Results from an enhanced recovery program for cardiac surgery

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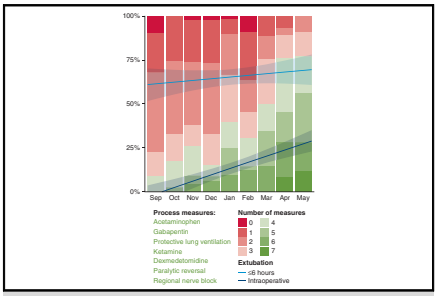
ABSTRACT

Objective: Enhanced recovery programs are multidisciplinary perioperative bundles of evidence-based process measures. Following the design and implementation of preanesthesia and intraoperative enhanced recovery programs for cardiac surgery guidelines, we evaluated the association between compliance and key clinical outcomes.

Methods: Consecutive patients undergoing cardiac surgery at a single tertiary medical center from September 2017 to June 2018 were included. Patients were stratified into low (0-4 measures) and high (5-7 measures) compliance groups and then 1-to-3 propensity matched on the basis of 15 patient and surgical covariables. The primary outcome of interest was time to postoperative extubation. Secondary outcomes included interval time point extubation rates and intensive care unit, floor, and hospital lengths of stay.

Results: A total of 451 patients were included in the study. After propensity matching (n = 315), patients in the high compliance group (n = 84) had a significant reduction in time to extubation ($P < .001$), floor length of stay ($P = .01$), and hospital length of stay ($P = .03$) compared with patients in the low compliance group (n = 231). Patients in the high compliance group were more likely to be extubated in the operating room (odds ratio, 35.8; 95% confidence interval, 10.66-168.75; $P < .001$) and within 6 hours of surgery (odds ratio, 2.6; 95% confidence interval, 1.18-6.07; $P < .02$). High compliance was associated with a median estimated time reduction of 3.4 hours to postoperative extubation ($P < .001$) and 19.4 hours in hospital length of stay ($P = .01$) compared with low compliance counterparts. There were no reintubations reported among patients extubated in the operating room (0/62 patients).

Conclusions: There is value in developing phase-specific enhanced recovery programs guidelines, which improve rates of early extubation and affect the duration of stay after cardiac surgery. These results are hypothesis generating, and further prospective study is necessary to identify clinical impact of further program expansion. (J Thorac Cardiovasc Surg 2019;■:1-10)



Compliance is associated with increased rates of early and intraoperative extubation.

Central Message

There is value in developing phase of care guidelines for ERPs for cardiac surgery, which may improve rates of early extubation and reduce LOS after cardiac surgery.

Perspective

ERPs for cardiac surgery are multidisciplinary perioperative bundles of evidence-based process measures. Compliance with intraoperative guidelines is shown to improve rates of intraoperative and early extubation, as well as reduce LOS. There is value in engaging intraoperative providers to improve rates of recovery after cardiac surgery.

See Commentary on page XXX.

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Abbreviations and Acronyms

CABG = coronary artery bypass grafting
CI = confidence interval
CPB = cardiopulmonary bypass
ERP = enhanced recovery program
ICU = intensive care unit
LOS = length of stay
STS = Society of Thoracic Surgeons

Scanning this QR code will take you to the article title page to access supplementary information.

Enhanced recovery programs (ERPs) are multidisciplinary perioperative pathways designed to reduce surgical insult, prevent healthcare-associated conditions, and hasten patient recovery through the bundled application of evidence-based process measures.[1-4] Borrowing from the original colorectal version of the program, groups have now applied ERP principles to numerous additional service lines.[5-7] Success among these procedures has led providers to adapt ERP frameworks to cardiac surgery, for which limited early examples have shown that an ERP for cardiac surgery is equal parts feasible, advisable, and potentially effective,[8-13] with at least 1 recent study that reported reduced length of stay (LOS) and improved indices of patient satisfaction associated with their program.[14]

ERPs have relied thus far on the theory of marginal gains, whereby results are based on the summation of incremental—and often statistically imperceptible—benefits.[8,12,13] Therefore, researchers have been unable to formally assess the relative contribution of measures from individual phases of care (ie, preoperative, intraoperative, postoperative) to overall outcomes. Because of the designed pragmatic stepwise implementation of an institutional ERP for cardiac surgery, our group was able to assess the impact of individual phases of program deployment. We detail the conception and implementation of the preanesthesia and intraoperative care process measures, the initial phase of program deployment, and their association with clinical milestones including postoperative extubation and phase of care lengths of stay.

MATERIALS AND METHODS

Institutional Enhanced Recovery Programs for Cardiac Surgery Overview

The institutional ERP for cardiac surgery is an extension of an existing pathway instituted by the cardiac surgery Clinical Communities Committee, a multidisciplinary collaboration among surgery, anesthesiology, perioperative nursing, and others. Details of the Clinical Communities initiatives have been outlined previously.[15,16] The program is sponsored by the Johns Hopkins Armstrong Institute for Patient Safety and Quality, which provides administrative support, and the Cardiovascular Thoracic Comprehensive Unit-Based Safety Program, which identifies and develops unit-specific safety and quality initiatives. In July of 2017, the group developed a pragmatic stepwise implementation strategy, which involved rolling out the ERP for cardiac surgery in a phase-of-care fashion, which includes process measures specific to the following:

Phase 1: preanesthesia and intraoperative;

Phase 2: preoperative [time from surgical consultation to date of surgery]; and

Phase 3: postoperative [immediate post-surgery to hospital discharge] care settings.

This strategy was used to allow for each phase to be both championed and evaluated independently. We report the results of preanesthesia and intraoperative stages of implementation.

Study Overview

After the appropriate Institutional Review Board approval, the requirement for written informed consent was waived by the Institutional Review Board. From the period of September 2017 through June 2018, data were prospectively collected and analyzed for patients undergoing cardiac surgery at Johns Hopkins Hospital, an approximately 1100-bed tertiary care academic medical center. All patients undergoing coronary artery bypass grafting (CABG), aortic, mitral, tricuspid valve, or combination procedures were included in the Enhanced Recovery After Cardiac Surgery pathway. Although patients undergoing heart transplantation or left ventricular assist device, aortic, and other cardiac procedures were also included, they were excluded from study analysis. All surgeries were performed by 1 of 6 primary board-certified cardiac surgeons. During the study period, there were no changes in staffing with regard to the surgeons, anesthesiologists, or intensive care unit (ICU) physicians.

Preanesthesia and Intraoperative Enhanced Recovery Programs for Cardiac Surgery Guidelines

Specific process measures included within the intraoperative guidelines were developed from a combination of literature review and institutional experience, and ultimately agreed upon by cardiothoracic anesthesiologists, surgeons, and perfusionists. These guidelines consisted of patient care process measures used throughout the preanesthesia and intraoperative phases of care (Figure E1). Patients enrolled as part of the ERP initiative were intended to receive all pathway measures unless contraindicated based on existing medical comorbidities. The decision to withhold or alter a specific intervention was guided by both the pathway outline (ie, recommended medication dose modification based on glomerular filtration rate) and individual anesthesiologist discretion. Process measure compliance rates, along with relevant patient-specific variables such as age, gender, procedure, Society of Thoracic Surgeons (STS) score, left ventricular ejection fraction, laboratory data, cardiopulmonary bypass (CPB) time, and outcomes of interest, were collected and analyzed.

Outcome Variables

Primary outcomes for each phase of program implementation were selected on the basis of their relationship to that specific phase of care as supported by the available literature. The primary outcome for this phase was time to endotracheal extubation after completion of surgery. This end point was selected because early extubation is highlighted as an STS marker for quality and has been previously used as an end point for fast-track cardiac surgery protocols.[17-19] Phase-specific secondary

outcomes included intraoperative extubation (defined as removal of the endotracheal tube at the completion of surgery before transfer of care to the ICU), early extubation (≤6 hours of mechanical ventilation after completion of surgery), interval extubation (12 and 24 hours), ICU LOS, and floor and hospital LOS. The decision to extubate patients in the operating room was made on the basis of the discretion of individual surgical and anesthesia teams at the completion of surgery. To investigate the association between process measures and outcomes, auditing of compliance data was performed and analyzed on the following 7 interventions:

1. Acetaminophen (ie, 1000 mg; administered orally in preanesthesia area or via intravenous route in the operating room).
2. Gabapentin (ie, administered orally in the preanesthesia area; 600 mg standard dose, reduced to 300 mg if age >70 years or if renal clearance <60 mL/min).
3. Ketamine (ie, intraoperative infusion; 0.25 mg/kg/h).
4. Dexmedetomidine (ie, intraoperative infusion; 0.2-0.7 μg/kg/h; administered at the time of cardiopulmonary bypass and throughout transport to the ICU and titrated on the basis of hemodynamic and sedation goals).
5. Regional nerve block (ie, serratus anterior plane block; administered at the end of surgery under ultrasound guidance via "single-shot" technique; bupivacaine 0.25%-0.375%, 20-30 mL bilaterally).
6. Protective lung ventilation (ie, tidal volumes 6-8 mL/kg predicted body weight, positive end-expiratory pressure ≥5 cm water, F_{IO_2} <100%).
7. Full paralytic reversal (ie, intraoperative, administration of combination neostigmine/glycopyrrolate, or sugammadex).

These 7 process measures were chosen because (1) each measure may be reasonably hypothesized to impact the primary outcome of interest, and (2) they were uniformly adopted into practice as part of the ERP. For example, our group did not study preexisting process measures such as the use of a continuous antibiotic infusion or goal-directed perfusion protocol because these had been introduced through quality improvement initiatives before ERP deployment.

Data Collection and Statistical Analysis

Data were obtained by querying the existing institutional information system (Epic Systems Corporation, Verona, Wis). All relevant data for each patient were combined into a single patient database. Patients were categorized into high (5-7 total process measures administered per encounter) and low (0-4 measures) compliance groups to determine if overall process measure compliance was associated with selected outcomes. This cutoff was selected on the basis of a preliminary receiver operator characteristic curve, which suggested this represented the point of greatest inflection in sensitivity/specificity to predict extubation within 6 hours of surgery (Figure E2). Initial univariable and subsequent multivariable logistic regression models were developed for primary outcomes in a stepwise fashion while adjusting for key covariates and independent associations were identified and reported. High compliance patients were 1-to-3 propensity matched to low compliance patients (control), and the score was estimated with logistic regression based on 15 patient-level variables to control for relevant patient and surgical covariables (Figure E3). Matching was performed for the following procedures only: CABG, aortic valve replacement, mitral valve replacement, and CABG + aortic valve replacement because of the small number of operations that incorporated other procedure types. Matching was greedy without replacement with caliper width 0.0245. Covariates' balance was assessed in R with Cobalt package v. 3.4.1 (N. Greifer). Standardized mean differences were calculated with pooled variances. The adjustment validation requirement included absolute standardized mean differences less than 0.1 and variance ratios less than 2 for all the covariates. The Love Plot depicting the covariates' balance is shown in Figure E3. Overall results are expressed in unmatched and matched forms. For continuous variables, data are expressed as mean value ± standard deviation. For unmatched binary variables, data are expressed as count (percentage). Finally, for matched binary variables, data are expressed as weighted count (percentage) (unweighted count [percentage]). Comparisons are analyzed by Mann–Whitney or Fisher exact test where appropriate. Kaplan–Meier plots for each outcome are analyzed using the log-rank test. To estimate the median time reduction to extubation and in LOS, we used a censored quantile regression doubly robust model (ie, censored quantile regression was run for weighted matched observations with the same covariates as for propensity score estimation). Median difference was expressed as time difference in hours with 95% confidence interval (CI). Data were processed and analyzed with the software programs Excel, v. 14.0 (Microsoft Inc, Redmond, Wash), Stata v. 14.2 (StataCorp, LP, College Station, Tex), and R v. 3.5.0 (R Core Team) statistical packages.

RESULTS

Study Population and Demographics

In total, 451 consecutive patients were included in our cohort, with patient characteristics represented in Table 1. Among unmatched patients, the high compliance group was represented by patients with lower STS scores (1.38 vs 2.45%; $P < .001$) and shorter CPB time (100.7 vs 121.3 minutes; $P = .002$) compared with the low compliance group. Overall procedure breakdown is also remarkable for fewer combination procedures in the high compliance group (4.8% vs 15.3%; $P = .04$) as well. After propensity score matching, there were 315 patients (n = 231 and 84 in the low and high compliance groups, respectively).

Process Measure Compliance and Time to Postoperative Extubation

The association between process measure compliance and time to extubation is shown in Figure 1. Overall, high compliance was associated with earlier postoperative extubation compared with low compliance counterparts (Figure 1, *A*: unmatched; Figure 1, *B*: matched; $P < .001$ for each, respectively). Within the matched cohort, high compliance patients were significantly more likely to be extubated in the operating room (Table E1; odds ratio, 35.8; CI, 10.7-168.8; $P < .001$) compared with low compliance patients, with 47.6% of high and 4.8% of low compliance patients extubated at the time of surgical completion. Within the matched cohort, high compliance patients were also more likely to be extubated at 6 hours (odds ratio, 2.6; 95% CI, 1.18-6.07; $P < .02$) compared with low compliance patients. The overall rate of reintubation was 5.3% (unmatched data; 24/451), with 5.8% (20 of 347) in the low compliance group and 3.8% (4 of 104) in the high compliance group. Among patients who were extubated intraoperatively (46 in the high and 16 in the low compliance group), there were no subsequent reintubations. Figure 2 depicts the patient-specific individual and composite process measure compliance over the duration of the study. As shown, compliance improved throughout the study period, with the final individual and

TABLE 1. Patient cohort demographics stratified according to process measure compliance and propensity-matching statistics

	Unmatched				Matched			
	All cases	0-4 process measures	5-7 process measures	*P* value	All cases	0-4 process measures	5-7 process measures	Absolute standardized mean difference
Cases, No.	451 (100.0%)	347 (100.0%)	104 (100.0%)	–	315 (100.0%)	231 (100.0%)	84 (100.0%)	–
Gender, male	332 (73.6%)	249 (71.8%)	83 (79.8%)	.13	249 (79.0%)	181 (78.4%)	68 (81.0%)	0.012
Age, y	63.8 (±11.8)	64.2 (±11.9)	62.6 (±11.6)	.21	64.1 (±10.6)	64.0 (±11.4)	64.1 (±9.9)	0.016
STS score, %*	2.21 (±3.48)	2.45 (±3.74)	1.38 (±2.26)	<.001	1.55 (±2.23)	1.65 (±2.01)	1.44 (±2.44)	0.066
Ejection fraction, %	53.30 (±12.13)	52.75 (±12.46)	55.14 (±10.78)	.06	53.84 (±11.54)	53.57 (±11.91)	54.11 (±11.22)	0.046
Preoperative hemoglobin, g/dL	12.97 (±2.16)	12.96 (±2.21)	12.98 (±1.98)	.81	13.05 (±2.00)	13.01 (±2.08)	13.10 (±1.92)	0.037
Creatinine, mg/dL	1.22 (±1.09)	1.23 (±1.18)	1.17 (±0.72)	.70	1.19 (±0.92)	1.20 (±1.04)	1.18 (±0.78)	0.013
Lactate, mmol/L	0.98 (±0.49)	0.98 (±0.52)	0.96 (±0.38)	.86	0.96 (±0.37)	0.97 (±0.40)	0.94 (±0.34)	0.089
Weight, kg	86.69 (±20.45)	86.88 (±21.66)	86.04 (±15.83)	.87	87.65 (±18.00)	87.27 (±20.64)	88.02 (±15.03)	0.053
Height, m	1.72 (±0.10)	1.72 (±0.10)	1.73 (±0.09)	.60	1.73 (±0.09)	1.73 (±0.10)	1.73 (±0.09)	0.046
BSA, m^2	2.01 (±0.26)	2.01 (±0.27)	2.01 (±0.21)	.99	2.03 (±0.23)	2.02 (±0.26)	2.03 (±0.20)	0.053
Cardiopulmonary bypass time, min	116.5 (±53.8)	121.3 (±57.0)	100.7 (±37.3)	.002	106.4 (±40.7)	108.3 (±45.1)	104.5 (±36.0)	0.086
CABG	303 (67.2%)	225 (64.8%)	78 (75.0%)	.06	257 (81.6%)	190 (82.3%)	67 (79.8%)	0
AVR	42 (9.3%)	31 (8.9%)	11 (10.6%)	.57	16 (5.1%)	10 (4.3%)	6 (7.1%)	0
MVR	41 (9.1%)	34 (9.8%)	7 (6.7%)	.44	27 (8.6%)	20 (8.7%)	7 (8.3%)	0
CABG + AVR	36 (8.0%)	32 (9.2%)	4 (3.8%)	.10	15 (4.8%)	11 (4.8%)	4 (4.8%)	0
CABG + MVR	9 (2.0%)	9 (2.6%)	0 (0.0%)	.13	0 (0.0%)	0 (0.0%)	0 (0.0%)	–
AVR + TVR	1 (0.2%)	1 (0.3%)	0 (0.0%)	1.00	0 (0.0%)	0 (0.0%)	0 (0.0%)	–
AVR + MVR + TVR	2 (0.4%)	2 (0.6%)	0 (0.0%)	1.00	0 (0.0%)	0 (0.0%)	0 (0.0%)	–
AVR + MVR	6 (1.3%)	6 (1.7%)	0 (0.0%)	.34	0 (0.0%)	0 (0.0%)	0 (0.0%)	–
TVR	7 (1.6%)	4 (1.2%)	3 (2.9%)	.20	0 (0.0%)	0 (0.0%)	0 (0.0%)	–
AVR + MVR + CABG	2 (0.4%)	1 (0.3%)	1 (1.0%)	.41	0 (0.0%)	0 (0.0%)	0 (0.0%)	–
MVR + TVR	2 (0.4%)	2 (0.6%)	0 (0.0%)	1.00	0 (0.0%)	0 (0.0%)	0 (0.0%)	–

Data expressed as mean value ± standard deviation. *STS*, Society of Thoracic Surgeons; *BSA*, body surface area; *CABG*, coronary artery bypass grafting; *AVR*, aortic valve replacement/repair; *MVR*, mitral valve replacement/repair; *TVR*, tricuspid valve replacement/repair. *STS score in unmatched data is the composite of CABG, AVR, MVR, and combination thereof procedures.

composite compliance reaching greater than 70%. The Figure 3 depicts the percentage of patients who received a certain number of process measures over the duration of the study. As compliance increased, so did the percentage of patients who were extubated in the operating room as well as within 6 hours of surgery.

Multivariable regression analysis revealed that lower STS risk score ($P = .002$) and shorter CPB time ($P < .001$) were independently associated with extubation 6 hours or less. Whereas reversal of paralysis ($P < .001$), use of gabapentin ($P = .003$), regional analgesia ($P = .01$), and dexmedetomidine ($P = .02$) were independently associated with intraoperative extubation, only reversal of paralytic in the operating room was also independently associated with extubation 6 hours or less ($P < .001$; Table E2).

Process Measure Compliance and Intensive Care Unit Length of Stay

The association between process measure compliance and ICU LOS in hours is shown in Figure E4. Although high compliance was associated with a shorter LOS compared with low compliance counterparts among unmatched results (Figure E4, *A*; $P = .01$), there was no difference in ICU LOS between groups in the propensity-matched cohort (Figure E4, *B*; $P = .66$).

Process Measure Compliance and Floor Length of Stay

The association between process measure compliance and floor LOS in hours is shown in Figure E5. High compliance was associated with a significantly shorter floor LOS

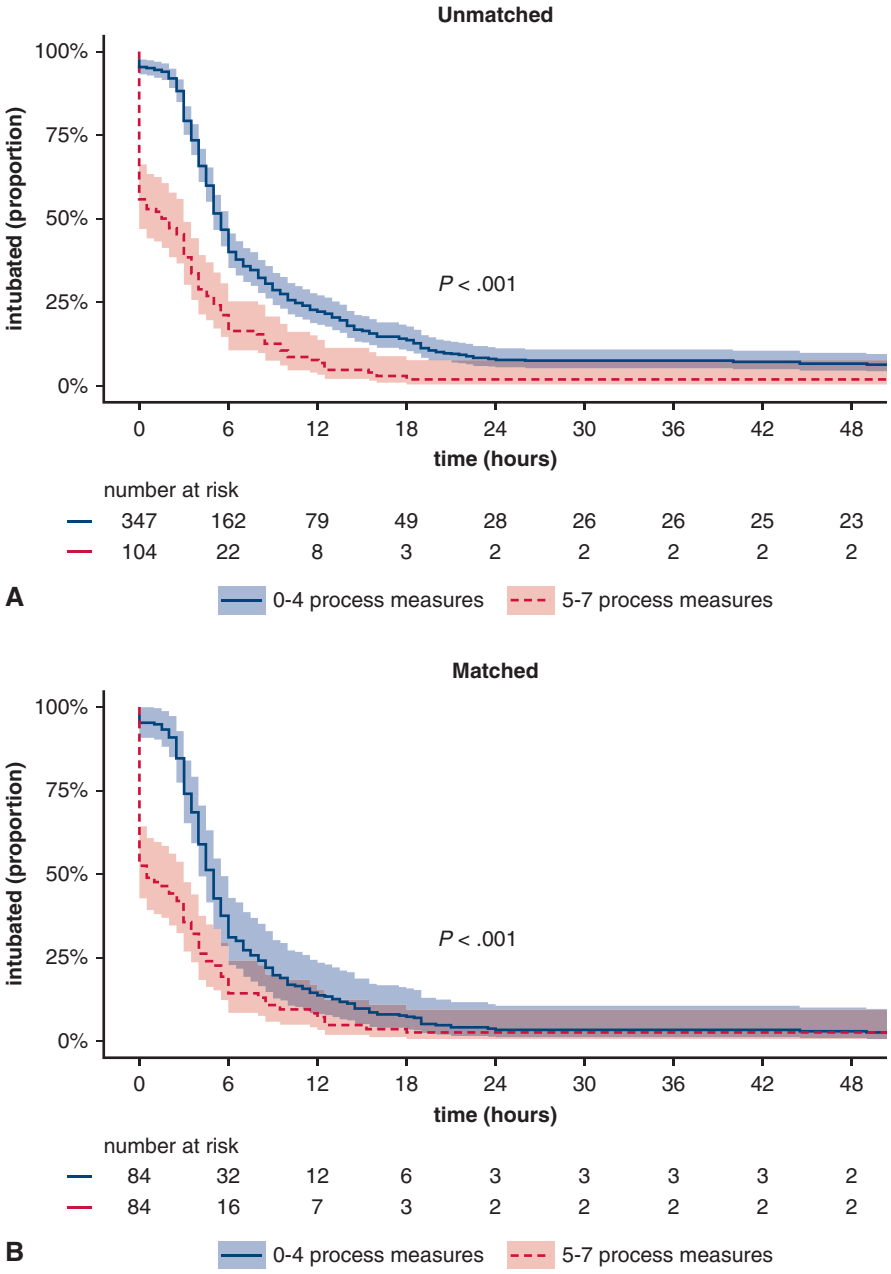

FIGURE 1. Time to postoperative extubation as a function of compliance with phase-specific process measures. Unmatched (A) and propensity-matched (B) cohorts. As shown, high compliance with phase of care guidelines (*red*; 5-7 process measures) is associated with a significant reduction in time to extubation at intraoperative and 6-hour time frames compared with low compliance (*blue*; 0-4 process measure) counterparts.

(difference between floor LOS and ICU LOS) compared with low compliance among unmatched (Figure E5, *A*; $P < .001$) and propensity-matched (Figure E5, *B*; $P = .01$) cohorts.

Process Measure Compliance and Hospital Length of Stay

The association between process measure compliance and hospital LOS in hours is shown in Figure 4. High compliance was associated with a significantly shorter length of hospital stay compared with low compliance patients among unadjusted (Figure 4, *A*; $P < .001$) and propensity-matched (Figure 4, *B*; $P = .03$) cohorts.

Median Time Reduction Analysis

Results of the doubly robust censored quantile regression analysis are expressed in Table 2. As shown, high compliance patients have a shorter time to extubation (propensity

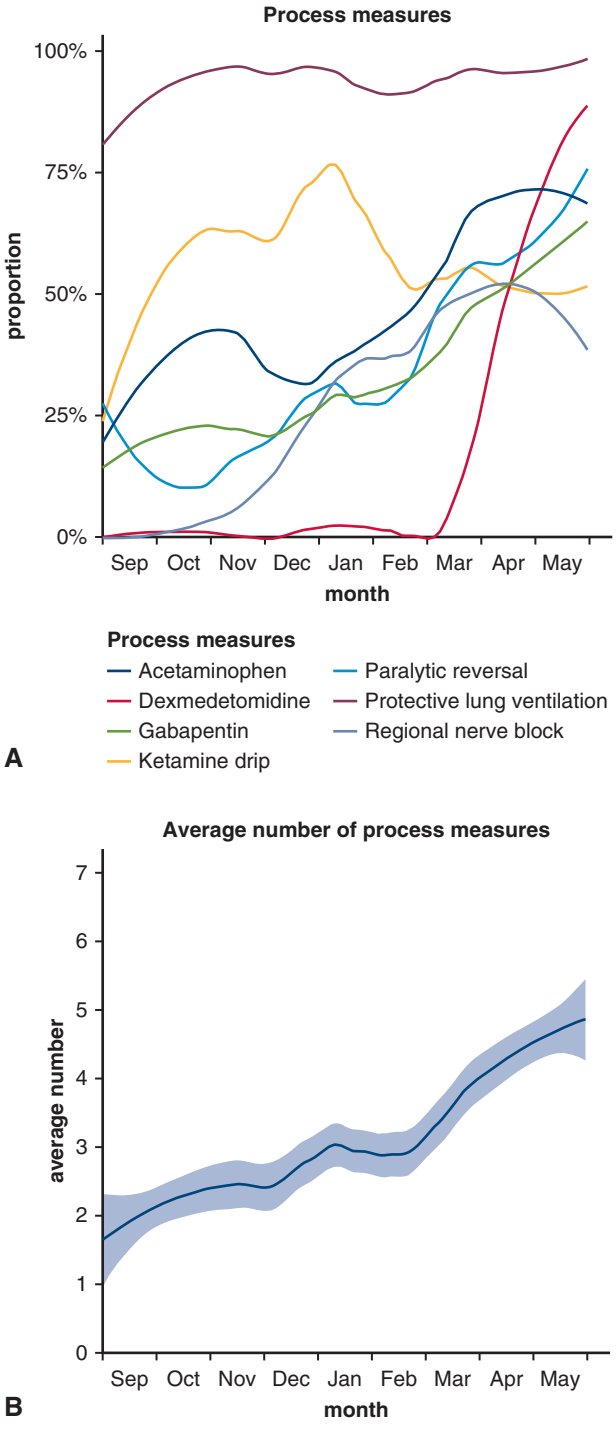

FIGURE 2. Monthly interval compliance with individual (A) and composite (B) process measures over the duration of the study period. As shown, compliance was shown to improve with study duration for the majority of the selected process measures. In conjunction, composite process measure compliance was more than 70% by study conclusion.

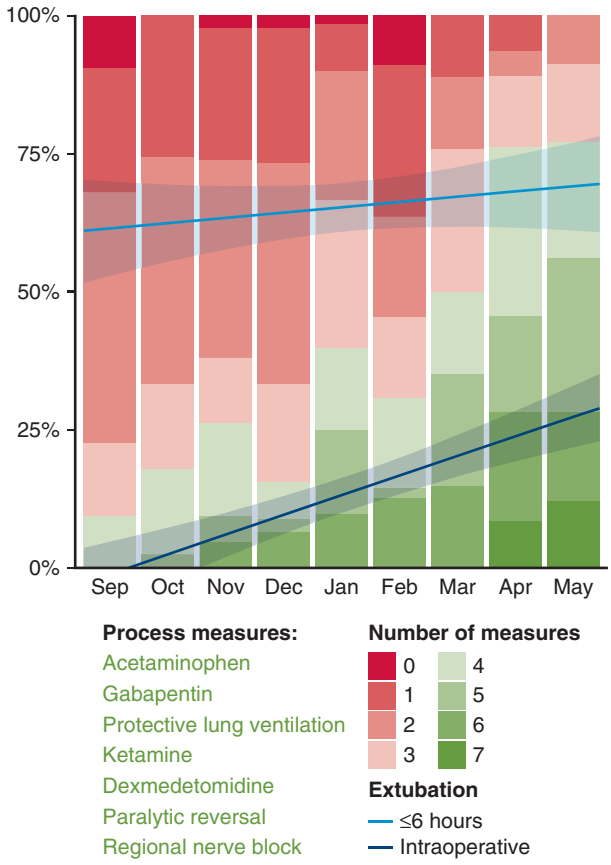

FIGURE 3. The percentage of patients who received a certain number of process measures, which are delineated on the right, as a function of study month. Overlying, the best fit (±95% CI) percentages of patients who were extubated in the operating room and within 6 hours are depicted. As overall compliance improved during the study, there was an associated increase in the rate of intraoperative and early extubation.

matched; 0.5 vs 5 hours) compared with low compliance counterparts, resulting in a median estimated time reduction of 3.4 hours ($P < .001$). High compliance patients also have a shorter floor (98.5 vs 119 hours) and hospital (142 vs 163 hours) LOS compared with low compliance patients with a median estimated time reduction of 20.5 hours ($P = .006$) and 19.4 hours ($P = .01$), respectively.

DISCUSSION

Compliance with preanesthesia and intraoperative process measures is associated with earlier rates of postoperative extubation, a statistically significant effect noted at the intraoperative and 6-hour time points. Although it does not affect ICU LOS, compliance is associated with a significant reduction in floor and overall hospital LOS, with the high compliance cohort experiencing a median reduction in hospital LOS of approximately 20 hours compared with low compliance counterparts. These findings suggest that interventions isolated to the preanesthesia and intraoperative setting may provide value throughout the duration of the cardiac surgical encounter. To our knowledge, this represents the first evaluation of a phased implementation

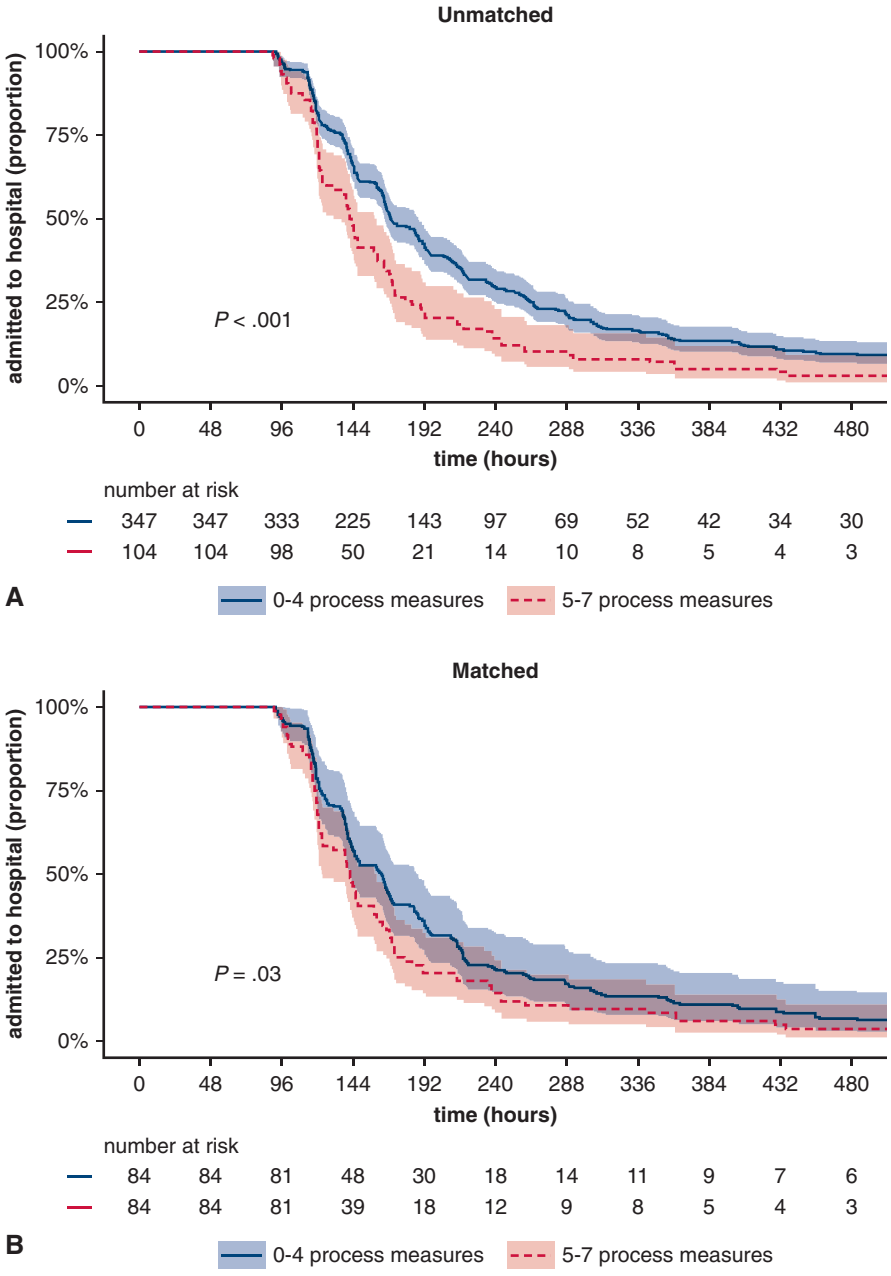

FIGURE 4. Overall hospital LOS as a function of compliance with phase-specific process measures. Unmatched (A) and propensity-matched (B) cohorts. As shown, high compliance with phase of care guidelines (*red*; 5-7 process measures) is associated with a significant reduction in length of hospital stay compared with low compliance (*blue*; 0-4 process measure) counterparts.

strategy and assessment of the impact of process measure compliance on clinical outcomes in an ERP for cardiac surgery. An overview of the study and key results are provided in Video 1.

The selected interventions introduced in this study are borne from existing literature that supports their use as measures to hasten recovery from anesthesia, optimize multimodal analgesia, and limit the harmful impact of mechanical ventilation. They include preventative multimodal acetaminophen, gabapentin, intraoperative ketamine infusions, and regional analgesia, which have been shown to reduce perioperative opioid administration in cardiac and other types of surgery,[20-26] and therefore may reduce the impact of the anesthetic on rates of recovery. We incorporated a lung protective mechanical ventilation strategy, evidenced to reduce rates of postoperative lung injury and pneumonia.[27] Perioperative sedation was facilitated through the use of dexmedetomidine, which is shown

TABLE 2. Estimated median time reduction to extubation and length of stay

	Unmatched: Median time, h		Matched: Median time, h		Reduction for 5-7 vs 0-4 process measures	
	0-4 process measures	5-7 process measures	0-4 process measures	5-7 process measures	Medians' difference, h	*P* value
Extubation	5.5 (5, 6)	1.75 (0, 3)	5 (4, 5.5)	0.5 (0, 3)	3.4 (2.1, 4.8)	<.001
Admission in ICU	44 (40, 47)	27.25 (24.5, 41)	29.5 (25, 46)	28.25 (25, 44)	–0.8 (–4.8, 4.5)	.90
Admission on floor	122 (119, 136.5)	99.25 (96, 116)	119 (101, 140.5)	98.5 (94.5, 113.5)	20.5 (4.4, 33.3)	.006
Admission in hospital	169.5 (165, 188)	142.5 (131, 158.5)	163 (142.5, 187)	142 (123, 160)	19.4 (3.7, 34.4)	.013

Data expressed as value in hours with 95% CIs. *ICU*, Intensive care unit.

to reduce incidence of postoperative delirium and increase the likelihood of 8-hour extubation compared with propofol.[28,29] Finally, providers were encouraged to fully reverse muscle relaxation in the operating room, thereby hastening return of spontaneous ventilation and potentiate assessment for early extubation.

A great deal of prior work has been devoted to cardiac surgical pathway development, with perhaps the most noteworthy example being fast-track cardiac surgery. These pathways were designed to reduce the use of opioid-based anesthetics and hasten time to postoperative extubation.[30-32] Although fast-track cardiac surgery led to shorter durations of mechanical ventilation, a recent meta-analysis determined that this did not necessarily translate into improved downstream clinical outcomes because there were similar overall LOS.[19] As a result, there remains controversy regarding the true clinical impact of early extubation. A recent editorial suggested that early extubation after cardiac surgery may be a marker for patient or disease severity rather than a clinically relevant end point.[33] Although several other trials have found that system interventions such as application of rapid weaning protocols, lean frameworks, and multidisciplinary teams may reduce intubation times,[17,34-37] what has remained elusive is a strategy to consistently translate these early interval successes into meaningful downstream clinical outcomes.

The results of our study suggest that compliance with a concerted set of guidelines may not only hasten extubation but also subsequently lead to a significant reduction in overall hospital LOS. There are several potential explanations for this effect. First, it is possible that earlier postoperative achievements (ie, extubation) allow for subsequent elements of care to be provided in a hastened fashion. This would suggest that extubation is not only an outcome associated with the intraoperative management but also a key intermediary to subsequent care. If this were entirely true, it is unlikely that early extubation alone could account for a nearly full day of LOS reduction. Alternatively, it may be true that the multidisciplinary decision to extubate early is an independent predictor of early discharge as well—essentially that healthier patients are selected for earlier extubation. Although possible, propensity matching suggests that among similar patients, high compliance was more strongly associated with both early extubation and LOS. Most likely, our findings suggest that early extubation is both facilitated by and a marker of optimal intraoperative management. A goal-oriented intraoperative plan may allow for immediate de-escalation in organ support (ie, extubation), management that is typically reserved for the "next" phase of care (ie, reversal of paralysis, removal of sedation, weaning of vasopressors in the ICU). Subsequent pathway elements (ie, oral feeding, ambulation, and Foley and central line removal) may continue on the basis of individual patient milestones rather than discrete patient location (ie, ICU vs intermediate care unit vs surgical ward). Further, patients are optimized to tolerate subsequent care elements because of the goal-directed nature of their intraoperative care. This approach stands in contrast to prior early extubation strategies, which have underemphasized the role of the anesthesia and analgesia plan. In this study, de-escalation planning actually begins more or less at the surgical outset through the use of select anesthetics and analgesics that reduce ongoing impact beyond the completion of surgery. Extubation, although an important milestone, is less an outcome of the program and perhaps more a marker of sound intraoperative management.

VIDEO 1. Dr Michael Grant explains the design and key findings of an enhanced recovery program for cardiac surgery at Johns Hopkins University. Video available at: https://www.jtcvs.org/article/S0022-5223(19)31136-5/fulltext.

One compelling finding in this study is the significant increase in the rate of intraoperative extubation within the high compliance group. Because of the retrospective nature of our study design, we were unable to conclusively separate the impact of process measure compliance from the providers' decision to extubate. As a result, although it is likely that intraoperative extubation in particular led to improved overall rates of early extubation, we are unable to make larger conclusions regarding the importance of intraoperative extubation overall. Certainly, intraoperative extubation is an uncommon practice in cardiac surgery and thus far generally unstudied. Therefore, it remains unclear whether intraoperative extubation is associated with superior outcomes compared with early (<6 hours) extubation, and this remains an opportunity for future prospective study. Although our findings do not suggest harm in the practice, we hesitate to promote its widespread adoption based on these limited results. Further, even in institutions where providers prefer to adhere to an initial postoperative observation period to evaluate for patient stability before extubation, the results of our study suggest that compliance with these measures are likely to facilitate improved rates of early postoperative extubation.

The ERP for cardiac surgery program highlighted several important barriers and facilitators to implementation. As shown, compliance was notably poor at the outset. Although reasons for poor compliance are speculative, they likely stem from failure to prospectively address system-level obstacles, including preanesthesia nursing workflow, formal and consistent education of staff in each phase of care, medication formulary restrictions, comfort of the intraoperative providers to administer individual process measures (ie, regional anesthesia), and consistent multidisciplinary acceptance. Mitigation strategies included, in kind, the development of electronic preanesthesia order sets and nursing education, identification of individual discipline program champions, work to gain medication approval/availability, and a continuous auditing and provider feedback process. In addition, there were intraoperative workflow delays, especially at program inception, associated with the administration of regional nerve blocks and intraoperative extubation. These were, at times, met with resistance, something that may be particularly true in high-turnover centers where these efforts are perceived as bottlenecks to efficiency. Regular communication of the ultimate program goals, development of strategies to ensure improvement in efficacy and timing of measures, and publication of local compliance/outcome data helped to reinforce support from surgery and anesthesiology.

Finally, it should be noted that whereas the ICU had previously established an early extubation algorithm, additional support and communication were necessary to potentially receive and recover an extubated patient, including adequate nursing and respiratory staff, bedside advanced providers, rescue airway specialists, and the presence of noninvasive ventilation devices (ie, high-flow nasal cannula or bilevel positive airway pressure). Recognition of existing barriers and deployment of their associated solutions that fostered program success were the product of an established culture of perioperative pathway development via multidisciplinary collaboration, top-down administrative support, and use of similar strategies to address potential patient harms in other clinical arenas.

Study Limitations

There are several important limitations to this study. Data presented are specific to a single academic institution. Interpretation and extrapolation of results should be done with caution, because they are potentially influenced by unmeasured factors such as local medication formulary, unique workforce structure, unit-level protocols/workflows, and intangibles such as service line culture. Although it is likely that foundational principles such as the establishment of a multidisciplinary team, use of evidence-based interventions, guideline development, and system auditing are transferrable, we are unable to comment on the potential impact of adoption of a similar program elsewhere. Because of pragmatic rather than randomized nature of our study, the most significant limitation is the potential for bias, because healthier patients undergoing less complex procedures are typically more likely to tolerate care elements and advance along the pathway. Therefore, it is possible that intraoperative observations by the anesthesiologist led them to deviate from the pathway guidelines. Although we attempt to mitigate for confounders such as patient or surgery-specific variables through the use of propensity score matching and multivariable regression strategies, we cannot exclude the potential for provider or selection bias. Full accounting for intraoperative surgical complications such as bleeding, hemodynamic instability, or other untoward events is not feasible. We recommend these results be viewed as hypothesis generating and recognize the importance of further discovery in this area.

CONCLUSIONS

We outlined the initial conception, design, and implementation of an institutional ERP for cardiac surgery. The results suggest that deployment and compliance with a concerted preanesthesia and intraoperative set of evidence-based guidelines may lead to early extubation and translate into shorter lengths of hospital stay after cardiac surgery. Future study is anticipated to assess the impact of greater program expansion, including preoperative and postoperative process measures, on additional clinical outcomes.

Conflict of Interest Statement

Grant is on the Executive Board of the ERAS Cardiac Society. All other authors have nothing to disclose with regard to commercial support.

References

1. Ljungqvist O, Scott M, Fearon KC. Enhanced recovery after surgery. A review. *JAMA Surg*. 2017;1:292-8.
2. Gustafsson UO, Scott MJ, Schwenk W, Demartines N, Roulin D, Francis N, et al. Guidelines for perioperative care in elective colonic surgery: Enhanced Recovery After Surgery (ERAS®) Society recommendations. *Clin Nutr Edinb Scotl*. 2012; 31:783-800.
3. Ban KA, Gibbons MM, Ko CY, Wick EC, Cannesson M, Scott MJ, et al. Evidence review conducted for the agency for healthcare research and quality safety program for improving surgical care and recovery: focus on anesthesiology for colorectal surgery. *Anesth Analg*. 2018;128:879-89.
4. Grant MC, PioRoda C, Canner J, Sommer P, Galante D, Hobson D, et al. The impact of anesthesia influenced process measure compliance on length of stay: results from an enhanced recovery after surgery (ERAS) for colorectal surgery cohort. *Anesth Analg*. 2019;128:68-74.
5. Mortensen K, Nilsson M, Slim K, Schäfer M, Mariette C, Braga M, et al. Consensus guidelines for enhanced recovery after gastrectomy: enhanced Recovery after Surgery (ERAS®) Society recommendations. *Br J Surg*. 2014;101: 1209-29.
6. Thorell A, MacCormick AD, Awad S, Reynolds N, Roulin D, Demartines N, et al. Guidelines for perioperative care in bariatric surgery: Enhanced Recovery After Surgery (ERAS) Society recommendations. *World J Surg*. 2016;40: 2065-83.
7. Grant MC, Gibbons MM, Ko CY, Wick EC, Cannesson M, Scott MJ, et al. Evidence review conducted for the agency for healthcare research and quality safety program for improving surgical care and recovery: focus on anesthesiology for bariatric surgery. *Anesth Analg*. 2019;129:51-60.
8. Li M, Zhang J, Gan TJ, Qin G, Wang L, Zhu M, et al. Enhanced recovery after surgery pathway for patients undergoing cardiac surgery: a randomized clinical trial. *Eur J Cardiothorac Surg*. 2018;54:491-7.
9. Noss C, Prusinkiewicz C, Nelson G, Patel PA, Augoustides JG, Gregory AJ. Enhanced recovery for cardiac surgery. *J Cardiothorac Vasc Anesth*. 2018;32: 2760-70.
10. Yang L, Kaye AD, Venakatesh AG, Green MS, Asgarian CD, Luedi MM, et al. Enhanced recovery after cardiac surgery: an update on clinical implications. *Int Anesthesiol Clin*. 2017;55:148-62.
11. Krzych Ł, Kucewicz-Czech E. It is time for enhanced recovery after surgery in cardiac surgery. *Kardiol Pol*. 2017;75:415-20.
12. Zaouter C, Imbault J, Labrousse L, Abdelmoumen Y, Coiffic A, Colonna G, et al. Association of robotic totally endoscopic coronary artery bypass graft surgery associated with a preliminary cardiac enhanced recovery after surgery program: a retrospective analysis. *J Cardiothorac Vasc Anesth*. 2015;29:1489-97.
13. Fleming IO, Garratt C, Guha R, Desai J, Chaubey S, Wang Y, et al. Aggregation of marginal gains in cardiac surgery: feasibility of a perioperative care bundle for enhanced recovery in cardiac surgical patients. *J Cardiothorac Vasc Anesth*. 2016;30:665-70.
14. William JB, McConnell G, Allender JE, Woltz P, Kane K, Smith PK, et al. One-year results from the first US-based enhanced recovery after cardiac surgery (ERAS Cardiac) program. *J Thorac Cardiovasc Surg*. December 8, 2018 [Epub ahead of print].
15. Wu CL, Benson AR, Hobson DB, Roda CP, Demski R, Galante DJ, et al. Initiating an enhanced recovery pathway program: an anesthesiology department's perspective. *Jt Comm J Qual Patient Saf*. 2015;41:447-56.
16. Wick EC, Galante DJ, Hobson DB, Benson AR, Lee KH, Berenholtz SM, et al. Organizational culture changes result in improvement in patient-centered outcomes: implementation of an integrated recovery pathway for surgical patients. *J Am Coll Surg*. 2015;221:669-77.
17. Richey M, Mann A, He J, Daon E, Wirtz K, Dalton A, et al. Implementation of an early extubation protocol in cardiac surgical patients decreased ventilator time but not intensive care unit or hospital length of stay. *J Cardiothorac Vasc Anesth*. 2018;32:739-44.
18. Crawford TC, Magruder JT, Grimm JC, Sciortino C, Conte JV, Kim BS, et al. Early extubation: a proposed new metric. *Semin Thorac Cardiovasc Surg*. 2016;28:290-9.
19. Wong WT, Lai VK, Chee YE, Lee A. Fast track cardiac care for adult cardiac surgical patients track. *Cochrane Database Syst Rev*. 2016;9:CD003587.
20. Knotkova H, Fine PG, Porteney RK. Opioid rotation: the science and the limitations of the equianalgesic dose table. *J Pain Symptom Manage*. 2009;38:426-39.
21. Jelacic S, Bollag L, Bowdle A, Rivat C, Cain KC, Richebe P. Intravenous acetaminophen as an adjunct analgesic in cardiac surgery reduces opioid consumption but not opioid-related adverse effects: a randomized controlled trial. *J Cardiothorac Vasc Anesth*. 2016;30:997-1004.
22. Maitra S, Baidya DK, Bhattacharjee S, Som A. Perioperative gabapentin and pregabalin in cardiac surgery: a systematic review and meta-analysis. *Rev Bras Anestesiol*. 2017;67:294-304.
23. Lahtinen P, Kokki H, Hakala T, Hynynen M. S(+)-ketamine as an analgesic adjunct reduces opioid consumption after cardiac surgery. *Anesth Analg*. 2004; 99:1295-301.
24. Mazzeffi M, Johnson K, Paciullo C. Ketamine in adult cardiac surgery and the cardiac surgery intensive care unit: an evidence-based clinical review. *Ann Card Anaesth*. 2015;18:202-9.
25. Mamoun NF, Lin P, Zimmerman NM, Mascha EJ, Mick SL, Insler SR, et al. Intravenous acetaminophen analgesia after cardiac surgery: a randomized, blinded, controlled superiority trial. *J Thorac Cardiovasc Surg*. 2016;152:881-9.
26. Kumar KN, Kalyane RN, Singh NG, Nagaraja PS, Krishna M, Babu B, et al. Efficacy of bilateral pectoralis nerve block for ultrafast tracking and postoperative pain management in cardiac surgery. *Ann Card Anaesth*. 2018;333-8.
27. Yang D, Grant MC, Stone A, Wu CL, Wick EC. A meta-analysis of intraoperative ventilation strategies to prevent pulmonary complications: is low tidal volume alone sufficient to protect healthy lungs? *Ann Surg*. 2016; 263:881-7.
28. Djaiani G, Silverton N, Fedorko L, Carroll J, Styra R, Rao V, et al. Dexmedetomidine versus propofol sedation reduces delirium after cardiac surgery: a randomized controlled trial. *Anesthesiology*. 2016;124:362-8.
29. Herr DL, Sum-Ping ST, England M. ICU sedation after coronary artery bypass graft surgery: dexmedetomidine-based *versus* propofol-based sedation regimens. *J Cardiothorac Vasc Anesth*. 2003;17:576-84.
30. Ender J, Borger MA, Scholz M, Funkat AK, Anwar N, Sommer M, et al. Cardiac surgery fast-track treatment in a postanesthetic care unit: six-month results of the Leipzig fast-track concept. *Anesthesiology*. 2008;109:61-6.
31. Camp SL, Stamou SC, Stiegel RM, Reames MK, Skipper ER, Madjarov J, et al. Quality improvement program increases early tracheal extubation rate and decreases pulmonary complications and resource utilization after cardiac surgery. *J Card Surg*. 2009;24:414-23.
32. Cheng DC, Karski J, Peniston C, Asokumar B, Raveendran G, Carroll J, et al. Morbidity outcome in early versus conventional tracheal extubation after coronary artery bypass grafting; a prospective randomized controlled trial. *J Thorac Cardiovasc Surg*. 1996;112:755-64.
33. Goeddel LA, Hollander KN, Evans AS. Early extubation after cardiac surgery: a better predictor of outcome than metric of quality? *J Cardiothorac Vasc Anesth*. 2018;32:745-7.
34. Cove ME, Ying C, Taculod JM, Oon SE, Oh P, Kollengode R, et al. Multidisciplinary extubation protocol in cardiac surgical patients reduces ventilation time and length of stay in the intensive care unit. *Ann Thorac Surg*. 2016;102:28-34.
35. Fitch ZW, Debesa O, Ohkuma R, Duquaine D, Steppan J, Schneider EB, et al. A protocol-driven approach to early extubation after heart surgery. *J Thorac Cardiovasc Surg*. 2014;147:1344-50.
36. Chan JL, Miller JG, Murphy M, Greenberg A, Iraola M, Horvath KA. A multidisciplinary protocol-driven approach to improve extubation times after cardiac surgery. *Ann Thorac Surg*. 2018;105:1684-90.
37. Gutsche JT, Erickson L, Ghadimi K, Augoustides JG, Dimartino J, Szeto WY, et al. Advancing extubation time for cardiac surgery patients using lean work design. *J Cardiothorac Vasc Anesth*. 2014;28:1490-6.

Key Words: enhanced recovery after surgery, cardiac surgical pathways, perioperative medicine, bundled health care, quality improvement

Enhanced Recovery Program for Cardiac Surgery
Preanesthetic and Intraoperative Guidelines

Preanesthesia:
Goals: liberation of NPO status, multimodal analgesia to limit reliance upon opioids, beta blockade

- Recommend preoperative analgesic medication bundle to be taken with a sip of water in the PACU:
  - ***Gabapentin*** 600 mg PO x1
    - Do *not* give to patients on hemodialysis, consider holding in Stage IV chronic renal insufficiency; reduce dose to 300mg in patients >70 years of age
      [Rev Bras Anestesiol. 2017 May - Jun;67(3):294-304.]
  - ***Acetaminophen*** 1 gm PO x1
    - Do *not* give to patients with liver failure/cirrhosis and consider reduction to 650 mg in patients with ALT/AST >10x ULN
      [J Cardiothorac Vasc Anesth. 2016 Aug;30(4):997-1004; J Cardiothorac Vasc Anesth 2016;30:997-1004]
  - ***Beta-blocker*** (home agent and dose) PO x1
    - For CABG patients ONLY [Cardiac SCIP/STS Measure]

Intraoperative (Prior to CPB):
Goals: multimodal analgesia to minimize opioid use, prevention of surgical site infection, tight glucose control, protective lung ventilation to avoid pulmonary complication

- Consider ***Midazolam at induction*** (or pre-treatment): 0.02-0.05 mg/kg bolus (1-5 mg) for anxiolysis, treatment of PONV and offset potential hallucination side effect of unopposed ketamine (below)
  - Recommend reducing or omitting use in elderly (age > 70) or frail patients
    [Anesth Analg. 2016 Mar;122(3):656-63]
- Consider ***Ketamine:*** 0.25 mg/kg/hr infusion initiated after induction; discontinue at time of transport
  - Bolus dosing (in isolation) has been shown to be ineffective in reducing perioperative opioid use or improving pain scores; *provider discretion* if boluses may aide in more stable induction
    [Mazzeffi M, et al. *Ann Card Anaesth* 2015;18:202-209; Lahtinen P, et al. *Anesth Analg* 2004;99:1295-1301; Lancet. 2017 Jul 15;390(10091):267-275]
- Recommend initiating ***dexmedetomidine*** infusion (no bolus; 0.5 – 0.7 mcg/kg/hr) prior to (just after central line placement) or during CPB . Continue throughout the case and upon admission to the ICU
  [Anesthesiology. 2016 Feb;124(2):362-8]
- For CABG: if patient did NOT take ***beta-blocker*** prior to surgery, please administer metoprolol IV unless the patient's heart rate is < 50 bpm
  - If you do not give beta-blocker, please document the rationale in the electronic record
- ***Cefazolin*** 2 gm (3 gm if > 120kg) + 1 gm/hr (reduce to 0.5 g/hr if CrCl30-60 mL/min, or to 0.33 g/hr if CrCl <30 or patient receiving dialysis) infusion during surgery; stop infusion prior to transport
  - If penicillin allergic: ***vancomycin*** 15 mg/kg bolus over 1 hour prior to surgical incision
    [J Cardiothorac Vasc Anesth. 2015 Dec;29(6):1582-7.]
- ***Lung protective ventilation*** strategy – 6 mL/kg tidal volume predicted body weight + 5 cm H20 of PEEP (Reference Chart for Tidal Volumes)

FIGURE E1. The Johns Hopkins Medical Institutions preanesthesia and intraoperative ERP for cardiac surgery guidelines. *NPO*, Nil per os; *PACU*, post-anesthesia care unit; *PO*, per os; *ALT*, alanine aminotransferase; *AST*, aspartate aminotransferase; *ULN*, upper limit of normal; *CABG*, coronary artery bypass graft; *hr*, hour, *bpm*, beats per minute; *PEEP*, positive end expiratory pressure; *Fi02*, fraction of inhaled oxygen; *PaO2*, partial pressure of oxygen; *SaO2*, oxygen saturation; *ABG*, arterial blood gas; *VBG*, venous blood gas; *Q1 hour*, every hour; *ACT*, activated clotting time; *FFP*, fresh frozen plasma; *MAP*, mean arterial pressure; *TEG*, thromboelastography; *CPB*, cardiopulmonary bypass.

PM

- Recommend FiO2 60% or less
- If PaO2 < 80 or SaO2 < 92%, perform standard recruitment on AYSIS GE machine (35 mmHg for 15 seconds) every 30 minutes unless contraindicated
- Recommend holding mechanical ventilation while on bypass; no clear strategy that definitively improves postoperative outcome
[Ann Surg. 2016 May;263(5):881-7; J Cardiothorac Vasc Anesth. 2012 Jun;26(3):448-54]

-Recommend an initial arterial and venous blood gas (ABG, VBG) + ACT at start of case
-Recommend repeating ABG + "CORE4" + lactate Q1 hour for case duration

-***Insulin*** bolus + infusion as indicated based upon the protocol (Intraoperative Insulin Protocol; goal glucose <180)

****IV fentanyl or IV hydromorphone***: Intermittent intravenous opioid at provider discretion
-*AVOID* ultra-short acting opioids with high incidence of medication-induced tachyphylaxis and hyperalgesia (i.e. remifentanil).
-*AVOID* long-acting opioids (i.e. methadone) given unpredictable metabolism profile and potential association with postoperative ileus

Intraoperative (During CPB):
Goals: Adequate anticoagulation, anti-fibrinolysis and cardiopulmonary perfusion

-***Heparin*** 350 unit/kg bolus (ACT goal > 480); initiate heparin infusion at rate = 1/3rd of bolus dose/hr throughout cardiopulmonary bypass
- If ACT < 480, please administer an additional 10,000 units of heparin and repeat ACT
- If ACT is still < 480 after a total heparin dose of ≥650 units/kg, consider either lower ACT goal, administration of antithrombin III (ATIII) concentrate per protocol (ATIII Concentrate Protocol), or FFP 2-3 units (if available in the room)

-At time of heparin bolus, ***tranexamic acid*** 10 mg/kg bolus over 10 minutes through the Alaris pump + 1 mg/kg bolus in the CPB circuit + 1 mg/kg/hr infusion through the Alaris pump throughout the surgery
[N Engl J Med. 2017 Jan 12;376(2):136-148]

-***Goal-directed perfusion*** per our institutional guidelines (Goal Directed Perfusion Protocol)
-If perfusion utilizes > 1,000 mcg of phenylephrine and increased flow (cardiac index > 2.4; per perfusion) do not maintain MAP > 60, please initiate a ***norepinephrine infusion*** during CPB
[J Thorac Cardiovasc Surg. 2017 Jan;153(1):118-125.]

Intraoperative (During Rewarming):
Goals: Goal directed transfusion, adequate warming

-Send ***coagulation labs*** (platelet count, fibrinogen and cardiac TEG) when aortic cross-clamp is removed; transfuse as appropriate based upon abnormalities **PLUS** active bleeding (Coagulation Study Protocol)

-Goal ***hemoglobin transfusion trigger recommendation is 7.5***, regardless of patient age or comorbidities provided no active large volume bleeding
-Please discuss transfusion(s) with anesthesiology, surgery and perfusion personnel at surgical timeout and again at the time of decision to transfuse [N Engl J Med. 2017 Nov 30;377(22):2133-2144]

-Turn on ***bear hugger*** to boost and ***increase room temperature*** to 68 degrees to ensure adequate warming and assist in the prevention of coagulopathy (goal postop temperature of > 36.0 degrees)

FIGURE E1. (*continued*).

-Hypothermia is a reason for failure to extubate the patient within 6 hours

Intraoperative (After CPB Separation):
Goals: adequate hemostasis, electrolyte repletion, multimodal analgesia to minimize opioid use and mechanical ventilator weaning

-Ensure adequate heparin reversal after ***protamine*** administration via ACT (goal ~ baseline ACT), consider repeating coagulation laboratories after factor/platelet administration

-Ensure adequate repletion of ***calcium*** (goal iCal 1.1) and ***potassium*** (goal K > 4.0) by case completion
-Remember: epinephrine +/- insulin +/- acidosis all impact plasma K levels

-Recommend ***magnesium infusion***: 4 gm administered over approximately 30 minutes upon separation from CPB [Anesthesiology. 2013 Jul;119(1):178-90; J Cardiothorac Vasc Anesth. 2012 Aug;26(4):643-50.]

-Recommend ***IV acetaminophen 1000 mg x1*** at 6-8 hours after initial oral preoperative administration if still in the operating room. Do *not* give if AST/ALT >10x ULN [J Thorac Cardiovasc Surg 2016;152:881-9]

-Recommend ***Regional Analgesia Block:*** 0.25 – 0.375% bupivacaine 20-30 mL via ultrasound guidance bilateral at the time of surgical drape removal
- **NOTE:** If you plan to perform an this block please do NOT perform a surgical incision block due to the risk of local anesthesia toxicity

-Multidisciplinary discussion to determine if ***extubation in the operating room*** is appropriate. If so, paralysis should be fully reversed, weaned to pressure support, titrate analgesics and extubate trachea
- If extubation is not desired or is inappropriate, then at the time of ICU handoff, all patients should have their ***muscle paralysis fully reversed***
-Recommend the use of ***dexmedetomidine*** infusion over propofol for transportation to ICU

FIGURE E1. (*continued*).

PM

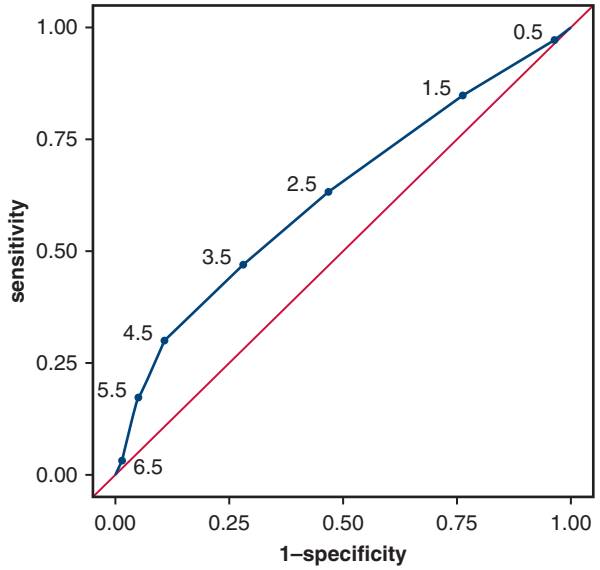

FIGURE E2. Results of a preliminary receiver operator characteristic curve, which helped to establish the cutoff number (between 4 and 5) of measures necessary for maximal sensitivity and specificity to predict postoperative extubation within 6 hours of surgery.

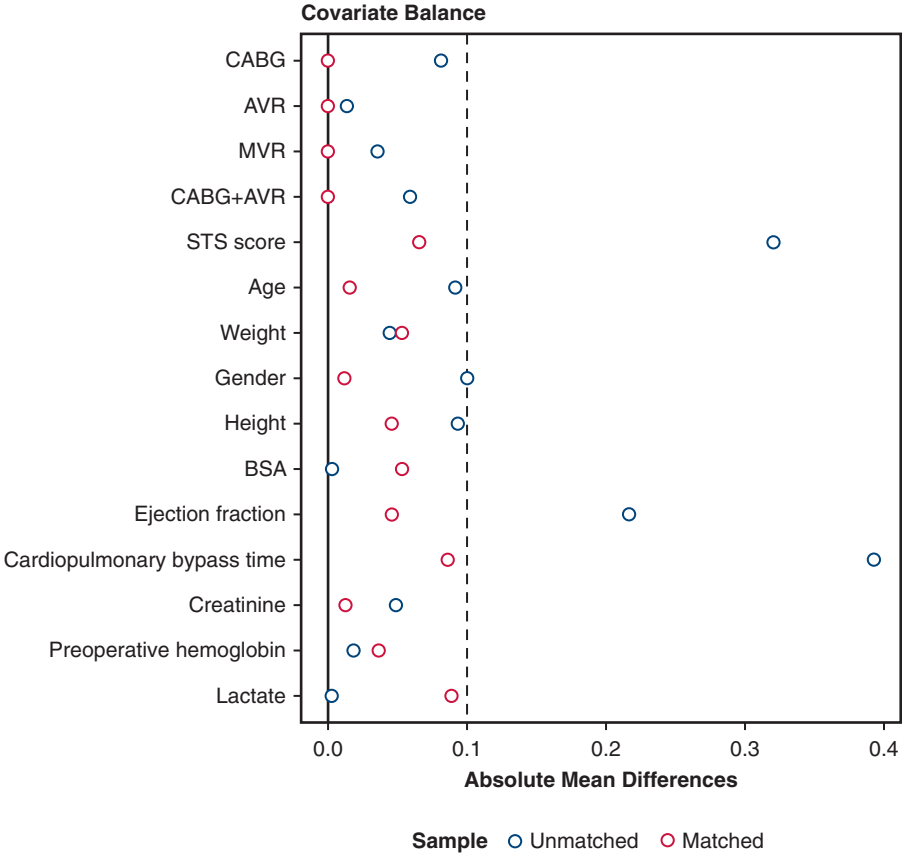

FIGURE E3. The Love plot depicting the results of propensity matching. Although among unmatched data, there is a significant difference between high compliance and low compliance cohorts with respect to STS score, ejection fraction, and CPB time, there is excellent matching between groups as evidenced by an absolute standardized mean difference of less than 0.1 and variance ratio less than 2 for all 15 selected covariates. *CABG*, Coronary artery bypass grafting; *AVR*, aortic valve replacement; *MVR*, mitral valve replacement; *STS*, Society of Thoracic Surgeons; *BSA*, body surface area.

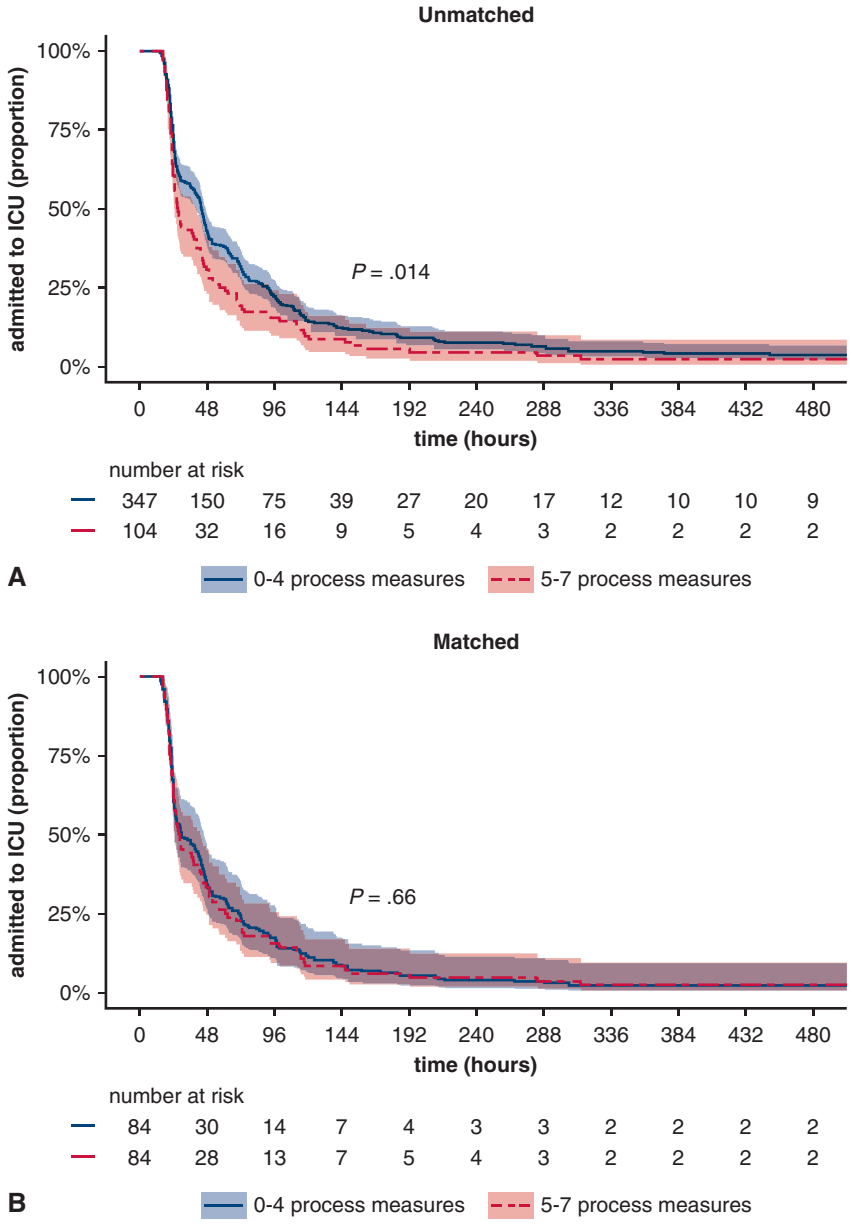

FIGURE E4. ICU LOS as a function of compliance with phase-specific process measures. Unmatched (A) and propensity-matched (B) cohorts. As shown, there is no difference in ICU LOS between high (*red*; 5-7 process measures) and low compliance (*blue*; 0-4 process measure) cohorts. *ICU*, Intensive care unit.

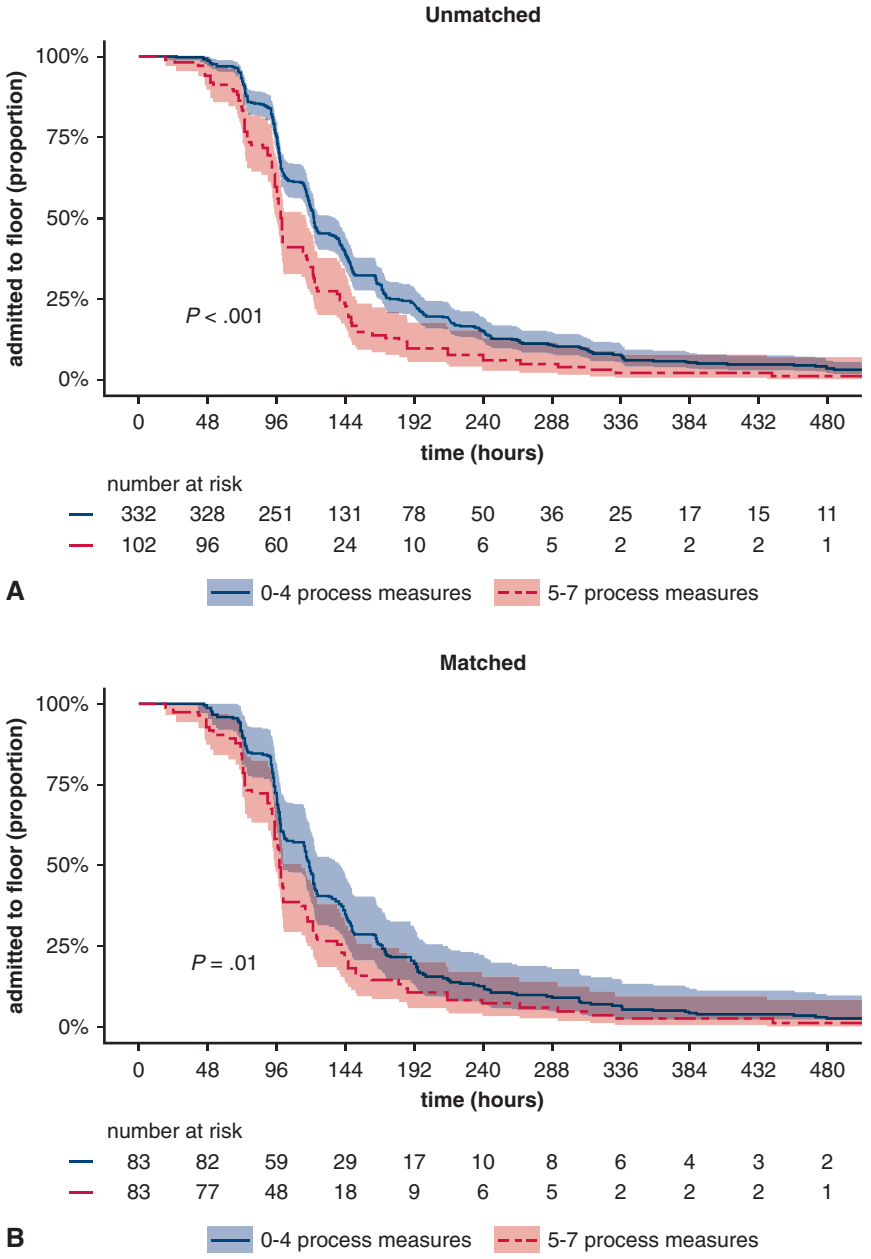

FIGURE E5. Floor LOS as a function of compliance with phase-specific process measures. Unmatched (A) and propensity-matched (B) cohorts. As shown, high compliance with phase of care guidelines (*red*; 5-7 process measures) is associated with a significant reduction in length of floor stay compared with low compliance (*blue*; 0-4 process measure) counterparts.

TABLE E1. Odds of extubation based on compliance group

Extubation time	OR; 5-7 vs 0-4 process measures	*P* value
Intraoperative	35.76 (10.66, 168.75)	<.001
≤6 h	2.62 (1.18, 6.07)	.02
≤12 h	1.79 (0.59, 5.90)	.31
≤24 h	0.72 (0.01, 8.14)	.79

The ORs were computed with logistic regression doubly robust model. *OR*, Odds ratio.

TABLE E2. Results of multivariable regression analysis on various timeframes of extubation

	Intraoperative extubation		Extubation (≤6 h)		Extubation (≤12 h)		Extubation (≤24 h)	
	OR	*P* value	OR	*P* value	OR	*P* value	OR	*P* value
Ketamine	1.46 (0.60, 3.57)	.40	0.84 (0.50, 1.38)	.48	0.82 (0.44, 1.52)	.54	0.48 (0.14, 1.49)	.22
Paralytic reversal (operating room)	13.92 (5.37, 40.44)	**<.001**	2.96 (1.59, 5.69)	**<.001**	2.32 (1.03, 5.66)	**.051**	2.14 (0.47, 13.17)	.36
Dexmedetomidine	0.33 (0.12, 0.83)	**.023**	0.56 (0.27, 1.16)	.12	0.56 (0.22, 1.45)	.22	0.52 (0.11, 3.17)	.44
Acetaminophen	1.94 (0.58, 6.44)	.27	1.61 (0.82, 3.28)	.18	1.42 (0.62, 3.51)	.43	0.76 (0.19, 3.84)	.71
Regional Analgesia	2.75 (1.25, 6.24)	**.013**	1.13 (0.62, 2.11)	.69	1.88 (0.85, 4.45)	.13	3.10 (0.60, 25.37)	.22
Gabapentin	4.73 (1.77, 14.39)	**.003**	1.03 (0.47, 2.20)	.94	1.03 (0.38, 2.69)	.95	1.79 (0.27, 11.09)	.53
Protective lung ventilation	1.88 (0.17, 50.56)	.64	0.34 (0.10, 1.04)	.072	0.49 (0.12, 1.64)	.28	0.70 (0.07, 4.26)	.73
Age	1.00 (1.00, 1.00)	.18	1.00 (1.00, 1.00)	.81	1.00 (1.00, 1.00)	.15	1.00 (1.00, 1.00)	.10
STS score	0.73 (0.45, 0.99)	.13	0.82 (0.72, 0.92)	**.002**	0.84 (0.75, 0.93)	**.001**	0.87 (0.76, 0.98)	**.026**
Ejection fraction	1.02 (0.98, 1.06)	.40	1.01 (0.99, 1.03)	.20	1.03 (1.00, 1.05)	**.022**	1.03 (0.99, 1.08)	.097
Preoperative hemoglobin	0.99 (0.79, 1.26)	.96	1.00 (0.87, 1.15)	.96	1.01 (0.86, 1.19)	.86	1.31 (1.00, 1.71)	.048
Creatinine	1.01 (0.52, 1.70)	.97	0.99 (0.77, 1.23)	.93	1.28 (0.96, 1.86)	.14	1.20 (0.85, 1.90)	.37
Lactate	0.91 (0.31, 2.58)	.86	0.48 (0.25, 0.93)	**.029**	0.74 (0.35, 1.63)	.44	0.52 (0.15, 1.80)	.30
Weight	1.09 (0.99, 1.20)	.075	0.99 (0.94, 1.05)	.78	0.99 (0.93, 1.07)	.85	1.07 (0.93, 1.24)	.35
Gender	1.68 (0.45, 6.41)	.44	0.71 (0.33, 1.51)	.38	0.54 (0.21, 1.31)	.18	1.82 (0.38, 8.54)	.44
Height	1499.15 (0.56, >2000)	.08	1.47 (0.01, 183.30)	.88	2.84 (0.01, 978.08)	.73	3.01 (0.00, >2000)	.83
BSA	0.00 (0.00, 0.60)	**.044**	4.43 (0.02, 1002)	.59	3.81 (0.00, 2880)	.69	0.00 (0.00, 904)	.39
Cardiopulmonary bypass time	1.0007 (0.99, 1.01)	.89	0.9904 (0.99, 0.10)	**<.001**	0.9925 (0.99, 0.10)	**.003**	0.9836 (0.98, 0.10)	**<.001**
AVR vs CABG	2.98 (0.88, 9.79)	.073	4.24 (1.58, 13.85)	**.008**	5.61 (1.34, 41.82)	**.042**	35.75 (1.39, 4060)	.088
MVR vs CABG	6.62 (1.52, 29.35)	**.012**	0.84 (0.34, 2.15)	.71	0.50 (0.18, 1.50)	.20	4.69 (0.54, 80.91)	.22
CABG + AVR vs CABG	2.75 (0.47, 13.52)	.23	1.01 (0.43, 2.46)	.98	0.38 (0.15, 0.98)	.040	1.68 (0.30, 12.39)	.58

Bold values represent statistical significance based on the established threshold of <.05. *OR*, Odds ratio; *STS*, Society of Thoracic Surgeons; *BSA*, body surface area; *AVR*, aortic valve replacement; *CABG*, coronary artery bypass grafting; *MVR*, mitral valve replacement.

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000 Results from an enhanced recovery program for cardiac surgery

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There is value in developing phase of care guidelines for ERPs for cardiac surgery, which may improve rates of early extubation and reduce LOS after cardiac surgery.