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FOCUS ISSUE: ASPIRIN

Prior Aspirin Use and Outcomes in Elderly Patients Hospitalized With Acute Myocardial Infarction

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OBJECTIVES We sought to assess the association between prior aspirin use and mortality, all-cause readmission, and condition-specific readmission at one month and six months in a national sample of Medicare beneficiaries hospitalized with a confirmed myocardial infarction (MI).

BACKGROUND Prior aspirin use is considered a marker of higher risk in patients with MI, yet the prognostic significance of this factor has been debated.

METHODS Medicare beneficiaries ≥65 years old hospitalized with MI were evaluated to determine whether there was an association between prior aspirin use and mortality (n = 118,992), all-cause readmission, and condition-specific readmission (n = 78,975) at one month and six months.

RESULTS One-third of the patients (n = 39,531, 33.2%) were using aspirin before admission. Those with prior aspirin use had significantly lower mortality at one month (16.1% vs. 19.0%, $p < 0.0001$) and six months (24.7% vs. 27.5%, $p < 0.0001$). After multivariable adjustment, prior aspirin use was found to be associated with a lower risk of one-month (relative risk ratio 0.93, 95% confidence interval [CI] 0.90 to 0.96) and six-month mortality (hazard ratio 0.94, 95% CI 0.91 to 0.96). Prior aspirin use tended to reduce all-cause or coronary artery disease readmissions at one month or six months.

CONCLUSIONS Prior aspirin use is not a marker of increased mortality in patients ≥65 years old hospitalized with MI. (J Am Coll Cardiol 2005;46:967–74) © 2005 by the American College of Cardiology Foundation

Although prior aspirin use is considered a marker of higher risk in acute myocardial infarction (MI) (1), the prognostic significance of this factor has been debated. Several studies have reported that patients who present with MI despite chronic aspirin use have a higher risk of adverse short-term outcomes (1–10). These studies, however, were limited by their small size (3,4,7,9), lack of detailed data on baseline characteristics (3–5,7,8,10), and use of patients drawn from randomized controlled trial populations (1–3,6,8,10). In contrast, the Global Registry of Acute Coronary Events (GRACE) trial found that aspirin use before admission was associated with less severe presentation, fewer in-hospital complications, and lower adjusted risk of in-hospital mortality in patients with acute coronary syndromes (11). However, this study was unable to ascertain if prior aspirin use was associated with a higher or lower risk of long-term adverse events or mortality.

In view of these conflicting studies, we sought to assess whether prior aspirin use was associated with short- and long-term mortality and readmission in a national sample of elderly patients hospitalized in the U.S. with MI. We specifically sought to assess whether prior aspirin use reflected a marker of higher risk in elderly patients with MI or was independently associated with patient outcomes after accounting for confounding characteristics.

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Abbreviations and Acronyms

CABG = coronary artery bypass graft surgery
CAD = coronary artery disease
CI = confidence interval
CK = creatine kinase
CVA = cerebrovascular accident
HR = hazard ratio
LDH = lactate dehydrogenase
MI = myocardial infarction
NSTEMI = non–ST-segment elevation myocardial infarction
PTCA = percutaneous transluminal coronary angioplasty
RR = relative risk ratio

METHODS

Study sample. The Cooperative Cardiovascular Project, described in detail elsewhere (12), was a national quality improvement initiative of the Health Care Financing Administration (currently the Centers for Medicare & Medicaid Services) to improve the quality of care for Medicare beneficiaries with acute MI. The 234,769 patients in the cohort constitute all fee-for-service Medicare beneficiaries who were discharged from nongovernmental acute care hospitals in the U.S. with a primary discharge diagnosis of acute MI (code 410.xx of the International Classification of Diseases, 9th Revision, Clinical Modification) (13) between January 1994 and February 1996, excluding patients for whom the hospitalization had been a readmission for acute MI (code 410.x2). Patients' records were abstracted for clinical data including medical history, clinical presentation, comorbid conditions, and medication use before admission.

We restricted our cohort to the initial admission of patients ≥65 years of age with a confirmed MI, excluding 17,593 patients age <65 years because Medicare beneficiaries in this age group are not representative of the general under-age-65 population due to the selective criteria for Medicare coverage in the younger population, and 31,186 patients without a confirmed MI, defined as creatine kinase (CK)-MB level ≥5%, lactate dehydrogenase (LDH) level >1.5 times normal, and LDH-1 level ≥LDH-2, or a two times increase of the CK level and evidence of MI on the presenting electrocardiogram. If patients had more than one admission during the study time period, only the first admission was included to avoid having patients counted more than once. This approach excluded 23,773 admissions from the study sample. In addition, 34,409 patients who had been transferred to the study hospital were excluded from analysis. Because prior aspirin use was the focus of our analysis, we excluded 19,378 patients whose medical records were missing documentation of previous chronic medication use. Patients with contraindications to aspirin use (allergy to aspirin, history of bleeding, current bleeding, or other conditions associated with an increased risk of bleeding) (n = 23,520) were also excluded from analysis. We excluded 4,617 patients with terminal illness because their treatment before admission may not have been oriented toward improving survival, and thus likely did not incorporate aspirin use. Patients with missing data for mortality (n = 325) and readmission (n = 8,740) were excluded from analysis. In total, 115,777 (49.3%) of the original 234,769 patients met at least one criterion for exclusion; the 118,992 remaining patients (50.7%) constituted our study cohort.

Prior aspirin use. Patients were classified as using aspirin before admission if aspirin was included in the medical record of chronic medications taken before admission. Aspirin administered only in the ambulance or emergency room during admission was not considered to constitute prior aspirin therapy.

Outcomes. The primary outcomes were death at one and six months from the date of admission, as determined by review of the Medicare Enrollment Database (14). Secondary outcomes included all-cause readmission and readmissions for acute MI, coronary artery disease (CAD), and cerebrovascular accident (CVA) at one and six months from the date of discharge as determined by review of patients' Medicare Part A data. For the analysis of these secondary outcomes, we excluded patients (n = 40,017) who died during hospitalization or patients who were transferred out to other acute care hospitals because the starting point for these analyses is hospital discharge.

Statistical analysis. We compared the demographic and clinical characteristics of patients who had used aspirin before admission and those who had not using chi-square tests for categorical variables and *t* tests for continuous variables. These included patient demographics (age, gender, race), clinical presentation (Killip class, left ventricular ejection fraction, systolic blood pressure, heart rate, creatinine, white blood cell count, hemoglobin, anterior MI, atrial fibrillation, Q-wave MI, ST-segment elevation MI, cardiac arrest on admission, angina before admission), medical history (hypertension, diabetes mellitus, MI, heart failure, current smoker, cerebrovascular disease, peripheral vascular disease, peptic ulcer disease, percutaneous transluminal coronary angioplasty [PTCA], coronary artery bypass graft surgery [CABG]), comorbid conditions (dementia, chronic obstructive pulmonary disease), mobility, urinary continence, admission from nursing home, and medications before admission (angiotensin-converting enzyme inhibitors, diuretics, nonsteroidal anti-inflammatory drugs, digoxin, nitrates, beta-blockers, calcium-channel blockers, warfarin).

We compared crude rates of mortality, all-cause readmission, and cause-specific readmissions at one month and six months between patients using aspirin before admission and those who were not, using chi-square tests. To further assess the association of prior aspirin use with outcomes, we performed multivariable analysis using logistic regression and Cox proportional hazards models. Factors were entered as covariates in the models based on clinical judgment and bivariate analysis. For one-month outcomes, we did logistic

regression analysis and converted the odds ratio into relative risk ratio (RR) for better interpretability (15). In the multivariable Cox proportional models for mortality within six months of admission, we considered the days from admission to death as time variable and truncated at six months of admission. In the multivariable Cox proportional models for readmission (all-cause, acute MI, CAD, CVA) within six months of discharge, we considered the days from discharge to the day of first readmission as time variable and truncated at six months of discharge, and also censored at the time of death for patients who died within six months of discharge and were not readmitted before death. These model analyses were repeated for all outcomes separately and adjusted for patients' demographic characteristics, clinical presentation, medical history, comorbidities, and other prior medications. Analyses were repeated restricted to the following subgroups: the prescription of aspirin at discharge (yes/no/unknown); ST-segment elevation MI (yes/no)—defined as those without documented ST-segment elevation MI, new left bundle branch block, or Q-wave MI; age is <75 years (yes/no).

In the analysis, we imputed missing as "no" for categorical variables with "yes/no" responses, and median for continuous variables. For a categorical variable with "yes/no" responses or a continuous variable with missing values more than 5%, we created a dummy variable to represent the missing values and included it in the model with the corresponding variable. All categorical variables with "yes/no" responses and all continuous variables in our analyses had fewer than 10% missing values. The missing values in a categorical variable with responses other than "yes/no" were merged into the category of "unknown," or a separate category of "unknown" was added to the categorical variable; dummy variables were created corresponding to each of the categories including "unknown" and then added into the model leaving one out as the reference group. All categorical variables with responses other than "yes/no" had fewer than 10% missing values except for left ventricular ejection fraction. The effect of aspirin use before admission on outcomes was not very different among the multivariable Cox proportional regression analyses with different adjustments. Accordingly, we only reported the results from the model with full adjustment of patients' demographic characteristics, clinical presentation, medical history, comorbidities, and other prior medications. In secondary analyses, we excluded patients who died during hospitalization or patients who were transferred out to other acute care hospitals (n = 40,017) in order to assess outcomes from hospital discharge.

Statistical analyses were performed using SAS version 8.2 (SAS Inc., Cary, North Carolina). Analysis of the Cooperative Cardiovascular Project database was approved by the Yale University School of Medicine Human Investigation Committee.

RESULTS

Baseline characteristics. Approximately one-third of patients in the study cohort (n = 39,531, 33.2%) were using aspirin before admission. These patients were, on average, younger than patients who had not used aspirin (Table 1). A greater proportion of patients who used aspirin before admission were white, male, had a prior MI, documented peripheral vascular disease, cerebrovascular disease, prior coronary revascularization, and used angiotensin-converting enzyme inhibitors, digoxin, nitrates, beta-blockers, and calcium-channel blockers before admission compared with patients who had not used aspirin before admission. In contrast, patients who had used aspirin before admission had lower rates of anterior MI, Q-wave MI, ST-segment elevation MI, diabetes, peptic ulcer disease, smoking, dementia, chronic obstructive pulmonary disease, difficulty walking, urinary incontinence, and admission from a nursing home compared with patients who had not used aspirin before admission.

Mortality. Patients with prior aspirin use had lower crude mortality at one month (16.1% vs. 19.0%, $p < 0.0001$) and six months (24.7% vs. 27.5%, $p < 0.0001$) compared with patients who had not used aspirin before admission (Table 2). After multivariable adjustment, prior aspirin use remained associated with a lower risk of one-month mortality (RR 0.93, 95% confidence interval [CI] 0.90 to 0.96) and six-month mortality (hazard ratio [HR] 0.94, 95% CI 0.91 to 0.96) (Table 3, Figs. 1 and 2).

Readmissions. Patients who used aspirin before admission had higher crude rates of readmission for acute MI (4.1% vs. 3.8%, $p = 0.018$ at one month; 10.5% vs. 9.0, $p < 0.001$ at six months) and CVA (4.2% vs. 3.9%, $p = 0.028$ at one month; 11.4% vs. 10.3%, $p < 0.001$ at six months) but had similar rates of readmission for all causes (21.2% vs. 21.4%, $p = 0.5$ at one month; 44.8% vs. 44.8%, $p = 0.9$ at six months) and CAD (20.7% vs. 20.8%, $p = 0.7$; 43.8% vs. 43.6%, $p = 0.5$ at six months) compared with patients who were not using aspirin before admission (Table 2).

Most of these crude associations were attenuated after multivariable adjustment, including prior aspirin use and readmissions for all causes (RR 0.98, 95% CI 0.96 to 1.01), acute MI (RR 1.04, 95% CI 0.97 to 1.11), CAD (RR 0.99, 95% CI 0.96 to 1.01), and CVA (RR 1.00, 95% CI 0.93 to 1.07) at one month and readmission for all causes (HR 0.97, 95% CI 0.95 to 1.00), CAD (HR 0.98, 95% CI 0.95 to 1.00), and CVA (HR 1.01, 95% CI 0.96 to 1.06) at six months. However, patients who had used aspirin before admission tended to have an increased risk of readmission for acute MI at six months (HR 1.05, 95% CI 1.00 to 1.11) (Table 4, Figs. 1 and 2).

Subgroup analysis. Among the 37,537 patients who presented with non–ST-segment elevation MI (NSTEMI), 36.7% (n = 13,779) had used aspirin before hospitalization. As with the general population of patients, prior aspirin use was associated with a trend toward improved adjusted

Table 1. Patient Characteristics and Use of ASA Before Admission

	Overall (118,992) n (%) or Mean (SD)	Without ASA (71,461) n (%) or Mean (SD)	With ASA (39,531) n (%) or Mean (SD)	p Value
Demographic characteristics				
Age	76.4 (7.3)	76.6 (7.4)	76.1 (7.2)	<0.0001
Women	58,938 (49.5)	42,102 (53.0)	16,836 (42.6)	<0.0001
Race				<0.0001
White	107,308 (90.2)	70,743 (89.0)	36,565 (92.5)	
Black	7,272 (6.1)	5,452 (6.9)	1,820 (4.6)	
Other	4,412 (3.7)	3,266 (4.1)	1,146 (2.9)	
Clinical presentation				
Killip class				<0.0001
I	60,211 (50.6)	39,795 (50.1)	20,416 (51.6)	
II	14,370 (12.1)	9,646 (12.1)	4,724 (12.0)	
III	41,863 (35.2)	28,138 (35.4)	13,725 (34.7)	
IV	2,548 (2.1)	1,882 (2.4)	666 (1.7)	
Left ventricular ejection fraction				<0.0001
Unknown	15,082 (12.7)	10,139 (12.8)	4,943 (12.5)	
<20	36,542 (30.6)	24,522 (30.9)	11,930 (30.2)	
20–39	22,802 (19.2)	14,987 (18.9)	7,815 (19.8)	
40–54	2,036 (1.7)	1,387 (1.7)	649 (1.6)	
≥55	42,620 (35.8)	28,426 (35.8)	14,194 (35.9)	
Systolic blood pressure	145.40 (32.6)	145.1 (33.0)	146.0 (31.7)	<0.0001
Heart rate	87.7 (24.2)	88.2 (24.4)	86.6 (23.9)	<0.0001
Creatinine	1.3 (0.6)	1.3 (0.7)	1.3 (0.6)	0.05
White blood cell count	10.8 (4.3)	11.0 (4.4)	10.5 (4.1)	<0.0001
Hemoglobin	13.6 (1.8)	13.5 (1.8)	13.6 (1.8)	<0.0001
Anterior infarction	55,242 (46.4)	37,526 (47.2)	17,716 (44.8)	<0.0001
Left bundle branch block	7,931 (6.7)	5,158 (6.5)	2,773 (7.0)	0.0006
Atrial fibrillation	11,138 (9.4)	7,822 (9.8)	3,316 (8.4)	<0.0001
2nd- or 3rd-degree heart block	1,590 (1.3)	1,126 (1.4)	464 (1.2)	0.0006
Q-wave infarction	70,563 (59.3)	48,579 (61.1)	21,984 (55.6)	<0.0001
ST-segment elevation infarction	33,979 (28.6)	23,804 (30.0)	10,175 (25.7)	<0.0001
Cardiac arrest on admission	3,928 (3.3)	2,857 (3.6)	1,071 (2.7)	<0.0001
Duration of symptoms before admission (h)				<0.0001
Unknown	11,016 (9.3)	7,534 (9.5)	3,482 (8.8)	
None	63,076 (53.0)	40,854 (51.4)	22,222 (56.2)	
<6	10,907 (9.2)	7,220 (9.1)	3,687 (9.3)	
6–12	16,145 (13.6)	10,942 (13.8)	5,203 (13.2)	
>12	17,848 (15.0)	12,911 (16.2)	4,937 (12.5)	
Medical history				
Hypertension	76,452 (64.2)	51,205 (64.4)	25,247 (63.9)	0.05
Diabetes mellitus	38,626 (32.5)	26,268 (33.1)	12,358 (31.3)	<0.0001
Prior myocardial infarction	35,989 (30.2)	19,441 (24.5)	16,548 (41.9)	<0.0001
Prior heart failure	25,622 (21.5)	16,979 (21.4)	8,643 (21.9)	0.05
Current smoker	16,742 (14.1)	11,607 (14.6)	5,135 (13.0)	<0.0001
Cerebrovascular disease	16,586 (13.9)	9,842 (12.4)	6,744 (17.1)	<0.0001
Peripheral vascular disease	12,820 (10.8)	7,611 (9.6)	5,209 (13.2)	<0.0001
Peptic ulcer disease	12,738 (10.7)	8,918 (11.2)	3,820 (9.7)	<0.0001
PTCA	8,254 (6.9)	3,253 (4.1)	5,011 (12.7)	<0.0001
CABG	15,655 (13.2)	7,044 (8.9)	8,611 (21.8)	<0.0001
Comorbid conditions				
Dementia	6,885 (5.8)	4,866 (6.1)	2,019 (5.1)	<0.0001
COPD	24,034 (20.2)	16,878 (21.2)	7,156 (18.1)	<0.0001
Mobility				<0.0001
Unknown	3,062 (2.6)	2,189 (2.8)	873 (2.2)	
Independent	94,346 (79.3)	62,242 (78.3)	32,104 (81.2)	
Unable to walk independently	21,584 (18.1)	15,030 (18.9)	6,554 (16.6)	
Urinary continence				<0.0001
Unknown	2,544 (2.1)	1,857 (2.3)	687 (1.7)	
Continent	108,158 (90.9)	71,674 (90.2)	36,484 (92.3)	
Incontinent	8,290 (7.0)	5,930 (7.5)	2,360 (6.0)	
Admitted from a nursing home	6,125 (5.1)	4,398 (5.5)	1,727 (4.4)	<0.0001

Continued on next page

Table 1 Continued

	Overall (118,992) n (%) or Mean (SD)	Without ASA (71,461) n (%) or Mean (SD)	With ASA (39,531) n (%) or Mean (SD)	p Value
Medications before admission				
Angiotensin-converting enzyme	26,386 (22.2)	17,121 (21.5)	9,265 (23.4)	<0.0001
Diuretics	43,393 (36.5)	29,423 (37.0)	13,970 (35.3)	<0.0001
NSAID	16,368 (13.8)	11,951 (15.0)	4,417 (11.2)	<0.0001
Digoxin	24,621 (20.7)	16,301 (20.5)	8,320 (21.0)	0.03
Nitrates	44,920 (37.8)	25,020 (31.5)	19,900 (50.3)	<0.0001
Beta-blockers	22,000 (18.5)	12,267 (15.4)	9,733 (24.6)	<0.0001
Calcium-channel blockers	44,528 (37.4)	26,515 (33.4)	18,013 (45.6)	<0.0001
Warfarin	8,587 (7.2)	7,367 (9.3)	1,220 (3.1)	<0.0001

ASA = aspirin; CABG = coronary artery bypass graft surgery; COPD = chronic obstructive pulmonary disease; NSAID = nonsteroidal anti-inflammatory drug; PTCA = percutaneous transluminal coronary angioplasty.

survival at one month (RR 0.94, 95% CI 0.89 to 1.01) and at six months (HR 0.95, 95% CI 0.91 to 1.00) (Table 3). Prior aspirin use among NSTEMI patients was not associated with readmissions for all causes (RR 0.96, 95% CI 0.92 to 1.01), acute MI (RR 1.04, 95% CI 0.93 to 1.17), CAD (RR 0.97, 95% CI 0.93 to 1.02), and CVA (HR 0.91, 95% CI 0.81 to 1.02) at one month. At six months, prior aspirin use was independently associated with lower risk of readmission for all causes (HR 0.95, 95% CI 0.92 to 0.99) and CAD (HR 0.96, 95% CI 0.92 to 1.00), but not for acute MI (HR 1.04, 95% CI 0.96 to 1.13) and CVA (HR 0.97, 95% CI 0.90 to 1.05) (Table 4).

Among the 61,455 patients with aspirin prescription at discharge, 38.9% (n = 23,929) had used aspirin before hospitalization. Prior use of aspirin in this group of patients was not significantly associated with reduced risk of mortality at one month (RR 0.98, 95% CI 0.89 to 1.08) and at six months (HR 1.00, 95% CI 0.95 to 1.05) (Table 3), and tended to reduce the risk of readmissions for all causes (RR 0.97, 95% CI 0.93 to 1.00) and CAD (RR 0.97, 95% CI

Table 2. Outcomes and Use of ASA Before Admission

	Overall (118,992) n (%) Total (118,992)	Without ASA (71,461) n (%)	With ASA (39,531) n (%)	p Value
Mortality (from admission)				
1-month	21,477 (18.0)	15,096 (19.0)	6,381 (16.1)	<0.0001
6-month	31,575 (26.5)	21,828 (27.5)	9,747 (24.7)	<0.0001
Readmissions (from discharge)*	(78,975)	(52,262)	(26,661)	
1-month: any cause	16,836 (21.3)	11,184 (21.4)	5,652 (21.2)	0.5325
6-months: any cause	35,384 (44.8)	23,446 (44.8)	11,938 (44.8)	0.8543
1-month: AMI	3,092 (3.9)	1,987 (3.8)	1,105 (4.1)	0.0184
6-months: AMI	7,537 (9.5)	4,729 (9.0)	2,808 (10.5)	<0.001
1-month: CAD	16,381 (20.7)	10,868 (20.8)	5,513 (20.7)	0.7201
6-months: CAD	34,473 (43.7)	22,788 (43.6)	11,685 (43.8)	0.5188
1-month: CVA	3,185 (4.0)	2,052 (3.9)	1,133 (4.2)	0.0283
6-months: CVA	8,443 (10.7)	5,401 (10.3)	3,042 (11.4)	<0.001
	In Patients With Non–ST-Segment Elevation MI (37,537)			
Mortality (from admission)				
1-month	4,883 (13.0)	3,175 (13.4)	1,708 (12.4)	0.007
6-month	8,409 (22.4)	5,459 (23.0)	2,950 (21.4)	0.0004
Readmissions (from discharge)*				
1-month: any cause	5,862 (22.0)	3,713 (22.1)	2,149 (21.9)	0.7959
6-months: any cause	12,393 (46.6)	7,898 (47.0)	4,495 (45.9)	0.0922
1-month: AMI	1,179 (4.4)	715 (4.3)	464 (4.7)	0.0631
6-months: AMI	2,861 (10.8)	1,715 (10.2)	1,146 (11.7)	0.0001
1-month: CAD	5,706 (21.4)	3,598 (21.4)	2,108 (21.5)	0.8048
6-months: CAD	12,089 (45.4)	7,678 (45.7)	4,411 (45.0)	0.3294
1-month: CVA	1,191 (4.5)	742 (4.4)	449 (4.6)	0.5120
6-months: CVA	3,182 (12.0)	1,975 (11.7)	1,207 (12.3)	0.1595

*Patients who were transferred out or died in the hospital were excluded for the outcomes of readmission.
AMI = acute myocardial infarction; ASA = aspirin; CAD = coronary artery disease; CVA = cerebrovascular accident.

Table 3. Independent Effect of Aspirin Use Before Admission on Mortality*

Description	n	1 Month Relative Risk Ratio (95% CI)	6 Months Hazard Ratio (95% CI)
Total	118,992	0.93 (0.90–0.96)	0.94 (0.91–0.96)
Aspirin at discharge			
Unknown	27,715	0.98 (0.96–1.01)	0.95 (0.92–0.98)
No	29,982	1.22 (1.11–1.35)	1.07 (1.00–1.14)
Yes	61,455	0.98 (0.89–1.08)	1.00 (0.95–1.05)
ST-segment elevation MI			
No	37,537	0.94 (0.89–1.01)	0.95 (0.91–1.00)
Yes	81,455	0.93 (0.90–0.97)	0.93 (0.90–0.96)
Age <75 yrs			
No	63,835	0.95 (0.91–0.99)	0.95 (0.92–0.98)
Yes	53,157	0.91 (0.89–0.96)	0.90 (0.86–0.95)

*Subgroups stratified by prescription of aspirin at discharge, ST-segment elevation MI, and age <75 years.
CI = confidence interval; MI = myocardial infarction.

0.93 to 1.00) at one month, but was not associated with readmission for acute MI (RR 1.06, 95% CI 0.97 to 1.16) and CVA (RR 1.02, 95% CI 0.93 to 1.12) at one month. At six months, prior aspirin use tended to reduce the risk of readmission for all causes (HR 0.97, 95% CI 0.95 to 1.00) and CAD (HR 0.98, 95% CI 0.95 to 1.01), but to increase the risk of readmission for acute MI (HR 1.08, 95% CI 1.02 to 1.15) and CVA (HR 1.07, 95% CI 1.00 to 1.13) (Table 4).

DISCUSSION

Previous studies (1–10) have reported that prior aspirin use is a risk factor for poor outcomes in patients presenting with acute coronary syndromes, and prior aspirin use has been included in risk scores (1). However, in our nationally representative cohort of Medicare beneficiaries with confirmed MI, after adjusting for demographic characteristics, clinical presentation, medical history, comorbidities, and other prior medications, aspirin use was associated with a lower risk of death (at both one and six months). The rates of readmission were not significantly associated with prior aspirin use at one month.

These results differ from those of previous studies that found prior aspirin use to be a marker for poor outcomes. Subgroup analyses of large randomized controlled trials (1,2,8) have limited generalizability to the overall population, specifically the elderly, because these trials target a younger, healthier population. Furthermore, although attempts were made in the cited trials to account for differences in baseline characteristics and MI extent, they were unable to control for a broad range of comorbid conditions. In a study based on the Thrombolysis In Myocardial Infarction-11b (TIMI-11b) and the Efficacy and Safety of

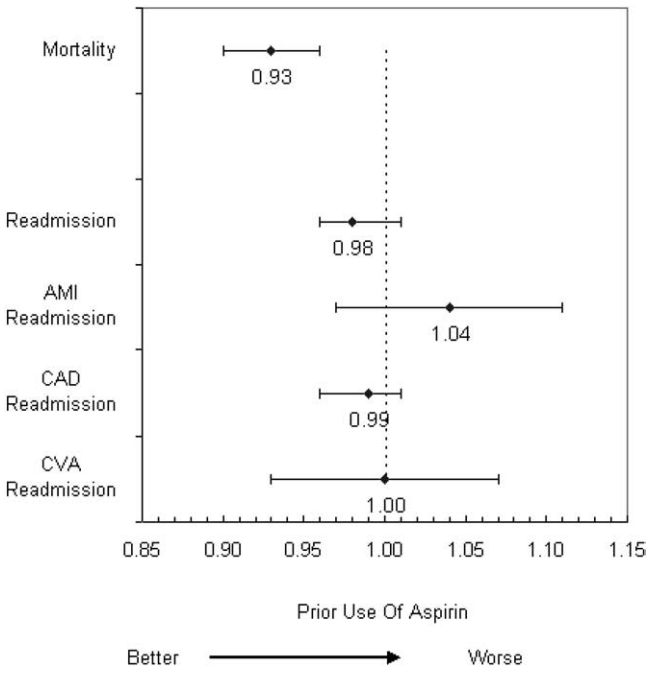

Figure 1. Adjusted 30-day risk of death and readmission: relative risk ratio and its 95% confidence interval. AMI = acute myocardial infarction; CAD = coronary artery disease; CVA = cerebrovascular accident.

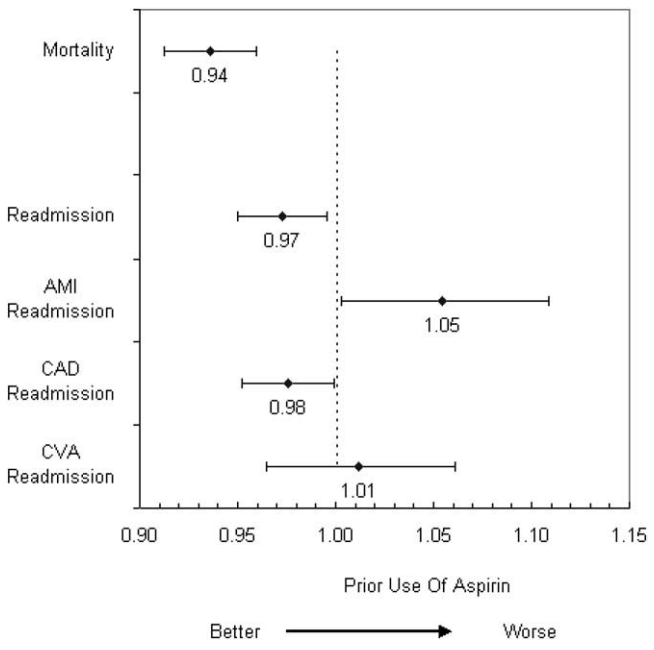

Figure 2. Adjusted six-month risk of death and readmission: hazard ratio and its 95% confidence interval. AMI = acute myocardial infarction; CAD = coronary artery disease; CVA = cerebrovascular accident.

Table 4. Effect of ASA Use Before Admission on Readmission*

Description	n	All Cause	MI	CAD	CVA
1 month, relative risk ratio (95% CI)					
Total	78,975	0.98 (0.96–1.01)	1.04 (0.97–1.11)	0.99 (0.96–1.01)	1.00 (0.93–1.07)
ASA at discharge					
Unknown	2,810	1.02 (0.93–1.12)	0.95 (0.77–1.19)	1.02 (0.93–1.12)	1.04 (0.84–1.30)
No	11,570	0.98 (0.93–1.03)	0.99 (0.87–1.13)	0.98 (0.93–1.04)	0.94 (0.83–1.08)
Yes	53,429	0.97 (0.93–1.00)	1.06 (0.97–1.16)	0.97 (0.93–1.00)	1.02 (0.93–1.12)
ST-segment elevation MI					
No	26,606	0.96 (0.92–1.01)	1.04 (0.93–1.17)	0.97 (0.93–1.02)	0.91 (0.81–1.02)
Yes	52,369	0.99 (0.96–1.03)	1.04 (0.95–1.13)	0.99 (0.96–1.03)	1.05 (0.96–1.15)
Age <75 yrs					
No	45,015	0.99 (0.95–1.02)	1.06 (0.97–1.16)	0.99 (0.95–1.02)	0.98 (0.90–1.07)
Yes	33,960	0.98 (0.94–1.03)	1.01 (0.90–1.13)	0.99 (0.94–1.03)	1.03 (0.92–1.14)
6 months, hazard ratio (95% CI)					
Total	78,975	0.97 (0.95–1.00)	1.05 (1.00–1.11)	0.98 (0.95–1.00)	1.01 (0.96–1.06)
ASA at discharge					
Unknown	2,810	1.03 (0.90–1.17)	1.16 (0.87–1.54)	1.03 (0.90–1.18)	1.00 (0.78–1.29)
No	11,570	0.97 (0.93–1.02)	0.99 (0.89–1.09)	0.97 (0.92–1.02)	0.93 (0.84–1.02)
Yes	53,429	0.97 (0.95–1.00)	1.08 (1.02–1.15)	0.98 (0.95–1.01)	1.07 (1.00–1.13)
ST-segment elevation MI					
No	26,606	0.95 (0.92–0.99)	1.04 (0.96–1.13)	0.96 (0.92–1.00)	0.97 (0.90–1.05)
Yes	52,369	0.98 (0.95–1.01)	1.07 (1.00–1.14)	0.99 (0.96–1.02)	1.04 (0.98–1.10)
Age <75 yrs					
No	45,015	0.98 (0.95–1.01)	1.06 (1.00–1.13)	0.98 (0.95–1.01)	1.03 (0.97–1.09)
Yes	33,960	0.97 (0.93–1.00)	1.04 (0.95–1.13)	0.97 (0.93–1.01)	0.99 (0.92–1.07)

*Subgroups stratified by prescription of aspirin at discharge, ST-segment elevation MI, and age <75 years.
ASA = aspirin; CAD = coronary artery disease; CI = confidence interval; CVA = cerebrovascular accident; MI =myocardial infarction.

Subcutaneous Enoxaparin in Non–Q-Wave Coronary Events (ESSENCE) trials, aspirin use in the seven days before admission was associated with an almost two-fold increase in the odds of the combined end point of all-cause mortality, MI, or urgent revascularization (odds ratio 1.86, 95% CI 1.26 to 2.73) (1). This risk was greater than that for all other independent variables including age ≥65 years and elevated serum cardiac markers. While both of these trials adjusted for typical risk factors (age, gender, past medical and family history, and so on), other clinically relevant factors such as renal failure, severe hypertension, planned use of coronary intervention or fibrinolytic therapy, and other comorbid conditions (chronic obstructive pulmonary disease, dementia, mobility, or urinary continence status) were either excluded from the trial or not included in the risk adjustment. In an analysis of the Platelet Glycoprotein IIb/IIIa in Unstable Angina: Receptor Suppression Using Integrilin Therapy (PURSUIT) trial, prior aspirin use was associated with an increased likelihood of death or MI at 30 days (odds ratio 1.16, 95% CI 1.00 to 1.33) and at 6 months, although this did not reach statistical significance at 6 months (odds ratio 1.14, 95% CI 0.98 to 1.33) among patients presenting with unstable angina/NSTEMI (2). In the Platelet Receptor Inhibition in Ischemic Syndrome Management in Patients Limited by Unstable Signs and Symptoms (PRISM-PLUS) trial, there was evidence of poor outcomes in prior aspirin users (8). In contrast to these studies, our analysis of a community-based sample of patients presenting with NSTEMI shows that prior aspirin use is associated with a lower rate of mortality that was statistically significant.

The present study suggests that prior aspirin use is a marker of a higher-risk patient. Prior aspirin users were more likely to be men and had more frequent medical histories of vascular disease (prior MI, cerebrovascular disease, PTCA, or CABG). The patients using aspirin before admission were also more likely to be using other cardiac medications (beta-blockers, calcium-channel blockers, nitrates, and digoxin) before admission. The finding that aspirin use at discharge was more than 13% lower in the group that was not taking aspirin before admission may be because patients taking a medication on admission are more likely to be discharged on it. However, admission aspirin use was independently associated with reduced mortality even after adjusting for other cardiac medications. This finding suggests that aspirin use is not solely a surrogate marker for improved quality of care.

In contrast to previous reports, our findings suggest that prior aspirin use has a protective role in acute MI. While different than the findings of the large randomized controlled trials, our findings corroborate those of multiple smaller studies that have shown that prior aspirin use affects the presentation and severity of acute MI (5–7,9,11). For example, Col et al. (5) reported that patients taking aspirin before admission were more likely to have a non–Q-wave infarction (65% vs. 49%, odds ratio 1.91, $p < 0.001$) and to sustain a small MI compared with nonaspirin users (30% vs. 22%, odds ratio 1.57, $p < 0.001$). In a study using more recent data, Spencer et al. (11) reported that in both patients with history of CAD and those without, prior aspirin use was associated with a significant reduction in the likelihood

of presenting with a STEMI (odds ratio 0.52, 95% CI 0.44 to 0.61 and odds ratio 0.35, 95% CI 0.3 to 0.4, respectively).

Certain issues should be considered in the interpretation of our results. As an observational study based on retrospective chart review, our study is subject to the typical limitations of this type of design. Despite our efforts to control for confounding variables, we could not exclude unmeasured factors that may have affected the results. We defined prior aspirin use as the taking of aspirin before admission, excluding patients who received aspirin in the ambulance or in the emergency department. Although we cannot comment on the exact chronicity of aspirin use, we believe this is a suitable definition for comparison to previous trials where prior aspirin use was defined as aspirin use for at least 7 to 14 days before admission. Finally, we cannot comment on the effects of aspirin dosage and outcomes. However, given the findings that dosages of 81 to 325 mg of aspirin are effective in reducing events (16) and that most patients treated with aspirin in 1993 to 1994 were probably treated with dosages within this range, these results are likely valid.

Conclusions. In this nationally representative, community-based cohort of older patients, prior aspirin use was associated with a lower risk of death after presentation with acute MI. This finding raises questions about the appropriateness of its incorporation as an independent variable into risk adjustment models.

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