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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