# Factors Affecting Mortality in Ebstein's Anomaly of the Tricuspid Valve

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**Abstract**

Ebstein's anomaly of the tricuspid valve is a relatively uncommon congenital heart defect. Twenty-one patients (11 boys and 10 girls) with Ebstein's anomaly were reviewed regarding clinical characteristics and factors related to the outcome of this lesion. Their ages at presentation ranged from 1 day to 13 years (median = 11 months). Eleven patients presented in infancy period, 6 of them were neonates. Common clinical findings were systolic murmur (85.7%) and cyanosis (57.1%). Laboratory findings included cardiomegaly on chest X-rays (95.2%), right bundle branch block pattern (76.2%) and right atrial enlargement (61.9%) on electrocardiography. Diagnosis and grading of severity were established by echocardiography. Among 21 patients, 4 were lost during follow-up. Seventeen patients were followed for 3–72 months. Six patients (28.6%) required surgery, 5 of whom died following surgery. Two patients died during the medical follow-up. Factors affecting cardiac death were the younger age at presentation, onset of cyanosis in infancy period, associated PS or PA, the lower insertion of the septal leaflet of the tricuspid valve and the higher ratio of the combined area of right atrium and atrialized right ventricle to that of functional right ventricle and left heart chambers.

**Key word :** Ebstein's Anomaly, Tricuspid Valve, Factor Affecting Mortality

Ebstein's anomaly of the tricuspid valve is a relatively uncommon congenital heart defect. Its incidence was reported to be approximately 0.2 to 0.4 per cent of all cases of congenital heart disease (1). In a multicenter study in Thailand, the incidence was 0.8 per cent of congenital heart disease in 742 infants born in 1994(2). It was first described by Wilhelm Ebstein in 1866 in a 19-year-old laborer who died of severe congenital malformation of the tricuspid valve with tricuspid regurgitation(3). Tourniaire diagnosed this anomaly in a living subject in 1949(4). There is an extremely variable natural history, which may present at any age, ranging from neonatal death to asymptomatic survival into late adulthood. There was only one report on Ebstein's anomaly in adolescents and adults in Thailand(5).

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There has been no report on natural history of this lesion in pediatric age group. This study is a retrospective review of infants and children diagnosed with Ebstein's anomaly at Ramathibodi Hospital. Clinical presentations and predictors of outcome were evaluated.

**Abbreviations:**

PS = pulmonary stenosis
VSD = ventricular septal defect
PA = pulmonary atresia
PDA = patent ductus arteriosus
ASD = atrial septal defect
TGA = transposition of the great arteries
TR = tricuspid regurgitation
BT = Blalock-Taussig

## PATIENTS AND METHOD

Medical records, chest radiography, electrocardiography (ECG) and echocardiography of all patients (n = 21) under the age of 15 years who were diagnosed as having Ebstein's anomaly in Pediatric Cardiology Unit, Ramathibodi Hospital between 1989 and 1998 were reviewed.

The diagnosis was confirmed by echocardiography in all cases. The diagnostic criterion was the inferior displacement of septal tricuspid leaflet of more than 8 $mm/m^2$ body surface area[6].

Echocardiographic grading of severity was calculated by using the ratio of the combined area of the right atrium and atrialized right ventricle to that of the functional right ventricle, left atrium and left ventricle in four-chamber view at end-diastole as described by Celermager[7]. The severity of TR was graded by measurement of the spatial distribution of the TR jet on the color Doppler examination, categorized into mild, moderate and severe[8]. Other associated lesions were recorded.

### Statistics

Student *t*-test, Fisher exact test and Odd ratio were used in analytical statistics in predicting the outcome. A p value of less than 0.05 was considered significant.

## RESULTS

Twenty-one patients (11 boys and 10 girls) were enrolled in the study. Their ages ranged from 1 day to 13 years (median 11 months). Eleven patients (52.4%) presented in infancy period, six of them were neonates. Cyanosis was the most common presenting symptom (Table 1). Associated cardiac defects were present in 17 patients (81%) which included pulmonary atresia and pulmonary stenosis, 2 patients each (Table 2).

Chest radiography demonstrated cardiomegaly in 20 of the 21 (95%) patients. The ECG showed evidence of right atrial enlargement in 13 patients (61.9%) and incomplete right bundle branch block in 16 patients (76.2%). Echocardiography demonstrated mild TR in 5 patients (23.8%), moderate TR in 9 patients (42.8%) and severe TR in 5 patients (23.8%).

Six patients were operated on (Table 3); the indications for surgery were persistent severe cyanosis. Of the 6 patients, 2 had pulmonary valvulotomy, 2 had BT shunt and 2 had repair tricuspid valve combined with bidirectional Glenn operation. Five patients died following the surgery giving the mortality rate of 83.3 per cent. One who survived had right modified BT shunt at 5 days of age. Now she is 4 years of age with cardiac functional class 2 and oxygen saturation of 80-90 per cent.

**Table 1. Symptoms and ages at first presentation.**

| Symptoms at first presentation | Number of patients Ages at first presentation | | | Total (%) |
|---|---|---|---|---|
| | < 1 mo | >1-12 mo | 1-15 yr | |
| Cyanosis | 6 | 3 | 3 | 12 (57.1) |
| Asymptomatic | | 1 | 3 | 4 (19.1) |
| Congestive heart failure | - | 1 | 2 | 3 (14.2) |
| Supraventricular tachycardia | - | - | 1 | 1 (4.8) |
| History of brain abscess | - | - | 1 | 1 (4.8) |
| Total (%) | 6 (28.6) | 5 (23.8) | 10 (47.6) | 21 (100) |

There were 4 patients who were lost in follow-up. Two patients who did not undergo surgery died due to severe cyanosis at 3 and 8 months of age. Ten patients had been monitored for 3-72 months; and the cardiac functional class revealed: 6 patients in class 1, 2 in class 2, 3 and 1 each in class 3 and 4. Seven patients who died and 10 patients who survived were comparitively studied in various aspects including : ages at presentation, cyanosis in infancy period, cardiomegaly on chest films, right bundle branch block on ECG, associated PA or severe PS, the distance between tricuspid and mitral valve leaflets, severity of TR and the ratio of the combined area of right atrium and atrialized right ventricle to that of functional right ventricle, left atrium and left ventricle (Table 4). The poor prognostic factors included younger age at presentation, early onset of cyanosis in infancy period, associated PS or PA, the lower insertion of the septal leaflet of the tricuspid valve and the higher ratio. Six of 9 patients (66.7%) with the ratio greater than one died (Table 5).

**Table 2. Associated cardiac defects.**

| Associated cardiac defects | Number of patients | % |
|---|---|---|
| ASD, secundum | 4 | 19.0 |
| Severe PS | 2 | 9.6 |
| PA, PDA | 2 | 9.6 |
| Small muscular VSD | 2 | 9.6 |
| PDA | 2 | 9.6 |
| Supravalvular PS | 1 | 4.8 |
| Inlet VSD, ASD, muscular VSD | 1 | 4.8 |
| Dilated cardiomyophathy | 1 | 4.8 |
| Corrected TGV, VSD | 1 | 4.8 |
| Endocardial fibroelastosis, ASD | 1 | 4.8 |
| None | 4 | 19.0 |

## DISCUSSION

Watson[9] reported an international cooperative study of 505 cases of Ebstein's anomaly of the tricuspid valve with 314 of them presented under 15 years of age. Thirty-five of 314 cases (11.1%) studied were in infancy and 279 (88.9%) were between 1 and 15 years of age. Pramod et al[10] also reported in the same percentage, in a study of

**Table 3. Type and age of surgery and outcome.**

| Type of surgery | Number | Age at surgery | Number of deaths |
|---|---|---|---|
| Pulmonary valvulotomy | 2 | 4 mo, 1 yr 6 mo | 2 |
| Blalock-Taussig shunt | 2 | 5 days, 7 days | 1 |
| Repair of TV# and Bidirectional Glenn operation | 2 | 2 yr, 3 yr | 2 |

# TV = tricuspid valve

**Table 4. Factors affecting death.**

| Factors | Death (n = 7) | Alive (n = 10) | Odd ratio | P |
|---|---|---|---|---|
| Mean age at presentation | 2.35 ± 2.97 | 63.21 ± 6069 | | 0.01* |
| Male sex | 4 (57.1%) | 4 (40%) | 2 | 0.48 |
| Cyanosis in infancy | 6 (85.7) | 1 (10%) | 54 | 0.002* |
| Cardiomegaly in chest film | 7 (100%) | 10 (100%) | | |
| RBBB in ECG | 3 (42%) | 9 (90%) | 0.08 | 0.04 |
| PA or severe PS | 4 (57.1%) | 0 (0%) | | |
| Moderate to severe TR | 5 (71.4%) | 6 (60%) | 1.67 | 0.63 |
| Mean TV-MV distance$ | 5.47 ± 1.83 | 2.5 ± 1.37 | - | 0.001* |
| Mean ratio# | 1.36 ± 0.38 | 0.80 ± 0.32 | - | 0.006* |

$ The distance between mitral and tricuspid valve leaflets ($cm/m^2$)
# The ratio of the combined area of right atrium and atrialized right ventricle to that of right ventricle proper and left heart chambers
* Statistical significance

**Table 5. Echocardiographic features in 17 patients with Ebstein's anomaly and outcome.**

| Grade | Ratio* | No. of patients | Cardiac death (%) |
|---|---|---|---|
| 1 | < 0.5 | 2 | 0 (0) |
| 2 | 0.5 to 0.99 | 6 | 1 (16.7) |
| 3 | 1 to 1.49 | 8 | 5 (62.5) |
| 4 | ≥ 1.5 | 1 | 1 (100) |

* Ratio = The ratio of combined area of right atrium and atrialized right ventricle to that of left ventricle, left atrium and functional right ventricle

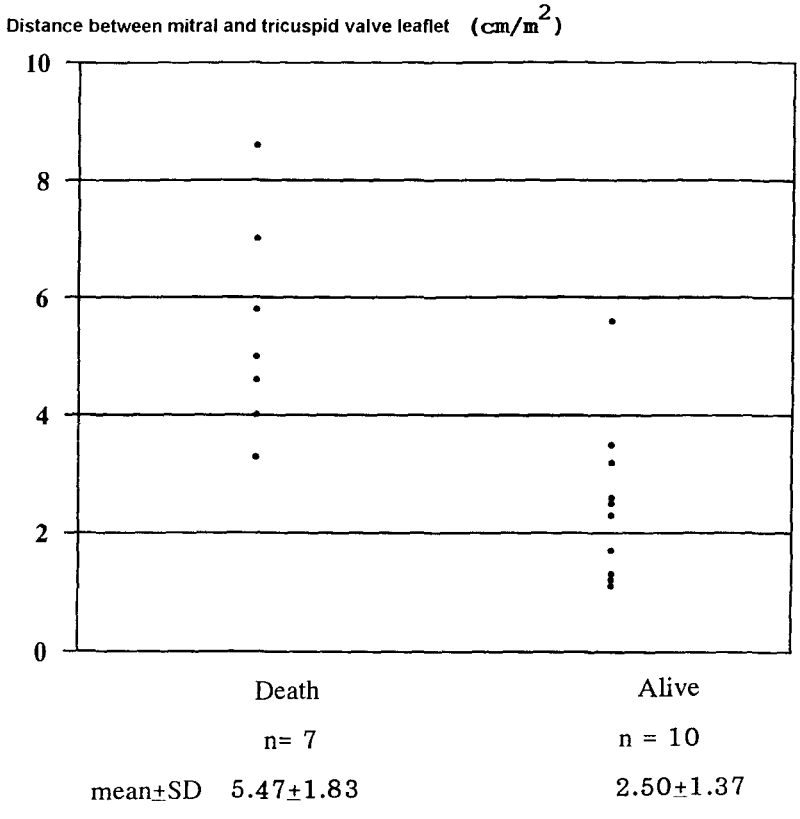


**Fig. 1. Distance between mitral and tricuspid valve leaflet in death and alive patients.**

63 cases, 21 cases studied were under 15 years of age, 3 of 21 cases (14.3%) were in infancy and 18 (85.7%) were between 1-15 years of age. This study showed that 52.4 per cent of Ebstein's anomaly were in infancy period and 47.6 per cent were between 1 and 15 years of age. The reasons for the higher percentage of patients who presented in infancy in our study probably were the small number of cases and the undetected older age group, who were usually asymptomatic.

The poor prognostic predictors in our study were the onset of cyanosis in infancy, the distance between the mitral and tricuspid valve leaflets, and the ratio of the combined area of right atrium and atrialized right ventricle to that of right ventricular proper and left heart chambers. This ratio, proposed by Celermajer[7], reflects both the anatomic tricuspid valve displacement in which the greater the displacement, the larger the area of the atrialzed right ventricle, and the physiologic conse-

quences of tricuspid valve stenosis and regurgitation, or both, in which the more severe the lesion, the larger the area of the right atrium. This ratio can be easily and reliably measured by echocardiogram in an apical four-chamber view. The younger age at presentation and early cyanosis in infancy imply that the more secere the disease, so the earlier the symptoms occurred.

The distance between tricuspid and mitral valve leaflets had a high correlation with mortality, when corrected by the body surface area. The lower the insertion of the septal leaflet of the tricuspid can cause the greater the atrialized right ventricle and the less the right ventricle proper, which determined a lower antegrade flow across the pulmonary valve. This distance of $\geq$ 4 cm/m$^2$ was related with the high mortality rate. Six of 7 patients who died and only 1 of 10 who survived had this distance (Fig. 1).

Associated PS or PA can cause less pulmonary blood flow and aggravate the severity of cyanosis. In this study, all patients associated with PS or PA died.

The severity of TR was not a predictor of mortality in this study. The validation of grading in retrospect is probably the factor. Certainly the impact of TR causing progressive dilatation of the atrium and the atrialized right ventricle, probably play roles in the death of the patients.

The management of Ebstein's anomaly depends on age at presentation, degree of cyanosis, anatomic severity of the lesion, and presence of associated lesions. The indication for early surgical intervention in Ebstein's anomaly is severe cyanosis. Yetman et al[11] reported poor outcome in cyanotic neonates with Ebstein's anomaly. Thirty-five per cent of patients underwent surgical intervention and the total mortality was 70 per cent. Starnes et al[12] reported palliative treatment consisting of tricuspid closure with autologous pericardium and an aorto-pulmonary shunt of 4 mm polytetra-fluoroethylene tubing and then further Fontan procedures, which represent their definitive operative management, with good results in 2 patients. This study showed poor outcome in the surgical patients. One patient who survived, presented with cyanosis early in the neonatal period, and underwent right modified BT shunt. The cyanosis improved and she is doing well up to 4 years of age with oxygen saturation of 80 to 90 per cent. The other patient who underwent BT shunt, died after the surgery. This palliative shunt generally has a low risk and can improve the cyanosis in the patient with Ebstein's anomaly.

## SUMMARY

The poor prognostic factors included the younger age at presentation, onset of cyanosis in infancy period, associated PS or PA, the lower insertion of the septal leaflet of the tricuspid valve, and the higher ratio of the combined area of right atrium and atrialized right ventricle to that of the functional right ventricle and left heart chambers.

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## ปัจจัยที่มีผลต่อการตายในผู้ป่วยที่เป็น Ebstein's anomaly ของ tricuspid valve

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Ebstein's anomaly ของ tricuspid valve เป็นโรคหัวใจพิการแต่กำเนิดที่พบได้ไม่บ่อย การศึกษาย้อนหลังตั้งแต่ปี พ.ศ.2532 ถึง 2541 พบผู้ป่วยเด็กที่ได้รับการวินิจฉัยว่าเป็น Ebstein's anomaly จำนวน 21 ราย เป็นชาย 11 ราย และหญิง 10 ราย อายุตั้งแต่ 1 วันถึง 13 ปี (median 11 เดือน) พบว่ามีเด็ก 11 รายที่มีอาการในช่วงวัยทารกและในจำนวนนั้นมีทารกแรกเกิดจำนวน 6 ราย อาการและอาการแสดงที่พบได้บ่อยคือ เสียงหัวใจฟู่ (systolic murmur) คิดเป็นร้อยละ 85.7 และอาการเขียว (cyanosis) คิดเป็นร้อยละ 57.1 นอกจากนี้พบว่ามีหัวใจโตจากการถ่ายภาพรังสีของทรวงอก (cardio-megaly) คิดเป็นร้อยละ 95.2 และจากการตรวจคลื่นไฟฟ้าหัวใจ พบว่ามี right bundle branch block คิดเป็นร้อยละ 76.2 กับ right atrial enlargement คิดเป็นร้อยละ 61.9 การตรวจด้วยคลื่นเสียงสะท้อน (echocardio-graphy) สามารถให้การวินิจฉัย และบอกถึงความรุนแรงของโรคได้ ในจำนวนผู้ป่วยทั้งหมด มีผู้ป่วยที่ขาดการติดตามผลการรักษา 4 ราย ผู้ป่วยจำนวน 17 รายได้รับการติดตามการรักษาเป็นเวลาตั้งแต่ 3 เดือน ถึง 72 เดือน ผู้ป่วยทั้งสิ้น 6 รายได้รับการผ่าตัดรักษา พบเสียชีวิต 5 ราย มีผู้ป่วยอีก 2 คนที่ยังไม่ได้รับการผ่าตัดแต่เสียชีวิต ปัจจัยที่มีผลต่อการเสียชีวิตคือ เริ่มแสดงอาการของโรคตั้งแต่อายุน้อย ระยะเวลาของการเกิดอาการเขียวในช่วงวัยทารก การมีลิ้นพัลโมนารี่ตีบหรือตันร่วมด้วย การมี septal leaflet ของ tricuspid เกาะต่ำมากมาก และการมีอัตราส่วนที่สูงกว่าของพื้นที่ของ right atrium กับ atrialized right ventricle ต่อ functional right ventricle กับ left heart chambers

**คำสำคัญ** : Ebstein's Anomaly, Tricuspid Valve, Factor Affecting Mortality

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