

Tricuspid valve septal displacement cutoff value for mortality risk following biventricular repair in Ebstein anomaly

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ABSTRACT

Background : Surgical intervention is the definitive treatment for Ebstein anomaly, offering both biventricular and nonbiventricular repair options. The objective of this study is to identify a specific cutoff value for tricuspid septal leaflet displacement, which will be a crucial factor in determining the selection of a surgical approach with lower mortality risk in biventricular repair.

Methods and Results : This is a retrospective cohort study of consecutive patients with Ebstein anomaly undergoing surgical intervention at the National Cardiovascular Center Harapan Kita from January 2010 to December 2023. A total of 83 patients with Ebstein anomaly were treated surgically; 43 of those underwent biventricular repair, whereas the remaining underwent nonbiventricular repair. Echocardiography was performed, and the Great Ormond Street Echocardiography score was calculated. Several risk factors were identified and stratified for patients with biventricular repair ($n = 43$). Tricuspid septal leaflet displacement was measured for each patient, and there was a statistically significant higher mortality risk directly proportional to higher displacement in patients with biventricular repair ($P < 0.05$). A cutoff value of 43.5 mm/m² for the tricuspid septal leaflet displacement is the best predictor of mortality risk in biventricular repair with 83.3% sensitivity and 93.3% specificity.

Conclusions : In patients with Ebstein anomaly undergoing a biventricular repair, mortality rates are significantly elevated in patients with a higher tricuspid septal leaflet displacement distance. The results of the study indicated that the mortality risk in biventricular repair can be predicted based on the tricuspid septal leaflet displacement distance using a cutoff value of 43.5 mm/m².

Keywords : Cone repair, outcomes of Ebstein anomaly, tricuspid septal leaflet displacement

INTRODUCTION

Ebstein anomaly is a rare congenital heart disease, representing <1% of all congenital heart defects. Ebstein

anomaly is characterized by the presence of a tricuspid septal leaflet attached to the myocardium, a shift of

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the functional annulus to the apex, dilatation of the right ventricle (RV) that is experiencing atrialization, and dilatation of the right atrioventricular junction.^[1,2] This anatomical abnormality will cause dilatation of the right atrium and RV, congestive heart failure, and even ventricular arrhythmia.^[1,3] The degree of apical displacement of the septal leaflet (≥ 8 mm/m² body surface area) is an essential feature in diagnosing the Ebstein anomaly.^[4]

The primary diagnostic procedure for Ebstein anomaly is echocardiography.^[5,6] Echocardiography can evaluate the heart's pump function, the location and degree of tricuspid valve regurgitation, the presence of pulmonary atresia, and the Great Ormond Street Echocardiography (GOSE) score can assist the selection of surgical procedures and assess the prognosis. Celermajer *et al.* described an echocardiographic grading score for neonates with Ebstein anomaly, as shown in Table 1.^[7] However, additional examinations, including cardiac magnetic resonance, can be used to quantify and qualify RV and left ventricle (LV) size and function, the electrocardiogram examination assesses the presence of arrhythmia, and the chest X-ray examination assesses the size of the cardiothoracic ratio (CTR). A CTR ≥ 0.65 indicates a poor prognosis.^[1,2] Surgical treatment with biventricular and nonbiventricular repair is influenced by anatomical abnormalities and the patient's condition. The characteristics of the patient's condition are assessed before the surgery, such as heart pump function, degree of tricuspid valve regurgitation, other existing congenital anomalies, and right ventricular size.^[8,9]

Ebstein anomaly requires surgical repair as the definitive treatment, with biventricular and nonbiventricular repair as the surgical options. In Indonesia, data from the National Cardiovascular Center Harapan Kita Hospital showed that Ebstein anomaly are generally found in infants and adults, with neonatal cases constituting <5% of the patient population. There is limited research on the cutoff value of the displacement distance of the tricuspid septal leaflet to predict mortality risk in biventricular repair. This retrospective study aims to establish the cutoff value of tricuspid septal leaflet displacement to guide surgical repair in Ebstein anomaly.

Table 1: Celermajer index or Great Ormond Street Echocardiography score and mortality risk estimation

GOSE score	Index (RA + RV)/ (RV + LA + LV)	Risk of mortality (%)
Grade 1	<0.5	0
Grade 2	0.5–0.99	10
Grade 3	1–1.49	44–100
Grade 4	≥ 1.5	100

RA: Right atrium, RV: Right ventricle, LA: Left atrium, LV: Left ventricle, GOSE: Great Ormond Street Echocardiography

METHODS

We retrospectively reviewed medical records and analyzed biventricular repair surgery performed between January 2010 and December 2023 in patients with Ebstein anomaly. A total of 83 patients with Ebstein anomaly underwent surgical repair during that period, with preoperative oxygen saturation levels ranging from 70% to 100%. Forty-three patients had biventricular repair. Patients with incomplete echocardiography data were excluded from the study. We collected demographic baseline and perioperative information from various sources, including registries, pediatric cardiac surgery conferences, medical records, surgical reports, and echocardiography reports. The patient's age was determined as age at the surgery, arrhythmia was determined based on preoperative electrocardiography, the right ventricular function was determined based on tricuspid annular plane systolic excursion in preoperative echocardiography, tricuspid regurgitation (TR) was determined based on qualitative and quantitative measurement in echocardiography with severe regurgitation was categorized as significant and mild-to-moderate regurgitation was categorized as nonsignificant. The displacement of the tricuspid septal leaflet was determined by the distance of displacement per body surface area (mm/m²) in preoperative echocardiography. The GOSE score was determined based on the cardiac chamber size calculation in preoperative echocardiography. A score of 1 and 2 was categorized as low, and a score of 3 and 4 was classified as high. The CTR was determined based on a preoperative chest X-ray.

The decision to pursue biventricular or nonbiventricular repair was made during the multidiscipline pediatric cardiac surgery conference, guided by the patient's condition, the GOSE score, and echocardiography findings. Due to resource limitations, magnetic resonance imaging (MRI) was not utilized for preoperative assessment. The cone procedure was the predominant surgical intervention for most biventricular repair.

The data that had been collected and verified were then processed using the IBM SPSS version 25.0 program software (SPSS, Inc., Chicago, IL, USA). The existing data are stratified based on the surgical procedure, and the data of patients who have undergone biventricular repair were further analyzed. The Fisher's exact test, the Mann-Whitney test, and the unpaired *t*-test were used in the analysis. Relative risks are displayed along with 95% confidence intervals (CIs). The *P* value limit for significance is < 0.05. Factors with *P* < 0.2 in bivariate analysis were included in multivariate analysis using logistic regression. Numerical variables statistically significant in bivariate and multivariate analysis were then entered into the receiver operating characteristic (ROC) to find the cutoff value.

RESULTS

The characteristics of patients with Ebstein anomaly who underwent biventricular repair are presented in Table 2. The proportion of males and females was 41.9% and 58.1%, respectively. The median age was 108.5 (2.67–608.58) months. Preoperative arrhythmia was found in 35.9% of subjects, and the right ventricular dysfunction was found in 16.3% of subjects; significant TR was found in 62.8% of subjects, and a CTR of more than equal to 0.65 was found in 48.8% of subjects. The median value of the displacement of the tricuspid

septal leaflet in patients who underwent biventricular repair was 24.59 (9.29–127.27) mm² per meter. Of the 43 patients, 27.9% had high GOSE scores, whereas 72.1% had low GOSE scores.

The findings from the bivariate analysis of biventricular repair patients are summarized in Table 3. Notably, statistical significance in mortality risk was observed in three variables: RV dysfunction ($P = 0.045$), tricuspid septal leaflet displacement distance ($P = 0.014$), and GOSE score ($P = 0.042$).

Four variables were included in the multivariate analysis as described in Table 4. The distance of displacement of the tricuspid septal leaflet was statistically significant in predicting mortality ($P = 0.049$) and qualified as the independent predictor for mortality risk in biventricular repair. The four variables included in the multivariate analysis accounted for 77.0% of the factors influencing mortality risk in biventricular repair (Nagelkerke $R^2 = 0.770$).

Tricuspid septal leaflet displacement was found to be an independent predictor of mortality risk. Therefore, a ROC analysis was used to determine the diagnostic value based on sensitivity and specificity assessments of various cutoff values. Diagnostic power was quantified by calculating the area under the curve (AUC) value. This analysis was conducted to determine the impact of tricuspid septal leaflet displacement on mortality risk in biventricular surgery. This variable demonstrated statistical significance in both bivariate and multivariate analysis. The ROC curves are described in Figure 1, and the diagnostic values are described in Table 5.

The cutoff point value is based on the Youden index. Table 5 shows the ROC analysis results in the form of AUC values, P values, cutoff points, sensitivity, and specificity.

Table 2: Baseline characteristics of all patients who underwent biventricular repair

Patient's characteristics	n (%)
Number of patients	43 (51.8)
Gender	
Male	18 (41.9)
Female	25 (58.1)
Age (months)	108.5 (2.67–608.58)
Arrhythmia	
Yes	17 (39.5)
No	26 (60.5)
RV function (cm)	
Dysfunction (TAPSE <1.7)	7 (16.3)
Good (TAPSE ≥ 1.7)	36 (83.7)
TR	
Significant	27 (62.8)
Nonsignificant	16 (37.2)
CTR	
≥0.65	21 (48.8)
<0.65	22 (51.2)
Tricuspid septal leaflet displacement (mm/m ²)	24.59 (9.29–127.27)
GOSE score	
High (3–4)	12 (27.9)
Low (1–2)	31 (72.1)

TAPSE: Tricuspid annular plane systolic excursion, TR: Tricuspid regurgitation, GOSE: Great Ormond Street Echocardiography, RV: Right ventricle, CTR: Cardiothoracic ratio

Table 3: Bivariate analysis factors in biventricular repair on postoperative outcomes

Risk factor	Biventricular		P	Bivariate RR (95% CI)
	Yes, n (%)	No, n (%)		
Age (months)	58.733 (2.67–482.2)	112 (7.6–608.58)	0.233	-
Arrhythmia				
Yes	1 (5.9)	16 (94.1)	0.376	0.31 (0.04–2.4)
No	5 (19.2)	21 (80.8)	Reference	0.04–2.4
RV function (cm)				
Dysfunction (TAPSE <1.7)	3 (42.9)	4 (57.1)	0.045	5.1
Good (TAPSE ≥ 1.7)	3 (8.3)	33 (91.7)	Reference	1.29–20.45
TR				
Significant	5 (18.5)	22 (81.5)	0.386	2.96
Nonsignificant	1 (6.3)	15 (93.8)	Reference	0.38–23.16
CTR				
≥0.65	4 (19)	17 (81)	0.412	2.09
<0.65	2 (9.1)	20 (90.9)	Reference	0.43–10.26
Tricuspid septal leaflet displacement (mm/m ²)	58.56±35.99	21.96±11.13	0.014	-
GOSE score				
High (3–4)	4 (33.3)	8 (66.7)	0.042	5.17
Low (1–2)	2 (6.5)	29 (93.5)	Reference	1.07–24.61

TAPSE: Tricuspid annular plane systolic excursion, TR: Tricuspid regurgitation, GOSE: Great Ormond Street Echocardiography, CI: Confidence interval, RR: Relative risk, RV: Right ventricle, CTR: Cardiothoracic ratio

DISCUSSION

Tricuspid valve repair has been performed for many years and has evolved through many techniques and functional modifications. The patient's preoperative condition influences the choice of surgical treatment for Ebstein anomaly. Before 2020, biventricular and nonbiventricular repair were determined in our center based on echocardiography to analyze the function of the right and LVs. In the period between 2020 and the present, the GOSE score assessment has been utilized. The GOSE score Grades 1 and 2 will undergo biventricular repair. In this research conducted at the National Cardiovascular Centre Harapan Kita, from the 6 patients who had mortality following biventricular repair, the distance of displacement of the tricuspid septal leaflet in each patient who died was 127.27, 96.35, 62.31, 54.81, 43.87, and 30.81 mm/m². Four patients with tricuspid septal leaflet displacement distances of 127.27, 96.35,

54.81, and 43.87 mm/m² developed severe right heart failure in intensive care, and all patients remained unresponsive and died. One patient with tricuspid septal leaflet displacement of 62.31 mm/m² developed respiratory failure and sepsis in the intensive care unit. One patient with a tricuspid septal leaflet distance of 30.81 mm/m² developed malignant arrhythmia in postoperative care without any preoperative arrhythmia. The higher the tricuspid septal leaflet distance, the wider the atrialized RV area, and the GOSE score will increase.^[10]

According to other studies, many factors have been associated with mortality: age at diagnosis, CTR, male sex, associated cardiac lesions, degree of TR, and residual RV function.^[11,12] Compared to the existing literature, the results are based on more objective and reproducible measurements of the size and function of the RV (cardiac MRI vs. echocardiography). Furthermore, we found age to be an essential risk factor for early mortality, especially if a massively enlarged RV and impaired RV function are coexistent.^[13] The Nagelkerke $R^2 = 0.770$ in the logistic regression of the four factors shows good results, namely that the four factors compose 77% of the factors that contribute to the mortality risk in biventricular repair in patients with Ebstein anomaly. However, 23% of other factors not examined in this study can still affect the mortality risk in biventricular repair patients with Ebstein anomaly. Some of these factors include the degree of heart failure, pulmonary hypertension, other congenital heart defects, congenital syndromes, duration of aortic cross-clamping and duration of heart-lung machine use, respiratory, neurological, renal, infectious complications, and various other factors.

In the study reported by da Silva, the mortality of biventricular repair with the cone procedure was 7% (3% short-term mortality, 4% long-term mortality), and other studies reported a mortality of 10%.^[14,15] Asou *et al.* stated that biventricular repair may be preferred as the surgical option, if possible, based on anatomy. However, univentricular palliation might be the treatment of choice for a safer and more effective approach in high-risk patients. This preference arises due to the severely compromised clinical conditions.^[16]

In this study, ROC analysis was carried out on the tricuspid septal leaflet displacement and the mortality risk in biventricular repair because the results of bivariate and multivariate tests showed statistical significance. Currently, there is no cutoff value for tricuspid septal leaflet displacement associated with

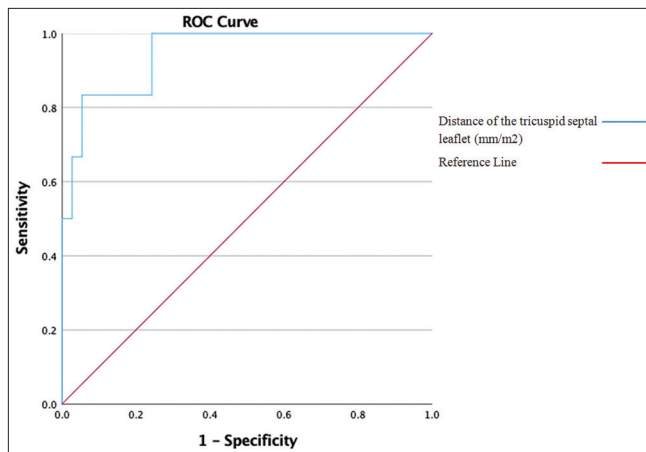


Figure 1: Receiver operating characteristic curve between the displacement distance of the tricuspid septal leaflet and risk of mortality in biventricular repair. ROC: Receiver operating characteristic

Table 4: Multivariate analysis factors in biventricular repair on postoperative outcomes

Risk factor	Multivariate analysis		
	Coefficient	P	aOR (95% CI)
RV function	3.951	0.075	51.97 (0.67–4014.22)
GOSE score	1.008	0.595	2.74 (0.07–112.85)
Tricuspid septal leaflet displacement (mm/m ²)	–0.152	0.049	-
Age (months)	2.447	0.392	11.56 (0.04–3130.27)

aOR: Adjusted odds ratio, CI: Confidence interval, GOSE: Great Ormond Street Echocardiography, RV: Right ventricle

Table 5: Receiver operating characteristic analysis of the distance of displacement of tricuspid septal leaflet on the risk of mortality in biventricular repair

Surgical repair	AUC	P	95% CI	Cut-off value	Sensitivity (%)	Specificity (%)
Biventricular	0.946	0.001	86.5%–100%	43.5	83.3	94.6

AUC: Area under curve, CI: Confidence interval

surgical treatment and postoperative outcome, either in biventricular or nonbiventricular repair. This study showed that in biventricular repair, the AUC value of the tricuspid septal leaflet displacement distance on the mortality risk was 94.6% (95% CI 86.5%–100%) with a cutoff value of 43.5 mm/m², which had a sensitivity of 83.3% and specificity of 94.6%. These results indicate that the displacement distance of the tricuspid septal leaflet has a solid diagnostic value in the mortality risk in biventricular repair patients with Ebstein anomaly. From the data, it can be inferred that a tricuspid septal leaflet displacement higher than 43.5 mm/m² is associated with a higher risk of mortality in biventricular repair but does not increase mortality risk in nonbiventricular repair. Therefore, this cutoff value can be proposed as a limit for selecting biventricular repairs as the preferred surgical treatment at cardiac surgery centers. This cutoff value will likely change in the future, along with the learning process at each cardiac surgery center, the improvement of health facilities, and further discovery in medicine that can optimize the patient's perioperative condition.

This study has limitations, such as the retrospective design and the single-center data. In addition, the hospital where the research was conducted is a referral center for cardiac surgery in Indonesia, with developing resources and facilities. The findings and outcomes might differ in a developed cardiac center. Nevertheless, we have reported significant findings and provided notable insight for other developing cardiac centers.

CONCLUSIONS

A higher tricuspid septal leaflet displacement is an independent predictor of higher mortality risk in patients with Ebstein anomaly undergoing biventricular repair. A 43.5 mm/m² cutoff value showed a high sensitivity and specificity. A prospective study with a larger sample is required to validate these findings.

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Conflicts of interest

There are no conflicts of interest.

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