PREDICTORS OF NEW-ONSET ATRIAL FIBRILLATION AFTER ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION IN THE ELDERLY

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ABSTRACT

Objective: *The predictors and outcomes of new-onset atrial fibrillation (AF) were evaluated among elderly patients with acute ST elevation myocardial infarction (STEMI).*

Material and Method: *Patients with STEMI who are older than 65 years were evaluated for new-onset AF and its complications. Patients with a previous history of AF and those found in AF at the time of admission were excluded.*

Results: *Of the 102 patients with STEMI, AF was not observed in 74 patients (Group I) and was observed in 28 patients (Group II) during hospitalization. Those 28 patients with AF were further divided into two subgroups according to the onset time of AF (early <24 hours and late >24 hours). Anterior MI was observed in 49% of patients in Group I and 71.4% of patients in Group II (p<0.05). In late onset AF group; pulse rate, systolic and diastolic blood pressure were significantly higher than Group I at admission to the hospital (p<0.05). All patients in Group II had higher Killip class and TIMI risk scores than Group I patients (p<0.05). Left ventricular ejection fraction was 30.4±4.0% in the late onset group and 44.4±8.8% in Group I (p<0.05). There was a significant difference in mortality rate among groups during hospitalization period; 36% in Group II, 9% in Group I (p<0.05).*

Conclusion: *AF is especially seen in elderly female patients with anterior MI and higher Killip Class. It is associated with higher rates of in-hospital mortality. Particularly, late-onset AFs are associated with lower LVEFs in older patients with STEMI and could be predictors of in hospital mortality.*

Keywords: *Myocardial infarction, atrial fibrillation, aging*
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YAŞLI HASTALARDA ST SEGMENT YÜKSELMELİ MİYOKARD İNFARKTÜSÜ SONRASI YENİ GELİŞEN ATRİYAL FİBRİLASYONUN GELİŞİMİNİ ÖNGÖRDÜRÜCÜ ETKENLER

ÖZET

Amaç: ST segment yükselmeli myokart infarktüsü (MI) tanılı yaşlı hastalarda yen atriyal fibrilasyonun (AF) öngördürücüleri ve sonuçları araştırıldı.

Materyal ve Metot: ST segment yükselmeli MI tanılı 65 yaş üzeri hastalar yeni AF gelişimi ve komplikasyonları açısından değerlendirildi. Öncesine ait AF öyküsü olan ve başvuru anında AF saptanan hastalar dışlandı.

Bulgular: Hastanede kaldıkları süre boyunca ST segment yükselmeli MI tanılı 102 hastanın 74'ünde AF gözlenmedi (Grup I) ve 28'inde AF saptandı (Grup II). AF gelişen 28 hasta AF gelişim zamanına göre (erken <24 saat ve geç >24 saat) iki alt gruba ayrıldı. Grup I'deki hastaların %49'unda ve Grup II'deki hastaların %71,4'ünde ön yüz MI gözlendi (p<0,05). Hastaneye başvuruda geç AF grubunda nabız hızı, sistolik ve diyastolik kan basıncı Grup I 'deki hastalara göre anlamlı olarak daha yüksek saptandı (p<0,05). Grup II'deki tüm hastalarda Grup I'deki hastalara göre daha yüksek Killip sınıfı ve TIMI risk skorları saptandı (p<0,05). Sol ventrikül ejeksiyon fraksiyonu geç AF grubunda %30,4±4,0 ve grup I'de ise %44,4±8,8 olarak saptandı (p<0,05). Hastane içi mortaliteye bakıldığında gruplar arasında istatiksel olarak anlamlı fark mevcuttu; Grup II'de %36 ve Grup I'de %9 (p<0,05).

Sonuç: AF özellikle daha yaşlı, ön yüz MI geçiren, daha yüksek Killip sınıfına sahip kadın hastalarda görüldü. Daha yüksek hastane içi mortaliteyle ilişkiliydi. ST segment yükselmeli MI tanılı hastalarda geç gelişen AF özellikle düşük sol ventrikül ejeksiyon fraksiyonu ve ileri yaşla ilişkilidir ve hastane içi mortalitenin de öngördürücüsü olabilir.

Anahtar kelimeler: Myokard infarktüsü, atriyal fibrilasyon, yaşlanma **Nobel Med 2015; 11(3): 22-27**

INTRODUCTION

Atrial fibrillation (AF) is the most common cardiac arrythmia and may lead major public health problems due to its severe complications. The incidence of AF increases with age. It has been well-shown that AF is associated with a higher mortality in specific clinical situations, such as acute myocardial infarction (MI), heart failure, renal failure, stroke, diabetes mellitus, hypertension (HT), and after cardiac surgery.[1-4] Varying trials have shown that AF is common, with an incidence of 5-15%, in patients with acute MI.[5,6] It can be classified in two categories as; early (<24h) and late (>24h)-developing AF in ST elevation myocardial infarction (STEMI). Early and late-developing AF with different underlying mechanisms, may vary in clinical expression and prognosis. Early development of AF is associated with right ventricular infarction, atrial perfusion impairment and severe lesions of coronary sinus or AV node. Differently, late-developing AF is usually associated with heart failure, low left ventricular ejection fraction, higher Killip class, and pericarditis.[7] We aimed to investigate the predictive and prognostic factors of new-onset AF after STEMI among elderly.

MATERIAL AND METHOD

A total of 102 consecutive patients, aged ≥65 years, were included in this study. The data of these patients were retrospectively analyzed. All patients had acute STEMI and were hospitalized in Coronary Care Unit in our hospital between January 1st and December 31st 2008. Acute MI was diagnosed as; persistent chest pain of 30 minutes or longer within 48 hours, typical pattern of ECG (ST segment elevation of ≥0.1 mV in at least two consecutive leads or new onset left bundle branch block, pathological Q waves) and increased levels of cardiac markers. The patients who were treated in the other hospitals-even partially or initially-during the acute phase of MI were excluded from this study. Patients with a medical use of antiarrythmics, rheumatic heart valve diseases, prosthetic heart valves, chronic AF at admission and hyperthyroidism were also excluded from the study. Since our clinic was a non-invasive center in 2008, all patients were treated by fibrinolytic therapy and transferred 48 hours later after succesful reperfusion. All patients who were transferred for primary PCI and rescue PCI were excluded from the study.

All patients were monitorized for 24 hours in Coronary Care Unit. ECG was performed at admission (first ECG), and during the coronary care unit at least three times. Electrolyte levels and cardiac markers were analyzed. Echocardiographic examination was performed with two-dimensional, colored, equipped with M-mode and doppler echocardiography.

AF was diagnosed based on the routine 12-lead electrocardiogram (ECG) records during the hospitalization. The patients with documented AF on their first ECG recorded on arrival in either Emergency Department or Coronary Care Unit and those with a

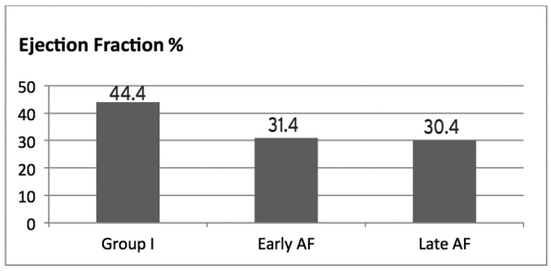

Figure. Mean left ventricular ejection fractions
AF: Atrial fibrillation

history of AF are excluded from the study. New-onset AF group consisted of patients with sinus rhythm who developed AF during hospitalization.

Patients were divided into two groups; without AF (Group I) and new-onset AF (Group II). Group II was classified in two subgroups according to the onset time of AF; early (<24 hours) and late (>24 hours). Killip class and TIMI risk score of patients were evaluated on admission.

In-hospital mortality, incidence of heart failure based on Killip class, stroke, and duration of hospitalization stay were determined and analyzed.

All data were presented as mean ± standard deviation (SD). The Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA) SPSS 16.0 software was used for statistical analysis. Student t test and Chi-square tests were used to determine the statistical significance of differences in patients with or without AF. Multivariate logistic regression analysis was performed to determine the clinical predictors of the incidence of AF and in-hospital mortality. A p value <0.05 was considered statistically significant.

RESULT

102 elderly patients (≥65 years old) that hospitalized after the diagnosis of STEMI in our Coronary Care Unit, between January 1st and December 31st 2008 were included in the study. New-onset AF was seen in 27.5% of the patients with acute STEMI during hospitalization. 74 patients (72.5%) without AF was labeled as Group I, 28 patients (27.5%) with new-onset AF was labeled as Grup II. The number of patients with early and late AF (<24 hours) was 16 (15.7%); and 12 (11.8%), respectively. Mean age in Group I, early AF group, and late AF group was 74.7±6.1, 76.1±6.1 and 86.1±4.8 years, respectively. The patients in late AF group were older than Group I (p<0.05). The number of women in Group I and II was 39.2% (29/74), 53.6% (15/28), respectively (p<0.05).

In Group II, the localization of MI was anterior in 71.4% and inferior or inferoposterior in 28.6% of the patients. In Group I, the localization of MI was anterior in 49% and inferior or inferoposterior in 51%.

Duration of the symptom onset to hospital admission for early onset AF, late onset AF, and Group I was 7.6±8.3, 9.9±10.7, 6.2±4.3 hours, respectively, without statistically significance. Also there was no significant difference between groups in terms of diabetes, family history, dyslipidemia and smoking. In group II, HT was present in 82% of patients (23/28) and in Group I, HT was seen in %53 of patients (39/74) (p<0.05).

Left ventricular ejection values were statistically measured higher in Group I (p<0.05) Mean heart rates on admission in patients with early AF group, late AF group and group I were 86± 24.1, 97.7±19.9, and 80±17.8 bpm, respectively, with a significant difference between late AF group and Group I (p<0.05). Similarly, the difference between Group I and late AF group for systolic and diastolic arterial blood pressure at admission was statistically significant (p<0.05). Systolic and diastolic arterial blood pressure levels for Group I, early AF group and late AF group were 131.2±23.5/76.2±15.5 mmHg, 121.1±27.9/72.2±20.4 mmHg, and 105±11.5/68.3±8.6 mmHg, respectively. Mean Killip class was 1.36±0.41 in Group I, 1.95±0.45 in early AF Group, and 2.15±0.66 in late AF group. There was no significant difference between early and late AF groups in terms of Killip classes however both late and early AF groups had higher Killip classes than Group I (p<0.05). TIMI risk scores of early AF group, late AF group and Group I were 8.1±2.1, 9.7±1.4, and 4.7±1.8, respectively. There was no significant difference between the groups including early and late AF, however the difference between Group I and II was significant (p<0.05).

Left ventricular ejection fraction (LVEF) values were 44.4±8.8%, 31.4±4.8%, 30.4±4.0% in Group I, early AF group and late AF group, respectively. Although there was no statistically significance between late and early AF groups, ejection fraction value was measured higher in Group I (p<0.05) (Figure).

There was no significant difference between groups in terms of hemoglobin, hematocrit, platelet, white blood cells, mean erythrocyte volume, mean platelet volume, LDL, HDL, AST, ALT levels however; urea, creatinine, LDH, peak CK-MB levels were significantly higher in Group II than Group I (p<0.05).

In hospital mortality rates were higher in Group II than Group I (36% vs. 9%, p<0.05), however there was no significant difference between early and late AF groups. None of the patients in both groups had stroke.

In 75% (21/28) of patients spontaneous conversion to sinus rhythm occurred. In early AF group its ratio was 87% (14/16), and in late AF group 58% (7/12) without statistically significance. Duration of hospitalization was longer in late AF group than early AF group, and Group I ($p<0.05$).

Multivariate analysis revealed that history of HT, heart rate at admission, TIMI risk score and Killip class were independent predictors for new onset AF after STEMI. Killip class and TIMI risk score predicted early AF as well as age, sex, systolic and dyastolic blood pressure, heart rate at admission, MI localization, Killip class, TIMI risk score, LVEF, urea-creatinine-LDH-peak CKMB levels predicted late AF. AF itself was associated with an increase in in-hospital mortality (mortality in Group I and II was 9%, and 36%,respectively, $p<0.05$) (Table).

Table. Comparison of Group I and II

	Group I (n=74)	Group II (n=28)	p
Female	39.2%	53.6%	<0.05
MI localization (anterior)	49%	71.4%	<0.05
HT frequency	53%	82%	<0.05
In-hospital mortality	9%	36%	<0.05
Diabetes mellitus	27%	32%	NS
Heart Failure	9%	78%	<0.05

MI: Myocard infarction, **HT:** Hypertension

DISCUSSION

In our study group, AF was mostly seen in female patients with anterior MI and was found associated with higher rates of in-hospital mortality. Specifically, late-onset AFs were observed in those patients with lower LVEFs after STEMI. This could be interpreted as; particularly late-onset AFs are predictors of in hospital mortality in STEMI, while early-onset AFs are not.

AF is the most common supraventricular arrhythmia in the early stages of STEMI.[8] Although the underlying mechanisms for development of AF in patients with acute MI are not clear; autonomic, anatomic, hemodynamic and iatrogenic factors may possibly be effective.[9] AF in patients with acute MI often results in marked deterioration of cardiac function and is associated with an increased in-hospital and long-term mortality, especially in patients with STEMI.[5,10-12] It is not clear whether the effect of new-onset AF on in-hospital mortality is due to the arrythmia itself or accompanying comorbid disorders.[9]

Incidence of new-onset AF during STEMI is reported as 10-23%.[6] However, in our study this ratio was determined higher than expected. Compared to the present literature, this higher percentage of new onset AF may depend on the lack of primary percutaneous coronary intervention (PCI). Recently, the incidence of new-onset AF during STEMI seems to decrease due to the common use of ACE inhibitors, ASA, beta blockers and cardiac revascularization therapies. AF is more frequent in patients with large MI, anterior localization, atrial infarction and pericarditis.[13]

The predictors of AF in diverse forms of acute coronary syndromes has been extensively studied.[14] New-onset AF is more common in elderly people, female sex, higher Killip class, heart failure, high heart rate, hypertension, diabetes and high blood pressure in the process of STEMI.[15]

There are conflicting opinions about the role of MI localization on the development of AF.[16] Although some studies documentated that AF was more frequently seen in patients with anterior MI, some studies show vice versa.[5,17,18] According to our results, AF was seen more common after anterior wall infarction in elderly (%71.4).

In GISSI-3 trial advanced age, high Killip class and elevated arterial blood pressure were found associated with new-onset AF among STEMI patients.[15] Development of AF was found to have higher mortality rates 1.98 fold than patients without AF, 1.78 fold for 4 years.[15] This finding was in correlation with our study results. In group II, mortality was higher than non AF group.

Early and late onset AF development was attributed to different mechanisms and the prognosis and clinical expression was also different. Early AF was associated with right ventricule infarction, impaired atrial perfusion and severe lesions of sinus or AV node vessels. Late AF was associated with heart failure, low left ventricular ejection fraction, high Killip class and pericarditis.

Konomi et al. showed that new-onset AF in first 24 hours was related to inferior MI and proximal occlusion of right coronary artery and AF developing after 24 hours was related to anterior MI and heart failure.[19] Sakata et al. investigated 1039 STEMI patients and found the incidence of new-onset AF as 8.2%. Early onset AF (<24h) was associated with inferior MI, higher left ventricular ejection fraction, higher right atrial pressure and RCA (right coronary artery) related MI. Late onset AF (>24h) was associated with anterior MI, low ejection fraction, more serious mitral regurjitation and LAD (left anterior descending artery) related MI. In late AF group, heart failure and pericardial effusion was

determined more often and in early AF group, right ventricular infarction and AV block was more frequent. At observational studies during long time follow-up, late onset AF group had 3.7 fold higher mortality rate than early onset AF group.[19]

Li Kang et al analyzed 967 STEMI patients over 65 years. Association of STEMI and AF was present among 100 (11.53%) patients and new onset AF was 6.51%. Patients with a history of coronary artery disease and cerebrovascular disease had more frequent AF. Among patients with new onset AF inferior MI and higher Killip class were significantly higher, and these patients had longer hospital stay and more frequent in-hospital complications. Also in hospital mortality attributed to heart failure with AF was higher.[20]

In CCP trial (The Cooperative Cardiovascular Project) 234,769 STEMI patients over 65 years were analyzed. Association of acute STEMI and AF were detected at 23,565 (21%) patients. The ratio of new onset AF was 11.3% during hospital stay. Patients with advanced age, higher heart rate, higher Killip class, low systolic blood pressure, anterior MI had higher AF development. Smoking had weak association and gender had no relationship with new onset AF. New onset AF patients had more frequent in hospital complications as reinfarction, heart failure, stroke and higher mortality rates for 30 days and one year. Association of STEMI and AF among elderly patients had poorer prognosis.[21]

HT was shown as a predictor of new onset AF after STEMI in mutlipte trials.[21,22] In our study, the incidence of HT was 82% in Group II supporting these data.

Altough intracranial hemorrhage is associated with thrombolytic therapy in elderly patients, none of our patients presented with this complication.[23] Also pericarditis, AV block and bleeding was not observed.

Generally our study was in correlation with the present literature about risk factors of new onset AF after STEMI and mortality predictors. The exact cause is still controversial regarding higher mortality in elder patients with new developing AF after STEMI.

The main limitation of our study was the retrospective design. Also we could not determine the exact time of the onset of AF and patients undergoing PCI were not included in the study.

CONCLUSION

In conclusion, AF is one of the common complications in elderly patients with acute STEMI. Different factors may contribute for developing AF in this group of patients. Patients with AF have more serious complications. In our study AF frequency was higher in the patients with anterior MI. AF was also correlated with age and these elderly patients with AF had poorer prognosis. In our opinion, elderly female patients with anterior STEMI without PCI should be closely monitored for new-onset AF, which is associated with higher in-hospital mortality rates. Besides optimal medical treatment, close attention should be given to this population due to high mortality risk. Specifically, late-onset AFs in elderly patients are in concordance with lower LVEFs after STEMI and could be interpreted as predictors of in hospital mortality after STEMI.

* The authors declare that there are no conflicts of interest.

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