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Original Article

Reasons for discontinuation of recommended therapies according to the patients after acute coronary syndromes

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ABSTRACT

Background: The prescription of recommended medical therapies is a key factor to improve prognosis after acute coronary syndromes (ACS). However, reasons for cardiovascular therapies discontinuation after hospital discharge are poorly reported in previous studies.
Methods: We enrolled 3055 consecutive patients hospitalized with a main diagnosis of ACS in four Swiss university hospitals with a prospective one-year follow-up. We assessed the self-reported use of recommended therapies and the reasons for medication discontinuation according to the patient interview performed at one-year follow-up.
Results: 3014 (99.3%) patients were discharged with aspirin, 2983 (98.4%) with statin, 2464 (81.2%) with beta-blocker, 2738 (90.3%) with ACE inhibitors/ARB and 2597 (100%) with P2Y12 inhibitors if treated with coronary stent. At the one-year follow-up, the discontinuation percentages were 2.9% for aspirin, 6.6% for statin, 11.6% for beta-blocker, 15.1% for ACE inhibitor/ARB and 17.8% for P2Y12 inhibitors. Most patients reported having discontinued their medication based on their physicians' decision: 64 (2.1%) for aspirin, 82 (2.7%) for statin, 212 (8.6%) for beta-blocker, 251 (9.1% for ACE inhibitor/ARB) and 293 (11.4%) for P2Y12 inhibitors, while side effect, perception that medication was unnecessary and medication costs were uncommon reported reasons (<2%) according to the patients.
Conclusions: Discontinuation of recommended therapies after ACS differs according the class of medication with the lowest percentages for aspirin. According to patients, most stopped their cardiovascular medication based on their physician's decision, while spontaneous discontinuation was infrequent.

1. Introduction

The prescription and continuation of recommended drug preventive therapies after hospitalization for acute coronary syndromes (ACS) are associated with an improvement of clinical outcome [1–3]. Current European and American guidelines recommend the long-term use of 5 classes of medications in secondary prevention after ACS: aspirin, statin, beta-blocker, angiotensin-converting enzyme inhibitor or angiotensin receptor blocker (ACEI or ARB) and in addition P2Y12 inhibitors for 1 year [4–8]. However, discontinuation to prescribed therapies after hospital discharge is common with adverse clinical outcomes in patients with ACS [9–12].

A recent meta-analysis on 376,162 patients reported that adherence to recommended therapies varied between 60 and 75% in secondary prevention [13]. In those studies, adherence was defined as the proportion of patients who had at least 75% of days covered by the drug over a defined time period using pharmacy prescription refill data. Patients who forgot to take medications on some days were considered to be non-adherent, although physicians could have stopped the treatment for a medical reason. Measuring non-adherence based on prescription

Abbreviations: ACS, acute coronary syndromes; ACE, angiotensin converting enzyme; ARB, angiotensin receptor blocker; CABG, coronary artery bypass graft; CHD, coronary heart disease; CR, cardiac rehabilitation; LVEF, left ventricular ejection fraction; NSTEMI, non-ST elevation myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction.

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claims databases might be flawed, because the appropriateness of medication discontinuation is not provided and discontinuation of recommended mediation is traditionally referred to as medication non-adherence [14–18]. Therefore, assessment of medication adherence and reasons for non-adherence by physicians are strongly recommended (Class I, Level A) by the 2012 European Society of Cardiology (ESC) guidelines on cardiovascular disease prevention [19].

Limited data exist about the reasons for medication discontinuation in the real practice after ACS according to patients' point of view [20]. Attributing medication discontinuation to patient non-adherence might be stigmatizing and asking patients the reasons for therapies discontinuation could provide a patient-centered care approach of the potential barriers regarding the long-term use of preventive therapies after ACS [21]. In this Swiss prospective multicenter cohort of patients with an ACS, we aimed at determining (1) the discontinuation percentage of recommended cardiovascular therapies one year after the index ACS event and (2) the reasons for cardiovascular medication discontinuation reported by the patients.

2. Methods

2.1. Patient population

The SPUM-ACS (Special Program University Medicine-Acute Coronary Syndrome, clinical trial number NCT01000701) cohort is a prospective cohort study of patients enrolled with a main diagnosis of ACS in four Swiss university hospitals (University hospital of Bern Geneva, Lausanne and Zürich) [22]. We included for this analysis patients enrolled from September 2009 to December 2012, aged >18 years, hospitalized within 5 days of symptom onset, and with a main diagnosis of ACS. ACS was defined as symptoms compatible with angina pectoris (chest pain, dyspnea) and at least one of the following characteristics: ST-segment elevation or depression, T-wave inversion or other dynamic ECG changes, evidence of positive troponin, and coronary heart disease (CHD) defined as history of myocardial infarction, coronary artery bypass graft (CABG), percutaneous coronary intervention (PCI) or newly documented ≥50% stenosis of an epicardial artery during the index angiography [4,5] and [23]. Exclusion criteria comprised severe physical disability if patients were unable to participate in the one year follow-up, inability to give informed consent and life expectancy of less than one year (for non-cardiac reasons). The final ACS diagnosis was classified as follows: STEMI (ST-segment elevation myocardial infarction), NSTEMI (non ST-segment elevation myocardial infarction) or unstable angina [23]. Patients were included in the catheterization laboratory in two participating hospitals (ZH and BE) and additionally while on ward in two participating hospitals (LA and GE) [22]. The study protocol was approved by the local ethical committees, and all participants provided written informed consent.

2.2. Medication assessment

We collected data on recommended secondary prevention medications at discharge and at one year. We also assessed the attendance to cardiovascular rehabilitation (CR) and medical follow-up rate during the year after the initial event. We defined discontinuation of treatment as a therapy prescribed at discharge but not continued at the one-year clinical assessment. The selection of recommended therapy was pre-specified according to the American and European guidelines: aspirin, P2Y12 inhibitors (clopidogrel, prasugrel, ticagrelor) if PCI, statin, beta-blocker or ACE inhibitor/ARB (Supplementary Tables 1 and 2) [8,19]. During interview, patients were asked to bring and read all of their current medications to the interviewer, including drug name, dose, and schedule, as done in a previous publication [3]. In case of medication discontinuation, we asked the following open question to the patient "Why did you stop taking the medication?" The question was openly asked without suggesting a specific answer. According to the statement obtained by the patients, we coded the answer into the following reasons: (1) "The physician stopped it or did not think it was necessary, (2) to avoid the side effects I suffered, (3) I could not afford it, (4) I felt it was unnecessary to continue and (5) other reasons reported by the patient." Only one reason was authorized per medication and the list of reasons was pre-specified based on a previous publication on long term adherence among patients after an ACS [20]. To estimate the accuracy of the patients' statement, we performed a cross-check validation among 115 participants using medical prescriptions or documentations. If the reason was unclear for the patient, we coded the reason post-hoc as «Unclear reason for the patient». We performed a subgroup analysis according to baseline LVEF, as the recommendation to give beta-blocker and ACE inhibitor/ARB in case the left ventricular ejection fraction (LVEF) ≤ 40% was strong (Class A, Level I),

2.3. Follow-up

Participants were contacted by a trained study nurse for a clinical visit one year after the ACS at the enrollment site. If patients were unable to come to an in-person clinical visit, visits were performed in the following order: (1) by phone calls, (2) by mails or emails, (3) by the family members and finally (4) by the primary care physician. We performed sensitivity analyses to assess whether the discontinuation percentages varied by the method of ascertainment. All data were entered by trained nurses in a web-based centralized data entry system (Cardiobase, Clinical Trial Unit and Department of Cardiology, Bern University Hospital, Switzerland, and 2mT, Ulm, Germany) fulfilling the principles of ICH/GCP guidelines quality control process of data management.

2.4. Co-variables

We collected baseline data on gender, age, use of cardiovascular medication (aspirin, P2Y12 inhibitor, statin, beta-blocker, ACE inhibitors/ARB, anticoagulant, diuretic, antiarrythmic, digoxine, calcium channel blocker, nitrate, antidepressant, immunosuppressive), previous myocardial infarction (MI), history of hypertension, history of hypercholesterolemia, history of diabetes mellitus, body mass index (BMI), working, marital and educational status, revascularization treatment, baseline LVEF, discharge treatment including prescription and documentation of contra-indications. The attendance to CR was assessed using data at discharge (direct transfer) and at one year asking the patients if they attended a CR program (inpatient or outpatient).

2.5. Statistical analysis

The proportion of discontinuation for each recommended medication, as well as reasons for discontinuation, was reported as frequencies for the five recommended therapies (aspirin, P2Y12 inhibitors if PCI, statin, β-blocker and ACE inhibitor/ARB). Exploratory stratified analyses were performed according to patients' characteristics (age, gender, educational, marital, baseline ACS diagnosis, attendance to CR and LVEF dysfunction). Those strata were preselected before analysis based on previous publication [15,17,20,24]. The level of significance was established a priori at 2-sided $P < 0.05$. All analyses were performed using Stata version 12.1 (Stata Corporation, College Station, Texas). The authors are responsible for the design, the conduct, statistical analysis, drafting and its final content.

3. Results

3.1. Baseline characteristics and follow-up data

The mean age of participants was 62.6 ± 12.2 years and 635 (20.8%) were females. Prior to hospitalization, 903 (29.7%) were on aspirin, 881 (29.0%) were on statin, 695 were (22.9%) on beta-blocker and 1025 (33.8%) were on ACE inhibitor/ARB. At the index hospitalization, 2635

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(86%) had PCI with stent, 138 (5%) had PCI with balloon, 59 (2%) had a coronary revascularization with CABG and 223 (7%) were treated conservatively. 2086 patients (70.5%) attended a CR program (inpatient or outpatient) after discharge (Table 1). Of the 3261 patients enrolled at baseline during the hospitalization for the index ACS event from September 2009 to December 2012, the follow-up was performed in 3055 patients (93.4%). Of the remaining patients, 84 (2.6%) died, 79 (2.4%) refused the follow-up and 43 (1.3%) were lost-to-follow-up. The follow-up was realized in 97.4% (2974) of cases with the patient, while the rest with the family, the treating physician or the staff of the nursing home. The visits with patients were performed in 2486 of cases by clinical visit (83.6%), in 448 by phone call (14.7%) and in 40 by mail or email (1.3%) (Supplemental Fig. 1). 2938 patients (98.4%) had a medical follow-up with a treating physician and 2247 (77.9%) had consulted a cardiologist during the year.

3.2. Medication discontinuation

Among patients with available one-year follow-up, 3014 (99.2%) were discharged with aspirin, 2983 (98.3%) with statin, 2464 (81.1%) with beta-blocker, 2738 (90.2%) with ACE inhibitors/ARB and 2597 (100%) with P2Y12 inhibitors if treated with coronary stent. At one year, 2938 (96.7%) participants used aspirin, 2819 (92.9%) statin, 2391 (78.8%) beta-blocker, 2465 (81.2%) ACE inhibitor/ARB and 2126 (81.9%) P2Y12 inhibitors (Table 2). The discontinuation rate one year after an ACS varied according to the class of medications: 2.9% (N = 88/3038) for aspirin, 6.6% (N = 201/3036) for statin, 11.6% (N = 351/3037) for beta-blocker, 13.5% (N = 413/3034) for ACE inhibitors/ARB and 17.8% (N = 461/2598) for P2Y12 inhibitors (Fig. 1). In patients treated with drug eluting stent, the discontinuation rate was lower (N = 315/2043, 15.4%) compared with those treated with bare metal stent (N = 155/545, 28.4%). Results were similar in sensitivity analyses after excluding data collection obtained from the general practitioners.

3.3. Reasons for medication discontinuation

Physicians' decision to stop was the most common cited reason of discontinuation among all recommended medication by the patients: 64 for aspirin (2.1%), 82 for statin (2.8%), 212 for beta-blocker (8.6%), 251 for ACE inhibitor/ARB (9.2%) and 293 (11.4%) for P2Y12 inhibitors, while side effects, perception that medication was unnecessary and medication costs were uncommon reported reasons (<2%) according to the patients (Table 3). Considering the relative percentages of reported reasons of discontinuation according to the patients, physicians' decision was a leading reason across all groups of medication: 89.1% for P2Y12 inhibitors, 84.1% for beta-blockers, 83.1% for aspirin, 81.2% for ACE inhibitor/ARB and 52.2% for statin (Fig. 2). The primary care physician stopped more frequently aspirin and statin, while cardiologist stopped more beta-blockers and ACE inhibitor/ARB. Side effects were an uncommon reported reason (4.6% for P2Y12 inhibitors, 7.8% for aspirin, 9.5% for beta-blocker and 12.6% for ACE inhibitor/ARB), except for statin (33.1%). Among 115 participants who reported to have discontinued therapies by their physician, 113 had an available documented confirmation for therapy discontinuation by the physicians. The reasons for therapy discontinuation were mainly related to clinical indications and side effects (bleeding, bradycardia, hypotension, muscular side effects, bare metal stent, end of P2Y12 inhibitors treatment, elderly, and fatigue). In 2 cases, therapy was switched for another drug of the same indication.

3.4. Patient characteristics and medication discontinuation

The discontinuation rates among the elderly (≥75 years old) were significantly higher for aspirin (4.7% vs. 2.5%), P2Y12 inhibitors (22.0% vs. 16.9%) and statin (8.6% vs. 6.2%) compared to younger patients (<75 years old). In patients who did not attend a CR program, the discontinuation rates was significantly higher for aspirin (4.4% vs. 2.2%) and for statin (10.2% vs. 4.9%). The discontinuation rates in those with a baseline LVEF ≤ 40% were similar for beta-blocker (12.7% vs. 11.6%), but less for ACE inhibitor/ARB (8.1% vs. 15.0%) (Table 4). No significant differences were found according to the educational status, while we observed a lower rate of aspirin discontinuation (2.4% vs.4.0%) and

Table 1
Baseline characteristics of 3055 patients with follow-up.

Variables[a]	
Women, n (%)	635 (21)
Age, mean (±SD)	62.6 (±12.2)
Elderly ≥ 75 years old, n (%)	563 (18)
BMI categories, n (%)	
<25 kg/m^2	947 (32)
25–29.9 kg/m^2	1387 (46)
≥30 kg/m^2	662 (22)
ACS diagnosis, n (%)	
STEMI	1634 (54)
NSTEMI	1278 (42)
Unstable angina	133 (4)
Marital status, n (%)	
Married/partnership	2052 (68)
Divorced/widowed/single	968 (32)
Educational status, n (%)	
Apprenticeship/vocational school or lower, n (%)	1996 (74)
University/High school graduation, n (%)	702 (26)
Working status, n (%)	
Full time, n (%)	1183 (41)
Part time, n (%)	236 (8)
No employment/retired, n (%)	1496 (51)
History of MI, n (%)	449 (15)
History of diabetes, n (%)	529 (17)
History of hypercholesterolemia, n (%)	1873 (62)
History of hypertension, n (%)	1711 (56)
Previous use of aspirin, n (%)	903 (30)
Previous use of statin, n (%)	881 (29)
Previous of beta-blockers, n (%)	695 (23)
Previous use of ACE inhibitor/ARB, n (%)	1025 (34)
Current smoker, n (%)	1222 (41)
Index revascularization therapy, n (%)	
PCI with stent	2635 (86)
PCI with balloon	138 (5)
CABG	59 (2)
Conservative	223 (7)
Attendance to CR, n (%)	2086 (71)

Abbreviations: ARB, angiotensin receptor blocker; ACS, acute coronary syndrome; ACE, angiotensin converting enzyme; BMI, body mass index; CABG, coronary artery bypass graft; CR, cardiac rehabilitation; MI, myocardial infarction; NSTEMI, non-ST elevation myocardial infarction; PCI, percutaneous coronary intervention; SD, standard deviation; STEMI, ST-elevation myocardial infarction.

[a] Missing values: 59 for BMI, 10 for ACS diagnosis, 35 for marital status, 357 for educational status, 140 for working status, 7 for previous MI, 4 for ACE inhibitors/ARB.

Table 2
Use of recommended therapies at discharge and at one year.

Therapies[a]	At discharge[b]	At one year[b]
	N (%)	N (%)
Aspirin	3014 (99.3)	2935 (96.7)
Statin	2983 (98.4)	2815 (92.8)
Beta-blocker	2464 (81.2)	2387 (78.7)
ACE inhibitor/ARB	2738 (90.3)	2465 (81.3)
P2Y12 inhibitor if PCI	2597 (100.0)	2126 (81.9)

Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; PCI, percutaneous coronary intervention.

[a] Among 3055 patients, those with had missing values for discharge and one year follow-up medications were excluded: 20 for aspirin, 23 for statin, 22 for beta-blocker, 24 for ACE inhibitors/ARB and 38 for P2Y12 inhibitor. Therefore, the percentages were calculated using following total number for each class of medications: 3035 for aspirin, 3032 for statin, 3033 for beta-blockers, 3031 for ACE inhibitor/ARB and 2597 for P2Y12 inhibitor.

[b] Medication at hospital discharge was collected based on medical records and at one year based on patients' statements.

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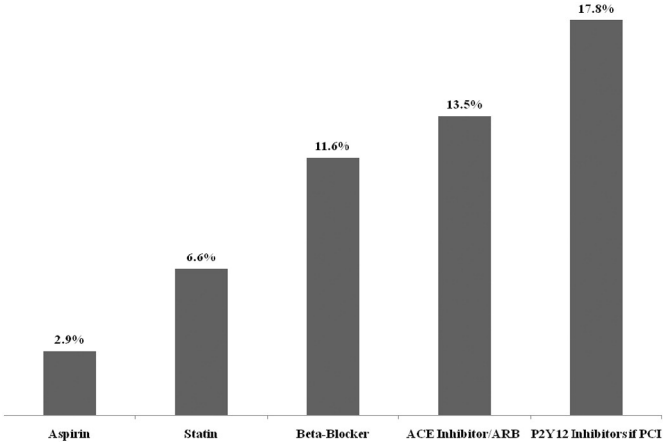

Fig. 1. Discontinuation of recommended therapies one year after acute coronary syndromes. Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; PCI, percutaneous coronary intervention.

statin discontinuation (5.8% vs. 8.0%) in married patients compared to non-married (single, widow and divorced).

4. Discussion

In this large prospective multicenter cohort of patients with an ACS, the discontinuation rate was highest for beta-blocker (14.3%), ACE inhibitor/ARB (15.1%) and P2Y12 inhibitors (17.9%) compared to aspirin (2.9%) and statin (6.7%). In patients with a LVEF ≤ 40%, the discontinuation rate was lower with ACE inhibitor/ARB (8.1%). The patients attributed predominantly the reasons of medication discontinuation to their physicians' decision for all classes of preventive medications, while side effects, educational issues or costs were uncommon reported reasons. Our findings suggest that patients after ACS stopped medication mostly after their physicians' decision, while spontaneous discontinuation of medication was infrequent.

4.1. Distinction between discontinuation and non-adherence

"To interpret our study, it is important to distinguish between discontinuation of therapies for specific reasons (appropriate or not) and non-adherence to prescribed therapies. Previous studies mainly focused on the prescription of recommended therapies at hospital discharge as an indicator of quality of care with a benefice on clinical outcome [1,2,22]. Studies assessing the continuation of medication after hospital discharge in the outpatient setting were based on pharmacy claims database corresponding to the filling of the drug prescription over a period of time [12, 17,18,24]. Two studies reported at 6 or 12 months the medication use after discharge by telephone interviews with patients, however the reasons and the appropriateness of drug discontinuation were not assessed [3,25]. Complete discharge medication card, hospital-based prevention programs and early follow-up were all associated with an improvement of the long-term use of medication [24–26]. A recent randomized controlled trial including pharmacists, patient education, voice messaging and collaboration between primary care physician and cardiologist improved the continuation of recommended therapies [18]. However, the authors used the term "adherence" for describing continuation of treatment therapies calculated as the proportion of days covered during the one year follow-up [18]. The improvement of medication adherence with all those interventions is likely linked to an increased motivation of patients enrolled in such motivational and educational programs. Therefore, secondary preventive measures, such as attendance to a CR program are strongly recommended by the European and American guidelines in secondary prevention [8,19]. In our study, we found that most discontinuations were attributed to physicians when questioning patients. Interestingly, none of those studies assessed the reasons for discontinuation."

4.2. Appropriateness of guidelines application

Interestingly, the patients attributed predominantly the reasons of medication discontinuation to their physicians' decision. The same observations were also reported by Sud et al. where physicians' decision to stop treatment was the leading cited reasons (between 50 and 60%) of therapies discontinuation [20]. The physician decision might have been motivated because of side effects or the prescription of a co-medication, which is also a frequent cause. The relevance of our findings might demonstrate a potential gap in the practice of the outpatient physicians or heterogeneity in the interpretation of guidelines [27]. Especially, there is a lack of explicit guidance on how to approach clinical-decision making for patients with multimorbidity. Current guidelines do not address the challenges in the care of patients with mutlimorbidity, as well as the quality of evidence available for summarizing benefits and harms and formulating recommendations for this specific population [28]. A strict application of the guidelines in real practice might be impaired by some aspects of the therapeutic relationship between the physicians and their patients or in the perceptions of the benefit/risk ratio for the beta-blocker and ACE inhibitors/ARB. This issue might especially be true in patients without heart failure or left ventricular dysfunction who had a better prognosis compared to those with ventricular dysfunction [29]. The favorable impact of the combination of all evidence-based therapies on mortality has been reported in observational studies [1,30]. The American secondary prevention guidelines recommend the pursuit of β-blocker at least three years after an ACS in patients without ventricular dysfunction, however the evidence is not strong [8]. Beta-blockers have been studied at times when the current invasive revascularization treatment was not available and some concerns were reported regarding their introduction in patients with unstable hemodynamic conditions [31]. The same observation might be also considered for ACE inhibitors/ARB

Table 3
Absolute numbers of reported reasons by the participants for medication discontinuation.

	Aspirin	Statin	Beta-blocker	ACE inhibitor/ARB	P2Y12 inhibitors if PCI
Number prescribed at discharge	N = 3014	N = 2983	N = 2464	N = 2738	N = 2579
Pre-specified reasons[a, b]	N (%)	N (%)	N (%)	N (%)	N (%)
Physician stopped it[c]	64 (2.1)	82 (2.7)	212 (8.6)	251 (9.2)	293 (11.4)
To avoid side effects	3 (0.1)	41 (1.4)	23 (0.9)	35 (1.3)	9 (0.3)
I could not afford it	3 (0.1)	11 (0.4)	1 (0.0)	4 (0.1)	6 (0.2)
I felt it was unnecessary to continue	4 (0.1)	17 (0.6)	13 (0.5)	14 (0.5)	9 (0.3)
Unclear reason for the patient	9 (0.3)	0 (0.0)	77 (3.1)	76 (2.8)	32 (1.2)
Other reasons reported by the patient	3 (0.1)	6 (0.2)	3 (0.1)	5 (0.2)	12 (0.5)

[a] Subjects could provide one reason. P2Y12 inhibitors or anticoagulants for aspirin, anticoagulants for P2Y12 inhibitors, other lipid-lowering therapies for statin, ACE inhibitor/ARB for beta-blocker and beta-blocker for ACE inhibitor/ARB.
[b] Missing values for reported reasons: 6 for aspirin, 44 for statin, 22 for beta-blockers, 28 for ACE inhibitors/ARB and 100 for P2Y12 inhibitor.
[c] Physician were defined by primary care physician, cardiologist or other specialists (see text in the methods).

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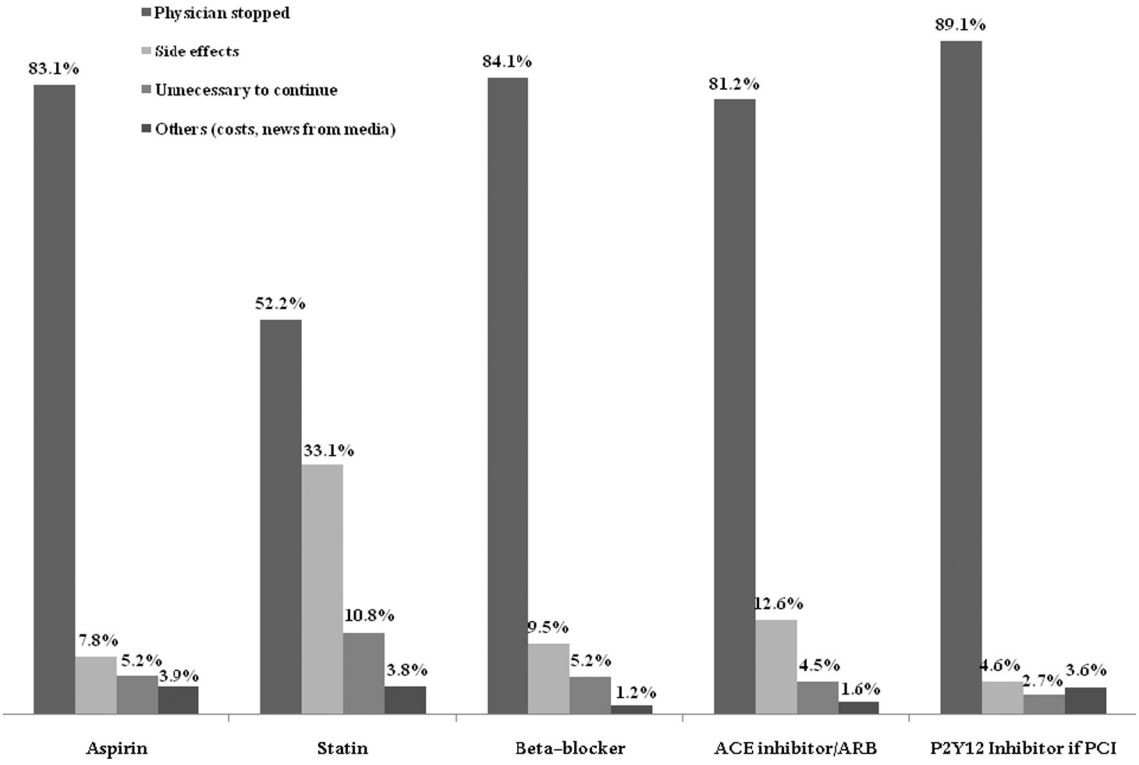

Fig. 2. Relative percentages of provided reasons for recommended therapies discontinuation according to the patients. Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker.

medications where previous studies reported some non-favorable benefits in patients with low risk or stable CHD [32,33]. It is possible that physicians preferred to stop beta-blocker or ACE inhibitor/ARB in case of a concomitant use of both medications. Regarding the P2Y12 inhibitors, guidelines recommend at least 12 months of treatment beyond PCI, although the duration might be shorter in case of bare metal stent implantation or high risk of bleeding. For this reason, the higher rate of discontinuation for P2Y12 inhibitors might be explained by an appropriate discontinuation of therapy by the physicians [4,5]. Our data suggest that in a great majority patients do not discontinue therapies without the approval or advice of their treating physicians. The Swiss health system is characterized by a strong network of primary care physicians and universal coverage of medical insurance with a small co-participation (10%) to medications costs. More than 98% of participants were followed by their physicians and 77% had a follow-up by the cardiologist during the year. In addition, the quality of care documented at hospital discharge was high, as well as the attendance to a CR program after hospital discharge (more than 70% of patients).

4.3. Future perspectives

Adherence to therapy is not only a major issue for patients, but also for care-providers and the health-care system. The reasons for medication non-adherence are multifactorial, such as medical conditions, patients' preferences, therapy complexities, socioeconomic factors, poor coordination within the healthcare system and incomplete physician communication or education [34–36]. The 2012 European Society of Cardiology guidelines on cardiovascular disease prevention recommend physicians to assess adherence to medication and to identify reasons for non-adherence in order to tailor interventions to the individual needs of the patient [19]. Improvement of communication skills and working on an improved patient–physician alliance has been shown to improve medication adherence [37,38]. Besides continuing and improving patients' education and secondary preventive efforts at discharge and during CR phase, the pertinence of studying interventions in the outpatient settings, including treating physicians, might be a critical step for improving the application for evidence in clinical practice and the prognosis of patients after an ACS [19]. Patients' perception about the need of medication continuation warrants better understanding, especially the way of communication of the physicians and the comprehension of the disease [38]. Further research is needed to explore the physicians' decisions and the factors that guide therapy discontinuation in secondary prevention after an ACS. More data are needed to fully understand whether the discontinuation reasons are appropriate or not. In addition, a patient-centered approach dedicated to the patients' needs and interests will be a critical step in designing clinical research based on the patient's point of view and their participation in the process of care [21,36].

4.4. Limitations

The continuation of medication was self-reported and not validated with a direct measure, such as pharmacological dispositive counter. However, self-reported adherence has been used widely in several studies and been associated with clinical outcomes [13,34,39]. We also asked patients to bring the list of medications, as well as the pill boxes to confirm their statement. In addition, we collected reasons for medication discontinuation according to the patients and confirm the reasons with each single physicians in a randomly selected sample of 115 non compliant patients. Therefore a social desirability bias or recall bias could not be excluded, such as the attribution of discontinuation to the physician instead of patients, as well as the exact cause of medication discontinuation by the physician (mild bleeding, hypotension or side effects). However, communication between patients and physicians might be improved, as the reason of discontinuation was not clear for many patients. Furthermore the lost-to follow-up and withdrawal rates of the participants were especially low (<2%) in our cohort. Along these lines, we did not have collected data on the LVEF evolution, thus limiting a potential justification of beta-blocker discontinuation. This cohort might also not represent the real world population admitted

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Table 4
Discontinuation of therapies according to the patient characteristics in those prescribed at discharge.

Patient characteristics[a]	Aspirin discontinuation	Statin discontinuation	Beta-blocker discontinuation	ACE inhibitor/ARB discontinuation	P2Y12 inhibitors discontinuation
	N (%)	N (%)	N (%)	%	%
Age					
<75 years old	62 (2.5)	153 (6.2)	290 (11.7)	338 (13.7)	364 (16.9)
≥75 years old	26 (4.7)	48 (8.6)	61 (10.9)	75 (13.4)	97 (22.0)
P value	0.01	0.03	0.60	0.89	0.01
Gender					
Men	63 (2.6)	141 (5.9)	276 (11.5)	326 (13.7)	359 (17.3)
Women	25 (4.0)	60 (9.5)	75 (11.9)	87 (13.8)	102 (19.4)
P value	0.07	0.00	0.76	0.87	0.22
Educational level					
High	7 (1.8)	26 (6.8)	52 (13.6)	58 (15.1)	63 (19.0)
Low	66 (2.9)	154 (6.7)	258 (11.2)	300 (13.1)	318 (16.1)
P value	0.24	0.95	0.19	0.27	0.19
Married/partnership					
Yes	49 (2.4)	118 (5.8)	236 (11.6)	280 (13.7)	296 (16.7)
No	38 (4.0)	80 (8.4)	110 (11.5)	128 (13.4)	157 (19.3)
P value	0.02	0.008	0.97	0.82	0.07
ACS Diagnosis					
STEMI	37 (2.3)	99 (6.1)	184 (11.3)	218 (13.4)	251 (16.6)
NSTEMI/UA	51 (3.6)	101 (7.2)	166 (11.9)	195 (13.9)	210 (19.5)
P value	0.03	0.22	0.64	0.69	0.055
Attendance to CR					
Yes	46 (2.2)	101 (4.9)	234 (11.3)	275 (13.3)	305 (16.7)
No	38 (4.4)	88 (10.2)	97 (11.3)	115 (13.4)	127 (18.7)
P value	0.001	<0.001	0.98	0.94	0.25
LVEF ≤ 40%					
Yes	18 (3.6)	31 (6.1)	64 (12.7)	41 (8.1)	95 (21.5)
No	59 (2.7)	146 (6.7)	253 (11.6)	328 (15.0)	318 (17.0)
P value	0.29	0.66	0.48	<0.001	0.03

Abbreviations: ACS, acute coronary syndrome; CR, cardiac rehabilitation; LVEF, left ventricular ejection fraction; NSTEMI, non ST-elevation myocardial infarction; STEMI, ST-elevation myocardial infarction; and UA, unstable angina.

[a] Missing values: 10 for ACS diagnosis, 35 for marital status,, 98 for attendance to CR, 357 for educational status and 342 for LVEF.

for an ACS. Patients were included in the catheterization laboratory and the emergency wards. It is probable that recruitment in the cat lab strategy was more successful and favored the inclusion of STEMI patients in our study. Notably, the proportion of ACS patients with STEMI (54%) was higher in our study compared to other European registries (40–47%) [40–42]. The rate of discontinuation of the recommended therapies might be not representative of other European countries and patients hospitalized for ACS in other hospitals in Switzerland. We also observed a higher rate of attendance to CR compared with other cohorts, a higher quality in the prescription at discharge, as well as higher follow-up rate with physicians (99%) during the year, which all are likely to have improved medical adherence. Furthermore, the Switzerland health system guarantees universal insurance coverage, the patients' participation to the medication costs is small and the educational level of the population is high.

5. Conclusion

Discontinuation of recommended cardiovascular therapies one year after acute coronary syndrome differs according to the class of medications. The discontinuation was the lowest for aspirin compared to other recommended therapies, such as statin, beta-blocker, angiotensin-converting enzyme inhibitor or angiotensin receptor blocker and P2Y12 inhibitors. Interestingly, the main reason for cardiovascular medication discontinuation reported by the patients was the physicians' decision more than potential side effects or the patients' spontaneous decision to stop. Further studies are needed to explore among physicians the reasons of cardiovascular therapy discontinuation and the impact of their patients' point of view in clinical decision.

Disclosures

Dr Mach reports receiving research grants to the institution from Amgen, AstraZeneca, Boston Scientific, Biotronik, Medtronic, MSD, Eli Lilly and St. Jude Medical. Dr Klingenberg received lecture fees from Eli Lilly, Servier and Bayer. Dr Lüscher reports receiving research grant to the institution from Abbott, Biosensors, Biotronik, Boston Scientific, and Medtronic, and consultant payments from AstraZeneca, Boehringer Ingelheim, Bayer, Merck, and Pfizer. Dr Matter reports receiving grants from MSD, Eli Lilly, AstraZeneca, and Bayer; expert testimony from MSD, payment lectures from MSD, AstraZeneca, and Roche. Dr Windecker reports receiving research contracts to the institution from Abbott, Biotronik, Boston Scientific, Biosensors, Cordis, Medtronic, St. Jude Medical and speaker fees from: Abbott, Biotronik, Boston Scientific, Biosensors, Medtronic, Eli Lilly, and Astra Zeneca. All other authors have no conflict of interest to declare.

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Appendix A. Supplementary data

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