Preoperative percutaneous oxygen saturation is a predictor of postoperative adverse events after Ebstein's anomaly reconstruction

Yao Yang[1], Wei Zhang[1], Yang Liu[1], Gang Li[1], Han Zhang[1], Xing Fan[1], Junwu Su[1], Yinglong Liu[1], Xiangming Fan[1]

1. Pediatric Cardiac Center, Beijing Anzhen Hospital, Capital Medical University, Beijing, China

Correspondence

Xiangming Fan, Pediatric Cardiac Center, Beijing Anzhen Hospital, Capital Medical University, No. 2 Anzhen Rd, Chaoyang District, Beijing, 100029, China.

Chief physician, Deputy director of pediatric cardiac surgery, Beijing Anzhen Hospital, specializes in the diagnosis and treatment of complex congenital heart disease.

E-mail: fanxiangming@126.com

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Funding statement

Funding: None.

Conflict of interests

The authors declare that there are no conflict of interests.

Ethics approval statement

The study has been approved by the ethics committee of Beijing Anzhen Hospital.

Informed consent statement

All patients involved in this retrospective study have informed consent.

Abstract

Background

Ebstein's anomaly (EA) is a kind of congenital heart disease, which is currently widely treated by cone reconstruction. However, prediction of postoperative recovery is still challenging.

Methods

A retrospective analysis was performed on EA cases undergoing cone reconstruction from January 2010 to January 2016. Univariate and multivariate logistic regression analyses were performed, with postoperative adverse events defined as dependent variable and pre- and intra-operative parameters defined as independent variables. Predictive capacity of preoperative SPO_2 and Great Ormond Street (GOS) score was evaluated using areas under the curve of receiver operating characteristic (ROC).

Results

Preoperative SPO_2 was 95.7 ± 5.20%. Cardiopulmonary bypass, aortic cross-clamp, postoperative mechanical ventilation, and hospitalization time were 101.7 ± 28.26 min, 60.9 ± 18.04 min, 16 hours (8, 22), and 8 days (7, 11), respectively. The incidence of total postoperative adverse events including low cardiac output syndrome, mechanical ventilation more than 3 days, postoperative hospitalization more than 2 weeks, postoperative re-intubation, extracorporeal membrane oxygenation assistance, and death was 13.1% (n=13). Low pre-operative SPO_2 (P=0.001, OR=0.834), GOS score (P=0.021, OR=0.368), and cardiopulmonary bypass time (P=0.034, OR=1.021) were risk factors for adverse events. Multivariate logistic regression analysis showed that low preoperative SPO_2 (P=0.002, OR=0.846) and GOS score (P=0.043, OR=0.577) were independent risk factors for adverse events. The areas of SPO_2 and GOS score under the ROC curve were 0.764 and 0.740, respectively.

Conclusions

Low pre-operative SPO_2 and GOS score were predictors of adverse events after cone reconstruction, and SPO_2 was more convenient and objective than GOS score.

Key words

GOS score, preoperative percutaneous oxygen, Ebstein's anomaly, cone reconstruction

1 | Introduction

Ebstein's anomaly (EA), first reported by doctor Ebstein in 1866 [1], accounts for less than 1% of congenital heart defects[2]. This anomaly typically involves displacement of the septal and posterior leaflets of the tricuspid valve, with varying degrees of abnormal leaflet and subvalvular structure development [3].

Severe cyanosis and cardiac insufficiency in infancy in severe cases may require an emergency palliative surgery, followed by single-ventricular correction [4], whereas valvuloplasty is considered for stable cases. Current valvuloplasty methods for EA include Denilson's[5] method, Carpentier's[6] method, and cone reconstruction[7]. Cone reconstruction can reduce tricuspid regurgitation and reduce the right ventricular end-diastolic volume. Moreover, it can reduce right ventricular stroke volume without reducing right ventricular ejection fraction, while left ventricular end-diastolic volume and left ventricular stroke volume can be increased [8]. Both the short- and long-term prognosis is satisfactory [7, 9, 10]. However, postoperative adverse events are not uncommon in severe cases, and recovery prediction is still challenging.

We performed cone reconstruction on EA patients since January 2010, and analyzed predictive factors of postoperative adverse events.

2 | Materials and methods

The study has been approved by the ethics committee of Beijing Anzhen Hospital. All patients involved in this retrospective study have informed consent.

2.1 | General information

Patients with EA who had undergone cone reconstruction at our pediatric cardiac center from January 2010 to January 2016 were systematically reviewed. Patients' demographic data (gender, age, weight, and height) and preoperative percutaneous oxygen saturation (SPO_2) were collected. Echocardiography was performed in all of the cases before surgery, and GOS score[11] was calculated. The degree of tricuspid regurgitation, GOS score, atrial communication, combined deformities, cardiopulmonary bypass time, and aortic cross-clamp time were recorded.

SPO_2 was measured as follows. After the patient was sedated by tranquillizer and fell asleep for 10 min, SPO_2 was read by Philips monitor central station with room air. GOS score was calculated as the ratio between the area $_{(ARV+RA)}$ and area $_{(LV+LA+FRV)}$, where ARV is atrialized right ventricle, RA - right atrium, LA - left atrium, LV - left ventricle, and FRV - functional right ventricle.

2.2 | Definition of adverse events

Adverse events included low cardiac output syndrome, more than 3 days of mechanical ventilation, re-intubation, extracorporeal membrane oxygenation assistance, and death.

Diagnostic criteria for low cardiac output syndrome in children included tachycardia, hypotension, decreased pulse pressure, poor tissue perfusion (low peripheral skin temperature, weak pulse, and prolonged capillary filling time), oliguria, or anuria occurring simultaneously [12].

2.3 | Surgical methods

The main steps of cone reconstruction were as follows: 1. Abnormal attachments of the anterior and posterior leaflet were cut off; 2. Fenestration of the fused chordae tendineae; 3.

Rotate the anterior and posterior lobes clockwise; 4. Cut off the attachment of the septal leaflet from the ventricular septum; 5. Suture the edge of the anterior leaflet with the septal leaflet to form a cone; 6. Fix the valves to the normal annulus [7].

If *Z* score of the new tricuspid valve annulus was less than -2 after the cone reconstruction, bidirectional cavopulmonary shunt was performed.

2.4 | Statistical methods

Categorical variables were expressed as frequency and percentage. Continuous variables were expressed as mean ± standard deviation, or median and interquartile range. Unpaired t test or Mann–Whitney U test was used to analyze the statistical significance of differences between the means or medians, as appropriate. Univariate and multivariate logistic regression analyses were performed to evaluate the association between pre- and intra-operative parameters and postoperative adverse events. Postoperative adverse events were considered as dependent variable, while pre- and intra-operative parameters (age, sex, body mass index, SPO_2, GOS score, existence of preoperative atrial level communication, ventricular septal defect, right ventricular outlet tract obstruction, degree of pre-operative tricuspid regurgitation, existence of pre-operative Wolff-Parkinson-White syndrome, intra-operative cardiopulmonary bypass time, and aortic cross-clamp time) were defined as independent variables. The predictive capacity of pre-operative SPO_2 and GOS scores was evaluated using area under the curve (AUC) of receiver operating characteristic (ROC). Pearson linear or Spearman rank correlation was used for correlation analysis. All of the *P* values were two-sided, and $P<0.05$ was considered to be statistically significant. SPSS 22.0 software was used for statistical analysis.

3 | Results

3.1 | Demographic characteristics

A total of 99 patients who underwent cone reconstruction over the 7-year observation period were selected for this study. The demographic characteristics are listed in Table 1. Concomitant malformation included atrial communication in 64 (64.6%) cases, ventricular septal defect in 9 (9.1%) cases, right ventricular outflow tract obstruction in 3 (3.0%) cases, pericardial effusion in 1 (1.0%) case, and Wolff-Parkinson-White syndrome in 11 (11.1%) cases. Pre-operative SPO_2 was 95.7 ± 5.20. Pre-operative tricuspid regurgitation was mild in 27 (27.3%), moderate in 33 (33.3%), and severe in 39 cases (39.4%).

3.2 | Clinical results

The incidence of total postoperative adverse events was 13.1% (n=13), including low cardiac output syndrome in 5 (5.1%) cases, mechanical ventilation more than 3 days in 6(6.1%) cases, postoperative hospitalization more than 2 weeks in 9 (9.1%) cases, re-intubation in 2 (2.0%) cases, extracorporeal membrane oxygenation assistance in 1 (1.0%) case, and death in 4 (4.0%) cases.

Cardiopulmonary bypass, aortic cross-clamp, postoperative mechanical ventilation, and hospitalization were 101.7 ± 28.26 min, 60.9 ± 18.04 min, 16 h (8, 22), and 8 days (7, 11), respectively. Bidirectional cavopulmonary shunt was performed in 25 (25.3%) patients.

Table 1. Preoperative and intraoperative data

Parameters	Total (n=99)	No adverse events (n=86)	Adverse events (n=13)	*P* value
Age (years)	5.6 (2.3, 13.0)	5.6 (2.4, 12.9)	4.2 (1.0, 20.8)	0.571
Sex (male, %)	43 (43.3%)	41 (47.7%)	2 (15.4%)	χ^2=4.792
				P=0.036
BMI (kg/m^2)	16.6 (15.1, 18.4)	16.4 (15.0, 18.4)	17.4 (15.0, 19.3)	0.425
Preoperative SPO_2	95.7 ± 5.20	96.7 ± 3.78	90.1 ± 7.91	0.004
GOS score	0.89 ± 0.127	0.86 ± 0.095	1.09 ± 0.134	0.000
Degree of preoperative TR				0.670
Mild (n, %)	27 (27.3%)	24	3	
Moderate (n, %)	33 (33.3%)	29	4	
Severe (n, %)	39 (39.4%)	33	6	
Atrial communication (n, %)	64 (64.6%)	52 (60.5%)	12 (92.3%)	χ^2=5.010
				P=0.029
VSD (n, %)	9 (9.1%)	9 (10.5%)	0 (0)	χ^2=1.497
				P=0.221
ROVTO (n, %)	3 (3.0%)	2 (2.3%)	1 (7.7%)	χ^2=1.107
				P=0.293
WPW syndrome (n, %)	11 (11.1%)	9 (10.5%)	2 (15.4%)	χ^2=0.277
				P=0.635
CPB time (min)	101.7 ± 28.26	99.3 ± 27.17	117.8 ± 31.05	0.044
Aortic cross-clamp time (min)	60.9 ± 18.04	60.6 ± 18.20	62.8 ± 17.54	0.700

Abbreviations: BMI: body mass index, SPO_2: Percutaneous oxygen saturation, TR: tricuspid regurgitation, ROVTO: right ventricular outflow tract obstruction, VSD: ventricular septal defect, WPW syndrome: Wolff-Parkinson-White syndrome, CPB: cardiopulmonary bypass. Categorical variables were expressed as frequency and percentage. Continuous variables were expressed as mean ± standard deviation, or median and interquartile range.

3.3 | Univariate logistic regression analysis

Univariate logistic regression analysis was performed to analyze the association between postoperative adverse events and 12 pre- and intra-operative variables. Preoperative SPO_2 (*P*=0.001, *OR*=0.834) and GOS score (P=0.021, OR=0.386) were associated with lower risk of postoperative adverse events (Table 2). Cardiopulmonary bypass time (*P*=0.034, *OR*=1.021) was associated with higher risk of postoperative adverse events (Table 2).

Table 2. Univariate logistic regression analysis

Influencing factors	*OR*	95% *CI*	*P* value
Age	1.014	0.958–1.073	0.632
Sex	0.044	0.042–0.954	0.200
BMI	1.060	0.903–1.243	0.479
Pre-operative SPO_2	0.834	0.753–0.925	0.001
GOS score	0.386	0.324–2.384	0.021
Degree of pre-operative TR	1.218	0.583–2.545	0.601
ROVTO	0.286	0.024–3.396	0.321
Atrial communication	0.127	0.016–1.026	0.053
WPW syndrome	0.643	0.123–3.372	0.601
CPB time	1.021	1.002–1.041	0.034
Aortic cross-clamp time	1.007	0.975–1.040	0.681

Abbreviations: BMI: body mass index, SPO_2: percutaneous oxygen saturation, TR: tricuspid regurgitation, ROVTO: right ventricular outflow tract obstruction, VSD: ventricular septal defect, WPW syndrome: Wolff-Parkinson-White syndrome, CPB: cardiopulmonary bypass.

3.4 | Multivariate logistic regression analysis

Multivariate logistic regression analysis of the same factors showed that low preoperative SPO_2 (*P*=0.002, *OR*=0.846, 95% CI=0.763-0.939) and GOS score (*P*=0.043, *OR*=0.577, 95% CI= 0.157-6.901) were independent risk factors for adverse events (Table 3).

Table 3. Multivariate logistic regression analysis

Influencing factors	*OR*	95% *CI*	*P* value
Preoperative SPO_2	0.846	0.763–0.939	0.002
GOS score	0.577	0.157–6.901	0.043
CPB time	1.016	0.994–1.038	0.162

Abbreviations: SPO_2: percutaneous oxygen saturation, CPB: cardiopulmonary bypass. OR: odds ratio, CI: confidence interval.

3.5 | ROC curve

The areas under the ROC curve of oxygen saturation and GOS score were 0.764 and 0.740, respectively (Figure 1).

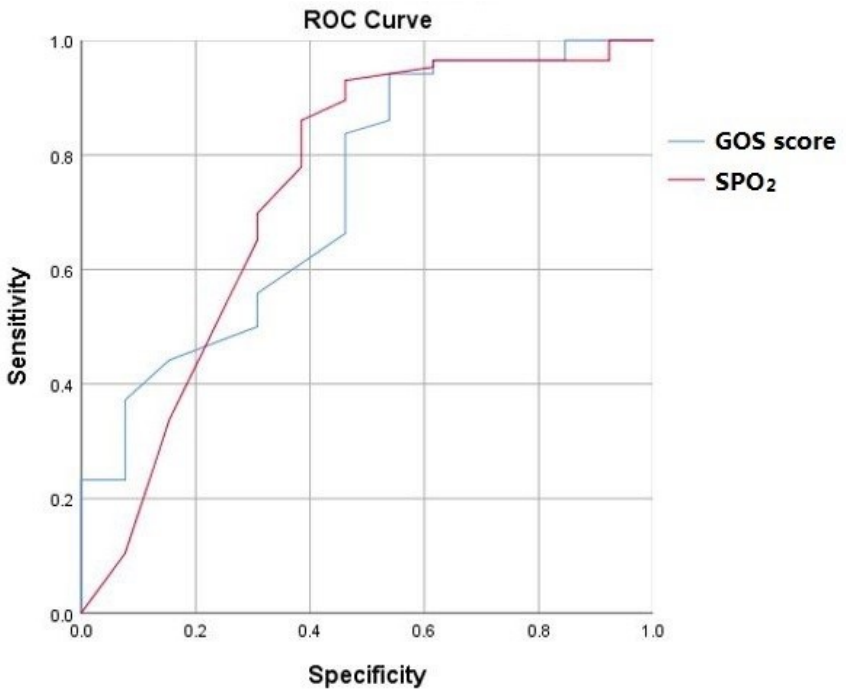

Figure 1. ROC curve of GOS score and SPO_2.

3.6 | Correlation analysis between pre-operative SPO_2 and tricuspid regurgitation

There was no significant correlation between pre-operative SPO_2 and tricuspid regurgitation (*P*=0.838, *r*=-0.026).

4 | Discussion

In this study, we found that low pre-operative SPO_2 and GOS score were predictive factors of adverse events after cone reconstruction for EA.

4.1 | Preoperative tricuspid regurgitation in EA

In this group of patients, there were 27 cases (27.3%) of mild regurgitation, 33 cases (33.3%) of moderate regurgitation, and 39 cases (39.4%) of severe regurgitation. Univariate regression analysis showed that the degree of pre-operative tricuspid regurgitation was not a risk factor for postoperative adverse events (*P*=0.601, *OR*=1.218). Among the 4 deaths in this group, 1 case had a moderate pre-operative tricuspid regurgitation and three cases had severe pre-operative tricuspid regurgitation, but unpaired t test shows that was not significant (*P*=0.523).

Many previous scoring systems focused on cardiac structure and did not involve pre-operative tricuspid regurgitation, but a recent study showed consistency between them [13]. However, here we find that pre-operative tricuspid regurgitation was not a risk factor for EA after cone reconstruction. Severe pre-operative tricuspid regurgitation was associated with a greater functional right ventricle [14]. According to the experience of pediatric cardiac center of Anzhen hospital, severe tricuspid regurgitation does not seem to affect surgical outcome in the presence of a sufficiently large functional right ventricle and a sufficiently large and active anterior leaflet. The results of this study differ from previous studies, which may originate from different methods

for measurement of tricuspid regurgitation. Future studies should use 3D ultrasound and tissue Doppler to quantitatively measure the relationship between functional right ventricular volume and tricuspid regurgitation.

4.2 | GOS score

David Celermajer defined an echocardiographic grading for severity of EA by calculating the ratio (GOS score) between the combined area of the right atrium and atrialized right ventricle and the combined area of the functional right ventricle, left atrium, and left ventricle in a four-chamber view at end-diastole. The ratio was used to define four grades: grade I, ratio < 0.5; grade II, 0.5 to 0.99; grade III, 1 to 1.49; and grade IV, ≥ 1.5 [11]. Tobler recommended that atrialized right ventricular volume was independently related to aerobic capacity, which may express severity of disease[14]. However, due to the complex anatomical structure of EA, there is no accurate method to measure functional right ventricular volume [15]. Therefore, severity of EA could be evaluated according to ratio of the right ventricular end-diastolic dimension to the left ventricular end-diastolic dimension measured by magnetic resonance imaging [13]. However, it is always difficult to perform magnetic resonance imaging in children. This study is expected to use clinically accessible data for convenient and effective evaluation for severity of EA.

4.3 | Pre-operative SPO_2 in EA

For pre-operative patients, blood indices such as hemoglobin, hematocrit, and brain natriuretic peptide levels correlated with right ventricular function measured by magnetic resonance imaging and patients' activity ability [16]; however, factors influencing postoperative results were not discussed.

We found that low pre-operative SPO_2, rather than the degree of pre-operative tricuspid regurgitation, is an independent risk factor for postoperative adverse events after cone reconstruction for EA. We carried out the correlation analysis of the above two variables for this seemingly contradictory results, and found no significant correlation between the two variables. The possible explanation is that increased right atrial pressure results in right-to-left shunt, but increased right atrial pressure may not only be caused by the degree of pre-operative tricuspid regurgitation but also by insufficient volume of functional right ventricle and increased right ventricular ejection resistance[17].

Decreased SPO_2 can be found in patients with atrial septal defect or patent foramen ovale in case of right-to-left shunt. Right ventricular enlargement results in leftward septal shift which increases left end-diastolic pressure and consequently also pulmonary arterial wedge pressure[17], which may also explain the decrease in SPO_2.

5 | Conclusion

Low pre-operative SPO_2 and GOS scores were predictors of adverse events after EA cone reconstruction. Compared with the complex EA deformity scoring system, SPO_2 is recorded by peripheral oxygen saturation detector, which is more convenient and objective.

6 | Limitations

This study was a retrospective analysis without classification of atrial level communication. According to the experience of our center, EA-related atrial level communications can be divided

into atrial septal defect and patent foramen ovale. In EA, patent foramen ovale tends to be larger than usual, which is considered to be a forced right-to-left shunt due to increased right atrial pressure. In such cases, it may indicate adverse postoperative events.

References

[1] W E. Über einen sehr seltencn Fall von Insuffizienz der Valvula tricuspidalis bedingt durch eine angeborene hochgradige Missbildung derselben [J]. Arch Anat Physiol. 1866; 328: 238-254.

[2] Li X, Wang S M, Schreiber C, et al. More than valve repair: Effect of cone reconstruction on right ventricular geometry and function in patients with Ebstein anomaly [J]. Int J Cardiol. 2016; 206: 131-137.

[3] Schreiber C, Cook A, Ho S Y, et al. Morphologic spectrum of Ebstein's malformation: revisitation relative to surgical repair [J]. J Thorac Cardiovasc Surg. 1999; 117: 148-155.

[4] Kumar S R, Kung G, Noh N, et al. Single-Ventricle Outcomes After Neonatal Palliation of Severe Ebstein Anomaly With Modified Starnes Procedure [J]. Circulation. 2016; 134: 1257-1264.

[5] Danielson G K, Maloney J DandDevloo R A. Surgical repair of Ebstein's anomaly [J]. Mayo Clin Proc. 1979; 54: 185-192.

[6] Carpentier A, Chauvaud S, Mace L, et al. A new reconstructive operation for Ebstein's anomaly of the tricuspid valve [J]. J Thorac Cardiovasc Surg. 1988; 96: 92-101.

[7] da Silva J P, Baumgratz J F, da Fonseca L, et al. The cone reconstruction of the tricuspid valve in Ebstein's anomaly. The operation: early and midterm results [J]. J Thorac Cardiovasc Surg. 2007; 133: 215-223.

[8] Beroukhim R S, Jing L, Harrild D M, et al. Impact of the cone operation on left ventricular size, function, and dyssynchrony in Ebstein anomaly: a cardiovascular magnetic resonance study [J]. J Cardiovasc Magn Reson. 2018; 20: 32.

[9] Holst K A, Dearani J A, Said S, et al. Improving Results of Surgery for Ebstein Anomaly: Where Are We After 235 Cone Repairs? [J]. Ann Thorac Surg. 2018; 105: 160-168.

[10] Ibrahim M, Tsang V T, Caruana M, et al. Cone reconstruction for Ebstein's anomaly: Patient outcomes, biventricular function, and cardiopulmonary exercise capacity [J]. J Thorac Cardiovasc Surg. 2015; 149: 1144-1150.

[11] Celermajer D S, Cullen S, Sullivan I D, et al. Outcome in neonates with Ebstein's anomaly [J]. J Am Coll Cardiol. 1992; 19: 1041-1046.

[12] Masse LandAntonacci M. Low cardiac output syndrome: identification and management [J]. Crit Care Nurs Clin North Am. 2005; 17: 375-383.

[13] Liu X, Zhang Q, Yang Z G, et al. Morphologic and functional abnormalities in patients with Ebstein's anomaly with cardiac magnetic resonance imaging: Correlation with tricuspid regurgitation [J]. Eur J Radiol. 2016; 85: 1601-1606.

[14] Tobler D, Yalonetsky S, Crean A M, et al. Right heart characteristics and exercise parameters in adults with Ebstein anomaly: new perspectives from cardiac magnetic resonance imaging studies [J]. Int J Cardiol. 2013; 165: 146-150.

[15] Yalonetsky S, Tobler D, Greutmann M, et al. Cardiac magnetic resonance imaging and the assessment of ebstein anomaly in adults [J]. Am J Cardiol. 2011; 107: 767-773.

[16] Hosch O, Ngyuen T T, Lauerer P, et al. BNP and haematological parameters are markers of severity of Ebstein's anomaly: correlation with CMR and cardiopulmonary exercise testing [J]. Eur Heart J Cardiovasc Imaging. 2015; 16: 670-675.

[17] Mysore M M, Bilchick K C, Ababio P, et al. Right atrial to left atrial volume index ratio is associated with increased mortality in patients with pulmonary hypertension [J]. Echocardiography. 2018; 35: 1729-1735.