Effect of venoarterial extracorporeal membrane oxygenation initiation timing on tricuspid valve surgery outcomes

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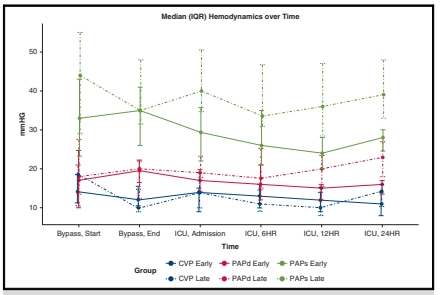
ABSTRACT

Objectives: Tricuspid valve surgery is associated with high rates of shock and in-hospital mortality. Early initiation of venoarterial extracorporeal membrane oxygenation after surgery may provide right ventricular support and improve survival. We evaluated mortality in patients undergoing tricuspid valve surgery based on the timing of venoarterial extracorporeal membrane oxygenation.

Methods: All consecutive adult patients undergoing isolated or combined surgical tricuspid valve repair or replacement from 2010 to 2022 requiring venoarterial extracorporeal membrane oxygenation use were stratified by initiation in the operating room (Early) versus outside of the operating room (Late). Variables associated with in-hospital mortality were explored using logistic regression.

Results: There were 47 patients who required venoarterial extracorporeal membrane oxygenation: 31 Early and 16 Late. Mean age was 55.6 years (standard deviation, 16.8), 25 (54.3%) were in New York Heart Association class III/IV, 30 (60.8%) had left-sided valve disease, and 11 (23.4%) had undergone prior cardiac surgery. Median left ventricular ejection fraction was 60.0% (interquartile range, 45-65), right ventricular size was moderately to severely increased in 26 patients (60.5%), and right ventricular function was moderately to severely reduced in 24 patients (51.1%). Concomitant left-sided valve surgery was performed in 25 patients (53.2%). There were no differences in baseline characteristics or invasive measurements immediately before surgery between the Early and Late groups. Venoarterial extracorporeal membrane oxygenation was initiated 194 (23.0-840.0) minutes after cardiopulmonary bypass in the Late venoarterial extracorporeal membrane oxygenation group. In-hospital mortality was 35.5% (n = 11) in the Early group versus 68.8% (n = 11) in the Late group ($P = .037$). Late venoarterial extracorporeal membrane oxygenation was associated with in-hospital mortality (odds ratio, 4.00; 1.10-14.50; $P = .035$).

Conclusions: Early postoperative initiation of venoarterial extracorporeal membrane oxygenation after tricuspid valve surgery in high-risk patients may be associated with improvement in postoperative hemodynamics and in-hospital mortality. (JTCVS Open 2023;14:171-81)



Comparison of hemodynamics in Early and Late VA-ECMO groups.

CENTRAL MESSAGE

Early postoperative initiation of VA-ECMO after TV surgery in high-risk patients may be associated with improvement in postoperative hemodynamics and in-hospital mortality.

PERSPECTIVE

Prior studies detail the benefit of VA-ECMO after TV surgery, but none discuss VA-ECMO initiation timing. The current analysis supports early, proactive initiation of VA-ECMO due to the improved clinical and hemodynamic outcomes without a corresponding increase in complications compared with a later, more reactive approach.

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Abbreviations and Acronyms

IQR = interquartile range
LVEF = left ventricular ejection fraction
OR = odds ratio
PAP = pulmonary artery pressure
RV = right ventricle
RVEDV = right ventricular end-diastolic volume
SD = standard deviation
TR = tricuspid regurgitation
TV = tricuspid valve
VA-ECMO = venoarterial extracorporeal membrane oxygenation
VIS = Vasoactive Inotrope Score

Tricuspid regurgitation (TR) is common[1] and associated with increased mortality independent of concomitant cardiac comorbidities.[2] Although rates of tricuspid valve (TV) surgery have been increasing nationally, TV surgery remains associated with a high incidence of postoperative shock and mortality in both multivalve and isolated TV surgeries.[3,4]

One potential means of mitigating the effect of postoperative shock and its morbid sequelae is the use of venoarterial extracorporeal membrane oxygenation (VA-ECMO) after cardiac surgery. In the setting of hemodynamic compromise after TV surgery, VA-ECMO support may prevent end-organ ischemia and reduce common postoperative complications, including multisystem organ failure.[4] However, VA-ECMO carries its own set of complications including bleeding and stroke.[5] Although survival among patients put on VA-ECMO for postcardiotomy shock has improved since its inception in 1973,[6] in-hospital mortality remains high, at an estimated 25% to 52%.[7]

Early initiation of VA-ECMO has been shown in prior studies to improve survival in other cardiac operations;[6,8,9] however, no definitive conclusions have been drawn regarding the benefit of early VA-ECMO in the setting of TV surgery.[10] Early initiation, that is, the immediate transfer from cardiac bypass to VA-ECMO in the operating room, compared with late initiation (after transfer to the intensive care unit), is theoretically appealing in the setting of TV surgery given that the right ventricle (RV) is poorly equipped to handle acute increases in afterload seen with acute resolution of TR.

The goal of this study was to determine the association between in-hospital mortality and early versus late VA-ECMO initiation after TV surgery complicated by cardiogenic shock. We hypothesized that early initiation of VA-ECMO would be associated with lower in-hospital mortality due to the prevention of end-organ hypoperfusion and more rapid improvement of right-sided cardiac function.

MATERIALS AND METHODS

Institutional Review Board approval for this study (AAAR-3154 approved 6/2/2022) was granted, and informed consent was waived.

We performed a multicenter, retrospective review based on hospital records of all adult patients at Columbia University Irving Medical Center and Aarhus University Hospital undergoing isolated or combined surgical TV repair or replacement between 2010 and 2022 requiring postoperative VA-ECMO in the operating room or within 2 weeks after surgery while an inpatient. Patients with concomitant LVAD were excluded. Patients were stratified by VA-ECMO initiation in the operating room (Early VA-ECMO) versus outside of the operating room after the completion of the operation (Late VA-ECMO).

Time to VA ECMO was defined as the difference in minutes between cessation of cardiopulmonary bypass and initiation of VA-ECMO. Postoperative Vasoactive Inotrope Score (VIS) was calculated using vasoactive drug doses in μg/kg/min, as follows: dobutamine + dopamine + (10 * [phenylephrine + milrinone]) + (100 * [epinephrine + norepinephrine]) + (10,000 * vasopressin), as previously described.[11]

Missing data are noted in each respective table and excluded from percentage counts and regressions. Missing data were not imputed because of the small sample size.

The decision to initiate VA-ECMO in the Early or Late group was not prespecified given the retrospective nature of the analysis. The primary indication for VA-ECMO was cardiogenic shock in all cases, and timing and cannulation strategy were left to the individual surgeon. However, robust strategies for VA-ECMO cannulation are present at both institutions, and all patients during and after cannulation remain under the care of specialized VA-ECMO teams.[12]

Statistical Analysis

The 'tableone' and 'ggplot2' packages of R statistical software (version 4.0.3, R Foundation for Statistical Computing) were used for statistical analysis and all figures. Data are expressed as frequencies and percentages for categorical variables. Continuous variables are expressed as mean (standard deviation [SD]) or median (interquartile range [IQR]) depending on normality (evaluated via Shapiro–Wilk test) and were compared using the *t* test or Mann–Whitney *U* test, respectively. Categorical variables were compared using chi-square or Fisher exact test depending on size (>5). Univariable logistic regression was performed for all variables enumerated next. Qualitative echocardiographic assessment of RV size and function was categorized as less than moderate and greater than or equal to moderate dilation or dysfunction, respectively, for logistic regression.

Definitions

Stroke was defined as a physician diagnosed newly developed focal neurologic deficit lasting more than 72 hours beginning during index hospitalization.

Renal replacement therapy was defined as new postoperative requirement for continuous veno-venous hemofiltration or intermittent hemodialysis during index hospitalization.

Vascular complication was defined according to Valve Academic Research Consortium 2 recommendations as aortic dissection, aortic rupture, annulus rupture, left ventricle perforation, distal embolization, new apical aneurysm/pseudo-aneurysm, access-related vascular injury (dissection, stenosis, perforation, rupture, arteriovenous fistula, pseudoaneurysm, hematoma, irreversible nerve injury, compartment syndrome, percutaneous closure device failure) leading to death, life-threatening or major bleeding, visceral ischemia, or neurological impairment.[13] Major bleeding was defined as a decrease in hemoglobin of 3 g/dL or the need for transfusion, as defined by Valve Academic Research Consortium 2.[13]

Preoperative and postoperative echocardiography were conducted to establish baseline cardiac function and to assess the effects of interventions

on cardiac function, respectively. Variables were categorized as mild, moderate, or severe. Echocardiographic variables were extracted based on Columbia University Irving Medical Center/Aarhus University Hospital clinical echocardiography laboratory reporting. Echocardiography readings were done by echocardiography board-certified anesthesiologists. Grading of TR was assessed according to semiquantitative and quantitative criteria as recommended by the American Society of Echocardiography guidelines.[14]

RESULTS

Baseline Characteristics

Of all TV operations performed during the study period requiring VA-ECMO, 31 were classified as Early VA-ECMO and 16 were classified as Late VA-ECMO, comprising the study group. There were no significant differences in baseline characteristics between groups (Table 1). Mean age was 55.6 (16.8) years, and 53.2% of patients were male. Comorbidities included diabetes (34.0%), coronary artery disease (36.2%), atrial fibrillation (57.4%), and endocarditis (23.4%). Congenital heart disease was present in 25.5% of patients, and 21.3% had an RV pacemaker or implantable cardioverter defibrillator lead. The majority of patients (60.8%) had a history of left-sided valve disease, and 23.4% were reoperative patients. Baseline New York Heart Association class III/IV was 54.3%, and 32.6% had a history of heart failure hospitalization (Table 1). Key echocardiographic variables include median LVEF 60.0% (IQR, 45.0%-65%), moderately or more increased RV size in 60.5%, and moderately or more reduced RV function in 51.1% (Table 2).

Surgical Variables

Isolated TV surgery was performed in 17.0% of patients (n = 8), and replacement (vs repair) was performed in 51.1% of patients (n = 24). Concomitant procedures included left-sided valve surgery 53.2% (n = 25) and coronary artery bypass grafting in 10.6% (n = 5) (Table 3). Mean cardiopulmonary bypass time in the Early VA-ECMO group was 241 minutes (IQR, 174-327.5) versus 169.5 minutes (IQR, 136.5-215.5) in the Late VA-ECMO group ($P = .027$). Crossclamp time was 155.2 ± 65.3 minutes versus 130.3 ± 59.6 minutes in the Early VA-ECMO and Late VA-ECMO groups, respectively ($P = .233$) (Table 3). Early VA-ECMO group required significantly more transfusions than the Late VA-ECMO group (4 units [IQR, 2-7] vs 0.5 units [IQR, 0-2], $P = .002$). Time from cardiopulmonary bypass cessation to VA-ECMO initiation was significantly shorter in the Early versus Late VA-ECMO group (67.5 [IQR, 2.0-160.0] vs 1682 [IQR, 792.5-3187.5] minutes, $P < .001$) (Table 4).

Hemodynamics

Hemodynamic evaluation via Swan Ganz catheter at the initiation of anesthesia revealed no difference in Early versus Late VA-ECMO central venous pressure (14 [IQR, 9.75-17.5] vs 18.5 [IQR, 10.5-21.0] mm Hg, $P = .276$), systolic pulmonary artery pressure (PAP) (30.5 [IQR, 22.0-40.8] vs 44.0 [IQR, 29.0-55.0], $P = .062$) or diastolic PAP (17 [IQR, 10.0-24.3] vs 18 [13.5-27.5], $P = .271$) (Figure 1 and Table E1). However, there was significant difference in systolic PAP (27.5 [SD, 7.17] vs 42.18 [SD, 14.45] mm Hg, $P = .005$) and diastolic PAP (16.0 [IQR, 12.5-17] vs 23.0 [IQR, 18.0-27.0] mm Hg, $P = .011$) in Early versus Late VA-ECMO groups 24 hours postoperatively. There was no difference in central venous pressure at 24 hours postoperatively (11.65 [SD, 4.06] vs

TABLE 1. Baseline characteristics

Variable	No. missing	All (n = 47)	ECMO Early (n = 31)	ECMO Late (n = 16)	*P* value
Demographics					
Age, mean [SD]	0	55.6 (16.8)	55.1 (16.3)	56.6 (18.3)	.771
Male sex, n (%)	0	25 (53.2)	17 (54.8)	8 (50.0)	.995
Diabetes, n (%)	0	16 (34.0)	8 (25.8)	8 (50.0)	.182
CAD, n (%)	0	17 (36.2)	12 (38.7)	5 (31.2)	.753
Prior MI, n (%)	0	5 (10.6)	4 (12.9)	1 (6.2)	.648
Atrial fibrillation, n (%)	0	27 (57.4)	17 (54.8)	10 (62.5)	.758
RV lead (PPM/AICD), n (%)	0	10 (21.3)	7 (22.6)	3 (18.8)	1
Congenital heart disease, n (%)	0	12 (25.5)	10 (32.3)	2 (12.5)	.176
History of HFH, n (%)	1	15 (32.6)	10 (32.3)	5 (33.3)	1
NYHA III/IV, n (%)	1	25 (54.3)	15 (50.0)	10 (62.5)	.538
Reoperation, n (%)	0	11 (23.4)	10 (32.3)	1 (6.2)	.07
History of left-sided valve disease, n (%)	0	30 (60.8)	20 (64.5)	10 (62.5)	1
ESRD	0	12 (25.5)	9 (29.0)	3 (18.8)	.505
Endocarditis	0				.131
Recent (within 12 mo)		10 (21.3)	9 (29.0)	1 (6.2)	
Remote (>12 mo)		1 (2.1)	1 (3.2)	0 (0)	

ECMO, Extracorporeal membrane oxygenation; *SD*, standard deviation; *CAD*, coronary artery disease; *MI*, myocardial infarction; *RV*, right ventricle; *PPM*, permanent pacemaker; *AICD*, automatic implantable cardiac device; *HFH*, heart failure hospitalization; *NYHA*, New York Heart Association; *ESRD*, end-stage renal disease.

TABLE 2. Echocardiography and hemodynamics

Variable	No. missing	All (n = 47)	ECMO Early (n = 31)	ECMO Late (n = 16)	*P* value
LVEDd, mean [SD]	11	4.71 (0.91)	4.75 (0.93)	4.65 (0.91)	.753
LVEF, median [IQR]	6	60.0 (45.0-65.0)	59.0 (45.0-65.0)	60.0 (50.0-65.0)	.865
RV size, n (%)	5				.434
Normal		6 (14.0)	3 (11.1)	3 (18.8)	
Mild enlargement		11 (25.6)	7 (25.9)	4 (25.0)	
Moderate enlargement		14 (32.6)	11 (40.7)	3 (18.8)	
Severe enlargement		12 (27.9)	6 (22.2)	6 (37.5)	
RV function, n (%)	0				.938
Normal		19 (40.4)	12 (38.7)	7 (43.8)	
Mild impairment		4 (8.5)	3 (9.7)	1 (6.2)	
Moderate impairment		13 (27.7)	8 (25.8)	5 (31.2)	
Severe impairment		11 (23.4)	8 (25.8)	3 (18.8)	
Moderate or greater aortic stenosis	3	8 (18.2)	3 (10.3)	5 (33.3)	.099
Moderate or greater aortic regurgitation	2	11 (24.4)	7 (24.1)	4 (25.0)	1
Moderate or greater mitral stenosis	5	9 (21.4)	5 (18.5)	4 (26.7)	.698
Moderate or greater mitral regurgitation	3	21 (47.7)	12 (42.9)	9 (56.2)	.588
Hemodynamics					
CVP, median [IQR]	11	15.0 (9.0-20.3)	14.0 (9.8-17.5)	18.5 (10.5-21.0)	.276
PAPs, median [IQR]	12	34.0 (26.0-45.0)	30.5 (22.0-40.8)	44.0 (29.0-55.0)	.062
PAPd, median [IQR]	12	18.0 (12.5-25.0)	17.0 (10.0-24.3)	18.0 (13.5-27.5)	.271
PAPm, median [IQR]	12	24.0 (17.5-33.5)	22.0 (17.0-26.3)	25.0 (21.5-35.0)	.053
PCWP, mean [SD]	27	19.4 (10.1)	20.1 (9.9)	18.3 (10.9)	.701
CI, median [IQR]	25	2.12 (1.85-2.49)	2.37 (2.14-3.10)	1.81 (1.61-2.06)	.005
PVR, median [IQR]	28	2.34 (2.00-4.30)	2.17 (1.81-3.05)	2.93 (2.36-5.59)	.398

Echocardiography and hemodynamics

Variable	No. Missing	All (n = 47)	ECMO Early (n = 31)	ECMO Late (n = 16)	*P* value
LVEDd, mean [SD]	11	4.71 (0.91)	4.75 (0.93)	4.65 (0.91)	.753
LVEF, median [IQR]	6	60.0 (45.0-65.0)	59.0 (45.0-65.0)	60.0 (50.0-65.0)	.865
RV size, n (%)	5				.434
Normal		6 (14.0)	3 (11.1)	3 (18.8)	
Mild enlargement		11 (25.6)	7 (25.9)	4 (25.0)	
Moderate enlargement		14 (32.6)	11 (40.7)	3 (18.8)	
Severe enlargement		12 (27.9)	6 (22.2)	6 (37.5)	
RV function n (%)	0				.938
Normal		19 (40.4)	12 (38.7)	7 (43.8)	
Mild impairment		4 (8.5)	3 (9.7)	1 (6.2)	
Moderate impairment		13 (27.7)	8 (25.8)	5 (31.2)	
Severe impairment		11 (23.4)	8 (25.8)	3 (18.8)	
Moderate or greater aortic stenosis	3	8 (18.2)	3 (10.3)	5 (33.3)	.099
Moderate or greater aortic regurgitation	2	11 (24.4)	7 (24.1)	4 (25.0)	1
Moderate or greater mitral stenosis	5	9 (21.4)	5 (18.5)	4 (26.7)	.698
Moderate or greater mitral regurgitation	3	21 (47.7)	12 (42.9)	9 (56.2)	.588
Hemodynamics					
CVP, median [IQR]	11	15.0 (9.0-20.3)	14.0 (9.8-17.5)	18.5 (10.5-21.0)	.276
PAPs, median [IQR]	12	34.0 (26.0-45.0)	30.5 (22.0-40.8)	44.0 (29.0-55.0)	.062
PAPd, median [IQR]	12	18.0 (12.5-25.0)	17.0 (10.0-24.3)	18.0 (13.5-27.5)	.271
PAPm, median [IQR]	12	24.0 (17.5-33.5)	22.0 (17.0-26.3)	25.0 (21.5-35.0)	.053

ECMO, Extracorporeal membrane oxygenation; *LVEDd*, left ventricular end-diastolic diameter; *SD*, standard deviation; *LVEF*, left ventricular ejection fraction; *IQR*, interquartile range; *RV*, right ventricle; *CVP*, central venous pressure; *PAP*, pulmonary artery pressure; *PAPd*, diastolic pulmonary artery pressure; *PAPm*, mean pulmonary artery pressure; *PAPs*, systolic pulmonary artery pressure; *PCWP*, pulmonary capillary wedge pressure; *CI*, cardiac index; *PVR*, pulmonary vascular resistance.

TABLE 3. Surgical variables

Variable	No. missing	All (n = 47)	ECMO Early (n = 31)	ECMO Late (n = 16)	*P* value
TV replacement (vs repair)	0	24 (51.1)	16 (51.6)	8 (50.0)	1
Isolated tricuspid surgery, n (%)	0	8 (17.0)	7 (22.6)	1 (6.2)	.234
Concomitant left-sided valve surgery, n (%)	0	25 (53.2)	14 (45.2)	11 (68.8)	.22
Concomitant CABG, n (%)	0	5 (10.6)	2 (6.5)	3 (18.8)	.32
CPB time, median [IQR]	5	215.0 (158.5-295.0)	241.0 (174.0-327.5)	169.5 (136.5-215.5)	.027
Crossclamp time (min), mean [SD]	9	146.1 (63.7)	155.2 (65.3)	130.3 (59.6)	.233
RBC transfusion (No. of units), median [IQR]	0	2.0 (0-6.0)	4.0 (2.0-7.0)	0.5 (0-2.0)	.002

ECMO, Extracorporeal membrane oxygenation; *TV*, tricuspid valve; *CABG*, coronary artery bypass grafting; *CPB*, cardiopulmonary bypass; *IQR*, interquartile range; *SD*, standard deviation; *RBC*, red blood cell.

13.21 [SD, 4.87] mm Hg, $P = .286$) (Figure 1). Peak pre–VA-ECMO VIS was significantly higher in the Late VA-ECMO group (44.98 [SD, 15.47] vs 17.02 [SD, 11.19], $P < .001$) (Figure 2). There was no difference in peak pre–VA-ECMO serum lactate (5.15 vs 5.90 mmol/L, $P = .863$).

Clinical Outcomes

In-hospital mortality occurred in 35.5% (n = 11) of the Early VA-ECMO group versus 68.8% (n = 11) of the Late VA-ECMO group ($P = .037$) (Table 4). There was no difference in need for renal replacement therapy (25.8% vs 50.0%, $P = .182$) or stroke (12.9% vs 18.8%, $P = .676$) in Early VA-ECMO versus Late VA-ECMO groups, respectively. There was no difference in vascular complications (3.2% vs 12.5%, $P = .264$) or major bleeding (32.3% vs 43.8%, $P = .648$) between groups.

Univariable logistic regression for the primary outcome of in-hospital mortality revealed a significant association with Late VA-ECMO (odds ratio [OR], 4.00; 1.10-14.50; $P = .035$) and a history of diabetes (OR, 6.30; 1.62-24.53; $P = .008$) (Table 5). There was no significant association with time to VA-ECMO (OR, 1.00; 1.00-1.00; $P = .959$) or peak pre–VA-ECMO lactate (OR, 1.07; 0.88-1.30; $P = .507$) (Table 5).

DISCUSSION

This study explored the role of VA-ECMO initiation timing in improving TV surgery outcomes (Figure 3). VA-ECMO is a useful tool after cardiac surgery to facilitate myocardial recovery by providing circulatory support. VA-ECMO has the capacity to reverse metabolic dysfunction resulting from prolonged low cardiac output and can also prevent end-organ ischemia.[5,6] Some studies

TABLE 4. Outcomes

Variable	No. missing	All (n = 47)	ECMO Early (n = 31)	ECMO Late (n = 16)	*P* value
CPB to ECMO time (min), median [IQR]	6	194.0 (23.0-840.0)	67.50 [2.00-160.00]	1682.00 [792.50-3187.50]	<.001
Peak VIS (pre-ECMO), median [SD]	0	26.54 (18.41)	17.02 (11.19)	44.98 (15.47)	<.001
Peak lactate (pre-ECMO), mean [SD]	1	5.35 (3.90-8.20)	5.15 [3.70-8.15]	5.90 [4.28-8.27]	.863
Hemoglobin, post-CPB, g/dL [IQR]	3	8.5 (7.7-9.6)	8.3 (7.4-10.0)	8.5 (8.4-9.1)	.366
Hemoglobin, ICU, g/dL [SD]	0	8.6 (1.4)	8.5 (1.2)	8.7 (1.7)	.737
Mechanical ventilation (d), median [IQR]	0	14.0 (6.0-24.5)	8.0 [4.5-23.0]	18.5 [14.0-24.3]	.045
Vascular complication, n (%)	0	3 (6.4)	1 (3.2)	2 (12.5)	.264
Major bleeding, n (%)	0	17 (36.2)	10 (32.3)	7 (43.8)	.648
Infection, n (%)	0	28 (59.6)	18 (58.1)	10 (62.5)	1
New-onset renal replacement therapy, n (%)	0	16 (34.0)	8 (25.8)	8 (50.0)	.182
New-onset atrial fibrillation, n (%)	0	7 (14.9)	4 (12.9)	3 (18.8)	.676
Stroke, n (%)	0	7 (14.9)	4 (12.9)	3 (18.8)	.676
MI, n (%)	0	1 (2.1)	0 (0.0)	1 (6.2)	.34
ICU LOS (d), median [IQR]	0	21.0 (12.5-34.5)	21.0 [9.0-35.0]	21.0 [14.8-29.0]	.537
Hospitalization LOS (d), median [IQR]	0	27.0 (16.0-42.5)	32.0 [14.5-45.5]	23.5 [17.3-36.8]	.84
In-hospital mortality, n (%)	0	22 (46.8)	11 (35.5)	11 (68.8)	.037

ECMO, Extracorporeal membrane oxygenation; *CPB*, cardiopulmonary bypass; *IQR*, interquartile range; *VIS*, Vasoactive Inotrope Score; *SD*, standard deviation; *ICU*, intensive care unit; *MI*, myocardial infarction; *LOS*, length of stay.

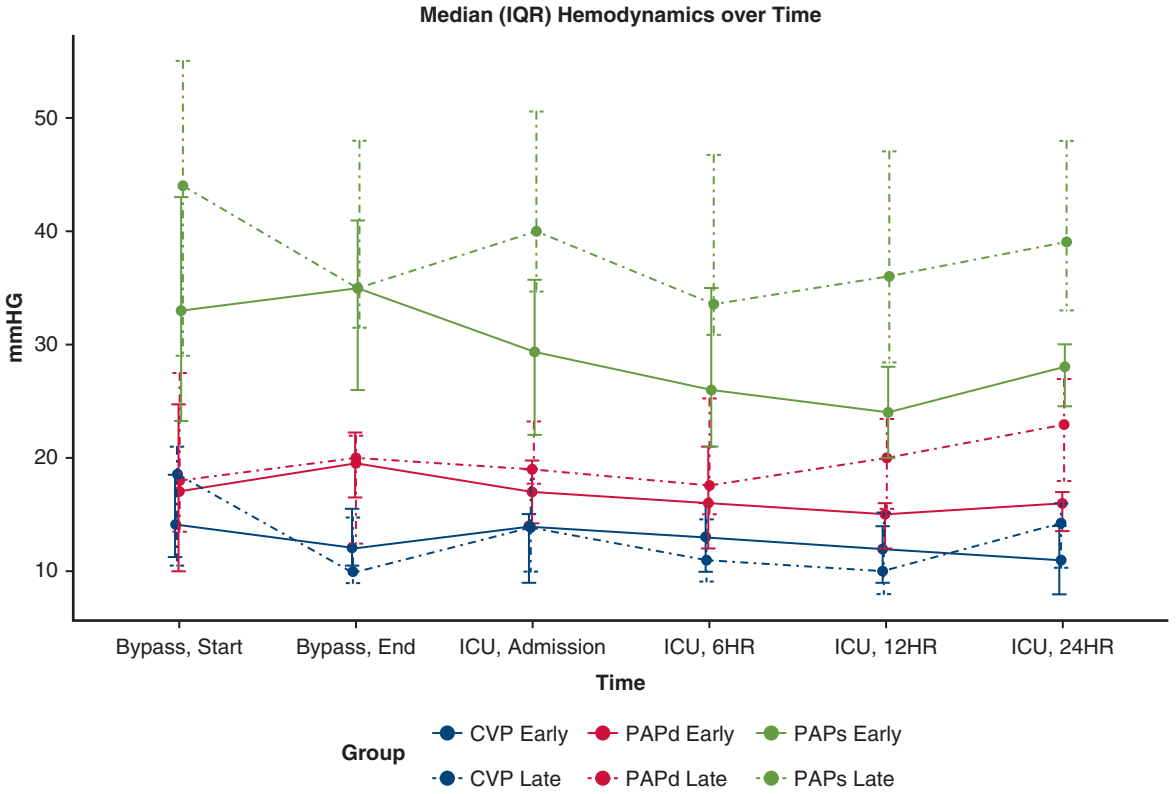

FIGURE 1. The difference in median cardiovascular pressure and PAP, both PAPs and PAPd, in mm Hg between Early and Late VA-ECMO groups. The *solid lines* represent the Early groups, and the *dashed lines* represent the Late groups. The *green lines* represent PAPs, the *red* lines represent PAPd, and the *blue lines* represent central venous pressure. This demonstrates similar preoperative pressures, but a reduction in postoperative PAPs in the Early VA-ECMO group postoperatively ($P < .01$). *IQR*, Interquartile range; *CVP*, central venous pressure; *PAPd*, diastolic pulmonary artery pressure; *PAPs*, systolic pulmonary artery pressure; *ICU*, intensive care unit.

suggest that VA-ECMO initiation timing can play a crucial role in the outcomes of cardiac surgery in general and demonstrates the benefit of early initiation.[6,10] Early initiation of VA-ECMO after TV surgery may reduce complications and mortality associated with this procedure. Our study showed (1) an association between early VA-ECMO initiation in patients undergoing TV surgery and reduced in-hospital mortality; (2) improvement in hemodynamics in the Early VA-ECMO group reflected by lower pulmonary arterial pressures and lower VIS postoperatively; and (3) no difference in vascular complications, bleeding, stroke, or mechanical ventilation requirements between the 2 groups. The current analysis may support consideration of early, proactive initiation of VA-ECMO postoperatively due to the improved clinical and hemodynamic outcomes without a corresponding increase in complications compared with a later, more reactive approach.

VA-ECMO use after cardiac surgery has been extensively researched. A retrospective review of 517 patients, 4.3% of whom underwent TV repair, espoused the morbidity and mortality benefits of using VA-ECMO for patients with postcardiotomy cardiogenic shock.[10] However, although this study supported the benefits of VA-ECMO in cardiac surgery in general, including in TV surgery, it did not address the issue of VA-ECMO initiation timing. A 2019 retrospective study, focused on 36 propensity-matched sets of patients scheduled for cardiac surgery from 2010 to 2017 who were deemed to be at high risk for cardiogenic shock,[6] found that those with early VA-ECMO initiation had lower mortality, pulmonary infection rate, and renal replacement therapy rate, as well as improved cardiac index and lactate clearance.[6] Early VA-ECMO initiation was also shown to have better outcomes in 214 postcardiac transplant recipients experiencing primary graft dysfunction and myocardial rejection with hemodynamic instability.[15] To our knowledge, ours is the first study to examine the impact of VA-ECMO timing in a cohort of patients undergoing TV surgery specifically.

Our study data are notable for a few reasons. First, baseline demographics and hemodynamic characteristics suggest no statistically significant differences between the Early and Late groups (Table 2). This reduces the likelihood

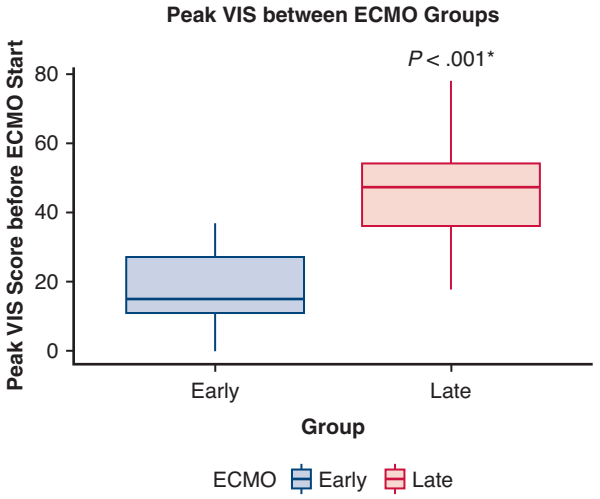

FIGURE 2. Box and whisker plot showing the difference in pre–VA-ECMO VIS in μg/kg/min between Early (*blue*) and Late (*red*) VA-ECMO groups. The *upper and lower lines of the box* represent the 25th and 75th percentiles. The *middle horizontal line* represents the median. The *upper and lower whiskers* represent the minimum and maximum values. This demonstrates an elevated VIS in the Late VA-ECMO group ($P < .001$). *VIS*, Vasoactive Inotrope Score; *ECMO*, extracorporeal membrane oxygenation.

of preoperative conditions confounding our results and allows for focus on intraoperative management. Next, our results showed an increased peak VIS pre–VA-ECMO in the Late VA-ECMO initiation group (Figure 2 and Table 4), demonstrating a higher pressor requirement and a greater need for cardiac support before VA-ECMO initiation in the Late VA-ECMO group, thereby illustrating significantly worse hemodynamics and perfusion before circulatory support. Despite longer bypass time and crossclamp time, and increased transfusion requirement (suggesting more complicated operation), the Early VA-ECMO group had lower mortality. This highlights the importance of circulatory support despite these complicating factors.

The physiology behind these findings may be explained by the effects that VA-ECMO incurs on cardiac hemodynamics. The patients in our cohort were experiencing a mixed cardiogenic shock and vasoplegic shock with RV failure. VA-ECMO works to reduce preload in these patients and thus RV work via cardiopulmonary bypass and direct drainage from the right atrium.[16] Increased preload, as seen by increased right ventricular end-diastolic volume (RVEDV), leads to increased force of contraction and RV work. Further, the Starling curve demonstrates that beyond a certain RVEDV, no further compensatory increase in carbon monoxide occurs, only preload-induced myocyte stretching/damage that may be irreversible.[17] TV surgery eliminates or reduces the RV's means of reducing RVEDV through regurgitation, which thus increases afterload faced by the RV and may precipitate RV failure. Thus, the greater the VA-ECMO flow, the greater the decrease in preload, thereby unloading the RV.[11] The reduction of flow through the heart poses an increased risk of intracardiac thrombosis.[18] In those receiving VA-ECMO, there is a reported incidence of thrombosis of 17%, making it one of the more prevalent complications.[18] Potential strategies to mitigate this risk include lower-flow VA-ECMO, inotropic therapy, and insertion of short-term intra-aortic balloon pump.[18] Thus, the determination of the desired level of VA-ECMO support must balance prioritizing preload reduction with the maintenance of appropriate forward flow and pulsatility to avoid thrombus.

To determine which patients will benefit most from early VA-ECMO initiation, it is important to risk stratify which patients are most likely to experience RV failure and cardiogenic shock. Comprehensive assessment of RV function, congestion, and afterload via both invasive (pulmonary artery catheterization) and noninvasive (echocardiography) means may help identify patients with adverse remodeling and RV decompensation at high risk of postoperative cardiogenic shock. Additionally, echocardiography allows for evaluation of left ventricular function and concomitant valvular disease that may place the patient at higher risk of postoperative shock. One additional consideration is the use of VIS, previously associated with unfavorable outcomes including mortality, as a means of predicting right heart failure.[19] In our study, subjects in the Late VA-ECMO group have significantly greater peak VIS before VA-ECMO initiation, suggesting greater decompensation before full hemodynamic support. Despite longer bypass and crossclamp times, the Early VA-ECMO group had lower peak pre–VA-ECMO VIS and favorable outcomes, suggesting that the prevention of hemodynamic compromise, rather than reaction to it, is paramount in preventing postoperative mortality. Despite these indicators of complications, the Early VA-ECMO group still had improved mortality. It is possible that increased transfusion volume was factored into the decision that was made to place these patients on early VA-ECMO. No demographic or baseline characteristics demonstrated any significant differences between the 2 groups or demonstrated any prediction of right heart failure. Large, multicenter, randomized control trials should be conducted to substantiate our conclusions and further delineate which patients are most likely to experience right heart failure and cardiogenic shock such that the population who would benefit most from early VA-ECMO initiation can be promptly identified.

Study Limitations

Our study does have several limitations. Our study sample is small and limited to the experience at 2

TABLE 5. Univariable logistic regression for characteristics associated with in-hospital mortality

Variable	No. missing (n)	OR (95% CI)	*P* value
ECMO late	0	4.00 (1.10-14.50)	.035
CPB to ECMO time (min)	6	1.00 (1.00-1.00)	.959
Peak VIS (pre-ECMO)	0	1.03 (0.99-1.06)	.102
Peak lactate (pre-ECMO)	1	1.07 (0.88-1.30)	.507
Age	0	1.00 (0.96-1.03)	.936
Male sex	0	0.79 (0.25-2.48)	.681
History of HFH	1	1.06 (0.31-3.66)	.923
NYHA III-IV	1	1.76 (0.54-5.73)	.347
DM	0	6.30 (1.62-24.53)	.008
ESRD	0	1.19 (0.32-4.41)	.797
CAD	0	1.47 (0.45-4.86)	.527
MI	0	0.73 (0.11-4.85)	.748
Congenital heart disease	0	0.47 (0.12-1.86)	.283
History of left-sided valve surgery	0	0.98 (0.30-3.24)	.979
Reoperation	0	0.34 (0.08-1.47)	.148
CVP	11	1.02 (0.96-1.09)	.568
PAPs	12	1.05 (1.00-1.10)	.054
PCWP	12	0.96 (0.88-1.06)	.445
Cardiac index	25	0.75 (0.25-2.29)	.615
PVR	28	0.93 (0.72-1.22)	.617
LVEF	6	0.99 (0.94-1.04)	.704
RV size, moderate/severe increased	4	0.67 (0.21-2.12)	.492
RV function, moderate/severe reduced	0	0.43 (0.13-1.42)	.166
Concomitant left-sided valve surgery, any	0	0.79 (0.25-2.48)	.681
Concomitant CABG	0	1.82 (0.27-12.01)	.536

OR, Odds ratio; *CI*, confidence interval; *ECMO*, extracorporeal membrane oxygenation; *CPB*, cardiopulmonary bypass; *VIS*, Vasoactive Inotrope Score; *HFH*, heart failure hospitalization; *NYHA*, New York Heart Association; *DM*, diabetes mellitus; *ESRD*, end-stage renal disease; *CAD*, coronary artery disease; *MI*, myocardial ischemia; *CVP*, central venous pressure; *PAPs*, systolic pulmonary artery pressure; *PCWP*, pulmonary capillary wedge pressure; *PVR*, pulmonary vascular resistance; *LVEF*, left ventricular ejection fraction; *RV*, right ventricle; *CABG*, coronary artery bypass grafting.

high-volume TV surgery centers. Moreover, this small sample size with few mortalities limited our ability to fully account for potential confounding influences in our comparison of Early versus Late groups. Likewise, limited group size precluded robust propensity score approaches. Per a recent analysis, underpowered trials with weakly significant *P* values have a 50% false-positive risk.[20] Although our study presents and supports a novel theory, as a small study with a heterogenous sample by necessity, the conclusions we can definitively draw are limited. The difficulty of interpreting invasive hemodynamic data in a retrospective fashion is substantial, and clinical decision making in the operating room to start or delay VA-ECMO includes many factors that may not have been captured in this analysis, such as surgeon fatigue, suitability of peripheral vessels for VA-ECMO initiation, and risk of valvular thrombosis with VA-ECMO leading to delay of VA-ECMO until worsened hemodynamics. Furthermore, hemodynamic values obtained after anesthesia are confounded by the medication used to initiate anesthesia and the patient's position. It is also challenging to interpret the effect of multivalvular surgery in this cohort. All surgery that included TV surgery was included. Given the heterogeneous nature of the patient population we studied, the 95% confidence interval for association of late ECMO with mortality was large (1.10-14.50), and the results should be interpreted with this information in mind. Left-sided ventricular events could have impacted these results, although no major events were apparent from review of the operative notes or hemodynamics. Likewise, major surgical events such as catastrophic bleeding or arrythmias could have affected the decision to start VA-ECMO. Nevertheless, this is, to our knowledge, the largest cohort of patients undergoing TV surgery receiving subsequent VA-ECMO analyzed for initiation timing to date. Further, multicenter randomized trials must be conducted to confirm these results.

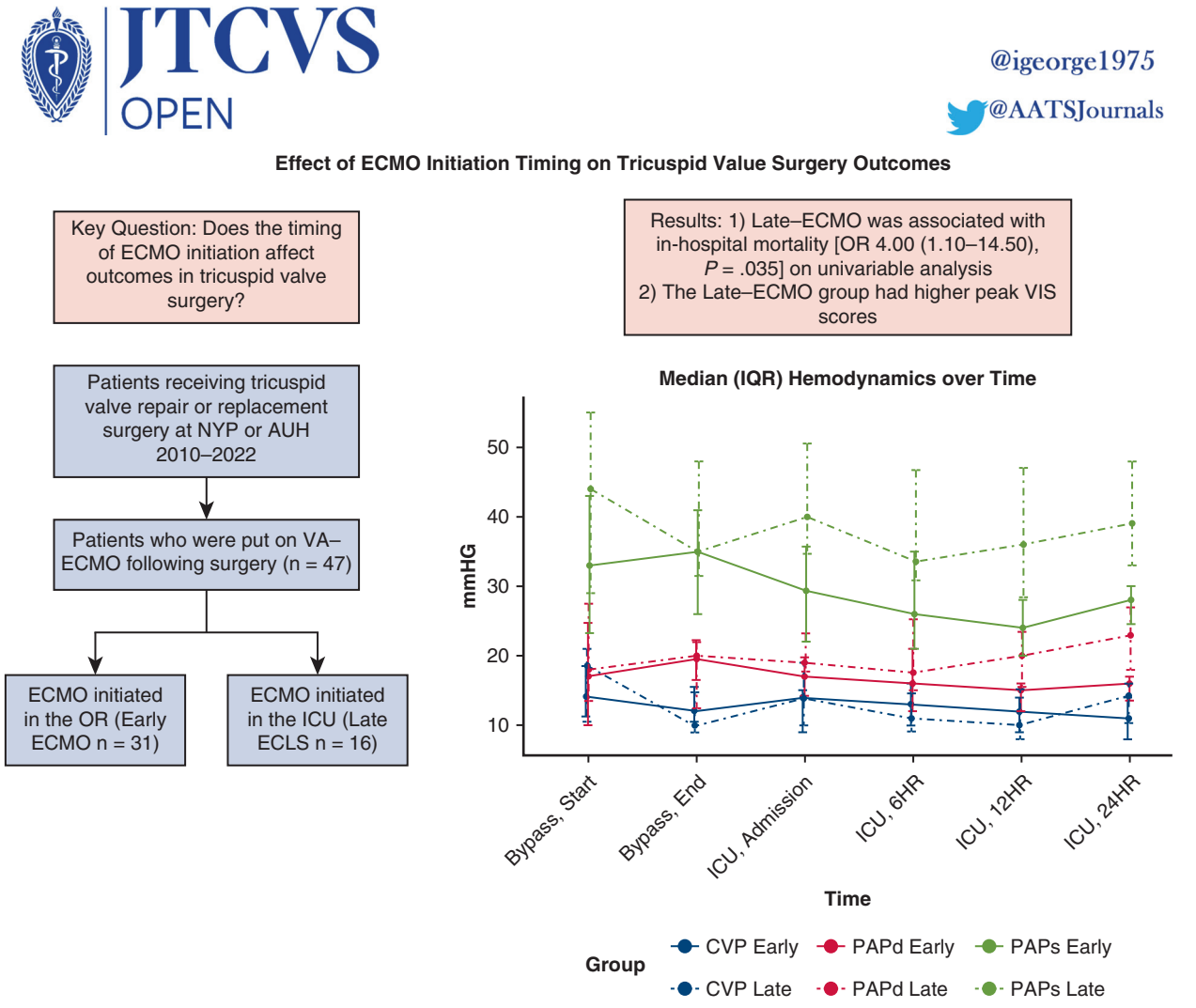

FIGURE 3. Graphical Abstract detailing cohort selection via identification of all patients who were placed on VA-ECMO after TV surgery at New York Presbyterian Hospital and Aarhus University Hospital, as well as division of the cohort into Early and Late VA-ECMO initiation groups. Primary results show Late VA-ECMO was associated with in-hospital mortality (OR, 4.00; 1.10-14.50; $P = .035$) on univariable analysis and had higher peak VIS scores. Early postoperative initiation of VA-ECMO after TV surgery in high-risk patients may be associated with improvement in postoperative hemodynamics and in-hospital mortality. Created with Biorender. *ECMO*, Extracorporeal membrane oxygenation; *OR*, odds ratio; *VIS*, Vasoactive Inotrope Score; *NYP*, New York Presbyterian Hospital; *AUH*, Aarhus University Hospital; *IQR*, interquartile range; *CVP*, central venous pressure; *PAPd*, diastolic pulmonary artery pressure; *PAPs*, systolic pulmonary artery pressure; *VA-ECMO*, venoarterial extracorporeal membrane oxygenation; *ICU*, intensive care unit.

CONCLUSIONS

Postoperative cardiogenic shock requiring VA-ECMO after TV surgery often results in death. Early initiation of VA-ECMO may be associated with improvement in postoperative hemodynamics and lower in-hospital mortality.

Conflict of Interest Statement

I.G.: Consultant (honoraria) for Zimmer Biomet, AtriCure, Neosurgery, Neptune Medical, AbbVie, Johnson & Johnson, Boston Scientific, Edwards Lifesciences, Medtronic, and Help-TheraX; Advisory Boards: Edwards Surgical, Medtronic Surgical, Trisol Medical, AbbVie, Johnson & Johnson, Foldax Medical, Zimmer Biomet, Neosurgery, AbbVie, and Boston Scientific; Equity: Valcare Medical, Durvena, CardioMech, Vdyne, MitreMedical, and MITRx; Institutional funding to Columbia University: Edwards Lifesciences, Medtronic, Abbott Vascular, Boston Scientific, and JenaValve. M.L.: Institutional grant funding

to Columbia University: Edwards Lifesciences. All other authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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Key Words: heart failure, tricuspid valve regurgitation, VA-ECMO

TABLE E1. Hemodynamics

	First operating room*				Bypass end time				ICU admission				ICU, 6 h				ICU, 12 h				ICU, 24 h			
Variable	No. missing	ECMO Early	ECMO Late	*P* value	No. missing	ECMO Early	ECM Late	*P* value	No. missing	ECMO Early	ECMO Late	*P* value	No. missing	ECMO Early	ECMO Late	*P* value	No. missing	ECMO Early	ECMO Late	*P* value	No. missing	ECMO Early	ECMO Late	*P* value
HR									0	90.00 [81.00, 100.00]	86.50 [82.75, 97.00]	.77	1	87.48 (14.91)	95.13 (17.18)	.128	2	86.00 (15.61)	89.29 (19.42)	.548	2	88.97 (13.29)	90.71 (18.88)	.723
SBP									2	107.83 (26.54)	98.31 (18.21)	.209	2	100.73 (15.38)	97.33 (17.70)	.51	3	101.87 (18.30)	97.79 (21.69)	.52	2	102.87 (19.55)	102.29 (16.22)	.923
DBP									2	67.00 (14.44)	52.69 (12.40)	.002	2	64.70 (9.77)	52.33 (7.72)	<.001	3	63.30 (8.61)	52.21 (9.37)	<.001	2	59.39 (8.78)	53.00 (10.02)	.036
CVP	12	14.00 [9.75, 17.50]	18.50 [10.50, 21.00]	.276	17	12.00 [10.00, 16.00]	10.00 [9.00, 14.75]	.231	2	13.30 (5.00)	14.67 (6.09)	.426	2	12.50 [10.00, 14.00]	11.00 [9.00, 14.50]	.699	3	11.87 (4.06)	11.36 (5.61)	.734	7	11.65 (4.06)	13.21 (4.87)	.286
PAPs	13	30.50 [22.00, 40.75]	44.00 [29.00, 55.00]	.062	18	33.07 (8.61)	39.33 (14.79)	.167	16	28.58 (8.83)	43.08 (10.97)	<.001	17	26.00 [21.25, 35.75]	33.50 [31.00, 46.75]	.049	18	24.50 (9.62)	39.09 (16.23)	.005	24	27.50 (7.17)	42.18 (14.45)	.005
PAPd	13	17.00 [10.00, 24.25]	18.00 [13.50, 27.50]	.271	19	17.86 (6.53)	18.60 (8.13)	.789	16	16.26 (4.52)	20.58 (4.83)	.017	17	15.94 (5.88)	19.25 (5.88)	.142	18	13.50 (4.79)	20.55 (7.12)	.004	25	16.00 [12.50, 17.00]	23.00 [18.00, 27.00]	.011
PAPm	13	22.00 [17.00, 26.25]	25.00 [21.50, 35.00]	.053	20	24.85 (6.76)	26.07 (9.22)	.697	16	20.37 (5.01)	25.67 (9.19)	.046	17	21.06 (6.91)	25.67 (7.25)	.09	18	17.00 [16.00, 18.75]	24.00 [21.00, 31.00]	.011	24	18.00 (4.35)	28.18 (8.64)	.002
VIS	0	0.00 [0.00, 4.14]	0.00 [0.00, 2.33]	.781	0	14.20 [0.00, 23.35]	16.73 [11.00, 21.45]	.55	0	24.22 (13.27)	32.94 (12.70)	.036	1	24.35 (13.24)	37.27 (16.45)	.006	1	24.59 (12.93)	34.50 (16.37)	.031	2	21.88 [14.50, 31.25]	27.93 [22.85, 43.57]	.053

ICU, Intensive care unit; *ECMO*, extracorporeal membrane oxygenation; *HR*, heart rate; *SBP*, systolic blood pressure; *DBP*, diastolic blood pressure; *CVP*, central venous pressure; *PAPs*, systolic pulmonary artery pressure; *PAPd*, diastolic pulmonary artery pressure; *PAPm*, mean pulmonary artery pressure; *VIS*, Vasoactive Inotrope Score. *First operating room refers to the first values obtained in the operating room during the tricuspid valve surgery.