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ORIGINAL RESEARCH

Balancing intubation time with postoperative risk in cardiac surgery patients – a retrospective cohort analysis

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Introduction: Intubation time in patients undergoing cardiac surgery may be associated with increased mortality and morbidity. Premature extubation can have serious adverse physiological consequences. The aim of this study was to determine the influence of intubation time on morbidity and mortality in patients undergoing cardiac surgery.

Methods: We performed a retrospective analysis of data on 1,904 patients undergoing isolated coronary artery bypass grafting (CABG) and stratified them by duration of intubation time after surgery – 0–6, 6–9, 9–12, 12–24 and over 24 hours. Postoperative complications risk analysis was performed using multivariate logistic regression analysis for patients extubated ≤12 and >12 hours.

Results: Intubation percentages in each time cohort were as follows: 0–6 hours – 7.8%, 6–9 hours – 17.3%, 9–12 hours – 26.8%, 12–24 hours – 44.4% and >24 hours – 3.7%. Patients extubated ≤12 hours after CABG were younger, mostly males, more often smokers, with lower preoperative risk. They had lower 30-day mortality (2.02% vs 4.59%, P=0.002), shorter hospital stay (7.68±4.49 vs 9.65±12.63 days, P<0.001) and shorter intensive care unit stay (2.39 vs 3.30 days, P<0.001). Multivariate analysis showed that intubation exceeding 12 hours after CABG increases the risk of postoperative delirium (OR 1.548, 95% CI 1.161–2.064, P=0.003) and risk of postoperative hemofiltration (OR 1.302, 95% CI 1.023–1.657, P=0.032).

Conclusion: Results indicate that risk of postoperative complications does not increase until intubation time exceeds 12 hours. Shorter intubation time is seen in younger, men and smokers. Intubation time >12 hours is a risk factor for postoperative delirium and hemofiltration after cardiac surgery.

Keywords: intubation, cardiac surgery, CABG, mortality, complications, delirium

Introduction

Prolonged intubation time in patients undergoing cardiac surgery can be associated with increased mortality and morbidity.[1–3] Studies have shown that patients extubated earlier after the operation have shorter ICU and hospital length of stay (LOS).[4,5] The guidelines of the Society of Thoracic Surgeons (STS) indicate a 6-hour time point as a definition of "early extubation" and intubation longer than 24 hours as "prolonged intubation".[6] The advocated early extubation time, ie, within 6 hours after the procedure as compared to conventional extubation practices, has been associated with a reduced rate of infections, renal failure, stroke and mortality.[7–9] However, the time between 6 and 24 hours has not been adequately studied. Dichotomization of patients into two sub-groups divided by a single time point may miss some of the important information regarding the intermediate time intervals. Advances in surgical and anesthetic

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techniques bring an on-going interest in early extubation in order to reduce the negative outcomes associated with delayed extubation, as well as any additional costs.[10]

Despite the advocated early 6-hour extubation time, many patients do not fulfill criteria for extubation at this time. One of the reasons is the cardiopulmonary bypass (CPB), responsible for inducing a generalized inflammatory response (complement and neutrophil activation, pro-inflammatory mediator release) that may result in the post-CPB syndrome characterized by an increase in alveolar–arterial oxygen partial pressure gradients ($AaDO_2$), decreased lung compliance and increased extravascular lung water.[11,12] Premature extubation can have serious adverse physiological consequences, including atelectasis, respiratory distress, hypercarbia and hypoxemia.[13]

Studies have reported numerous interventions and perioperative protocols aimed at meeting the 6-hour time point that were implemented in the cardiac ICUs as an effort to reduce the intubation time.[14,15] The heterogeneity of patient populations undergoing cardiac surgery may have limited the success of previously suggested protocols and risk prediction models.[16–19] The inflection point at which the complications rate rises has not been adequately determined. To verify the validity of previously identified predictors in a homogenous group of relatively low-risk patients, we performed this study with an aim to determine the influence of intubation duration on postoperative morbidity and mortality in patients undergoing isolated coronary artery bypass grafting (CABG) under general anesthesia.

Methods

Study design and patient selection

We performed a retrospective analysis of data from a prospectively collected institutional database including all operations performed at the Department of Cardiac Surgery of a tertiary university hospital with entries between January 1, 2014 and December 31, 2016. We included all patients undergoing isolated CABG, excluding any patients undergoing a valvular procedure performed in addition to CABG and all CABG without the use of cardio-pulmonary bypass (off-pump CABG [OPCAB]). Among 3,065 records in the database that included all cardiac surgery patients, we extracted data on 1,904 patients undergoing isolated CABG. Data on concomitant diseases and demographic information (age, gender, body mass index [BMI], history of smoking and admission type) were extracted from the medical documentation. The following co-morbidities were recorded: heart failure according to New York Heart Association (NYHA) and ejection fraction, arterial hypertension, myocardial infarction, atrial fibrillation, extracardiac arteriopathy, internal carotid artery stenosis, COPD, renal failure, stroke and transient ischemic attack. Perioperative risk was calculated using the EuroScore Logistics 2 scale. Laboratory results were part of routine perioperative blood sampling. Induction of general anesthesia was performed intravenously with fentanyl and etomidate, and a muscle relaxant (pancuronium) to allow tracheal intubation. Maintenance of general anesthesia was inhalational, using sevoflurane with additional doses of fentanyl and a muscle relaxant. After the surgery patients were transferred to a postoperative cardiac ICU, still intubated and mechanically ventilated, sedated to achieve adequate sedation depth (Richmond Agitation Sedation Scale [RASS] between −1 and +1) with adequate pain control, using intravenous morphine infusion and a non-opioid analgesic. The initial mode for mechanical ventilation was synchronized intermittent mechanical ventilation with continuous positive airway pressure when the patient regained their respiratory drive and the weaning process was initiated. Patients were extubated when they met pre-defined criteria: normal body temperature, Glasgow Coma Scale 14–15 points, no focal neurological deficit, pain under control, drainage <100 mL/h, hemodynamic stability (noradrenaline or adrenaline <0.05 μg/kg/min), absence of significant arrhythmias, $PaO_2 >60$ mmHg, $PaCO_2 <45$ mmHg, $SpO_2 >95\%$ with $FiO_2 <0.45$, no respiratory distress and normal respiratory rate. Patients were extubated to passive oxygen therapy (facial mask with O_2 at 5–7 L/min). An arterial blood gas was obtained 30 minutes after extubation to ensure patient safety.

Ethical concerns

The study was performed in accordance with the Declaration of Helsinki due to its retrospective character a waiver was granted from the Bioethical Committee of the Pomeranian Medical University in Szczecin, Poland, decision no KB-0012/254/06/18. The data entered into the prospectively collected database required written informed consent for surgery, anesthesia and data collection at the time of hospital admission from each patient, as part of routine preoperative assessment, therefore patient consent to review their medical documentation was waived by the Bioethical Committee. To ensure patient data safety only de-identified data was used for analysis.

Intubation time cohorts

The intubation time (in hours, rounded to tenths) was calculated for each patient as a difference between the time when patient left the operating room to be transferred to the cardiac ICU and the time of extubation after the surgery and. We used five pre-defined time intervals of postoperative intubation: 0–6, 6–9, 9–12, 12–24 and over 24 hours.

The time stratification approach indicated a threshold of 12-hours at which the risk of 30-day mortality increased, for which a complications risk analysis was performed.

Primary and secondary outcomes

The primary outcome was death within 30 days after the operation, regardless of the cause and ICU LOS (days) and hospital LOS (days). Secondary outcomes included postoperative complications – neurological (stroke, transient ischemic attack, delirium, seizures), respiratory (pneumonia, respiratory failure), renal (acute kidney injury, hemofiltration), cardiovascular (heart failure, cardiogenic shock, atrial fibrillation), and infectious (sepsis).

Statistical analyses

We performed descriptive analysis using the Student's *t*-test for continuous variables, presented as means with SD according to distribution. The chi-squared test was used for categorical variables, which were presented as proportions. A mortality-matched analysis was performed for pre-defined time points (0–6, 6–9, 9–12, 12–24, and >24 hours), which showed a statistically significant mortality increase in patients intubated for longer than 12 hours and the whole cohort was further sub-divided into ≤12 hours and >12 hours. The *P*-value of <0.05 was regarded as statistically significant. Univariate logistic regression analysis was used for subgroups ≤12 hours and >12 hours for each variable and presented as ORs with 95% CI. Risk factors that were significant in univariate analysis and presented with narrow CI and a *P*-value of <0.05 were manually entered for multivariate logistic regression analysis. All statistical analyses was performed using licensed software Statistica 12 (StatSoft, Inc., Tulsa, OK, USA), license no JPZP602C295824AR-V.

Results

Results for all time cohorts

The average intubation time after CABG was 14.93±8.63 hours. The intubation percentages in each time cohort were (Figure 1): 0–6 hours – 7.8% (148/1,904), 6–9 hours – 17.3% (329/1,904), 9–12 hours – 26.8% (511/1,904), 12–24 hours – 44.4% (846/1,904) and >24 hours – 3.7% (70/1,904). The majority of the patients were extubated within 12 hours – 52.5%. All data on patients with a stratification according to pre-defined time points are shown in Table 1. Age increase was seen across all five cohorts (*P*<0.001). Patients extubated earlier had higher BMI (*P*=0.032) were mostly men (*P*<0.001), more often smokers (*P*=0.003), with a lower operative risk (based on EuroScore logistic 2, *P*<0.001). The admission type did not differ between study cohorts. When accounting for concomitant diseases, patients extubated earlier had less heart failure (NYHA III and IV, *P*<0.001), less low ejection fraction <30% (*P*=0.023), less internal carotid artery stenosis (*P*=0.048), less chronic renal failure (*P*<0.001) and extracardiac arteriopathy (*P*=0.002) than patients with longer intubation times.

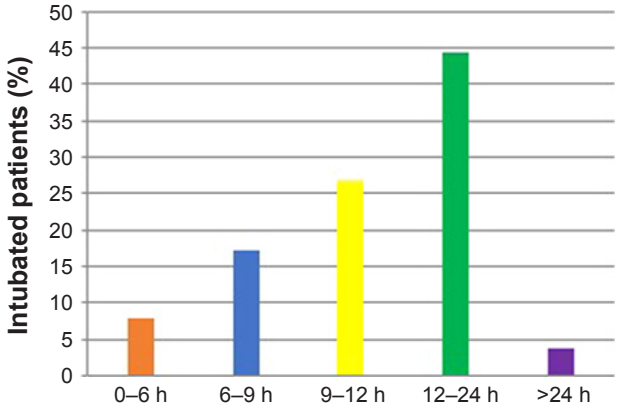


Figure 1 Percentages of patients according to the length of intubation after CABG.
Abbreviation: CABG, coronary artery bypass grafting.

Both primary and secondary outcomes data showed significant differences across all time cohorts (Table 2), with lower mortality (*P*<0.001) and shorter ICU (*P*<0.001) and hospital stay (*P*<0.001) for patients extubated earlier.

The differences in mortality across all five time cohorts for post-CABG intubation (Table 3) showed that the OR for mortality increases in patients intubated for longer than 12 hours (OR 2.831, 95% CI 1.216–6.594, *P*=0.016) and further increases if intubation time exceeded 24 hours (OR 8.514, 95% CI 3.283–22.079, *P*<0.001).

Results for patients with intubation times ≤12 and >12 hours

Patients extubated within 12 hours after intubation (52.4%, 998/1,904) were younger, mostly males (83.4% vs 72.4%, *P*<0.001), more often active smokers with lower preoperative risk as shown in Table 4. There were no differences regarding the BMI or the admission type between the two subgroups. When analyzing the comorbid conditions, only heart failure (NYHA III/IV) internal carotid artery stenosis and acute renal failure was more frequent in patients extubated >12 hours; preoperative hemoglobin was lower and serum creatinine was higher in these patients. The length of CPB and aortic cross-clamping time did not differ between ≤12-hour and >12-hour intubation times. The rate of reoperation (*P*<0.001) and intraoperative hemofiltration (*P*<0.001) was significantly higher in patients extubated after 12 hours. Patients intubated for longer than 12 hours

Table 1 Study group characteristics and perioperative data for each intubation time cohort

Data	Intubation time					
	0–6 hours, n=148 (7.77%)	**6.1–9 hours, n=329 (17.28%)**	**9.1–12 hours, n=511 (26.84%)**	**12.1–24 hours, n=846 (44.43%)**	**>24.1 hours, n=70 (3.68%)**	***P*-value**
Demographic data						
Age [years] (mean ± SD)	61.98±8.49	63.08±7.55	66.00±7.88	68.07±8.01	70.36±8.31	<0.001
BMI [kg/m^2] (mean ± SD)	29.99±4.58	29.05±4.15	28.94±4.42	28.74±4.32	28.46±4.40	0.032
Gender, male, n (%)	132 (89.19)	291 (88.45)	401 (78.47)	618 (73.05)	44 (64.29)	<0.001
Smoking, n (%)	27 (18.24)	67 (20.43)	91 (17.88)	111 (13.18)	15 (21.74)	<0.001
BMI, n (%)						
Normal	17 (11.49)	51 (15.50)	88 (17.22)	160 (18.91)	18 (25.71)	NS
Overweight	62 (41.89)	147 (44.68)	230 (45.01)	367 (43.38)	28 (40.00)	
Obese	69 (46.62)	131 (39.82)	193 (37.77)	319 (37.71)	24 (34.29)	
Admission type, n (%)						
Elective	100 (67.57)	225 (68.39)	354 (69.41)	579 (68.44)	46 (65.71)	NS
Accelerated	37 (25.00)	84 (25.53)	123 (24.12)	208 (24.59)	18 (25.71)	
Emergency	11 (7.43)	20 (6.08)	33 (6.47)	59 (6.97)	6 (8.57)	
Concomitant diseases						
Ejection fraction <30%, n (%)	7 (4.73)	21 (6.38)	32 (6.26)	49 (5.79)	11 (15.71)	0.023
NYHA III and IV, n (%)	13 (9.85)	24 (8.33)	48 (10.55)	93 (12.30)	17 (27.42)	<0.001
Diabetes mellitus, n (%)	71 (47.97)	144 (43.77)	236 (46.18)	404 (47.75)	29 (41.43)	NS
Glucose intolerance, n (%)	8 (5.41)	10 (3.04)	15 (2.94)	32 (3.78)	3 (4.29)	NS
Transient ischemic attack, n (%)	2 (1.35)	2 (0.61)	5 (0.98)	12 (1.42)	1 (1.43)	NS
Stroke, n (%)	6 (4.05)	21 (6.38)	34 (6.65)	45 (5.32)	7 (10.00)	NS
Arterial hypertension, n (%)	110 (74.32)	241 (73.25)	379 (74.17)	650 (76.83)	54 (77.14)	NS
Myocardial infarction, n (%)	80 (54.05)	170 (51.6)	256 (50.1)	462 (54.61)	47 (67.14)	NS
PTCA/Stenting, n (%)	48 (32.43)	124 (37.69)	168 (32.88)	267 (31.56)	20 (28.57)	NS
Atrial fibrillation paroxysmal, n (%)	10 (6.76)	18 (5.47)	29 (5.86)	57 (6.74)	6 (8.57)	NS
Atrial fibrillation persistent, n (%)	8 (5.41)	11 (3.34)	16 (3.13)	27 (3.19)	2 (2.86)	NS
Internal carotid artery stenosis, n (%)	7 (4.73)	20 (6.08)	33 (6.46)	73 (8.63)	10 (14.29)	0.048
COPD, n (%)	7 (4.73)	18 (5.47)	28 (5.48)	49 (5.79)	7 (10.00)	NS
Chronic renal failure, n (%)	5 (3.38)	16 (4.86)	31 (6.07)	45 (5.32)	12 (17.14)	<0.001
Acute renal failure, n (%)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	6 (0.71)	NS
Extracardiac arteriopathy, n (%)	16 (10.81)	43 (13.07)	101 (19.77)	159 (18.79)	20 (28.57)	0.002
Operative risk						
EuroScore Logistic 2 [%] (mean ± SD)	1.87±1.99	1.96±1.97	2.15±2.45	2.42±3.08	5.10±8.80	<0.001
Preoperative factors						
Ejection fraction [%] (mean ± SD)	46.57±9.67	46.63±10.41	47.07±9.82	47.14±9.95	43.51±11.33	NS
CKMB [U/L] (mean ± SD)	27.95±35.65	23.77±17.72	25.15±24.18	34.03±94.88	82.66±142.61	<0.001
Hemoglobin [mmol/L] (mean ± SD)	8.62±0.99	8.69±0.92	8.48±0.92	8.43±0.94	8.12±1.16	<0.001
Creatinine [mg/dL] (mean ± SD)	1.00±0.74	0.99±0.64	0.97±0.47	1.04±0.79	1.21±0.53	<0.001
GFR [mL/min/1.73 m^2] (mean ± SD)	85.68±19.97	84.26±18.39	81.88±30.79	77.71±31.41	63.83±22.22	<0.001
Intraoperative factors						
CPB time [min] (mean ± SD)	53.16±17.29	48.87±13.35	50.37±13.68	50.02±15.94	60.40±37.05	NS
Aortic cross-clamping time [min] (mean ± SD)	31.85±10.52	30.10±10.09	30.45±9.07	29.66±8.78	30.78±15.80	NS
Re-operation, n (%)	5 (3.38)	5 (1.52)	9 (1.76)	45 (5.32)	14 (20)	<0.001
Intraoperative hemofiltration, n (%)	28 (18.92)	40 (12.16)	92 (18.00)	178 (21.04)	34 (48.57)	<0.001

(*Continued*)

Table 1 (*Continued*)

Data	Intubation time					
	0–6 hours, n=148 (7.77%)	**6.1–9 hours, n=329 (17.28%)**	**9.1–12 hours, n=511 (26.84%)**	**12.1–24 hours, n=846 (44.43%)**	**>24.1 hours, n=70 (3.68%)**	***P*-value**
Postoperative factors						
CKMB day 1 [U/L] (mean ± SD)	61.01±67.44	54.59±55.28	55.87±58.40	72.57±148.09	188.12±301.22	<0.001
Drainage day 1 [mL] (mean ± SD)	473.82±306.40	461.96±277.51	443.66±317.96	485.93±435.79	697.57±767.97	0.002
Creatinine (highest) day 1 [mg/dL] (mean ± SD)	1.15±0.77	1.21±1.13	1.24±0.79	1.38±1.03	1.88±0.83	<0.001
Hemoglobin day 1 [mmol/L] (mean ± SD)	6.79±0.77	6.81±0.80	6.66±0.83	6.58±0.85	6.13±0.91	<0.001
GFR (lowest) [mL/min/1.73 m^2] (mean ± SD)	78.31±25.29	76.02±23.54	69.64±24.75	63.04±25.03	41.63±21.52	<0.001
PRBC transfusion [units] (mean ± SD)	2.63±1.74	2.70±2.20	2.62±1.42	3.11±2.22	4.62±3.04	<0.001

Note: The statistical analysis showed $p>0.05$, therefore this is statistically not significant (NS).
Abbreviations: BMI, body mass index; CK, creatinine kinase MB fraction; CPB, cardio-pulmonary bypass; FFP, fresh frozen plasma; GFR, glomerular filtration rate; n, number of patients; NS, not significant; NYHA, New York Heart Association; PRBC, packed red blood cells; PTCA, percutaneous coronary angioplasty.

had higher creatinine level at day 1 and required transfusion of more packed red blood cells, although the volume of postoperative drainage did not differ significantly between the two groups.

Patients intubated for longer than 12 hours had higher 30-day mortality (2.02% vs 4.59%, $P=0.002$), longer hospital LOS (9.65 vs 7.68 days, $P<0.001$) and longer ICU LOS (3.30 vs 2.39 days, $P<0.001$), but more patients had stroke ($P<0.001$), postoperative delirium ($P<0.001$), cardiogenic shock ($P=0.003$), pneumonia ($P<0.001$) and respiratory failure ($P<0.001$), acute kidney failure ($P<0.001$) and hemofiltration ($P<0.001$), as depicted in Table 5.

Univariate and multivariate analyses

Univariate analysis showed multiple factors to be associated with intubation exceeding 12 hours (Table 6), yet the multivariate analysis showed that intubation exceeding 12 hours after CABG did not increase the risk of 30-day mortality or

Table 2 Primary and secondary outcomes data for each intubation time cohort

Postoperative outcomes	Intubation time					
	0–6 hours (n=148)	**6.1–9 hours (n=329)**	**9.1–12 hours (n=511)**	**12.1–24 hours (n=846)**	**>24.1 hours (n=70)**	***P*-value**
Primary outcome data						
Mortality – 30 days, n (%)	7 (4.73)	5 (1.52)	8 (1.57)	31 (3.66)	11 (15.71)	<0.001
Hospital LOS (mean ± SD)	7.05±2.82	7.77±5.35	7.80±4.25	9.13±11.73	15.89±19.63	<0.001
ICU LOS (mean ± SD)	2.23±0.76	2.49±2.77	2.38±1.63	2.96±5.10	7.37±12.31	<0.001
Secondary outcome data – complications						
Stroke, n (%)	2 (1.35)	4 (1.22)	4 (0.78)	19 (2.25)	11 (15.71)	<0.001
TIA, n (%)	1 (0.68)	3 (0.91)	4 (0.78)	10 (1.18)	0 (0)	NS
Delirium, n (%)	15 (10.14)	25 (7.6)	56 (10.96)	140 (16.55)	15 (21.43)	<0.001
Seizures, n (%)	1 (0.68)	0 (0.00)	0 (0.00)	3 (0.35)	4 (5.71)	<0.001
Cardiogenic shock, n (%)	3 (2.03)	2 (0.61)	5 (0.98)	16 (1.89)	12 (17.14)	<0.001
Pneumonia, n (%)	1 (0.68)	7 (2.13)	10 (1.96)	35 (4.14)	18 (25.71)	<0.001
Respiratory failure, n (%)	6 (4.05)	12 (3.65)	16 (3.13)	48 (5.67)	34 (48.57)	<0.001
AKI, n (%)	7 (4.73)	4 (1.22)	17 (3.33)	46 (5.44)	18 (25.71)	<0.001
AKI requiring hemofiltration, n (%)	7 (4.73)	14 (4.26)	15 (2.94)	64 (7.57)	26 (37.14)	<0.001
Atrial fibrillation, n (%)	32 (21.62)	55 (16.72)	110 (21.53)	186 (21.99)	15 (21.43)	NS
Sepsis, n (%)	1 (0.68)	0 (0.00)	1 (0.20)	1 (0.12)	2 (2.68)	<0.001

Abbreviations: AKI, acute kidney injury; ICU, intensive care unit; LOS, length of stay; n, number of patients; *P*, statistical significance; TIA, transient ischaemic attack.

Table 3 Differences in 30-day mortality for different intubation time-points

Mortality at 30 days	OR	95% CI	*P*-value
Intubation time 0–6 hours	0.661	0.271–1.614	NS
Intubation time 6–9 hours	0.916	0.341–2.460	NS
Intubation time 9–12 hours	1.513	0.620–3.692	NS
Intubation time 12–24 hours	2.831	1.216–6.594	0.016
Intubation time >24 hours	8.514	3.283–22.079	0.000

Abbreviations: NS, not significant; *P*, statistical significance.

Table 4 Baseline characteristics and perioperative data for patients intubated for ≤12 hours and >12 hours during and after CABG

Data	Intubation time		
	≤12 hours (n=988)	>12 hours (n=916)	*P*-value
Demographic data			
Age [years] (mean ± SD)	64.43±8.04	68.25±8.05	<0.001
BMI [kg/m^2] (mean ± SD)	29.14±4.37	28.72±4.32	NS
Gender, male, n (%)	824 (83.40)	663 (72.38)	<0.001
Smoking, n (%)	185 (18.78)	126 (13.83)	<0.001
BMI, n (%)			
Normal	156 (15.79)	180 (19.48)	NS
Overweight	439 (44.43)	397 (42.97)	
Obesity	393 (39.78)	347 (37.55)	
Admission type, n (%)			
Elective	679 (68.79)	632 (68.40)	NS
Accelerated	244 (24.72)	235 (25.43)	
Emergency	64 (6.48)	65 (7.09)	
Concomitant diseases			
Ejection fraction <30%, n (%)	60 (6.07)	60 (6.55)	NS
NYHA III and IV, n (%)	85 (9.71)	110 (13.45)	0.016
Diabetes mellitus, n (%)	451 (45.65)	433 (47.27)	NS
Glucose intolerance, n (%)	33 (3.34)	35 (3.82)	NS
Transient ischemic attack, n (%)	9 (0.91)	13 (1.42)	NS
Stroke, n (%)	61 (6.17)	52 (5.68)	NS
Arterial hypertension, n (%)	730 (73.89)	704 (76.86)	NS
Myocardial infarction, n (%)	506 (51.21)	509 (55.57)	NS
PTCA/Stenting, n (%)	340 (34.41)	287 (31.33)	NS
Atrial fibrillation paroxysmal, n (%)	57 (5.77)	63 (6.88)	NS
Atrial fibrillation persistent, n (%)	35 (3.54)	29 (3.17)	NS
Internal carotid artery stenosis, n (%)	60 (6.07)	83 (9.06)	0.013
COPD, n (%)	53 (5.36)	56 (6.11)	NS
Chronic renal failure, n (%)	52 (5.26)	57 (6.22)	NS
Acute renal failure, n (%)	0 (0.0)	6 (0.66)	0.032
Extracardiac arteriopathy, n (%)	160 (16.19)	179 (19.54)	NS
Operative risk			
EuroScore Logistic 2 [%] (mean ± SD)	2.05±2.23	2.63±3.88	<0.001
Preoperative factors			
Ejection fraction [%] (mean ± SD)	46.85±9.9	46.86±10.11	NS
CKMB [U/L] (mean ± SD)	25.10±24.38	37.76±100.09	NS

(*Continued*)

Table 4 (*Continued*)

Data	Intubation time		
	≤12 hours (n=988)	>12 hours (n=916)	*P*-value
Hemoglobin [mmol/L] (mean ± SD)	8.57±0.93	8.40±0.96	<0.001
Creatinine [mg/dL] (mean ± SD)	0.98±0.58	1.06±0.77	0.004
GFR [mL/min/1.73 m^2] (mean ± SD)	83.24±25.76	76.65±31.01	<0.001
Intraoperative factors			
CPB time [min] (mean ± SD)	50.29±14.23	50.81±18.60	NS
Aortic cross-clamping time [min] (mean ± SD)	30.54±9.65	29.74±9.48	NS
Reoperation, n (%)	19 (1.92)	59 (6.44)	<0.001
Intraoperative hemofiltration, n (%)	160 (16.19)	212 (23.14)	<0.001
Postoperative factors			
CKMB day 1 [U/L] (mean ± SD)	56.19±58.75	81.20±167.04	NS
Drainage day 1 [mL] (mean ± SD)	454.27±303.23	502.10±472.26	NS
Creatinine [highest] day 1 [mg/dL] (mean ± SD)	1.22±0.91	1.42±1.02	<0.001
Hemoglobin day 1 [mmol/L] (mean ± SD)	42.63±10.18	43.45±12.38	NS
GFR [lowest] day 1 [mL/min/1.73 m^2] (mean ± SD)	73.06±24.67	61.46±25.40	<0.001
PRBC transfusion, units (mean ± SD)	2.65±1.72	3.29±2.38	<0.001

Abbreviations: BMI, body mass index; CK, creatinine kinase MB fraction; CPB, cardio-pulmonary bypass; FFP, fresh frozen plasma; GFR, glomerular filtration rate; n, number of patients; NS, not significant; NYHA, New York Heart Association; PTCA, percutaneous coronary angioplasty; PRBC, packed red blood cells.

length of ICU or hospital stay, but was associated only with increases in the occurrence of postoperative delirium (OR 1.580, 95% CI 1.188–2.102, *P*=0.003) and postoperative hemofiltration due to acute kidney injury (OR 1.302, 95% CI 1.023–1.657, *P*=0.032).

Discussion

The length of intubation and mechanical ventilation after cardiac surgery is a balance between the necessity to extubate the patient early to allow spontaneous breathing and regaining of respiratory independence and the risk of extubating

Table 5 Postoperative complications and mortality for patients intubated ≤12 and >12 hours

Postoperative outcomes	Intubation time		
	≤12 hours (n=988)	>12 hours (n=916)	*P*-value
Primary outcome			
Mortality at 30 days, n (%)	20 (2.02)	42 (4.59)	0.002
Hospital LOS, days (mean ± SD)	7.68±4.49	9.65±12.63	<0.001
ICU LOS, days (mean ± SD)	2.39±2.00	3.30±6.07	<0.001
Secondary outcome			
Stroke, n (%)	10 (1.01)	30 (3.28)	<0.001
TIA, n (%)	8 (0.81)	10 (1.09)	0.69
Delirium, n (%)	96 (9.72)	155 (16.92)	<0.001
Seizures, n (%)	1 (1.01)	7 (0.76)	0.06
Cardiogenic shock, n (%)	10 (1.01)	28 (3.06)	0.003
Pneumonia, n (%)	18 (1.82)	53 (5.79)	<0.001
Respiratory failure, n (%)	34 (3.44)	82 (8.95)	<0.001
AKI, n (%)	28 (2.83)	64 (6.99)	<0.001
AKI requiring hemofiltration, n (%)	36 (3.64)	90 (9.83)	<0.001
Atrial fibrillation, n (%)	197 (19.94)	201 (21.94)	NS
Sepsis, n (%)	2 (0.20)	3 (0.33)	NS

Abbreviations: AKI, acute kidney injury; ICU, intensive care unit; LOS, length of stay; n, number of patients; NS, not significant; *P*, statistical significance; TIA, transient ischaemic attack.

Table 6 Univariate and multivariate analysis for intubation longer than 12 hours after CABG

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	***P*-value**	**OR (95% CI)**	***P*-value**
Primary outcomes				
Mortality 30 days, n (%)	2.326 (1.355–3.992)	0.002	1.248 (0.628–2.480)	NS
Hospital LOS (mean ± SD)	1.044 (1.024–1.063)	<0.001	1.017 (0.996–1.034)	NS
ICU LOS (mean ± SD)	1.075 (1.034–1.119)	<0.001	1.030 (0.991–1.071)	NS
Secondary outcomes				
Stroke, n (%)	3.312 (1.610–6.813)	0.001	1.416 (0.642–3.125)	NS
Delirium, n (%)	1.893 (1.441–2.485)	<0.001	1.548 (1.161–2.064)	0.003
Cardiogenic shock, n (%)	3.084 (1.489–6.385)	0.002	1.813 (0.800–4.107)	NS
Pneumonia, n (%)	3.310 (1.924–5.693)	<0.001	1.584 (0.844–2.974)	NS
Respiratory failure, n (%)	2.759 (1.830–4.159)	<0.001	1.159 (0.683–1.968)	NS
Acute Kidney Injury (AKI), n (%)	2.575 (1.636–4.054)	<0.001	1.158 (0.643–2.085)	NS
AKI requiring hemofiltration, n (%)	1.558 (1.240–1.959)	<0.001	1.302 (1.023–1.657)	0.032
Heart failure, n (%)	2.881 (1.936–4.288)	<0.001	1.349 (0.779–2.337	NS

Abbreviations: CABG, coronary artery bypass grafting; n, number of patients; ICU, intensive care unit; LOS, length of stay; *P*, statistical significance.

too early and causing atelectasis and secondary respiratory failure and re-intubation.

The results of our pragmatic analysis indicate that the risk of postoperative complications does not increase until the intubation time exceeds 12 hours. The majority of the patients were extubated within 12 hours (52.5%) and only 3.7% remained intubated after 24 hours. Shorter intubation time was seen in younger patients, men, with higher BMI and more often in smokers. The multivariate analysis showed that intubation exceeding 12 hours after CABG does not increase the risk of 30-day mortality or length of ICU or hospital stay, but increases the occurrence of postoperative delirium and postoperative hemofiltration due to acute kidney injury.

Not surprisingly, shorter intubation time is seen in younger patients. Many studies reported that age is a significant predictor of delayed extubation with older patients having longer intubation times.[20–23] In a study by Shahbazi and Kazerooni, age was the only predictive factor for delayed extubation.[23] Suematsu et al has shown that age above 70 years was a predictor for delayed extubation time.[22] In a study by Cislaghi et al, age above 65 years was associated with prolonged mechanical ventilation in patients undergoing cardiac surgery.[20,21]

Shorter intubation times in patients who are overweight or obese comply with the obesity paradox, with increasing BMI being a protective factor associated with improved outcome after cardiac surgery.[24–26] According to Stamou et al, the hospital outcome and survival were better for overweight patients undergoing cardiac surgery when compared with patients with normal BMI.[24] A cohort study and meta-analysis performed by Mariscalco et al showed that obesity was associated with lower risks for cardiac surgery patients, excluding reverse causation.[25]

This is the first study to show that intubation time is shorter in patients who are active smokers. Intuitively, smoking should be associated with worse postoperative outcome, being a risk factor for complications after cardiac surgery. It has been reported that cessation of smoking over 1 month prior to cardiac surgery may gradually improve ciliary function and macrophage phagocytic function, decrease the amount of sputum, resulting in the reduction of postoperative pulmonary complications in a few weeks.[27,28] The relationship between smoking and extubation time in cardiac surgery was reported by Ji et al.[29] Persistent smokers had a higher incidence of pulmonary complications following CABG when compared with non-smokers. Smoking cessation more than 1 month before surgery was expected to reduce early major morbidities following CABG surgery.[29] Contrary to our findings, the smoking group in the study by Ji et al had a significantly higher incidence of postoperative pulmonary complications (7.1% vs 4.5%, $P=0.0010$) and significantly longer duration of mechanical ventilation (9.8±2.6 hour vs 9.4±2.4 hour, $P<0.0001$) when compared with the non-smoking group.[29]

Association with sex was also seen in many previous studies, indicating that men perform better after cardiac surgery.[20] Studies have shown that female sex may be a non-modifiable risk factor for prolonged intubation after cardiac surgery.[30]

The rate of postoperative complications increases with the length of intubation time. According to Heringlake et al, postoperative intubation time prolongation was associated with AKI in cardiac surgical patients.[31] Our results indicated that

intubation exceeding 12 hours may be associated with AKI requiring hemofiltration (usually due to decreased diuresis and/or fluid overload). Oliver et al hypothesized that perioperative hemofiltration and steroids may attenuate the inflammatory response during CPB, but only hemofiltration reduced time to tracheal extubation for adults after CABG.[32]

This is the first study to show directly that the intubation time over 12 hours increases the risk of postoperative delirium, a well-recognized complication of cardiac surgery.[33] Previous studies have shown that delirium was associated with prolonged ventilation time after cardiac surgery, but used a >24 hours intubation time-frame.[34–36] Jannati et al reported that the ventilator time was associated with delirium during the first 24 hours after cardiac surgery.[34] Kazmierski et al identified prolonged intubation as a risk factor for delirium, yet again this involved intubation >24 hours.[35] Kobayashi et al indicated that intubation duration of 88.3±212.5 hours vs 37.2±92 hours (P=0.0296) was associated with delirium after CABG in patients aged over 75 years.[36]

Studies performed in the 1990s have shown that intubation exceeding 24 hours (prolonged intubation) is associated with increased mortality and morbidity after cardiac surgery.[1,37,38] On the other side of the spectrum lies the shorter, 6-hour intubation time, associated with reduced risk of adverse postoperative events and decreased treatment cost.[1,39] The intermediate period between 6 and 24 hours has not been adequately studied and it is still unclear, what is the ideal time above which the patient deteriorates and their outcome worsens. The 6-hour STS target seems arbitrary. Current guidelines of intubation times should be revisited allowing for more liberal length of postoperative intubation, less aggressive ventilation weaning and extubation after CABG. According to Camp et al, a 9-hour threshold was advocated.[39] Crawford et al have shown that insignificant differences were observed in those extubated in 6–9 hours vs 0–6 hours nor in 9–12 hours vs 0–9 hours; an identical trend was observed for secondary outcomes of PLOS and reintubation.[14] According to Crawford et al, a 12-hour benchmark for maximum duration of intubation may be advisable as the new target in the vulnerable population.[14]

The major limitation of this study is its retrospective character, although data were collected prospectively and not all data were available in the dataset. The multitude of factors that contribute to the duration of intubation after cardiac surgery makes this analysis difficult and prone to bias. The definite strength of our study is a very large number of patients included and the pragmatic evaluation of risk factors for intubation time points in patients undergoing one of the most common surgical interventions worldwide.

Conclusion

The results of this real-life analysis of intubation practices after CABG indicate that earlier extubation occurs in younger patients, males, and surprisingly in smokers. Intubation exceeding 12 hours does not increase the risk of 30-day mortality or hospital and ICU LOS, but is associated with the risk of postoperative delirium and AKI requiring hemofiltration. This study is another voice in the discussion about the new extubation metric that should guide both cardiac anesthetists and surgeons to stratify the risk of prolonged intubation after cardiac surgery and to allocate the resources.

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Author contributions

KK provided the concept and design of the study, selection of the study group, collection of material, development and interpretation of research results, wrote the manuscript, collected literature, provided substantive supervision. AS was involved in the design of the study, performed statistical analysis, analyzed the results, was involved in revised the manuscript. ML designed the study, collected the data, analyzed the results, and provided critical revision of the manuscript. MK, KL, SD analyzed the results, collected literature and provided critical revision of the manuscript. MB, IR, and MŻ provided critical revision of the manuscript. All authors contributed to data analysis, drafting and revising the article, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflict of interest in this work.

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