Table 1. Baseline clinical and procedural characteristics (P0 vs P2)							
		CABG (N=872)			Valve (N=640)		
Variables	**Value**	**P0**	**P2**	***P*-value**	**P0**	**P2**	***P*-value**
Patient Age	n	151	721		174	466	
	mean	65.87±10.18	65.98±9.74	0.906	66.37±14.21	65.12±11.80	0.299
Sex	Female	39 (25.83%)	171 (23.72%)		55 (31.61%)	197 (42.27%)	0.014
	Male	112 (74.17%)	550 (76.28%)		119 (68.39%)	269 (57.73%)	
Predicted Morbidity or Mortality	mean	0.16±0.09	0.13±0.10	<.001	0.18±0.11	0.15±0.10	0.002
Predicted Risk of Mortality	mean	0.02±0.02	0.02±0.03	0.547	0.03±0.03	0.02±0.02	0.081
Predicted Prolonged Ventilation	mean	0.10±0.07	0.09±0.08	0.006	0.11±0.09	0.10±0.08	0.134
RF-Chronic Lung Disease	No	131 (86.75%)	599 (83.08%)	0.703	150 (86.21%)	389 (83.48%)	0.229
	Mild	12 (7.95%)	69 (9.57%)		13 (7.47%)	46 (9.87%)	
	Moderate	5 (3.31%)	21 (2.91%)		4 (2.30%)	15 (3.22%)	
	Severe	3 (1.99%)	21 (2.91%)		2 (1.15%)	12 (2.58%)	
	Lung disease, severity unknown	0 (0.00%)	10 (1.39%)		4 (2.30%)	4 (0.86%)	
	Unknown	0 (0.00%)	1 (0.14%)		1 (0.57%)	0 (0.00%)	
Classification-NYHA	Class I	25 (16.56%)	51 (7.07%)	0.021	27 (15.52%)	55 (11.80%)	<0.001
	Class II	47 (31.13%)	128 (17.75%)		63 (36.21%)	105 (22.53%)	
	Class III	28 (18.54%)	93 (12.90%)		43 (24.71%)	95 (20.39%)	
	Class IV	4 (2.65%)	21 (2.91%)		4 (2.30%)	14 (3.00%)	
	Not documented	0 (0.00%)	22 (3.05%)		0 (0.00%)	35 (7.51%)	
Hemo Data-EF	mean	50.89±11.60	51.10±11.69	0.841	57.38±11.03	58.81±9.70	0.133
Cross Clamp Time (min)	mean	67.44±20.60	69.11±21.05	0.393	67.13±24.32	76.96±30.43	<.001
Total Postoperative Ventilation Hours	median	11 (3 - 24)	6.22 (1.4 - 24)	<.001	10 (2 - 24)	6 (0 - 23)	<.001

Predicted risk of morbidity or mortality, predicted risk of mortality, and predicted prolonged ventilation are data points calculated from the Society of Thoracic Surgeons registry. They are computed for all patients undergoing cardiac surgery to estimate surgical risk.[i]
RF- Chronic lung disease denotes Risk Factor: Chronic lung disease is also defined by the STS as "whether the patient has chronic lung disease, and the severity level according to the following classification: No; Mild: FEV1 60% to 75% of predicted, or on chronic inhaled or oral bronchodilator therapy, Moderate: FEV1 50% to 59% of predicted, or on chronic oral/systemic steroid therapy aimed at lung disease, Severe: FEV1 < 50% or Room Air pO2 < 60 or pCO2 > 50. CLD present, severity not documented: Unknown"[ii]
Classification NYHA denotes the prevalence of heart failure symptoms as denoted by the New York Heart Association classification system.
Hemo Data EF refers to the preoperative left ventricular ejection fraction.

Table 2. Baseline clinical and procedural characteristics (P1 vs P2)							
		CABG (N=999)			Valve (N=652)		
Variables	**Value**	**P1**	**P2**	***P*-value**	**P1**	**P2**	***P*-value**
Patient Age	n	278	721		186	466	
	mean	65.96±9.60	65.98±9.74	0.984	65.47±12.18	65.12±11.80	0.733
Sex	Female	59 (21.22%)	171 (23.72%)	0.581	83 (44.62%)	197 (42.27%)	0.014
	Male	219 (78.78%)	550 (76.28%)		103 (55.38%)	269 (57.73%)	
Predicted Morbidity or Mortality	mean	0.16±0.10	0.13±0.10	<.001	0.16±0.09	0.15±0.10	0.337

Predicted Risk of Mortality	mean	0.02±0.02	0.02±0.03	0.749	0.02±0.03	0.02±0.02	0.880
Predicted Prolonged Ventilation	mean	0.10±0.07	0.09±0.08	<.001	0.11±0.09	0.10±0.08	0.801
RF-Chronic Lung Disease	n	151	721	0.703	174	466	0.229
	No	220 (79.14%)	599 (83.08%)	0.052	155 (83.33%)	389 (83.48%)	0.802
	Mild	41 (14.75%)	69 (9.57%)		17 (9.14%)	46 (9.87%)	
	Moderate	7 (2.52%)	21 (2.91%)		9 (4.84%)	15 (3.22%)	
	Severe	5 (1.80%)	21 (2.91%)		3 (1.61%)	12 (2.58%)	
	Lung disease, severity unknown	2 (0.72%)	10 (1.39%)		2 (1.08%)	4 (0.86%)	
	Unknown	3 (1.08%)	1 (0.14%)				
Classification-NYHA	Class I	45 (16.19%)	51 (7.07%)	<.001	36 (19.35%)	55 (11.80%)	<.001
	Class II	93 (33.45%)	128 (17.75%)		55 (29.57%)	105 (22.53%)	
	Class III	41 (14.75%)	93 (12.90%)		60 (32.26%)	95 (20.39%)	
	Class IV	10 (3.60%)	21 (2.91%)		5 (2.69%)	14 (3.00%)	
	Not documented	0 (0.00%)	22 (3.05%)		0 (0.00%)	35 (7.51%)	
Hemo Data-EF	mean	50.89±11.60	51.10±11.69	0.841	57.38±11.03	58.81±9.70	0.133
Cross Clamp Time (min)	mean	67.44±20.60	69.11±21.05	0.393	67.13±24.32	76.96±30.43	<.001
Total Postoperative Ventilation Hours	median	11 (3 - 24)	6.22 (1.4 - 24)	<.001	10 (2 - 24)	6 (0 - 23)	<.001

Table 3. Patient characteristics of samples used in logistic regressions (a binary outcome 'P0' VS 'P2')

		CABG (N=828)				**Valve (N=603)**			
Variables	**Value**	**P0**	**P2**	**Total**	***P*-value**	**P0**	**P2**	**Total**	***P*-value**
Patient Age	n	140	688	828		174	429	603	
	mean	65.61±10.33	65.87±9.83	65.82±9.91	0.784	66.37±14.21	64.97±11.72	65.38±12.49	0.25
Sex	Female	34 (24.29%)	167 (24.27%)	201 (24.28%)	0.997	55 (31.61%)	177 (41.26%)	232 (38.47%)	0.027
	Male	106 (75.71%)	521 (75.73%)	627 (75.72%)		119 (68.39%)	252 (58.74%)	371 (61.53%)	
Predicted Morbidity or Mortality	mean	0.16±0.08	0.13±0.10	0.13±0.10	<.001	0.18±0.11	0.15±0.10	0.16±0.10	0.002
Predicted Risk of Mortality	mean	0.02±0.02	0.02±0.03	0.02±0.02	0.843	0.03±0.03	0.02±0.02	0.02±0.03	0.075
Predicted Prolonged Ventilation	n	140	688	828		174	429	603	
	mean	0.10±0.07	0.08±0.08	0.09±0.07	0.004	0.11±0.09	0.10±0.08	0.10±0.08	0.123
RF-Chronic Lung Disease	No	123 (87.86%)	570 (82.85%)	693 (83.70%)	0.636	150 (86.21%)	358 (83.45%)	508 (84.25%)	0.275
	Mild	11 (7.86%)	67 (9.74%)	78 (9.42%)		13 (7.47%)	43 (10.02%)	56 (9.29%)	
	Moderate	4 (2.86%)	20 (2.91%)	24 (2.90%)		4 (2.30%)	13 (3.03%)	17 (2.82%)	
	Severe	2 (1.43%)	20 (2.91%)	22 (2.66%)		2 (1.15%)	11 (2.56%)	13 (2.16%)	
	Lung disease, severity unknown	0 (0.00%)	10 (1.45%)	10 (1.21%)		4 (2.30%)	4 (0.93%)	8 (1.33%)	

	Unknown	0 (0.00%)	1 (0.15%)	1 (0.12%)		1 (0.57%)	0 (0.00%)	1 (0.17%)	
Hemo Data-EF	mean	51.16±11.37	51.63±10.89	51.55±10.97	0.643	57.38±11.03	58.68±9.67	58.31±10.09	0.174
Cross Clamp Time (min)	mean	67.44±20.60	69.12±21.07	68.84±20.99	0.389	67.13±24.32	72.54±25.76	70.98±25.45	0.018
Total Postoperative Ventilation Hours	median	11 (4 - 24)	6.205 (1.4 - 24)	7 (1.4 - 24)	<.001	10 (2 - 24)	6 (0 - 23)	7 (0 - 24)	<.001

Appendix A:

Patients who had undergone isolated CABG surgery would be eligible for an early extubation if they met the following criteria: temperature between 35° and 39 °C, heart rate between 50 – 120 beats per min, systolic blood pressure between 95 and 200 mmHg receiving less than 4 units per hour of vasopressin and/or 8 micrograms per minute of norepinephrine, a left ventricular ejection fraction greater or equal to 40%, minimal post-operative bleeding, recovery from neuromuscular blockade, oxygen saturation greater than 94% on less than 7 cm H_2O of positive end expiratory pressure (PEEP), and a pH between 7.33 and 7.47. Patients with pre-existing pulmonary hypertension, a requirement for mechanical circulatory support, concern for graft ischemia, reoperative sternotomy, a known or suspected difficult intubation, a history of congenital heart surgery, neurologic impairment, or end stage renal disease were excluded.

Laboratory studies including a basic metabolic panel, complete blood count, arterial blood gas, mixed venous blood gas, PT/INR, and PTT were obtained and gross deficiencies were corrected. The laboratory oxygen saturation was correlated with the value from the pulse oximeter. Sedation infusions were stopped and and boluses of 25-50 micrograms of fentanyl were administered for a critical-care pain observation tool (CPOT) score of greater than 3. A green sign was placed on the patient's door displaying the time they arrived from the OR to the ICU with a target extubation time of four hours later. Mechanical ventilation settings were standardized to a tidal volume of 8 cc/kg and 5 cm H_2O of PEEP. The fraction of inspired oxygen was then titrated down to a goal of 40% or lower to maintain an oxygen saturation of greater than or equal to 92%. Once the patient's respiratory rate was greater than the set rate on the ventilator, a spontaneous breathing trial was started with pressure support of 10 cm, titrated for a tidal volume of 6-8 cc/kg with 5 cm H_2O PEEP. If the patient continued to meet weaning clinical criteria with a Rapid Shallowing Breathing Index (RSBI) of less than or equal to 105, a negative inspiratory force (NIF) test was performed. Patients with a NIF of less than or equal to -20 were then evaluated by a member of the house staff, physician assistant, or nurse practitioner and at their discretion, an order was given for extubation.

Appendix B

1. Univariate analysis

For statistical analysis, 5 categorical variables and 8 continuous variables were compared between three time periods (P0, P1 and P2) for CABG and Valve patients.

1.1. Categorical variables

The 5 catergorical variables are sex, Chronic Lung Disease classification, NYHA classification (NYHA), and Procedure type (procedure, CABG vs. Valve).

The associations between period (PI vs. P2) and other categorical variables were tested using Pearson's Chisq test.

As the p-value indicates, we can discover that the Chronic Lung disease Classification and NYHA classification are associated with period. However, the NYHA classification have a high missingness (about 50%).

1.2. Continuous variables

The 7 continuous variables are age, Predicted Morbidity or Mortality (PMM), Predicted Risk of Mortality (PRM), Predicted Prolonged Ventilation (PPV), Hemodynamic Data – Left Ventricular Ejection Fraction (Hemo), Cross Clamp Time (XCT), and Total Postoperative Ventilation Hours (TPVH). Descriptive statistics within P1 and P2 periods are shown below and boxplot and histogram attached at the end.

The associations between period and each continuous variable were tested using two-sample t-test.

2. Logistic regression

2.1.CABG patient

2.1.1.1.Model building for CABG patients comparing P2 to P0.

Due to a large missingness of NYHA (over 50% are missing), we did not consider variable NYHA. A backward model selection was performed. The confounding effect of the eliminated variable was also accessed (> 10% change of the TPVH coefficient) and non-confounding variables were eliminated.

Variable deleted in sequence	Highest P-value	Coefficient of TPVH before remove	Coefficient of TPVH after remove	Sample size
Age	0.988	-0.153	-0.153	828
Sex	0.633	-0.153	-0.153	828
Hemo	0.433	-0.153	-0.153	828
PPV	0.430	-0.153	-0.153	828
XCT (min)	0.400	-0.153	-0.152	828
Chronic Lung Disease classification	0.163	-0.152	-0.153	828

The covariates remained after backward selection are PMM and PRM. TPVH has a coefficient of -0.153 after adjusting for PMM and PRM, which means P2 associates with reduced TPVH after adjustment, for every hour decrease in TPVH, the odds of being in P2 is 1.165 comparing being in P0.

Variable (N = 999)	Coefficients	Standard Error	P-value
TPVH	-0.153	0.019	**<0.0001**
PMM	-8.382	2.135	**<0.0001**
PRM	47.732	12.089	**<0.0001**

PMM is negatively associated with P2. It means patients with higher PMM are more likely to be in P0, which is consistent with the descriptive statistics.

PRM is positively associated with P2. It means patients with higher PRM are more likely to be in P2, which is consistent with descriptive statistics.

2.2. Valve patient

2.2.1. Logistic regression

2.2.1.1. Model building for Valve patients comparing P2 to P0.

For Valve patients, the remained covariates after backward selection are PMM, PPV, age and XCT. The coefficient of TPVH is -0.160 after adjusting for PMM, PPV, age and XCT, which means P2 is associated with reduced TPVH after adjustment, for every hour decrease in TPVH, the odds of being in P2 is 1.165 comparing being in P0.

Variable (N = 603)	Coefficients	Standard Error	P-value
TPVH	-0.160	0.020	<0.0001
Age	0.024	0.009	0.007
PMM	-27.430	4.955	<0.0001
PPV	31.809	6.122	<0.0001
XCT (min)	0.018	0.005	<0.0001

2.3. One single logistic model for CABG and Valve

In order to have the same model for CABG and Valve, we used union of the covariates selected in CABG and in Valve: PMM, PRM, PPV, and XCT. Logistic model for CABG patient

For CABG patients

Variable (N = 828)	Coefficients	Standard Error	Odds Ratio	P-value
TPVH	-0.152	0.019	0.467	0.0002
Age	-0.002	0.012	0.976	0.833
PMM	-6.635	3.419	0.936	0.052
PRM	52.557	14.482	1.691	0.0003
PPV	-3.389	4.485	0.967	0.484
XCT (min)	-0.004	0.005	1.141	0.361

The odds of being in P2 is 0.467 for every 5-hour increase in TPVH.
The odds of being in P2 is 0.976 for every 10-year increase in age.
The odds of being in P2 is 0.936 for every 0.01 unit increase in PMM.
The odds of being in P2 is 1.691 for every 0.01 unit increase in PRM.
The odds of being in P2 is 0.967 for every 0.01 unit increase in PPV.
The odds of being in P2 is 1.141 for every 30 minutes increase in XCT.

For ABG patients, simple logistic regression without adjusting for covariates

Variable (N = 828)	Coefficients	Standard Error	Odds Ratio	P-value
TPVH	-0.148	0.018	0.477	<0.0001

The coefficient of TPVH after adjusting age, PMM, PRM, PPV and XCT does not change much comparing to that of simple logistic model.

New descriptive table within the subset of N=953 patients for CABG with complete information on Period and covariates.

Variable (Continuous)		P1 (N=264)	P2 (N=689)	Total (N=953)	P-value
Age		264	689	953	0.86
	Mean±SD	66.00±9.72	65.88±9.83	65.91±9.79	
	Median	67	67	67	
	Range	(35 - 89)	(28 - 90)	(28 - 90)	
PMM		264	689	953	**<0.0001**
	Mean±SD	0.1569±0.0937	0.1279±0.0965	0.1359±0.0965	
	Median	0.1334	0.0984	0.1068	
	Range	(0.0433 - 0.6736)	(0.0241 - 0.6285)	(0.0241 - 0.6736)	
PRM		264	689	953	0.55
	Mean±SD	0.0182±0.0199	0.0173±0.0254	0.0175±0.0240	
	Median	0.0117	0.0103	0.0109	
	Range	(0.0024 - 0.1658)	(0.0023 - 0.3025)	(0.0023 - 0.3025)	
PPV		264	689	953	**0.0001**
	Mean±SD	0.1054±0.0772	0.0840±0.0760	0.0899±0.0769	
	Median	0.0856	0.0595	0.0664	
	Range	(0.0249 - 0.5953)	(0.0116 - 0.5584)	(0.0116 - 0.5953)	
XCT (min)		264	689	953	0.11
	Mean±SD	71.6±22.25	69.11±21.05	69.80±21.41	
	Median	69.00	67.00	68.00	
	Range	(25 - 149)	(12 - 181)	(12 - 181)	
TPVH		264	689	953	**<0.0001**
	Mean±SD	10.02±4.80	7.84±4.73	8.44±4.85	
	Median	9.00	6.22	7.00	
	Range	(0 - 24)	(0 - 24)	(0 - 24)	

* P-value of t-test for association with period. Significant p-value (<0.05) are indicated in bold

2.3.1. Logistic model for Valve patient

Variable (N = 603)	Coefficients	Standard Error	Odds Ratio	P-value
TPVH	-0.161	0.020	0.447	**<0.0001**
Age	0.026	0.009	1.297	**0.005**
PMM	-26.876	4.990	0.764	**<0.0001**
PRM	-7.138	9.092	0.931	0.432
PPV	32.966	6.347	1.390	**<0.0001**
XCT (min)	0.019	0.005	1.754	**<0.0001**

The odds of being in P2 is 0.447 for every 5-hour increase in TPVH.
The odds of being in P2 is 1.297 for every 10-year increase in age.
The odds of being in P2 is 0.764 for every 0.01 unit increase in PMM.
The odds of being in P2 is 0.931 for every 0.01 unit increase in PRM.
The odds of being in P2 is 1.390 for every 0.01 unit increase in PPV.

The odds of being in P2 is 1.754 for every 30 minutes increase in XCT.

2.3.2. Simple logistic regression over same sample

Variable (N = 603)	Coefficients	Standard Error	Odds Ratio	P-value
TPVH	-0.149	0.018	0.475	<0.0001

From both simple and multiple logistic regressions, we can observe that the TPVH are significantly different between period 0 and period 2 within valve procedure patients.

The magnitude of the association between TPVH and period changed from OR=0.475 to OR=0.447 after adjusting for covariates (Age, PMM, PRM, PPV, and XCT).

New descriptive table within the subset of N=603 patients for Valve with complete information on Period and covariates.

Variable (Continuous)		P1 (N=174)	P2 (N=429)	Total (N=603)	P-value
Age		174	429	603	0.75
	Mean±SD	65.31±11.92	64.97±11.72	65.07±11.77	
	Median	68	67	68	
	Range	(28 - 88)	(22 - 90)	(22 - 90)	
PMM		174	429	603	0.32
	Mean±SD	0.1597±0.0858	0.1516±0.0999	0.1539±0.0960	
	Median	0.1361	0.1237	0.1289	
	Range	(0.0525 - 0.5964)	(0.0308 - 0.6907)	(0.0308 - 0.6907)	
PRM		174	429	603	0.85
	Mean±SD	0.0236±0.0286	0.0231±0.0240	0.0232±0.0254	
	Median	0.0162	0.0162	0.0162	
	Range	(0.0025 - 0.2421)	(0.0022 - 0.2200)	(0.0022 - 0.2421)	
PPV		174	429	603	0.84
	Mean±SD	0.0976±0.0694	0.0990±0.0834	0.0986±0.0795	
	Median	0.0778	0.0722	0.0747	
	Range	(0.0227 - 0.4759)	(0.0163 - 0.6378)	(0.0163 - 0.6378)	
XCT (min)		174	429	603	0.02
	Mean±SD	67.74±21.62	72.54±25.76	71.15±24.71	
	Median	64.00	66.00	65.00	
	Range	(35 - 154)	(34 - 178)	(34 - 178)	
TPVH		174	429	603	**0.0002**
	Mean±SD	8.93±4.59	7.36±4.77	7.81±4.77	
	Median	8.00	6.00	6.07	
	Range	(2 - 24)	(0 - 23)	(0 - 24)	

2.4. Test for Interaction TPVH*Surgical Procedure

To test if there is a significant TPVH reduction from P0 to P2 between CABG patients and valve patients, we pooled the patients with complete information from the previous two models (N =

802+603 = 1405) and perform a logistic regression model with interaction between TPVH and surgical procedure (CABG vs. Valve).

Variable (N =1405)	Coefficients	Standard Error	P-value
TPVH	-0.144	0.018	**<0.0001**
Age	0.013	0.007	0.053
PMM	-14.837	3.092	**<0.0001**
PRM	11.834	6.210	0.057
PPV	14.565	3.985	**0.0003**
XCT (min)	0.011	0.003	**0.0007**
Procedure (Valve)	-0.572	0.299	0.055
TPVH * Procedure (Valve)	0.014	0.026	0.596

The TPVH*surgical procedure is not statistically significant, which means the TPVH reduction from P0 to P2 is not significantly different between CABG patients and valve patients.

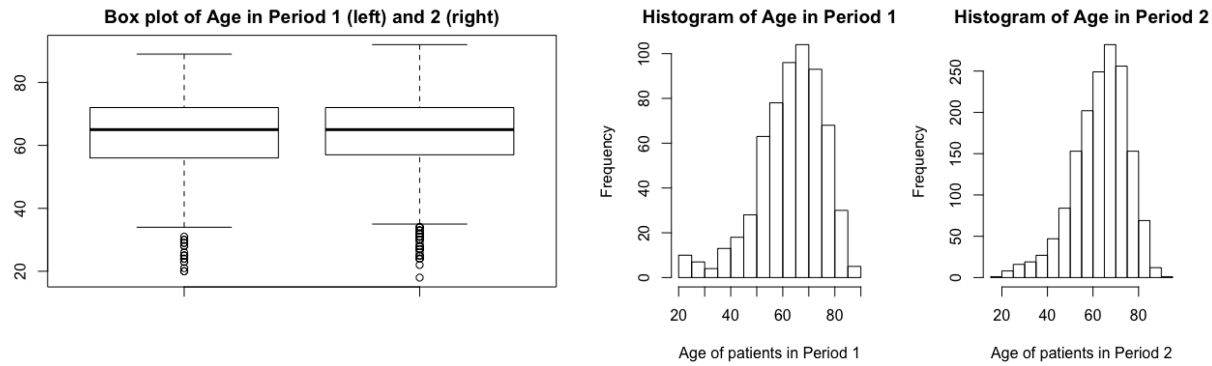
2.5. Combined model

We finally introduce the surgical procedure type (procedure) as a categorical variable (CABG vs. Valve) into the multivariate logistic regression.

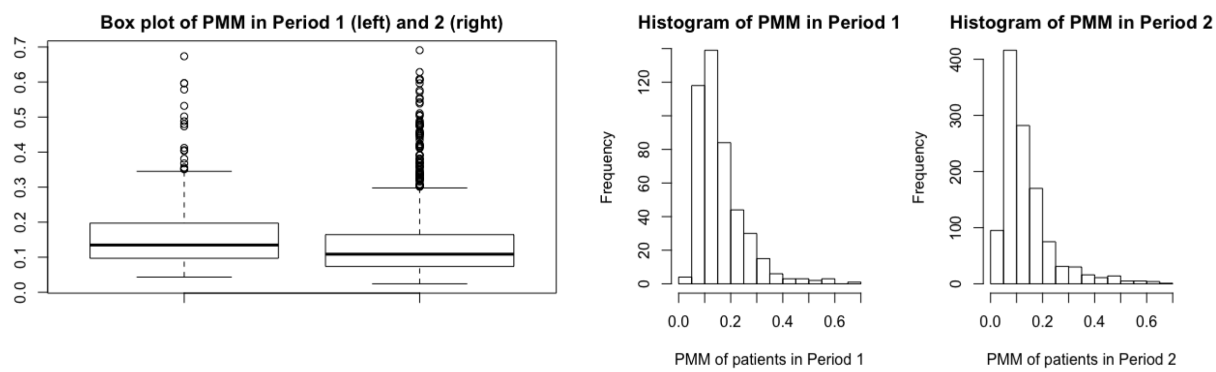
Variable (N = 1405)	Coefficients	Standard Error	Odds Ratio	P-value
TPVH	-0.151	0.014	0.470	**<0.0001**
Age	0.013	0.007	1.142	0.057
PMM	-14.825	3.091	0.862	**<0.0001**
PRM	11.771	6.184	1.125	0.057
PPV	14.579	3.981	1.157	**0.0003**
XCT (min)	0.011	0.003	1.375	**0.0008**
Procedure (Valve)	-0.710	0.146	2.034	**<0.0001**

The odds of being in P2 is 0.470 for every 5-hour increase in TPVH.
The odds of being in P2 is 1.142 for every 10-year increase in age.
The odds of being in P2 is 0.862 for every 0.01 unit increase in PMM.
The odds of being in P2 is 1.125 for every 0.01 unit increase in PRM.
The odds of being in P2 is 1.157 for every 0.01 unit increase in PPV.
The odds of being in P2 is 1.375 for every 30 minutes increase in XCT.
The odds of being in P2 is 2.034 for patients received Valve procedure vs. CABG procedure.

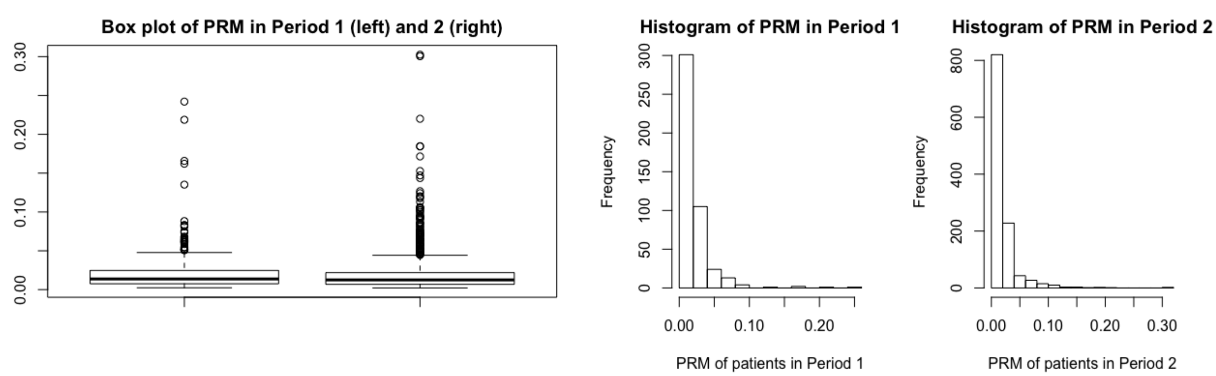
Age by Period



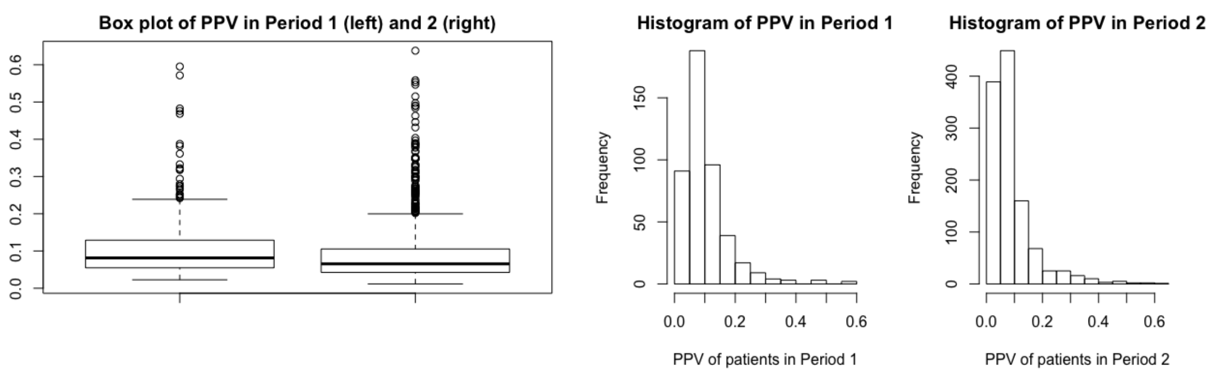
Predicted Morbidity or Mortality by Period



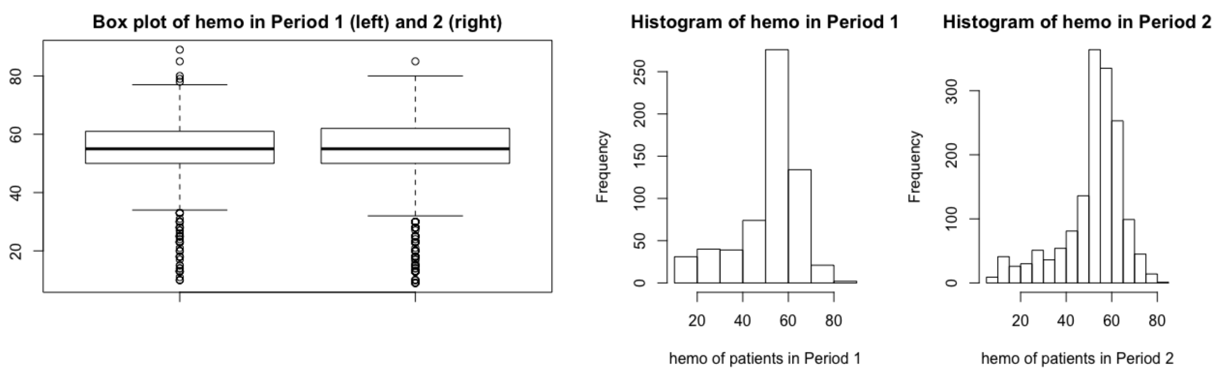
Predicted Risk of Mortality by Period



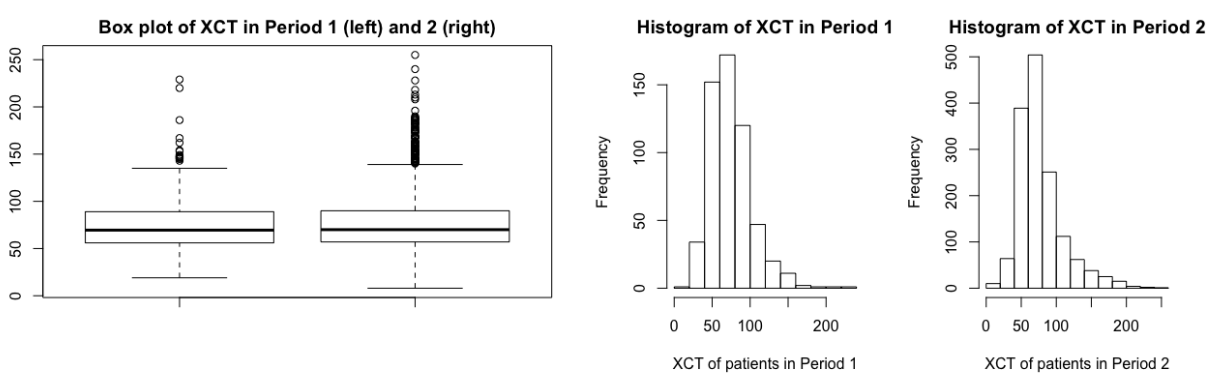
Predicted Prolonged Ventilation by period



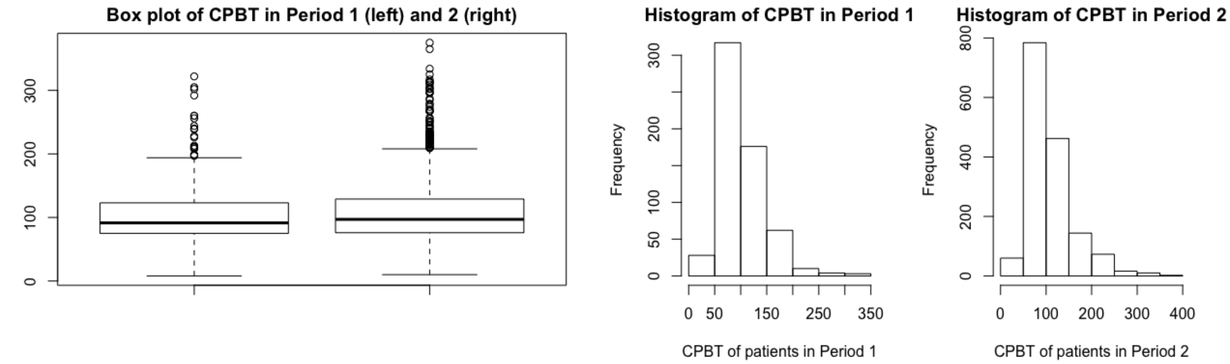
Hemo Data-EF by Period



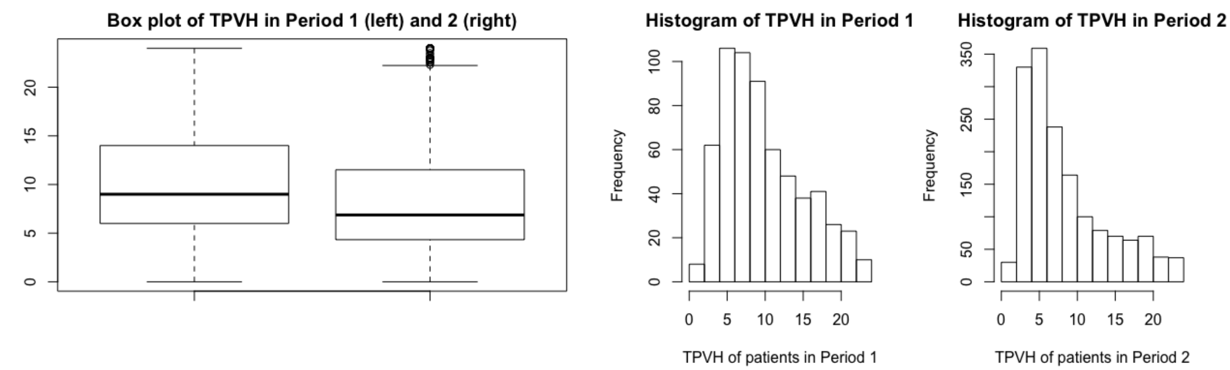
Cross clamp time (XCT) by Period



Cardiopulmonary Bypass Time (CPBT) by Period



Total Postoperative Ventilation Hour (TPVH) by Period



Appendix C

Interrupt time series analysis

Content:

Description

Time period:

P0, P1, and P2

Patients group:

CAB and Valve

Outcome variable:

Post-operative ventilation time

Plot

Analysis

Part 1: Single Interrupt Time Series Analysis (SITSA)

P0 vs P1, P1 vs P2 and P0 vs P2 for CAB only and Valve only separately.

Part 2. Multiple Interrupt Time Series Analysis (MITSA)

P0 vs P1, P1 vs P2 and P0 vs P2 for comparison of CAB (as control) and Valve.

Description:

Three time periods:

P0: 07/2015-12/2015 Pre-intervention

P1: 01/2016-08/2016 Intervention tuning

P2: 09/2016-05/2018 Intervention implementation

Patients group:

CAB

Valve

Outcome variable:

1. Excluded the patients with a post-operative ventilation time over 24hours.
2. Calculated monthly median ventilation time of patients within 24 hours.

Analysis

Part 1. Single Interrupt Time Series Analysis (SITSA)

$$y = \alpha + \beta_1 T + \beta_2 X + \beta_3 XT + \varepsilon$$

T: time
X: Period (P0, P1, P2)
TX: Time and period interaction with modification.

The primary coefficients of interest are β2 and β3 (for X and XT) which respectively indicate the change in level from pre- to post-interruption and the change in slope from pre- to post-interruption (Penfold & Zhang, 2013).

The post-interruption slope can be determined by summing coefficients β1 and β3 (Linden, 2015) with statistical significance obtained using post-estimation procedures.

P0 vs P1
CAB

Parameter	Interpretation	Estimate	StdErr	prob
b0	Intercept	10.86667	0.8373	<.0001
b1	Pre- Trend	0.157143	0.2150	0.4816
b2	Post- Level Change	-0.05952	0.9564	0.9516
b3	Post- Trend Change	-0.78214	0.2559	0.0121
b1+b3	Post- Trend	-0.625	0.1388	<.0001

Valve

Parameter	Interpretation	Estimate	StdErr	prob
b0	Intercept	9.366667	1.2922	<.0001
b1	Pre- Trend	0.3	0.3318	0.3872
b2	Post- Level Change	-1.38095	1.4762	0.3716
b3	Post- Trend Change	-0.71071	0.3949	0.1021
b1+b3	Post- Trend	-0.41071	0.2142	0.0552

P1 vs P2

CAB

Parameter	Interpretation	Estimate	StdErr	prob
b0	Intercept	11.75	0.6240	<.0001
b1	Pre- Trend	-0.625	0.1236	<.0001
b2	Post- Level Change	0.109286	0.6313	0.8640
b3	Post- Trend Change	0.584481	0.1269	0.0001
b1+b3	Post- Trend	-0.04052	0.0289	0.1603

Valve

Parameter	Interpretation	Estimate	StdErr	prob
b0	Intercept	9.785714	0.7737	<.0001
b1	Pre- Trend	-0.41071	0.1532	0.0128
b2	Post- Level Change	-0.52905	0.7827	0.5053
b3	Post- Trend Change	0.406753	0.1573	0.0159
b1+b3	Post- Trend	-0.00396	0.0358	0.9119

P0 vs P2

CAB

Parameter	Interpretation	Estimate	StdErr	prob
b0	Intercept	10.86667	0.8788	<.0001
b1	Pre- Trend	0.157143	0.2257	0.4932
b2	Post- Level Change	-4.95024	0.8058	<.0001
b3	Post- Trend Change	-0.19766	0.2282	0.3954
b1+b3	Post- Trend	-0.04052	0.0340	0.2336

Valve

Parameter	Interpretation	Estimate	StdErr	prob
b0	Intercept	9.366667	1.0569	<.0001
b1	Pre- Trend	0.3	0.2714	0.2804
b2	Post- Level Change	-5.19571	0.9691	<.0001
b3	Post- Trend Change	-0.30396	0.2745	0.2795
b1+b3	Post- Trend	-0.00396	0.0409	0.9229

Part 2. Multiple Interrupt Time Series Analysis (MITSA)

$$y = \alpha + \beta_1 T + \beta_2 X_t + \beta_3 XT + \beta_4 Z + \beta_5 ZT + \beta_6 ZX + \beta_7 ZXT + \varepsilon$$

T: time
X: Period (P0, P1, P2)
TX: Time and period interaction with modification
Z: Indicator of treatment and control (CAB as control = 0, Valve as treatment =1)
ZT: Interaction of treatment and time with modification
ZX: Interaction of treatment and period with modification
ZXT: Interaction of treatment , time and period with modification

Coefficients β1 to β3 reflect properties of the control series as described in Eq 1, and all other variables are as described in Eq 1. Coefficients β4 and β5 indicate level and slope differences, respectively, between treatment and control series during the pre-interruption phase. Where series are comparable prior to the interruption, these coefficients will be non-significant (e.g., $p > 0.05$).
β6 indicates the difference in level between treatment and control series in the post-interruption phase, while β7 indicates the change in slope difference between treatment and control series from pre- to post-interruption (a “difference-in-differences of slopes” (Linden, 2015)).

P0 vs P1
CAB as control

Parameter	Interpretation	Estimate	StdErr	Probt
b0	Intercept	10.86667	1.0888	<.0001
b1	Control Pre- Trend	0.157143	0.2796	0.5803
b2	Control Post- Level Change	-0.05952	1.2437	0.9623
b3	Control Post- Trend Change	-0.78214	0.3328	0.0291
b4	Treatment/Control Pre- Level Difference	-1.5	1.5398	0.3416
b5	Treatment/Control Pre- Trend Difference	0.142857	0.3954	0.7216
b6	Treatment/Control Post- Level Difference	-1.32143	1.7589	0.4612
b7	Treatment/Control Change in Slope Difference Pre- to Post-	0.071429	0.4706	0.8809

P1 vs P2
CAB as control

Parameter	Interpretation	Estimate	StdErr	Probt
b0	Intercept	11.75	0.7028	<.0001
b1	Control Pre- Trend	-0.625	0.1392	<.0001
b2	Control Post- Level Change	0.109286	0.7110	0.8785
b3	Control Post- Trend Change	0.584481	0.1429	0.0002
b4	Treatment/Control Pre- Level Difference	-1.96429	0.9939	0.0537
b5	Treatment/Control Pre- Trend Difference	0.214286	0.1968	0.2815
b6	Treatment/Control Post- Level Difference	-0.63833	1.0056	0.5284
b7	Treatment/Control Change in Slope Difference Pre- to Post-	-0.17773	0.2021	0.3834

P0 vs P2
CAB as control

Parameter	Interpretation	Estimate	StdErr	Probt
b0	Intercept	10.86667	0.9719	<.0001
b1	Control Pre- Trend	0.157143	0.2496	0.5320
b2	Control Post- Level Change	-4.95024	0.8912	<.0001
b3	Control Post- Trend Change	-0.19766	0.2524	0.4376
b4	Treatment/Control Pre- Level Difference	-1.5	1.3745	0.2808
b5	Treatment/Control Pre- Trend Difference	0.142857	0.3530	0.6875
b6	Treatment/Control Post- Level Difference	-0.24548	1.2603	0.8464
b7	Treatment/Control Change in Slope Difference Pre- to Post-	-0.1063	0.3569	0.7672

[i] Shahian DM, Jacobs JP, Badhwar V, Kurlansky PA, Furnary AP, Cleveland JC Jr, Lobdell KW, Vassileva C, Wyler von Ballmoos MC, Thourani VH, Rankin JS, Edgerton JR, D'Agostino RS, Desai ND, Feng L, He X, O'Brien SM. The Society of Thoracic Surgeons 2018 Adult Cardiac Surgery Risk Models: Part 1-Background, Design Considerations, and Model Development. Ann Thorac Surg. 2018 May;105(5):1411-1418.

[ii] Ibid