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Effect of preoperative inspiratory muscle training on right ventricular systolic function in patients after heart valve replacement surgery



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ABSTRACT

Background: The reduction of right ventricular function after heart valve surgery was associated with mortality and morbidity after cardiac surgery, prolonged ICU length of stay, and higher hospital cost. Inspiratory muscle training can be considered for improving right ventricular systolic function by optimizing afterload and cardiac contractility. The study aims to determine the effect of inspiratory muscle training on right ventricular systolic function in patients after heart valve surgery.

Methods: Patients undergoing heart valve surgery were randomized into a conventional preoperative rehabilitation group and conventional preoperative rehabilitation added high-intensity inspiratory muscle training at least 14 days before surgery. Echocardiography examination was performed before rehabilitation and after cardiac surgery.

Results: There were 24 subjects consist of 12 control group and 12 intervention group. By using independent t-test or Mann Whitney test, we found significant differences on right ventricular function between intervention and control group, by using RV free wall strain ($17.7 \pm 3.0\%$ and $14.4 \pm 4.0\%$; $p=0.033$), RV FAC ($43.2 \pm 4.9\%$ and $35.1 \pm 8.8\%$; $p=0.006$), and TAPSE (12.7 ± 3.4 mm and 9.9 ± 2.7 mm; $p=0.039$). ICU length of stay in the intervention group was significantly shorter than the control group (3.2 ± 0.8 and 4.2 ± 1.3 days; $p=0.044$).

Conclusion: Patients underwent conventional preoperative rehabilitation added inspiratory muscle training had better right ventricular systolic function than patients in control group.

Keywords: right heart, valve surgery, outcome, respiration.

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INTRODUCTION

Valvular heart disease is one of heart failure etiology and caused high morbidity and mortality. Due to heart failure symptoms, patients were needed to undergo surgery.^{1,2} One of the common problems after heart valve surgery is reducing the right ventricular function associated with the increasing risk of mortality and morbidity after cardiac surgery and increasing hospital cost.³⁻⁵

The right ventricular function can be determined by preload, afterload, and contractility of the right ventricle. The right ventricle's structure was sensitive to sudden afterload changes. Some theories explained the reduction of right ventricle contractility during heart surgery such as pericardiotomy, inflammations due to cardiopulmonary bypass usage, mechanical ventilator usage,

and pulmonary dysfunction after cardiac surgery.^{4,6,7}

One of the new preoperative cardiac rehabilitation program concepts in heart surgery is maintaining good exercise capacity using aerobic and inspiratory muscle training programs.⁸ Patients with heart failure commonly have inspiratory muscle weakness associated with complications and exercise capacity reduction after cardiac surgery. In heart failure patients, inspiratory muscle weakness was associated calcium regulation changes, calpain activation, and increasing inflammatory mediators.⁹⁻¹¹ These problems may have a role in reducing myocardial contractility.^{12,13}

Inspiratory muscle training has been used as preoperative and cardiac rehabilitation program in patients with heart failure.^{8,14-16} This study aimed to establish the role of inspiratory muscle

training in patients' right ventricular function after heart valve surgery.

METHODS

Patient Population

We randomized 30 stable heart failure patients (NYHA I – II), aged 18 – 60 years old in Kariadi General Hospital, scheduled for elective heart valve surgery into control and intervention groups. This study was conducted in August 2019 until November 2019. Patients with comorbidities such as coronary heart disease, congenital heart disease, chronic pulmonary obstructive disease were excluded in this study. Patients with cardiopulmonary bypass time > 150 minutes, history of septic shock after surgery, and exercise discontinuation for more than three days were dropped out. The local ethics committee approved the study protocol.

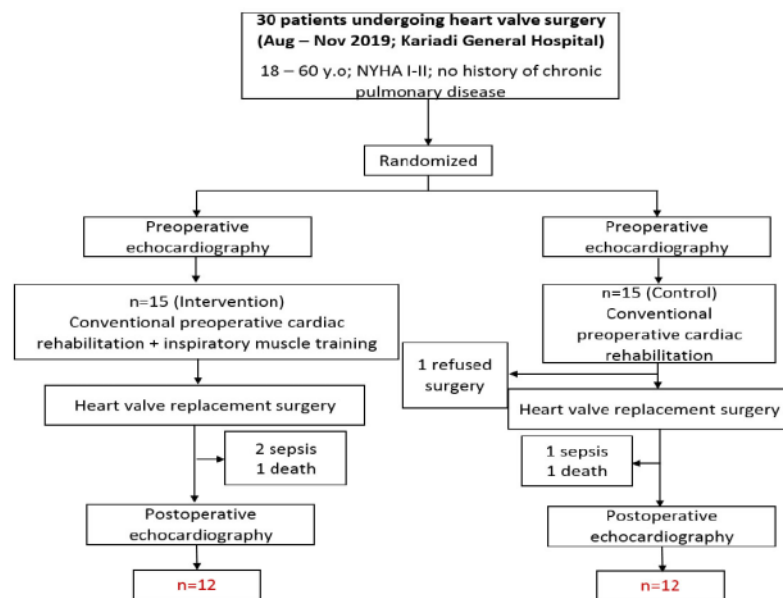


Figure 1. Patients selection

Definitions

Inspiratory muscle training was performed at home at least 14 days before heart valve surgery, twice a day (10 minutes each exercise), with 5 x 10 Repetition Maximum (RM) intensity. The resistance was increased on the 8th day of training. Exercise will be halted when the patient's shows worsen clinical signs and heart failure symptoms such as dyspnea, palpitations, fatigue, or cyanotic. Home-based exercise was supervised daily using video call. Both groups received standard preoperative exercise programs such as aerobic training, breathing techniques, ankle pump exercise, and range of motion exercise.^{15,17,18}

Right ventricular systolic function was measured by echocardiography using three methods: right ventricular free wall strain (RV free wall strain), right ventricular fractional area changes (RV FAC), and Tricuspid Annular

Plane Systolic Excursion (TAPSE). All methods were analyzed using Philips Qlab Software. RV free wall strain was assessed by tracing the right ventricular base, mid, and apex on apical four-chamber view. RV free wall strain <20% indicates abnormal right ventricular function. RV FAC percentage was measured using

the difference between right ventricle end-diastolic area and end-systolic area divided by end-diastolic area multiplied by one hundred. RV FAC < 35% indicates RV systolic dysfunction. TAPSE was measured by aligning an M-mode cursor parallel with the RV free wall as it meets the tricuspid annulus from the RV apical four-chamber view. TAPSE < 17 mm indicates RV systolic dysfunction.^{4,19,20} Echocardiography examinations were performed before patients underwent preoperative cardiac rehabilitation and were discharged from the hospital.

Pulmonary hypertension probability was assessed using echocardiography measurement by sPAP (systolic pulmonary arterial pressure) assessment and supportive echocardiography signs.²¹ Tricuspid regurgitation severity was evaluated by measuring the tricuspid regurgitation's vena contracta jet width in apical four-chamber view.²² Other rhythm besides sinus rhythm on electrocardiogram were considered as arrhythmia.

Statistical analysis

Baseline characteristics data were analyzed using descriptive statistics. The normality of data was tested using the Saphiro-Wilk test. Numerical values were

expressed as mean \pm standard deviation (normally distributed data) or median and interquartile range (non-normally distributed data) and compared using independent t-test or Mann-Whitney test, as appropriate. The p-value threshold was set at 0.05. Statistical analyses were performed with IBM SPSS statistic version 23.

RESULTS

Thirty patients joined the study. Two patients had septic shock and one patient was died after surgery in intervention group. Patients who refused surgery had septic shock, and died were considered dropped out in the control group. There were 12 patients left in both groups. No differences were found between control and intervention groups for age, sex, height, weight, vital signs, diagnosis, medical therapies, surgery, arrhythmia, six-minute walking distance, cardiopulmonary bypass time, aortic cross-clamp time, surgery duration, echocardiography measurement, right ventricular function measured using RV free wall strain, RV FAC, and TAPSE. Some patients had decreased right ventricular function before cardiac surgery but there was no statistical difference in decreased right ventricular function patients' numbers between intervention and control groups (Table 1).

The echocardiography evaluation after cardiac surgery showed a significant difference in right ventricular systolic function which measured by using RV free wall strain ($-17.7 \pm 3.0\%$ vs $-14.4 \pm 4.0\%$; $p=0.033$), RV FAC ($43.2 \pm 4.9\%$ vs $35.1 \pm 8.8\%$; $p=0.006$), and TAPSE (12.7 ± 3.4 mm vs 9.9 ± 2.7 mm; $p=0.039$) between intervention and control group after cardiac surgery. Inspiratory muscle training group had better right ventricular function based on echocardiography measurement after cardiac surgery (Table 2 and Figure 2).

We performed interrater reliability and found an excellent reliabilities between two measurements for RV free wall strain (IC=0.998), RV FAC (IC=0.998), and TAPSE (IC=0.998). There was good interrater reliability between two observers for RV free wall strain (IC=0.996), RV FAC (IC=0.998), and TAPSE (IC=0.998).

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Table 1. Baseline characteristics

	Groups		p
	Intervention (n=12)	Control (n=12)	
Age (year)	44.9 ± 9.5	41.2 ± 11.6	0.406 ^a
Sex			1.1
Female (n)	6 (50%)	6 (50%)	1.0 ^b
Height (cm)	162 ± 8.8	160.3 ± 8.4	0.607 ^a
Weight (kg)	57.5 ± 11.2	58.1 ± 8.2	0.888 ^a
SBP (mmHg)	111.0 ± 9.4	112.9 ± 8.6	0.734 ^a
DBP (mmHg)	69.2 ± 7.9	68.5 ± 8.4	0.951 ^a
HR (times/minute)	75.0 ± 12.9	79.3 ± 14.8	0.259 ^a
Diagnosis (n)			
- Mitral stenosis	8 (67%)	6 (50%)	0.679 ^b
- Mitral regurgitation	5 (42%)	8 (67%)	0.413 ^b
- Aortic stenosis	0 (0%)	1 (8%)	1.0 ^b
- Aortic regurgitation	3 (25%)	4 (33%)	1.0 ^b
- Tricuspid regurgitation	12 (100%)	12 (100%)	1.0 ^b
Medical therapies			
- Diuretic (n)	7 (59%)	7 (59%)	1.0 ^b
- ACEi/ARB (n)	4 (33%)	5 (42%)	1.0 ^b
- MRA (n)	10 (83%)	6 (50%)	0.194 ^b
- Warfarin (n)	9 (75%)	8 (67%)	1.0 ^b
- Digoxin (n)	10 (83%)	9 (75%)	1.0 ^b
- Beta blocker (n)	10 (83%)	10 (83%)	1.0 ^b
Surgery (n)			0.589 ^c
- MVR	9 (75%)	8 (67%)	
- DVR	3 (25%)	3 (25%)	
- AVR	0 (0%)	1 (8%)	
Echocardiography measurements			
- LVEF (%)	65.5 ± 8.5	64.7 ± 7.8	0.805 ^a
- mPAP (mmHg)	26.3 ± 13.2	31.9 ± 12.7	0.292 ^a
- sPAP (mmHg)	44.2 ± 24.3	50.1 ± 19.9	0.520 ^a
- eRAP (mmHg)	7.8 ± 3.4	9.6 ± 5.7	0.498 ^a
- PVR (WU)	2.7 ± 1.5	3.2 ± 1.5	0.382 ^a
- RV base (mm)	42.0 ± 9.5	42.0 ± 9.2	0.604 ^a
- RV mid (mm)	32.6 ± 5.7	32.9 ± 8.7	0.912 ^a
- RV major axis (mm)	71.0 ± 15.6	71.0 ± 14.0	1.0 ^a
- PH probability (n)			0.607 ^c
- No PH	3 (25%)	3 (25%)	
- Possible	7 (58%)	5 (42%)	
- Likely	2 (17%)	4 (33%)	
- Tricuspid regurgitation severity (n)			0.315 ^c
- Severe	1 (8%)	4 (33%)	
- Not severe	11 (92%)	8 (67%)	
- RV free wall strain			0.637 ^c
- >20%	8 (67%)	10 (83%)	
- <20%	4 (33%)	2 (17%)	
- RV FAC			1.0 ^c
- >35%	12 (100%)	11 (92%)	
- <35%	0 (0%)	1 (8%)	
- TAPSE			0.637 ^c
- >17 mm	8 (67%)	10 (83%)	
- <17 mm	4 (33%)	2 (17%)	

	Groups		p
	Intervention (n=12)	Control (n=12)	
Arrhythmia (n)	9 (75%)	8 (67%)	1.0 ^b
6MWT (meter)	377 ± 79	326 ± 47	0.092 ^a
CPB time (minutes)	48.3 ± 20.2; 38.5 (38 – 90)	52.6 ± 16.3; 51.5 (33 – 90)	0.193 ^a
AoX time (minutes)	32.8 ± 16.1; 24.5 (22 – 62)	33.3 ± 13.9; 28.5 (22 – 69)	0.416 ^a
Surgery duration (minutes)	147.5 ± 31.0; 142.5 (110 – 200)	145 ± 29.7; 127.5 (120 – 190)	0.814 ^a
TVr (n)	10 (83%)	11 (92%)	1.0 ^b

^aindependent t-test with alternative Mann-Whitney test; ^bFischer-exact test; ^cchi square test

SD: standard deviation; SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: heart rate; ACEi: Angiotensin-Converting Enzyme inhibitor; ARB: angiotensin receptor blocker; MRA: MVR: mitral valve replacement; AVR: aortic valve replacement; LVEF: left ventricular ejection fraction; RVs FW: right ventricular free wall strain; RV FAC: right ventricular fractional area changes; TAPSE: Tricuspid Annular Plane Systolic Excursion; mPAP: mean pulmonary arterial pressure; sPAP: systolic pulmonary arterial pressure; eRAP: estimated right atrial pressure; PVR: pulmonary vascular resistance; RV: right ventricular; PH: pulmonary hypertension; 6MWT: 6-minute walking test; CPB: cardiopulmonary bypass; AoX: aortic cross-clamp; TVr: tricuspid valve repair.

Table 2. Right ventricular function before cardiac rehabilitation programs and after cardiac surgery

	Mean±SD; Median (Minimum-Maximum)		p
	Intervention (n=12)	Control (n=12)	
RV free wall strain (%)			
• Pre	-20.2 ± 3.7; -19.5 [-11.3 – (-27)]	-20.6 ± 4.6; -20.6 [-13.3 – (-28)]	0.794 ^a
• Post	-17.7 ± 3.0; -16.9 [-12.3 – (-24)]	-14.4 ± 4.0; -15.4 [-6.3 – (-19)]	0.033 ^a
RV FAC (%)			
• Pre	44.3 ± 4.1; 43.5 (39 – 52)	42.0 ± 8.5; 42.5 (19 – 56)	0.562 ^b
• Post	43.2 ± 4.9; 42.5 (36 – 56)	35.1 ± 8.8; 37 (17 – 51)	0.006 ^b
TAPSE (mm)			
• Pre	20.3 ± 4.4; 21 (13 – 28)	20.4 ± 5.2; 19.5 (12 – 34)	0.839 ^b
• Post	12.7 ± 3.4; 11.5 (9 – 20)	9.9 ± 2.7; 9 (6 – 15)	0.039 ^a

^aindependent t-test ^bMann-Whitney test

DISCUSSIONS

Our study found the reduction on right ventricular function by echocardiography using RV free wall strain, RV FAC, and TAPSE. These results were similar to Singh et al. and Jadhav et al. study on right ventricular function reduction after cardiac surgery.^{23,24} Surgical procedures may not become a confounding factors since all patients received the same procedures such as cold cardioplegia usage, off-pump cardiac surgery, and pericardial incision size, which was known as the etiology for reducing right ventricular function after cardiac surgery.⁴

Right ventricular function was determined by preload, afterload, and contractility. Preload states can be excluded from the confounding factor because there was no significant estimated right

atrial pressure difference/eRAP (p=0.698) measured using echocardiography between two groups. No significant differences on TVr procedures between two groups that may cause preload changes (p=1.0).^{20,25,26}

We hypothesized that afterload changes might be the cause of right ventricular function reduction, but we didn't find any significant difference between two groups afterload which measured using pulmonary vascular resistance/PVR (p=0.23) and sPAP (p=0.95) by echocardiography; and no significant differences on postoperative pulmonary complications in both groups (p=0.665) that may increase right ventricle afterload due to prolonged mechanical ventilators and acute respiratory distress syndromes. Parati et al. stated that breathing exercise reduced sPAP significantly in patients

with chronic heart failure.¹⁶ In this study, we found no increasing afterload because PVR and sPAP were reduced after cardiac surgery in both groups. This also explained why the patients were in excellent clinical conditions despite reduced right ventricular function.²³

Right ventricle contractility may reduce after cardiopulmonary bypass which caused myocardial and systemic inflammations. Patients with heart failure with inspiratory muscle Weakness has role in increasing pro-inflammatory factors and raising calpain activities which known resulted in decreasing myocardial contractility. Patients in intervention group may have better inspiratory muscle strength than patients in the control group. Although we didn't measure respiratory muscle strength using micro RPM, there was significant load progression (13% load

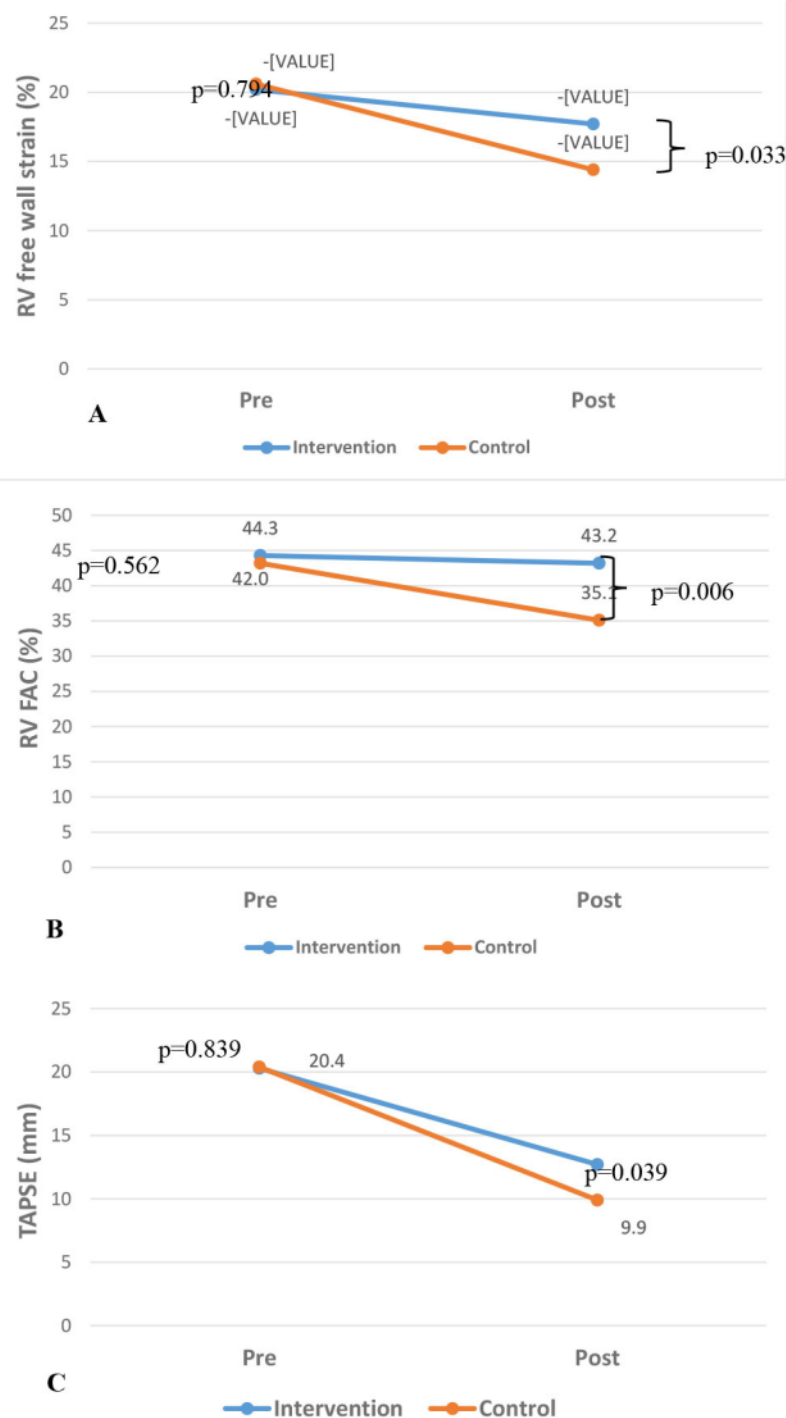


Figure 2. RV free wall strain (A), RV FAC (B), and TAPSE (C) changes in intervention and control group before cardiac rehabilitation and after cardiac surgery.

progression, $p=0.000$) after inspiratory muscle training in the intervention group. Strengthening the inspiratory muscle may reduce the risk of decreasing myocardial contractility due to inflammation after cardiac surgery.^{4,18,27} Donauer et al. stated that the RV lateral and inferior wall's longitudinal contraction, the RV outflow tract, and the interventricular septum are impaired at the end of surgery. An increase in circumferential contraction compensates this impairment without changes in RV ejection fraction (RVEF).²⁸ We didn't perform RVEF examination but RV FAC represents right ventricle global function and has a good correlation with RVEF. It may explain that RV FAC didn't reduce to abnormal values in this study.^{19,29} This also explains TAPSE reduction below normal cut-off value in both groups because TAPSE only represents longitudinal not global right ventricular function.^{20,23}

We found lower RV free wall strain reduction in intervention and control group (12% vs. 30%). Singh et al. stated that RV free wall strain reduction >20% might cause clinical implications.²³ Other clinical implications as Shukla et al. stated, RV free wall strain < -16.2% is the cut-off that increases mortality risk in pulmonary hypertension with multiple etiologies (OR= 3.67; CI 95% 2.82 – 4.77; $p<0.001$).³⁰ We found that mean RV free wall strain in intervention group was higher than the cut-off point ($-17.7 \pm 3.0\%$) and the control group means were below cut off point ($-14.4 \pm 4.0\%$). The ICU length of stay (LOS) was significantly shorter in patients in intervention vs control group (3.2 ± 0.8 vs 4.2 ± 1.3 days; $p=0.044$). Katsura et al. stated that inspiratory muscle training reducing hospital LOS ($p=0.03$).¹⁵ Bootsma et al study showed that low RVEF (20 – 30%) was associated the increasing risk for longer ICU LOS (OR 3.25; $p<0.001$).³

STUDY LIMITATIONS

The authors didn't perform invasive hemodynamic measurements to get PVR and sPAP values. We didn't perform the inspiratory muscle strength using standard micro RPM and small sample size in our study. The inflammatory biomarkers weren't measured in this study, and they

may have roles in myocardial contractility differences between two groups in this study.

CONCLUSION

Patients underwent conventional preoperative rehabilitation added inspiratory muscle training had better right ventricular systolic function than patients in control group.

ETHICAL APPROVAL

This research has ethical approval from Health Research Ethics Committee RSUP Dr. Kariadi Semarang No. 309/EC/KEPK-RSDK/2019.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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AUTHOR CONTRIBUTIONS

Hari Hendriarti Satoto had full access to all of the data in the study and took responsibility for the integrity of the data and the data analysis accuracy.

Study concept and design: all authors.

Acquisition, analysis, or interpretation of data: all authors.

Drafting of the manuscript: Hari Hendriarti Satoto.

Critical revision of the manuscript for important intellectual content: all authors. Statistical analysis: Hari Hendriarti Satoto, Suhartono.

Administrative, technical, or material support: Hari Hendriarti Satoto, Aditya Pramitha, Sri Hastuti Barata.

Study supervision: Sugiri, Suhartono, Sri Wahyudati, Sefri Noventi Sofia.

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