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Retrospective Evaluation of In-Hospital and Thirty-Month Mortality Parameters in Cases of Acute Coronary Syndrome

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ABSTRACT

Objectives: The aim of this study is to retrospectively assess, from the hospital records of patients, the clinical data of patients and the treatment strategies practiced on patients who were diagnosed as Acute Coronary Syndrome (ACS) and hospitalized and treated in the Hospital of Faculty of Medicine to research the effect of these data on occurrence of cardiovascular events and 30 months mortality.

Methods: It is a retrospective screening study in which patients hospitalized with the diagnosis of ACS between June 2007 and December 2008 in the Hospital of Faculty of Medicine Cardiology Clinic are evaluated by using patient file information and electronic data recording system information, and by calling patients. In-hospital and long-term follow-up deaths were the endpoints of the study. Statistical analysis was performed using SPSS (Version 15.0).

Results: 985 patients were included in the study who were diagnosed as ACS, hospitalized and treated in the hospital. The categorization of the patients subjected to the analysis (n:901) according to their diagnosis is as follows: 339 (38%) cases diagnosed as UAP, 206 (23%) cases diagnosed as NSTEMI, and 356 (39%) cases diagnosed as STEMI. 78,4 % of cases were male while 21,6 % were female. It was found that cases with hypertension, hyperlipidemia, obesity risk factor, and with a history of cardiovascular disease fall into the NSTEMI and UAP groups with a larger proportion. Among the groups, the UAP diagnosed cases have the largest and the STEMI diagnosed cases have the smallest ratio of using medicine groups such as beta blocker, calcium-canal blocker, ACE inhibitor, ARB, diuretic, statin, fibrate and nitrate before being hospitalized. In-hospital mortality was frequently encountered with a percentage of 7.6 % in STEMI cases, 2.4 % in NSTEMI cases, and 0.6 % in UAP cases. 30-months of follow-up data were obtained in all diagnosis groups for long-term mortality assessment. 70 (7.8 %) deaths were observed within the follow-up. According to diagnosis groups, death was observed in 22 (6.5 %) of UAP cases, 22 (10.7 %) of NSTEMI cases, and 26 (7.3 %) of STEMI cases. Correlation between long-term survival (30 months) and in-hospital statin usage and statin usage in discharge was not significant (p value respectively 0.1 and 0.16). Correlation between an approximate 30-months-survival and in-hospital ACE inhibitor/ARB inhibitor usage and ACE inhibitor/ARB inhibitor usage during discharge was significant ($p = 0.007$ and $p = 0.004$). It is also found that there was a significant correlation between survival in the same period of time and in-hospital beta blocker usage ($p = 0.01$). There was not a significant correlation between beta blocker usage during discharge and long-term survival ($p = 0.779$).

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Conclusion: Results of the unicentral retrospective scanning study which involves 901 ACS diagnosed patients prove to be similar to the ones obtained from GRACE and Euro Heart Survey prospective studies which were carried out in multi-central environment and among outnumbered patients.
Key words: Acute Coronary Syndrome, Beta Blocker, Mortality, RAS Blocker, Statin

Coronary artery disease, which is the most serious and most common clinical consequence of the atherosclerotic process, is one of the leading causes of death in today's developed countries. The clinical picture that occurs with sudden myocardial ischemia is called acute coronary syndrome (ACS). ACS patients constitute a heterogeneous group clinically in terms of severity of ischemia, anatomical features of coronary arteries, and prognostic features.

The term ACS is a broad concept which includes myocardial infarction with ST-segment elevation (STEMI), non-ST-segment elevation myocardial infarction (NSTEMI) and unstable angina pectoris (UAP). Serious reductions in both morbidity and mortality rates in acute coronary syndromes have been reported thanks to advanced treatment applications, increase in medical treatment options and clinical experience gained in the light of large-scale studies. As a matter of fact, intervention and treatment methods that reduce acute, short and long-term mortality and morbidity in acute coronary syndromes are recommended in detail in current treatment guidelines prepared in the light of clinical studies. [1, 2] However, the data on the drugs and applications recommended in these guidelines are obtained from clinical studies in which treatment regimens are applied under optimal conditions. In actual clinical practice, however, there is not enough research on the treatment approach in acute coronary syndromes and their effects on cardiovascular (CV) events. In other words, it is not known to what extent the positive results of the treatments shown in the guidelines in acute coronary syndromes are reflected in actual clinical practice.

This study aims at retrospectively evaluating the treatment strategies applied (Beta blocker, ACEinh/ARB and statin usage in particular) and clinical data based on hospital records of patients hospitalized with ACS diagnosis in University Hospital between June 2007 and December 2008, and investigating the effect of these clinical data to the CV mortality development within an approximately 30-months period. It is planned to use a retrospective method in order to ensure that the study reflects actual clinical practice.

METHODS

Before starting the research, ethics committee approval (No. 10-10/3) was obtained from the EUMF Research Ethics Committee on October 15, 2010. It is a retrospective screening study in which patients hospitalized with the diagnosis of ACS between June 2007 and December 2008 in the Hospital of Faculty of Medicine Cardiology Clinic are evaluated by using patient file information and electronic data recording system information, and by calling patients, who do not have sufficient follow-up data, by phone. In the light of the data obtained from the patient files of the patients hospitalized with the diagnosis of ACS, it was aimed to determine the effects of symptoms, physical examination, laboratory and imaging findings on mortality both in the in-hospital and in the follow-up periods. Symptoms at admission, CAD risk factors and accompanying diseases, physical examination findings, drug use histories, admission ECG findings, laboratory examinations (kidney function tests, hemogram, cardiac enzymes, thyroid function tests if performed, CRP, and HbA1C values), the procedures and timings (echocardiography, coronary angiography and percutaneous coronary intervention, thrombolytic therapy, stress test, CABG, etc.) obtained from the file records of the cases in the hospital archive were recorded in the case report forms. Complications developed during the in-hospital period (heart failure, shock, arrhythmia, infection, death, bleeding, cerebrovascular accident), drug groups used by the patients before hospitalization, drug therapy started at hospitalization, and treatment given during discharge were recorded in the case report forms. In order to obtain long-term survival data after discharge, the date of the last registration to the hospital and the information about the last application were recorded in the hospital registry system. Cases for whom sufficient data could not be reached from this registry system or those who did not apply to hospital again were called by phone and their current status was questioned and the information obtained was added to the case report forms.

In-hospital and long-term follow-up deaths were the endpoints of the study. In-hospital deaths were divided into two groups as cardiovascular and non-cardiac causes. While cardiogenic shock, pulmonary edema, cardiac arrest, ventricular fibrillation, cerebrovascular accident and pulmonary embolism are the causes of in-hospital cardiovascular death, non-cardiac causes of death involve bleeding, infection and other causes. Long-term cardiovascular deaths include sudden cardiac death, early period pump failure after coronary artery bypass surgery (CABG), myocardial infarction (MI), congestive heart failure (CHF), mesenteric ischemia and cerebrovascular accident, non-cardiac causes of death, kidney failure, infections, chronic obstructive pulmonary disease disease (COPD), malignancies, and other causes.

Statistical analysis was performed using SPSS (Version 15.0). Data are shown as mean ± standard deviation for continuous variables and as percentages for discontinuous variables. Variance analysis was used to compare group means, and chi-square test was used to compare percentages. Spearman (rho) test was used in correlation analyzes to determine in-hospital CV event development, mortality and mortality determinants in follow-up. In-hospital mortality was evaluated by logistic regression analysis, and mortality at follow-up was evaluated by Cox-regression analysis. Kaplan-Meier curves were drawn to evaluate the survival effect of beta-blocker, statin, and ACE inhibitor/ARB use. The probability value of $p \leq 0.05$ was accepted as statistically significant.

RESULTS

985 cases from archive information were sampled sequentially. When their diagnoses were examined, it was detected that 369 (37%) cases were followed with UAP, 236 (24%) cases with NSTEMI and 380 (39%) cases with STEMI. Eighty-four cases (30 UAP, 30 NSTEMI, and 24 STEMI diagnosed) whose follow-up data could not be reached through the hospital

Table 1. Characteristics of the cases in terms of cardiovascular disease and risk factors

Feature	*STEMI (356) n, (%)*	*NSTEMI (206) n, (%)*	*UAP (339) n, (%)*
Diabetes Mellitus	96 (27)	73 (35.4)	90 (26.5)
Hypertension	152 (42.7)	132 (64.1)	229 (67.6)
Hyperlipidemia	151 (42.4)	109 (52.9)	199 (58.7)
Obesity	137 (38.5)	92 (44.7)	151 (44.5)
Smoking	259 (72.7)	126, (61.2)	190 (56)
Family history	127 (35.7)	77 (37.4)	144 (42.5)
Alcohol	49 (13.8)	29 (14.1)	46 (13.6)
CVD history (total)	89 (25)	98 (47.6)	177 (52.2)
MI history	44 (12.4)	47 (22.8)	80 (23.6)
CHF history	3 (0.8)	2 (1)	5 (1.5)
Coronary angiography history	51 (14.3)	74 (35.9)	151 (44.5)
CABG history	16 (4.5)	40 (19.4)	61 (18)
PCI history	32 (9)	25 (12.1)	73 (21.5)
Valvuler intervention history	0	1 (0.5)	2 (0.6)
Peripheral artery disease history	6, (1.7)	4 (1.9)	8 (2.4)
History of atrial fibrillation	1, (0.3)	5 (2.4)	1 (0.3)
History of cerebrovascular accident	14, (3.9)	13 (6.3)	17 (5)
CIED history	1, (0.3)	1 (0.5)	3 (0.9)

STEMI: ST-elevation myocardial infarction; NSTEMI: non-ST-elevation myocardial infarction; UAP: unstable angina pectoris; CVD: cardiovascular disease, MI: myocardial infarction, CHF: congestive heart failure, CABG: coronary artery bypass graft, PCI: percutaneous coronary intervention, CIED: Cardiac Implantable Electronical Device

electronic data recording system and phone calls were not included in the analysis due to insufficient data. Statistical analysis was performed on a total of 901 (91.5%) remaining patients whose mortality data were available. The mean age of the study population was 60 ± 12.15 years, with 195 (21.6%) females and 706 (78.4%) males. The distribution of the patients included in the statistical evaluation according to their diagnoses is composed of 339 UAP (38%), 206 NSTEMI (23%) and 356 STEMI (39%) of cases.

The characteristics of the cases in terms of CV disease and risk factors are summarized in Table 1. The cases with diabetes in the NSTEMI group and the cases with hypertension, hyperlipidemia, obesity risk factors and a previous history of CV disease in the NSTEMI and UAP groups were found to be higher in percentage. It was observed that the history of smoking was higher in the STEMI group.

The drug groups used by the cases before hospitalization are summarized in Table 2. While the history of aspirin use was seen at higher rates in NSTEMI and UAP cases, the history of clopidogrel use was found at a higher rate in the UAP group. Among the diagnostic groups, the rate of use of beta-blockers, calcium channel blockers, ACE inhibitors, ARBs, diuretics, statins, fibrates and nitrates before hospitalization was the highest in patients with UAP, while the lowest rates were recorded in patients with STEMI (Table 2).

The drug groups administered in the hospital are summarized in Table 3 according to the diagnosis groups. Beta blocker, ACE inhibitor/ARB and statin treatments were found to be used at high rates in all groups. It was observed that these drug groups were used most frequently in NSTEMI cases among the diagnostic groups, followed by STEMI and UAP cases in order of frequency.

In-hospital complications and mortality

The complications developed within the hospital are summarized in Table 3. These complications include heart failure, sudden onset pulmonary edema, cardiogenic shock, cardiac arrest, severe ventricular arrhythmias (VT/VF), mechanical complications, development of AV block, bleeding, infection, deep vein thrombosis, pulmonary thromboembolism,

Table 2. Drug groups used before hospitalization according to diagnosis groups

Features	*STEMI (356)* *n, (%)*	*NSTEMI (206)* *n, (%)*	*UAP (339)* *n, (%)*
Acetylsalicylic acid	79 (22.2	83 (40.3)	181(53.4)
Clopidogrel	17 (4.8)	9 (4.4)	38 (11.2)
Other antiaggregants	1 (0.3)	5 (2.4)	5 (1.5)
Warfarin	0	5 (2.4)	6 (1.8)
Beta blockers	57 (16)	45 (21.8)	155 (45.7)
CCB	29 (8.1)	28 (13.6)	54 (15.9)
ACE inh.	42 (11.8)	53 (25.7)	100 (29.5)
ARB	21 (5.9)	28 (13.6)	79 (23.3)
Diuretics	33 (9.3)	46 (22.3)	117 (34.5)
Digitalis	2 (0.6)	4 (1.9)	8 (2.4)
Statins	37 (10.4)	34 (16.5)	93 (27.4)
Fibrates	2 (0.6)	1 (0.5)	11 (3.2)
Niacin	0	0	0
Ezetimibe	0	1 (0.5)	1 (0.3)
Antiarrhythmics	4 (1.1)	1 (0.5	3 (0.9)
Nitrates	34 (9.6)	37 (18)	113 (33.3)
Oral antidiabetics	42 (11.8)	39 (18.9)	65 (19.2)
Insulin	16 (4.5)	19 (9.2)	16 (4.7)

STEMI: ST-elevation myocardial infarction; NSTEMI: non-ST-elevation myocardial infarction; UAP: unstable angina pectoris; ACE: Angiotensin converting enzyme, ARB: Angiotensin I receptor blocker, PPI: proton pump inhibitor, CCB: calcium channel blockerbloker

Table 3. Beta blockers, RAS blockers and statins given to the diagnosis groups at the hospital

DRUG GROUP	*UAP* *n, (%)*	*NSTEMI* *n, (%)*	*STEMI* *n, (%)*
Beta blockers	291 (85.8)	184 (89.3)	291 (81.7)
ACE inh. / ARB	284 (83.8)	188 (91.3)	310 (87.1)
Statin	282 (83.2)	195 (94.7)	329 (92.4)

STEMI: ST-elevation myocardial infarction; NSTEMI: non-ST-elevation myocardial infarction; UAP: unstable angina pectoris, ACE inhibitor: Angiotensin converting enzyme inhibitor, ARB: Angiotensin I receptor blocker

cerebrovascular accident, and infection. All types of complications were seen at a higher rate in STEMI cases.

Cardiogenic shock (20 patients, 2.2%) was the leading cause of in-hospital mortality. The other 14 causes of death are as follows: 7 (0.8%) VF, 2 (0.2%) cardiac arrest, 2 (0.2%) pulmonary edema, 1 (0.1%) cerebrovascular accident, 1 (0.1%) gastrointestinal system bleeding, and 1 (0.1%) pulmonary embolism.

In-hospital mortality was detected with a frequency of 7.6% in STEMI, 2.4% in NSTEMI and 0.6% in UAP cases. In-hospital CV death was observed with the rates of 7% in STEMI, 2.4% in NSTEMI, and 0.6% in UAP cases (Table 4).

Beta blockers, RAS blockers and statins given at discharge

The distribution of drug groups given to the discharged cases is summarized in Table 5. Beta blocker use was found to be above 80% in all three groups. While ACE inhibitor use was higher in NSTEMI and STEMI cases, it was seen that the ARB group was more frequently applied in UAP cases. It was observed that the statin group was used most

Table 4. In-hospital complications observed in the diagnostic groups

In-hospital complication	*UAP* *n (%)*	*NSTEMI* *n (%)*	*STEMI* *n (%)*
Congestive Heart Failure	0	5 (2.4)	16 (4.5)
Acute Pulmonary Edema	0	4 (1.9)	13 (3.7)
Cardiogenic Shock	0	3 (1.5)	23 (6.5)
Cardiac Arrest	1 (0.3)	6 (2.9)	27 (7.6)
Ventricular fibrillation	1 (0.3)	2 (1.0)	27 (7.6)
Atrial fibrillation	1 (0.,3)	5 (2.4)	10 (2.8)
Sustained Ventricular Tachycardia	1 (0.3)	2 (1.0)	6 (1.7)
Mechanical complication	0	0	4 (1.1)
AV Block	2 (0.6)	2 (1.0)	12 (3.4)
Acute renal failure	3 (0.9)	11 (5.3)	17 (4.8)
Deep Vein Thrombosis	0	0	0
Pulmonary Thromboembolism	1 (0.3)	0	0
Cerebrovascular Accident	2 (0.6)	3 (1.5)	5 (1.4)
Bleeding	12 (3.5)	10 (4.9)	25 (7.0)
Bleeding with ERT tx	7 (2.1)	2 (1.0)	13 (3.7)
Infection	7 (2.1)	15 (7.3)	26 (7.3)
Mortality	2 (0.6)	5 (2.4)	27 (7.6)
Cardiovascular mortality (*)	2 (0.6)	5 (2.4)	25 (7.0)

STEMI: ST-elevation myocardial infarction; NSTEMI: non-ST-elevation myocardial infarction; UAP: unstable angina pectoris, AV: atrioventricular, ERT Tx: erythrocyte transfusion

(*) Pulmonary edema or cardiac arrest or VF or pulmonary embolism or cardiogenic shock

Table 5. Beta blocker, RAS blocker and statin rates given at discharge

Drug groups	*UAP n, (%)*	*NSTEMI n, (%)*	*STEMI n, (%)*
Beta blockers	273 (80.5)	183 (88.8)	305 (85.7)
ACE inh.	199 (58.7)	161 (78.2)	282 (79.2)
ARB	76 (22.4)	13 (6.3)	12 (3.4)
Statins	290 (85.5)	189 (91.7)	315 (88.5)

STEMI: ST-elevation myocardial infarction; NSTEMI: non-ST-elevation myocardial infarction; UAP: unstable angina pectoris, ACE inhibitor: Angiotensin converting enzyme inhibitor, ARB: Angiotensin I receptor blocker.

Table 6. Long-term mortality rates by diagnosis groups

Long-term mortality type	*UAP*	*NSTEMI*	*STEMI*
All-cause mortality	22 (%6.5)	22 (%10.7)	26 (%7.3)
Cardiovascular death (*)	13 (%3.8)	19 (%9.2)	18 (%5.1)
Death from non-cardiac causes	9 (%2.7)	3 (%1.5)	8 (%2.2)

*(Sudden cardiac death, pump failure after CABG, MI, CHF, mesenteric ischemia, cerebrovascular accident)

frequently in NSTEMI cases (91.7%) which was followed by STEMI cases (88.5%). (Table 5).

Long term mortality rates after discharge

In order to determine the long-term mortality rates of the patients after discharge, long term mortality rates were calculated by using the hospital electronic data recording system or by calling the patients who did not have a follow-up record in the data recording system. The mean follow-up period of the cases was calculated as 30.02 ± 7.41 months in the UAP group, 30 ± 9.21 months in the NSTEMI group, and 29.86 ± 8.62 months in the STEMI group.

Overall mortality

In the follow-up, death was observed in 70 (7.8%) cases in general. When distributed according to diagnostic groups, there were 22 (6.5%) deaths in UAP cases, 22 (10.7%) in NSTEMI cases, and 26 (7.3%) deaths in STEMI cases.

Mortality rates from cardiovascular and non-cardiac causes

It was determined that 50 (5.5%) cases died due to CV, and 20 (2.2%) cases died due to non-cardiac

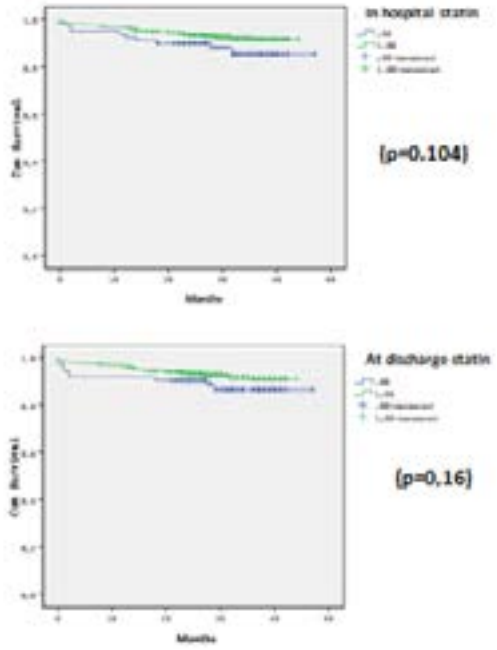

Fig. 1. Relationship between long-term mortality and the use of statins in-hospital and discharge

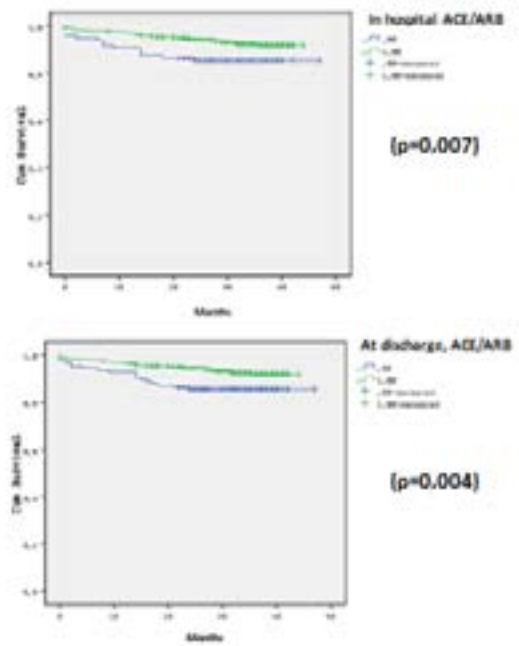

Fig. 2. Relationship between long-term mortality and the use of ACE inhibitors/ARBs

causes. When 50 cases who were found to have died due to CV events are distributed according to their diagnoses, 13 (3.8%) out of 339 cases (mean follow-up of 30.02 ± 7.41 months) with UAP, 19 (9.2%) out of 206 cases (mean follow-up of 30 ± 9.21 months) diagnosed with NSTEMI and 18 (5.1%) out of 356 cases (mean 29.86 ± 8.62 months follow-up) diagnosed with STEMI died. During follow-up, 26% (13) of CV deaths occurred in the UAP group, 38% (19) in the NSTEMI group, and 36% (18) in the STEMI group.

In the follow-up of the cases, death from non-cardiac causes was recorded in 9 (2.7%) cases in the UAP group, in 3 (1.5%) cases in the NSTEMI group, and in 8 (2.2%) cases in the STEMI group (Table 6).

Relationship between long-term mortality and the use of statins, ACE inhibitors/ARBs, and beta-blockers in-hospital and discharge

When evaluated with the Kaplan-Meier curve:

During hospitalization, no reducing effect of statin use on long-term mortality was found (p = 0.14) (Fig. 1). It was detected that long-term mortality was significantly reduced with the use of ACE inhibitor / ARB (p = 0.007) (Fig. 2). It was found that the long-term mortality-reducing effect of beta-blocker use was significant (p = 0.014) (Fig. 3).

At discharge, the statin administration did not significantly affect long-term mortality (p = 0.16) (Fig. 1). However, the administration of ACE/ARB was significantly effective in long-term mortality (p = 0.004) (Fig. 2). It was detected that beta-blocker administration did not have a significant effect in long-te

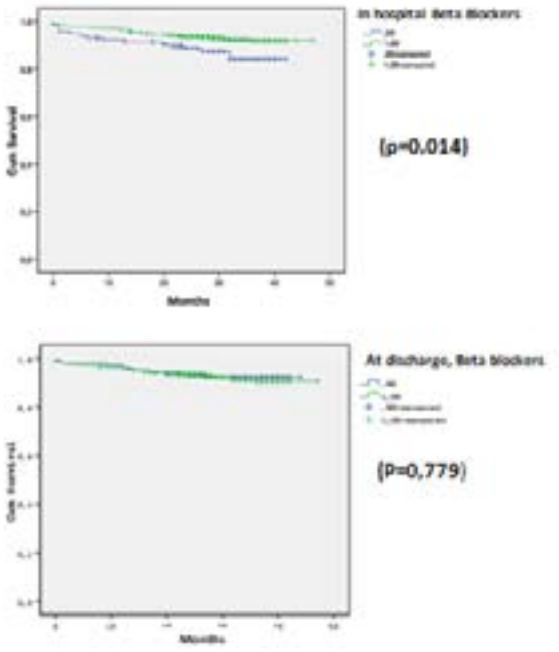

Fig. 3. Relationship between long-term mortality and the use of beta-blockers in-hospital and discharge

DISCUSSION

In this study, 339 (38%) cases diagnosed with UAP, 206 (23%) cases diagnosed with NSTEMI, and 356 (39%) cases diagnosed with STEMI were included in the analysis. In GRACE registry, the cases consisted of 29% with UAP, 30% with NSTEMI and 34% with STEMI. [3] The reasons why the UAP group was found to be proportionally higher in our case is that patients who did not undergo coronary imaging and misdiagnosed as UAP, not actually having ACS, could have been evaluated in the study. Another point is that there were 85 cases whose data could not be reached and therefore were excluded from the analysis, which may have contributed to the higher proportion of those diagnosed with UAP.

In terms of gender distribution, 706 out of 901 patients were male (78.4%), and 195 (21.6%) patients were female. This rate was similar to the rates found in the GRACE, Euro Heart Survey ACS and ENACT studies. [3-5] The gender distribution of the cases in our study reminds us the fact that male gender is an important risk factor for coronary artery disease.

The mean age of the patients was calculated as 57 in the STEMI group and 62 in the NSTEMI and UAP groups. In a study by Tokgözoğlu *et al*., when compared to EUROASPIRE III, the most important difference was that Turkish patients were younger than Europeans, and had higher rates of continued smoking, inactivity, and low HDL after MI. [6]

Among the other values determined in terms of CV disease and risk factors of the cases, the rates of hyperlipidemia, hypertension, diabetes, PCI and CABG history were found to be compatible with GRACE registry. [3]

When CV disease histories were evaluated before hospitalization, it was found that 75% of STEMI cases, 52% of NSTEMI cases and 48% of cases with UAP did not have a previous CV event. Another conclusion that can be drawn from this is that the frequency of ACS can be reduced by disseminating preventive treatments (hypertension, hyperlipidemia, Diabetes. etc) and strategies (weight management, avoiding smoking, avoiding sedantery life sytle, etc).

In the light of the evidences of studies such as HOPE, EUROPA, PEACE, ONTARGET, the effects of Renin Angiotensin System (RAS) blockers used for blood pressure control in primary prevention are clear. [7-9]

Another goal in primary prevention is the treatment of hyperlipidemia. In our study, it was found that 42% of STEMI cases, 53% of NSTEMI cases, and 58% of UAP cases had hyperlipidemia risk factors. These rates are also consistent with the data of the GRACE and Euro Heart Survey ACS study. [3, 4] The average LDL values were found to be 116 mg/dl in the STEMI group, 108 mg/dl in the NSTEMI group, and 113 mg/dl in the UAP group. These values are above the target values recommended by the treatment guidelines. 10 Some researchers, like Rosensen, sugges that there is a change in serum levels of plasma proteins as an acute phase response after MI, a decrease in lipid and lipoprotein levels starts in 24-48 hours and reaches a maximum in 4-7 days, and they return to their true value within 2 months after infarction. 11 This may explain the fact that the mean LDL levels of the cases were not excessively high. In primary prevention studies such as HPS, ASCOTT-LLA, and WOSCOPS, it is known that statins reduce the risk of mortality and major CV events in individuals with high CV risk. [12-14]

In the subgroups, no difference was found between the total cholesterol, HDL and TG values measured at hospitalization with the "post-hoc" evaluation. Mean total cholesterol measured for all groups was 189 ± 48 mg/dl, HDL was 42 ± 11mg/dl, and TG was 178 ± 134 mg/dl.

In a meta-analysis using the data of beta-blocker studies after MI, it was found that the odds ratio decreased by 23% in the long term and by 4% in the short term. 15 In a study by Gottlieb *et al*., involving 70000 patients using metoprolol, atenolol and propranolol, they showed 40% improvement in 2-year survival. 16 Beta-blockers are used in the acute phase of ACS because of their antiarrhythmic and antianginal effects, as well as their infarct-limiting effects. In the COMMIT/CCS study, it is emphasized that i.v. beta-blockers should be administered carefully, especially in patients with a high Killip class. 17 In our study, the rates of in-hospital beta-blocker use in STEMI, NSTEMI and UAP cases were 82%, 89% and 86% respectively. The rates of beta-blocker use during discharge in STEMI, NSTEMI and UAP cases was found 86%, 89% and 81% respectively. While a significant relationship was found between long-term (approximately 30 months) survival and in-hospital use of beta-blockers ($p = 0.01$), no significant relationship was found between use of beta-blockers at discharge and long-term survival ($p = 0.779$). This result suggests that beta-blockers are much more effective in the acute phase of ACS. Failure to use adequate doses and titration at the time of discharge may explain the lack of effect on long-term survival. Moreover, failure to use medications properly after discharge may also be related to the lack of expected long-term benefits. However, there are also publications in the literature showing that there may not be a long-term reduction in mortality with the use of high-dose titrated beta-blockers after ACS. 18

Given the lack of strong randomized controlled trial on the duration of beta-blocker usage in post-MI patients, a more personalized approach should be adopted (based on the LVEF, arrhythmias, etc). If the LVEF is low (< 40%), beta-blockers should be used for longer periods of time. [1, 2] For most of the patients with preserved ejection fraction, the evidence suggests short-term use of beta-blockers to reduce the risk of reinfarction and angina. Nasasra *et al*. evaluated 7392 ACS patients (without heart failure or left ventricular systolic dysfunction) between 2000 and 2016 and found that beta-blockers were prescribed to 6007 cases. The 30-day major adverse cardiac events (MACE) rates were similar in patients using and not receiving beta-blockers at discharge (9.0% and 9.5%, respectively). One-year survival was not significantly different between beta-blockers users and non-users (HR 0.8, 95% CI 0.58 to 1.11, $p = 0.18$). 19 In the GULF-COAST trial (a prospective multicenter cohort of ACS) in-hospital, 6-month and 12-month mortality were studied, in relation to beta blocker use: prior to admission, 24-hour post-admission and on discharge. Patients with LVEF > 40% were included in the study. Prior beta blocker use or its administration in 24 hours decreased in-hospital mortality (OR = 0.25, 95% CI [0.09-0.67]; OR = 0.16, 95% CI [0.08-0.35]; respectively). Beta blocker on discharge lowered 1-month mortality (OR = 0.28, 95% CI [0.11-0.72]), but had a neutral effect on mortality and reinfarction at 6 and 12 months. 20 Further studies are needed to understand the optimal duration of beta-blocker therapy post-MI. The REDUCE SWEDHEART study, which is planned to be completed in 2025, will help answer the questions that come to mind regarding the use of beta blockers in this patient group. [21]

The positive effects of ACE inhibitors/ARBs in ACS cases have been shown in many studies. These positive effects include the Inhibition of ventricular remodeling, improvement of endothelial functions, slowing of atherogenesis process and anti-inflammatory response. In the light of the studies of AIRE (with ramipril), GISSI-3 (with lisinopril), CONSENSUS-II (with enalapril), SAVE (with

captopril), ISIS-4 (with captopril), SMILE (with zofenopril), and TRACE (with trandolapril), it is recommended to start ACE inhibitor therapy in the early period (within 24 hours). 22-28 Angiotensin II receptor-1 blockers (ARB) are recommended as an alternative treatment for patients who cannot tolerate ACE inhibitor therapy. In the VALIANT study (with valsartan), in the CHARM-alternative subgroup (with candesartan), positive effects were demonstrated with the use of ARBs in these patients. [29-31]

In our study, the rates of in-hospital use of ACE inhibitor/ARB group drugs in STEMI, NSTEMI and UAP cases were determined as 87%, 91% and 84% respectively. The rates of administration of ACE inh/ARB to the cases during discharge in STEMI, NSTEMI and UAP cases were determined as 83%, 85% and 81% respectively. The relationship between survival of approximately 30 months and ACE inhibitor/ARB use in hospital and at discharge was significant (p = 0.007 and p = 0.004). This can be explained by the early onset of the hemodynamic regulating effects of RAS blockers (such as reduced afterload, reducing the risk of lung congestion) and the addition of anti-inflammatory, antiatherogenic and remodeling effects in the long term.

Sud *et al*. followed up a total of 165058 patients with a diagnosis of coronary artery disease (mean age 75 years, 65.5% male, 64.7% prescribed RAS blockers) for 4 years. They found that CV death and the frequency of MI or USAP were significantly lower in those receiving RAS blockers. In subgroup analyzes, it was determined that the decrease in MACE was more pronounced in those with a previous history of MI. [32]

As for statins, whose positive effects have been shown in large studies in primary and secondary prevention of coronary artery disease, it was detected that they were used in STEMI, NSTEMI and UAP at rates of 92%, 95%, and 83% respectively, during the in-hospital period, and were prescribed at rates of 89%, 92%, and 86%, respectively, in STEMI, NSTEMI, and UAP patients at discharge. Large statin studies in ACS cases can be listed as PROVE-IT, MIRACLE and A to Z. [33-35] The positive effects of statins in acute coronary syndromes may be related to their LDL-lowering and/or pleiotropic effects. [36] Among these effects are regulation of endothelial functions, anti-inflammatory effects, reduction of matrix metalloproteinase levels and tissue factor expression. In our study, the relationship between long-term survival and statin use in the hospital and at discharge was not found to be significant (p values 0.1 and 0.16, respectively). This may be related to the fact that high-dose statin therapy is not used, especially in the acute period. However, the efficacy and safety of high-dose statin use has been demonstrated in the PROVE-IT, MIRACLE, and A to Z studies. In a meta-analysis involving 26497 patients (including 16 randomized controlled trials), which assess high-intensity and standard statin regimens for efficacy and safety in patients with ACS, high-intensity statin therapy resulted in more clinical benefits regarding MACE compared with standard statin treatment in both Asian (RR = 0.77; 95%CI, 0.61-0.98; P = 0.03) and non-Asian (RR = 0.79; 95%CI, 0.71-0.89; P < 0.0001) patients. 37 The fact that a sufficient number of cases failed to reach the target LDL levels in the long term may be due to treatment non-compliance or treatment inadequacy after discharge, which can be shown as a reason for not detecting a statistical relationship with mortality.

In-hospital mortality rates were reported as 8% in STEMI cases, 5% in NSTEMI cases, and 3% in UAP cases in GRACE registries. [3] In-hospital mortality rates in our study were observed with a frequency of 7.6% in STEMI cases, 2.4% in NSTEMI cases, and 0.6% in UAP cases. In-hospital CV-related death was found to be 7% in STEMI, 2.4% in NSTEMI, and 0.6% in UAP. Among the causes of CV death were pulmonary edema, cardiac arrest, VF, cardiogenic shock and pulmonary embolism. Cardiogenic shock was the leading cause of in-hospital death in STEMI and NSTEMI cases, and according to our records, it accounts for 59% of in-hospital deaths.

In our study, an average of 30-month follow-up data was obtained in all diagnostic groups for long-term mortality assessment. During the follow-up, 70 (7.8%) cases died. When distributed according to diagnostic groups, 22 (6.5%) deaths occurred in UAP cases, 22 (10.7%) deaths in NSTEMI cases, and 26 (7.3%) deaths in STEMI cases. When 50 patients who died due to CV events are distributed according to their diagnoses, 13 (3.8%) of 339 patients were diagnosed with UAP (mean follow-up of 30.02 ± 7.41 months), 19 (9,2%) of 206 patients with NSTEMI (mean follow-up of 30 ± 9.21 months), and 18 (5.1%) of 356 patients with STEMI (mean follow-up of 29.86 ± 8.62 months). During follow-up, 26% (13) of CV-related deaths were seen in the UAP group, 38% (19) in the NSTEMI group, and 36% (18) in the STEMI group. Polonski *et al*. evaluated 13441 cases with MI (8250 STEMI, 5191 NSTEMI cases). In the 2-year follow-up of the cases, the long-term prognosis was

worse in the NSTEMI group. The frequency of death, re-infarction, stroke and CABG was found to be higher in the NSTEMI group ($p < 0.0001$). 38 In their observational study data, Terkelsen *et al*. reported that mortality rates were higher in NSTE-ACS cases than in STEMI cases, and there was a two-fold difference between the groups at the end of 4 years. [39] This difference in the medium and long term may be due to the different patient profiles, as seen in our study, because patients diagnosed with NSTE-ACS are older, and comorbidities such as diabetes and kidney failure are more common in these patients. This difference may be related to the more diffuse atherosclerotic process and the more intense inflammation in these cases. [40, 41]

CONCLUSION

In conclusion, our study, as a retrospective study, clearly demonstrates the clinical approach applied to the cases treated with the diagnosis of ACS in a university hospital clinic. Although it is a point to be criticized that the study is not prospective, it should be noted that in prospective studies it is highly probable that a more ideal treatment or application would be given to the patients. Therefore, the physician will be influenced by the study (bias). However, in this retrospective study, both the pre-hospital and in-hospital period and the following 2-year retrospective follow-up period were presented in a more realistic way without any influence. Obtained mortality, complication and treatment rates proved the truth, and these rates are objective data reflecting daily clinical practice as can be expected.

The most important limitation of our study was that the retrospective data obtained in the study was reliable to the extent which hospital electronic record system, patient file data and telephone feedback from patients allowed. Another limitation is that the study data were obtained from patients who were followed up and treated in the clinic about 15 years ago rather than current ACS patients, and that current drugs (for example, new antiaggregants) and clinical approaches (more widespread use of primary percutaneous coronary intervention) could not be applied to patient groups. Further multi-centered, retrospective and prospective clinical studies, in which current treatment recommendations are applied and more patient populations are included, will contribute to diminish the knowledge gap on this subject.

Authors' Contribution

Study Conception: BA, LMK,; Study Design: BA, LMK,; Supervision: LMK,; Materials: YBA, LMK,; Data Collection and/or Processing: BA,; Statistical Analysis and/or Data Interpretation: YBA, LMK,; Literature Review: BA, ISA,; Manuscript Preparation: BA, ISA and Critical Review: BA, ISA.

Conflict of interest

None declared.

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