



Examining the Correlation Between the GOSE Index and Atrial Arrhythmia Development with Electrocardiographic P-wave Properties in Patients with Ebstein's Anomaly

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ABSTRACT

Introduction: Ebstein's anomaly (EA) is a congenital malformation of the tricuspid valve. In the present study, the aim was to examine the relationship between the Great Ormond Street Score (GOSE) index and P-wave characteristics in patients with EA.

Patients and Methods: Unoperated patients with EA were evaluated retrospectively. Echocardiographic GOSE indices were calculated for each patient. The P-wave characteristics on the 12-channel electrocardiography (ECG) were also evaluated simultaneously.

Results: There were EA 24 cases in the study. The median age was 12 months (range, 1 day-8 years). The median P-wave dispersion was 18 ms (range, 8-36 ms), median P-max duration was 86 ms (range, 58-104 ms), median P-min duration was 62 ms (range, 18-88 ms), and median P amplitude was 2.7 mm (range, 1.2-5 mm). Atrial arrhythmia was detected in eight cases. In the arrhythmia group, the P dispersion and P-max duration were significantly higher than in the non-arrhythmic group ($p < 0.05$). The median GOSE index was measured as 0.62 (range, 0.2-1.3). The GOSE index grade was detected as Grade 1 in 8 cases, Grade 2 in 12 cases, and Grade 3 in 4 cases. When the patients' GOSE index and P-wave characteristics were evaluated, a positive correlation was found between the P-max ($r = 0.5$, $p = 0.02$) and P amplitude ($r = 0.780$, $p = 0.001$). There was no significant correlation between the P dispersion and P-min durations ($p > 0.05$).

Conclusion: In EA cases, the GOSE index can be estimated, especially by evaluating the P-wave maximum duration and amplitude. Thus, clinicians may have an idea about the prognosis of cases with EA by evaluating the P-wave changes in ECG and especially the development of supraventricular arrhythmia.

Key Words: Children; Ebstein's anomaly; GOSE index; P-wave characteristics

Ebstein Anomalili Hastalarda Elektrokardiyografik P Dalga Özellikleri ile "GOSE İndeksi" ve Atriyal Aritmi Gelişmesi Arasında Korelasyon Var mı?

ÖZET

Giriş: Ebstein anomalisi (EA) triküspit kapağın konjenital bir malformasyonudur. Bu çalışmada EA'lı olgularda "Great Ormond Street Score (GOSE)" indeksi ile P dalga özellikleri arasındaki ilişkinin incelenmesi amaçlandı.

Hastalar ve Yöntem: Ameliyat olmamış ve EA tanısı alan olgular retrospektif olarak değerlendirildi. Hastaların ekokardiyografik olarak GOSE indeksleri hesaplandı. Eş zamanlı çekilen 12 kanallı elektrokardiyografi (EKG)'deki P dalga özellikleri (P maksimum, P minimum, P dispersiyon, P amplitüdü) ölçüldü. Sonuçlar değerlendirildi.

Bulgular: Çalışmada EA'lı 24 olgu mevcuttu. Ortanca P dalga dispersiyonu 18 ms (aralık: 8-36 ms), ortanca P-maks süresi 86 ms (aralık: 58-104 ms), ortanca P-min süresi 62 ms (aralık: 18-88 ms) ve ortanca P amplitüdü 2.7 mm (aralık: 1.2-5 mm) olarak hesaplandı. Atriyal aritmi 8 olguda saptandı. Aritmisi olan grupta nonaritmik grupta P dispersiyon ve P-maks süresi anlamlı olarak daha yüksekti ($p < 0.05$). Ortanca GOSE indeksi 0.62 (aralık: 0.2-1.3) olarak ölçüldü. GOSE indeksi derecesi 8 olguda Grade 1; 12 olguda Grade 2 ve 4 olguda Grade 3 olarak saptandı. Hastaların GOSE indeksi ile P dalga özellikleri değerlendirildiğinde; P-maks ($r = 0.5$, $p = 0.02$) ve P amplitüdü ($r = 0.780$, $p = 0.001$) arasında pozitif yönde bir ilişki saptandı. P dispersiyonu ve P-min süreleri arasında anlamlı ilişki gözlenmedi ($p > 0.05$).

Sonuç: EA'lı olgularda özellikle P dalga maksimum süresi ve amplitüdü değerlendirilerek GOSE indeksi tahmin edilebilir. Böylece klinisyenler EKG'deki P dalga değişiklikleri ile EA'lı olguların prognozu hakkında ve özellikle supraventriküler aritmi gelişimi yönünden fikir sahibi olabilirler.

Anahtar Kelimeler: Çocuk; Ebstein anomalisi; GOSE indeksi; P dalga özellikleri

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INTRODUCTION

Ebstein's anomaly (EA) is a rare congenital cardiac malformation characterized by apical displacement of the septal and posterior tricuspid valve leaflets, leading to the atrialization of the right ventricle with a variable degree of malformation and displacement of the anterior leaflet⁽¹⁻³⁾.

Its prognosis depends on the severity of the disease, and the severity of the disease can be determined by several techniques. One of them is the Great Ormond Street Score (GOSE index=Celermajer index), which is the ratio of the combined area of the right atrium and atrialized right ventricle to that of the functional right ventricle and left heart in a four-chamber view at the end-diastole⁽⁴⁾.

The P wave is a simple electrocardiographic (ECG) finding used to evaluate the intra-atrial and inter-atrial interactions. The importance of the duration of the P wave in various clinical conditions such as paroxysmal atrial fibrillation and left atrial dilation has been demonstrated⁽⁵⁻⁷⁾.

The increment of the atrialized chamber is directly leading to an increase in the GOSE index, and the increment of the size of the atrialized chamber also causes an increase in the P-wave amplitude in a 12-lead ECG. Although it is a well-known fact that the P-wave amplitude increases in cardiac diseases with right atrial (RA) dilation, the data about the relation of the P-wave amplitude and the GOSE index in patients with Ebstein's anomaly are insufficient. In this study, we investigated the relationship between the GOSE index and ECG P-wave indices.

PATIENTS and METHODS

The study included patients with EA who were monitored at the Pediatric Cardiology Department between January 2016 and January 2018. This retrospective study was approved by the institutional Ethics Committee (2018-35) and was conducted in accordance with the principles of the Declaration of Helsinki.

The demographic data regarding age, weight, cardiothoracic ratio, associated cardiac defects and echocardiographic findings, the GOSE index, the GOSE index severity grade, and ECG recordings were evaluated.

The GOSE index was calculated using echocardiography. The echocardiographic GOSE index measurements were performed by the same pediatric cardiologists (PA, T.K, E.O). The GOSE index was calculated as the ratio of the combined area of the RA and atrialized right ventricle (aRV) divided by the combined area of the remaining RV, left atrium, and left ventricle on a four-chamber view at the end of diastole. There were four grades of increasing severity defined: Grade 1, ratio < 0.5; Grade 2, ratio 0.5-0.99; Grade 3, ratio 1-1.49; and Grade 4, ratio ≥ 1.5 ⁽⁴⁾. The degree of tricuspid regurgitation (TR) was determined by a semi-quantitative measurement depending on

the vena contracta width. The left ventricular ejection fraction was calculated using Simpson's biplane method⁽⁸⁾.

Patients underwent 12-lead ECG (GE Healthcare, MAC 1600, Lewis Center, OH, USA) at the initial diagnosis. All the measurements and analyses were carried out with the MUSE-Citrix ECG system (Citrix, Santa Clara, CA, USA) with a 100% magnification. The P wave (min, max, axis, and dispersion), PR interval, QRS (axis and duration), QT (max, min, duration, dispersion), and T axis were calculated. The P-wave duration was defined as the distance between the initiation of the P wave on the isoelectric line and the point where the wave ended. It was measured for three consecutive beats on each derivation, and the average was calculated^(5,6). P dispersion was defined as the difference between the longest and shortest P-wave duration. An ECG analysis was conducted by the same pediatric cardiologists (E.O, T.K, P.A) to exclude the interobserver variability.

Patients with clinical symptoms and patients with documented tachyarrhythmia on ECG during periodic controls or on 24-hour holter monitoring or 12-channel ECGs required in accordance with symptoms were accepted as having tachyarrhythmia. Wolff-Parkinson-White (WPW) syndrome was defined as the presence of a short PR interval and delta wave. Inappropriate sinus tachycardia syndrome was defined as a resting daytime heart rate (HR) > 100 bpm with a normal P-wave morphology and axis obtained from standard 12-lead ECGs recorded on ≥ 2 separate days and an average HR of > 90 bpm on 24-hour ECG recording⁽⁹⁾. Atrial flutter was defined as an atrial HR between 240 and 400 beats per minute and an AV node conduction block. In addition, it was characterized by a sawtooth ECG pattern in leads II and III and aVF.

A diagnosis of focal atrial tachycardia was based on ECG, 24-hour Holter, or event monitor data consistent with the following electrophysiological criteria: (a) narrow complex tachycardia with visible P waves at an inappropriate rate given the patient's age and activity level; (b) identical abnormal P-wave morphology in the first and all subsequent tachycardia beats; (c) progressive increase in the atrial rate with tachycardia onset (warm-up); (d) variable rate depending on autonomic tone; and (e) first- or second-degree atrioventricular block in the presence of continued tachycardia^(10,11).

Statistical Analysis

The Statistical Package for the Social Sciences for Windows (SPSS) version 15 (SPSS, Chicago, IL, USA) was used for a statistical analysis. Continuous variables were expressed as median (range); and categorical variables were expressed as percentages. The correlations between the GOSE index and other parameters were measured by Pearson's correlation coefficient. A p-value < 0.05 was considered statistically significant.

RESULTS

There were 24 cases in the study group. Twelve (50%) of the patients were female. The median weight was 15 kg (range, 2.5-60 kg). The median age was 12 months (range, 1 day-8 years). The cardiothoracic (CT) ratio was > 0.55 in 6 cases (25%).

The ECG revealed the right bundle branch block in 6 cases (25%) and pre-excitation syndrome (WPW) in 5 cases (21%). P dispersion, P-wave max duration, P-wave min duration, and P-wave amplitudes were 18 msec (8-36 msec), 86 msec (58-104 msec), 62 msec (18-88 msec), and 2.7 mm (1.2-5 mm), respectively.

The ECG also showed significant tricuspid regurgitation in 9 of the cases (38%). The most common congenital associated lesions were patent foramen ovale in 11 (46%) cases and atrial septal defect in 7 (29%) cases. The median GOSE index was measured as 0.62 (range, 0.2-1.3). The GOSE indices were Grade 1 in 8 cases, Grade 2 in 12 cases, and Grade 3 in 4 cases.

The median duration of follow-up was 36 months (range, 12-44 months).

The demographic features, ECG, and echocardiographic characteristics of the patients were shown in Table 1.

Atrial arrhythmias were present in eight patients. Five of them were SVT, 2 were inappropriate sinus tachycardia, and 1 was atrial flutter/fibrillation. Three of the supraventricular tachyarrhythmias demonstrated narrow QRS morphology, while the two had wide QRS morphology. The Mahaim accessory pathway was demonstrated by an electrophysiological study of patients with wide QRS morphology. All patients with narrow QRS SVT were diagnosed with atrioventricular reentry tachycardia. When the P-max, P-min, P dispersion, and P amplitude were compared among those patients with arrhythmia and without arrhythmia, the P-dispersion duration was significantly higher in the arrhythmia group ($p < 0.05$). There was no difference between the P max, P min, and P amplitudes. The GOSE value and GOSE grades were significantly higher in the arrhythmia group ($p < 0.05$) (Table 2).

There was no significant correlation between the GOSE index and P dispersion ($r = 0.260$, $p = 0.24$). There was no significant correlation between the GOSE index and P-min duration ($r = 0.30$, $p = 0.10$). There was a statistically significant correlation between the GOSE index and the P-wave max duration ($r = 0.500$, $p = 0.02$) and the GOSE index and the P-wave amplitude ($r = 0.780$, $p = 0.001$).

Correlation of the P-wave properties with the GOSE index are presented in Figure 1.

When the relation between the P-wave dispersion and tricuspid valve insufficiency, TV displacement, and associated

Table 1. Patient characteristics

Patient characteristics	n= 24
Sex (male/female)	12/12
Median age-month (range)	12 months (1 day-8 years)
< 6 months n (%)	8 (33)
6-12 months n (%)	6 (25)
> 12 months n (%)	10 (42)
Median body weight-kg (range)	15 (2.5-60)
Median Cardiothoracic (CT) ratio	0.50 (0.42-0.68)
CT ratio ≥ 0.55 n (%)	6 (25)
CT ratio ≥ 0.65 n (%)	2 (8)
Electrocardiographic variables	
P-min median (range), msec	62 (18-88)
P-max median (range), msec	86 (58-104)
P dispersion median (range), msec	18 (8-36)
P amplitude median (range), mm	2.7 (1.2-5)
PR interval	130 (80-180)
RBBB, n (%)	6 (25)
Right axis deviation, n (%)	10 (42)
QRS pre-excitation, n (%)	5 (21)
Echocardiographic variables	
LV ejection fraction, median(range)	65 (50-75)
Ejection fraction $< 55\%$, n (%)	2 (8)
TV displacement, mm/m ² , median (range)	
Severe TR, n (%)	15 (9-28)
GOSE index median (range)	9 (38)
GOSE grade, n (%)	0.62 (0.2-1.3)
1	8 (33)
2	12 (50)
3	4 (17)
4	-
Associated anomaly	
Atrial septal defect n (%)	7 (29)
Patent foramen ovale n (%)	11 (46)
Ventricular septal defect n (%)	2 (8)
Mitral valve pathologies n (%)	2 (8)
Pulmonary stenosis n (%)	1 (4)
RV or LV non-compaction n (%)	3 (13)

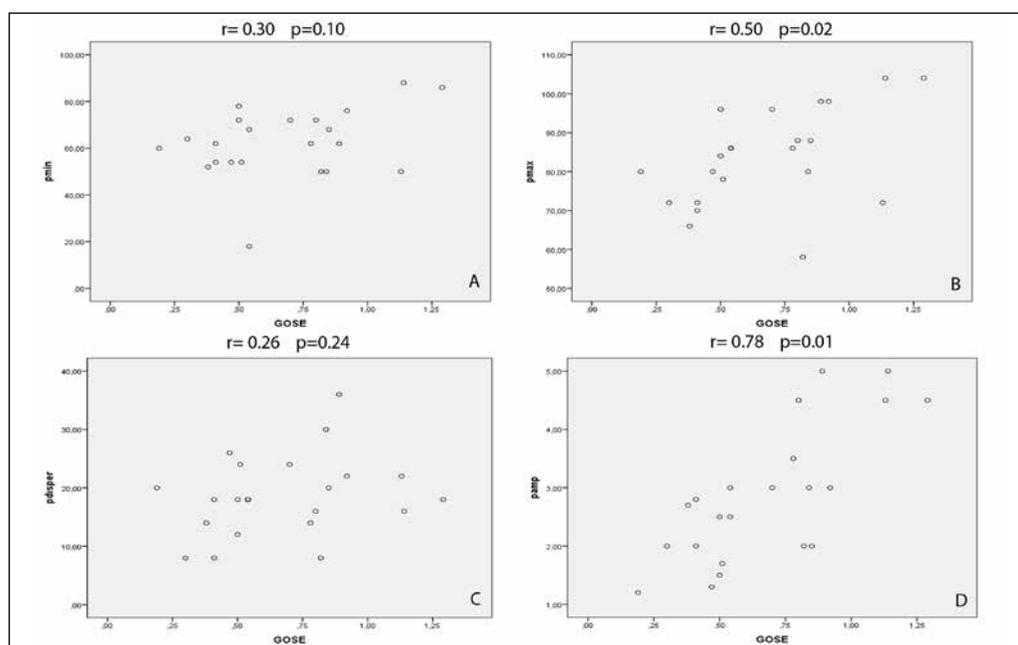
GOSE: Great Ormond Street Score, RBBB: Right bundle branch block, LV: Left ventricle, TV: Tricuspid valve, TR: Tricuspid regurgitation, RV: Right ventricle.

anomalies were evaluated, the median P-wave dispersion was 20 msec (range, 8-36 msec) in patients with severe tricuspid valve insufficiency, while it was 16 msec (range, msec 8-30) in patients without any insufficiency or with mild-to-medium insufficiency ($p = 0.850$). The median P-wave dispersion was 20 msec (range, 14-36 msec) in patients with associated anomalies, while it was 17 msec (range, 8-30 msec) in patients without any associated anomalies ($p = 0.100$). There was no correlation between the P-wave dispersion and TV displacement ($r = 0.220$, $p = 0.32$).

Table 2. Baseline atrial arrhythmias, the GOSE index, and P-wave characteristics

	(+) Arrhythmia (n= 8)	(-) Arrhythmia (n= 16)	p
P-min median (range), msec	60 (50-72)	65 (50-88)	0.650
P-max median (range), msec	80 (66-104)	90 (72-104)	0.219
P dispersion median (range), msec	24 (16-36)	16 (8-22)	0.020
P amplitude median (range), mm	2.5 (1-4)	3.5 (1-5)	0.060
Severe TR, n (%)	3 (38)	5 (31)	0.900
GOSE index median (range)	0.88 (0.41-1.33)	0.58 (0.19-0.89)	0.025
GOSE grade, n (%)			
1	1 (12)	8 (50)	0.030
2-4	7 (88)	8 (50)	

GOSE: Great Ormond Street Score, TR:Tricuspid regurgitation.

**Figure 1.** Correlation of P-max (A), P-min (B), P dispersion (C), and P amplitude (D) with the GOSE index.

DISCUSSION

In this study, we examined the presence of a correlation between the GOSE index, an important factor to predict the prognosis and clinical severity in pediatric patients with EA, and P-wave characteristics in ECG. It was determined that there was a high correlation between the GOSE index and P amplitude; and a mid-level correlation with P-max duration. In addition, P dispersion was significantly higher in cases of EA with atrial arrhythmia. To the best of our knowledge, these characteristics have not been reported in literature in children before.

EA is characterized by apical displacement of the tricuspid valve, and it corresponds to less than 1% of all congenital heart defects. It is often associated with other malformations, such as

ventricular septal defect, and is often accompanied by WPW syndrome. Its clinical manifestations depend on the severity of the anatomical changes, and surgical indications have been well established⁽¹²⁾.

The inter-atrial communication (ASD or PFO) has been reported as 50%-89% and the interventricular communication (VSD) as 2%-8% among different studies on EA^(13,14). In a study of 51 cases, including adult cases, ASD was detected in 37% (n= 19) of the cases; PFO was detected in 10% (n= 5), and PFO and VSD together were detected in 2% (n= 1)⁽³⁾.

In the present study, 75% of the cases had an inter-atrial connection (ASD or PFO) and 8% had VSD in accordance with the literature.

The EA prognosis varies from one patient to another, depending on the morphology of the heart, burden of arrhythmias, and resultant clinical sequelae. In an adult cohort of 72 unoperated patients over the age of 25 years, survival was 89% at 1 year, 76% at 10 years and 41% at 20 years of follow-up⁽¹²⁾. In another study, it was suggested that the GOSE index was the most effective prognosis factor. The GOSE index was categorized by a scoring system (if index < 0.5, GOSE score= 1; if index 0.5-1, score= 2; if index 1-1.4, score= 3; and if index > 1.5 score= 4). According to this scoring system, the mortality rate was 8% in patients with a score of 1-2; the mortality in patients with a score of 3 without a cyanotic disease was 10% in the early phase and 45% in the late phase; and the mortality was 100% in patients with a score of 4 and the cyanotic score 4.

In the present study, the highest GOSE index was 1.3, and none of the patients was lost during the follow-up period.

The ECG is usually abnormal in patients with EA. P waves are often quite tall and peaked (Himalayan P waves). A QR pattern can be seen in leads V1 to V4. There can be some intraventricular conduction delay with a widened QRS with or without a right bundle branch pattern. Pre-excitation, in the form of WPW syndrome and manifest pre-excitation, may be present in 18%-44% of the cases. There is usually a right-sided bypass tract present in the right posterior or right posteroseptal region. Multiple accessory pathways may be present^(12,15).

In the present study, 21% of the cases had pre-excitation, and multiple accessory pathways were detected in 2 cases.

The atrial function under various pressure and volume loading, and thus the secondary changes in the atrial tissue due to these loads, has caused a decreased intra-atrial and inter-atrial conduction and irregularity of conduction. The prolongation of intra-atrial and inter-atrial conduction times and heterogeneous conduction of sinus stimuli were the main electrophysiological disorders seen in atrial arrhythmias.

Atrial tachycardia (AT) had been common in patients with the Ebstein malformation. Both the P-wave duration and dispersion on ECG were known predictors of AT. A more heterogeneous and tortuous pathway of atrial activation in addition to a prolonged activation time seemed to be responsible for the widening of P-wave dispersion^(3,16,17).

In addition, it has been found that the P dispersion and P maximum values also changed after atrial surgery, but these measurements were performed on Holter monitoring, and no relationship was found between these measurements and atrial tachycardia⁽¹⁸⁾.

Shiina et al. evaluated 24 operated adult patients to assess P-wave characteristics in adults with Ebstein's malformation and its relationship with AT and RA fibrosis. The P-wave duration and dispersion in adults with EA has been shown to correlate

with RA fibrosis and predicted preoperative atrial arrhythmia. P-wave dispersion was found to increase after surgery, despite a mid-term reduction in paroxysmal AT. P-wave characteristics are surrogates of atrial fibrosis and noninvasive predictors of paroxysmal AT in Ebstein malformation⁽¹⁹⁾.

In the present study, eight cases with arrhythmias had a higher P dispersion and P-max durations than patients without arrhythmia. Similar to Shiina et al., these factors can be used as a predictor factor in atrial arrhythmias⁽¹⁹⁾.

Limitations

This study was limited by the retrospective single-center nature of the data available for analysis. Other limitations included low GOSE grades and an unknown percentage of cardiac fibrosis cases. Additionally, a 21% WPW incidence in overall patient population might influence the effect of arrhythmia development on P-wave morphology.

CONCLUSION

A significant correlation between the GOSE index and P-wave max duration and P-wave amplitude was demonstrated so that the clinicians might gather opinion about prognosis after evaluating ECG P-wave indices. In addition, cases with a high P dispersion are risky in terms of the development of atrial arrhythmia. Further studies with a large number of patients are needed to predict the relationship between the GOSE index, prognosis, and ECG P-wave indices.

CONFLICT of INTEREST

The authors reported no conflict of interest related to this article.

AUTHORSHIP CONTRIBUTIONS

Concept/Design: TK, PA

Analysis/Interpretation: EÖ, CT

Data Acquisition: PA, TK, CT

Writing: TK, EÖ

Critical Revision: YE, AG

Final Approval: All of authors.

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