Post-myocardial Infarction (MI) Care: Medication Adherence for Secondary Prevention After MI in a Large Real-world Population

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ABSTRACT

Purpose: Secondary medication prevention after acute myocardial infarction (MI) is strongly recommended in international guidelines, but actual use, adherence, and outcomes in current clinical practice are largely unknown. Therefore, the aims of this study were to determine the current adherence to medications for secondary prevention after MI and to estimate the association between medication adherence and mortality and major adverse cardiovascular events (MACE) in a large real-world population.

Methods: Using a large health care claims database, patients were selected who had been hospitalized with MI between 2012 and 2015 (N = 4349). Adherence to drug therapy after discharge was measured as the medication possession rate (MPR) per year (0%−100%, indicating the number of days with medication supplied relative to the total number of days) for the individual drug classes. The relationship between MPR and the risk of MACE and death was assessed by using Cox proportional hazards regression models.

Findings: A high proportion of patients with low MPR (0%−79%) was observed for all drug classes (47.6% for dual antiplatelet therapy (DAPT), 23.5% for lipid-lowering drugs (LLDs), 47.3% for angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, and 88.1% for beta-blockers (BB). Women and elderly patients were less likely to receive LLDs. Patients with high adherence to DAPT, LLDs, and angiotensin-converting enzyme inhibitors/angiotensin receptor blockers (MPR ≥80%) had a significantly reduced risk for all-cause mortality and MACE (LLD-group).

Implications: In a real-life setting, adherence to drug therapy for secondary cardiovascular prevention after MI was only moderate. Increased use of evidence-based treatment such as DAPT and LLDs in current clinical practice may improve long-term outcomes of patients with MI. Moreover, providing clear information, improved care transition, and a close collaboration between clinicians and physicians involved in an early outpatient follow-up is required. (*Clin Ther*. 2019;41:107−117)

Key Words: adherence, cohort study, drugs, heart, myocardial infarction, secondary prevention.

INTRODUCTION

Ischemic heart disease is the single most common cause of death.[1] However, mortality rates in patients with acute coronary syndromes have declined in recent years due to a greater use of early reperfusion therapy, primary percutaneous coronary intervention (PCI), modern antithrombotic therapy, and implementation of secondary prevention. Indeed, use

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of antithrombotic and lipid-lowering drugs (LLDs), treatment of heart failure, and risk factor control play an essential role for improving long-term outcomes in patients with acute myocardial infarction (MI).[2–4] Nevertheless, all-cause and cardiac death rates remain substantial, with a 5-year mortality risk >20% after acute coronary syndromes.[5] Current guidelines for the treatment of patients with MI are derived from a large body of evidence showing the beneficial effects of several single-drug therapies such as dual antiplatelet therapy (DAPT) with aspirin and a $P2Y_{12}$ inhibitor (prasugrel, ticagrelor, or clopidogrel), LLDs, angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs), and beta-blockers (BBs).[2,3] However, because these guidelines are based on findings from individual studies that evaluated, in most cases, only the effect of one single medication, actual use of multiple drugs and patient characteristics that determine medication adherence and outcomes in real life are largely unknown.[6] Moreover, previous studies on the care of patients with acute coronary syndromes are mostly based on the design of a randomized controlled trial (RCT) that lack information on translation of treatment guidelines into routine clinical practice. This point in view is remarkable given the growing debate about the advantages and disadvantages of RCTs compared with observational, real-life studies, particularly because medication nonadherence is a common and costly problem in a significant proportion of patients.[7–10]

Despite the evidence for improved long-term outcomes in patients with MI who receive optimal therapy, available data on currently recommended care delivered in routine clinical practice are limited and challenged by small patient numbers and limitations in study design.[2,3] Therefore, the aims of the present study were, first, to determine the current adherence to medications for secondary prevention after MI, and, second, to estimate the association between adherence and mortality and major adverse cardiac events (MACE) in a comprehensive real-world population.

PATIENTS AND METHODS

Study Design and Population

This retrospective population-based cohort study was based on a large anonymized health care claims database including pharmacy, medical, and health services records of obligatory health–insured persons in Switzerland (Helsana Insurance Group), covering the years 2012–2015. Helsana is one of the largest and most comprehensive national health insurance groups with ~1.2 million subjects (15% of the entire Swiss population) and is considered approximately representative of the general population. We considered all health care invoices submitted to Helsana for reimbursement. However, deductibles (ranging from 300 to 2500 Swiss francs [SFr]) and cost-sharing with 10% of the costs per year (maximum up to SFr 700) are compulsory for all insured persons in Switzerland. The deductible of SFr 300 is seen as standard but can be chosen as a higher deductible (SFr 500, 1500, 2000, or 2500) in exchange for reduced premiums. Furthermore, persons have the choice between a standard care model and a managed care model. Managed care models included health plans with capitation, family physician models, or telemedicine models. The database comprises longitudinal information on patients' sociodemographic characteristics, prescribed drugs (substance, dose), clinical diagnosis, health care utilization, and date of death. We included all patients aged ≥18 years who were discharged from the hospital with a primary diagnosis of acute MI (World Health Organization International Classification of Diseases codes I.21 and I.22) between January 1, 2012, and December 31, 2015. Patients who died within the first month after hospital discharge were excluded from the study group.

Medication Use and Adherence

Medication use was assessed within the first month after hospital discharge of patients with MI and considered for the following medications recommended for secondary prevention: aspirin, $P2Y_{12}$ inhibitors (clopidogrel, prasugrel, and ticagrelor), LLDs, ACE inhibitors/ARBs, and BBs. Adherence to medication after discharge was evaluated by using the proportion of patients who were prescribed DAPT, LLDs, ACE inhibitors/ARBs, or BBs after hospital discharge. For each medication, we determined the medication possession rate (MPR), which is a valid standard measure of adherence calculated by dividing the number of days of medication supplied (numerator) by the number of days (denominator) in a time period of 1 year (365 days).[11,12] If patients were hospitalized due to a

recurrent MI or died before the end of the 1-year time period, these cases were included for determining adherence as well. The MPR ranges from 0% (completely nonadherent) to 100% (completely adherent). Overall, 2 patient groups with different adherence levels were defined: patients with "low adherence" if their individual MPR was 0%−79%, and patients with "high adherence" if their MPR was ≥80%.

Variables

Baseline characteristics of patients were determined at the index date and included sex, age, type of health plan, and type of cost-sharing. Patients' comorbidity status was measured by using 4 indicators: (1) coexisting illnesses at index hospitalization (diabetes mellitus, hypertension, unstable angina, congestive heart failure, stroke, and atrial fibrillation); (2) medication use 1 year before index hospitalization; (3) history of MI (previous year); and (4) a summarized comorbidity index (Charlson Comorbidity Index 0, 1−2, 3−4, ≥5), measured within 1 year before index hospitalization. The Charlson Comorbidity Index is a valid method for classifying comorbid diseases that might influence the mortality risk for use in longitudinal studies.[13,14] Health outcomes included the risk of recurrent hospitalization for MACE including MI, unstable angina and stroke, and death within the follow-up period from January 1, 2012, to December 31, 2015.

Statistical Analysis

Initially, data were analyzed by using frequency tables. Descriptive results are given as number (percentage) of patients for categorical variables and as mean values with standard deviation (SD). Density plots are provided to display the distribution of the MPR as a continuous variable for each drug treatment group. We further used a multivariable logistic regression model to estimate the effect of patient characteristics on the probability of adherence to the secondary prevention drug therapy. The predictive performance of the regression model was assessed by calculating the c-statistic, which is equivalent to the AUC. Cox proportional hazards regression models were used to assess the relationship between medication adherence (MPR <80% "nonadherent" vs MPR ≥80% "adherent") and the risk of MACE and death. All analyses were performed by using R version 3.2.0 (R Development Core Team, 2015; R Foundation for Statistical Computing, Vienna, Austria). P values < 0.05 were considered statistically significant. According to the national ethical and legal regulation (the Swiss Federal Law of data protection), an ethical approval and patient consent were not needed.

RESULTS

The study population comprised a total of 4349 patients with MI, who survived for at least 30 days without recurrent MI after discharge. Table I summarizes the baseline characteristics of the study population. The mean age of the patients was 68.5 years; almost 70% were men. Cardiovascular risk factors, including diabetes mellitus in 900 patients (20.7%) and hypertension in more than one half of the patients (56.6%), were frequently present; the summary comorbidity measure (Charlson Comorbidity Index) showed moderate disease severity with a mean of 0.5 condition. About 11% of patients had a history of MI in the year before the index event. The most frequent medications used before hospital admission were ACE inhibitors/ARBs (49.1%), aspirin (42.5%), LLDs (37.4%), and BBs (34.3%) (Table II).

The proportions of the prescribed drugs for secondary prevention after MI within 30 days after discharge from the hospital are displayed in Figure 1. Approximately 86% of the study patients had at least 1 prescription for antiplatelet therapy, but only 63.0% received DAPT within 30 days after discharge. The majority were prescribed at least 1 of the 3 drug classes (LLDs, ACE inhibitors/ARBs, or BBs); therapy consisting of all 3 drug classes was used in 45.3%. The proportion of patients who were prescribed all 3 drug classes as well as DAPT was 38.4%.

The distribution of medication adherence, defined as the MPR (ranging from 0% [0.0] completely nonadherent to 100% [1.0] completely adherent) for DAPT, LLDs, ACE inhibitors/ARBs, and BBs is depicted in Figure 2 (density plot). The mean MPR was 91.2% (SD, 25.0) for DAPT, 82.2% (SD, 33.9) for LLDs, 66.8% (SD, 38.4) for ACE inhibitors/ARBs, and 32.9% (SD, 35.2) for BBs. According to the predefined cutoff point of MPR ≥80% (low/high adherent), a significant proportion of patients with low adherence was consistently observed in most drug treatment groups (MPR 0%−79%, 47.6% for

Table I. Baseline characteristics of the study patients (N = 4349).

Characteristic	Value
Sociodemographic characteristics	
Male	3015 (69.3%)
Mean age, SD, y	68.5 (12.9)
Age groups	
18–44 y	149 (3.4%)
45–54 y	528 (12.1%)
55–64 y	948 (21.8%)
65–74 y	1160 (26.7%)
75–84 y	1117 (25.7%)
≥85 y	447 (10.3%)
Health insurance status (at index hospitalization)	
Managed care model	1935 (44.5%)
Deductible	
High (SFr >500)	710 (16.3%)
Low (SFr 300/500)	3639 (83.7%)
Comorbidity	
Coexisting illness (at index hospitalization)	
Diabetes	900 (20.7%)
Hypertension	2463 (56.6%)
Unstable angina	66 (1.5%)
Congestive heart failure	754 (17.3%)
Stroke	34 (0.8%)
Atrial fibrillation	528 (2.1%)
History of myocardial infarction	461 (10.6%)
Charlson Comorbidity Index	
0	3310 (76.1%)
1–2	752 (17.3%)
3–4	179 (4.1%)
≥5	108 (2.5%)
Mean Charlson Comorbidity Index	0.5 (1.2)

SFr = Swiss Francs.

Table II. Medication and health care use of the study patients.

Characteristic	Value
Medication use (1 year before hospitalization)	
Antidiabetic agents	798 (18.3%)
Aspirin	1850 (42.5%)
Clopidogrel	403 (9.3%)
Prasugrel	50 (1.1%)
Ticagrelor	86 (2.0%)
Lipid-lowering drugs	1626 (37.4%)
ACE inhibitors/ARBs	2134 (49.1%)
Beta-blockers	1493 (34.3%)
Health care use (1 year before hospitalization)	
Visit to a primary care physician	
≥1 visit	3618 (83.2%)
No. of visits	6.8 (7.8)
Visit to a cardiologist	
≥1 visit	681 (15.7%)
No. of visits	0.3 (1.3)
Visit to another specialist	
≥1 visit	2792 (64.2%)
No. of visits	4.1 (8.1)
Hospitalizations for acute care	
≥1 hospitalization	1413 (32.5%)
No. of hospitalizations	0.5 (0.9)
Length of stay in acute care, SD, d	2.5 (8.3)
Hospitalizations for rehabilitation	
≥1 hospitalization	118 (2.7%)
No. of hospitalizations	0.04 (0.3)
Length of stay in rehabilitation, SD, d	0.6 (4.4)

ACE = angiotensin-converting enzyme; ARBs = angiotensin receptor blockers.

DAPT, 47.3% for ACE inhibitors/ARBs), with the highest percentage in the BB group (88.1%) (Table III). In contrast, the adherence to aspirin and at least one of the $P2Y_{12}$ inhibitors and adherence to the LLDs were higher, with an MPR ≥80% of 88.1% and 76.5%, respectively.

Multivariate logistic regression analyses were used to identify factors that are associated with medication adherence to 4 drug classes (Table IV). We observed that increased age (75–84 years and ≥85 years) was significantly associated with nonadherence to DAPT and BB treatment; the strongest effect was found for patients aged ≥85 years in all drug treatment groups.

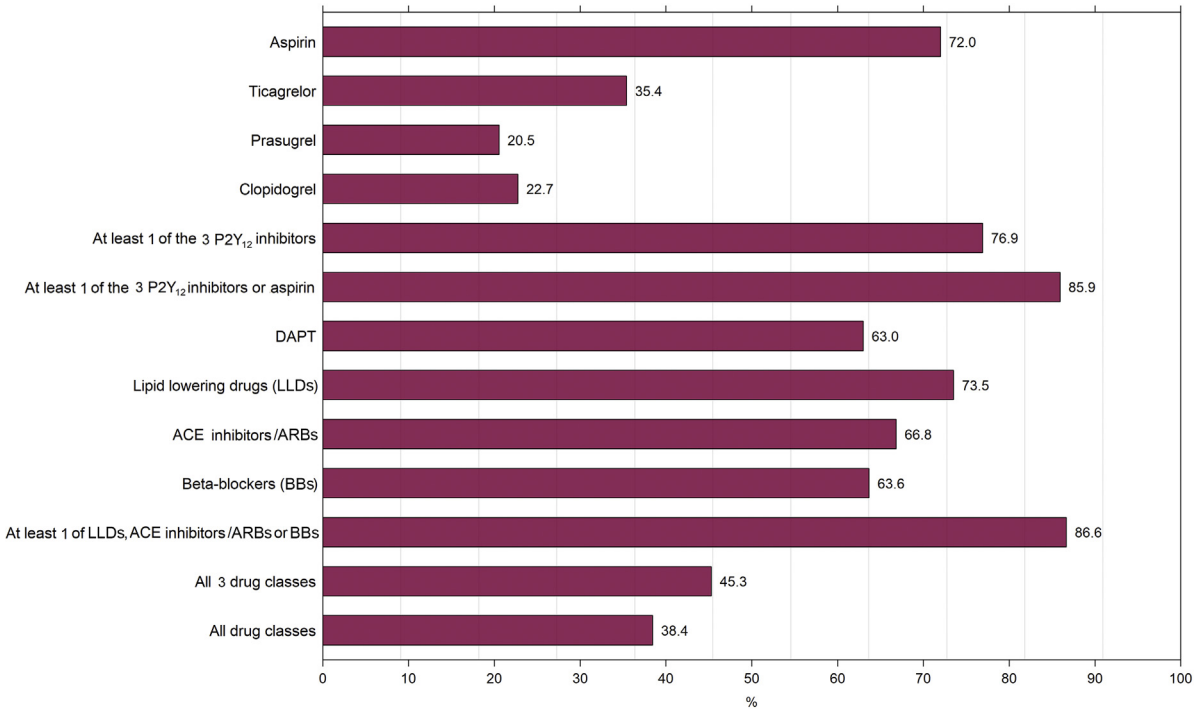

Figure. 1. Use of medication within 30 days after discharge in patients with myocardial infarction. ACE = angiotensin-converting enzyme; ARBs = angiotensin receptor blockers; BBs = beta-blockers; DAPT = dual antiplatelet therapy; LLDs = lipid-lowering drugs.

Women were more likely to be adherent to BBs (OR, 1.39 [95% CI, 1.14−1.70]; $P = 0.001$) but less likely to be adherent to LLDs than men (OR, 0.74 [95% CI, 0.63−0.86]; $P < 0.001$). Patients who experienced comorbidities such as diabetes, hypertension, and congestive heart failure had a higher likelihood of being adherent to ACE inhibitors/ARBs as well as to BBs compared with those without these concomitant diseases (c-statistic of all performed models ranged from 0.61 to 0.67). Enrollment in a managed care health insurance model was significantly associated with good adherence to LLDs (OR, 1.18 [95% CI, 1.02−1.37]; $P = 0.029$) and ACE inhibitors/ARBs (OR, 1.14 [95% CI, 1.01−1.29]; $P = 0.036$), whereas having a high deductible class exhibited no significant influence on the adherence to these drug treatment groups.

As shown in Table V, good medication adherence was significantly associated with a lower likelihood for mortality for almost all drug classes (DAPT hazard ratio, 0.68 [95% CI, 0.50−0.91]; LLD hazard ratio, 0.59 [95% CI, 0.45−0.77]; ACE inhibitor/ARB hazard ratio, 0.73 [95% CI, 0.56−0.95]), with the exception of the BB group. The probability of MACE was 45% lower in patients who were adherent to LLD therapy compared with nonadherent patients. As expected, the likelihood for mortality increased significantly with age and the extent of comorbidities.

DISCUSSION

Secondary prevention medication plays an essential role in improving long-term outcomes in patients with MI.[2,3] Here, based on a large health care claims dataset, we report that use and adherence to such therapy is only moderate in a real-life setting. Conversely, in patients with high adherence to recommended therapy such as DAPT, LLDs, and ACE inhibitors/ARBs, we found a reduced risk for MACE or all-cause mortality, indicating that maintaining adherence to evidence-based medication

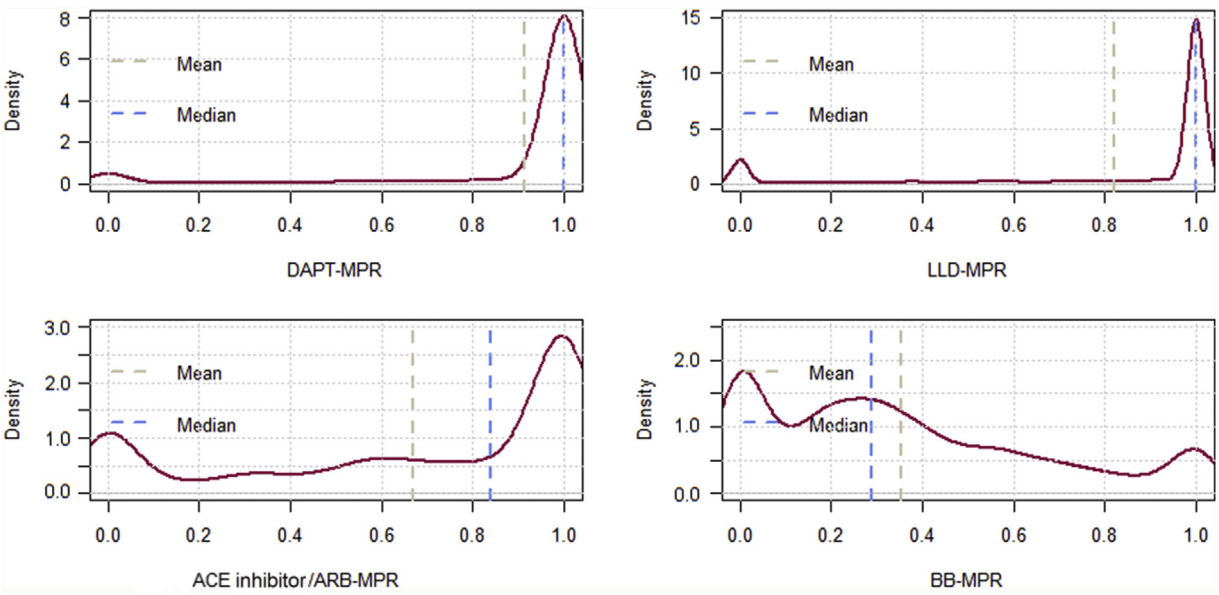

Figure 2. Density plots: medication adherence (MPR) for secondary prevention after myocardial infarction for all drug classes. ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; BB = beta-blocker; DAPT = dual antiplatelet therapy; LLD = lipid-lowering drug.

may substantially improve quality of care and clinical outcomes.

Medication nonadherence is widely recognized as a common and costly problem, although it is undetected and undertreated in a significant proportion of patients.[9,10] It has previously been shown that people who are prescribed self-administered daily medications take only about one half of their recommended doses, which may be particularly relevant for therapies consisting of multiple compounds intended to reduce the risk of future cardiovascular events. Indeed, beneficial effects of treatment may not be apparent because, at best, coronary events do not occur, whereas adverse drug reactions may impair the patient's quality of life.[15] Previous studies reported ~45%–65% adherence to medications prescribed for secondary prevention, with few differences between drug classes.[16,17] However, actual use of individual therapies and patient characteristics that determine medication adherence and effects on outcomes in current clinical practice are largely unknown.

DAPT is recommended in patients with MI for up to 12 months unless there are contraindications such as an excessive bleeding risk. DAPT reduces rates of fatal or nonfatal MI, stroke, and stent thrombosis after PCI.[18] We observed that at least 1 antiplatelet drug was prescribed to the majority of patients, whereas DAPT was used only in two thirds of patients, with high medication adherence in one half of the study population. Low DAPT use was associated with increasing age and the presence of atrial fibrillation, likely reflecting patients who are at high risk of bleeding complications such as concomitant oral anticoagulation.[19] Of note, we have no information on the number of patients being diagnosed with bleeding complications, with type 2 MI (eg, in which DAPT may be contraindicated due to severe anemia), or who have not been treated with PCI (eg, not requiring DAPT to minimize the risk for stent thrombosis).[18] However, given that 64% of patients were aged <75 years and that 98% had no history of atrial fibrillation, our data indicate that adherence to DAPT may be inadequately low in a considerable number of patients.

Similar to DAPT, we found that high adherence to LLD therapy is strongly associated with reduced mortality as well as MACE, although only ~75% of patients regularly used such medications after hospital

Table III. Medication adherence after discharge, defined according to the medication possession ratio (MPR).

Variable	Low Adherence: MPR 0%–79%	High Adherence: MPR ≥80%
Drugs		
Clopidogrel, prasugrel, ticagrelor, or aspirin	517 (11.9%)	3832 (88.1%)
DAPT	2069 (47.6%)	2280 (52.4%)
Lipid-lowering drugs	1023 (23.5%)	3326 (76.5%)
ACE inhibitors/ARBs	2059 (47.3%)	2290 (52.7%)
Beta-blockers	3831 (88.1%)	518 (11.9%)
All 3 drugs (LLDs, ACE/ARBs, BBs)	4051 (93.1%)	298 (6.9%)
All 5 drugs(+ DAPT)	4159 (95.6%)	190 (4.4%)

ACE = angiotensin-converting enzyme; ARBs = angiotensin receptor blockers; BBs = beta-blockers; DAPT = dual antiplatelet therapy; LLDs = lipid-lowering drug.

Table IV. Association between patient characteristics and medication adherence (medication possession ratio ≥80%). Values are given as odds ratios (95% CIs).

Variable	DAPT	LLDs	ACE Inhibitors/ARBs	BBs
Sex (female)	1.03 (0.90–1.19)	0.74 (0.63–0.86)	1.01 (0.88–1.16)	1.39 (1.14–1.70)
Age groups				
45–54 y	0.88 (0.59–1.32)	1.62 (1.01–2.60)	0.89 (0.62–1.29)	0.78 (0.45–1.35)
55–64 y	0.76 (0.52–1.12)	1.54 (0.99–2.39)	1.09 (0.77–1.55)	0.78 (0.46–1.30)
65–74 y	0.54 (0.37–0.79)	1.04 (0.68–1.61)	1.03 (0.72–1.46)	0.65 (0.39–1.09)
75–84 y	0.32 (0.22–0.48)	0.65 (0.43–1.01)	1.00 (0.70–1.43)	0.59 (0.35–1.00)
≥85 y	0.25 (0.17–0.38)	0.27 (0.17–0.43)	0.55 (0.37–0.81)	0.38 (0.21–0.68)
Managed care plan	1.10 (0.97–1.25)	1.18 (1.02–1.37)	1.14 (1.01–1.29)	0.87 (0.72–1.05)
High deductible (SFr >500)	1.36 (1.13–1.62)	1.08 (0.87–1.35)	0.90 (0.76–1.07)	0.72 (0.54–0.97)
Comorbidity (at index)				
Diabetes	0.80 (0.68–0.94)	0.93 (0.78–1.12)	1.22 (1.05–1.43)	1.44 (1.16–1.79)
Hypertension	0.90 (0.79–1.02)	1.08 (0.93–1.26)	1.91 (1.68–2.17)	1.29 (1.05–1.57)
Congestive heart failure	0.89 (0.75–1.06)	1.11 (0.91–1.35)	1.24 (1.05–1.47)	1.53 (1.22–1.93)
Angina	0.74 (0.44–1.24)	0.63 (0.37–1.08)	0.53 (0.31–0.88)	1.00 (0.47–2.13)
Stroke	0.93 (0.46–1.90)	1.05 (0.46–2.40)	0.66 (0.33–1.32)	1.13 (0.38–2.64)
Atrial fibrillation	0.36 (0.29–0.45)	0.82 (0.67–1.02)	0.96 (0.79–1.16)	1.60 (1.23–2.07)
MI (1 year before)	0.87 (0.72–1.06)	0.72 (0.58–0.89)	0.96 (0.79–1.16)	0.91 (0.67–1.23)

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; BBs = beta-blockers; DAPT = dual antiplatelet therapy; LLDs = lipid-lowering drugs; MI = myocardial infarction; SFr = Swiss Francs.

discharge. Indeed, long-term therapy with a high-intensity statin (with consideration of adding ezetimibe if treatment goals cannot be reached) is recommended in patients with acute coronary syndromes to reduce the occurrence of future cardiovascular events and mortality, as shown in large clinical trials.[2,3,20–22] In our study, elderly patients were less likely to use LLD therapy. The safety of statin therapy is of special concern in the elderly due to comorbidities, interactions with multiple medications, and altered pharmacokinetic and pharmacodynamic variables.[23] Evidence for treatment effects, particularly in patients >80 years of

Table V. Prediction of patient outcomes according to medication adherence (medication possession ratio [MPR] ≥80%). Values are given as hazard ratios (95% CI).

Variable	Mortality	MACE
Sex (female)	0.86 (0.66–1.12)	0.89 (0.71–1.11)
Age groups		
18–44 y	Ref.	Ref.
45–54 y	1.09 (0.23–5.12)	0.83 (0.39–1.77)
55–64 y	0.96 (0.22–4.25)	1.05 (0.52–2.11)
65–74 y	2.35 (0.56–9.76)	1.11 (0.56–2.24)
75–84 y	4.35 (1.06–17.90)	1.54 (0.77–3.10)
≥85 y	11.93 (2.89–49.23)	1.75 (0.84–3.63)
Managed care plan	0.65 (0.49–0.86)	1.08 (0.88–1.33)
Medication adherence (MPR)		
DAPT	0.68 (0.50–0.91)	1.09 (0.87–1.36)
LLDs	0.59 (0.45–0.77)	0.54 (0.43–0.68)
ACE inhibitors/ARBs	0.73 (0.56–0.95)	1.15 (0.93–1.43)
Beta-blockers	2.10 (1.51–2.93)	2.15 (1.66–2.80)
Charlson Comorbidity Index score		
0	Ref.	Ref.
1–2	0.86 (0.60–1.24)	1.22 (0.94–1.57)
3–4	2.37 (1.63–3.46)	0.79 (0.48–1.29)
≥5	4.04 (2.58–6.30)	0.90 (0.50–1.60)
Drugs used 1 year before index		
Antidiabetic agents	0.94 (0.68–1.30)	1.19 (0.93–1.53)
Beta-blockers	1.14 (0.86–1.51)	1.04 (0.82–1.33)
ACE inhibitors/ARBs	1.10 (0.83–1.46)	1.11 (0.87–1.41)
LLDs	1.25 (0.94–1.67)	1.31 (1.03–1.67)
Clopidogrel	1.12 (0.81–1.57)	1.46 (1.10–1.94)
Prasugrel	1.58 (0.56–4.40)	1.57 (0.82–3.02)
Ticagrelor	0.94 (0.34–2.55)	0.68 (0.30–1.54)
Aspirin	0.85 (0.64–1.12)	1.16 (0.91–1.47)

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; DAPT = dual antiplatelet therapy; LLDs = lipid-lowering drugs; MACE = major adverse cardiovascular events.

age, is limited, although registry data indicate that statin therapy is associated with lower cardiovascular mortality in the very elderly when used as secondary prevention after MI.[23,24] Although we have no information on adverse drug reactions, our data support the view that the use of and adherence to LLDs in clinical practice can be increased in this population.

In contrast to antiplatelet and LLD therapies, the use of and adherence to ACE inhibitors/ARBs and BBs display greater variability. Both drug classes are first-line therapies for heart failure and reduced left ventricular ejection fraction with a more frequent clinical use in these patients being supported by our data.[2,3] In addition, ACE inhibitors/ARBs improve cardiovascular outcomes in patients with diabetes or hypertension and are generally well tolerated.[25] This finding likely explains the higher prescription rate and adherence compared with BBs, which are typically being used more frequently in women as well as for rate control in patients with atrial fibrillation. In patients without heart failure or impaired ventricular function who have been fully

revascularized, the effect of prolonged BB therapy has not been studied in large clinical trials.[2,3] Furthermore, use of BBs was found to be unrelated to cardiovascular event risk in a large observational study of stable outpatients with a history of MI.[26] Because we do not have information on left ventricular function or coronary anatomy of our study population, conclusions on the appropriate use of ACE inhibitors/ARBs or BBs may be limited.

In contrast to randomized clinical trials, which often do not adequately represent patients with extensive comorbidities or at high age, our study is based on a comprehensive health care claims dataset from a large population-based patient sample reflecting the translation of treatment guidelines into routine clinical practice.[7,8] Such information may be of particular importance when considering the strong demand to assess and further improve the quality of care delivered.[10] Conversely, our study has certain limitations inherent to its design. First, we had no information about socioeconomic characteristics and other patient-related factors such as adverse drug reactions and contraindications to certain medications, which may partly explain the observed use of and adherence to individual therapies. Second, although being considered a highly reliable source of data reflecting clinical practice, our data reflect medication acquisition rather than actual consumption.[15] Third, as in all retrospective approaches, the revealed associations may not reflect actual causal links. Conversely, this method has a high likelihood of blinding patients and providers, and also includes patients dropping out of regular care, representing the most severe form of nonadherence. Fourth, we used the MPR instead of the proportion of days covered, which in the meantime can be considered the more conservative method. Nevertheless, the MPR is a well-validated, useful instrument for measuring medication adherence, and thus we do not assume a meaningful effect on the validity of our results. Finally, a small proportion of invoices were systematically not considered in our analysis. We estimated that ~3% of all claims invoices were not reimbursed by the health insurer but directly paid by the patient (eg, out-of-pocket payments). This scenario may have led to a possible bias in estimating the medication adherence.

The time for implementing secondary prevention may be limited during hospitalization, particularly because early ambulation and discharge is common practice in low-risk patients with MI.[3] Thus, a close collaboration between clinicians and physicians involved in outpatient follow-up is required. In addition, providing clear information, simplified treatment regimens, and improved care transition with early follow-up may increase adherence to treatment.[27] Strategies such as structured follow-up programs, the use of repeated text messages, or even simple telephone calls to remind patients about their medication, as well as the development of single pills combining multiple compounds to reduce the number of tablets, may help to accomplish this difficult task.[28,29]

CONCLUSIONS

According to our findings, adherence to drug therapy for secondary cardiovascular prevention after acute coronary syndromes was only moderate, despite being associated with positive health outcomes in current clinical practice. With limitations regarding the observational study design in mind, quality of care regarding the use of and adherence to evidence-based treatment such as DAPT and LLD therapy should be improved, which may help to reduce mortality in patients with MI.

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Dr. Huber, Prof. Steffel, Prof. Rosemann, and Dr. Reich initiated and conceptualized the project, and developed the study design; Dr. Huber and Dr. Reich made the funding acquisition; and Dr. Huber handled the data and performed the statistical analysis. Dr. Huber and Dr. Meyer wrote the first draft, and all authors read and critically commented on the manuscript during its development and gave final approval of the version to be submitted.

CONFLICTS OF INTEREST

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