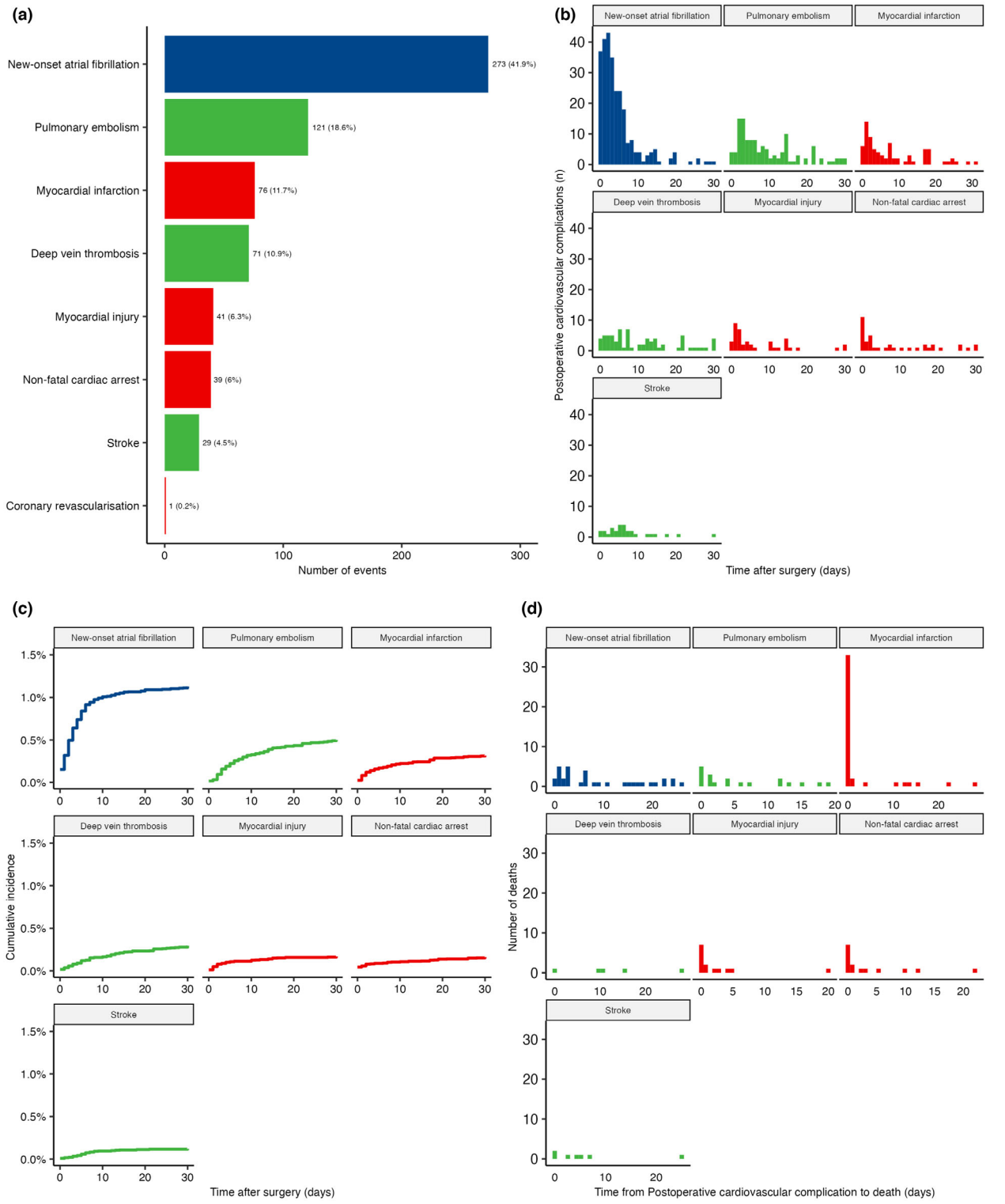


Figure 2 Incidence (a), time of onset after surgery (b), cumulative incidence (c) and time from onset to death of individual postoperative cardiac complications in patients undergoing major abdominal surgery (d). Blue, new-onset atrial fibrillation; green, thromboembolic event; red, myocardial event.

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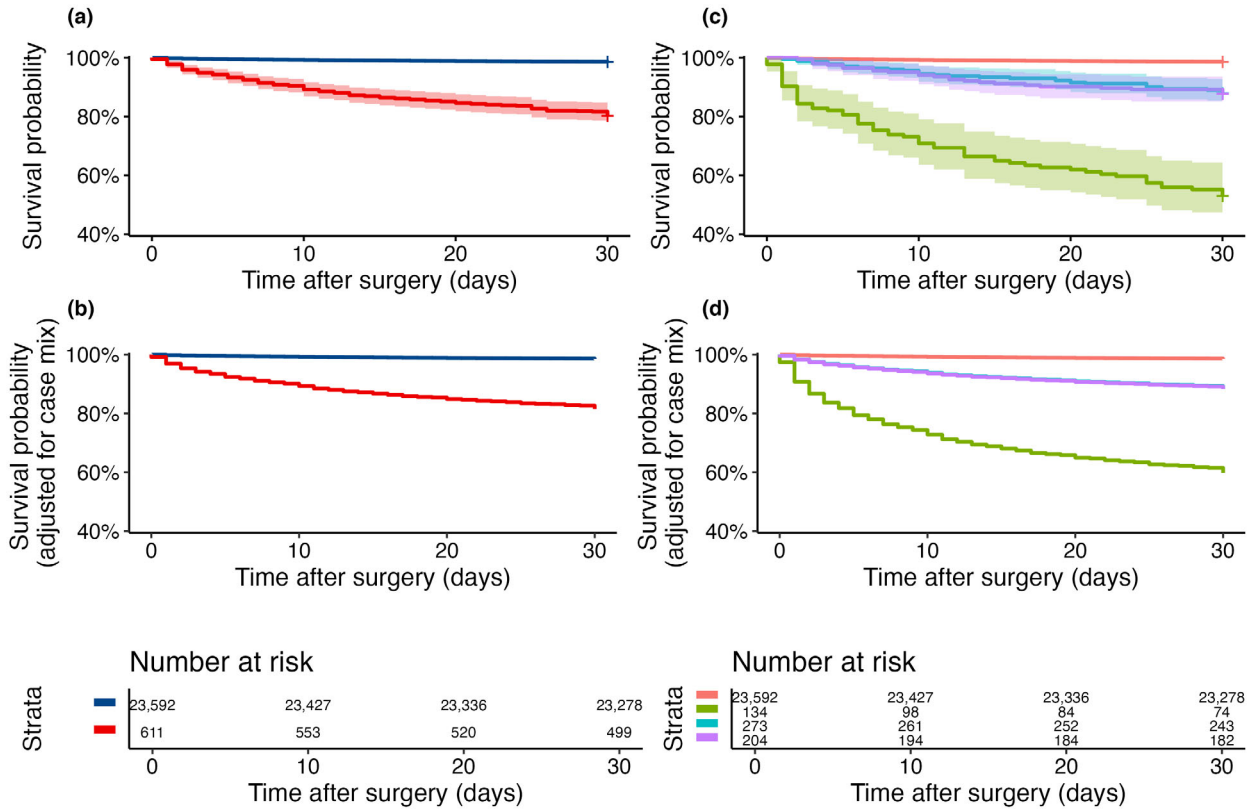


Figure 3 Kaplan–Meier survival curves of survival data in relation to postoperative cardiovascular complications, with follow-up duration of 30 days after major abdominal surgery. (a) Unadjusted Kaplan–Meier survival estimates by postoperative cardiovascular complications; (b) adjusted Kaplan–Meier survival estimates by postoperative cardiovascular complications; (c) unadjusted Kaplan–Meier survival estimates by postoperative cardiovascular complications subgroup and (d) adjusted Kaplan–Meier survival estimates by postoperative cardiovascular complications subgroup. Blue, no postoperative cardiovascular complications; red, postoperative cardiovascular complications; orange; no postoperative cardiovascular complications; green, myocardial event; light blue, new-onset atrial fibrillation; purple, thromboembolic event.

to postoperative mortality. However, there are important limitations to recognise. First, we collected routine data with no change to clinical care pathways. It is well established that new-onset atrial fibrillation, myocardial injury and venous thromboembolism in particular are underdiagnosed due to frequent lack of routine testing of troponin levels [3]. Therefore, while the reported rates of postoperative cardiovascular complications may be an underestimation, the most clinically significant complications would be expected to be captured. Nonetheless, it is possible that a proportion of postoperative deaths may be due to undiagnosed postoperative cardiovascular complications and so the contribution to postoperative mortality may be even higher. Second, results of the study are limited to only participating countries in Europe and may not be generalisable to centres from low/middle-income countries or non-participating high-income countries. This cohort study did not collect data for all possible risk factors or other specific postoperative complications which may also contribute to death, as data were restricted to what was routinely recorded and practical to be collected across international health systems. Finally, since the data were collected during the COVID-19 pandemic, it remains unclear if this may have had an impact on the results. Further analyses of the dataset will be undertaken to explore the role of peri-operative anaemia and prevalence of multimorbidity in patients undergoing major abdominal surgery and their impact on postoperative major complications.

This study has important implications. First, it has established the growing scale and impact of postoperative cardiovascular complications on mortality in patients undergoing major abdominal surgery. This is important as we move towards an era of increasingly complex surgery performed on patients with frailty who may also have multiple long-term conditions [26]. Second, findings from this study can be used to inform the design of future interventional trials to reduce postoperative cardiovascular

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Table 2 Summary of mixed-effects multivariable Cox proportional hazards regression models and counterfactual analysis of postoperative cardiovascular complications and postoperative death within 30 days of surgery, by outcome subgroup. Values are number proportion, hazard ratio (95%CI) and risk reduction (95%CI).

	30-day mortality rate	Association with 30-day mortality		Treatment effect on 30-day mortality	
		Unadjusted hazard ratio	Adjusted hazard ratio	Absolute risk reduction	Relative risk reduction
All postoperative cardiovascular complications	121/611 (19.8%)	11.54 (8.91–14.95)*	4.15 (3.14–5.48)*	0.42% (0.32–0.52)*	21.6%
Subgroup by type of complication					
New-onset atrial fibrillation	33/273 (12.1%)	8.79 (6.15–12.57)*	3.09 (2.12–4.49)*	0.10% (0.00–0.25)	6.5%
Myocardial event	63/134 (47.0%)	44.33 (33.87–58.04)*	11.86 (8.70–16.18)*	0.25% (0.17–0.33)*	14.4%
Thromboembolic event	25/204 (12.3%)	8.97 (5.98–13.47)*	3.56 (2.32–5.45)*	0.08% (0.02–0.33)	13.0%

Variables adjusted for in the model are: age; sex; BMI; presence of multiple long-term health conditions and operative factors such as urgency, indication, approach (open or minimally invasive); contamination (clean; clean – contaminated; contaminated – dirty) and speciality.
*$p < 0.001$.

complications through complex trial designs involving routine risk stratification, input across multidisciplinary teams and routine surveillance. Finally, the evidence base for the scale of postoperative cardiovascular complications in low/middle-income countries is limited, highlighting the need for a future cohort study to better understand the impact of postoperative cardiovascular complications in these countries.

Postoperative cardiac complications remain an urgent clinical concern that needs to be addressed, especially with the rising rates of multimorbidity and cardiovascular disease of patients undergoing surgery. As the capacity of surgical services is expanded over the next decade to meet the growing demands in healthcare systems worldwide, an urgent clinical need exists to better identify risk reduction strategies to reduce rates and impact of postoperative cardiovascular complications on patients undergoing major surgery. This is particularly important for patients with myocardial disease; the development of validated prediction tools that are clinically relevant in a global context is a research priority.

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Supporting Information

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Appendix S1. STARSurg and EuroSurg collaborators.

Figure S1. International variation in the unadjusted and adjusted rates of postoperative cardiovascular complications.

Figure S2. Causal model linking the postoperative cardiac complications and 30-day mortality.

Table S1. Summary of definitions used for postoperative cardiovascular complications after major abdominal surgery.

Table S2. Patient data submitted and hospitals involved in the CASCADE cohort study by country.

Table S3. Mixed-effects multivariable logistic regression models of postoperative cardiovascular complications within 30 days of surgery.

Table S4. Univariate and mixed-effects multivariate Cox proportional hazards regression analysis of association between postoperative cardiovascular complications and 30-day postoperative mortality.

Table S5. Univariate and mixed-effects multivariate Cox proportional hazards regression analysis of association between postoperative cardiovascular complication subgroups and 30-day postoperative mortality.

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