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CLINICAL PROFILE AND MANAGEMENT OF PATIENTS WITH INCIDENT AND RECURRENT ACUTE MYOCARDIAL INFARCTION IN ALBANIA – A CALL FOR MORE FOCUS ON PREVENTION STRATEGIES

KLINIČNI PROFIL IN ZDRAVLJENJE PACIENTOV S PRVIM IN PONOVNIM POJAVOM AKUTNEGA MIOKARDNEGA INFARKTA V ALBANIJI – POZIV ZA VEČJO POZORNOST NA PODROČJU PREVENTIVNIH STRATEGIJ

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ABSTRACT

Background. The clinical profile of acute myocardial infarction (AMI) patients reflects the burden of risk factors in the general population. Differences between incident (first) and recurrent (repeated) events and their impact on treatment are poorly described. We studied potential differences in the clinical profile and in-hospital treatment between patients hospitalised with an incident and recurrent AMI.

Methods. A total of 324 patients admitted in the Coronary Care Unit of 'Mother Teresa' hospital, Tirana, Albania (2013-2014), were included in the study. Information on AMI type, complications and risk factors was obtained from patient's medical file.
Logistic regression analyses were used to explore differences between the incident and recurrent AMIs regarding clinical profile and in-hospital treatment.

Results. Of all patients, 50 (15.4%) had a prior AMI. Compared to incident cases, recurrent cases were older (P=0.01), more often women (P=0.01), less educated (P=0.01), and smoked less (P=0.03). Recurrent cases experienced more often heart failure (HF) (OR=2.48; 95% CI: 1.31–4.70), impaired left ventricular ejection fraction (OR=1.97; 95% CI: 1.05–3.71), and multivessel disease (OR=6.32; 95% CI: 1.43–28.03) than incident cases. In-hospital use of beta-blockers was less frequent among recurrent compared to incident cases (OR=0.45; 95% CI: 0.24–0.85), while no statistically significant differences between groups were observed regarding angiotensin-converting enzyme inhibitor/angiotensin receptor blocker, statin, aspirin or invasive procedures.

Conclusion. A more severe clinical expression of the disease and underutilisation of treatment among recurrent AMIs are likely to explain their poorer prognosis compared to incident AMIs.

Keywords:
acute myocardial infarction, epidemiology, in-hospital treatment, prevention, Albania

IZVLEČEK

***Ozadje**. Klinični profil pacientov z akutnim miokardnim infarktom (AMI) odraža breme dejavnikov tveganja v splošni populaciji. Razlike med prvim in ponovnimi pojavi in njihovim vplivom na zdravljenje so slabo opisani. Raziskali smo morebitne razlike v kliničnem profilu in bolnišničnim zdravljenjem pri pacientih s prvim pojavom AMI in tistih s ponovnim pojavom.*

***Metode**. V raziskavo je bilo skupno vključenih 324 pacientov, ki so bili v letih 2013-2014 sprejeti na Enoto za koronarno nego bolnišnice Matere Terezije v Tirani v Albaniji. Iz kartotek pacientov so pridobili podatke o vrsti AMI, zapletih in dejavnikih tveganja.*
Za ugotavljanje razlik med prvimi in ponovnimi AMI so bile uporabljene analize logistične regresije z upoštevanjem kliničnega profila in bolnišničnega zdravljenja.

***Rezultati**. Med vsemi pacienti jih je 50 (15,4%) že enkrat doživelo AMI. V primerjavi s pacienti s prvim pojavom so bili tisti s ponovnimi pojavi starejši (P=0,01), pogosteje so bile to ženske (P=0,01), imeli so nižjo izobrazbo (P=0,01) in so manj kadili (P=0,03). Pacienti s ponovnimi pojavi so v primerjavi s pacienti s prvim pojavom pogosteje izkusili odpoved srca (OR=2,48; 95% CI: 1,31-4,70), oslabljeno izmetno frakcijo levega prekata (OR=1,97; 95% CI: 1,05-3,71) in multivaskularno bolezen (OR=6,32; 95% CI: 1,43-28,03). Uporaba beta-blokatorjev v bolnišnični obravnavi je bila manj pogosta pri pacientih s ponovnim pojavom v primerjavi s pacienti s prvim pojavom AMI (OR=0,45; 95% CI: 0,24-0,85), medtem ko ni bilo opaziti statistično pomembnih razlik v zvezi z uporabo zaviralcev angiotenzinske konvertaze/blokatorjev receptorjev angiotenzina, statinov, aspirina ali invazivnih postopkov.*

***Zaključek**. Resnejša klinična slika bolezni in manjša poraba zdravil med pacienti s ponovnim pojavom AMI tako lahko razložita njihovo slabšo prognozo v primerjavi s pacienti s prvim pojavom AMI.*

Ključne besede:
akutni miokardni infarkt, epidemiologija, bolnišnično zdravljenje, preventiva, Albanija

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1 BACKGROUND

Acute myocardial infarction (AMI) is the most serious clinical expression of coronary heart disease (CHD). The substantial reduction in mortality following an incident (first) AMI (1-4), combined with aging of the population has led to a growing number of AMI survivors who are at risk of experiencing a recurrent (repeated) event. Although recurrent events account for the minority of all AMI-related hospitalisations (5, 6), their prognosis is poor (7-9), contributing thus substantially to the overall cardiovascular mortality.

Incident events reflect the burden of coronary risk factors in the population at large (10), whereas recurrences are further influenced by the quality of coronary care during the acute phase of the incident event and secondary prevention (11).

In Albania, CHD death rates are among the highest in the Southeast Europe (12). The burden of CHD (both mortality and hospitalisations) has increased in the last decades (13), rendering it the main cause of premature mortality in Albania (14). Simultaneously, the prevalence of classical coronary risk factors in the population is high. A health survey conducted in 2001 in Tirana, reported that among 1120 participants aged 25 years or older, the prevalence of obesity, diabetes mellitus (DM), hypertension and smoking (current) was 29% (15), (9.7%) (16), 31.8% (17) and 28% (18), respectively. Later reports confirmed the high burden of these risk factors; the prevalence of hypertension and obesity (in 2008) and smoking (in 2011) were 36.5%, 21.6% and 26% (19), respectively. Despite these unfavourable developments, the difficult transition from a totalitarian communist regime toward a free, marked-oriented economy in Albania was characterised by the lack of sufficient resources allocated to health care (20). As a consequence, preventive strategies have not been considered a priority. No structured national or regional primary prevention strategies have been applied at the population at large, despite their proven role in reducing CHD burden (21). Further, no structured rehabilitation programmes are available to coronary patients, and secondary prevention is confined to medical advice provided by specialists upon hospital discharge and, occasionally, during check-ups at the family doctor's office. The consequences of such lack of preventive strategies on the clinical profile of AMI patients and their management are not studied in Albania, and are poorly described elsewhere.

Thus, the objective of the current study was to explore the clinical profile and in-hospital treatment of patients hospitalized with an AMI, with a special focus on the differences between patients with and without history of prior AMI.

2. SUBJECTS AND METHODS

2.1 Study Population

This study included 324 consecutive patients hospitalized during 2013-2014, with an AMI in the Coronary Care Unit (CCU) of the University Hospital Centre 'Mother Teresa',' the only public hospital providing specialized coronary care in Tirana, the capital of Albania.

2.2 Data Collection

Information on patients' age, gender, educational attainment, height and weight, systolic and diastolic blood pressure, AMI type [ST-elevation myocardial infarction (STEMI) versus non-ST-elevation myocardial infarction (NSTEMI)], location, major complications [including heart failure (HF), ventricular fibrillation (VF) and 2nd or 3rd degree atrioventricular block (AVB)], and in-hospital treatment was obtained from patients' medical charts.

To derive the prevalence of each major risk factor, we combined self-reported information on risk factors and medication use prior to hospitalisation with blood pressure, fasting glucose, and total cholesterol values measured during admission (22). A history of prior AMI was defined as a previous hospitalisation with AMI as the main discharge diagnosis.

2.3 Statistical Analyses

Continuous variables were presented as means and standard deviations (SD), and categorical variables were presented as percentages. Independent sample t-test was used to compare mean values of the continuous variables. Categorical variables were compared using the chi-square test or Fisher's exact test in cases of small sample sizes.

Logistic regression models were used to explore differences between incident and recurrent cases regarding AMI complications and in-hospital treatment. They were adjusted for covariates known to influence the outcome, and showed association with the exposure in our data. To account for the role of comorbidities in a potentially influencing use of beta-blockers [chronic obstructive pulmonary disease (COPD), systolic blood pressure (SBP)<85 mm Hg or AVB], angiotensin-converting enzyme inhibitors (ACEI)/angiotensin receptor blockers (ARB) (SBP<85 mm Hg) and aspirin (peptic ulcer), we repeated the analyses after excluding patients with any of these conditions. The results of these analyses (referred to in the text as 'additional analyses') are presented as supplemental material online.

We tested and did not find a statistically significant interaction between gender and history of prior AMI. All models were adjusted for age and gender, and results expressed as odds ratios (OR) and 95% confidence intervals (CI) for prevalent versus incident (the reference

category) AMIs. Two-sided tests with the 0.05 significance level were used. Analyses were performed using STATA software, version 13.

3. RESULTS

3.1 Characteristics of the Study Population

Characteristics of the study population are summarized in Table 1. The mean (SD) age of the cohort was 64.4 (11.4) years and the majority (73.8%) were men. Overall, 44.1% of patients had attained only primary education and 55.9% secondary or tertiary education.

The prevalence of current smoking, hypertension, diabetes mellitus (DM), and hypercholesterolemia was 59.9%, 83.3%, 50.6% and 55.3%, respectively. At least one major risk factor was observed in 98.8%, and all four major risk factors in 13.9% of the study cohort.

3.2 The Clinical Profile of Patients

STEMI accounted for 83.9% of the study population (Table 2). AMI was complicated with HF in 33.6% of the patients. The proportion of impaired LVEF, 2nd or 3rd degree AVB or VF in the study population were 31.2%, 4.0% and 4.9%, respectively. Compared to incident cases, recurrent cases had multivessel CHD (P=0.03), HF (P<0.01), or impaired LVEF (P=0.01) (Table 2).

Table 1. Characteristics of the study population.

Patient characteristics	All patients (n=324)	Incident cases (n=274)	Recurrent cases (n=50)	P value
Age (years), mean (SD)	64.4 (11.4)	63.7 (11.5)	68.4 (10.1)	0.01
Gender (male), n (%)	239 (73.8)	210 (76.6)	29 (58.0)	0.01
Education, n (%)				
Primary	143 (44.1)	113 (41.2)	30 (60.0)	0.01
Secondary or higher	181 (55.9)	161 (58.8)	20 (40.0)	
Coronary risk factors, n (%)				
Smoking	194 (59.9)	171 (62.4)	23 (46.0)	0.03
Hypertension	270 (83.3)	229 (83.6)	41 (82.0)	0.78
Diabetes	164 (50.6)	135 (49.3)	29 (58.0)	0.26
Hypercholesterolemia	179 (55.3)	149 (54.4)	30 (60.0)	0.46
At least one risk factor	320 (98.8)	270 (98.5)	50 (100.0)	0.39
All four risk factors	45 (13.9)	39 (14.2)	6 (12.0)	0.63
Comorbidities, n (%)				
Atrial fibrillation	39 (12.1)	26 (9.4)	13 (27.7)	<0.01
Peripheral artery disease	23 (7.1)	20 (7.2)	3 (6.4)	0.84
Cerebrovascular disease	25 (7.4)	19 (6.9)	6 (12.8)	0.16
COPD	17 (5.3)	14 (5.1)	3 (6.4)	0.71
eGFR<60 mL/min/1.73m^2	77 (23.8)	59 (21.5)	18 (36.0)	0.03
Peptic ulcer	23 (7.1)	19 (6.9)	4 (8.0)	0.79
Pulse (beats/min), mean (SD)	78 (16.8)	77 (16.5)	80 (18.5)	0.37
Hemoglobin* (g/dl), mean (SD)	12.8 (1.9)	12.9 (1.8)	11.9 (1.9)	<0.01

COPD: chronic obstructive pulmonary disease; eGFR: estimated glomerular filtration rate.

* 4% of patients had missing values

Incident cases were younger (P=0.01), more often men (P=0.01), and had attained a higher education (P=0.01) than recurrent cases. No statistically significant differences between groups were observed regarding hypertension, DM, and hypercholesterolemia. Smoking was more frequent among the incident cases (P=0.03).

Table 2. Clinical profile and in-hospital treatment of patients with an acute myocardial infarction.

	All patients (n=324)	Incident cases (n=274)	Recurrent cases (n=50)	P value
		Clinical profile		
STEMI, n (%)	271 (83.9)	230 (84.3)	41 (82.0)	0.69
Multivessel CAD, n (%)	164 (75.9)	136 (73.1)	28 (93.3)	0.03
Heart failure, n (%)	109 (33.6)	81 (29.6)	28 (56.0)	<0.01
LVEF<0.45, n (%)	101 (31.2)	77 (28.1)	24 (48.0)	0.01
AVB (2nd/3rd degree), n (%)	13 (4.0)	10 (3.7)	3 (6.0)	0.44
VF, n (%)	16 (4.9)	11 (4.0)	5 (10.0)	0.07
		In-hospital treatment		
Beta-blockers	192 (59.3)	172 (62.8)	20 (40.0)	0.01
ACEI/ARBs	206 (63.6)	179 (65.3)	27 (54.0)	0.12
Statins	314 (96.9)	268 (97.8)	46 (92.0)	0.05
Aspirin	308 (95.1)	261 (95.3)	47 (94.0)	0.71
All four drug classes	144 (44.4)	128 (46.7)	16 (32.0)	0.05
Invasive procedures				
Coronary angiography	222 (68.5)	192 (70.1)	30 (60.0)	0.16
Revascularization*	139 (64.4)	122 (65.6)	17 (56.7)	0.34

STEMI: ST-segment elevation myocardial infarction; CAD: coronary artery disease; LVEF: left ventricular ejection fraction; AVB: atrioventricular block; VF: ventricular fibrillation; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker.
* Percutaneous coronary intervention or coronary artery bypass grafting among patients undergoing coronary angiography.

The results of age and gender-adjusted analyses revealed an increase in the odds of HF (OR=2.48; 95% CI: 1.31–4.70), impaired LVEF (OR=1.97; 95% CI: 1.05–3.71), or multivessel CAD (OR=6.32; 95% CI: 1.43–28.03) among recurrent cases compared to incident ones. No statistically significant differences were observed between groups regarding AMI type and other complications (Figure 1).

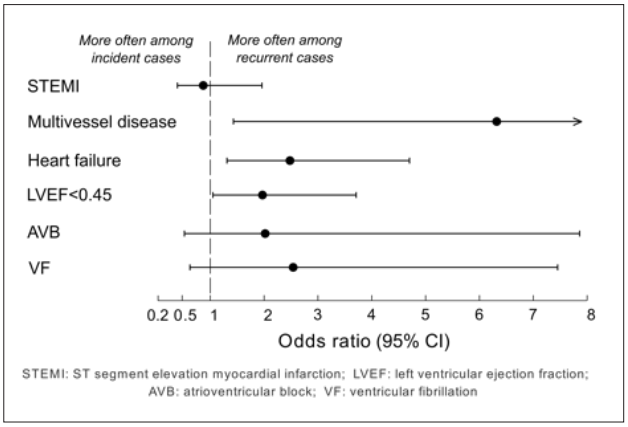

Figure 1. Differences in the clinical profile between patients hospitalized with an incident and recurrent acute myocardial infarction.

3.3 In-Hospital Treatment

The utilisation rates for beta-blockers, angiotensin-converting enzyme inhibitors (ACEIs)/angiotensin receptor blockers (ARBs), statins, and aspirin were 59.3%, 63.6%, 96.9%, and 95.1%, respectively (Table 2).

Less than half (44.4%) of the study population received all four drug classes. Only 68.5% of the patients underwent coronary angiography. Of those, 64.4% received coronary revascularisation. The proportion of patients receiving a beta-blocker or statin was lower among recurrent compared to incident cases (P=0.01 and P=0.03, respectively). No statistically significant differences in the utilisation of other drug classes or invasive diagnostic and treatment procedures were observed between the two groups.

Adjusted analyses revealed lower utilisation rates of beta-blockers among recurrent cases as compared to incident cases (OR=0.45; 95% CI: 0.24–0.85) (Figure 2).

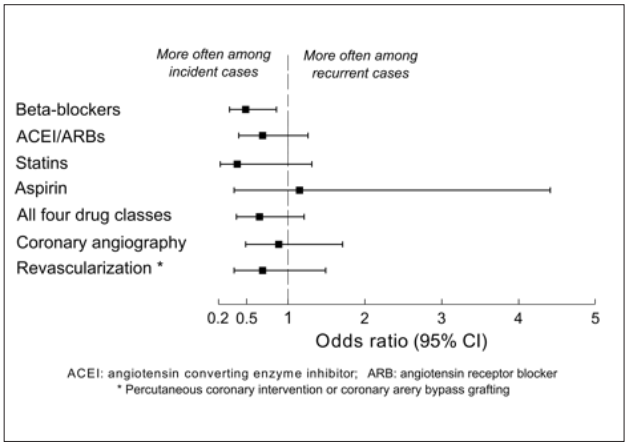

Figure 2. Differences in the in-hospital treatment between patients hospitalized with incident and recurrent acute myocardial infarction.

No statistically significant differences between groups were observed regarding ACEIs/ARBs, statins or aspirin use [(OR=0.67; 95% CI: 0.36–1.26), (OR=0.34; 95% CI: 0.12–1.31) and (OR=1.15; 95% CI: 0.30–1.31), respectively].
A similar pattern was observed in the use of invasive diagnostic and treatment procedures. No statistically significant differences between the two groups were found with regard to coronary angiography (OR=0.88; 95% CI: 0.45–1.71) or revascularisation (OR=0.67; 95% CI: 0.30–1.49).

The results of additional analyses were similar to those of the main analyses in terms of direction of the association and level of significance (Table 1, supplementary material online).

4. DISCUSSION

4.1 Main Findings

The burden of coronary risk factors in our study was very high among both incident and recurrent cases. The prevalence of HF, impaired LVEF, and multivessel CAD (all reliable indications of AMI's clinical severity) were higher among recurrent compared to incident cases. The use of evidence-based drugs in our study varied widely and, compared to incident cases, recurrent cases seemed to use less often evidence-based treatment, including revascularisation. However, the differences were statistically significant only with regard to the use of beta-blockers.

4.2 A Comparison with Other Studies

Data from a case-control study conducted in Tirana between 2003 and 2006, and enrolling 467 acute coronary syndrome (ACS) patients (i.e., a combination of AMI and unstable angina pectoris – UAP), revealed that the prevalence of obesity (BMI≥30), hypertension, DM, and current smoking were 20.6%, 29.6%, 15.8%, and 42.2%, respectively (23). Among 809 incident ACS cases admitted to CCU in Tirana in 2009, the prevalence of current smoking, hypertension, family history of CHD, and overweight/obesity were 63%, 58%, 33%, and 30%, respectively. All patients had at least two coronary risk factors (24).

Several factors may have contributed to the higher burden of coronary risk factors in our study, compared to other studies conducted in Albania (23, 24). We included in the analyses, only AMI patients, while others combined AMI and UAP patients. Further, the study by Balla et al. (24) included only incident cases, while our study population was a mixture of incident and prevalent cases. Our study population comprised severely ill patients requiring hospitalisation in CCU, whereas in the study by Burazeri et al. (23), patients were recruited from CCU and hospital wards. Despite these differences in the populations studied, a worrying increase in the burden of risk factors over time cannot be rule out, and needs further investigation.

Internationally, the prevalence of smoking, hypertension, DM, and hyperlipidaemia among 122 458 CHD patients enrolled in 14 randomised control trials was 37.9%, 43.2%, 17.5%, and 34.8%, respectively. Eighty-two percent of patients had at least one, whereas 1.0% of the cohort had all four major coronary risk factors (25). Data from the National Cardiovascular Registry (NCDR) showed that 71.4% of AMI patients reported to suffer from hypertension, and 30.5% from DM (26).

We could not identify previous publication from Albania comparing incident and recurrent cases regarding their clinical profile or in-hospital treatment. International studies have suggested that recurrent cases presented

more often with pulmonary oedema, cardiogenic shock and asystole (27), and have a higher incidence of HF (28), compared to incident cases.

The results of the analyses comparing in-hospital treatment between incident and recurrent cases have been less consistent. In the Netherlands, utilisation rates of aspirin, beta-blockers, and statins among 4718 STEMI patients were higher in incident, compared to recurrent cases (9). In the USA, similar rates were reported in incident and recurrent cases (28). With regard to revascularisation procedures, higher rates were observed in incident, compared to recurrent cases in the USA (28) and Israel (27). The direction of the association in our study suggests a more severe clinical expression of the disease with concurrent lower utilisation rates of medications in recurrent compared to incident cases. However, due to the lack of statistical significance (possibly affected by the relatively small sample size), these findings should be interpreted with caution.

A direct comparison of our findings with previously published analyses on the use of invasive procedures is challenging, as the use of these procedures is largely influenced by patients' age, gender, comorbidities, prior AMI status, and the study period – all factors that differ widely between the published studies.

4.3 Potential Mechanisms and Implications

The high burden of coronary risk factors reflects the lack of prevention measures in the population at large in Albania. Interventions aiming at reducing the burden of coronary risk factors have proven to be cost-effective (29), and can reduce CHD mortality up to 75% (30-33). Nevertheless, the majority of resources in the past 2-3 decades were allocated into tertiary care institutions, aiming at modernising the system and improving the quality of care. The observed unfavourable trends in CHD mortality in Albania, combined with our findings, point out to the immediate need for a shift in the focus of attention toward preventive measures. In 2014, health authorities launched a nationwide health campaign, inviting citizens aged 40-65 years (expanded lately to include those aged 35-70 years) to undergo a medical examination aiming at screening for CVD (with a special focus on CHD), cancer, and other relevant conditions. This was the first step in the long process of identifying the burden of coronary risk factors in the population. This campaign can lay the ground for policy and legislative changes to tackle many aspects related to diet and lifestyle, aiming at reducing the burden of risk factors and, subsequently, CHD in Albania.

Another worrying finding is the prevalence of risk factors among recurrent cases, which – with an exception of smoking – is similar to (if not higher than) that of incident cases. This reflects the failure of patients with overt CHD to change their risk profile and conduct a healthy lifestyle. Many factors may have contributed to this failure, including i) the lack of personalised recommendations upon discharge from the hospital, ii) lack of rehabilitation programs, iii) poor adherence to treatment, iv) no coordination between different actors involved in the health care system (i.e., the family doctor and specialist) during the follow up. Further studies are needed to tackle each potential component individually and provide a new insight into this phenomenon. Further, national guidelines specifying treatment goals, frequency of follow up visits and role of specialist (versus the family doctor) during the follow up are needed to optimise medical care and reduce the rate of new coronary events in this vulnerable subset of population.

Recurrent cases present with a more severe form of the disease, yet, the medication use among them tend to be suboptimal compared to that in incident cases. The reasons for these differences are not clearly explained. One hypothesis is that certain comorbidities and/or AMI complications represent contraindications to individual cardiac drugs. We addressed this issue by conducting additional analyses where we excluded patients with such comorbidities and/or AMI complications. This was associated with a slight increase in the use of beta-blockers (+ 2.4%), ACEI/ARBs (+2.4%), statins (+0.9%), and all four drug classes (+3.8%). However, the differences in the use of cardiac drugs between recurrent and incident cases did not change substantially, indicating that factors other than comorbidities might be involved.

Another reason might be related to the fact that medical staff is reluctant to perform revascularisation procedures among severely ill patients due to a poorer outcome compared to that in uncomplicated AMI cases (34).

4.4 Study Limitations

Our study has several limitations. The relatively small sample size and low number of patients with a recurrent event, is most probably responsible for the statistically non-significant findings, even though the point estimates indicate that recurrent AMIs present at the hospital with a more severe clinical expression, and underutilise the recommended drug classes compared to incident AMIs.

Our sample size did not allow us to explore the role of medications taken prior to hospitalisation on the burden of risk factors, either. Furthermore, we could not determine the proportion of patients with controlled level of risk factors. In addition, we did not know the proportion of patients who might have been scheduled to receive revascularisation upon AMI discharge, as follow-up information was not available. We therefore restricted our focus on treatment during MI hospitalization. The

distinction between 'never' and 'former' smokers was not available in our study. Consequently, we could not discriminate between patients who smoked and gave up smoking, and those who never smoked. This distinction would have been of particular interest among recurrent cases. We also lacked information on the time from symptom onset to arrival at the hospital; an important factor influencing the decision to perform coronary angiography and revascularisation.

5 CONCLUSIONS

Recurrent cases seemed to be admitted with a more severe clinical form of AMI and received optimal treatment less often, compared to incident cases. A more aggressive treatment approach combined with the implementation of preventive strategies would help improving the prognosis of patients suffering a recurrent AMI.

CONFLICTS OF INTEREST

The authors declare that no conflicts of interest exist.

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None

ETHICAL APPROVAL

The study was approved by the National Committee for Bio-Medical Ethics in Albania.

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