Non Communicable Diseases

Inadequate management of cardiovascular risk factors prior to admission for an acute coronary event

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Keywords

Cardiovascular risk factors • Primary prevention • Secondary prevention • Acute coronary syndrome • Diabetes mellitus

Summary

Objectives. *Optimal regulation of modifiable risk factors has been proposed as the standard of care both for primary and secondary prevention of cardiovascular disease (CVD). The aim of this study was to assess primary and secondary cardiovascular risk management received before admission for an acute coronary event.*

Methods. *Data were analyzed for 185 consecutive hospitalized patients with a diagnosis of acute coronary syndrome (ACS) in the Cardiology department of a University hospital during an annual period (1/7/2019 until 30/6/2020). The study population was divided into two groups, the primary and secondary prevention subgroups, according to previous medical history of cardiovascular disease (CVD).*

Results. *The mean age of the participants was 65.5 ±12.2 years and most patients were male (81.6%). Previous CVD was present in 51 patients (27.9%). Fifty-seven patients (30.8%) had a history of diabetes mellitus (DM) and 97 (52.4%) had a history of dyslipidemia. Hypertension was present in 101 (54.6%) patients. In the secondary prevention group, the LDL-C was on target in only 33.3% of the patients, while 20% patients did not use statins. The use of antiplatelet/anticoagulant agents was 94.5%. Among patients with diabetes, only 20% had been using a GLP-1 receptor agonist or/and an SGLT-2 inhibitor, while the HbA_{1c} was on target in 47.8%. Twenty-five percent of the patients were active smokers. In the primary prevention group, the use of statins was overall low (25.8%) but more frequent in patients with diabetes and those without diabetes at very high-risk for CVD (47.1% and 32.1% respectively). The LDL-C was on target in less than 23.1% of the patients. The use of antiplatelet/anticoagulant agents was low (20.1%), but higher in those with diabetes (52.9%). In the diabetic group, HbA_{1c} was on target in 61.8%. Active smoking was practiced by 46.3% of the patients.*

Conclusions. *Our data show that in a substantial proportion of patients presenting with ACS, previous CVD prevention, both primary and secondary, fails to meet the current recommendations provided by scientific societies.*

Introduction

Acute coronary syndrome (ACS) is associated with significant morbidity and mortality, despite advances in pharmacological and non-pharmacological management [1]. The prevalence of coronary artery disease (CAD) worldwide remains high due to aging of the population, improved survival after an initial cardiovascular (CV) event and increasing prevalence of certain CV risk factors such as diabetes and obesity [2]. Primary and secondary prevention of CV disease (CVD) through aggressive modification of classical risk factors has been proposed as the most effective way to reduce the incidence and severity of ACS and its long-term complications [3, 4]. In order to implement aggressive primary and secondary prevention of CVD, several risk stratification scores have been developed[5]. The European Society of Cardiology and the European Atherosclerosis Society (ESC/EAS) have adopted the SCORE (Systematic Coronary Risk Estimation) system for risk stratification in individuals without known CVD, while they have further proposed a global risk stratification to encompass the entire spectrum of the population at risk [6].

Aim of the present study was to investigate if individuals who suffered an ACS had previously been receiving adequate preventive care against risk factors for CVD.

Methods

The Institutional Review Board of Laiko General Hospital, a University tertiary hospital in Athens, Greece, approved the study protocol, which conforms to the principles outlined in the 1975 Declaration of Helsinki [7]. An informed consent was obtained from all participants prior to their involvement in the study.

We prospectively enrolled all patients with a diagnosis of ACS who were hospitalized at the Cardiology department during a one-year period (between 1/7/2019 and 30/6/2020) and analyzed their clinical characteristics. ACS was defined as unstable angina, non-ST elevated myocardial infraction or ST elevated myocardial infraction, as indicated by the admission ICD-10 code and further adjudicated by the investigators on the basis of clinical features, electrocardiogram and cardiac enzymes on admission and during hospitalization.

Data regarding the patients' previous medical history, use of medications, demographics, somatometric

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features and laboratory parameters on admission were recorded. Body weight was measured on admission only in ambulatory patients. The presence of diabetes mellitus (DM), hypertension and dyslipidemia were ascertained by self-reporting and/or previous intake of relevant medications. The use of medications preceding the ACS was also self-reported and ascertained on the basis of a dispensed prescription (from the national prescription electronic database) up to three months before admission.

In order to assess the adequacy of the antecedent risk factor management, individuals were classified, as being "at very high risk" (VHR), "at high risk" (HR), "at moderate risk" (MR) or "at low risk" (LR), according to the 2016 ESC/EAS guidelines [8], which rely on factors such as history of established CVD, presence duration and possible end-organ damage of diabetes, presence of chronic kidney disease, SCORE levels etc.

The study participants were initially divided into two groups, according to the absence or presence of established CVD prior to the indexed ACS, comprising the primary and secondary prevention group, respectively. Patients with established CVD were identified as those with a medical history of previous coronary artery disease or/and previous cerebrovascular accident or/and previous peripheral artery disease as reported and ascertained on the basis of their medical files/documents. All individuals in the secondary prevention group were considered as VHR. In the primary prevention group, the risk stratification of individuals without DM was based on the SCORE for European populations at low cardiovascular disease risk, ranging from LR to VHR. The risk stratification of individuals with DM in the primary prevention group, depended on specific parameters indicated by the ESC/EAS guidelines, such as the presence of target organ damage (such as proteinuria or retinopathy) or the co-existence of a major risk factor such as smoking, hypertension or dyslipidemia [8]. An LDL-C target of < 70 mg/dl and < 100 mg/dl was considered as appropriate for the VHR and HR categories respectively, while an LDL-C target of < 115 mg/dl was considered for both the MR and LR categories [8]. For patients with diabetes, an HbA_{1c} of < 7% was considered as appropriate, according to the 2018 American Diabetes Association/European Association for the Study of Diabetes (ADA/EASD) guidelines (Fig. 1) [9].

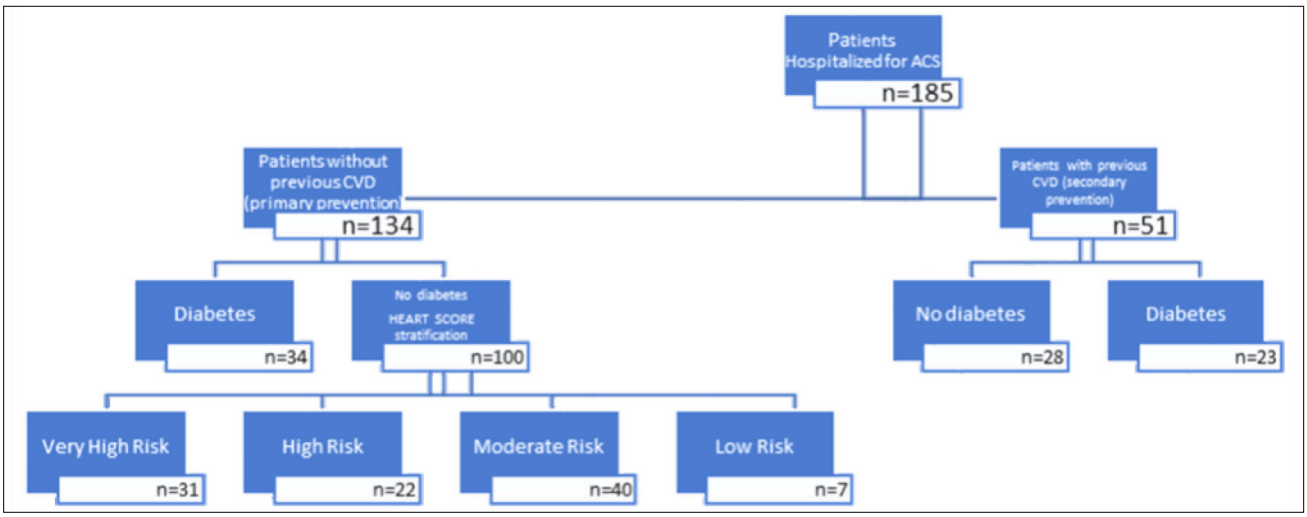
Statistical analysis was performed using IBM SPSS Version 28.0 (IBM Corporation, Armonk, NY, USA). Baseline characteristics were presented as means ± SD, median (25th-75th percentile) or counts (percentage). Between-group comparisons were performed using the chi-square test. In all instances, statistical significance was evaluated at the 0.05 level ($p < 0.05$).

Results

A total of 185 patients with ACS were hospitalized during the indicated period and were included in the present analysis. The mean age ± SD was 65.5 ± 12.2 years, and 81.6% were men. The main demographic and clinical characteristics of the study population are shown in Table I. A history of CVD was pre-existing in 51 (27.6%) patients (secondary prevention group) and, within this group, 23 patients (45.1%) had a history of DM (Tab. II). Out of the remaining 134 patients without previous CVD (primary prevention group), 34 (25.4%) had a history of DM (Tab. III). All the patients with DM were classified as VHR. Out of the non-DM patients of the primary prevention group, 53 were classified as VHR or HR and 47 as MR or LR (Tab. III). Out of the total study population, a history of hypertension was reported by 101 (54.6%) patients. This proportion was higher in patients with diabetes (61.4%) as compared to the patients without DM (51.6%).

Among the secondary prevention group (Tab. II), although 42/51 patients (82.4%) were previously treated with a statin and 22/51 (43.1%) with a high-intensity statin or a statin plus ezetimibe, LDL-C was on target in only

Fig. 1. Flowchart of the study.



Tab. I. Main demographic and clinical characteristics of the study population.

ACS	n = 185
Age (years)	65.5 (± 12.2)
Male sex n (%)	151 (81.6)
Height (cm)	171.6 (± 8.4)
Weight (kg)	84.4 (± 15)
BMI (kg/m2)	28.6 (± 4.6)
Hypertension n (%)	101 (54.6)
Diabetes n (%)	57 (30.8)
Lipid disorders n (%)	97 (52.4)
Coronary artery disease n (%)	51 (27.6)
Smoking n (%)	
Never	86 (46.5)
Active smokers	74 (40.0)
Ex-smokers	25 (13.5)
Family history of CVD n (%)	22 (11.9)
Chronic kidney disease n (%)	46 (24.9)
Prior PCI or CABG n (%)	47 (25.4)

17/51 (33.3%). The proportion of patients with LDL-C on target was higher in those receiving a statin (20/42 patients, 47.6%) than in those not on statin therapy (1/9, 11.1%, $p < 0.001$). The highest proportion of LDL-C target achievement was observed among patients under a high-intensity statin or a statin plus ezetimibe (59.1%, $p < 0.01$ *vs* those on low-intensity statin treatment). An antiplatelet agent had been received by 48 patients (94.1%), while active smoking had been practiced by 13 patients (25.5%). Among the patients with diabetes, 5/23 (21.7%) were previously being treated with a glucagon-like receptor agonist (GLP-1RA) or a sodium-glucose transporter-2 inhibitor (SGLT-2i) and 11/23 (43.7%) had an HbA_{1c} on target. The use of statins and/or antiplatelet agents, active smoking and LDL-C target achievement did not differ between patients with and without diabetes (Tab. II).

Among the primary prevention group (Tab. II), the use of a statin prior to the ACS event was overall low (25.8%) but more frequent in patients with diabetes and those without diabetes at VHR (47.1 and 32.1% respectively) than in those at HR (27.3%), MR (10%) and LR (14.3%), with all p values < 0.01. Accordingly, less than one quarter of patients achieved the appropriate LDL-C target across all the risk categories (Tab. II). The proportion of patients with LDL-C on target was higher in those receiving a statin (14/36, 38.8%) than in those not on statin therapy (17/98, 17.3%, $p < 0.001$). Among patients with diabetes, 21 (61.8%) had an HbA_{1c} on target. Antiplatelet/anticoagulant agents had been previously received by 52.9% of patients with diabetes, but, within the non-diabetic population, their use was, as expected, infrequent (Tab. II). More than one third of patients were active smokers, the proportion being lowest in those with diabetes (35.3%) and highest in those at HR (59.1%).

Hypertension was present in 102/185 (55.1%) of the total study population and its prevalence was highest among those with established CVD (80.4%) and diabetes (67.7%), while it was lowest in the primary prevention cohort among those at LR (14.3%) and at MR (17.5%) (Tabb. II, III). Among patients with hypertension, anti-hypertensive medications were used by 90.2% in the secondary cohort and by 72.1% in the primary cohort.

Discussion

Despite the progress being achieved in the pharmacological and supportive management of patients hospitalized for ACS over the last decades, coronary artery disease still remains the number one cause of morbidity and mortality worldwide [10]. Primary and secondary prevention of CVD, by aggressively modifying risk factors, is mandatory in order to prevent CV events and their complications. Nevertheless, according to the present study's findings, the majority of patients suffering from an ACS had been receiving insufficient prevention management of modifiable CVD risk factors prior to the event.

Among patients in the secondary prevention group requiring very aggressive management of risk factors, although the majority was receiving lipid-lowering medications, a notable proportion (15.7%) was no

Tab. II. Prevention measures, active smoking and target achievement in key metabolic parameters in patients with previous CVD (secondary prevention group).

Patients with previous CVD (secondary prevention group), n = 51			
	Diabetes n = 23	No diabetes n=28	p
Statin, n (%)	18 (78.2)	24 (86)	NS
Antiplatelet/anticoagulant, n (%)	20 (87)	28 (100)	NS
SGLT-2-i/GLP-1, n (%)	5 (21.7)	-	NA
Smoking, n(%)	6 (26)	7 (25)	NS
LDL-C on target, n (%)*	10 (43.5)	11 (39.3)	NS
LDL-C on target among those on statin n (%)*	9 (50%)	11 (45.8)	NS
HbA_{1c} on target n (%)**	11 (47.8)	-	NS
Hypertension	17 (73.9)	24 (85.7)	NS
Anti-hypertensive drugs	20 (86.9)	20 (71.4)	NS

NS: Not Significant at the level 0f 0.05; NA: Not Applicable.
* The LDL-C target for patients both with and without diabetes was considered as < 70 mg/dl. ** The HbA_{1c} target for patients with diabetes was considered as < 7.0%.

Tab. III. Prevention measures, active smoking and target achievement of key metabolic parameters in patients without previous CVD (primary prevention group).

Patients without previous CVD (primary prevention group), n = 134					
	Diabetes n = 34	No diabetes n = 100			
HEART Score		VHR n = 31	HR n = 22	MR n = 40	LR n = 7
Statin n (%)	16 (47.1)	10 (32.3)	6 (27.3)	4 (10)	0 (0)
Antiplatelet/anticoagulant	18 (52.9)	5 (16.1)	3 (13.6)	1 (2.5)	0 (0)
Hypertension	18 (52.9)	19 (61.2)	16 (72.7)	7 (17.5)	1 (14.3)
Anti-hypertensive drugs	16 (47)	14 (45.2)	10 (45.4)	4 (10)	0 (0)
SGLT-2-i/GLP-1, n (%)	7 (20.6)	-	-	-	-
Smoking	12 (35.3)	12 (38.7)	13 (59.1)	22 (55)	3 (42.7)
LDL-C on target n (%)*	8 (23.5)	8 (25.8)	2 (9,1)	12 (30)	1 (14.3)
LDL-C on target among those on statin n (%)*	4 (25)	4 (40)	2 (33,3)	4 (100)	-
HbA_{1c} on target n (%)**	21 (61.8)	-	-	-	-

* The LDL-C target for VHR and HR patients was considered as < 70 mg/dl, for MR as < 100 mg/dl and for LR as < 115 mg/dl. ** The HbA_{1c} target for patients with diabetes was set at < 7.0%

under such treatment at all, while a remarkable fraction (43.1%) should have required treatment intensification. Disappointingly, active smoking was practiced by one quarter of the patients. In the diabetic subgroup, 52.2% of the patients seemed to need intensification of glucose-lowering treatment, while a substantial underuse of GLP-1RA and/or SGLT-2i was also noticed (21.7%), despite the latest ADA/EASD guidelines strongly recommending their use in patients with diabetes and established CVD [11]. Antiplatelet/anticoagulant treatment seemed to be the most well-established preventive treatment in this group, as it was followed by 94.2% of the patients.

In primary prevention, considerable heterogeneity regarding the previous CV risk status was noticed among. Almost two thirds of the patients in this group had been at HR or VHR to suffer an ACS (87/134, 64.9%), either because they had diabetes (and additional risk factors) or because of their calculated SCORE. Among them (at VHR/HR), 60% were not treated with any kind of lipid-lowering medications and only 25% had their LDL-C on target. Additionally, about one third of these patients were active smokers and about 40% of those with diabetes needed glucose-lowering treatment intensification. The proportion of patients with diabetes under GLP-1RA and/or SGLT-i was 20%, similar to that in the secondary prevention group. About one third were treated with an antiplatelet/anticoagulant, a proportion that was significantly higher in those with diabetes (52.6%) than in those without (16.1%). One third of the patients comprising the primary prevention group (and hence one quarter of the total study population) had been at MR or LR, previously to the indexed acute coronary event. Among these patients, only one quarter had their LDL-C on target, and, strikingly, more than 50% were active smokers.

Overall, the present study shows that the vast majority of patients suffering an ACS had been receiving insufficient preventive management of classical CV risk factors, while some individuals had not been receiving such management at all. A significant underuse/underdose of lipid-lowering medications, especially statins, in both primary and secondary prevention, was shown. An even greater underuse was noticed regarding the novel glucose-lowering medications (GLP-1Ras and SGLT-2i), which have been recently shown to reduce CV events in patients with DM at high CV risk. The use of antiplatelet/anticoagulant agents was sufficiently high in secondary prevention but relatively low in high and very high-risk patients of the primary prevention group, with the exception of patients with diabetes, in whom it slightly surpassed 50%. Last but not least, an alarming finding of the present study is the high proportion of active smokers in all groups. Vigorous counselling for smoking cessation and offering of structured smoking cessation programs are urgently needed.

In line with the results of the present study, previous studies have also shown concerning gaps in managing CV risk factors in patients with a history of CVD [12], diabetes [13] and acute myocardial infarction [14]. To our knowledge, however, no previous studies have considered the adequacy of CVD prevention management in the context of risk stratification according to the ESC/EAS guidelines in patients presenting with ACS. This approach offered the opportunity to eschew some limitations of larger registry-based studies, such as missing information and misclassification of CVD risk. The present analysis included a broad range of risk factor management, including lipid-lowering, glucose-lowering and antiplatelet medications. Importantly, very few studies have yet reported on the use of the newer glucose-lowering medications in this population. Additionally, the prospective inclusion of patients offered more accurate data collection and ascertainment of actual ACS events. Finally, the study population came from Greece, a medium-to-high income country under austerity measures, in which such an analysis has not been previously performed. On the other hand, the present study has some important limitations: first, this is a single-center study, a fact limiting representativeness of the sample population and generalizability of the results; second, the number of ACS events is relatively

small and third, some important factors related to CVD prevention such as diet habits and physical activity were not recorded. Importantly, however, the study population included patients admitted during the shift schedule of the single participating Cardiology clinic, which, being part of the Greek National Health System, allows access to virtually all inhabitants of the broader Athens area who need emergency care.

Physician's lack of awareness, clinical inertia, patients' non-adherence to follow up, the lack of a national program for systematic outpatient CVD prevention and high cost of newer hypolipidemic and glucose-lowering agents, are all probable contributing factors, explaining our results [15-17].

In conclusion, data from a single cardiology clinic of a tertiary hospital in Greece show that in a substantial proportion of patients presenting with ACS, previous CVD prevention, both primary and secondary, fails to meet the current recommendations. Establishing stricter local prescription protocols, implementing adequate follow up, enhancing physicians' awareness and addressing clinical inertia might serve as measures to improve management and achieve proper care.

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Authors' contribution

S.L., M.B. and J.B. conceived of the presented idea. C.S, C.K. and M.S processed the data and performed the analysis. C.S. and S.L. wrote the manuscript with input from all authors. All authors provided critical feedback and helped shape the research, analysis and manuscript.

Informed Consent Statement

Informed consent was obtained from all subjects involved in the study. Written informed consent has been obtained from the patients to publish this paper.

Conflict of interest statement

The authors declare no conflict of interest.

Ethical approval

The study was approved by the Ethics Committee of our institution and was carried out in accordance with the Declaration of Helsinki.

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