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Value of Admission HbA1c Level in Non-diabetic Patients With Unstable Angina

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Abstract

Introduction: There have been incompatible evidences about the prognostic value of HbA1c on the adverse outcomes in acute coronary syndrome. Also, these data are so limited in nondiabetic patients with unstable angina.

Methods: In this cross-sectional study, HbA1c level of 231 nondiabetic patients admitted with unstable angina, was measured using high performance liquid affinity chromatography (HPLC) at admission. Then transthoracic echocardiography (TTE) was performed for evaluation of ejection fraction (EF) using Simpson method.

Results: Our data revealed that HbA1c was significantly higher in patients with $EF \leq 50\%$ in comparison with $EF > 50\%$ group (P value = 0.01).

Conclusions: HbA1c may be a helpful prognostic marker in nondiabetic patients admitted in emergency department with diagnosis of unstable angina.

INTRODUCTION

Higher level of Glycated hemoglobin A1c (HbA1c) as a marker of chronic glucose dysregulation and accelerated atherosclerosis has been shown to be a prognostic factor in cardiovascular disease and congestive heart failure. Moreover, HbA1c has been suggested as a marker of adverse outcomes in the setting of acute coronary syndromes [1-5]. Stress induced hyperglycemia even in non-diabetics, is related with enhanced activation of stress responsive kinases and initiation of apoptosis and cardiac cell necrosis, which sequentially results in systolic and diastolic dysfunction [6, 7].

Although an association between HbA1c level and adverse outcomes has been explained in diabetic patients with acute coronary syndromes, there are limited data in nondiabetic patients with unstable angina [8].

Therefore, the primary objective of this study was to determine the association of HbA1c levels at admission and ejection fraction (EF) in nondiabetic patients with unstable angina.

METHODS

This was a cross-sectional study conducted from April 2013 to March 2014 on patients admitted in coronary chest pain unit of Modarres hospital. Those nondiabetic patients diagnosed with unstable angina were selected. The exclusion criteria were documented diabetes mellitus, ST elevation

MI (STEMI), None-ST elevation MI (NSTEMI), HbA1c $\geq 6.5\%$ or Lab test indicative of diabetes mellitus, history of definite MI, history of congestive heart failure and history of chronic kidney disease.

For each patient with diagnosis of unstable angina [9], HbA1c level was determined using high performance liquid affinity chromatography (HPLC) at admission. Then transthoracic echocardiography (TTE) was performed to evaluate EF using the Simpson method. Finally, patients were divided into two groups including $EF > 50\%$ and $EF \leq 50\%$. The Institutional Review Board approved the study protocol and patients provided informed written consent. Statistical analyses were performed by SPSS statistical software (version 16). Independent sample T-test was used for quantitative studies. P value < 0.05 was considered statistically significant.

RESULTS

In total, 231 patients including 122 males and 109 females, with diagnosis of unstable angina entered the study. Mean age of patients was 57.1 ± 4.5 years. 130 patients had $EF \leq 50\%$ and 101 patients $EF > 50\%$. The mean level of HbA1c was $5.1\% \pm 0.43\%$ for all patients. Mean level of HbA1c was $5.9\% \pm 0.51\%$ for $EF \leq 50\%$ group and $4.2\% \pm 0.37\%$ for $EF > 50\%$ group. Data analysis revealed that HbA1c was significantly higher in patients with $EF \leq 50\%$ in comparison with $EF > 50\%$ group (P value = 0.01). Table 1 shows demographic and biochemical data of the two groups.

Table 1. Demographic and Biochemical Data of the Two Groups of Non-diabetic Patients With Unstable Angina Including EF $\leq$ 50% Group and EF $>$ 50% Group. HbA1c Was Significantly Higher in Patients With EF $\leq$ 50% in Comparison With EF $>$ 50% Group

	EF $\leq$ 50% group, N = 122	EF $>$ 50% group, N = 109
Age	59.2 $\pm$ 3.3	55 $\pm$ 5.8
Gender		
Male	63 (51.6%)	59 (54.1%)
Female	59 (48.4%)	50 (45.9%)
HbA1c level, %	5.9 $\pm$ 0.51	4.2 $\pm$ 0.37

Data in table are presented as Mean $\pm$ SD or No. (%)

DISCUSSION

The key finding of the current study was that HbA1c level at admission is considerably related with reduced ejection fraction in diagnosed nondiabetic patients with unstable angina. Previous studies showed that enhanced HbA1c is related with higher cardiovascular risk in patients with and without diabetes [8, 10].

Another study on 50 patients with acute coronary syndrome including unstable angina, NSTEMI and STEMI determined that HbA1c at admission is a strong predictor of LV systolic dysfunction as a main adverse event of acute coronary syndrome in patients not known to be diabetics [11].

Measurement of glycated forms of hemoglobin presents a trustworthy reflection of the level of general glucometabolic status in the prior 8–12 weeks. It can be considered as an indicator for diabetic control. There have been inconsistent evidences about the prognostic value of HbA1c on adverse outcomes in acute coronary syndrome [3–5].

In a study performed in Asian Indians with normal glucose tolerance, a strong correlation of HbA1c and cardiovascular risk factors was established. Normal glucose tolerance patients with three or more metabolic abnormalities had the highest HbA1c levels and an HbA1c cut off point of $\geq$ 6.5% was found to be effective in predicting both metabolic syndrome and coronary artery disease [12, 13].

Our study focused only on patients with unstable angina and those with STEMI and NSTEMI were excluded. The study results emphasized on relation between HbA1c level as a marker of accelerated atherosclerosis and reduced EF on TTE in nondiabetic unstable angina patients. Moreover, another investigation showed HbA1c level as a predictor of fatal and nonfatal cardiovascular events in nondiabetic peritoneal dialysis patients [14].

On the other hand, one study suggested that HbA1c levels before admission are not related with short-term cardiovascular outcome in diabetic patients admitted with acute coronary syndrome [15]. This study can serve as a trigger for future investigations evaluating association of HbA1c and adverse outcomes in nondiabetic patients with unstable angina and developing new prognostic algorithm and cut off points for HbA1c in diabetic and nondiabetic patients with unstable angina.

Our study showed that HbA1c in unstable angina was considerably higher in nondiabetic patients with EF $\leq$ 50% in comparison with EF $>$ 50% group. This finding emphasizes this point that HbA1c may be a helpful prognostic marker in nondiabetic patients admitted in emergency departments

with unstable angina. Nevertheless, detailed data about the prognostic role of HbA1c is to somehow controversial, and this study with such a relatively small size cannot clarify all the remaining doubts.

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CONFLICT OF INTEREST

Authors declare that they have no conflict of interest.

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Reviewing EKGs in Thalassemia Patients to Evaluate Their Cardiac Function

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Abstract

Introduction: There are more than 18000 thalassemia patients in Iran. In a current study, a high rate of mortality in these patients due to heart failure, is shown. Main factors for evaluating this disorder in thalassemia patients were their electrocardiograms (EKGs) and Serum Ferritin Levels (SFLs).

Methods: We studied the cardiac function in 91 patients (73 major and 18 intermediate thalassemia patients) treated in Zafar Thalassemia Center, of whom 35 (38.45%) were male and 56 (61.55%) were female. The Factors in this study contains: EKGs, mean annual serum ferritin (at least, three SFL had been recorded in each patient treatment file in 2009), mean annual hemoglobin (Hb) levels and mean annual hematocrit (Hct) levels (average, 12 recorded hematocrit levels during 2009).

Results: Our findings have shown that Q-T interval did not correlate with ferritin ($r = 0.05$, $P > 0.05$). In both patients with LVH and without LVH, there was no significant difference in SFL ($P > 0.05$). Although, the mean rate among the thalassemia patients was 85.34 ± 12.91 , it did not correlate significantly with QRS duration and P-R Interval ($r = -0.08$, $P > 0.05$). In addition, ferritin did not correlate significantly with QRS duration and P-R Interval ($r = 0.1$, $r = 0.05$ and $P > 0.05$, $P > 0.05$). Furthermore, there was no difference in SFL in patients with normal cardiac axis and those with cardiac axis deviation.

Conclusion: There is no correlation between SFL and variations in EKG. Although EKG is an available method for checking cardiac function in thalassemic patients, especially in developing countries, physicians cannot rely on it for diagnosis or prognosis of cardiac failure in thalassemia patients. Therefore, other methods such as MRIT2* and Echocardiography are suggested to be used periodically in order to check the cardiac function in thalassemia patients.

INTRODUCTION

Thalassemia is a prevalent inherited blood disorder. According to Iranian Thalassemia Society, more than 18000 patients had been registered in Iran by 2006. During two last decades, mean age of the patients has increased due to the better care. However, like other parts of the world, cardiac failure is the most crucial problem among young and teenagers with thalassemia [1, 2]. Hadaegh F. reported that 21.8% (22.3% women and 18.8% men) of thalassemia patients in Tehran (capital of Iran) are affected by different levels of cardiac failure [3]. Therefore, it is a prioritized duty of care groups to check cardiac function in all patients in order to prevent cardiac failure. The main cardiac abnormalities reported in patients with thalassemia are iron overload and left ventricular systolic and diastolic dysfunction, pulmonary hypertension, valvulopathies, arrhythmias, and pericarditis [2]. Its prevalence varies according to the type of

thalassemia. Even though thalassemia intermedia patients require less transfusions than thalassemia major patients, they are still at risk of cardiac complications. With the introduction of new technologies, such as cardiac magnetic resonance T2*, the early detection of cardiac iron overload and associated cardiac dysfunction can be presently possible. In addition, an EKG and a chest radiograph (X-Ray) should also be obtained. Two-dimensional echocardiography helps differentiate systolic from diastolic dysfunction. However, MRIT2* is not accessible in all centers where thalassemia is of high prevalence and Echocardiography is an expensive method which can be conducted merely with an all - and - out expert [2, 4-6]. Hence, it is not possible to follow thalassemia patients relying on both methods in all parts of developing countries like Iran. As a result, EKG is used to determine the reliability of prognostication and prevention of cardiac dysfunction in thalassemia patients in Iran.

METHODS

In this study, the heart function in 91 patients (73 major thalassemia and 18 intermedia) treated in Zafar Thalassemia Center in Tehran, was studied. The patients were between 15 and 45 years old; 35 (38.45%) of these patients were male and 56 (61.55%) were female. EKG of patients was considered as well as the mean level of annual serum ferritin (at least three SFLs had been recorded in each patient treatment file in 2009), mean of annual hemoglobin and hematocrit levels (on average, 12 records of the results of hematocrit tests during 2009). Serum ferritin and hematocrit levels have been found in the patient's clinical files which are maintained in the clinic. A cardiologist has tested patients' heart function using EKG.

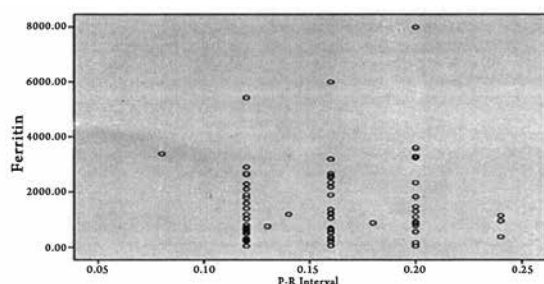


Figure 1: PCorrelation Between Ferritin and P-R Interval

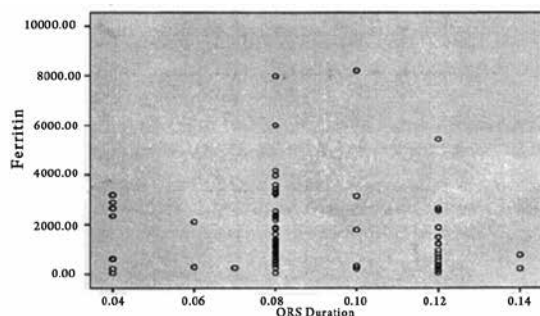


Figure 1: Correlation Between Ferritin and QRS Duration

RESULTS

Our findings show that Q-T interval did not correlate with ferritin ($r = 0.5$, $P > 0.05$). Both in patients with LVH and without LVH, there was no significant difference in serum ferritin level ($P > 0.05$). Although the mean rate among the

thalassemic patients was 85.34 ± 12.91 , it did not correlate significantly with serum ferritin level ($r = -0.08$, $P > 0.05$). In addition, ferritin did not correlate significantly with QRS Duration and P-R Interval ($r = 0.1$, $r = 0.05$ and $P > 0.05$, $P > 0.05$) (Figs 1 and 2). Furthermore, there was no difference between serum ferritin level in patients having normal axis and patient with axis deviation.

DISCUSSION

There is no correlation with serum ferritin level and contents of Electrocardiogram (EKG). Albeit EKG is an available and inexpensive method, especially in developing regions, to check patient's heart function physicians cannot find a logical correlation between EKG and ferritin to show whether the increase of level of ferritin could affect patient EKG. Furthermore, we are not able to correlate EKG to levels of hematocrit. Our findings prove that new methods like MRIT2* and Electrocardiography play a vital role in preventing and discriminating heart problems in thalassemia patients. At least, in case of patients with thalassemia, EKG cannot be reliable to diagnose the dysfunction in heart. Health care decision makers should be responsible to furnish new methods and make them available and free of charge for all thalassemics.

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CONFLICT OF INTEREST

Authors have no conflict of interest to declare.

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Drug-related Atrioventricular Block: Is It a Benign Condition?

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Abstract

Introduction: Prognosis of the patients with beta blocker or calcium channel blocker induced AV block is not well known to date.

Methods: All patients with symptomatic second-degree or third-degree atrioventricular block (AV) referred to our institution during one year were recruited prospectively and classified in two groups based on drug consumption (beta blocker/calcium channel blocker versus none). They were followed for six months and then collected data was analyzed.

Results: The study included 49 patients, 28 patients (age 60.1 ± 20 , 19 male) did not use any beta blocker or calcium channel blocker (No- DU group) and other 21 patients (age 73.5 ± 10.4 , 7 male) received beta blocker, calcium channel blocker or both at the time of AV block (DU group). No-DU group was significantly younger than DU group. The most common atrial rhythm in both groups was sinus. There was no significant difference in QRS wideness or ventricular rate. AV block regressed in 43% of the DU group after discontinuation of drug for five half-life, but, Mobitz type 2 or complete AV block occurred again during six months in 50% of them without consumption of the culprit drug.

Conclusions: More than two third of the patients who developed AV block on beta blocker and/or calcium channel blocker needed permanent pacemaker in six months of follow-up, so we concluded that the development of AV block was not as benign as it seems in these patients.

INTRODUCTION

According to ACC/AHA/HRS 2008 Guideline, permanent pacemaker implantation is indicated for third degree and advanced second-degree atrioventricular block (AV) at any anatomic level associated with symptomatic bradycardia or ventricular arrhythmias presumed to be due to AV block and also is indicated in symptom-free patients in sinus rhythm, with documented periods of asystole greater than or equal to 3.0 seconds, any escape rate less than 40 beat per minute (bpm), or with an escape rhythm that is below the AV node (class I) [1]. However, pacemaker

implantation is generally considered unnecessary if it caused by reversible etiologies such as electrolyte abnormalities [1].

It is documented that drugs such as calcium channel blockers and beta blockers, prolong AV nodal conduction and refractoriness in humans may cause AV block [2, 3]. But since the significant bradycardia is rare with therapeutic doses in normal heart [4], one of the theories can be unmasking of underlying AV node or his-purkinje diseases caused by these medications. So prognosis and natural history of the patients with drug related AV block need to be investigated.

METHODS

This prospective study was designed for assessment of mid term prognosis in patients with drug induced AV block. The study protocol was reviewed, and approved by the Review Board of Shaheed Rajaei Cardiovascular Medical and Research Center, and Iran University of Medical Sciences High Research Council. All patients with symptomatic second-degree or third-degree AV block referring to our institution between April 2010 and April 2011 were prospectively collected. Patients with concomitant myocardial infarction, electrolyte abnormalities, digitalis toxicity, vasovagal syncope, and those taking class I or III antiarrhythmics were excluded.

The type of AV block was determined by the surface electrocardiogram (ECG). Patients were classified into two groups to define a relationship between beta-blocker or calcium channel blocker therapy and AV block: (1) patients who developed AV block in the absence of drugs that affect AV conduction (No-DU group), (2) patients in whom AV block occurred on beta-blockers or calcium channel blockers therapy (DU-group).

Patients in group 2 were subclassified as follows: (1) patients in whom AV block resolved after the discontinuation of drug after 5 half-life (Soon-AVB-R) (2) patients in whom AV block was not resolved and persisted in spite of discontinuation of drug (Soon-AVB-NR).

All patients were monitored continuously during their hospitalization course until they had improved AV conduction within 4-6 days or received an implanted pacemaker (if AV block did not resolve). Patients with apparently normal AV conduction after discontinuation of drug, were discharged and recommended to visit arrhythmia clinic, for evaluation of AV conduction with surface ECG. Patients who had pacemaker placement have been followed in pace maker clinic on a regular basis.

Permanent pacemaker was implanted for all of the patients with recurrence of AV block during follow-up. Collection and analysis of data were authorized by the ethics committee of the hospital. Data were expressed as mean $\pm$ SD. Student's T

test, Chi square test and Fisher's exact probability test were used to analyze the data. Results were considered significant at an error probability level of $P < 0.05$.

RESULTS

Twenty eight of 49 patients who met the criteria and entered the study, didn't use any beta blocker or calcium channel blocker (No-DU group). Mean age of this group was 60.1 ± 20 years, 32.1% were female and 67.9% were male (Table 1). Other 21 patients with mean age of 73.5 ± 10.4 years (66.7% female; 33.3% male) were receiving beta blocker (81%), calcium channel blocker (9.5%) or both (9.5%) at the time of AV block (DU group). This group was significantly older than No-DU group ($P = 0.04$) and dominantly was female ($P = 0.02$) (Table 1).

Although Sinus rhythm was the most common atrial rhythm in both No-DU and DU patients (92.9% and 95.2%, respectively), the degree of AV block seemed to be some what different in both groups. In No-DU group, no patient had Mobitz type I (Wenckebach) AV block, 7.1% had Mobitz type 2, and 92.9% had 3rd degree AV block compared to 4.8, 33.3 and 61.9 in DU group, respectively. QRS duration and also ventricular rate were not significantly different between both groups (Table 1).

Follow-up after Five Half Life of Drug

AV block regressed in 43% (9 of 21) of the DU patients with discontinuation of drug after 5 half life (Soon-AVB-R). Mean age of this subgroup was 69.7 ± 10 years (55.6% female; 44.4% male). The remained 57% patients whose AV blocks persist in spite of discontinuation of drug (Soon-AVB-NR) candidate for permanent pacemaker implantation. The mean age of this subgroup was 76.4 ± 10 years (75% female; 25% male) which was not significantly different from previous subgroup. Analysis of these two subgroups didn't show any significant differences in degree of AV block, QRS duration, and ventricular rate (Table 2).

Table 1: Comparison Between the Patients Who Were on Medication and Who Weren't on Medication at the Time of Atrioventricular Block

	AV Block During Drug Therapy, (n = 21)	AV Block Without Drugs, (n = 28)	P Value
Age (y)	73.5 ± 10.4	60.1 ± 20	0.04
Male Gender	7 (33.3)	19 (67.9)	0.02
Sinus rhythm	20 (95.2)	26 (92.9)	1.0
Level of block			0.01
Wenckebach	1 (4.8)	0 (0)	
Mobitz type 2	7 (33.3)	2 (7.1)	
Complete AV block	13 (61.9)	26 (92.9)	
QRS duration > 120 msec	12 (57.1)	10 (35.7)	0.16
Ventricular rate < 40 bpm	13 (65)	22 (78.6)	0.34

Data are presented as mean $\pm$ SD and No. (%).

Table 2: Characteristic of the Patients with AV Block on Medication after Discontinuation of Drug for 5 Half Life

	AV Block Regressed after Discontinuation of Drug, (n = 9)	AV Block Remained after Discontinuation of Drug, (n = 12)	P Value
Age (y)	69.67 ± 10	76.42 ± 10	0.14
Male Gender	4 (44.4)	3 (25)	0.40
Level of block			0.79
Wenckebach	0 (0)	1 (8.3)	
Mobitz type 2	4 (44.4)	3 (25)	
Complete AV block	5 (55.6)	8 (66.7)	
QRS duration > 120 msec	4 (44.4)	8 (66.7)	0.40
Ventricular rate < 40 bpm	4 (44.4)	4 (33.3)	0.67

Data are presented as mean ± SD and No. (%).

Table 3: ECG Characteristics of the Patients Who Were on Medication at the Time of Atrioventricular Block after a 6-month Follow-up

	Drug User-Drug Related AV Block * (n = 4)	Drug User-Non-Drug Related AV Block ** (n = 16)	P Value
QRS duration > 120 msec	2 (50)	10 (62.5)	0.64
Ventricular rate < 40 bpm	2 (50)	4 (26.7)	0.32

*Patients with AV block during drug consumption whose AV block regressed with discontinuation of medication and didn't relapse in six months of follow-up

**patients with AV block during drug consumption whose AV block didn't regress or relapse in six months of follow-up despite the discontinuation of drug.

Data are presented as No. (%).

A Six-month Follow-up

In a six-month follow-up, one of the cases missed, in Soon-AVB-R group, 50% developed Mobitz type 2 or complete AV block that needed permanent pacemaker implantation. On the other side, 8.3% (one case) of the Soon-AVB-NRs in the absence of drug therapy (with betablocker and/or calcium channel blocker) and 3.6% (one case) of No-DUs showed disappearance of AV block and restoration of sinus rhythm in follow up. (Table 3)

If we pool all the patients with AV block during drug consumption who needed permanent pacemaker implantation till six months of follow-up as drug users, not drug related AV block group (DU-NDR), and who didn't need permanent pacemaker implantation as drug users, drug related group (DU-DR), and compare them, again there will be no significant differences according to QRS duration or ventricular rate.

DISCUSSION

In our study, most of the patients with AV block in No-DU was male, but most of the patients in DU was female. This can be concluded that increasing female consuming beta blockers or calcium channel blocker or these kinds of drugs results in increasing AV blocks. However, the main finding of our study was that nearly one half of the patients admitted in the hospital due to AV block (except those caused by digoxin toxicity, myocardial infarction, electrolyte imbalance and vasovagal response) was on beta blocker and/or calcium channel blocker. Drugs were discontinued in all of these patients, but in 43% of them, AV block didn't regress, and in 50% of them AV block resolved, relapse was seen in less than six months. So it seems that about 70% of patients who was on beta blocker and/or calcium channel blocker at the time of AV block, permanent pacemaker was needed in six months

of follow-up.

There are few other studies with the same result [5, 6]. A recent study reported that only 15% of AV blocks in patients treated with beta-blockers and/or calcium channel blocker, is truly caused by these drugs and in others, drug was only 'innocent bystanders' [5]. The authors concluded that as the effect of these drugs is slowing down the conduction of SA node and AV node and this would decrease conduction block in infra-nodal pathways, so in these patients, infra-nodal conduction disease expected to be more severe. In our study, we couldn't find any relationship between QRS duration or ventricular rate (as signs of supranodal or infra-nodal disease) [7-9] and AV block in drug users; in other word, ECG finding of supra or infra nodal block is not a predictor of permanent pacemaker requirement in patients who consumes drug and are on AV block.

Another study that assessed the prognosis of bradycardia related to drugs, evaluated 38 patients with symptomatic bradycardia during beta blocker or calcium channel blocker consumption, and showed that in 10 of 38 cases, bradycardia were not caused by drugs, but were revealed by drugs [10]. Interestingly, in this study, if we omit cases with AV block from that 31 patients who came with symptomatic sinus bradycardia, 27(87%) patients with bradycardia will be resolved by discontinuation of drugs [10].

Comparing these studies, one can argue when a patient referred due to symptomatic bradycardia on beta blocker or calcium channel blockers, if the bradycardia is caused by the second or third degree AV block, it is less probably that the drug induces and if it is caused by sinus bradycardia it is most probably that the drug induces and will regress by discontinuation of drug.

Study limitation: 1) We studied 49 cases prospectively and this limited numbers of patients prevent subgroup analysis. So some important features such as the effect of drug dose,

which may be a predictor of reversibility, were not evaluated in this study. 2) Although most of the clues in this and previous studies are compatible with infra-nodal disease of cases who developed AV block on beta blocker or calcium channel blocker, the studies on electrophysiology is needed.

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CONFLICT OF INTEREST

There is no conflict of interest for the present study.

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Validity of Initial Clinical Diagnosis of Unstable Angina Based on the Invasive and Noninvasive Studies

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Abstract

Introduction: A few studies have focused on diagnostic performance of residents for controlling the patients with acute chest pain referring to chest pain units. We aimed to assess diagnostic performance of cardiology residents for controlling the patients with acute chest pain, considering invasive and non-invasive diagnostic modalities as the key standards to confirm or refuse diagnosis of unstable angina.

Methods: One hundred and twenty nine patients with chest pain or angina referring to chest pain unit of Modarres hospital between 2013 and 2014 were assessed. The patients were categorized into two subgroups. The first group included 23 patients who were discharged by the resident in initial evaluation because of ruling-out diagnosis of unstable angina, but were assessed non-invasively by exercise test or SPECT as key standards. The second group included 106 patients who were hospitalized and admitted to CCU by residents' order and also were assessed invasively by coronary angiography or non-invasively by exercise test or SPECT.

Results: Overall, of 129 patients, 23 were initially diagnosed not to be necessarily hospitalized and thus were discharged by resident's order. Of those, assessing by SPECT indicated positive result in five of 19 patients and by exercise test indicated positive result in 1 of 4 patients yielding a sensitivity of 83.3%, a specificity of 17.6%, a PPV of 26.3%, a NPV of 75.0%, and an accuracy of 34.8% for assessing disease by resident. The remaining 106 patients were admitted to CCU ward in accordance with the resident's order. Among those patients, 85 underwent coronary angiography with positive results in 53 patients. Also, SPECT was positive in 10 of 19 patients and exercise test was positive in one of two patients yielding a sensitivity of 95.3%, a specificity of 0.0%, a PPV of 59.2%, a NPV of 0.0%, and an accuracy of 57.5%.

Conclusions: For patients with suspicion to unstable angina, the decision of residents in chest pain units for discharging or admitting patients suspected to unstable angina is accompanied with high sensitivity but unacceptable specificity and thus using supplement diagnostic tools such as exercise test or SPECT can be very helpful for diagnosing unstable angina.

INTRODUCTION

Approximately one percent of primary care office visits are for chest pain, and 1.5 percent of these patients will have unstable angina or acute myocardial infarction [1]. The initial goal in patients with chest pain was to determine if the patient needs to be referred for further testing to rule in or out acute coronary syndrome (ACS) and myocardial infarction (MI) [2]. The physician should consider patient characteristics and risk factors to help determine initial risk. Algorithmic approaches to the diagnosis and workup of the patient with chest pain in the office setting have not been specifically stud-

ied [3]. Differentiating ischemic from non-ischemic causes is often difficult, and patients with chest pain with an ischemic etiology often appear well [4]. As such, the initial diagnostic approach should always consider a cardiac etiology for the chest pain, unless other causes are apparent.

One recent meta-analysis concluded that the history and physical examination were mostly not helpful in diagnosing ACS or acute MI in patients with chest pain, especially in a low-prevalence setting [5]. Although individual characteristics may not rule in or out a diagnosis, a combination of signs and symptoms may increase diagnostic accuracy [6]. In this regard, the critical role of physicians admitting the patients

and assessing them initially is very important that misdiagnosis by the residents in emergency wards may lead to serious consequences and disease mismanagement [7, 8]. However, a few studies have focused on diagnostic performance of residents for controlling the patients with acute chest pain referring to chest pain units. Hence, we aimed to assess diagnostic performance of cardiology residents for controlling patients with acute chest pain, considering invasive and non-invasive diagnostic modalities as key standards to confirm or refuse diagnosis of unstable angina.

METHODS

To evaluate initial diagnostic performance of unstable angina by cardiovascular residents in chest pain unit, 129 patients with chest pain or angina referring to chest pain unit of Modarres hospital between 2013 and 2014 were assessed. Those patients with diagnosis of STEMI or NSTEMI due to evident changes in specific ECG patterns or serial cardiac enzymatic changes were excluded. The patients were categorized into two subgroups. The first group included 100 patients who were discharged by the resident in initial evaluation because of ruling-out diagnosis of unstable angina, but assessed non-invasively by exercise test or SPECT as key standards. The second group included 29 patients who were hospitalized and admitted to CCU by residents' order and also assessed invasively by coronary angiography or non-invasively by exercise test or SPECT. The study endpoint was to assess diagnostic performance of residents in both patient groups, considering diagnostic tools as key standards. The study protocol was reviewed, and approved by the Review Board of Cardiovascular Research Center, Shahid Beheshti University of Medical Sciences. For statistical analysis, sensitivity, specificity, and positive and negative predictive values of residents for the diagnosis of unstable angina were calculated using cross-tab analysis. In this regard, the SPSS software (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.) was used.

RESULTS

In total, 129 patients were initially assessed in chest pain unit with the mean age of 59.35 ± 10.68 years (ranged 35 to 88 years old). Among those assessed, 55.8% were male and 44.2% were female. Regarding general cardiovascular risk factors, 62.8% were hypertensive, 24.8% had family history of CAD, 5.4% were obese, 44.2% had hyperlipidemia, 28.7% were diabetics and 30.2% were passive and active smokers. With respect to the history of cardiac interventions, 12.4% underwent previously coronary artery bypass surgery and 14.7% underwent previous PCI. Two patients had also history of heart failure. Overall, of 129 patients, 23 were initially diagnosed not to be necessarily hospitalized and thus were discharged by resident's order. Of those, assessing by SPECT indicated positive result in five of 19 patients and by exercise test indicated positive result in one of four patients yielding a sensitivity of 83.3%, a specificity of 17.6%, a PPV of 26.3%, a NPV of 75.0%, and an accuracy of 34.8%. The remaining 106 patients were admitted to CCU ward in accordance with the resident's order. Among those patients, 85 underwent coronary angiography with positive results. Also, SPECT was positive in 10 of 19 patients and exercise test was positive in one of two patients yielding a sen-

sitivity of 95.3%, a specificity of 0.0%, a PPV of 59.2%, a NPV of 0.0%, and an accuracy of 57.5%.

DISCUSSION

Timely and accurately diagnosis of unstable angina can potentially affect both early and late consequences of the disease. In this regard, physicians in emergency wards and chest pain units have critical role. In fact, before basing invasive or non-invasive diagnostic modalities, diagnosing and controlling patients by the residents on initial manifestations of symptoms have major effects on patient's clinical outcome. However, the diagnostic performance of residents in chest pain units, especially in patients who suspected to unstable angina, remained uncertain. In the present study, we focused on two subgroups of the patients including the patients discharged without suspicion to unstable angina and those who were admitted to CCU wards after initial evaluation. In total, an acceptable sensitivity, but very low specificity for initial diagnosis by the residents indicating improper performance in diagnosing the patients suspected to unstable angina, was found. In this context, our findings are consistent with those of previous studies. In a study by Almas et al. in 2010, the sensitivity for resident's diagnosis was estimated to be 100%, but a specificity of 54.2% was obtained for diagnosing acute coronary syndrome [9]. In this regard, it seems that a combination of the changes in ECG patterns, clinical evidences or changes in cardiac biomarkers yielding low accuracy differentiates healthy subjects from patients with unstable angina. As shown previously by Goodacre et al. [10] in 2005, the sensitivity and specificity of ECG for initially assessing unstable angina was only 33% and 23%, respectively.

According to our observation, the resident-based diagnosis achieved high sensitivity but low specificity to diagnose unstable angina. In fact, the residents could successfully diagnose the patients with exact diagnosis of unstable angina based on the positive tests, but, could not correctly differentiate healthy individuals with the negative tests. This inability can be due to inappropriate educational or practical programs, prolonged clinical shifts leading to high workload or low diagnostic performance of ECG changes in final diagnosing unstable angina. Thus, it can be proposed that using diagnostic tools, especially non-invasive tools for initially assessing patients suspected to unstable angina, is necessary in initial evaluation in chest pain units.

In conclusion, for patients with suspicion to unstable angina, the decision of residents in chest pain units for discharging or admitting patients suspected to unstable angina is accompanied by high sensitivity but unacceptable specificity and thus using supplement diagnostic tools such as exercise test or SPECT that can be very helpful for diagnosing unstable angina.

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CONFLICT OF INTEREST

Authors declare that they have no conflict of interest.

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Pulmonary Hypertension and Its Determinants in β -thalassemia Major and Intermedia Considering Left Ventricular Functional State

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Abstract

Introduction: Pulmonary hypertension (PHT) is a common complication in β -thalassemia. We aimed to determine the prevalence of PHT and its main indicators in patients with β thalassemia Major (TM) and β -thalassemia Intermedia (TI), considering left ventricular function.

Methods: Pulmonary hypertension (PHT) is a common complication in β -thalassemia. We aimed to determine the prevalence of PHT and its main indicators in patients with β thalassemia Major (TM) and β -thalassemia Intermedia (TI), considering left ventricular function.

Results: The overall prevalence of PHT in TM and TI group was estimated to be 35.2% and 29.3%, respectively; while reduced LVEF was evident in 22.7% and 10.1% of patients with TM and TI, respectively. No significant correlation was observed between mean PAP and LVEF in the patients with TI (Pearson coefficient = -0.096, P value = 0.345); while, an adverse association was revealed between mean PAP and LVEF in patients with TM (Pearson coefficient = -0.227, P value = 0.033). Upon univariate analysis, the only significant association was observed between LVEF and pulmonary hypertension among TM patients (P value = 0.001). Our results did not indicate that male gender and aging may affect the development of PHT.

Conclusions: According to our findings, a considerable proportion of patients with TM and TI may have PHT. We detected an adverse association between mean PAP and LVEF in patients with TM. Left ventricular function was reduced in patients with PHT among TM group.

INTRODUCTION

β -thalassemia is an inherited hemoglobin disorder which results in chronic hemolytic anemia. Depending on the clinical severity, two forms are distinguished, including β -thalassemia Major (TM) and β -thalassemia Intermedia (TI) [1]. While TM is characterized by severe anemia

starting from the first year of life and therefore requiring lifelong transfusion therapy for survival, the TI form has a later clinical onset with a milder anemia that permits survival without regular transfusions and a longer life expectancy [2-4]. The diverse clinical severity of TM and TI and the different therapeutic approaches lead to a wide variety of clinical phenotypes. Findings regarding cardiac

status in these types of β -thalassemia are not completely comparable in both forms [5, 6].

With regard to the cardiac complications of β -thalassemia, Pulmonary Hypertension (PHT) is a common complication, especially among patients with TI [7]. It is considered to be the primary cause of congestive heart failure in such patients [8]. However, the majority of patients with increased Pulmonary Arterial Pressure (PAP) are asymptomatic [9]. Even, most of the patients may have normal left ventricular function in spite of severe PHT. Therefore, this condition is often unrecognized until patients develop heart failure and/or hypoxemia [10-12].

There is paucity of data regarding the prevalence of PHT in both forms of β -thalassemia and also its main determinants. In this line, the present study aimed to determine the prevalence of PHT and identify its main indicators in patients with TM or TI, considering normal or reduced left ventricular function.

METHODS

In this cross-sectional study performed at Firoozgar Hospital and Zafar Thalassemia Center in Tehran, patients with TM or TI referred between January 2009 and May 2009 were selected by simple sequential non-random sampling and enrolled into the study. In general, 187 consecutive patients without previous history of any cardiovascular or pulmonary disease (i.e. chronic obstructive pulmonary disease or ischemic heart disease) were selected. The Institutional Review Board (IRB) of Iran University of Medical Sciences (IUMS) approved the study protocol and patients provided informed written consent. Baseline characteristics including demographics and disease duration were collected by interviewing or reviewing medical records. Then, all participants were referred to Firoozgar Hospital for echocardiography evaluation in order to determine Pulmonary Artery Pressure (PAP) and Left Ventricular Ejection Fraction (LVEF). In this regard, PHT was defined as mean PAP higher than 25 mmHg. Also LVEF less than 50% was considered as left ventricular dysfunction in β -thalassemia patients. Echocardiography was performed by the same phy-

sician for all of the patients. Results were reported as mean $\pm$ standard deviation (SD) for the quantitative variables and percentages for the categorical variables. The groups were compared using the Student's t-test for the continuous variables and the chi-square test (or Fisher's exact test if required) for the categorical variables. Odds ratio (OR) and 95% confidence intervals (CI) were calculated. Association between the quantitative variables was examined by the Pearson's correlation coefficient test. P values of 0.05 or less were considered statistically significant. All the statistical analyses were performed using SPSS version 13.0 (SPSS Inc. Released 2005. SPSS for Windows, Version 13.0. Chicago, SPSS Inc.).

RESULTS

In the present study, 187 patients -88 in TM group and 99 in TI group - were studied among whom 46.6% and 50.5% were male, respectively. Patients in the TM group were significantly younger compared to the TI group (P value < 0.001). Table 1 shows some of the demographic and clinical characteristics of the patients in both groups. The overall prevalence of PHT in TM and TI groups was 35.2% and 29.3%, respectively. Left ventricular dysfunction based on reduced LVEF was also evident in 22.7% and 10.1% of patients with TM and TI, respectively. In patients with TI, prevalence of PHT in the subgroup with normal LVEF was 21.3% and in those with reduced ventricular function was 20.0% (P value = 0.921). In fact, the linear correlation between PAP and LVEF was not significant (Pearson coefficient = -0.096, P value = 0.345). In TM group, the overall prevalence of PHT in normal left ventricular function group was 13.2% and in left ventricular dysfunction group was 25% (P value = 0.294); while, an inverse correlation was revealed between mean PAP and LVEF in this group of patients (Pearson coefficient = -0.227, P value = 0.033). Table 2 shows the univariate association of PHT with gender, age and LVEF among both TM and TI patients. In this regard, the only significant association was observed between LVEF and PHT among TM patients (P value = 0.001).

Table 1: Comparison of demographics as well as pulmonary artery pressure (PAP) and left ventricular ejection fraction among thalassemia major (TM) and thalassemia intermedia (TI) groups (TM: thalassemia major, TI: thalassemia intermedia, PAP: pulmonary artery pressure, LVEF: left ventricular ejection fraction).

Variable	TM	TI	P value
Sex			0.66
Male	41 (46.6)	50 (50.5)	
Female	47 (53.4)	49 (49.5)	
Age (y)	24.93 $\pm$ 5.56	33.28 $\pm$ 11.23	0.001
PAP (mmHg)	31.4 $\pm$ 11.08	34.26 $\pm$ 18.08	0.20
LVEF (%)	55.81 $\pm$ 13.21	58.85 $\pm$ 9.53	0.07

Data are presented as mean SD and No. (%).

TM: Beta-thalassemia major; TI: Thalassemia intermedia; PAP: Pulmonary Artery Pressure; LVEF: Left ventricular ejection fraction

Table 2: The Univariate associations between Pulmonary Hypertension (defined as PAP>25 mmHg) and Gender, Age and LVEF among thalassemia major (TM) and thalassemia intermedia (TI) patients (TM: thalassemia major, TI: thalassemia intermedia, LVEF: left ventricular ejection fraction, PAP: pulmonary artery pressure).

	TM			TI		
	PAP > 25 mmHg	PAP < 25 mmHg	P value	PAP > 25 mmHg	PAP < 25 mmHg	P value
Sex			0.84			0.55
Male	14	27		16	34	
Female	17	30		13	36	
Age (y)	24.1 ± 5.2	25.4 ± 7.2	0.42	30.5 ± 11.4	34.5 ± 10.9	0.13
LVEF (%)	53.0 ± 14.9	60.8 ± 7.0	0.001	54.9 ± 9.8	58.6 ± 9.4	0.67

Data are presented as mean SD and No. (%).

TM: Beta-thalassemia major; TI: Thalassaemia intermedia; LVEF: Left ventricular ejection fraction

DISCUSSION

In this study, the prevalence of PHT in the TM group was 35.2% and in the TI group was 29.3%, which was not significantly different. The obtained prevalence of PHT in our survey was in the range published in most of the previous reports. In a study by Vlahos et al. [13], PHT was observed in 18.5% of TM patients and in another study by Aessopos et al. [14], PHT prevalence was estimated to be 23% in patients with TI. Generally speaking, it could be concluded that PHT is a partially common finding in both forms of thalassemia, even more frequent in TI patients.

Another important finding of our study was that PAP and LVEF were not associated in our patients. Also, the prevalence of PHT is independent to left ventricular function state in both types of β -thalassemia. Thus, prevalence of PHT in patients with normal left ventricular function and those with impaired ventricular function is not different that is consistent with most of the previous studies. Vlahos et al. [13] similarly showed that despite normal systolic and diastolic ventricular function, 18.5% of TM patients had PHT. In another study by Aessopos et al. [14], despite the high prevalence of PHT 60%, right heart failure was detected in only 5% of patients and left ventricular dysfunction was reported in none. Aessopos also indicated no cases of left ventricular dysfunction in thalassemia patients with PHT [4]. Also, upon univariate analysis of our data, the only significant association was observed between LVEF and pulmonary hypertension among TM patients. Our results did not indicate that male gender and aging may affect the development of PHT.

In summary, our obtained prevalence of PHT is reported in most of the previous observations and a considerable proportion of patients in both TM and TI groups had PHT that was more prevalent in the former group. We detected an adverse association between mean PAP and LVEF in patients with TM. Left ventricular function was reduced in patients with PHT among TM group.

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CONFLICTS OF INTEREST

Authors declare that they have no conflict of interest.

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Change in Atrial Activation Pattern during Ablation of Atrial Flutter

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Catheter Ablation

Abstract

Different types of supraventricular tachycardia have been reported in patients with history of surgical repair of Tetralogy of Fallot. This report presents appearance of focal atrial tachycardia during radiofrequency ablation of the cavotricuspid isthmus in typical atrial flutter.

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INTRODUCTION

Supraventricular tachycardia occurs in about 20% of patients with previous surgical Tetralogy of Fallot (TOF) repair [1, 2]. Increased right atrial pressure due to chronic right ventricular pressure overload and anatomical obstacle due to atriotomy scar can cause atrial arrhythmias, mainly cavotricuspid (CTI)-dependent atrial flutter (AFL) and non-CTI-dependent AFL around the atriotomy scar or both [3].

Radiofrequency ablation of these arrhythmias has been reported in this group of patients. Electroanatomical mapping has an important role in identification of reentry circuits in patients with postoperative right atrial incisional scar and flutter and it is necessary to ablate both scar-related and typical AFL to prevent long-term recurrence [4].

CASE PRESENTATION

A 31-year-old man who performed total surgical correction of TOF at 5 years old, was referred for catheter ablation of persistent typical AFL. His baseline electrocardiogram revealed negative flutter waves in leads II, III, aVF, V5 and V6, and positive waves in lead V1 consistent with typical counterclockwise AFL with 4:1 AV conduction and right bundle branch block (RBBB) pattern.

A decapolar catheter was advanced with its proximal 9 and 10 poles placed in the proximal coronary sinus (CS) and a duodecapolar halo catheter was positioned along the tricuspid annulus, such that the distal bipole of the halo catheter

was in the low lateral right atrium.

The atrial activation sequence and entrainment mapping were compatible with typical counterclockwise AFL. Linear radiofrequency ablation of CTI during arrhythmia was performed which resulted in termination of AFL, but appearance of another arrhythmia (change in atrial cycle length from 300 milliseconds to 326 milliseconds and with a different sequence of atrial activation) without restoration of sinus rhythm. P waves became positive in leads II, III and aVF and biphasic in lead V1 (Fig. 1A). This arrhythmia was compatible with focal atrial tachycardia as the atrial activation accounted for less than 60% of atrial cycle length [5]. Activation mapping was performed conventionally and arrhythmia was successfully ablated at the lateral of right atrium where the earliest activation signal achieved (96 milliseconds) (Fig. 1B).

DISCUSSION

Change of the first arrhythmia without restoration of the sinus rhythm can be described by different theories. It is probable that the second arrhythmia started de novo at the termination of the first arrhythmia. The other theory is that both arrhythmias were presented initially, but as the AFL rate was faster than the atrial tachycardia, the second arrhythmia could not be manifested. In this theory, one can argue that the mechanism of atrial tachycardia was microreentry (maybe around previous surgical scar of lateral atriotomy), so AFL

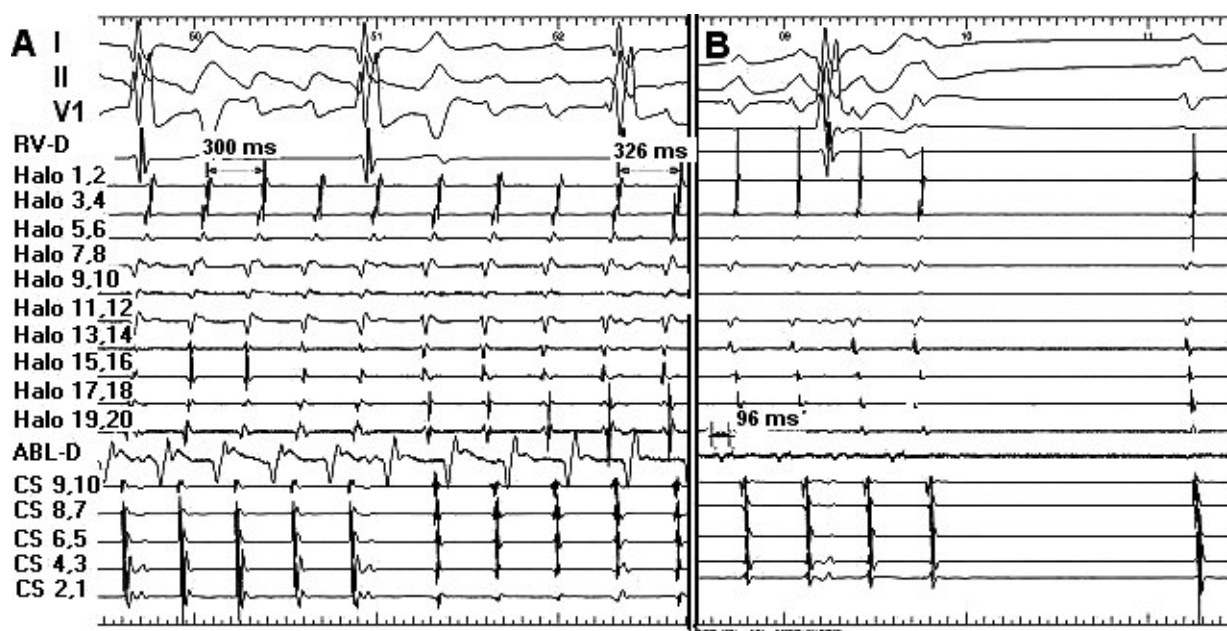


Figure 1: A) Termination of atrial flutter (300 ms) and appearing of focal atrial tachycardia (CL = 326 ms) during ablation of cavotricuspid isthmus. Note Change of intracardiac sequence and cycle length, and P wave morphology. B) Termination of focal atrial tachycardia during radiofrequency application in lateral of right atrium. Signal in ablation catheter is 96 ms earlier than surface P wave.

entrained the cycle of the micro reentry, but could not terminate it, or if the mechanism of atrial tachycardia was automaticity, due to a lower rate, it was hidden under AFL. Although it is difficult to define the mechanism of a focal AT, some principles may help to find that. Initiation and termination with programmed atrial stimulation and insensitivity to adenosine can be in favor of reentrant mechanism. Criteria for entrainment may be useful to prove the mechanism of reentrant, but due to small circuit size, it is difficult to demonstrate. By the way, regardless of the mechanism of focal atrial tachycardia, ablation can be performed with mapping the tachycardia focus. In our case we did not try to find out the main mechanism and just found its focus and ablated it [6].

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CONFLICT OF INTEREST

None of the authors had any conflicts of interest.

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Acute Myocardial Infarction in a Patient With Elevated ST-Segment in aVR Lead and Diffuse ST Segment Depression in Other Leads: A Case Report

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Abstract

ST elevation in aVR in conjunction with diffuse ST depression in precordial leads may indicate occlusion of very proximal portion of the left anterior descending artery. We present a 54-year old man, with crushing retrosternal pain and ST-segment elevation only in aVR lead and diffuse ST-segment depression in inferior, lateral and precordial leads. The patient was scheduled for emergent coronary angiography, which showed that left anterior descending (LAD) artery was cut off at very proximal portion and urgent CABG was performed for the patient.

INTRODUCTION

ST elevation in aVR lead has precise significance in ECG interpretation. This finding could be supportive in diagnosis of myocardial infarction due to left main coronary artery occlusion. However, this finding may be overlooked in emergency units, particularly in the absence of ST segment abnormalities like ST elevation in other leads. ST elevation in aVR in conjunction with diffuse ST depression in precordial leads may be a sign of occlusion of very proximal portion of the left anterior descending artery.

CASE PRESENTATION

A 54-year old man, without previous history of ischemic heart disease referred to our hospital with crushing retroster-

nal pain with radiation to lower mandible and cold sweating, from 3 hours before. 12 lead ECG revealed ST-segment elevation only in aVR lead and diffuse ST-segment depression in inferior, lateral and precordial leads. The patient was scheduled for emergent coronary angiography, which showed that left anterior descending (LAD) artery was cut off at very proximal portion and well-developed obtuse marginal (OM) artery was cut off at proximal portion with no ante grade run off. Urgent CABG was performed for the patient (LIMA on LAD and one SVG on OM).

The patient had no complication after CABG. Transthoracic echocardiography revealed ejection fraction of 40% and discharged one week later with ASA 80 mg daily, atorvastatin 40 mg, captopril 12.5 mg twice daily and carvedilol 6.25mg twice daily.

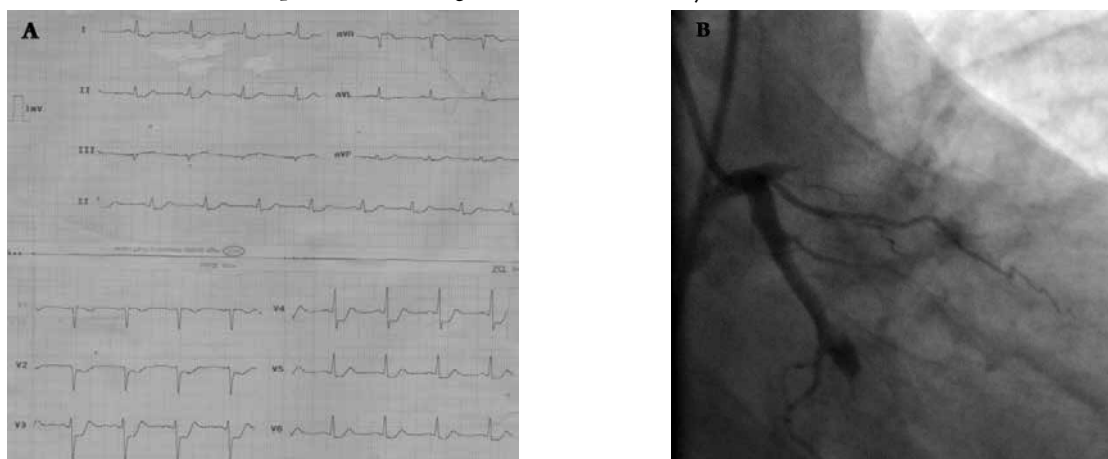


Figure 1: A, 12 lead ECG Revealed ST-segment Elevation Only in aVR Lead and Diffuse ST-segment Depression in Inferior, Lateral and Precordial Leads. B, Emergent Coronary Angiography Which Showed That Left Anterior Descending (LAD) Artery Was cut off at Very Proximal Portion and Well-developed Optus Marginal Artery Was Cut off at Proximal Portion With no Ante Grade Run off

DISCUSSION

ST elevation in aVR lead has particular importance in ECG interpretation. This finding could be helpful in diagnosis of myocardial infarction due to left main coronary artery occlusion. However, this finding may be ignored in emergency units, especially in the absence of ST segment abnormalities like ST elevation in other leads [1, 2].

ST elevation in aVR in conjunction with diffuse ST depression in precordial leads may indicate occlusion of very proximal portion of the left anterior descending artery [3].

This is a challenging condition, particularly in centers that are not equipped for emergent coronary angiography and angioplasty. Therefore, the only therapeutic revascularization option is thrombolytic agent. On the other hand, complications of thrombolytic agents including bleeding catastrophes is not inevitable and it is a difficult and challenging decision to use thrombolytic agents in the setting of single ST-segment elevation in aVR lead and diffuse ST-segment depression in other leads. Last updated guidelines recommended class IIb for administration of thrombolytic in this challenging circumstance [4, 5].

As a conclusion, emergency clinicians and cardiologists should be familiar with the importance of ST-segment elevation only in aVR lead, especially in conjunction with diffuse ST segment depression in other leads, which could be indicative of LAD occlusion in the setting of myocardial infarction.

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CONFLICT OF INTEREST

Authors declare that they have no conflict of interest.

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Products

(Medical Equipment)



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- Ablation Products (Catheter-Based) for Atrial Fibrillation
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- Implantable Cardioverter Defibrillators (ICDs)
- Leads
- Pacemakers
- Patient Management (Data Connectivity Solutions)



Cardiovascular

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- Cannulae (Adult and Pediatric)
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- Catheters
 - Balloon Dilatation Catheters
 - Guide Catheters
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- Coronary Stents
- Electrosurgical Products
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- MiniMed Paradigm 715 Insulin pump
- IPro 2 Professional CGM
- Guardian REAL-Time System
- Iport Injection Port



Products

(Medical Equipment)



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- Drug Infusion Systems for Chronic Pain
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- Nerve Monitoring Products
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