ORIGINAL ARTICLE

Long-term follow-up of antithrombotic management patterns in acute coronary syndrome patients

Akut koroner sendromlu hastalarda antitrombotik yönetim yaklaşımlarının uzun dönem takibi

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ABSTRACT

Objective: The aim of this study was to evaluate the long-term, post-discharge follow-up of antithrombotic management patterns (AMPs), clinical outcomes, and real-life health status of patients hospitalized acute coronary syndrome (ACS).

Methods: A total of 1034 patients hospitalized for ACS within 24 hours of symptom onset who survived to discharge were included. Of those, 514 had ST-segment elevation myocardial infarction (STEMI) and 520 had unstable angina (UA)/ non-STEMI (NSTEMI). Data on follow-up AMPs, clinical outcomes, and health status were collected during 24 months of follow-up.

Results: The overall all-cause mortality was 6.4% (6.7% in UA/NSTEMI and 6.0% in STEMI patients), cardiovascular (CV) events had occurred in 9.4% (9.8% in UA/NSTEMI and 8.9% in STEMI patients), and bleeding events in 2.0% (2.3% in STEMI and 1.7% in UA/NSTEMI patients) of patients at 2 years after discharge. EuroQol-visual analogue scales scores increased from 78.9 to 81.6 in STEMI patients, and from 76.0 to 76.2 in UA/NSTEMI patients. Discharge and 2-year post-discharge scores for the EuroQol-5D index were 0.7 and 0.9, respectively in STEMI patients, while it was 0.8 for each period in UA/STEMI patients. Overall, 57.5% of the patients on dual antiplatelet (AP) therapy at discharge remained on this treatment at 2 years after discharge. The use of 1AP/0 anticoagulant (AC) and ≥2AP/0AC were associated with a CV event risk of 10.5% and 8.9%, a mortality risk of 10.5% and 5.8%, and a bleeding event risk of 0.9% and. 2.2%, respectively.

Conclusion: These findings in a real-life population of ACS patients emphasize the importance of longer-term follow-up of ACS patients surviving hospitalization and support the likelihood of more favorable long-term outcomes in ACS management with the current treatment practices.

ÖZET

Amaç: Akut koroner sendrom (AKS) nedeni ile yatışı yapılan hastalarda taburcu olma sonrası uzun dönem takip sonuçlarının antitrombotik yönetim yaklaşımları (AYY), klinik sonuçlar ve sağlık durumu açısından gerçek yaşam koşullarında değerlendirilmesidir.

Yöntemler: Bu kayıt çalışması semptom başlangıcını takiben 24 saat içinde AKS tanısı ile hastaneye yatışı yapılan ve taburcu edilebilen 1034 hastada (514'ü ST-segment yükselmeli miyokart enfarktüsü [STYME] ve 520'si kararsız angina/ ST-segment yükselmesiz miyokart enfarktüsü [KA/STYzME] tanılı) yürütüldü. AYY, klinik sonuçlar ve sağlık durumu açısından 24-aylık takip verileri kaydedildi.

Bulgular: Taburcu edilme sonrası 2 yıl için genel tüm-nedenli mortalite oranı %6.4 (KA/STYzME için %6.7 ve STYME için %6.0) olup, kardiyovasküler (KV) olay hastaların %9.4'ünde (KA/STYzME için %9.8 ve STYME için %8.9) ve kanama komplikasyonu ise hastaların %2.0'sinde (STYME için %2.3 ve KA/STYzME için %1.7) gözlendi. EuroQol-görsel analog skala skorları STYME'li hastalarda 78.9'dan 81.6'ya, KA/STYzME'li hastalarda 76.0 dan 76.2'ye yükseldi. Taburcu edilme sırasında ve takip eden 2 yıl sonunda EuroQol-5D indeks skorları STEMI grubunda sırasıyla 0.7 ve 0.9, UA/STEMI grubunda ise her iki dönemde de 0.8 idi. Taburcu olurken ikili antitrombosit (AT) tedavi altında olan hastaların %57.5' i taburcu olma sonrası 2 yıl süresince de aynı tedavi altında idi. 1AT/0 antikoagülan (AK) ve ≥2AT/0AK kullanımı ile ilişkili KV olay riski sırasıyla %10.5% ve %8.9, mortalite riski sırasıyla %10.5 ve %5.8 ve kanama riski sırasıyla %0.9 ve %2.2 olarak bulundu.

Sonuç: AKS'li hastaların gerçek yaşam koşullarında değerlendirilmesine yönelik sonuçlarımız, taburcu edilen AKS'li hastalarda uzun dönem takibin önemine ve AKS yönetimi güncel tedavi uygulamalarının daha iyi takip sonuçları ile olası ilişkisine işaret etmektedir.

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Acute coronary syndrome (ACS) is a clinical syndrome with acute plaque disruption or erosion leading to an abrupt imbalance between myocardial oxygen supply and demand.[1] Current medical therapies for patients with ACS focus on the coagulation cascade and platelet inhibition.[2,3]

However, despite progress in evidence-based treatments, a high 5-year mortality rate indicates that the consequences of ACS are still serious.[4] Thus, the management of ACS remains a clinical challenge.[4]

There is a shortage of evidence concerning physicians' practices in the use of antithrombotic drugs in different settings and countries, as well as the benefits and risks of the many potential antithrombotic agent combinations used in a real-life.[5]

Therefore, the present study, representing the Turkish arm of the multinational non-interventional EPICOR (long-tErm follow-up of antithrombotic management Patterns In acute CORonary syndrome patients) study, described the antithrombotic management patterns (AMPs) used for patients hospitalized with ACS and evaluated the relationship between AMPs and post-discharge clinical outcomes and health status in a real-life setting.

METHODS

Study population

EPICOR is a multinational, multicenter, observational, prospective, longitudinal cohort study. A total of 10,568 consecutive patients surviving an ACS (4943 with ST-segment elevation myocardial infarction [STEMI], and 5625 with unstable angina [UA]/non-ST-segment elevation myocardial infarction [NSTEMI]) were enrolled. The study was conducted between September 1, 2010 and March 31, 2011 at 555 hospitals in 20 countries including Argentina, Belgium, Brazil, Denmark, Finland, France, Germany, Greece, Italy, Luxembourg, Mexico, Netherlands, Norway, Poland, Romania, Slovenia, Spain, Turkey, UK, and Venezuela.[5] This is a subgroup analysis of data collected from 1034 patients (514 with STEMI and 520 with UA/NSTEMI) from 34 hospitals (3 regional/community/rural, 6 non-university general, 24 university general [n=24] and 1 other type of hospital) in Turkey. All 34 centers had a coronary/intensive care unit, and 33 (97.1%) centers had catheterization laboratory facilities, and a 24/7 primary percutaneous coronary intervention (PCI) program was available in 32 (97.0%).

Abbreviations:

AC	*Anticoagulant*
ACS	*Acute coronary syndrome*
AMP	*Antithrombotic management pattern*
AP	*Antiplatelet*
CV	*Cardiovascular*
DAPT	*Dual antiplatelet therapy*
NSTEMI	*Non-ST-segment elevation myocardial infarction*
PCI	*Percutaneous coronary intervention*
STEMI	*ST-segment elevation myocardial infarction*
UA	*Unstable angina*
VAS	*Visual analogue scale*

Men and women aged 18 years or older were eligible for inclusion in the study if (1) they were hospitalized for the first time within 24 hours of the onset of symptoms of the index event, and had a final diagnosis of STEMI or UA/NSTEMI, (2) they provided written informed consent, and (3) they completed a contact order form, in which they agreed to be contacted by telephone for regular follow-up interviews during a post-discharge phase of 24 months. Patients were not eligible to participate in the study if any of the following exclusion criteria were present: (1) ACS was a complication of or precipitated by surgery, trauma, or gastrointestinal bleeding, or was post-PCI; (2) ACS occurred during hospitalization for other reasons; (3) any condition/circumstance which, in the opinion of the investigator, could significantly limit the complete follow-up of the patient was present; (4) previous enrollment in the EPICOR study; (5) current participation in another clinical trial; or (6) presence of serious/severe comorbidities which, in the opinion of the investigator, may limit short-term (i.e., 6-month) life expectancy.

All of the patients underwent routine clinical assessments and received standard medical care, as determined by the treating physician. The patients did not receive any experimental intervention or treatment as a consequence of their participation in the study. The study was approved by the institutional ethics committee and was conducted in accordance with the Helsinki Declaration, the International Conference on Harmonization Good Clinical Practice Guideline, and local legislation.

Study procedures

The pre-hospital and in-hospital data were collected in the acute phase of the study. Follow-up information (until 2 years after discharge) was obtained through telephone interviews at 6 weeks and then every 3 months after the index event. During the interviews, data on follow-up medications, clinical outcomes

(cardiovascular [CV] events [myocardial infarction, UA, ischemic stroke, and transient ischemic attack], bleeding events, and death) and health status via the EuroQol-5D (EQ-5D) questionnaire were collected. The impact of AMPs on clinical outcomes was investigated by comparing 4 AMP subgroups (0 antiplatelet [AP]/0 anticoagulant [AC]; 1AP/0AC, ≥2AP/0AC and any AC).

Study parameters

Patient demographics; the rate of CV events, bleeding events, and death; the percentage of patients who remained on the AMP prescribed at discharge and variations in AMP following the index event up to 2 years post discharge with respect to bleeding vs. CV events; the final diagnosis of the index event (STEMI vs. UA/NSTEMI); and AMP subgroups were the study parameters. The EQ-5D scores at discharge and during follow-up were determined. The EQ-5D is a standardized measure evaluating the health status of patients that comprises 5 dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) at 3 levels (no problems, some problems, and severe problems).[6] Due to the non-interventional character of the study, there was no proactive safety data collection.

Statistical analysis

The data were expressed as mean, standard deviation (SD), count, and percent, as appropriate. Kaplan-Meier curves were created for clinical outcomes (CV events, bleeding events, and deaths). All statistical analyses were performed using the SAS statistical software system (version 9.2; SAS Institute, Inc., Cary, NC, USA).

RESULTS

Baseline characteristics

Of the 1034 patients enrolled in the study, 520 (50.3%) patients were diagnosed with UA/NSTEMI and 514 (49.7%) with STEMI. The majority of the patients were male (83.5%) and Caucasian (94.3%). The mean (SD) age of all of the patients was 56.5 (11.20) years. Overall, 48.1% had completed primary school education. The mean (SD) body mass index (BMI) was 26.9 (4.03) kg/m^2. A comparison of baseline characteristics and the final diagnosis of the index event revealed that patients in the STEMI and UA/NSTEMI groups were aged a mean (SD) 55.1 (11.7) years and 57.9 (10.6) years, with 460 (89.5%) and 403 (77.5) males, respectively. Most of the patients were primary school graduates (249 [48.4%] patients in the STEMI group and 248 [47.7%] patients in UA/NSTEMI group). The mean (SD) BMI (kg/m^2) was 26.8 (3.7) and 27.0 (4.3) in the STEMI and UA/NSTEMI patients, respectively.

Patient disposition

Two years of follow-up data were collected in 98.1% (n=504) of STEMI patients and 97.3% (n=506) of UA/NSTEMI patients; 4.9% were prematurely withdrawn from the study due to death, and there was a voluntary discontinuation 2.6%. Follow-up information was provided by the patient in 711 (68.8%) cases, and by the patient or a relative in 991 (95.8%) of 1034 over the 2 years.

Post-discharge clinical outcomes

The mortality rate 6 months post discharge was 3.9% (n=40), and 4.9% (n=51) died within the first year. Overall, 66 patients (6.4%) died during the entire 2-year follow-up period: 1.5% of CV, none of bleeding events.

From discharge to 6 months, 1 year, and 2 years of follow-up, 10 (0.97%), 14 (1.35%), and 21 (2.0%) patients had experienced a physician-confirmed bleeding event, respectively. In addition, 36 (3.5%), 52 (5.0%), and 97 (9.4%) patients had CV events within 6 months, 1 year, and 2 years post discharge.

Examination of the clinical outcomes during the entire 2-year follow-up period according to the final diagnosis of the index event (STEMI vs UA/NSTEMI) indicated that the incidence of a CV event in the STEMI and UA/NSTEMI groups was 12 (2.3%) and 24 (4.2%) in the first 6 months, 18 (3.5%) and 34 (6.5%) in the first year, and 46 (8.9%) and 51(9.8%) during the 2 years following discharge, respectively. The incidence of bleeding events in the STEMI and UA/NSTEMI groups was 5 (0.97%) and 5 (0.96%) at 6 months, 6 (1.2%) and 8 (1.5%) at 1 year, and 12 (2.3%) and 9 (1.7%) at 2 years after discharge, respectively. The incidence of death in the STEMI and UA/NSTEMI groups was 20 (3.9%) in each group at 6 months, 27 (5.3%) and 24 (4.6%) in the first year, and 31 (6.0%) and 35 (6.7%) at 2 years post discharge, respectively.

Post-discharge clinical outcomes according to antithrombotic management pattern

At the final assessment, 114 patients were taking only 1 AP (1AP/0AC group), while 910 patients were on ≥2 APs without an AC (≥2AP/0AC group) (Table 1). Use of 1AP/0AC and ≥2AP/0AC was associated with a CV event rate of 10.5% and 8.9%, a mortality rate of 10.5% and 5.8%, and a bleeding event rate of 0.9% and. 2.2%, respectively (Table 1). Kaplan-Meier estimates of the clinical outcomes by AMP group and the STEMI and UA/NSTEMI subgroups are shown in Figure 1.

Change in discharge antithrombotic medication during follow-up

Overall, 57.5% of the patients placed on dual antiplatelet therapy (DAPT; acetylsalicylic acid [ASA]+another antiplatelet) at discharge continued this treatment for 2 years, and this was similar in both STEMI and UA/NSTEMI patients (Table 2 and Table 3). Evaluation of the data indicated that of those who had experienced at least 1 bleeding event at the 1-year and 2-year mark, 5 of 13 (38.5%) and 3 of 19 (15.8%) remained on DAPT, respectively, while 101 of 130 (77.7%) and 91 of 145 (62.8%) maintained DAPT

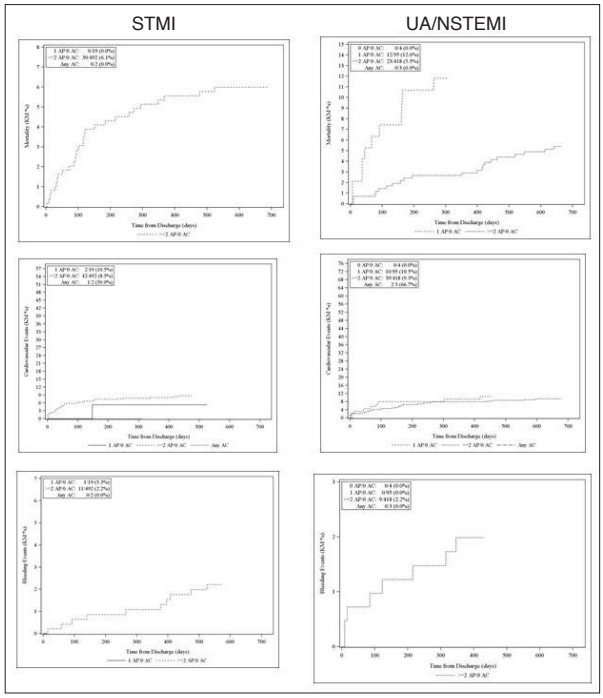

Figure 1. Kaplan-Meier estimates of mortality, cardiovascular events, and bleeding events by final diagnosis of the index event in antithrombotic management pattern groups. STEMI: ST-segment elevation myocardial infarction; UA/NSTEMI: Unstable angina/non-STEMI.

Table 1. Cardiovascular events, bleeding events, and mortality at 2-year post-discharge follow-up by index event final diagnosis according to antithrombotic management pattern group

	AMP groups							
	0AP/0AC		1AP/0AC		≥2AP/0AC		any AC	
	N	n_{event} (%)	N	n_{event} (%)	N	n_{event} (%)	N	n_{event} (%)
CV events								
STEMI	–	–	19	2 (10.5)	492	42 (8.5)	2	1 (50.0)
UA/NSTEMI	4	0 (0.0)	95	10 (10.5)	418	39 (9.3)	3	2 (66.7)
Total	4	0 (0.0)	114	12 (10.5)	910	81 (8.9)	5	3 (60.0)
Bleeding events								
STEMI	–	–	19	1 (5.3)	492	11 (2.2)	2	0 (0.0)
UA/NSTEMI	4	0 (0.0)	95	0 (0.0)	418	9 (2.2)	3	0 (0.0)
Total	4	0 (0.0)	114	1 (0.9)	910	20 (2.2)	5	0 (0.0)
Mortality								
STEMI	–	–	19	0 (0.0)	492	30 (6.1)	2	0 (0.0)
UA/NSTEMI	4	0 (0.0)	95	12 (12.6)	418	23 (5.5)	3	0 (0.0)
Total	4	0 (0.0)	114	12 (10.5)	910	53 (5.8)	5	0 (0.0)

AC: Anticoagulant; AP: Antiplatelet; AMP: Antithrombotic management pattern; CV: Cardiovascular; NSTEMI: Non-ST-segment elevation myocardial infarction; STEMI: ST-segment elevation myocardial infarction; UA: Unstable angina.

Table 2. Changes to discharge antithrombotic medications during follow-up and bleeding and cardiovascular events

	6 months	1 year	2 years*
	n (%)	n (%)	n (%)
Those on ASA+another antiplatelet at discharge (n=895)			
ASA+another antiplatelet	733 (85.8)	644 (76.8)	457 (57.5)
ASA only	53 (6.2)	71 (8.5)	161 (20.3)
Other antiplatelet only	59 (6.9)	104 (12.4)	143 (18.0)
Neither	9 (1.1)	20 (2.4)	34 (4.3)
Died	28	37	52
Lost to follow-up	13	19	48
At least 1 bleeding event	9 (1.1)	13 (1.5)	19 (2.4)
At least 1 cardiovascular event	112 (13.1)	144 (17.2)	166 (20.9)
Those on ASA+clopidogrel at discharge (n=866)			
ASA+clopidogrel	707 (85.7)	620 (76.4)	439 (57.2)
ASA only	50 (6.1)	67 (8.3)	153 (19.9)
Clopidogrel only	59 (7.2)	104 (12.8)	142 (18.5)
Neither	9 (1.1)	20 (2.5)	34 (4.4)
Died	28	36	51
Lost to follow-up	13	19	47
At least 1 bleeding event	8 (1.0)	11 (1.4)	17 (2.2)
At least 1 cardiovascular event	101 (12.2)	132 (16.3)	154 (20.1)
Those on ASA+ticlopidine at discharge (n=29)			
ASA+ticlopidine	26 (89.7)	24 (85.7)	18 (66.7)
ASA only	3 (10.3)	4 (14.3)	8 (29.6)
Ticlopidine only	0 (0.0)	0 (0.0)	1 (3.7)
Neither	0 (0.0)	0 (0.0)	0 (0.0)
Died	0	1	1
Lost to follow-up	0	0	1
At least one bleeding event	1 (3.4)	2 (7.1)	2 (7.4)
At least one cardiovascular event	11 (37.9)	12 (42.9)	12 (44.4)

ASA: Acetylsalicylic acid; CV: Cardiovascular. *The study follow-up had a total duration of 24 months. The last interview, corresponding to 24 months, was conducted within a timeframe of ±2 weeks. When a patient had the last phone call before 24 months (e.g., 1 or 2 weeks in advance), he/she became "lost" (i.e., a patient on drug was assumed to remain on drug until last known contact, but not any longer). For this reason, medication status until 23 months, rather than 24 months (when a large proportion of patients would appear as "lost"), is included.

among those who experienced at least 1 CV event in the first year and within 2 years, respectively.

Health status assessment

An increase in the EQ-5D index score from a mean (SD) of 0.8 (0.2) at discharge to 0.9 (0.2) in 1 year and to 0.9 (0.3) in 2 years post discharge was noted, as well as a change in the visual analogue scale (VAS) score from a mean (SD) of 77.4 (16.7) at discharge to 78.5 (19.5) at 2 years post discharge. The improvement in health status scores from discharge to 2 years post discharge was observed in both STEMI and UA/NSTEMI patients in terms of VAS scores (from 78.9 to 81.6 in STEMI patients and from 76.0 to 76.2 in UA/NSTEMI patients) and in the EQ-5D index (from 0.7 to 0.9 in STEMI patients and from 0.8 to 0.8 in UA/STEMI patients).

DISCUSSION

The survival and prognosis of patients who suffered an ACS in Turkey has not been well documented.

Table 3. Changes to discharge acetylsalicylic acid+another antiplatelet treatment up to 23 months and the index event final diagnosis

	STEMI	UA/NSTEMI
	n (%)	n (%)
Those on ASA+another antiplatelet at discharge	486	409
At 6 months post discharge		
ASA+another antiplatelet	392 (85.8)	341 (85.9)
ASA only	35 (7.7)	18 (4.5)
Antiplatelet only	26 (5.7)	33 (8.3)
Neither	4 (0.9)	5 (1.3)
Died	20	8
Lost to follow up	9	4
At least 1 bleeding event	4 (0.9)	5 (1.3)
At least 1 CV event	64 (14.0)	48 (12.1)
At 1 year post discharge		
ASA+another antiplatelet	338 (75.6)	306 (78.1)
ASA only	46 (10.3)	25 (6.4)
Antiplatelet only	52 (11.6)	52 (13.3)
Neither	11 (2.5)	9 (2.3)
Died	27	10
Lost to follow up	12	7
At least 1 bleeding event	5 (1.1)	8 (2.0)
At least 1 CV event	75 (16.8)	69 (17.6)
At 2 years* post discharge		
ASA+another antiplatelet	246 (57.1)	211 (58.0)
ASA only	95 (22.0)	66 (18.1)
Antiplatelet only	75 (17.4)	68 (18.7)
Neither	15 (3.5)	19 (5.2)
Died	31	21
Lost to follow up	24	24
At least 1 bleeding event	10 (2.3)	9 (2.5)
At least 1 CV event	85 (19.7)	81 (22.3)

ASA: Acetylsalicylic acid; CV: Cardiovascular; NSTEMI: Non-ST-segment elevation myocardial infarction; STEMI: ST-segment elevation myocardial infarction; UA: Unstable angina.

One year post discharge, the all-cause mortality rate (4.9%) in our cohort is in line with data from the main EPICOR study (3.9% of 10,568 patients).[7] In our cohort, no difference was noted in the 6-month post-discharge mortality rate, while a greater all-cause mortality was seen at 1 year post discharge in the STEMI patients and at 2 years post discharge in the UA/NSTEMI patients. This seems consistent with the greater mortality rate in NSTEMI patients starting from 1 year post discharge that have been reported in the literature.[8–10] Hence, effective implementation of adjunctive therapeutic strategies aimed at mortality reduction in the first months after primary PCI in STEMI patients and secondary prevention practices aimed at treating co-morbidities and other modifiable factors in NSTEMI patients seem to be helpful in ACS patients surviving hospitalization.[11,12] Notably, the 1-year mortality rates identified in our cohort were lower in both groups than seen in the literature.[8–10] The post-discharge 1-year and 2-year mortality rates of 4.9% and 6.4% in our cohort support the encouraging trends noted in the post-discharge death rates for both STEMI and NSTEMI patients and the improved long-term outcome using current treatment practices in ACS management.[13]

The high rate of CV events during the entire 2-year post-discharge follow-up period in our UA/NSTEMI patients is in line with the suggestion of non-ST-elevation-ACS contributing to more than twice as many high-risk patients as STEMI in the main EPICOR study[7] and consideration of NSTEMI as the ACS subtype most often associated with unfavorable outcomes, and thus the greater longer-term mortality and adverse risk factor profile when compared with STEMI patients.[14] Hence, our findings emphasize the importance of longer-term follow-up in ACS patients surviving hospitalization.

Our findings are consistent with data from the overall Eastern European cohort in terms of the rate of CV events and mortality during the 2-year follow-up period, as well as the percentage of patients who remained on DAPT (76.8% vs 80.7%). Global data from the overall cohort of the EPICOR study across Europe and Latin America revealed that of 8593 patients discharged on DAPT, 4859 (57%) remained on uninterrupted DAPT at the end of follow-up.[15] The authors also reported an association between DAPT interruption and an increased risk of CV events in the following week (hazard ratio: 2.29; 95% confidence interval: 1.08 to 4.84).[15] The fact that 76.8% of our patients remained on discharge DAPT at 1 year post discharge seems notable, given the strong association reported between the premature discontinuation of antiplatelet therapy within 1 year and increased CV events and death.[15,16] Also, unlike data from several

registries that highlight the underutilization of recommended post-discharge treatment, especially DAPT in ACS patients,[17,18] our findings indicate adherence to the guidelines pertaining to post-discharge 1-year AMPs, which may explain a lower 1-year mortality rate and a lower incidence of bleeding events in our cohort.

The percentage of patients who remained on the discharge DAPT regimen at 12 months and 23 months post discharge in our cohort was 38.5% and 15.8%, respectively, in patients with at least 1 bleeding event, and 77.7% and 62.8%, respectively, in patients with at least 1 CV event. In this regard, our findings highlight consideration of a 2.1% absolute reduction in the risk of death from CV causes, nonfatal myocardial infarction, or stroke at 12 months to offset a 1% absolute increase in risk of major/severe bleeding in the guidelines and the likelihood that this balance of benefit to risk will continue beyond 12 months.[19]

Overall bleeding events were less commonly observed in the Turkish cohort than in the overall Eastern European cohort (2.0% vs 3.2 %), particularly for NSTEMI patients (1.7% vs 3.7%). Considering the impact of selected AMPs on clinical outcomes, the use of 1AP/0AC and ≥2AP/0AC was associated with bleeding event rates of 0.9% and 2.2%, and a CV event rate of 10.5% and 8.9%, respectively, regardless of the index event diagnosis. All-cause mortality rate in cases of 1AP/0AC usage was 10.5% in the overall cohort, while it was 12.6% and 0.0% in the UA/NSTEMI and STEMI patients, respectively.

Notably, regarding the impact of different AMPs on clinical outcomes, data from the Eastern European cohort of the EPICOR study revealed "any AC" type of AMP to be associated with the highest rates of CV events (13.4%), mortality (8.9%), and bleeding events (6.3%), as compared with the 1AP/0AC and ≥2AP0AC categories. In our cohort, the "any AC" category was also associated with the highest mortality rate, while no CV events or bleeding was observed in patients under "any AC" AMP. However, one must remain prudent when comparing these results, given that only 5 of 1034 patients were under "any AC" type of AMP in our cohort, and therefore, categorical conclusions cannot be drawn.

The PEGASUS-TIMI 54 (Prevention of Cardiovascular Events in Patients with Prior Heart Attack Using Ticagrelor Compared to Placebo on a Background of Aspirin-Thrombolysis in Myocardial Infarction 54) trial report indicated that the addition of intensive AP therapy with ticagrelor to low-dose aspirin significantly reduced the risk of CV death, myocardial infarction, and stroke, and increased the risk of major bleeding in high-risk patients with a history of myocardial infarction.[20] A recent, adjusted, indirect meta-analysis demonstrated that both prasugrel and ticagrelor were significantly superior to clopidogrel in terms of 12-month risk of mortality without any significant difference in major bleeding.[21]

In our cohort, the majority of patients were on ASA+clopidogrel therapy at discharge, while only 29 were on ASA+ticlopodine therapy, and none were on ASA+prasugrel or ticagrelor therapy. The rates of mortality and CV events under a ≥2AP/0AC regimen at the 2-year post-discharge mark in our cohort of ACS patients surviving hospitalization emphasizes the likelihood of better clinical outcomes in the long-term with more prevalent use of these novel agents. Furthermore, bleeding rates were minimal and no event was fatal in our cohort. Given the lower rate of continuation of medication in patients with at least 1 bleeding event post discharge, our findings support the likelihood of improved management and better use of guideline-recommended therapies in ACS patients via the more frequent use of newer AC and AP agents with a potentially lower bleeding risk.[22]

In our study, a younger age at ACS presentation was evident compared with registries such as the contemporary FAST-MI 2010 (French Registry on Acute ST-elevation and non ST-elevation Myocardial Infarction 2010)[23] registry and the GRACE (Global Registry of Acute Coronary Events)[24] registry. The EUROASPIRE III (European Action on Secondary and Primary Prevention by Intervention to Reduce Events III) survey also revealed a greater percentage of young patients with myocardial infarction (<50 years: 20% vs 12.7%) in the Turkish cohort.[25] Hence given the greater long-term mortality rate expected in the elderly compared with younger ACS patients and the demonstration of age as the most significant independent predictor of 1-year mortality at hospital discharge after an ACS in the main EPICOR study,[7] the lower overall long-term mortality rate in our cohort may also be associated with the younger age distribution.

In addition, given that the EQ-5D was listed among the highly significant independent predictors of 1-year mortality at hospital discharge after an ACS in the main EPICOR study,[7] the markedly improved EQ-5D scores from discharge to 2 years post discharge in the STEMI group (rather than in UA/NSTEMI patients) in our cohort seems significant.

It should also be noted that analysis of differences between Turkey and other European countries included in the EUROASPIRE III survey revealed a greater likelihood of no current follow-up by a physician in the Turkish cohort (12% vs 2.2%).[24] In the present cohort, a lack of follow-up information from the patient or a relative was noted in 4.2% of patients, while in 31.2% of patients, no follow-up data was available based on information from the patient, per se.

Study limitations

Certain limitations to this study should be considered. First, while a naturalistic design provides a good guarantee of the external validity of the results, our study was limited by issues inherent in the observational methodology, including the potential of not capturing or of misclassifying factors that affect clinical decision-making. Second, since treatment alterations may be related to various clinical approaches, including a new ischemic event necessitating more antithrombotic drugs or bleeding leading to restriction in antithrombotic drug use, a causal relationship cannot be made. Third, since only hospital survivors were recruited, the nature of the relationship when fatal events are considered is not known. Fourth, due to the exclusion of patients who died in the hospital, usually older and sicker patients, EPICOR recruited a slightly younger group than that seen in registries of all-comers. This represents a limitation for the assessment of total in-hospital treatments and outcomes as chosen by several previous registries, mostly focused on acute care. However, given the low current in-hospital mortality of ACS, it will still be useful to demonstrate the most frequently used AMPs during hospitalization as well as variability. Moreover, this potential limitation has no influence on the validity of the long-term results of the study, which will demonstrate the real profile of ACS patients surviving hospitalization, the main focus of EPICOR.

Conclusion

In conclusion, our findings in a real-life population of ACS patients surviving hospitalization enrolled in the Turkish arm of the EPICOR study revealed CV events in 9.4%, bleeding events in 2.0%, and mortality in 6.4% of the overall population. In all, 57.5% of the patients were continuing the discharge AMP at the end of the 2-year post-discharge follow-up. Our findings underscore the importance of longer-term follow-up of ACS patients surviving hospitalization and support the idea that current evidence-based treatment practices are likely to offer improved long-term outcomes for ACS patients surviving hospitalization. The impact of the index event final diagnosis as well as different AMPs on clinical outcomes, along with distinct mortality trends in STEMI and NSTEMI patients, depending on the duration of follow-up, are also emphasized.

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Keywords: Acute coronary syndrome; antithrombotic management; non-ST-segment elevation myocardial infarction; real-life setting; ST-segment elevation myocardial infarction; Turkey.

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