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ST Segment Yükselmeli Hastalarda Trombolitik Tedavi Sonrası İnfark Genişliği ve QRS Aks Değişikliği Arasındaki İlişki

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Abstract

Objective: Electrocardiography (ECG) may be a practical guiding tool for prognostic infarct sizing in ST elevation acute myocardial infarction (STEAMI). In this study, we sought to find a relation between the infarct size and the change in the QRS axis after thrombolytic therapy.

Materials and Methods: Patients with STEAMI who received thrombolytic therapy were selected retrospectively. The mean QRS axes of two ECGs (before and 90 minutes after thrombolytic therapy) were calculated. Creatinine kinase MB (CKMB) was used as the marker of infarct size.

Results: We did not detect any correlation between infarct size and change in the QRS axis with respect to any myocardial infarction MI localizations (p=0.80). However, in the isolated inferior MI group, there was a good correlation between CKMB and change in the QRS axis (r=-0.52 p=0.049).

Conclusion: The change in the QRS axis is rarely emphasized, providing a practical and promising tool for evaluating both the efficiency of the thrombolytic therapy and prognostic infarct sizing.

Key Words: Acute coronary syndrome, Acute myocardial infarction with ST elevation, Infarct size, QRS axis, Thrombolytic therapy

Özet

Amaç: Elektrokardiyografi (EKG) ST yükselmeli akut miyokard infarktüsü (STYAMİ) ile gelen hastalarda prognostik infarkt genişliğini belirlemede pratik ve yönlendirici bir araç olabilir. Bu çalışma ile infarkt genişliği ile trombolitik tedavi sonrası QRS aks değişim miktarı arasında bir ilişki olup olmadığını bulmaya çalıştık.

Gereç ve Yöntem: Bu çalışmada trombolitik tedavi alan STYAMİ hastaları retrospektif olarak seçildi. İki EKG'de (trombolitik tedavi öncesindeki ve tedavi sonrası 90. dakikadaki) ortalama QRS aksı bir formül yardımıyla hesaplandı. İnfarkt genişliğini belirlemede belirteç olarak kreatinin kinaz MB (CKMB) kullanıldı.

Bulgular: Tüm Mİ altgrupları gözönüne alındığında infarkt genişliği ile QRS aksı değişimi arasında korelasyon saptamadık (p=0.80). Sadece izole inferior Mİ grubunda CKMB ile QRS aksı değişimi arasında iyi derece korelasyon saptadık (r=-0.52 p=0.049).

Sonuç: QRS aksı değişimi, trombolitik tedavinin etkinliğinin değerlendirilmesinde ve prognostik infarkt genişliğinin belirlenmesinde çok vurgulanmamış, pratik ve gelecek vadeden bir araç gibi gözükmektedir.

Anahtar Kelimeler: Akut koroner sendrom, ST yükselmeli akut miyokard infarktüsü, İnfarkt genişliği, QRS aksı, Trombolitik tedavi

Introduction

Acute coronary syndromes (ACS) are the leading cause of death in the world [1]. There has been a measurable decrement in mortality and morbidity associated with ACS as a result of not only the recent achievements in pharmacological therapy but also the increased convenience and accessibility of medical help. However, ACS are still serious health problems that must be handled rapidly and effectively. ST elevation acute myocardial infarction (STEAMI) constitutes the most exclusive group amongst ACS. Improved survival due to widespread usage of thrombolytic therapy emphasizes the importance of restoration of blood flow. The main goal of therapy in the management of ACS is to focus on the improvement of the systems to provide restoration of blood flow to infarcting myocardium as soon as possible. The loss of jeopardized

myocardium and the related increment in mortality and morbidity when reperfusion is not achieved necessitates an early assessment of reperfusion and prognostic infarct sizing, which can be performed faster noninvasively. Among noninvasive methods, the most practical and guiding one is undoubtedly electrocardiography (ECG). To date, there are no data on the change in the QRS axis associated with ACS. In this study, we sought to find a relation between infarct size and the change in the QRS axis after thrombolytic therapy.

Materials and Methods

Patients who were hospitalized in the Ankara Ataturk Education and Research Hospital Coronary Care Unit with the diagnosis of ST elevation acute coronary syndrome between the 1st of January, 2007, and the 1st of January, 2009, were included in this study. Among these patients, those who received thrombolytic therapy were used in this study. Two ECGs, (one before thrombolytic therapy and one 90 minutes after thrombolytic therapy) were obtained. The mean QRS axes of these two ECGs were calculated by a formula 01 [2]:

Electrical Axis (EA)= ±arctan $[2 \times aVF/ sqr(3) \times I]$ [2]

$aVF=II–\frac{1}{2}\times I$ [3]
$6\times aVF=6\times II–3\times I$

$aVR=-\frac{1}{2}\times I–\frac{1}{2}\times II$ [3]
$8\times aVR=-4\times I–4\times II$

$aVL=I–\frac{1}{2}\times II$ [3]
$4\times aVL=4\times I–2\times II$

$6\times aVF+8\times aVR+4\times aVL=(6\times II–3\times I)+(-4\times I–4\times II)+(4\times I–2\times II)$
$6\times aVF+8\times aVR+4\times aVL=-3\times I$
$6\times aVF=-8\times aVR–4\times aVL–3\times I$
$aVF=-(8\times aVR+4\times aVL+3\times I)/6\times I$

Electrical Axis (EA)= ± arctan $\{-2 [(8\times aVR+4\times aVL+3\times I)/6\times I]/sqr(3)\times I\}$

This formula is generated and modified by geometrical summation of I, aVL and aVR in a hexa-axial plane. To estimate the QRS axis of patients with inferior MI, geometric summation of any derivations II, III or aVF were avoided because ST segment elevation may cause false changes in the mean QRS axis. If there were any reciprocal changes in the I or aVL leads, those patients were excluded from the study. Creatinine kinase MB (CKMB) was selected as a marker of infarct size. Patients who had branch blocks or an abnormal QRS axis in their ECGs, who developed branch blocks during thrombolytic therapy or who had renal failure were excluded.

Statistical analysis

Data analysis was performed in SPSS 15 for Windows, a statistical software application (SPSS Inc., Chicago, Illinois). Means±SD and proportions were used to summarize the characteristics of the study sample. After employing normality tests for continuous variables, the Wilcoxon Rank Summation test was used to evaluate the QRS axis difference between pre- and post-thrombolytic therapy because of the non-normally distributed character of the values. Because CK-MB and the degree of QRS axis change values are not normally distributed, Spearman correlation analysis was performed to evaluate the relation between CK-MB and the degree of QRS axis change in all patients and subgroups. Statistical significance was accepted at p<0.05. Simple regression analysis could not be performed because the data distribution did not meet the regression analysis criteria.

Results

The total number of patients included in this study was 85, and the mean age of the patients was 60.6±10.7 years (Table 1). Among these patients, 35 (42.1%) were admitted with anterior myocardial infarction (MI), 15 (17.6%) were admitted with inferior MI, 16 (18.8%) were admitted with inferior+right MI, 8 (9.4%) were admitted with inferoposterolateral MI, 1 (1.2%) was admitted with lateral MI, 2 (2.4%) were admitted with posterolateral, and 1 (1.2%) was admitted with posterior MI. The mean left ventricular ejection fraction (LVEF) of the patients was 39.7%±10.1%. The change in the QRS axis before and after the thrombolytic therapy was significant (Z=-2, 33 p=0.02). In this particular study, we did not detect any significant correlation between infarct size and change in the QRS axis with respect to any MI localizations (p=0.80). However, regarding all of the MI localizations, CKMB and LVEF were found to be negatively correlated (r=-0.34 p=0.002) (Table 2). During subgroup analysis, there was good correlation between CKMB and change in the QRS axis (r=-0.52 p=0.049) only in the isolated inferior MI group. According to the scatter plot diagram, there may be a linear regression between the change in the QRS axis and infarct size in the isolated inferior MI patients (Figure 1). There was no significant correlation for other MI localizations (Table 3).

Discussion

The beneficial effects of thrombolytic therapy on patient survival and LVEF set the primary goal of the therapy as restoration of blood flow as soon as possible in STEAMI. ST resolution after thrombolytic therapy shows epicardial, microvascular and tissue reperfusion [4]. However, because reperfusion cannot be achieved in all patients and in some patients silent

Table 1. Clinical characteristics according to MI localization

Groups (n=85)	Age (Mean+SD)	Male Number (%)	CK-MB (Mean+SD)	LVEF (Mean+SD)	HT (%)	DM (%)
Anterior (n=35)	60.5±10.9	26 (39.4%)	132.5±126.0	32.6±8.9	12/35	12/35
Inferior (n=15)	59.8±9.6	13 (19.7%)	65.3±32.2	42.3±8.3	3/15	4/15
Inferior+Right (n=16)	62.3±9.4	11 (16.7%)	104.6±74.6	47.2±7.7	5/16	6/16
Inferoposterior (n=8)	60.8±11.2	6 (9.1%)	182.0±129.3	39.3±6.7	5/8	1/8
Inferoposterolateral (n=7)	57.6±14.6	7 (10.6%)	109.2±32.4	45.7±6.7	2/7	0/7
Lateral (n=1)	42.0±0	1 (1.5%)	179±0	50±0	0/1	0/1
Inferolateral (n=2)	70.0±2.8	1 (1.5%)	151.0±186.7	50.0±0	1/2	0/2
Posterior (n=1)	69.0±0	1 (1.5%)	169.0±0	40.0±0	1/1	0/1
Mean (n=85)	60.6±10.7	66 (77.6%)	119.6±102.9	39.7±10.0	29/85	23/85

Table 2. Correlation analysis between CKMB, the change in the QRS axis and the left ventricular ejection fraction

Variables	LV ejection fraction		The change in QRS axis	
	Rho	P	rho	P
Infarct size (CK-MB)	-0.342	0.002	-0.027	0.804

Spearman Correlation Analysis (rho: correlation coefficient)
CK-MB: Creatine kinase; LV: left ventricle; MI: Myocardial infarction

reocclusion occurs, evaluation of reperfusion and prognostic infarct sizing with noninvasive methods are becoming more and more important [5]. The tool for this evaluation is, undoubtedly, ECG. ECG is a perfect tool for understanding reperfusion, but there is not enough data about the role of ECG in infarct sizing. Until now, the studies on jeopardized myocardium and infarct sizing have primarily used ST deviations and QRS scores [6-8]. In fact, biochemical markers, primarily CK-MB and troponin (Tn) T, have long been used for infarct sizing [9-14]. In this context, for infarct sizing, markers like CK-MB and myoglobin are more appropriate than Tn T because of the higher rate of rising and falling serum levels. The correlation between the CK-MB release slope, infarct size and clinical outcomes has been known for many years [15]. Higher CK-MB values indicate more necrosis, wider infarcts and worse patient prognosis when compared to the slow and late completing nature of the release slope obtained by the usage of Tn T for infarct sizing.

In this particular study, the correlation between the infarct size and the change in the QRS axis of STEAMI patients is presented for the first time. The QRS axis in ECG represents the direction or angle of the ventricular depolarization. In fact, a normal QRS axis is neither sensitive nor specific, which means that a heart with a normal QRS axis may be normal or may have a serious pathology. Although there is no real consensus on the normal values of the QRS axis, in 2009, the ACC/AHA ECG guidelines updated the accepted values of a normal QRS axis to -30 and +90 degrees [16]. The QRS axis is calculated via the hexa-axial reference system. There are a number of different methods for calculating the QRS axis, but the geometric summation of projections of ventricular depolarization of the QRS axis on the hexa-axial plane is the most common. Computer software can also be used, but studies have shown that there is a high correlation between the QRS axes calculated by either inspection, computer or vector method [17]. Therefore, for practical purposes, we chose a formula derived from the original methodology prepared with the voltage values of I and aVF [2, 18]. Some believe that there may be a significant difference between patients, even in normal QRS axis ranges, and it would not be appropriate to use the QRS axis alone. Instead, as the QRS axis is made by all functioning myocardial cells, it can be foreseen that under life threatening conditions like ACS, which may endanger the contractile function or even the survival of cells, the QRS axis may change. Therefore, it is reasonable to use the change in the QRS axis as our measurement.

In STEAMIs, after cessation of the blood flow in the infarcted artery, a group of myocytes will not be functional, and a group of them will survive and continue to contract. Thrombolytic therapy has proven to be beneficial for survival and post-MI LVEF. In other words, it is effective to reduce the number of cells that lose function or the cells that have a high risk for losing function. Therefore, the change in the QRS axis immediately after the lytic therapy may be associated with the efficacy of thrombolytic therapy. It is possible that the more the cells are under risk, the more the cells could be salvaged. To put it another way, it may be thought that greater changes in the QRS axis are associated with smaller infarct sizes. Infarct size is determined primarily by the cells that lose function and become necrotic. In this study, we did not find a correlation between infarct size and the QRS axis change in any STEAMI patients. However, there was a good negative correlation between the QRS axis change and the infarct size in isolated inferior MIs. The significant negative

Table 3. Correlation analysis between CKMB, the change in the QRS axis and the left ventricular ejection fraction according to MI localization

Correlation analysis of variables according to MI localization		LV ejection fraction		The change in QRS axis	
		Rho	P	Rho	P
Infarct size (CKMB)	Anterior	-0.443	0.013	-0.249	0.150
	Inferior	-0.425	0.148	-0.517	0.0049
	Inferior+right	-0.480	0.060	-0.390	0.136
	Inferoposterior	-0.273	0.554	0.238	0.570
	Inferoposterolateral	-0.364	0.423	-0.250	0.589
	Lateral	-	-	-	-
	Inferoposterior	-	-	-	-
	Posterior	-	-	-	-
Spearman Correlation Analysis (rho:correlation coefficient) CK-MB: Creatine kinase; LV: left ventricle; MI: Myocardial infarction					
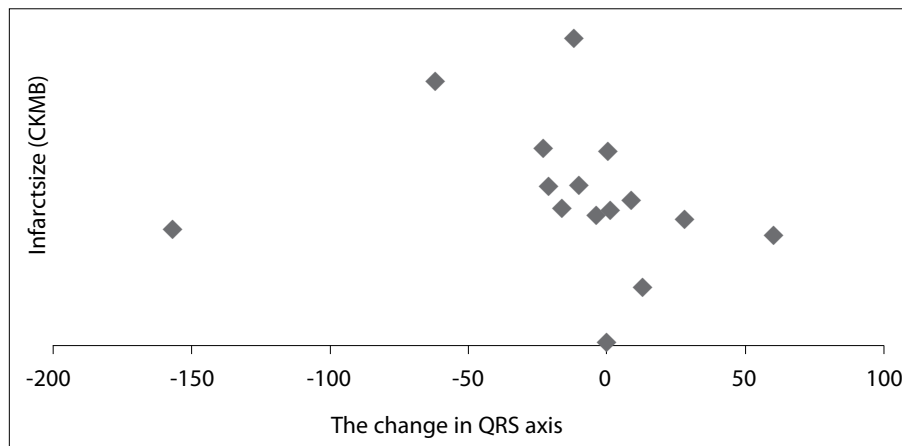
Figure 1. *Scatter plot diagram of infarct size and the change in the QRS axis in isolated inferior MI.*

correlation between LVEF and infarct size in anterior and right involved inferior MIs was an expected finding. To interpret these results, some points should be taken into consideration. The first is the concept of stunning. After an ischemic insult, contractile functions of ischemic myocardium are not restored immediately; they are restored long after the ischemia period [19]. If the ischemic insult is repeated, adapting to the changing environmental conditions, modulations occur in myocardial cells, and those cells cannot fulfill the contractile function even though they are alive. Under this condition, called "hibernation", if the flow is restored, then the time for myocardial cells to regain function may take months [20]. Due to this lengthy timeframe, in the very acute phase, reperfusion is achieved, and the life threatening condition is discarded. This means that the 90-minute period may not be adequate for the cells to regain function, which can lead to an underestimation of the actual number of cells that are

salvaged by thrombolytic therapy and a reduced statistical significance. Secondly, the negative correlation between the QRS axis change and infarct size in isolated inferior MIs may reveal that the change in the QRS axis may become more prominent in small infarcts where LVEF is mildly affected. In addition, a mildly affected LVEF may be associated with less stunning, which supports the idea that, in large infarcts where LVEF is more affected, less significant statistical results may be observed because there are more stunned cells.

In conclusion, as ACS are complex and dynamic processes, the use of a combination of noninvasive methods should be encouraged to choose the candidates for rescue percutaneous coronary intervention, which will restore early reperfusion. Although the change in the QRS axis is rarely emphasized, it is a practical and promising tool for evaluating both the efficiency of the thrombolytic therapy and prognostic infarct sizing.

Limitations

There are three main limitations to this study. The first limitation is the number of patients; to increase statistical power, more patients should have been included in the study. As with the previous limitation, MI subgroups may have been classified as anterior and inferior MI because more MI subgroups necessitate the inclusion of more patients in the study. The third limitation is that additional QRS axis change measurements should have been performed at the 24th hour and on the 7th day, in addition to the measurements made at the 90th minute. There may not have been sufficient time to see if the stunned myocardial cells regained contractile function.

Conflict of interest statement: The authors declare that they have no conflict of interest to the publication of this article.

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