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Impact of postoperative complications after cardiac surgery on long-term survival

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Abstract

Purpose: The impact of postoperative complications on long-term survival is not well characterized. We sought to study the prevalence of postoperative complications after cardiac surgery and their impact on long-term survival.

Methods: Operative survivors ($n = 26{,}221$) who underwent coronary artery bypass grafting (CABG) ($n = 13{,}054$, 49.8%), valve surgery ($n = 8667$, 33.1%) or combined CABG and valve surgery ($n = 4500$, 17.2%) from 1993 to 2019 were included in the study. Records were reviewed for postoperative complications and long-term survival. Propensity-match analysis was performed between patients who did and did not have a postoperative complication. The associations between postoperative complications and survival were assessed using a Cox-proportional model.

Results: Complications occurred in 17,463 (66.6%) of 26,221 operative survivors. A total of 17 postoperative complications were analyzed. Postoperative blood product use was the commonest ($n = 12{,}397$, 47.3%), followed by atrial fibrillation ($n = 8399$, 32.0%), prolonged ventilation ($n = 2336$, 8.9%), renal failure ($n = 870$, 3.3%), reoperation for bleeding ($n = 859$, 3.3%) and pacemaker/ICD insertion ($n = 795$, 3.0%). Stroke (hazard ratio [HR]: 1.55; 95% confidence interval [CI]: 1.36–1.77), renal failure (HR: 1.45; 95% CI: 1.33–1.58) and pneumonia (HR: 1.23; 95% CI: 1.11–1.36) had the strongest impact on long-term survival. Long-term survival decreased as the number of postoperative complications increased.

Conclusions: Postoperative complications after cardiac surgery significantly impact outcomes that extend beyond the postoperative period. Stroke, renal failure, and pneumonia are particularly associated with poor long-term survival.

KEYWORDS
long-term survival, postoperative complications

Abbreviations: CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; DSWI, deep sternal wound infection; GI, gastrointestinal; ICD, implantable cardioverter-defibrillator; LVEF, left ventricular ejection fraction; PPM, permanent pacemaker; TIA, transient ischemic attack.

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1 | INTRODUCTION

Postoperative complications after cardiac surgery are common and have been found to affect operative mortality, increase the length of intensive care and hospital stay and health care costs.[1–3] Identification of the most common complications may help to find opportunities to target improvement in patient outcomes and the delivery of cost-effective care.

While various studies have demonstrated the adverse effects of postoperative complications on the short-term outcomes after cardiac surgery, their impact on long-term outcomes has been less studied.[4] Most patients survive the hospital stay despite postoperative complications; however, the long-term consequences on survival is not well-known. The objective of the present study was to evaluate the prevalence of postoperative complications after cardiac surgery among operative survivors, and their impact on long-term survival. We hypothesize that postoperative complications have an adverse effect on long-term survival.

2 | METHODS

We retrospectively reviewed 31,248 adult patients (≥18 years) who underwent isolated coronary artery bypass grafting (CABG), valve surgery (repair or replacement), or a combination of CABG and valve surgery from January 1993 through October 2018 at Mayo Clinic, Rochester, Minnesota. Both primary and reoperative procedures were included. The study was approved by the Institutional Review Board at Mayo Clinic, Rochester, Minnesota. Individual patient consent requirement was waived as the study was deemed a minimal-risk retrospective study; however, patients without research authorization were excluded. Patient characteristics were obtained from the prospectively collected database based on definitions set forth by the Society of Thoracic Surgeons (STS) Adult Cardiac Database with additional review of patient records for supplementing missing information.[5]

Minimally invasive ($n = 1132$), transcatheter ($n = 511$) and robotic ($n = 401$) procedures were excluded. Operative mortalities ($n = 758$) were also excluded. Operative mortality was defined as any death, regardless of cause, occurring (1) within 30 days after surgery, or (2) during the same hospitalization as the index surgery, regardless of time. Patients with unknown 30-day status ($n = 562$), and surgeries from subjects who did not permit their records to be used for research ($n = 959$) were also excluded. Finally, there were some patients who had multiple surgeries that fit these criteria, only the first surgery done at our institution was analyzed to ensure independent samples (excluded $n = 704$ surgeries).

The postoperative complications studied were blood product transfusion, atrial fibrillation, prolonged ventilation, renal failure, gastro-intestinal events, anticoagulation-related events, sepsis, superficial, and deep wound infection, need for permanent pacemaker or implantable cardioverter-defibrillator (PPM/ICD), pneumonia, stroke, transient ischemic attack (TIA), reoperation for valve dysfunction, reoperation for bleeding, cardiac tamponade and cardiac arrest. Their clinical definitions were derived from the criteria set forth in the STS Database (Table S1).[6] The primary outcome was long-term survival.

Vital status was determined by combining information from the subject's electronic medical record and from retrievals from LexisNexis Accurint. If any death was found, that was used to determine the subject's vital status. When no deaths were found, the most recent of the subjects last diagnosis date or the last retrieval date of Accurin (back dated by 1 month) was used as last known alive status. The reverse Kaplan–Meier method (censoring deaths) was used to estimate the median time until last follow-up. Kaplan–Meier was used to estimate survival percentage. Univariate Cox-proportional hazards models were used to assess each complication with overall survival. A multivariable Cox-proportional hazards model was developed including variables with less than 1% missing data, including prespecified preoperative characteristics and studied complications. Sepsis and multisystem failure were not included in the multivariable as they highly correlated with other complications.

A supplemental propensity model was derived to balance the subjects with and without postoperative complications in terms of their preoperative characteristics. A gradient-boosted model (GBM) using preoperative characteristics was developed to predict the likelihood of subjects having at least one complication.[7,8] Threefold cross validation was replicated 100 times to determine the number of trees, the interaction depth, shrinkage parameter, and the minimum number of observations required in each node. The predictions from the GBM were kept on the logit scale and subjects with complications were matched to subjects without complications using a caliper of 0.2 times the *SD*s of the logit score among the cohort. A total of 8111 subjects with complications were matched to 8111 subjects without a complication. All complications were included in a multivariable model stratified by the matched pairs without adjustment for preoperative characteristics as all characteristics were found to be balanced with as determined by standardized differences all less than 0.1.

3 | RESULTS

The study cohort included 26,221 patients who underwent either isolated CABG ($n = 13,054$, 49.8%), isolated valve surgery (aortic valve repair/replacement, mitral valve repair/replacement, tricuspid valve repair/replacement or pulmonary valve replacement, $n = 8667$, 33.1%), or combined CABG and valve surgery ($n = 4500$, 17.2%). Patient demographics and operative characteristics are outlined in Table S2. The mean age was 67.6 ± 12.0 years, and 70.6% patients were male. Patients who underwent isolated valve surgery were younger, more often females, with fewer comorbidities and higher left ventricular ejection fraction.

TABLE 1 Number of postoperative complications stratified by procedure

No of complications, *n* (%)	CABG (*N* = 13,054)	CABG + valve (*N* = 4500)	Valve (*N* = 8667)	All (*N* = 26,221)
0	4500 (34.5)	929 (20.6)	3329 (38.4)	8758 (33.4)
1	5163 (39.6)	1730 (38.4)	3254 (37.5)	10147 (38.7)
2	2375 (18.2)	1148 (25.5)	1371 (15.8)	4894 (18.7)
3	648 (5.0)	403 (9.0)	401 (4.6)	1452 (5.5)
4	214 (1.6)	155 (3.4)	179 (2.1)	548 (2.1)
≥5	154 (1.2)	135 (3.0)	133 (1.5)	422 (1.6)

Abbreviation: CABG, coronary artery bypass grafting.

These patients also had shorter operative times evidenced by shorter cardiopulmonary bypass times.

The number of postoperative complications in each procedure type is shown in Table 1. At least one complication was seen in 66.6% (*n* = 17,463) of patients, while 1.6% (*n* = 422) of patients had five or more complications. The prevalence of postoperative complications stratified by procedure type is listed in Table 2. Postoperative blood product transfusion was the most common complication, seen in 47.3% of the patients, followed by atrial fibrillation in 32.0% and prolonged ventilation in 8.9%. Renal failure was present in 807 (3.3%) patients, of which 307 needed dialysis. The prevalence of most postoperative complications was higher in the combined CABG and valve surgery group. Sternal infections were more common in isolated CABG patients, and the

TABLE 2 Incidence of postoperative complications stratified by procedure

Variable, *n* (%)	CABG (*N* = 13,054)	CABG + valve (*N* = 4500)	Valve (*N* = 8667)	All (*N* = 26,221)	*p* Value
Blood product use	6311 (48.3)	2761 (61.4)	3325 (38.4)	12397 (47.3)	<.001
Atrial fibrillation	3889 (29.8)	1805 (40.1)	2705 (31.2)	8399 (32.0)	<.001
Prolonged ventilation	1030 (7.9)	660 (14.7)	646 (7.5)	2336 (8.9)	<.001
Renal failure	391 (3.0)	220 (4.9)	259 (3.0)	870 (3.3)	<.001
Reoperation for bleeding	365 (2.8)	209 (4.6)	285 (3.3)	859 (3.3)	<.001
PPM/ICD use	145 (1.1)	217 (4.8)	433 (5.0)	795 (3.0)	<.001
Pneumonia	339 (2.6)	167 (3.7)	209 (2.4)	715 (2.7)	<.001
GI event	254 (1.9)	153 (3.4)	191 (2.2)	598 (2.3)	<.001
Stroke	161 (1.2)	69 (1.5)	95 (1.1)	325 (1.2)	.100
Superficial sternal infection	179 (1.4)	52 (1.2)	63 (0.7)	294 (1.1)	<.001
Tamponade	71 (0.5)	56 (1.2)	149 (1.7)	276 (1.1)	<.001
Cardiac arrest	116 (0.9)	57 (1.3)	73 (0.8)	246 (0.9)	.040
Sepsis	92 (0.7)	44 (1.0)	77 (0.9)	213 (0.8)	.134
TIA	84 (0.6)	56 (1.2)	64 (0.7)	204 (0.8)	<.001
Deep sternal infection	104 (0.8)	29 (0.6)	20 (0.2)	153 (0.6)	<.001
Anticoagulation-related event	32 (0.2)	28 (0.6)	60 (0.7)	120 (0.5)	<.001
Reoperation for valve dysfunction	1 (0.0)	15 (0.3)	39 (0.4)	55 (0.2)	<.001

Abbreviations: CABG, coronary artery bypass grafting; GI, gastrointestinal, ICD, implantable cardioverter-defibrillator; PPM, permanent pacemaker; TIA, transient ischemic attack.

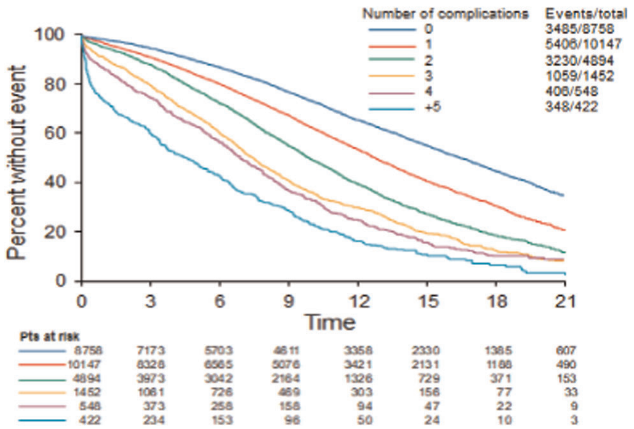

FIGURE 1 Kaplan–Meier survival curves stratified by number of postoperative complications

need for PPM/ICD was more common in patients that underwent isolated valve surgery.

3.1 | Late outcomes—survival

The median follow-up was 14.98 years (interquartile range: 7.85–20.32 years). The overall survival of the entire patient cohort at 1 and 5 years was 96.3% (95% confidence interval [CI]: 96.1–96.5) and 82.8% (95% CI: 82.3–83.2), respectively. Patients with no complications had a 1 and 5-year survival of 98.4% (95% CI: 98.2–98.7) and 89.8% (95% CI: 89.1–90.4), respectively. Long-term survival was adversely affected by the number of postoperative complications (Figure 1 and Table 3).

The type of complication also impacted survival differently. Stroke, anticoagulation-related events, renal failure, and pneumonia had the greatest impact on 1-year survival while renal failure, stroke, pneumonia, and gastrointestinal (GI) events had the greatest impact on 5-year survival (Figure 2 and Table 4). The median survival after each complication is also listed in Table 4.

The multivariable analysis is depicted in Table S3. It identified stroke, renal failure, anticoagulant-related events, pneumonia, TIA, PPM/ICD insertion, blood product use, GI events, prolonged ventilation, and atrial fibrillation as independent risk factors for late mortality.

3.2 | Propensity score

Our best efforts at matching yielded 8111 matched pairs of patients with and without postoperative complications. The distribution of propensity scores was similar with relatively small, standardized differences in baseline characteristics after matching (Table S4). The propensity match analysis is shown in Figure 3A,B. The results of the multivariable model (including all postoperative complications) among the matched subset (Table 5) were similar to the multivariable model among all subjects which did include adjustment of baseline characteristics. Renal failure, stroke, TIA, pneumonia, blood product use and atrial fibrillation remained associated with a significantly higher long-term mortality; however, the effect size was greater than that seen in the multivariable analysis.

4 | DISCUSSION

This study reports the impact of postoperative complications on long-term survival in more than 25,000 operative survivors after the most common cardiac surgery procedures. It highlights the profound impact that complications have on long-term survival underscoring the need for their prevention. In this study, 66.6% of operative survivors had at least one postoperative complication following CABG, isolated valve surgery or combined CABG and valve surgery. Blood product use, atrial fibrillation, prolonged ventilation, and renal failure were the most common complications. Both the number and type of postoperative complication impacted survival. Stroke, renal failure, and pneumonia were associated with particularly poor long-term survival.

In the present study, we analyzed 17 postoperative complications. Their prevalence ranges from 0.2% for reoperation for valve dysfunction to 47% for blood product transfusion with 66% of the patients having at least one complication. This provides a more granular description of the prevalence of a larger variety of complications beyond the STS-defined major morbidities[5] (prolonged ventilation, deep sternal wound infection [DSWI], renal failure, reoperation, and stroke) and demonstrated that many of them, not considered major complications, also impact long-term survival. In our study, the prevalence of one of the five complications defined by

TABLE 3 Unadjusted effect of the number of postoperative complications on long term survival

Number of complications	1-Year survival (95% CI)	5-Year survival (95% CI)	Median survival (years)
0	98.4 (98.2, 98.7)	89.8 (89.1, 90.4)	16.5
1	97.1 (96.8, 97.4)	84.1 (83.3, 84.8)	12.8
2	95.4 (94.8, 96)	77.9 (76.7, 79.1)	9.9
3	91.2 (89.8, 92.7)	67.2 (64.8, 69.8)	7.5
4	86.8 (84, 89.7)	63.1 (59.1, 67.5)	7.0
≥5	73.1 (68.9, 77.5)	47.9 (43.2, 53)	4.6

Abbreviation: CI, confidence interval.

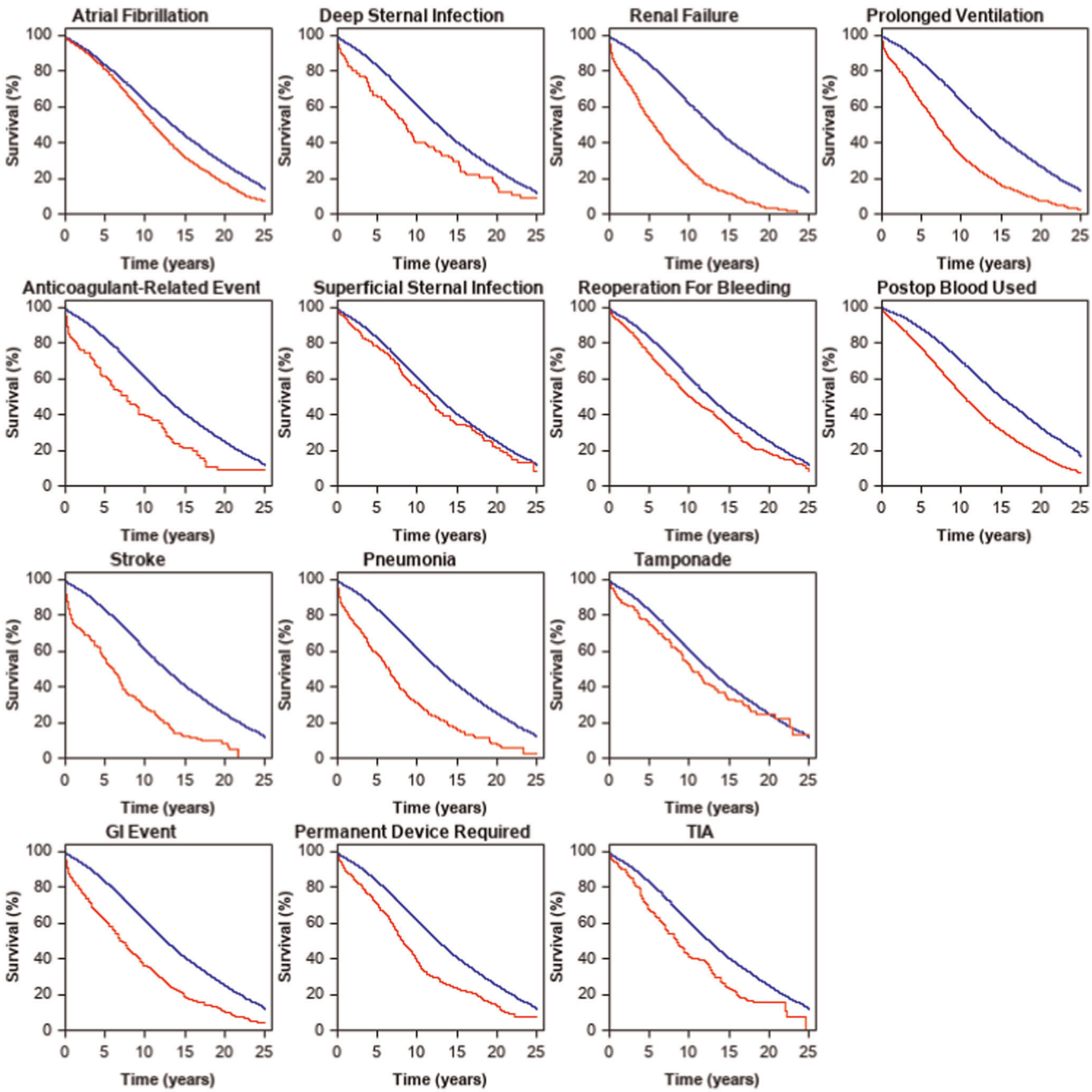

FIGURE 2 Kaplan–Meier survival curves for individual complications. Each plot is stratified by the complications indicated in the title. The blue line represents subjects without the complication and the red line represents subjects with the complication

the STS as major was 13.7% ($n = 3603$). This was similar to the findings recently reported by Seese et al.[4], where they found that 16.8% of their patients had at least one of these five complications.[4]

Postoperative stroke was associated with the highest risk for late mortality (hazard ratio [HR]: 1.55; 95% CI: 1.36–1.77; $p < .001$). Stroke was seen in 1.2% of the patients, and TIA in another 0.8%. Estimates for postoperative stroke have ranged from 1.6% to 5.2% in previous studies.[9–12] The 1 and 5-year survival after stroke in this study was 76% and 56%, respectively, which was congruent with the findings of other investigators.[13,14] Despite advances in stroke care, long-term prognosis remains a cause for concern. Sennfalt et al.[15] reported that at 5 years after stroke, over two in three patients with ischemic stroke, and over three in four patients with intracranial hemorrhage, were dead or in dependent care. Efforts to prevent stroke including epiaortic ultrasound, limited manipulation of the ascending aorta, higher arterial pressures during and after surgery are being pursued.[15]

Renal failure is a frequent complication after cardiac surgery, and has been associated with increased hospital stay, cost and higher operative mortality.[16] In the present study, renal failure was seen in 3.3% of patients, and was associated with the worst 5-year survival (54%).

TABLE 4 Unadjusted effect of individual postoperative complication on long term survival

Variable (%)	1-Year survival (95% CI)	5-Year survival (95% CI)	Median survival (years)
Overall	96.3 (96.1, 96.5)	82.8 (82.3, 83.2)	12.6
Superficial sternal infection	94.8 (92.3, 97.4)	78.8 (74.1, 83.8)	11.2
Atrial fibrillation	95.8 (95.4, 96.3)	81.2 (80.3, 82.1)	11.0
Blood product use	94.4 (94.0, 94.8)	77.1 (76.4, 77.9)	10.4
Tamponade	90.8 (87.4, 94.4)	75.1 (69.9, 80.8)	10.3
Reoperation for bleeding	93.4 (91.7, 95.1)	74.4 (71.4, 77.5)	10.2
Deep sternal infection	87.5 (82.4, 92.9)	65.9 (58.7, 74.1)	8.6
TIA	93.5 (90.2, 97.0)	67.0 (60.7, 73.9)	8.5
PPM/ICD use	89.9 (87.8, 92.1)	70.9 (67.6, 74.4)	8.1
Anticoagulant-related event	82.0 (75.3, 89.2)	62.3 (53.9, 71.9)	7.7
Cardiac arrest	87.0 (82.8, 91.4)	67.8 (61.9, 74.1)	7.3
GI event	83.9 (81.0, 87.0)	62.2 (58.3, 66.4)	7.2
Prolonged ventilation	87.4 (86.0, 88.7)	62.3 (60.3, 64.4)	7.0
Pneumonia	83.1 (80.3, 85.9)	58.6 (55.0, 62.5)	6.4
Stroke	76.1 (71.6, 81.0)	56.0 (50.5, 62.0)	6.0
Renal failure	82.3 (79.8, 84.9)	53.7 (50.4, 57.3)	5.6

Abbreviations: CI, confidence interval; GI, gastrointestinal; ICD, implantable cardioverter-defibrillator; PPM, permanent pacemaker; TIA, transient ischemic attack.

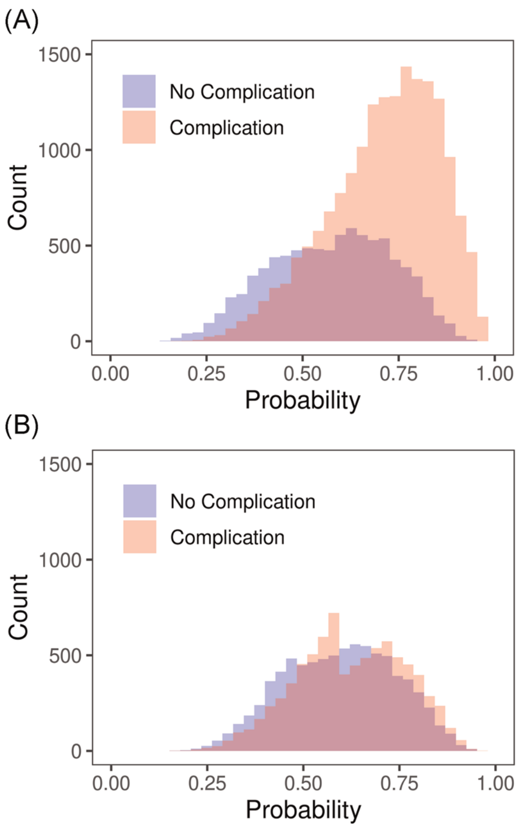

FIGURE 3 (A) Prepropensity match distribution of patients. (B) Postpropensity match distribution of patients

TABLE 5 Propensity matching—multivariable matched hazard ratio

Variable	Hazard ratio (95% CI)	*p* Value
TIA	3.38 (1.55, 7.32)	.002
Renal failure	2.87 (1.97, 4.20)	<.001
Stroke	2.05 (1.16, 3.62)	.014
Pneumonia	2.04 (1.33, 3.13)	.001
Blood product use	1.22 (1.11, 1.37)	<.001
Atrial fibrillation	1.14 (1.02, 1.28)	.019
Cardiac arrest	1.87 (0.85, 4.11)	.121
Superficial sternal infection	1.38 (0.77, 2.46)	.277
Anticoagulant-related event	1.22 (0.48, 3.12)	.675
Deep sternal infection	1.24 (0.61, 2.49)	.551
PPM/ICD use	1.16 (0.82, 1.64)	.405
Prolonged ventilation	1.07 (0.84, 1.36)	.604
GI event	1.06 (0.70, 1.61)	.779
Tamponade	0.91 (0.46, 1.76)	.768
Reoperation for bleeding	0.87 (0.63, 1.20)	.397

Abbreviations: CI, confidence interval; GI, gastrointestinal; ICD, implantable cardioverter-defibrillator; PPM, permanent pacemaker; TIA, transient ischemic attack.

The frequency of this complication in literature varies between 3% and 30% due to variable definitions of renal failure.[17] The reported 5-year survival has been between 36% and 63%[17–19] and worsens as the severity of renal failure increases.[20] Hobson et al.[17] reported that the risk of death associated with renal failure after cardiac surgery remains high for 10 years.[17] Other investigators have demonstrated that the early recovery of renal function after acute kidney injury is associated with improved long-term survival.[21] Renal failure after cardiac surgery maybe cardiopulmonary bypass-induced, drug-induced, due to volume depletion or vaso-spastic medications, or due to low cardiac output. Optimizing the patient's general condition, discontinuation of potentially nephrotoxic drugs and maintaining normovolemia are some of the documented ways of preventing renal failure.[22] Goal-directed perfusion, maintaining oxygen delivery ≥280 ml/minute/m^2, has been another recent strategy for renal protection during cardiopulmonary bypass.[23]

Blood product use was the most common complication in the present study, found in 47% of the patients. Use of postoperative blood products was associated with an increase in late mortality (HR: 1.18; 95% CI: 1.14–1.23; $p < .001$). This is congruent with a study performed by Jakobsen et al.[24] who reported that blood transfusion is associated with higher mortality. The deleterious effects of transfusion after cardiac surgery include the increased risk of nosocomial pneumonia, sternal wound infection, severe sepsis, and renal dysfunction.[25] Blood transfusion also carries a large inflammatory load and increases the already inflammatory state after CPB.[25] Interestingly, reexploration for bleeding was not associated with increased long-term mortality (HR: 0.95; 95% CI: 0.86–1.04, $p = .239$). Early reexploration in cases of postoperative bleeding could be a better alternative to blood product transfusion in terms of long-term outcomes.

Atrial fibrillation was found in 32% of the patients in the present study, and this is similar to the incidence reported by a few other studies.[26–28] Persistent atrial fibrillation increases risk of stroke, use of long-term anticoagulation and the complications associated with it, and increases long-term mortality.[29] It is, however, unclear whether duration of atrial fibrillation and rhythm and/or rate control strategies would impact long-term outcomes after cardiac surgery. Prolonged ventilation (>24 h) was another common complication, occurring in 9% of the patients. Prolonged ventilation is commonly seen associated with other complications as reported by Seese et al.[6] Patients suffering from a major stroke, cardiac arrest or all-cause reexploration may need longer ventilator support. In the present study, the 1 and 5-year survival after prolonged ventilation was 87% and 62%, respectively, and 5-year survival after pneumonia was 59%. This was similar to the 62% 5-year survival demonstrated by Ibanez et al.[30] in their propensity-matched analysis. These findings are also congruent with the findings of Shahian et al.[31] who found that prolonged intubation was highly associated with mortality. The concept of early extubation after cardiac surgery has been explored, and is evolving.[32] Clearly, not all patients after cardiac surgery will be candidates for early extubation, but an effort to reduce ventilation time may improve long-term outcomes.

The need for permanent pacemaker devices or defibrillators (PPM/ICD) was seen in 3% of the patients in this study. These findings were congruent with the findings of Raza et al.,[33] who had a PPM rate of 2.2%, and reported decreased long-term survival. Interestingly, 30% of their pacemaker patients were neither PPM-dependent nor paced regularly on long-term follow up (7.2 ± 5 years). A study from our institution also showed an increase in long-term mortality in patients who needed a PPM after aortic valve replacement.[34] Wiggins et al.[35] reported the use of PPM/ICD after cardiac surgery at 4.1% and although these patients may have increased early survival, the late survival is significantly lower than patients without these devices. The long-term effect of pacing devices on survival is likely related to ventricular dysfunction from chronic right ventricular pacing, tricuspid regurgitation, infectious complications, and complications related to device or lead exchange.[33,35]

The presence of DSWI was not identified as a risk factor for late mortality in the multivariable analysis (HR: 1.19; 95% CI: 0.99–1.44; $p = .063$). In the present study, DSWI was present in 0.6% of the patients and with such a small number of cases, there is most likely a lack of power to detect survival differences. It has a similar hazard ratio as blood product use, and it may have an impact on the long-term survival.

5 | LIMITATIONS

There are several limitations to this study. First, it is a retrospective single-institution study limited by its inherent selection bias. Second, multisystem failure and sepsis were not included in the multivariable model as they were highly associated with other complications. Finally, this retrospective study was conducted over a span of 25 years. The surgical techniques and definitions of postoperative complications have continued to evolve and may have contributed to variability of data over time.

6 | CONCLUSIONS

Postoperative complications were common in this large cohort of operative survivors after cardiac surgery followed for almost 15 years. The presence, number and type of postoperative complications adversely impact long-term survival. Stroke, renal failure, and pneumonia were the complications with the most severe impact on long-term survival. Prevention of postoperative complications not only impacts operative outcomes and cost but will likely have an important impact on long-term outcomes.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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