

## Is There A Correlation Between “gose Index” and Atrial Arrhythmia Development With Electrocardiographic P Wave Properties In Patients With Ebstein’s Anomaly?

Ebstein Anomalili Hastalarda Elektrokardiyografik P Dalga Özellikleri ile “gose İndeksi” ve Atriyal Aritmi Gelişmesi Arasında Korelasyon Var mı?

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### ABSTRACT

**Introduction:** Ebstein’s anomaly (EA) is a congenital malformation of the tricuspid valve. In this study, it is aimed to examine the relationship between Great Ormond Street Score (GOSE) index and P wave characteristics in patients with EA.

**Materials and Method:** Unoperated patients with EA were evaluated retrospectively. Echocardiographic GOSE indices were calculated for each patient. The p-wave characteristics on the 12-channel ECG were also evaluated simultaneously.

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

**Conclusion:** In cases with EA, 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.

**Keywords:** Children, Ebstein’s anomaly, GOSE index, p wave characteristics

**ÖZET**

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

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

**Bulgular:** Çalışmada EA'li 24 olgu mevcuttu. Ortanca p dalga dispersiyonu 18 msn (Aralık: 8-36 msn), ortanca p maksimum süresi 86 msn (aralık: 58-104 msn), ortanca P minimum süresi 62 msn (aralık: 18-88 msn) 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 maksimum 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 maksimum ( $r=0.5$ ,  $p=0.02$ ) ve p amplitüdü ( $r=0.780$ ,  $p=0.001$ ) arasında pozitif yönde bir ilişki saptandı. P dispersiyonu ve P minimum süreleri arasında anlamlı ilişki gözlenmedi ( $p>0.05$ ).

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

**Anahtar Kelimeler:** Çocuk, Ebstein Anomalisi, GOSE indeksi, p dalga özellikleri

**Geliş Tarihi:** 04.10.2018 - **Kabul Tarihi:** 01.11.2018

**Introduction:**

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

Prognosis depends on the severity of the disease and severity of the disease can be determined with several techniques. One of them is "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).

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

**Material and Method:**

The study involved patients with EA who have been monitored at Pediatric Cardiology Department between January 2016 and January 2018. This retrospective study was approved by the institutional Ethics Committee 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, GOSE index, GOSE index severity grade and ECG recordings were evaluated.

GOSE index was calculated by echocardiography. 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 RV (aRV) divided by the combined area of the remaining RV, left atrium, and left ventricle on a 4-chamber view at the end of diastole. Four grades of increasing severity were defined: Grade 1: ratio  $<0.5$ ; Grade 2:  $0.5$  to  $0.99$ ; Grade 3:  $1$  to  $1.49$ ; and Grade 4:  $\geq 1.5$  (4). The degree of tricuspid regurgitation (TR) was determined by a semi-quantitative measurement depending on 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 initial diagnosis. All the measurements and analysis were carried out with the MUSE-Citrix ECG system (Citrix, Santa Clara, CA, USA) with 100% magnification. P wave (min, max, axis, and dispersion), PR interval, QRS (axis and duration), QT (max, min, duration, dispersion), and T axis were calculated. P wave duration was defined as the distance between the initiation of 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. ECG analysis was conducted by the same pediatric cardiologists (E.O, T.K, P.A) in order to exclude interobserver variability.

Those with clinical symptoms and the ones with documented tachyarrhythmia on ECG during periodic controls or on 24 hours Holter monitorization or 12 channel ECGs required in accordance with symptoms were accepted as tachyarrhythmia. Wolff-Parkinson-White (WPW) syndrome was defined as presence of a short PR interval and delta wave. Inappropriate sinus tachycardia syndrome was defined as a resting daytime HR  $> 100$  bpm with a normal P wave morphology and axis obtained from standard 12-lead ECGs recorded on  $\geq 2$  separate days and an average HR of  $> 90$  bpm on 24-hour ECG recording (9). Atrial

flutter was defined as an atrial heart rate between 240 and 400 beats per minute and AV node conduction block. Additionally, it was characterized by a saw tooth ECG pattern in leads II, III and aVF.

A diagnosis of focal atrial tachycardia (FAT) was based on ECG, 24-hour Holter, or event monitor data consistent with the electrophysiological criteria described above: (a) narrow complex tachycardia with visible P waves at a rate inappropriate 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 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:**

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

**Results:**

There were 24 cases in the study group. Twelve (50%) of the patients were female. 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%).

ECG revealed right bundle branch block (RBBB) 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.

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

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 8 patients. Five of them were SVT, 2 were inappropriate sinus tachycardia and 1 was atrial flutter / fibrillation. Three of the supraventriküler tachyarrhythmias demonstrated narrow QRS morphology while the two had wide QRS morphology. Mahaim accessory pathway was demonstrated at electrophysiological study of the patients with wide QRS morphology. All of the patients with narrow QRS SVT were diagnosed as Atrioventricular reentry tachycardia (AVRT). When 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 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 GOSE index and p-dispersion ( $r=0.260$ ,  $p=0.24$ ). There was no significant correlation between GOSE index and p-min duration ( $r=0.30$ ,  $p=0.10$ ). There was a statistically significant correlation between GOSE index and p wave max duration ( $r = 0.500$ ,  $p = 0.02$ ), GOSE index and p wave amplitude ( $r = 0.780$ ,  $p = 0.001$ ).

Correlation of the p-wave properties with the GOSE index of the cases were shown in Fig. 1.

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

**Discussion:**

In this study, we examined the presence of a relationship 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 GOSE index and p amplitude; 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.

Ebstein's anomaly (EA) is characterized by apical displacement of the tricuspid valve, and corresponds to less than 1% of all congenital heart defects. It is often associated with other malformations, such as ventricular septal defect, and Wolff-Parkinson-White syndrome often accompanies. Its clinical manifestations depend on the severity of the anatomical changes, and surgical indications have been well established (12).

Interatrial communication (ASD or PFO) has been reported as 50-89% and interventricular communication (VSD) as 2-8% among different studies in Ebstein's anomaly (13-14). In a study of 51 cases involving adult cases; ASD was detected in 37 % (n = 19) of the cases; PFO was detected in 10 % (n = 5), PFO and VSD together was detected in 2 % (n = 1) (3).

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

The prognosis of EA 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 year, and 41 % at 20 years of follow-up (12). In another study, it was suggested that GOSE index was the most effective factor for prognosis. GOSE index was categorized by a scoring system (if index <0.5, GOSE score=1, if index 0.5-1, score= 2, if index1-1.4, score = 3, and if >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 cyanotic score 4.

In the present study, 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 Ebstein's anomaly. P waves are often quite tall and peaked (Himalayan P waves). A qR pattern can be seen in lead 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 Wolff-Parkinson-White 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 two of the cases.

Atrial function under various pressure and volume loading, and thus the secondary changes in the atrial tissue due to these loads have been caused 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 Ebstein malformation. Both 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).

In addition, it had been found that 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 right atrial (RA) fibrosis. 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, 8 cases with arrhythmias had higher P dispersion and P maximum durations than patients without arrhythmia. Similar to Shiina et al(19), these factors can be used as a predictor factor in atrial arrhythmias.

**Limitations:** This study was limited by the retrospective single-center nature of the data available for analysis. Other limitations included low GOSE grades, and unknown percentage of cardiac fibrosis

development. Additionally 21% WPW incidence in overall patient population might influence the effect of arrhythmia development on p wave morphology.

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

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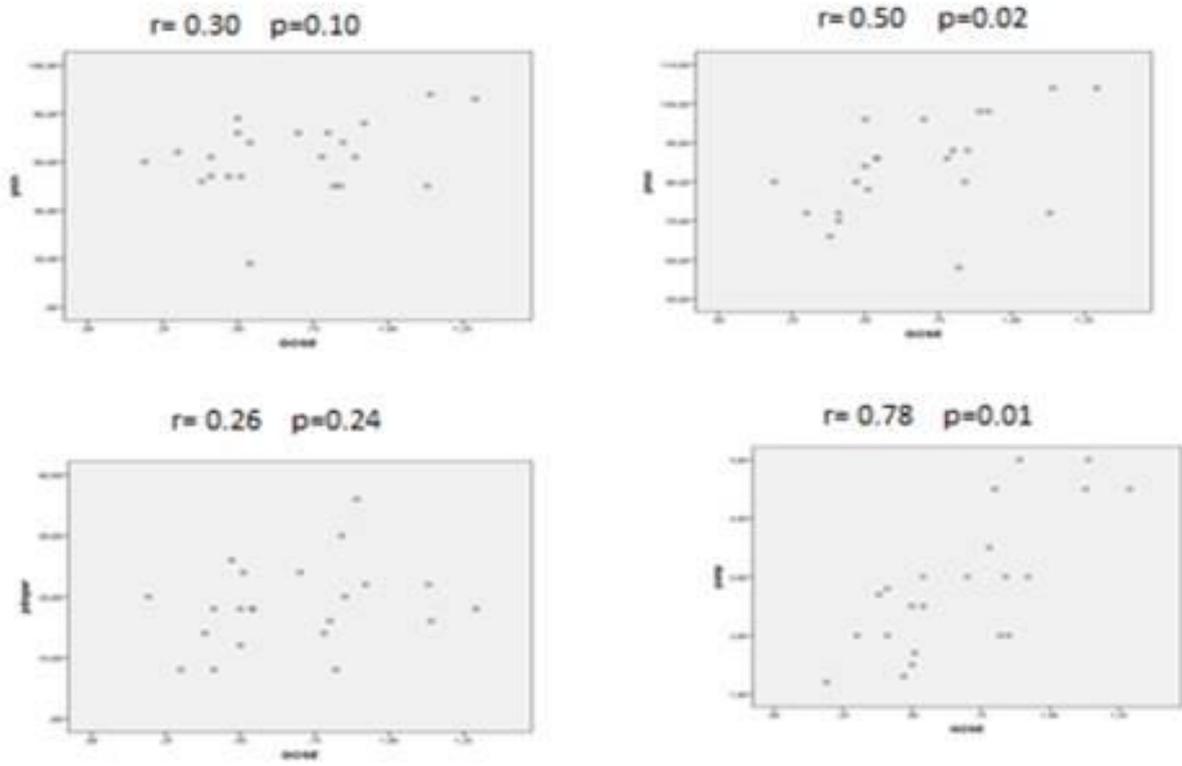


Figure-1: Correlation of p max(A), p min(B), p dispersion(C) and p amplitude(D) with GOSE index

**Table 1: Demonstration of patient characteristics**

Patient characteristics	n =24
<b>Sex (Male/Female)</b>	12/12
<b>Median age- month (range)</b>	12 months (1 day-8 years)
< 6 months n (%)	8(33)
6-12 months n (%)	6(25)
> 12 months n (%)	10(42)
<b>Median body weight- kg (range)</b>	15(2.5-60)
<b>Median Cardiothoracic(CT) ratio</b>	0.50 (0.42-0.68)
CT ratio $\geq$ 0.55 n (%)	6(25)
CT ratio $\geq$ 0.65 n (%)	2(8)
<b>Electrocardiographic variables</b>	
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)
<b>Echocardiographic variables</b>	
<b>LV ejection fraction, median(range)</b>	65(50-75)
<b>Ejection Fraction &lt; 55%, n (%)</b>	2(8)
<b>TV displacement, mm/m2, median(range)</b>	
<b>Severe TR, n (%)</b>	15(9-28)
<b>GOSE index median (range)</b>	9(38)
<b>GOSE grade, n (%)</b>	0.62(0.2-1.3)
1	
2	8 (33)
3	12(50)
4	4(17)
<b>Associated anomaly</b>	-
Atrial septal defect n (%)	
Patent foramen ovale n (%)	7(29)
Ventricular septal defect n (%)	11(46)
Mitral valve pathologies n (%)	2(8)
Pulmonary stenosis n (%)	2(8)
RV or LV non compaction n (%)	1(4)
	3(13)

**Table 2: Baseline atrial arrhythmias, 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)	<b>0,020</b>
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)	<b>0,025</b>
GOSE grade, n (%)			
1	1(12)	8(50)	<b>0,030</b>
2-4	7(88)	8(50)	