Secondary prevention advices after cardiovascular index event: From drug prescription to risk factors control in real world practice

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Abstract

The present study aims at evaluating the achievement of blood pressure, lipid and blood glucose targets, healthy lifestyle changes and appropriate drug prescription/adherence in patients attending secondary prevention/CR ambulatory visit after index cardiovascular event in a time period ranging 1 to 5 year. At ambulatory visit, a predetermined set of data collection was used, including demographic data, cardiovascular risk factors and lifestyle habits, type and time of index event, current symptoms, physical sign, biochemistry and current medical treatment (including type and dosage). Cardiovascular risk profile (smoking habits, physical activity and body weight), secondary prevention goals (LDL-cholesterol, blood pressure, resting heart rate, glycated haemoglobin level) and the use of recommended drugs were also evaluated and categorized. Study population consisted of 800 patients [644 men (84.5%), aged 69±10.9 years)]. Cardiovascular index events were coronary artery bypass graft (CABG) (20%) ST segment elevation myocardial infarction (STEMI) (28%), non-ST segment elevation myocardial infarction (NSTEMI) (21%) and stable angina (13%) by unstable angina (13%) and stroke (5%). About 30% of patients was symptomatic (angina or dyspnoea) at the time of ambulatory visit. Major comorbidities were hypertension (73%), dyslipidaemia (64%) and diabetes (40%). More than 80% of patients achieved target levels for blood pressure. Patients that have participated to cardiac rehabilitation programmes after cardiovascular index event showed best achievement in blood pressure target (83.8% *vs* 76.8%, p=0.02). LDL-cholesterol target (<70 mg/dl) was achieved in about 2/3 of patients; HbA1c target (<7%) was achieved in 56.4% of diabetic population. About 75% of study cohort was treated with RAAS inhibitors, 85% with beta-blockers, 92% with statins and 87% with acetylsalicylic acid. All drugs were increasingly adopted from index event. Implementing secondary prevention guidelines into the 'real world' clinical practice in "late" interval from 1 to 5 years after a cardiovascular event improved risk factors control and appropriate drug prescription. Whether these improvements translated into prognostic advantages remains to be elucidated.

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Introduction

Secondary prevention is the most critical intervention to be delivered after cardiovascular index event in order to reduce mortality or preventing a newer subsequent event [1]. Evidence-based interventions include optimal medical therapy, achievement of blood pressure, lipid and blood glucose targets, and appropriate lifestyle changes [2,3].

During the last decades, secondary prevention programmes evolved from simple bedside consultations of a few minutes into professionally led multidisciplinary interventions within cardiac rehabilitation (CR) units devoted at preventing future cardiac events and slowing disease progression [3,4]. Cardiac rehabilitation strategies include comprehensive lifestyle interventions based on behavioural change models (*i.e.* quit smoking, healthy food choices, stress/anxiety management and exercise training), with predominant involvement of the patient in making self-related health decisions [5-9].

Cardiovascular risk factor management, aiming at reaching blood pressure, lipids and glucose targets, as well as the appropriate prescription and adherence to drugs, are now integral parts of this approach [10]. Psychological interventions targeted at supporting coping strategies, decreasing psychosocial risk factors and improving patients' adherence to preventive interventions and behavioural changes, has become increasingly important [11,12].

However, in Europe, it is estimated that of eligible patients, only 14% to 35% of heart attack survivors and 31% of patients after coronary artery bypass surgery participate in secondary prevention programmes and that 70% of suitable patients do not receive dedicated secondary prevention interventions for risk factor reduction [13-15]. Conversely, in patients attending secondary prevention/CR programmes, few data are available regarding long-term achievement of cardiometabolic targets or appropriate drug prescription and adherence [6,7,16,17]. In fact, several studies previously assessed the status of secondary prevention in the first 12 months after index cardiovascular event [6,7,10]. On the other hand, there is a gap of knowledge on the control of risk factors beyond the first year after the first presentation of atherosclerotic disease. Accordingly, the present study aims at evaluating the secondary prevention strategy implementation (achievement of blood pressure, lipid and blood glucose targets, and healthy lifestyle changes and appropriate drug prescription/adherence) in patients enrolled in a time period ranging 1 to 5 year after index cardiovascular event.

Patients and Methods

From January 1st to April 30th 2018, 800 outpatients were recruited by the Secondary Prevention Units of Brescia and Passirana (ASST Rhodense). The study enrolled adult patients of both sexes with any clinical-instrumental manifestation of coronary artery disease (CAD) observed during routine follow-up visits in 2 different centres. The diagnosis of CAD was defined as: previous coronary artery bypass graft (CABG) or percutaneous coronary interventions (PCI) in election or in urgency; previous ST elevation myocardial infarction (STEMI) or non-ST elevation myocardial infarction (NSTEMI) regardless of revascularization; history of chest pain with positive stress perfusion myocardial scintigraphy imaging or with evidence of stenosis >70% of at least 1 coronary artery to coronary angiography. The patient was deemed eligible if the diagnosis of CAD was between 1 and 5 years before current evaluation.

During the clinical evaluation, a predetermined set of data collection was used, including demographic data, cardiovascular risk factors and lifestyle habits, type and time of index event, current symptoms, physical sign, biochemistry and current medical treatment (including type and dosage). Furthermore, cardiovascular risk profile (smoking habits, physical activity and body weight), secondary prevention goals (LDL-cholesterol, blood pressure, resting heart rate, glycated haemoglobin level) and the use of recommended drugs were evaluated and categorized. The therapeutic targets for blood pressure (<140/90 mmHg) refer to the current guidelines of the European Society of Cardiology [1]. Predefined therapeutic goals for LDL were set according to the European guidelines on dyslipidaemia: LDL-C levels <70 mg/dl for very high CV risk patients in secondary prevention [1,18]. Secondary prevention goal for glycated haemoglobin level was <7% [19]. The study was approved by the local Ethics Committee.

Statistical analysis

The results are presented in crude data and then divided by age, gender and diagnostic access category. Continuous variables were presented as mean ± standard deviation (SD); discrete variables as a percentage or proportions were appropriate. Comparisons between groups were performed by unpaired t test, chi-square test or Fischer's exact test as required. Multivariate analysis (Model 1) was performed with blood pressure target achievement as dependent variable and age, sex, ejection fraction, dyslipidaemia, diabetes, obesity, index event (CABG, stable and unstable angina, NSTEMI, STEMI, PCI, stroke/TIA, atrial fibrillation), and blood pressure lowering therapy as independent variables. Multivariate analysis (Model 2) was performed with LDL target achievement as dependent variable and age, sex, ejection fraction, arterial hypertension, diabetes, obesity, index event (CABG, stable and unstable angina, NSTEMI, STEMI, PCI, stroke/TIA, atrial fibrillation), attendance to cardiac rehabilitation programmes and blood pressure lowering therapy as independent variables. All analyses were performed using SPSS version 18.0 (SPSS Inc., Chicago, IL, USA) with significance set at $p<0.05$.

Results

Cardiovascular index event

Study population consisted of 800 patients [644 men (84.5%), aged 69±10.9 years)]. Table 1 shows anthropometrical, clinical and biochemical characteristics and cardiovascular index event of the study population. Cardiovascular index events were CABG (20%) STEMI (28%), NSTEMI (21%), stable angina (13%), unstable angina (13%) and stroke (5%). About 53% (n=429) of patients attended CR programmes. Clinical and drug therapy data were obtained in the whole population; lipid profile was obtained in 83% and glomerular filtration rate in about 50% of the study cohort.

The most common procedure was PCI (76.2%, in 12.1% at multiple site); and 20.1% of the study cohort underwent CABG. Notably, 15.6% had multivessel coronary artery disease. Overall, there were no significant gender-related differences in prevalence of index events, with the exception of NSTEMI and PCI (more frequent in women), and CABG (more frequent in men) (Table 1).

About 30% of patients (n=238, 77% males) was symptomatic at the time of ambulatory visit: 7% reported angina and 23% reported dyspnoea.

Comorbidities and traditional cardiovascular risk factors

Principal comorbidities and cardiovascular risk factors were reported in Table 2. Overall, 73% of patients had hypertension, 64% had dyslipidaemia and about 40% diabetes (Table 2). Twenty-nine percent of patients showed extra-coronary atherosclerosis (peripheral artery disease or carotid artery disease); 15.9% of study cohort had pacemaker or implanted cardioverter device (ICD) (Table 2). Notably, women showed higher prevalence of diabetes (48% *vs* 38.8%, p=0.02) and higher levels of Total-cholesterol (152.5±33.2 *vs* 140.0±31.6mg/dl, p=0.001) and LDL-cholesterol (79±28.8 *vs* 71.2±27.5mg/dl, p=0.004) compared to men, respectively (Table 2). Finally, women showed higher heart rate (67.5±10.5 *vs* 64.9±10.1 beats per minute, p=0.004) compared to men. About sixty-eight percent of the study population had eGFR ≥ 60 ml/min and 8.1% lower than 30 ml/min.

Data showed that 23.7% of the study population was still active smoker after cardiovascular event index; only 17.7% of patients never smoked in life and about 58.6% of patients quitted (Figure 1). Of note, women are still active smokers after acute index event compared to men (48.9% *vs* 18.8%, p<0.001, respectively) (Figure 1). Interestingly, there was no significant differ-

ences in smoking habits prevalence independent of time from index event (active smokers were 25.8% at 1 year; 13.3% at 2 years; 15.4% at 3 years; 25.3% at 4 years; 16.4% at 5 years from index event), confirming that smoking habits are very difficult to eradicate in cardiac patients.

Almost half of the study population was physically inactive: 45.7% of the study population performed moderate-intensity physical activity and only 2.7% was involved in vigorous activity (Figure 2). Notably, almost half of women cohort were sedentary (Figure 2).

Target achievement

Table 3 reported percentages of recommended targets according to International Guidelines based on history or clinical evaluation at the ambulatory visit.

More than 80% of patients achieved target levels for blood pressure (<140/90mmHg) (Table 3), independent of time of ambulatory visit from index event (generally ranging from 75 to 85% of target achievement). LDL-cholesterol target (<70mg/dl) was achieved in about 2/3 of patients. Interestingly, 76.5% of target achievement was obtained between 1 and 2 years from index event compared to longer periods (Table 3). LDL targets were achieved with a dose of simvastatin 10 mg in 12 patients, 20 mg in 34 patients and 4 0mg in 15 patients; with a dose of atorvastatin 10 mg in 17 patients, 20 mg in 75 patients, 40 mg in 115 patients and 80 mg in 38 patients; with a dose of rosuvastatin of 5 mg in 17 patients, 10 mg in 45 patients and 20 mg in 35 patients.

Patients that have participated to cardiac rehabilitation programmes after cardiovascular index event showed best achieve-

Table 1. Anthropometrical, clinical characteristics and cardiovascular index event of the study population.

	Total population (n=800)	Male (n=644, 80.5%)	Female (n=156, 19.5%)	p-value (M *vs* F)
Age (years)	69.0±10.9	67.9±10.8	73.6±10.6	<0.001
Waist circumference (cm)	100.8±12.7	101.3±12.5	98.4±13.7	0.173
SBP (mmHg)	130.7±17.7	130.6±17.2	131.1±19.6	0.739
DBP (mmHg)	76.2±9.5	76.3±9.3	75.8±10.4	0.594
Heart rate (beats/min)	65.4±10.3	64.9±10.1	67.5±10.5	0.004
Total cholesterol (mg/dl)	142.5±32.2	140.0±31.6	152.5±33.2	0.001
LDL- cholesterol (mg/dl)	72.7±27.8	71.2±27.5	79.0±28.8	0.004
HDL- cholesterol (mg/dl)	46.2±15.8	45.1±15.8	51.1±15.1	0.000
Triglyceridemia (mg/dl)	127.9±64.6	129.8±67.0	120.3±52.8	0.119
Glycemia (mg/dl)	115.2±37.9	114.2±37.2	119.6±40.4	0.125
Creatinine (mg/dl)	1.33±1.2	1.29±1.2	1.57±1.1	0.573
Uric acid (mg/dl)	5.8±4.0	5.9±3.4	5.6±5.8	0.474
Stable angina	127 (15.9%)	101 (15.7%)	26 (16.7%)	0.763
Unstable angina	128 (16.0%)	103 (16.0%)	25 (16.0%)	0.751
NSTEMI	200 (25.0%)	151 (23.4%)	49 (31.4%)	0.040
STEMI	253 (31.6%)	211 (32.8%)	42 (26.9%)	0.160
Multisite atherosclerotic disease	125 (15.6%)	96/403 (23.8%)	29/107 (27.1%)	0.484
CABG	161 (20.1%)	144 (22.4%)	17 (10.9%)	<0.001
PCI	610 (76.2%)	484 (75.1%)	126 (80.8%)	0.010
Multisite PCI	97 (12.1%)	81 (12.6%)	16 (10.3%)	0.229
LVEF (%)	50.4±9.7	50.2±10.0	51.4±8.1	0.172

SBP, systolic blood pressure; DBP, diastolic blood pressure; NSTEMI, non-ST segment elevation myocardial infarction; STEMI, ST segment elevation myocardial infarction; CABG, coronary artery by-pass graft; PCI, percutaneous coronary intervention; LVEF, left ventricular ejection fraction.

Table 2. Comorbidity and cardiovascular risk factors of the study population

	Total population (n=800)	Male (n=644, 80.5%)	Female (n=156, 19.5%)	p-value (M *vs* F)
Stroke/transient ischemic attack	36 (4.5%)	31 (4.8%)	5 (3.2%)	0.385
Atrial fibrillation	67 (8.4%)	49 (7.6%)	18 (11.5%)	0.112
PAD/carotid artery disease	232 (29.0%)	191 (29.7%)	41 (26.3%)	0.405
PMK/ICD	126 (15.8%)	101 (15.7%)	25 (16.0%)	0.916
Hypertension	584 (73.0%)	464 (72.4%)	120 (76.9%)	0.219
Dyslipidaemia	512 (64.0%)	418 (65.0%)	94 (60.2%)	0.748
Diabetes	318 (39.8%)	243 (37.7%)	75 (48.0%)	0.020
Obesity	130 (16.3%)	97 (15.1%)	33 (21.2%)	0.06
Active smoking	127/536 (23.7%)	84/448 (18.8%)	43/88 (48.9%)	<0.001

PAD, peripheral artery disease; PMK, pacemaker; ICD, implantable cardioverter defibrillator.

ment in blood pressure (83.8% *vs* 76.8%, p=0.02) and in LDL target (67.5% *vs* 63.5%, p=0.05). In patients with diabetes, HbA1c target (<7%) was achieved in 56.4% of diabetic population; target achievement was more frequent when ambulatory visit was up to 3 years after cardiovascular index event.

Notably, patients attending CR programmes were more likely at target for blood pressure (83% *vs* 76%, p=0.22), and showed lower LDL cholesterol levels (69±24 *vs* 78±32 mg/dl, p=0.001), respectively.

In Model 1, after adjusting for age, sex, ejection fraction, dyslipidaemia, diabetes, obesity, index event (CABG, stable and unstable angina, NSTEMI, STEMI, PCI, stroke/TIA, atrial fibrillation), and blood pressure lowering therapy, lower ejection fraction (β=-0.114, p=0.003) and unstable angina as index event (β=0.094, p=0.017), being not diabetic (β=-0.095, p=0.012) and attending CR programmes (β=0.109, p=0.006) were significantly associated to blood pressure targets achievement. In Model 2, after adjusting for age, sex, ejection fraction, arterial hypertension, diabetes, obesity, index event (CABG, stable and unstable angina, NSTEMI, STEMI, PCI, stroke/TIA, atrial fibrillation), attendance to cardiac rehabilitation programmes and statin therapy, being male (β=0.92, p=0.03), non-obese (β=0.86, p=0.041) and on statin therapy (β=0.143, p=0.001) were significantly associated to LDL targets achievement.

Drug therapy

Drug therapy was evaluated according to type (class); index event and time to index event in total population. Data were reported in Table 4.

About 75% of study cohort was treated with RAAS inhibitors (49.8% with ACE-inhibitors, 24.1% with ATII receptor antagonists). Eighty-five percent was on beta-blockers, 92% on statins

Table 3. Blood pressure, LDL-cholesterol and glycosylated haemoglobin (HbA1c) target achievement according to years from cardiovascular index event

		Years from cardiovascular index event					Total
		1	2	3	4	5	
Blood pressure target	No	5 (22.7%)	45 (17.0%)	35 (21.3%)	24 (16.4%)	39 (19.7%)	148 (18.6%)
	Yes	17 (77.3%)	220 (83.0%)	129 (78.7%)	122 (83.6%)	159 (80.3%)	647 (81.4%)
Total		22 (2.8%)	265 (33.3%)	164 (20.6%)	146 (18.4%)	198 (24.9%)	795
LDL-cholesterol target(<70 mg/dl)	No	4 (23.5%)	85 (38.1%)	43 (32.8%)	44 (34.4%)	49 (29.7%)	225 (33.8%)
	Yes	13 (76.5%)	138 (61.9%)	88 (67.2%)	84 (65.6%)	116 (70.3%)	439 (66.2%)
Total		17 (2.6%)	223 (33.6%)	131 (19.7%)	128 (19.3%)	165 (24.8%)	664
HbA1c target (<7%)	No	19 (39.6%)	4 (25.0%)	10 (41.7%)	9 (75.0%)	6 (60.0%)	48 (43.6%)
	Yes	29 (60.4%)	12 (75.0%)	14 (58.3%)	3 (25.0%)	4 (40.0%)	62 (56.4%)
Total		48 (43.6%)	16 (14.5%)	24 (21.8%)	12 (10.9%)	10 (9.1%)	110

HbA1c, glycosylated haemoglobin (only for diabetic patients).

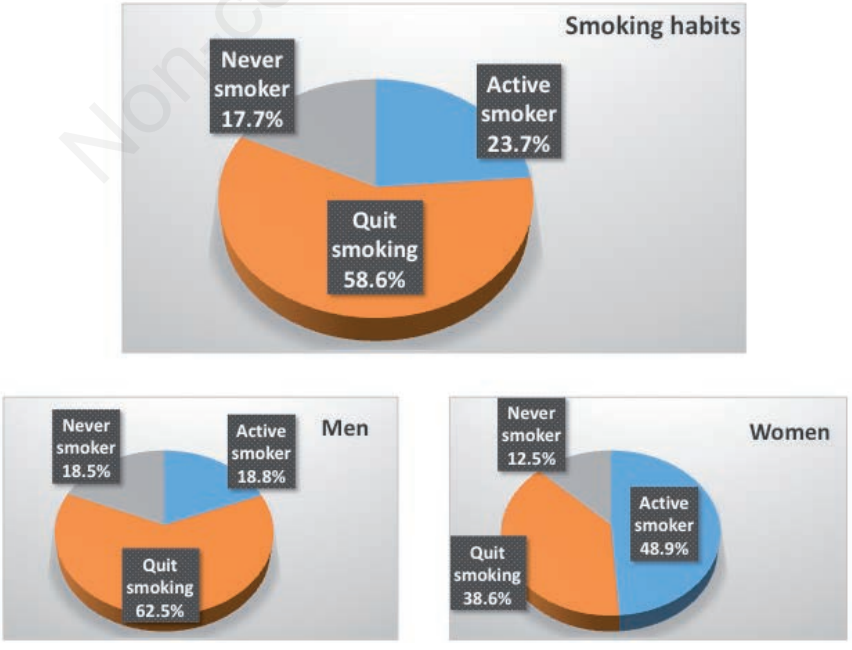

Figure 1. Smoking habits in study population.

and 87% on acetylsalicylic acid (Table 4). Interestingly, ACE-inhibitors were adopted in 34.8% at 1 year from index event up to 50.3% at 5 years. ATII receptor antagonists were adopted in about 30% of population at 1 year and at 5 years from index event; with a lower adoption at 2-4 years period after index event (ranging from 18 to 26%). Acetylsalicylic acid was increasingly adopted from index event (78.3% at 1 year after index event up to 87.4% at 5 years). Similarly, statins were increasingly adopted from index event (86.9% at 1 year after index event up to 93% at 5 years). A separate analysis was performed among high-dose statins users: Atorvastatin (40-80 mg OD) was adopted by 3% of study cohort at 12-24 months, 43.1% at 24-36 months; 18.2% at 36-48 months, 15.2% at 48-60 months and 20.5% at 60-72 months; Rosuvastatin (20-40 mg OD) was adopted by 5.8% of study cohort at 12-24 months, 23.2% at 24-36 months; 20.3% at 36-48 months, 18.8% at 48-60 months and 31.9% at 60-72 months. Proprotein convertase subtilisin/kexin type 9 (PCSK-9) inhibitors were not prescribed in 4 patients (0.5%), although criteria for prescription were satisfied. In this cohort, 7.4% of patients was on Ezetimibe (4.3% at 12-24 months up to 7.5% at 60-72 months), and 30.2% of them on dual antiplatelet therapy.

Discussion

The present study reported data on patients with different clinical presentation of CAD evaluated in an ambulatory setting in the time period ranging from 1 to 5 years after cardiovascular index event.

This study cohort likely represents the "real world" cardiac patients compared to the highly selected study population of randomized clinical trials. Notably, high mean age (70 years) and the presence of several comorbidities, usually considered exclusion criteria from randomized clinical trials, strongly characterized study cohort. Moreover, a relevant number of patients had extra-coronary localization of atherosclerosis (*i.e.* stroke, peripheral artery disease), chronic kidney disease, atrial fibrillation. In addition, about 15% of the study cohort had multivessel atherosclerotic CAD (diagnosed at angiography or history of multiple site PCI). This clinical complexity requires more accurate prognostic stratification together with more aggressive secondary prevention strategy. In fact, about one third of enrolled patients reported symptoms at the time of ambulatory visit, particularly dyspnoea, chest pain or

Table 4. Drugs use according to years from cardiovascular index event.

Drugs	Total	Years from cardiovascular index event				
		1	2	3	4	5
ACE-inhibitors	398/800(49.8%)	8/23 (34.8%)	144/268 (53.7%)	81/164 (49.4%)	66/146 (45.2%)	80/159 (50.3%)
ARBs	193/800(24.1%)	7/23 (30.4%)	50/268(18.7%)	33/164 (20.1%)	38/146 (26%)	48/159 (30.2%)
Statins	735/800(91.9%)	20/23 (86.9%)	239/268 (89.2%)	157/164 (95.7%)	136/146 (93.1%)	148/159 (93%)
Beta-blockers	679/800(84.9%)	21/23 (91.3%)	218/268 (81.3%)	139/164 (84.8%)	126/146 (86.3%)	138/159 (86.8%)
Acetylsalicylic acid	696/800(87.0%)	18/23 (78.3%)	233/268 (86.9%)	137/164 (83.5%)	131/146 (89.7%)	139/159 (87.4%)

ACEs, angiotensin-converting-enzyme inhibitors; ARBs, angiotensin II receptor blockers.

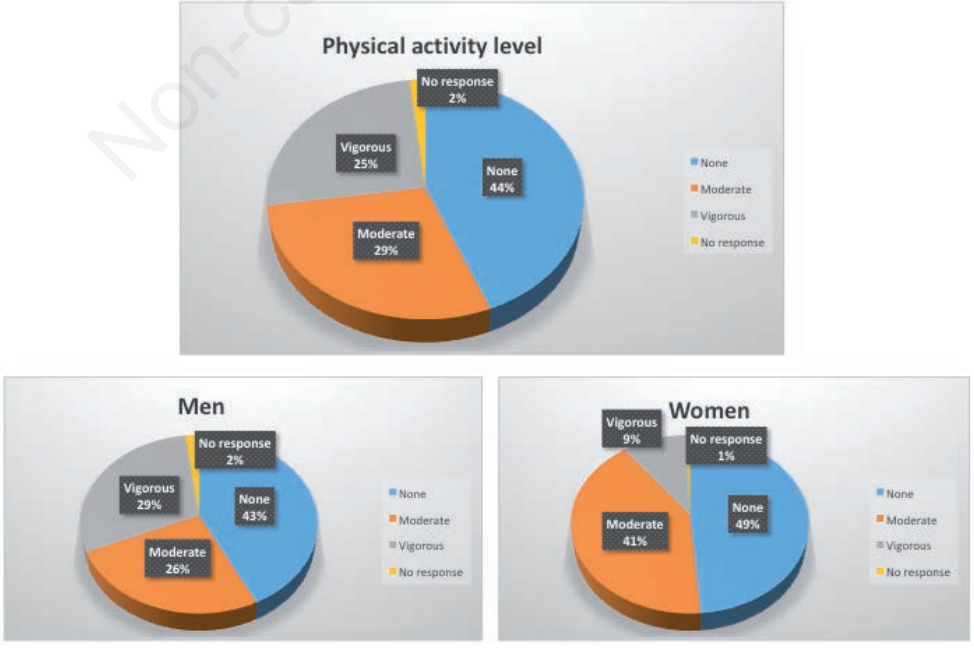

Figure 2. Physical activity level in study population.

palpitations. In addition, although this study was not designed for outcome evaluation, about 14% of study population (data available on 510/800 patients) reported angina or acute heart failure decompensation during the 12 months period before ambulatory visit. These data support the needing for a more structured follow-up even beyond the first year from index events, with strong attention both to achieving and maintaining secondary prevention targets. Cardiac rehabilitation programmes could represent the wiser strategy for significantly impact on long-term achieving and maintaining secondary prevention targets [6,7].

The study showed higher prevalence of traditional risk factors in this 'real world' population: more than 76% of the study cohort had hypertension, 64% had dyslipidaemia and 40% diabetes. In addition, patients referred to secondary prevention/cardiac rehabilitation units were usually older, had more comorbidity and multisite atherosclerotic disease. Such a clinical complexity underlies frail status, usually not well characterized in the setting of cardiac rehabilitation, although many studies have reported the measurement of frailty in patients with coronary syndromes in intensive care units or in cardiology wards, and others have highlighted the close link between frailty and chronic heart failure [20-22].

The present study documented a large use of RAAS inhibitors (75%), beta-blockers (85%), statins (91%) and acetylsalicylic acid (87%), according to secondary prevention Guidelines [1]. These data are in line with data from EUROASPIRE IV Registry [23,24] suggesting a correct approach and adherence to secondary prevention strategies. Interestingly, about 30% of the study cohort was on dual antiplatelet therapy, even after the 12-month limit suggested by the Guidelines [25-30].

However, data from our registry did not allow for distinguishing whether dual antiplatelet therapy continuation should be ascribed to latest Guidelines suggesting a more aggressive approach [31]; or might be due to a newer coronary event determining dual antiplatelet therapy re-adoption.

Although there was correct adoption of recommended drug regimen, therapeutic targets were not achieved or maintained, mostly after 12 months from index event. In fact, only about 65% of patients was on target LDL (<70 mg/dl), although statins were widely used, even at high dose regimen. Among diabetics, about 55% of this cohort was on target HbA1c (<7%). Better results were obtained in blood pressure target achievement (80% of study population had values <140/90 mmHg) or resting heart rate (HR) target (70% of patients had resting HR <70 beats/min). However, it should be noted that blood pressure and HR were acquired only during the ambulatory visit, thus reducing long-term prognostic value of these indexes.

These "real world" data indicated a better cardiovascular risk factors control compared to the most recent EUROASPIRE IV registry [23,24] and to different world region registries [32-35]. Compared to European studies, data from the SURF registry enrolling Asian population showed a poorer control of several risk factors including physical inactivity (41-45%), overweight and obesity (59-78%), and ongoing smoking (15%) [32]. Impressive data came out from PURE study: the use of secondary preventive drug therapies in patients with known CHD or stroke in South Asia is low, with over 80% receiving none of the effective drug treatments [33]. Interestingly, only 46.5% of participants with hypertension were aware of the diagnosis, with blood pressure control among 32.5% of those being treated [35]. In the present study, the observed better 'real world' risk factors control is more likely due to the fact that patients are referred to secondary prevention/cardiac rehabilitation units where healthcare professionals are particularly skilled on secondary prevention management. In fact, more than 50% of the cohort has been enrolled to cardiac rehabilitation programme. Among this cohort, LDL-cholesterol and blood pressure targets were more frequently reached; and sedentary habits were less reported. These findings are in line with other studies suggesting that patients attending a cardiac rehabilitation programme were more likely to achieve lifestyle targets [23,36-39].

Overall, data suggest that secondary prevention management guidelines were correctly adopted translating into appropriate drug prescription and risk factors control even up to 5 years after cardiovascular index event. However, 16% of the study cohort was classified obese and 12% was active smoker; confirming that weight control and smoking are still the long-term great challenges of secondary prevention [7,8,40,41].

Study limitation

Some limitation should be acknowledged. First, the relatively small sample size, predominantly men may limit conclusions; second, frailty was not evaluated. In addition, the relatively small sample size interfered with time-dependent analysis and did not allow to evaluate differences. Conversely, this study has several strengths since this cohort likely represent the "real world" cardiac patient (*i.e.* mean age 70 years and several comorbidities) compared to the highly selected cohorts of randomized clinical trials.

Conclusions

Implementing secondary prevention guidelines into the "real world" clinical practice in "late" interval from 1 to 5 years after a cardiovascular event improved risk factors control and appropriate drug prescription. Whether these improvements translated into prognostic advantages remains to be elucidated.

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