의학석사 학위논문

우심실-폐동맥 도관 교체 수술을 받은 환자의 단기 예후 인자로의 우심실-폐동맥 결합

Right ventricular-pulmonary arterial coupling as a prognostic factor for short-term outcome of right ventricular-pulmonary arterial conduit change operation

울산대학교 대학원

의 학 과

권 혁 진

우심실-폐동맥 도관 교체 수술을 받은 환자의 단기 예후 인자로의 우심실-폐동맥 결합

지도교수 유정진

이 논문을 의학석사 학위 논문으로 제출함

2023년 8월

울산대학교 대학원

의 학 과

권 혁 진

권혁진의 의학석사학위 논문을 인준함

심사위원장 백 재 숙 인

심사위원 유 정 진 인

심사위원 박 천 수 인

울산대학교 대학원

2023년 8월

Abstract

Author: Hyuck Jin Kwon

Affiliation: Department of Pediatrics, Division of Pediatric Cardiology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

Title: Right ventricular-pulmonary arterial coupling as a prognostic factor for short-term outcome of right ventricular-pulmonary arterial conduit change operation

Background: It is known that deterioration of right ventricular (RV)-pulmonary arterial (PA) coupling is associated with unfavorable outcomes in patients with RV diseases. We investigated whether RV-PA coupling indices are worse in the patients undergoing RV-PA conduit change surgery after Rastelli operation when compared to the healthy controls, and whether they can predict the short-term surgical outcomes.

Methods: Between January 2016 and February 2018, 77 pediatric patients underwent RV-PA conduit change operation in Asan Medical Center, Seoul, Korea. We retrospectively analyzed preoperative echocardiography and catheterization data and selected age- and sex- matched healthy controls of the same size as the final patient group. RV-PA coupling indices analyzed in the study included tricuspid annular plane systolic excursion (TAPSE)/RV end systolic area indexed with body surface area (ESAi), TAPSE/RV systolic pressure (RVSP), RV fractional area change (FAC)/RVSP, RV FAC/mean pulmonary artery pressure (mPAP), RV area change/RV ESA, tricuspid valve (TV) annular peak systolic velocity (s')/RV ESAi, TV s'/RVSP, and RV longitudinal strain (LS)/mPAP. Poor short-term surgical outcomes were defined as extended duration of ventilator use (>1 day), length of ICU stay (>1 day), and total hospital days (>10 days), with the median value as the reference point.

Results: The mean age of the 56 patients in the final patient group was 10.4 ± 6.5 years. All comparable RV-PA coupling indices, TAPSE/RV ESAi, TV s'/RV ESAi, RV area change/RV ESA, TAPSE/RVSP, TV s'/RVSP, RV FAC/RVSP, and RV LS/RVSP, were significantly decreased in the patient group (all $p < 0.001$), but none of the indices were proven to be associated with unfavorable short-term outcomes. In multivariate logistic regression analysis, smaller body surface area, lower RV

FAC, and longer cardiopulmonary bypass (CPB) time (all $p < 0.05$) were identified as independent predictors of poor short-term outcomes, particularly longer ICU stay (>1day).

Conclusion: In conclusion, we found that smaller body size, decreased RV contractility, longer CPB time as prognostic factors for short-term outcomes of RV-PA conduit change surgery after Rastelli operation. RV-PA coupling indices were significantly impaired in the patient group, but could not predict the short-term surgical outcomes.

Key words: Right ventricular-pulmonary arterial coupling, Right ventricular-pulmonary arterial conduit change operation, Rastelli operation

차 례

표 및 그림 차례

Introduction

The Rastelli operation was devised by Gian Carlo Rastelli and successfully performed first on July 26, 1968 by Dr. Robert Wallace at the Mayo Clinic[1,2]. This procedure involves the closure of a ventricular septal defect (VSD) and the installation of an extracardiac right ventricle (RV) to pulmonary artery (PA) conduit, typically employed in congenital heart diseases such as truncus arteriosus, VSD with pulmonary atresia, and double outlet right ventricle (DORV). However, the majority of the patients face conduit change operation over time due to conduit failure caused by conduit stenosis, conduit regurgitation or extrinsic compression, especially when the initial operation was performed at a younger age [3,4].

While the introduction of different types of RV-PA conduits with improved longevity have made some progress, the indications for conduit change operation are still not standardized and can vary depending on the centers. Generally, the operation is indicated when RV to PA gradient >40-50 mmHg in symptomatic patients or > 65-70 mmHg in asymptomatic patients [3-5]. Despite efforts to extend the lifespan of the RV-PA conduit through catheterization procedures like balloon dilatation or stent insertion, it is highly likely that patients will eventually require surgical intervention[4]. The availability of additional predictive indicators for surgical outcomes prior to conduit change surgery would be helpful in determining the optimal timing for the surgery.

Right ventricular (RV)-pulmonary arterial (PA) coupling, which refers to the relationship between RV contractility and afterload, has recently become a topic of extensive research in the context of RV related diseases including congenital heart disease [6,7]. In normal physiologic states, RV contractility increases commensurate with the augmentation of RV afterload, thereby maintaining RV-PA coupling. However, in decompensated states, RV contractility fails to rise sufficiently in response to increased afterload, leading to a decline in RV-PA coupling[8]. It has been established that this so-called RV-PA uncoupling is associated with adverse outcomes in a range of diseases involving the RV[9,10], including congenital heart disease such as Tetralogy of Fallot (TOF) or pulmonary stenosis (PS) with chronic pulmonary regurgitation (PR)[11,12]. In particular, in repaired TOF patients underwent for

Abbreviations and Acronyms

a’ = annular late diastolic peak velocity

EDAi = end diastolic area indexed by body surface area

EDP = end diastolic pressure

ESAi = end systolic area indexed by body surface area

e’ = annular early diastolic peak velocity

FAC = fractional area change

FS = fraction shortening

LS = longitudinal strain at apical 4 chamber view

LV = left ventricle

LVEDD = left ventricular end diastolic dimension

LVESD = left ventricular end systolic dimension

mPAP = mean pulmonary arterial pressure

PA = pulmonary artery

PASP = pulmonary artery systolic pressure

RV = right ventricle

RV-PA = right ventricular-pulmonary arterial

RVSP = right ventricular systolic pressure

SRs = longitudinal strain rate at systole

SRe = longitudinal strain rate at early diastole

SRa = longitudinal strain rate at late diastole

s’ = annular systolic peak velocity

TAPSE = tricuspid annular plane systolic excursion

TV = tricuspid valve

pulmonary valve replacement (PVR), two-thirds of them were found to be RV-PA uncoupled[13]. We hypothesized that RV-PA uncoupling could occur due to continuous loading of the RV and PA caused by conduit stenosis or regurgitation in pediatric patients with congenital heart disease who underwent

Rastelli surgery.

To our knowledge, there is no study regarding the relationship between RV-PA coupling and the short-term outcomes of the patients undergoing RV-PA conduit change surgery after Rastelli operation. We investigated whether the RV-PA coupling indices are aggravated in the patient group compared to the healthy controls, and whether they can be used as prognostic factors for short-term outcomes of RV-PA conduit change operation.

Materials and Methods

We conducted a retrospective review of the electronic medical records of all patients who underwent RV-PA conduit change operation at Asan Medical Center, Seoul, Republic of Korea, between January 2016 and February 2022. Patients whose echocardiographic data and catheterization data were not suitable for analysis were excluded from the study. Then we selected healthy controls who were matched by age and sex with the final patient group. The healthy controls were selected from patients who underwent echocardiography at the same center between June 2009 to May 2022 for symptoms such as chest pain, cardiac murmur, or palpitation, and were determined to have normal cardiac structure and function. This study was approved by the Institutional Review Board of the Asan Medical Center, Seoul, Republic of Korea (No. 2023-0093).

Medical records were reviewed for the following information: sex, main diagnosis, age at the initial Rastelli operation, age, height, weight, and body surface area(BSA) at the most recent and previous RV-PA conduit change operation, as well as at the time of echocardiography and catheterization before the last RV-PA conduit change operation. Additionally, the name of the most recent operation and the total number of conduit change operations were recorded.

The echocardiographic studies were performed using Vivid ultrasound machine (GE Healthcare, Fairfield, CT, USA), Philips EPIC CVx (Philips Andover, Andover, MA, USA), and Acouson SC2000 (Siemens Germany, North Rhine-Westphalia, Germany). Data were stored digitally and analyzed offline using the Tom Tec Image Arena software (Tom Tec Imaging Systems GmBH) by a qualified researcher. To test intraobserver reliability, the same researcher performed offline analyses of echocardiography for 15 randomly selected patients at least one week apart. To test interobserver reliability, a second qualified researcher performed offline analyses of echocardiography for the same 15 randomly selected patients who were tested for the intraobserver reliability. The results of the intra/interobserver reliability are shown in Supplemental table 2.

The following echocardiographic data were obtained: the severity and peak velocity of tricuspid regurgitation (TR), severity of pulmonary regurgitation (PR), left ventricular end diastolic dimension (LVEDD), LV end systolic dimension (LVESD), LV fraction shortening (FS), tricuspid annular plane systolic excursion (TAPSE), RV end diastolic area (EDA), RV EDA indexed to BSA (EDAi), RV end systolic area (ESA), RV ESA indexed to BSA (ESAi), RV fractional area change (FAC), tricuspid valve (TV) early diastolic inflow velocity (E), TV late diastolic inflow velocity (A), TV annular systolic peak velocity (s'), TV annular early diastolic peak velocity (e'), TV annular late diastolic peak velocity (a'), TV e'/a' ratio, TV E/e' ratio, LV longitudinal strain at apical 4 chamber view (LV LS), LV longitudinal strain rate at systole (LV SRs), at early diastole (LV SRe) and at late diastole (LV SRa), RV LS at apical 4 chamber view (RV LS), RV SRs, RV SRe, RV SRa. RV area change was calculated as the difference between RV EDA and RV ESA. RV FAC was calculated as (RV area change / RV EDA) x 100%.

Catheterization data were reviewed for the following information: right atrial mean pressure (RAP), right ventricular systolic pressure (RVSP), right ventricular end diastolic pressure (RVEDP), pulmonary artery systolic pressure (PASP), and mean pulmonary artery pressure (mPAP). Among laboratory data, Brain natriuretic peptide (BNP) level was collected from the electrical charts.

The study's primary outcomes were duration of ventilator use, length of intensive care unit (ICU) stay, and total hospital days after the last operation. We considered cases where the values of these factors exceeded the median value as a poor short-term outcome. Secondary outcomes included the application of extracorporeal membrane oxygenation (ECMO), early death (within 1 month), and late death (after 1 month).

The RV-PA coupling indices analyzed in the study were as follows:

Echocardiographic data only

· TAPSE/RV ESAi ratio [14]

· TV s'/RV ESAi ratio [14,15]

· RV area change/RVESA ratio [15-17]

Echocardiographic data and catheterization data mixed

· TAPSE/RVSP ratio [9,16,17]

· TV s'/RVSP ratio [9]

· RV FAC/RVSP ratio[18]

· RV FAC/mPAP ratio [16,19]

· TAPSE/mPAP ratio [19]

· RV LS/RVSP ratio[20]

When calculating RV-PA coupling indices, TAPSE, TV s', RV ESA, RV ESAi, RV area change, RV FAC, and RV LS were derived from echocardiographic data. For mPAP, the study used catheterization data. RVSP was also determined using catheterization data. However, when echocardiography was performed more than 3 months after catheterization and peak TR velocity was available, the formula of (peak TR velocity$(m/s)^2$ x 4 + estimated RA pressure) was used[7].

Statistical analysis

All statistical analyses were performed using SPSS software version 28.0 (IBM Corp., Armonk, NY, USA) R version 4.3.0 (R Studio, Boston, Massachusetts). Categorical variables are presented as number (percentage), and continuous variables as mean ± standard deviation (SD). The Chi-square test was used to compare categorical variables, and the Mann-Whitney test was used to compare continuous variables. Univariate & Multivariate logistic regression (LR) analyses were conducted to identify independent predictive factors of adverse short-term surgical outcomes, including prolonged duration of ventilator use (>1day), length of ICU stay (>1day), and total hospital days (>10 days). Intraclass correlation coefficient were used to assess interobserver and intraobserver reliability of echocardiographic parameters. *P* value <0.05 was considered statistically significant.

Results

1. Study Population and Baseline Diagnoses

Among the total 77 patients who underwent RV-PA conduit change operation, 8 were excluded due to inappropriate echocardiographic images and 13 were excluded due to unavailable cardiac catheterization data. The final patient group included 56 patients, who were matched by sex and age with 56 individuals in the control group. The basic characteristics between the patient group and the control group are compared in Table 1. In both the study and control groups, 27 out of 56 participants (48.2%) were females. The mean age of participants was comparable between the two groups (10.4 ± 6.5 years vs 10.0 ± 4.0 years, $p = 0.646$). Mean weight and BSA were similar between the two groups.

Baseline diagnoses of the patient group are shown in Supplemental table 1. Tetralogy of Fallot including pulmonary atresia with ventricular septal defect and/or Major aorto-pulmonary collateral arteries (MAPCAs) (n = 39/56, 69.6%) accounted for the largest portion of baseline diagnosis, followed by truncus arteriosus (n = 7/56, 12.5%), double outlet right ventricle (n = 4, 7.1%). Among the 56 patients included in the study, conduit change operation was performed once in 44 patients (78.6%), twice in 11 patients (19.6%), and 3 times in 1 patient (1.8%). The mean interval between echocardiography and surgery was 3.8months, whereas the mean interval between catheterization and surgery was 3.2 month.

2. Comparison between the patient group and the control group

2-1. Echocardiographic Findings

When comparing echocardiographic findings, the patient group exhibited significantly smaller LVEDD ($p = 0.006$) and LVESD ($p = 0.010$), but comparable LV FS ($p = 0.456$) compared to the control group. Both TAPSE and TAPSE Z score were significantly lower in the patient group (all p <0.001). Both RV EDAi and RV ESAi were increased in the patient group compared to the controls

Table 1. Comparison of basic characteristics between the patient group and the control group

Variable	Patient group (n=56)	Control group (n=56)	*p*
Demographic findings			
Female, n(%)	27 (48.2)	27 (48.2)	1.0
Age (years)	10.4 ± 6.5	10.0 ± 4.0	0.646
Height (cm)	128.5 ± 33.0	137.5 ± 21.0	0.214
Weight (kg)	32.2 ± 19.5	36.7 ± 17.0	0.077
BSA (m^2)	1.05 ± 0.44	1.17 ± 0.35	0.074
Echocardiographic findings (M-mode)			
LVEDD (mm)	37.0 ± 7.1	40.5 ± 5.1	0.006*
LVESD (mm)	23.2 ± 5.0	25.2 ± 3.8	0.010*
LV FS (%)	37.4 ± 6.3	37.9 ± 3.6	0.456
TAPSE (mm)	14.1 ± 3.1	20.9 ± 3.0	<0.001*
TAPSE (Z score)	-3.88 ± 1.91	0.47 ± 1.90	<0.001*
Echocardiographic findings (2D)			
RV EDAi (cm^2/m^2 BSA)	18.4 ± 5.9	11.7 ± 2.0	<0.001*
RV ESAi (cm^2/m^2 BSA)	11.4 ± 4.8	6.3 ± 1.1	<0.001*
RV FAC (%)	39.1 ± 8.1	45.9 ± 6.2	<0.001*
Echocardiographic findings (Doppler)			
TV E velocity (m/s)	0.79 ± 0.18	0.67 ± 0.12	0.001*
TV A velocity (m/s)	0.55 ± 0.15	0.47 ± 0.13	0.016*
TV E/A ratio	1.52 ± 0.45	1.48 ± 0.36	0.753

TV s’ (cm/s)	6.7 ± 1.4	11.4 ± 3.2	<0.001*
TV e’ (cm/s)	10.2 ± 2.9	14.6 ± 3.7	<0.001*
TV a’ (cm/s)	6.5 ± 2.2	9.0 ± 3.3	<0.001*
TV e’/a’ ratio	1.69 ± 0.72	1.84 ± 0.93	0.366
TV E/e’ ratio	8.5 ± 3.3	4.8 ± 1.5	<0.001*
Echocardiographic findings (Strain)			
LV LS (%)	-16.9 ± 4.6	-22.2 ± 3.5	<0.001*
LV SRs (m/s)	-0.88 ± 0.22	-1.00 ± 0.22	0.010*
LV SRe (m/s)	0.95 ± 0.32	1.02 ± 0.46	0.190
LV SRa (m/s)	0.35 ± 0.16	0.40 ± 0.17	0.349
RV LS (%)	-16.5 ± 4.3	-26.5 ± 3.3	<0.001*
RV SRs (m/s)	-0.76 ± 0.21	-1.12 ± 0.27	<0.001*
RV SRe (m/s)	0.87 ± 0.29	1.13 ± 0.33	<0.001*
RV SRa (m/s)	0.36 ± 0.15	0.46 ± 0.17	0.015*
Catheterization data			
Mean RAP (mmHg)	6.8 ± 4.1	-	-
RVEDP (mmHg)	10.1 ± 4.5	-	-
RVSP (mmHg)	76.9 ± 18.8	-	-
PASP (mmHg)	34.9 ± 17.0	-	-
Δ (RVSP – PASP) (mmHg)	41.6 ± 23.2	-	-
mPAP (mmHg)	18.8 ± 7.9	-	-
Operation time metrics			

Operation time (minutes)	318.7 ± 116.1	-	-
Cardiopulmonary bypass time (minutes)	103.5 ± 51.5	-	-
Circulatory arrest time (minutes)	21.6 ± 36.1	-	-

Abbreviations: BSA, body surface area; RV, right ventricle; EDAi, end diastolic area indexed by BSA; ESAi, end systolic area indexed by BSA; FAC, fractional area change; TAPSE, tricuspid annular plane systolic excursion; LVEDD, left ventricular end diastolic dimension; LVESD, left ventricular end systolic dimension; FS, fractional shortening; TV, tricuspid valve; E, early diastole; A, late diastole; s', annular peak systolic velocity; e', annular peak early diastole velocity; a', annular peak late diastole velocity; SRs, longitudinal strain rate at systole; SRe, longitudinal strain rate at early diastole; SRa, longitudinal strain rate at late diastole; LS, longitudinal strain at apical 4 chamber view; RAP, right atrial pressure; RVEDP, right ventricular end diastolic pressure; RVSP, right ventricular systolic pressure; PASP, pulmonary arterial systolic pressure; PAP pulmonary arterial pressure.

Values are presented as mean ± standard deviation.

* Statistically significant

(all p < 0.001), and RV FAC was significantly decreased in the patient group (39.1±8.1 % vs 45.9±6.2 %, p <0.001). In the patient group, TV E velocity (p = 0.001) and TV A velocity (p = 0.016) were increased, but there was no significant difference in TV E/A ratio (p = 0.753). TV annular peak velocity at systole (s'), early diastole (e') and late diastole (a') measured by tissue Doppler imaging were significantly decreased in the patient group (all p <0.001). TV E/e' ratio was increased statistically in the patient group (8.5±3.3 vs 4.8±1.5, p <0.001). In speckle tracking echocardiography, the patient group showed lower LV LS, LV SRs, RV LS, RV SRs, RV SRe, RV SRa compared to the control group (all p <0.05). LV SRe and LV SRa showed no significant difference.

2-2. Comparison of RV-PA Coupling Indices

A comparison of RV-PA coupling indices between the patient group and the control group is presented in Table 2. All comparable RV-PA coupling indices were significantly worse in the patient group compared to the control group (all p < 0.001). These indices include TAPSE/RV ESAi (1.46±0.57 vs 3.44±0.76), TV s'/RV ESAi (0.67±0.27 vs 1.89±0.71), RV area change/RV ESA (0.67±0.21 vs 0.88±0.25), TAPSE/RVSP (0.19±0.06 vs 0.99±0.22), TV s'/RVSP (0.09±0.03 vs 0.50±0.16), RV FAC/RVSP (0.54±0.18 vs 2.21±0.47), and RV LS/RVSP (-0.23±0.09 vs -1.25±0.28). However, RV FAC/mPAP and TAPSE/mPAP could not be compared between the study and control groups as there were no available catheterization data for mPAP in the control group.

3. Catheterization Data and Surgical Time Metrics

The catheterization data and surgery time metrics of the patients group are also included in Table 1. The average of RVSP was 76.9 ± 18.8 mmHg, and the average of PASP was 34.9 ± 17.0 mmHg. Mean PAP was 18.8 ± 7.9 mmHg. The average duration of operation was 318.7 ± 116.1 minutes, with a mean cardiopulmonary bypass (CPB) time of 103.5 ± 51.5 minutes and a mean circulatory arrest time of 21.6 ± 36.1 minutes.

4. Clinical Short-term Outcomes

Clinical short-term outcomes of the RV-PA conduit change surgery are shown in Table 3. The median duration of the ventilator use was 1 day or 9 hours, and the median length of ICU stay was 1 day or 22 hours. The median total hospital days were 10 days. During the study period, no patient required ECMO after the conduit-change operation. There were no early deaths reported within 1 month after surgery, but one patient died later.

5. Analysis of RV-PA Coupling Indices in Relation to Short-Term Surgical Outcomes

A comparison of the RV-PA coupling indices among patients with varying short-term surgic-

Table 2. Comparison of RV-PA coupling indices between the study group and the control group

RV-PA coupling indices	Study group(n=56)	Control group (n=56)	*p*
TAPSE/RV ESAi	1.46 ± 0.57	3.44 ± 0.76	<0.001*
TV s '/RV ESAi	0.67 ± 0.27	1.89 ± 0.71	<0.001*
RV area change/RV ESA	0.67 ± 0.21	0.88 ± 0.25	<0.001*
TAPSE/RVSP	0.19 ± 0.06	0.99 ± 0.22	<0.001*
TV s'/RVSP	0.09 ± 0.03	0.50 ± 0.16	<0.001*
RV FAC/RVSP	0.54 ± 0.18	2.21 ± 0.47	<0.001*
RV FAC/mPAP	2.60 ± 1.60	-	-
TAPSE/mPAP	0.93 ± 0.47	-	-
RV LS/RVSP	-0.23 ± 0.09	-1.25 ± 0.28	<0.001*

Abbreviations: RV, right ventricle; PA, pulmonary artery; TAPSE, tricuspid annular plane systolic excursion; ESAi, end systolic area indexed by body surface area; TV, tricuspid valve; s', annular peak systolic velocity; RVSP, right ventricular systolic pressure; FAC, fractional area change; mPAP, mean pulmonary arterial pressure; LS, longitudinal strain at apical 4 chamber view.

Values are presented as mean ± standard deviation.

* Statistically significant

al outcomes is presented in Supplemental table 3. We divided the patient group based on postoperative parameters: duration of ventilator use (≤1 day vs >1 day), length of ICU stay (≤1 day vs >1 day), and total hospital stay (≤10 days vs >10 days). Out of total 56 patients, 10.7% (n=6) were unable to be weaned off the mechanical ventilator within a day post-surgery, 21.4% (n=12) had an ICU stay longer than a day. Certain RV-PA coupling indices, including TV s'/RV ESAi, TAPSE/RVSP, RV FAC/RVSP, outcomes is presented in Supplemental table 3. We divided the patient group based on postoperative parameters: duration of ventilator use (≤1 day vs >1 day), length of ICU stay (≤1 day vs >1 day), and

Table 3. Short-term outcomes of RV-PA conduit change operation

Short-term outcomes	Median value (Interquartile range)
Primary outcomes	
Duration of ventilator use (days)	1 (1.0 – 1.0)
Duration of ventilator use (hours)	9 (6.0 – 13.0)
Length of ICU stay (days)	1 (1.0 – 1.0)
Length of ICU stay (hours)	22 (19.0 – 25.75)
Total hospital days	10 (8.0 – 15.0)
Secondary outcomes	
Application of ECMO	0
Early death (< 1month)	0
Late death (> 1 month)	1

Abbreviations: RV, right ventricle; PA, pulmonary artery; ICU, intensive care unit; ECMO, extracorporeal membrane oxygenation.

total hospital stay (≤10 days vs >10 days). Out of total 56 patients, 10.7% (n=6) were unable to be weaned off the mechanical ventilator within a day post-surgery, 21.4% (n=12) had an ICU stay longer than a day. Certain RV-PA coupling indices, including TV s'/RV ESAi, TAPSE/RVSP, RV FAC/RVSP, and RV FAC/mPAP, showed significant differences between patients who required more than one day of ventilation and those weaned off within a day (all p <0.05), as well as between patients with an ICU stay of more than a day compared to those discharged within a day (all *p* <0.05). Regarding the total hospital days, 41.1% of patients (n=23) stayed in hospital for more than 10 days, but there was no significant discrepancies observed in the RV-PA coupling indices between this group but there was

Table 4. Univariate logistic regression analyses conducted on various parameters associated with short-term outcomes of the RV-PA conduit change surgery after Rastelli operation.

	Duration of ventilator use (>1day)		**Length of ICU stay (>1day)**		**Total Hospital days (>10days)**	
	p	*β*	*p*	*β*	*p*	*β*
Demographics at operation						
Age	0.024*	0.622	0.125	0.909	0.006*	0.852
Weight	0.030*	0.776	0.031*	0.944	0.003*	0.944
Height	0.033*	0.968	0.013*	0.967	0.001*	0.962
BSA	0.023*	0.000	0.019*	0.081	0.002*	0.076
RV-PA indices						
TAPSE/RV ESAi	0.289	0.000	0.051	0.217	0.410	0.644
TV s'/RV ESAi	0.016*	0.000	0.024*	0.017	0.624	0.587
RV area change/RV ESA	0.006*	0.000	0.025*	0.013	0.461	0.380
TAPSE/RVSP	0.034*	0.000	0.030*	0.000	0.297	0.004
TV s'/RVSP	0.881	10.853	0.326	0.000	0.946	1.950

RV FAC/RVSP	0.030*	0.001	0.029*	0.007	0.879	0.790
RV FAC/mPAP	0.008*	0.131	0.070	0.490	0.568	0.900
TAPSE/mPAP	0.023*	0.000	0.123	0.157	0.484	0.619
RV LS/RVSP	0.900	0.532	0.322	64.162	0.862	0.573
Echocardiographic parameters						
LVEDD	0.007*	0.651	0.027*	0.875	0.002*	0.842
LVESD	0.007*	0.613	0.014*	0.789	0.020*	0.853
LVEDD (Z score)	0.264	0.585	0.830	1.088	0.718	0.892
LVESD (Z score)	0.323	0.651	0.396	0.747	0.498	1.218
TAPSE (mm)	0.023*	0.329	0.120	0.810	0.048*	0.807
TAPSE (Z score)	0.151	0.651	0.472	0.866	0.316	0.850
RV FAC	0.007*	0.772	0.013*	0.887	0.317	0.966
RV EDA	0.212	0.905	0.128	0.917	0.002*	0.807
RV ESA	0.968	1.004	0.571	0.960	0.009*	0.823
RV EDAi	0.006*	1.303	0.014*	1.168	0.207	1.063

RV ESAi	0.004*	1.639	0.006*	1.283	0.131	1.102
TV s’	0.426	0.758	0.225	0.725	0.181	0.748
TV e’	0.776	1.048	0.848	1.024	0.581	1.057
TV a’	0.036*	1.563	0.143	1.250	0.440	1.106
TV E/e’ ratio	0.604	1.098	0.508	1.095	0.490	0.926
LV LS	0.221	1.141	0.223	1.099	0.829	1.013
RV LS	0.995	1.001	0.800	1.019	0.650	1.029
Catheterization data						
RVSP	0.773	0.993	0.018*	1.028	0.660	0.993
PASP	0.134	1.031	0.018*	1.055	0.167	1.025
mPAP	0.055	1.095	0.009*	1.160	0.286	1.040
Laboratory data						
BNP	0.445	1.002	0.444	1.002	0.015*	1.019
Operation time metrics						
Operation time	0.986	1.000	0.070	1.005	0.642	1.001

CPB time	0.668	0.996	0.028*	1.014	0.992	1.000
Arrest time	0.479	0.987	0.245	1.009	0.601	1.004

Abbreviations: RV, right ventricle; PA, pulmonary artery; ICU, intensive care unit; BSA, body surface area; TAPSE, tricuspid annular plane systolic excursion; ESAi, end systolic area indexed by body surface area; TV, tricuspid valve; s’, annular peak systolic velocity; LS, longitudinal strain at apical 4 chamber view; RVSP, right ventricular systolic pressure; FAC, fractional area change; mPAP, mean pulmonary arterial pressure; LVEDD, left ventricular end diastolic dimension; LVESD, left ventricular end systolic dimension; EDAi, end diastolic area indexed by body surface area; e’, annular peak early diastolic velocity; a’, annular peak late diastolic velocity; BNP, brain natriuretic peptide; CPB, cardiopulmonary bypass.

* Statistically significant

Table 5. Multivariate logistic regression analyses associated with short-term outcomes of the RV-PA conduit change operation.

	Length of ICU stay (>1day)		Total Hospital days (>10days)	
	p	*β*	*p*	*β*
BSA	0.014*	0.012	0.003*	0.052
RV FAC (%)	0.013*	0.841	-	-
CPB time	0.010*	1.031	-	-

Abbreviations: RV, right ventricle; PA, pulmonary artery; ICU, intensive care unit; BSA, body surface area; FAC, fractional area change; CPB, cardiopulmonary bypass.

*Statistically significant

no significant discrepancies observed in the RV-PA coupling indices between this group and those who stayed for 10 days or less. Our investigation did not reveal any association between the severity of TR or PR and RV-PA coupling indices.

6. Prognostic factors for Short-Term Outcomes

The univariate LR analyses presented in Table 4 reveal significant associations between various parameters and the short-term outcomes post RV-PA conduit change surgery. The study discovered that patient demographics, specifically older age, increased weight, taller height, and a larger body surface area (BSA) were positively associated with favorable outcomes, such as a decrease in ventilator usage, shorter stays in ICU, and an overall reduction in duration of hospitalization (all $p < 0.05$), except for age for length of ICU stay ($p = 0.125$). Among the RV-PA coupling indices, RV area change/RV ESA ($p = 0.006$), and RV FAC/mPAP ($p = 0.008$) were found to be most significantly associated with the duration of ventilator use, and TV s'/RV ESAi ($p = 0.024$) and RV area change/RV ESA ($p = 0.025$) showed most significant associations with the length of ICU

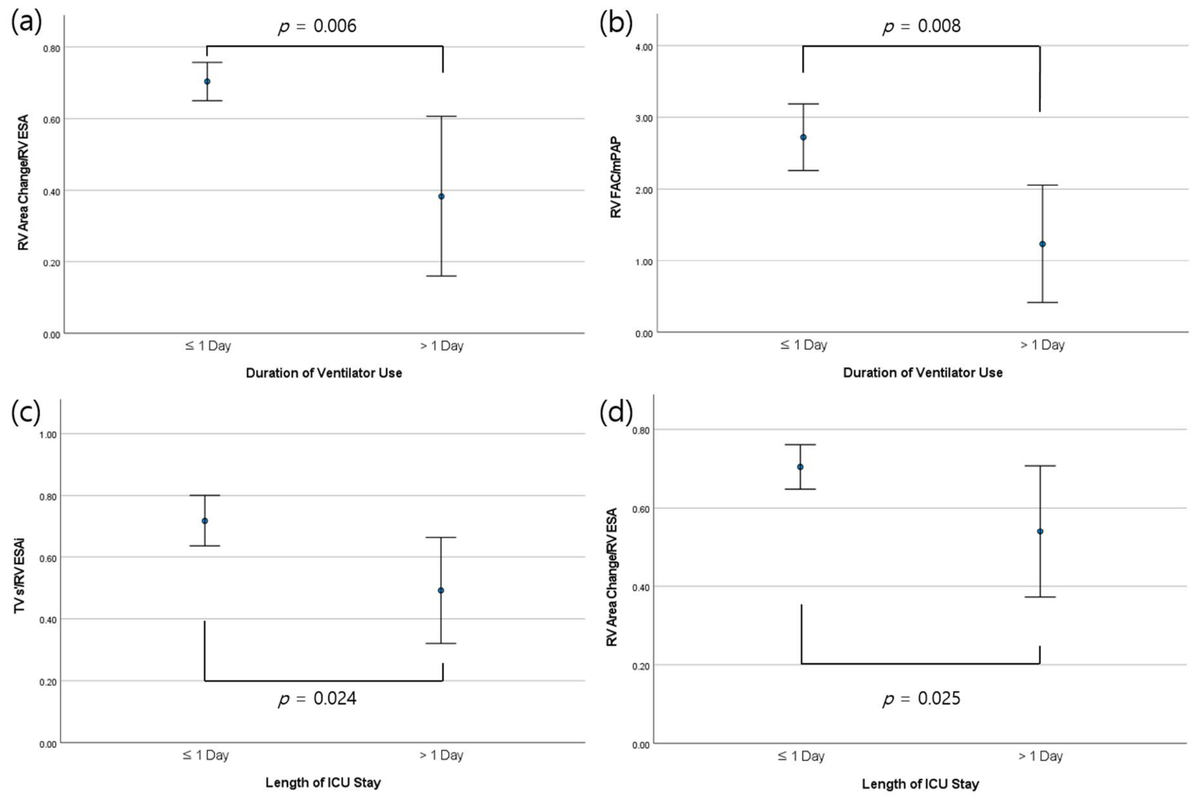

Figure 1. Comparison of RV-PA indices in relation to short-term outcomes of RV-PA conduit surgery after Rastelli operation. (a) RV area change/RV ESA on duration of ventilator use (p=0.006). (b) RV FAC/mPAP on duration of ventilator use (p=0.008). (c) TV s'/RV ESAi on length of ICU stay (p=0.024). (d) RV area change/RV ESA on length of ICU Stay (p=0.025). Abbreviations: *RV,* right ventricle; *PA,* pulmonary artery; *ESA,* end systolic area; *FAC,* fractional area change; *mPAP,* mean pulmonary artery pressure; *TV,* tricuspid valve; s’, annular peak systolic velocity; *ESAi* end systolic area indexed by body surface area

stay. These findings are depicted in Figure 1. The study also found that greater LVEDD and LVESD were associated with favorable short-term outcomes (all $p < 0.05$), but their z score did not showed any significance. Greater TAPSE level was associated with shorter ventilator use ($p = 0.023$) and shorter total hospital days ($p = 0.048$). On the other hand, higher RV EDAi and RV ESAi were linked to longer ventilator use and ICU stay (all $p < 0.05$). Furthermore, an increased TV a’ was associated with longer ventilator use (p = 0.036). Catheterization data including RVSP, PASP, and mPAP were found to be linked with longer ICU stays (all $p < 0.05$). Also, a higher preoperative BNP level was connected with extended hospital stays (*p* = 0.015. In terms of operative duration metrics, an elongated cardiopulmonary bypass (CPB) time was found to be associated with an extended ICU stay (*p* = 0.028).

The results of multivariable LR analyses are presented in Table 5. There was no significant predictable factor associated with the duration of ventilator use. Both higher BSA and higher RV FAC were independent predictable factors for shorter length of ICU stay. Longer CPB time during the operation could also predict longer ICU stay. BSA was the only predictable factor for total hospital days which had negative correlation. None of the RV-PA coupling indices could independently predict the short-term outcomes.

Discussion

In this study on patients with congenital heart diseases who underwent RV-PA conduit change surgery following Rastelli operation, the authors found that RV-PA coupling indices, derived from pre-surgical echocardiography and catheterization data, were significantly impaired compared to the healthy controls matched by sex and age. In multivariate LR analysis, smaller BSA, decreased RV FAC, and longer CPB time were identified as independent prognostic factors for unfavorable short-term outcomes, particularly prolonged ICU stays, while the RV-PA coupling indices showed no significance.

The patient group undergoing RV-PA conduit replacement operation exhibited significant deterioration in various echocardiographic parameters in comparison with the control group. RV enlargement and decrease in RV systolic and diastolic function, along with increase in RV filling pressure were prominent in the patient group, despite LV fractional shortening (FS) was rather preserved. Both RV and LV longitudinal strain (LS) and strain rate (SR), assessed using the speckle tracking method, showed an overall reduction in the patient group. Furthermore, one of the most significant finding of the study is that all comparable RV-PA coupling indices demonstrated a significantly worse value in patient group compared to the controls. These results are similar with recent studies on patients with repaired Tetralogy of Fallot (TOF), and are presumably due to a complex interplay of RV dysfunction and changes in the pulmonary arteries[12,13,15]. After RV-PA conduit placement in various congenital heart diseases, RV dilatation and dysfunction may progress due to increasing RV loading caused by conduit regurgitation, stenosis, or compression [3,4], and it can be speculated that RV-PA coupling will gradually deteriorate in this process.

The RV-PA coupling indices analyzed in this study were derived from readily obtainable surrogates using echocardiography and catheterization data collected prior to the surgery. However, the gold standard for assessing RV-PA coupling is measurement of the end-systolic/arterial elastance (Ees/Ea) ratio through invasive pressure-volume loops derived by specialized catheterization, which can be complemented by cardiac MRI [16,21]. Nevertheless, this technique is not routinely implemented in patients with congenital heart diseases due to its expensive cost and technical complexity. The optimal Ees/Ea ratio is known to be between 1.5 and 2, facilitating efficient blood ejection with minimal energy expenditure[21]. A ratio below 0.8, however, indicates a depletion of RV functional reserve and may herald the progression of RV failure[21]. Given the clinical utility of this method, there has been a concerted effort to identify alternative, more easily obtainable indicators through rigorous research. [8-11,16-18,20,22-25]. In this study, we aimed to examine the various possible RV-PA coupling indices and evaluate their applicability.

Univariate logistic regression (LR) analysis revealed a significant association between prolonged ventilator use (>1day) and ICU stay (>1day) with several common RV-PA indices, including TV s'/RV ESAi, RV area change/RV ESA, TAPSE/RVSP, and RV FAC/RVSP (all p <0.05). On the other hand, no significant differences were observed in RV-PA indices between patients with prolonged hospital days (>10days) and those without. This lack of significance may be attributed to the influence of various confounding factors, including the duration of antibiotic use and individual preferences of patients and their caregivers, which can also impact the length of hospital stay.

Among the surrogates of RV-PA index, TAPSE/pulmonary arterial systolic pressure (PASP) appears to be most widely studied in the literature. Tello et al. validated TAPSE/PASP ratio derived from echocardiography as a useful surrogate for Ees/Ea ratio in severe pulmonary hypertension, and suggested that a ratio of <0.31 mm/mmHg was associated with a worse prognosis [16]. Brener et al. conducted a study in patients who underwent transcatheter TV repair due to TR and showed that TAPSE/PASP ratio >0.317 mm/mmHg was associated with a significant difference in all-cause mortality, indicating that RV-PA index can be a powerful, independent predictor of mortality[10]. Lai et al. proposed a cut-off value of TAPSE/PASP ratio 0.194 mm/mmHg as a predictor of high-risk group in patients with systemic sclerosis-associated pulmonary arterial hypertension[23]. In our research, we used RVSP instead of PASP due to the substantial pressure gradient between the RV and PA, resulting from the presence of RV-PA conduit stenosis, rendering PASP an inadequate reflection of RV afterload. Furthermore, since the TAPSE normal range changes with age, applying the adult

TAPSE/PASP ratio cut-off value or establishing a new cut-off value for pediatric patients of various ages was not deemed suitable. However, in our study comparing patients with matched controls for age and gender, the average TAPSE/RVSP ratio showed a significant difference (0.19±0.06 vs 0.99±0.22, $p < 0.001$) and all the patients in the study exhibited values below than the -2 SD value of healthy controls. Univariate LR analysis further revealed that lower TAPSE/RVSP ratio value was associated with poor short-term outcomes such as prolonged ventilator use ($p = 0.034$) and extended ICU stay (p=0.030), but not in multivariate LR analysis.

Various research studies have examined the associations between the other RV-PA indices and clinical outcomes. In a study by Cheng et al., focusing on repaired TOF patients, the RV area change/RV ESA and TV s'/RV ESAi were found to be lower in the patient group compared to the controls. These indices were also found to be associated with the severity of RV and LV mechanics as well as TR and PR [15]. Additionally, Bleakley et al. demonstrated that RV FAC/RVSP exhibited association with pulmonary vascular resistance(PVR), RV EDAi, RV ESAi, measures of ventilation, and liver markers in critically ill COVID-19 ARDS patients[18]. Furthermore, Jentzer et al., in their study involving patients admitted to the cardiac ICU, revealed a significant association between TV s'/RVSP ratio and both short- and long-term mortality, suggesting its potential as a predictor of poor outcomes[9]. In our study, RV area change/RV ESA, TV s'/RV ESAi, RV FAC/RVSP, and TV s'/RVSP were all significantly worse in the patient group compared to the controls. However, in univariate LR analysis only the first three indices were found to be associated with prolonged duration of ventilator use and ICU stay (all $p < 0.05$), while the latter did not show significant differences in short-term prognosis within the patient group. Furthermore, Prins et al. suggested in their study that the reduction of pulmonary pulse wave transit time (pPTT) in patients with pulmonary arterial hypertension was due to the deterioration of RV-PA coupling[19]. They found that the RV FAC/mPAP ratio and TAPSE/mPAP ratio had strong associations with pPTT. In line with these findings, univariate LR analysis in our study revealed significant associations between these two indices and prolonged duration of ventilator use within the patient group.

In this study, using univariate logistic regression analysis, it was revealed that conventional factors, apart from RV-PA coupling indices, such as patient body size-related variables, RV dilatation, and decreased RV contractility were associated with poor short-term surgical outcomes of RV-PA conduit change surgery. Smaller values of age, weight, height, and body surface area (BSA), which reflect the patient's body size, as well as smaller values of LVEDD and LVESD, which reflect the size of the heart, were predominantly associated with poor short-term outcomes. Furthermore, smaller values of RV EDA and RV ESA were associated with longer total hospital days (all $p<0.05$). In many studies on congenital heart diseases, the smaller body size of patients has often been associated with adverse outcomes [3,4,26,27]. However, it is noteworthy that there have also been contradictory reports stating that age is not associated with early mortality and the risk of reoperation in the case of Tetralogy of Fallot (TOF) [28].

In addition, this study found that higher values of RV EDAi and RV ESAi, as well as decreased RV FAC, were significantly associated with prolonged ventricular use and ICU stay (all p <0.05). These findings are consistent with previous research that has demonstrated the adverse impact of RV dilatation and dysfunction on outcomes following TOF repair or pulmonary valve replacement in TOF [29-31]. TAPSE, one of the indicator reflecting right ventricular (RV) contractility, demonstrated an association with poor short-term outcomes, including prolonged ventilator use (p=0.023) and total hospital days (p=0.048). However, the TAPSE z score did not show any association with the short-term outcomes, indicating that TAPSE predominantly reflect patient size rather than solely focusing on RV contractility. TV s' showed no association with short-term outcomes.

Furthermore, this study has revealed that the increase in RVSP, PASP, and mPAP measured during catheterization is associated with prolonged ICU stay, emphasizing the importance of pulmonary arterial hypertension itself as a significant prognostic factor for mortality and morbidity in relation to cardiac surgery [32]. The study also showed that a significant association between high BNP levels and prolonged total hospital days (p=0.015). This finding aligns with previous research indicating that elevated BNP is associated with adverse outcomes, such as intubation duration, use of inotropic agents, and length of stay in the ICU in congenital heart diseases [33]. The finding that long cardiopulmonary bypass (CPB) time serves as an independent predictor of extended ICU stay in multivariate logistic regression analysis aligns with previous studies indicating that longer CPB time is associated with an increased risk of both early and late mortality in congenital heart diseases [3,28].

No patient involved in this study required ECMO or expired within a month following their surgical procedure. However, there was an instance of a late mortality occurring outside the hospital approximately 1.5 years after the procedure when the patient was 1.6 years old. The main diagnosis of the patient was pulmonary atresia with MAPCAs, and the patient underwent MAPCA unifocalization and Rastelli operation, followed by conduit change surgery. However, moderate to severe pulmonary hypertension and RV failure remained controlled, and it is presumed that the patient passed away due to an arrhythmia such as ventricular tachycardia. This patient had poor RV FAC of 16.3%, and small BSA of 0.49 and long CPB time of 179 min at the time and during the operation, and had experienced poor short-term surgical outcomes, with 9 days of ventilator use, 15 days in the ICU, and a total of 24 days of hospitalization. This suggests that further research is needed to apply our results on the long-term outcomes of the conduit-change surgery after Rastelli operation in the future.

Limitation

This study is a single-center retrospective study conducted on a relatively small sample of patients. However, due to the nature of rare congenital heart diseases in children, the sample size is inevitably limited, so the authors tried to complement the results of the study by comparison the patient group with healthy controls matched for gender and age.

Second, as the echocardiographic and catheterization data were obtained up to several months prior to the surgery, there is a possibility that the parameters derived from these exams may not accurately reflect the state of the patient just before the surgery. However, due to potential time delays between examinations and surgeries in high-workload clinical setting, it may be necessary to use the results to predict the surgical outcomes. Thus, in the clinical context, such attempts at prediction can be considered reasonable.

Third, all patients who underwent RV-PA conduit change surgery were included in the study without classifying the causes for reoperation. For example, surgeries due to endocarditis may extend hospitalization periods due to the duration of antibiotics usage, which could potentially confound the analysis of the effects of RV-PA coupling indices. However, even in such cases, it was considered that the RV-PA indices derived from the diagnostic process would have a significant impact on more acute outcomes such as the duration of ventilator use or ICU stay. Therefore, the authors intended to include all clinical situations in the study.

Fourth, there were inherent limitations and issues with the reliability of the echocardiographic modality itself. Particularly in the analysis of longitudinal strain using the speckle tracking method, we were not able to obtain significant results similar to those in other study[20]. This suggests that there might have been an influence of relatively low intra/interobserver reliability in our study.

Fifth, the classification of poor short-term surgical outcomes based on median duration in our study resulted in substantial discrepancies in sample sizes between the groups, which consequently undermined the statistical power. Future researches involving a larger patient population are recommended in order to strengthen and validate our findings, and further stratify the risk factors for outcomes of RV-PA conduit change surgery after Rastelli operation.

Conclusion

Our study found that RV-PA coupling indices were significantly impaired in patients undergoing RV-PA conduit change surgery after Rastelli operation compared to healthy controls, while none of these indices was able to predict the short-term surgical outcomes. Smaller patient body size, decreased RV contractility, and longer CPB time were identified as independent predictors of short-term surgical outcome. These findings will provide practical assistance in risk stratification for patients with congenital heart disease undergoing RV-PA conduit change operation.

Reference

1 Rastelli G (1969) A new approach to" anatomic" repair of transposition of the great arteries. Mayo Clinic Proceedings. pp 1-12

2 Rastelli G, WALLACE RB, ONGLEY PA (1969) Complete repair of transposition of the great arteries with pulmonary stenosis: a review and report of a case corrected by using a new surgical technique. Circulation 39: 83-95

3 Dearani JA, Danielson GK, Puga FJ, Schaff HV, Warnes CW, Driscoll DJ, Schleck CD, Ilstrup DM (2003) Late follow-up of 1095 patients undergoing operation for complex congenital heart disease utilizing pulmonary ventricle to pulmonary artery conduits. The Annals of thoracic surgery 75: 399-411

4 Mohammadi S, Belli E, Martinovic I, Houyel L, Capderou A, Petit J, Planché C, Serraf A (2005) Surgery for right ventricle to pulmonary artery conduit obstruction: risk factors for further reoperation. European journal of cardio-thoracic surgery 28: 217-222

5 Tweddell JS, Pelech AN, Frommelt PC, Mussatto KA, Wyman JD, Fedderly RT, Berger S, Frommelt MA, Lewis DA, Friedberg DZ (2000) Factors affecting longevity of homograft valves used in right ventricular outflow tract reconstruction for congenital heart disease. Circulation 102: Iii-130-Iii-135

6 Sanz J, Sánchez-Quintana D, Bossone E, Bogaard HJ, Naeije R (2019) Anatomy, function, and dysfunction of the right ventricle: JACC state-of-the-art review. Journal of the American College of Cardiology 73: 1463-1482

7 Shahim B, Hahn RT (2021) Right Ventricular-Pulmonary Arterial Coupling and Outcomes in Heart Failure and Valvular Heart Disease. Structural Heart 5: 128-139

8 Brener MI, Lurz P, Hausleiter J, Rodés-Cabau J, Fam N, Kodali SK, Rommel K-P, Muntané-Carol G, Gavazzoni M, Nazif TM (2022) Right ventricular-pulmonary arterial coupling and afterload reserve in patients undergoing transcatheter tricuspid valve repair. Journal of the American College of Cardiology 79: 448-461

9 Jentzer JC, Anavekar NS, Reddy YN, Murphree DH, Wiley BM, Oh JK, Borlaug BA (2021)

Right ventricular pulmonary artery coupling and mortality in cardiac intensive care unit patients. Journal of the American Heart Association 10: e019015

10 Fortuni F, Butcher SC, Dietz MF, van der Bijl P, Prihadi EA, De Ferrari GM, Marsan NA, Bax JJ, Delgado V (2021) Right Ventricular–Pulmonary Arterial Coupling in Secondary Tricuspid Regurgitation. The American Journal of Cardiology 148: 138-145

11 Egbe AC, Kothapalli S, Miranda WR, Pislaru S, Ammash NM, Borlaug BA, Pellikka PA, Najam M, Connolly HM (2019) Assessment of right ventricular-pulmonary arterial coupling in chronic pulmonary regurgitation. Canadian Journal of Cardiology 35: 914-922

12 Latus H, Binder W, Kerst G, Hofbeck M, Sieverding L, Apitz C (2013) Right ventricular–pulmonary arterial coupling in patients after repair of tetralogy of Fallot. The Journal of thoracic and cardiovascular surgery 146: 1366-1372

13 Sandeep B, Huang X, Li Y, Wang X, Mao L, Kan Y, Xiong D, Gao K, Zongwei X (2020) Evaluation of right ventricle pulmonary artery coupling on right ventricular function in post operative tetralogy of Fallot patients underwent for pulmonary valve replacement. Journal of Cardiothoracic Surgery 15: 1-9

14 Boulate D, Amsallem M, Kuznetsova T, Zamanian RT, Fadel E, Mercier O, Haddad F (2019) Echocardiographic evaluations of right ventriculo–arterial coupling in experimental and clinical pulmonary hypertension. Physiological reports 7: e14322

15 Cheng S, Li VW-Y, So EK-F, Cheung Y-F (2022) Right Ventricular–Pulmonary Arterial Coupling in Repaired Tetralogy of Fallot. Pediatric Cardiology 43: 207-217

16 Tello K, Wan J, Dalmer A, Vanderpool R, Ghofrani HA, Naeije R, Roller F, Mohajerani E, Seeger W, Herberg U (2019) Validation of the tricuspid annular plane systolic excursion/systolic pulmonary artery pressure ratio for the assessment of right ventricular-arterial coupling in severe pulmonary hypertension. Circulation: Cardiovascular Imaging 12: e009047

17 French S, Amsallem M, Ouazani N, Li S, Kudelko K, Zamanian RT, Haddad F, Chung L (2018) Non-invasive right ventricular load adaptability indices in patients with scleroderma-

associated pulmonary arterial hypertension. Pulmonary circulation 8: 2045894018788268

18 Bleakley C, Singh S, Garfield B, Morosin M, Surkova E, Mandalia MS, Dias B, Androulakis E, Price LC, McCabe C (2021) Right ventricular dysfunction in critically ill COVID-19 ARDS. International journal of cardiology 327: 251-258

19 Prins KW, Weir EK, Archer SL, Markowitz J, Rose L, Pritzker M, Madlon-Kay R, Thenappan T (2016) Pulmonary pulse wave transit time is associated with right ventricular–pulmonary artery coupling in pulmonary arterial hypertension. Pulmonary circulation 6: 576-585

20 Iacoviello M, Monitillo F, Citarelli G, Leone M, Grande D, Antoncecchi V, Rizzo C, Terlizzese P, Romito R, Caldarola P (2017) Right ventriculo-arterial coupling assessed by two-dimensional strain: A new parameter of right ventricular function independently associated with prognosis in chronic heart failure patients. International Journal of Cardiology 241: 318-321

21 Tello K, Dalmer A, Axmann J, Vanderpool R, Ghofrani HA, Naeije R, Roller F, Seeger W, Sommer N, Wilhelm J (2019) Reserve of right ventricular-arterial coupling in the setting of chronic overload. Circulation: Heart Failure 12: e005512

22 Todaro MC, Carerj S, Zito C, Trifirò MP, Consolo G, Khandheria B (2020) Echocardiographic evaluation of right ventricular-arterial coupling in pulmonary hypertension. American Journal of Cardiovascular Disease 10: 272

23 Lai J, Zhao J, Li K, Qin X, Wang H, Tian Z, Wang Q, Li M, Guo X, Liu Y (2022) Right Ventricle to Pulmonary Artery Coupling Predicts the Risk Stratification in Patients With Systemic Sclerosis-Associated Pulmonary Arterial Hypertension. Frontiers in Cardiovascular Medicine 9: 914

24 Li Y, Guo D, Gong J, Wang J, Huang Q, Yang S, Zhang X, Hu H, Jiang Z, Yang Y (2021) Right ventricular function and its coupling with pulmonary circulation in precapillary pulmonary hypertension: a three-dimensional echocardiographic study. Frontiers in Cardiovascular Medicine 8: 690606

25 Guazzi M, Bandera F, Pelissero G, Castelvecchio S, Menicanti L, Ghio S, Temporelli P, Arena

R (2013) Tricuspid annular plane systolic excursion and pulmonary arterial systolic pressure relationship in heart failure: an index of right ventricular contractile function and prognosis. American Journal of Physiology-Heart and Circulatory Physiology 305: H1373-H1381

26 Lim CYS, Lim JKB, Moorakonda RB, Ong C, Mok YH, Allen JC, Wong JJ-M, Tan TH, Lee JH (2019) The impact of pre-operative nutritional status on outcomes following congenital heart surgery. Frontiers in pediatrics 7: 429

27 Nomoto R, Sleeper LA, Borisuk MJ, Bergerson L, Pigula FA, Emani S, Fynn-Thompson F, Mayer JE, Del Nido PJ, Baird CW (2016) Outcome and performance of bioprosthetic pulmonary valve replacement in patients with congenital heart disease. The Journal of Thoracic and Cardiovascular Surgery 152: 1333-1342. e1333

28 Park CS, Lee JR, Lim H-G, Kim W-H, Kim YJ (2010) The long-term result of total repair for tetralogy of Fallot. European journal of cardio-thoracic surgery 38: 311-317

29 Knauth AL, Gauvreau K, Powell AJ, Landzberg MJ, Walsh EP, Lock JE, del Nido PJ, Geva T (2008) Ventricular size and function assessed by cardiac MRI predict major adverse clinical outcomes late after tetralogy of Fallot repair. Heart 94: 211-216

30 Therrien J, Provost Y, Merchant N, Williams W, Colman J, Webb G (2005) Optimal timing for pulmonary valve replacement in adults after tetralogy of Fallot repair. The American journal of cardiology 95: 779-782

31 Therrien J, Siu SC, McLaughlin PR, Liu PP, Williams WG, Webb GD (2000) Pulmonary valve replacement in adults late after repair of tetralogy of Fallot: are we operating too late? Journal of the American College of Cardiology 36: 1670-1675

32 Denault A, Deschamps A, Tardif J-C, Lambert J, Perrault L (2010) Pulmonary hypertension in cardiac surgery. Current cardiology reviews 6: 1-14

33 Cantinotti M, Giordano R, Scalese M, Molinaro S, Della Pina F, Storti S, Arcieri L, Murzi B, Marotta M, Pak V (2015) Prognostic role of BNP in children undergoing surgery for congenital heart disease: analysis of prediction models incorporating standard risk factors. Clinical Chemistry and Laboratory Medicine (CCLM) 53: 1839-1846

Supplemental table 1. Baseline characteristics of the study group

Variable	Final study population (n=56)
Baseline diagnosis	
TOF including PA VSD + MAPCAs	39 (69.6)
Truncus arteriosus	7 (12.5)
DORV	4 (7.1)
dTGA + VSD + PS	3 (5.4)
IAA type B	2 (3.6)
PA IVS	1 (1.8)
Number of conduit change	
1	44 (78.6)
2	11 (19.6)
3	1 (1.8)
Time gap between echocardiography and surgery (months)	3.8 (1.5 – 6.2)
Time gap between catheterization and surgery (months)	3.2 (2.0 – 4.8)

Abbreviations: RV, right ventricle; PA, pulmonary artery; TOF, tetralogy of Fallot; PA VSD, pulmonary atresia with ventricular septal defect; MAPCA, Major aorto-pulmonary collateral arteries; DORV, double outlet right ventricle; dTGA, dextro-Transposition of the great arteries; VSD, ventricular septal defect; PS, pulmonary stenosis; IAA, interruption of aortic arch; PA IVS, pulmonary atresia with intact ventricular septum.

Values are presented as number (percentage) for categorical variables, and mean ± standard deviation or median value (interquartile range) for continuous variables.

Supplemental table 2. Intraobserver and interobserver reliability test for echocardiographic findings

Echocardiographic parameters	Intraobserver reliability		Interobserver reliabiliy	
	Coefficient	*p*	Coefficient	*p*
TAPSE	0.857	<0.001	0.977	<0.001
RV EDA	0.906	<0.001	0.942	<0.001
RV ESA	0.938	<0.001	0.961	<0.001
RV FAC	0.778	0.004	0.848	0.001
TV E velocity	0.798	0.002	0.896	<0.001
TV A velocity	0.961	<0.001	0.977	<0.001
TV E/A ratio	0.983	<0.001	0.980	<0.001
s’	0.723	0.011	0.992	<0.001
e’	0.708	0.014	0.991	<0.001
a’	0.970	<0.001	0.983	<0.001
TV E/e’ ratio	0.957	<0.001	0.954	<0.001
LV LS	0.701	0.016	0.677	0.021
LV SRs	0.428	0.154	0.162	0.373
LV SRe	0.787	0.003	0.776	0.004
LV SRa	0.494	0.149	0.518	0.132
RV LS	0.635	0.035	0.655	0.028
RV SRs	0.553	0.072	0.095	0.427
RV SRe	0.768	0.005	0.771	0.005

RV SRa	0.586	0.117	0.896	0.001

Abbreviations: TAPSE, tricuspid annular plane systolic excursion; RV, right ventricle; EDA, end diastolic area; ESA, end systolic area; FAC, fractional area change; TV, tricuspid valve; E, early diastole; A, late diastole; s', annular peak systolic velocity; e', annular peak early diastole velocity; a', annular peak late diastole velocity; LV, left ventricle; LS, longitudinal strain at apical 4 chamber view; SRs, longitudinal strain rate at systole; SRe, longitudinal strain rate at early diastole; SRa, longitudinal strain rate at late diastole

Supplemental table 3. Comparison of RV-PA coupling indices between the patients with favorable and worse short-term surgery outcomes of the RV-PA conduit change operation

RV-PA indices	Duration of ventilator use			Length of ICU stay			Total Hospital days		
	≤ 1day (n=50)	>1 day (n= 6)	*p*	≤ 1day (n=44)	> 1day (n=12)	*p*	≤ 10day (n = 33)	> 10days (n= 23)	*p*
TAPSE/RV ESAi	1.55±0.50	0.46±0.18	<0.001*	1.54±0.51	1.11±0.72	0.096	1.51±0.48	134±0.71	0.473
TV s'/RV ESAi	0.71±0.25	0.30±0.13	<0.001*	0.72±0.26	0.49±0.24	0.022*	0.69±0.21	0.65±0.35	0.469
RV area change/RV ESA	0.70±0.19	0.38±0.21	0.002*	0.70±0.19	0.54±0.26	0.071	0.69±0.19	0.64±0.24	0.796
TAPSE/RVSP	0.20±0.06	0.12±0.01	0.003*	0.20±0.06	0.15±0.04	0.015*	0.20±0.06	0.18±0.06	0.291
TV s'/RVSP	0.09±0.03	0.09±0.06	0.507	0.09±0.03	0.08±0.04	0.071	0.53±0.16	0.53±0.21	0.930
RV FAC/RVSP	0.55±0.17	0.38±0.21	0.038*	0.56±0.15	0.43±0.24	0.015*	0.54±0.16	0.53±0.21	0.874
RV FAC/mPAP	2.72±1.63	1.24±0.78	0.004*	2.75±1.59	1.87±1.63	0.018*	2.67±1.78	2.41±1.41	0.790
TAPSE/mPAP	0.97±0.46	0.43±0.29	0.010*	0.98±0.46	0.71±0.45	0.113	0.96±0.49	0.87±0.44	0.635
RV LS/RVSP	-0.22±0.08	-0.23±0.10	0.867	-0.23±0.08	-0.20±0.09	0.285	-0.22±0.08	-0.23±0.09	0.967

Abbreviations: RV, right ventricle; PA, pulmonary artery; ICU, intensive care unit; TAPSE, tricuspid annular plane systolic excursion; ESAi, end systolic area indexed by body surface area; TV, tricuspid valve; s', annular peak systolic velocity; RVSP, right ventricular systolic pressure; FAC, fractional area change; mPAP, mean pulmonary arterial pressure; LS, longitudinal strain at apical 4 chamber view. * Statistically significant

국문요약

제목: 우심실-폐동맥 도관 교체 수술을 받은 환자의 단기 예후 인자로의 우심실-폐동맥 결합

목적: 우심실-폐동맥 결합의 악화가 다양한 우심실 질환 환자에서 불량한 예후와 연관이 있다는 사실은 잘 알려져 있다. 연구진은 라스텔리 수술 이후 우심실-폐동맥 도관 교체 수술을 받는 환자에서 우심실-폐동맥 결합 지표가 건강한 대조군에 비해 악화되어 있는지, 그리고 이 지표들이 수술의 단기 결과를 예측할 수 있는지 연구하고자 하였다.

방법: 2016년 1월부터 2018년 2월까지 77명의 소아 환자가 서울아산병원에서 우심실-폐동맥 도관 교체 수술을 받았다. 저자들은 이 환자들의 수술 전 심장 초음파와 심도자 검사 자료를 후향적으로 분석하였으며, 최종 환자군과 같은 수의 건강한 대조군을 연령과 성별을 매칭하여 선정하였다. 이번 연구에서 우심실-폐동맥 결합 지표는 tricuspid annular plane systolic excursion (TAPSE)/right ventricular end systolic area indexed with body surface area (RV ESAi), TAPSE/RV systolic pressure (RVSP), RV fractional area change (FAC)/RVSP, RV FAC/mean pulmonary artery pressure (mPAP), RV area change/RV ESA, tricuspid valve (TV) annular peak systolic velocity (s')/RV ESAi, TV s'/RVSP, and RV longitudinal strain (LS)/mPAP 를 이용하였다. 불량한 단기 수술 결과의 정의는 연장된 인공호흡기 사용 기간(>1일), 중환자실 체류 기간(>1일), 전체 입원 일수(>10일)로 하였고, 이는 중위수를 기준으로 하였다.

결과: 최종 환자군에 속한 56명의 평균 연령은 10.4 ± 6.5세였다. 비교 가능한 모든 RV-PA 결합 지표, 즉 TAPSE/RV ESAi, TV s'/RV ESAi, RV area change/RV ESA, TAPSE/RVSP, TV s'/RVSP, RV FAC/RVSP, RV LS/RVSP는 환자군에서 대조군에 비해 유의하

게 감소되어 있음이 확인되었으나($p < 0.001$), 단기 수술 예후의 독립적 예측 인자로 확인된 지표는 없었다. 다변량 로지스틱 회귀 분석에서는 환자의 작은 체표면적, 낮은 RV FAC, 그리고 긴 심폐 우회 시간이 불리한 단기 결과, 특히 중환자실 체류 기간이 긴 경우의 독립적 예측 인자로 확인되었다($p < 0.05$).

결론: 환자의 작은 체격, 우심실 수축 기능 저하, 긴 심폐 우회 시간이 라스텔리 수술 후 우심실-폐동맥 도관 교체 수술의 단기 예후 예측 인자로 밝혀졌다. 우심실-폐동맥 결합 지표는 환자 그룹에서 유의하게 악화되어 있었으나 단기 수술 결과의 예측인자로는 적용할 수 없었다.

중심 단어: 우심실-폐동맥 결합, 우심실-폐동맥 도관 교체 수술, 라스텔리 수술