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Comparison of in-hospital secondary prevention for different vascular diseases

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ABSTRACT

Background: Secondary prevention of coronary artery disease is highly effective and implemented on a large scale. However, studies testing adherence to recommended secondary prevention of other vascular diseases are rare. Our goal was to evaluate whether the kind of vascular disease influences prescription practice of secondary drug prophylaxis at hospital discharge and to which extent secondary prevention is actually complete.

Methods: A 3-month prospective observational review of the hospital discharge information of all patients hospitalized because of a vascular disease diagnosis: coronary artery disease (i.e. acute myocardial infarction [AMI] and chronic stable angina [CSA]); peripheral artery disease [PAD] and cerebrovascular disease [CVD]. The analysis was done by board registered internists with a structured form that founded on internationally accepted recommendations.

Results: From 271 patients 191 had coronary artery disease (105 AMI and 86 CSA), 88 PAD and 72 CVD. Global prescription rate (mean; 95% CI) of indicated secondary prophylaxis drugs was 74.1% (69.9–78.2) for AMI, 72.4% (67.2–77.5) for CSA, 74.7% (68.8–80.7) for PAD and 72.1% (66.9–77.3) for CVD. The proportion of patients who were prescribed a complete bundle of recommended medications was globally 29.5% (24.1–35.0).

Conclusions: We found similar global prescription rates of secondary prevention for the different vascular diseases. However, only one third of the studied collective gets a complete set of required prophylactic drugs.

1. Introduction

The pharmalogical secondary prophylaxis of cardiovascular risk factors has proven useful in lowering morbidity and mortality in coronary artery disease, and numerous international recommendations guide physicians towards a more adequate prescription of these drugs [1,2–4]. Over the last few years several studies have demonstrated clear improvements in the pharmacological prevention of coronary artery disease [5–7]. However, the targets are still not met and the most evident gaps may be found in older people, women, outpatients and diabetics [7–16].

As vascular diseases share common risk factors and pathomechanisms, comparable guidelines have been published for peripheral arterial (PAD) and ischemic cerebrovascular (CVD) disease [17–20]. However, studies testing adherence to these recommendations have been performed very rarely for PAD and CVD [21], and this minor attention might hide a reduced adherence to guidelines [11,13,22]. Moreover, previous research only reports prescription rates of the single preventive drugs, and does not analyze overall medication rates and to which degree patients are prescribed a complete set of recommended drugs [5–14,22–23].

The aim of this study was to assess the global prescription rate of secondary prophylactic medications at hospital discharge for each type of vascular disease, to analyze subgroups of patients at particular risk for undertreatment and finally to determine the proportion of patients being prescribed a complete secondary drug prophylaxis.

2. Methods

2.1. Study design and setting

This is a prospective, observational study and its methods were approved by the Cantonal Ethics Committee. The study was performed in the Department of General Internal Medicine at the Ospedale San Giovanni in Bellinzona, Switzerland.

2.2. Study protocol

We consecutively considered and analyzed the hospital discharge information of all patients hospitalized between March 1, 2007 and May 31, 2007 because of acute myocardial infarction (AMI: ST-segment elevation myocardial infarction [STEMI] and non-ST-segment elevation

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myocardial infarction [NSTEMI]), chronic stable angina (CSA), CVD (transient ischemic attack and ischemic stroke) or PAD. The analysis was done by means of a structured form based on internationally accepted recommendations for secondary prophylaxis of vascular diseases [2–4,18–20]. This study allowed us to observe our steady-state situation of drug prescription, since it was performed without previous information campaign.

From a total of 592 discharged patients, 271 (prevalence of vascular diseases: 46%) were included due to a pertinent diagnosis. We stratified the study population into 6 groups (STEMI, NSTEMI, CSA, embolic and atherosclerotic CVD, PAD) and recorded general patient characteristics and the presence of recommended secondary drug therapy (see point 2.3) in order to compute frequencies. Omission of medications justified by a clear contraindication (e.g. aldosteron antagonist omitted due to severe chronic kidney failure) was disregarded as a deficiency. We then calculated the global prescription rate of secondary prophylaxis (number of prescribed medications divided by the number of indicated medications) and the proportion of patients who were prescribed the complete set of necessary medications (patients lacking one or more required prophylactic drug were defined as incompletely treated). The prescription of certain drugs was dependent on cut-off levels (lipid-lowering therapy, arterial hypertension) or the presence of diabetes mellitus (defined according to WHO-criteria) [2–4,18–20,24]. Neglected measurement of lipid levels during hospital stay accounted as *non-adherence* as well as co-existent diabetes mellitus and/or arterial hypertension without a corresponding therapy (lifestyle changes and/or pharmacotherapy) or without an explicit suggestion for appropriate follow up.

2.3. Recommended secondary drug therapy and definitions of vascular diseases

For all vascular diseases the following Class I recommendations were required: 1) an antithrombotic agent such as aspirin or clopidogrel (if aspirin contraindicated) or aspirin plus clopidogrel (if current percutaneous coronary intervention with stent implantation), or warfarin (if atrial fibrillation, thrombo-embolic stroke or left ventricular thrombus); 2) a statin, if LDL-C $\geq$ 2.59 mmol/L (100 mg/dL); 3) an antihypertensive therapy for appropriate blood pressure control (BP<140/90 mm Hg or BP<130/85 mm Hg for concurrent chronic kidney disease or diabetes mellitus); and 4) a suitable diabetes management. The prescription of a beta-blocker was mandatory (diltiazem/verapamil if beta-blocker contraindicated) for all patients with AMI and for CSA in case of symptomatic disease. An angiotensin converting enzyme inhibitor or an angiotensin receptor blocker (if ACE contraindicated) was required for STEMI and for CSA with concurrent diabetes mellitus. Decreased left ventricular systolic function (ejection fraction <40%) was supposed to be treated with an angiotensin converting enzyme inhibitor (or angiotensin receptor blocker) and an aldosterone antagonist.

AMI was defined as the combination of typical symptoms and/or electrocardiographic signs with the characteristic course of biochemical markers of myocardial necrosis (rise of troponin I>0.10 µg/L). STEMI was diagnosed in case of ST-elevation in two contiguous leads ($\geq$0.2 mV in men or $\geq$0.15 mV in women in leads V_2–V_3 and/or $\geq$0.1 mV in other leads) or a new left bundle branch block. CSA was considered for a patient with known coronary artery disease and stable symptoms and when the current hospitalization was due to other causes. The definition of CVD was based on actual/past clinical evaluation, eventually supported by pathologic findings in brain imaging (in case of ischemic stroke). PAD was defined by typical clinical findings (history and physical examination) and ancillary examinations (invasive and noninvasive testing).

2.4. Data collection

The review process was performed in two steps. The initial step served as an assessment of accuracy between discharge summary reviewers and allowed the estimation of κ-values: during the first week of the project two experienced, board registered internists independently examined the same summaries. Reliability across reviewers was consecutively assessed by a third physician and scored using a previous reported scale [25]. Globally, inter-rater agreement was determined excellent (κ=0.86). During the second step of the review process (11 weeks), three internists jointly performed the analysis in order to further improve reliability. Thus, differences between the reviewers' judgments were resolved by discussion and a consensus was achieved.

2.5. Statistical analysis

All the analyses were done with S-Plus® 7.0 for Windows, Enterprise Developer, Insightful Corp. Differences between groups were tested with chi-square test for contingency tables (exact of Fisher when possible), or two-sided Student's *T* test for continuous variables. A multivariate logistic regression was performed to investigate the link between complete treatment adherence for different types of vascular disease and the following factors: gender, age, temporary stay in the Intensive Care Unit (ICU), number of drugs prescribed and length of hospital stay.

3. Results

During this 3-month period 271 consecutive patients were included in the study because of vascular disease diagnosis at discharge: 105 had AMI (28 STEMI and 77 NSTEMI), 86 CSA, 88 PAD and 72 CVD (8 embolic and 64 atherosclerotic). Their main characteristics are shown in Table 1. Women were (mean $\pm$ SD) older (76 $\pm$ 12 years vs 70 $\pm$ 12 years; p<.001), had more medications (8.2 $\pm$ 4.0 vs 7.3 $\pm$ 3.1; p=.046) and less AMI (23% vs 48%; p<.001) or PAD (24% vs 37%; p=.032) than male subjects, but tended to be affected more frequently from CSA (39% vs 27%; p=.067). Men suffered more often of multiple vascular disease (33% vs 18%, p=.010). Compared to the other groups, patients with PAD had more comorbidities, especially chronic kidney failure (82% vs 39%; p<.001), but the 12-month rates of mortality (p=.624) and hospital readmissions (p=.148) did not differ between groups.

Prescription rates of the single recommended drugs are listed in Table 2 according to the vascular diseases. Globally, an antithrombotic therapy (94%) was better prescribed than a treatment for concurrent diabetes mellitus (47%; p=.019), and these rates were independent of the pathology or gender (p=.778 for the antithrombotic therapy, p=.167 for diabetes mellitus). Patients with STEMI got more frequently a statin (p=.002) or an angiotensin converting enzyme inhibitor/angiotensin receptor blocker (p<.001) than subjects affected by other vascular diseases. A dual antiplatelet therapy was given to all 21 patients after percutaneous coronary intervention with stent placement. Eleven patients with coronary artery disease presented a contraindication to beta-blockers; in 10 (91%) cases that drug was substituted with either verapamil or diltiazem. After an AMI, beta-blockers and angiotensin converting enzyme inhibitors were prescribed (mean; 95% CI) at 50% (42–57) and 62% (53–70) of maximal recommended dosages. Antihypertensive therapy for CVD was realized in 21 of 50 (42%) patients with diuretics and in 26 of 50 (52%) patients with diuretics and/or ACE-inhibitors.

Global prescription rate of indicated secondary prophylaxis drugs was 74.1% (69.9–78.2) for AMI, 72.4% (67.2–77.5) for CSA, 74.7% (68.8–80.7) for PAD and 72.1% (66.9–77.3) for CVD (Fig. 1). Better results were observed for younger patients (<70 years: 79.8% vs 69.6%; p<.001) and shorter lengths of hospital stay (79.1% for <5 days, 71.7% for 5–14 days, 64.7% for >14 days; p=.002). There was also slight evidence for better adherence in case of a temporary stay in the Intensive Care Unit (p=.069) and for male patients (p=.066). In general, neither patients affected by multiple