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ORIGINAL RESEARCH

Association Between Subsequent Hospitalizations and Recurrent Acute Myocardial Infarction Within 1 Year After Acute Myocardial Infarction

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BACKGROUND: Patients who survive acute myocardial infarction (AMI) are at high risk for recurrence. We determined whether rehospitalizations after AMI further increased risk of recurrent AMI.

METHODS AND RESULTS: The study included Medicare fee-for-service patients aged ≥65 years discharged alive after AMI from acute-care hospitals in fiscal years 2009–2014. The outcome was recurrent AMI within 1 year of the index AMI. The Clinical Classifications Software (CCS) was used to classify rehospitalizations into disease categories. A Cox regression model was fit accounting for CCS-specific hospitalizations as time-varying variables and patient characteristics at discharge for the index AMI, adjusting for the competing risk of death. The rate of 1-year recurrent AMI was 5.3% (95% CI, 5.27%–5.41%), and median (interquartile range) time from discharge to recurrent AMI was 115 (34–230) days. Eleven disease categories (diabetes mellitus, anemia, hypertension, coronary atherosclerosis, chest pain, heart failure, pneumonia, chronic obstructive pulmonary disease, gastrointestinal hemorrhage, renal failure, complication of implant or graft) were associated with increased risk of recurrent AMI. Septicemia was associated with lower recurrence risk. Hazard ratios ranged from 1.6 (95% CI, 1.55–1.70, heart failure) to 1.1 (95% CI, 1.04–1.25, pneumonia) to 0.6 (95% CI, 0.58–0.71, septicemia).

CONCLUSIONS: Patient risk of recurrent AMI changed based on the occurrence of hospitalizations after the index AMI. Improving post–acute care to prevent unplanned rehospitalizations, especially rehospitalizations for chronic diseases, and extending the focus of outcomes measures to condition-specific rehospitalizations within 30 days and beyond is important for the secondary prevention of AMI.

Key Words: cardiovascular prevention ■ myocardial infarction ■ rehospitalization

Despite the marked decline in the rate of recurrent AMI over recent decades,[1–5] recurrence remains a significant threat to AMI survivors. Classifying patients according to their risk of recurrent AMI may be helpful in efforts to prevent the next AMI. Although patient baseline characteristics, postdischarge lifestyle, quality of care, and medication adherence are associated with risk of recurrent AMI,[6–10] subsequent hospitalizations after the initial AMI may also increase the risk of recurrence and, therefore, may be important when considering a patient's risk. Identifying subsequent hospitalizations associated with recurrent AMI could better inform patients, families, and physicians about any further increases in the risk of recurrent AMI and help ensure intensive follow-up and risk modification behaviors.

Efforts to identify risk markers and risk factors for long-term outcomes after AMI have focused on patient characteristics available at the time of the initial hospitalization for AMI.[8,11,12] Identification of postdischarge events as

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CLINICAL PERSPECTIVE

What Is New?

- This study addresses how subsequent hospitalizations after an acute myocardial infarction may influence the risk of a recurrent acute myocardial infarction.
- We show that many types of subsequent hospitalizations can increase the risk of a recurrent acute myocardial infarction.
- We are introducing the idea of dynamic risk prediction, in which subsequent events influence the likelihood of a future cardiovascular event.

What Are the Clinical Implications?

- Risk-stratification after an acute myocardial infarction is necessary to inform the choice of clinical strategies.
- We are showing that risk prediction should be updated as new information becomes available. In this case, subsequent hospitalizations modify risk.
- This study indicates the need to develop dynamic risk calculators that can be updated over time.

Nonstandard Abbreviations and Acronyms

AMI	acute myocardial infarction
CABG	coronary artery bypass grafting
CAD	coronary artery disease
CATH	cardiac catheterization
CCS	Clinical Classifications Software
COPD	chronic obstructive pulmonary disease
DM	diabetes mellitus
FY	fiscal years
HR	hazard ratio
HTN	hypertension
ICD-9-CM	*International Classification of Diseases, Ninth Revision, Clinical Modification*
IQR	interquartile range
PCI	percutaneous coronary intervention
UTI	urinary tract infection

risk markers for adverse outcomes is limited, and many of the available data focus on mortality.[13–16] There is scant information on the association between subsequent hospitalizations and recurrent AMI. A comprehensive, contemporary, national evaluation of such rehospitalizations could provide important information for the prevention of recurrent AMI, particularly among Medicare beneficiaries who are a high-risk population for AMI.

Accordingly, we used national Medicare inpatient claims data to assess the association between subsequent hospitalizations and recurrent AMI within 1 year after an initial AMI and identify clinically important hospitalizations that increased the risk of recurrence. This study, which was based on 100% national data and detailed follow-up information about patients with AMI, is ideally positioned to generate information to update risk stratification for recurrent AMI in the year after hospital discharge.

METHODS

Restricted by our Data Use Agreement with the Centers for Medicare & Medicaid Services (CMS), the Medicare data used for this study cannot be made publicly available to other researchers for purposes of reproducing the results or replicating the procedure. However, Medicare data are available from the Centers for Medicare & Medicaid Services upon request (https://www.cms.gov/Research-Statistics-Data-and-Systems/Files-for-Order/Data-Disclosures-Data-Agreements/DUA_-_Forms.html).

Study Sample

We used the Centers for Medicare & Medicaid Services Medicare denominator files to identify all beneficiaries aged 65 years or older enrolled in the fee-for-service program for at least 12 months in fiscal years (FY) 2009–2014 (October 1, 2008 to September 31, 2014), a period in which all diagnosis codes were classified according to the *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*). We linked these enrollment data to Medicare fee-for-service inpatient claims to identify beneficiaries who were discharged alive after hospitalization for AMI at an acute-care hospital in the United States. This was designated the index AMI hospitalization. If a patient had >1 AMI hospitalization during the study period, we selected the first AMI during the study period as the index AMI. Data from FY 2008 were used to identify patients who were rehospitalized with AMI in FY 2009; FY 2015 data were used to ensure 1 year of follow-up for patients hospitalized with AMI during FY 2014.

AMI was defined as an *ICD-9-CM* principal discharge diagnosis code of 410.xx. We excluded patients with *ICD-9-CM* codes 410.x2 because the codes represent subsequent episodes of care related to the index AMI. We also excluded patients who had a length of stay ≤1 day (because these patients were unlikely to have had an AMI), had conflicting dates of death and hospitalization, or were subsequently transferred to another acute-care hospital for continuing care after the initial AMI.

Patient Baseline Characteristics

Patient baseline characteristics included age (continuous), sex, race (white, black, other), and clinical comorbidities identified using the method employed by the Centers for Medicare & Medicaid Services to profile hospital 30-day mortality measures for AMI.[17] We determined comorbidities from secondary diagnosis codes for the index AMI hospitalization as well as the principal and secondary diagnosis codes from all hospitalizations during the 12 months before the index AMI. Because the maximum number of diagnosis codes in Medicare data increased from 10 to 25 in 2011,[18] we restricted the 2011–2015 data to the first 10 diagnosis codes to calculate comorbidities.

Outcome

The primary outcome was recurrent AMI within 1 year of discharge for the initial AMI. For patients with >1 recurrent AMI, the first recurrence was selected. Deaths during the 1-year follow-up period without a recurrent AMI hospitalization were treated as competing risks in the analysis. Secondary outcomes included 30-day all-cause mortality, 30-day all-cause readmission, and 1-year all-cause mortality using the index AMI discharge as the time zero. Mean length of stay and mean Medicare payment for the index AMI hospitalization were also assessed.

Subsequent Hospitalizations

We identified all subsequent hospitalizations within 1 year after discharge for the initial AMI. For patients with a recurrent AMI, subsequent hospitalizations were restricted to the period prior to the recurrent AMI. Because of the large volume of individual *ICD-9-CM* codes, we used the Clinical Classifications Software (CCS),[19] a diagnosis and procedure categorization algorithm developed by the Agency for Healthcare Research and Quality, to characterize the subsequent hospitalizations. Using the CCS single-level diagnosis-specific algorithm, we collapsed >14 000 individual *ICD-9-CM* principal discharge diagnosis codes into 285 clinically homogeneous, meaningful, and mutually exclusive disease categories (Table S1). If a patient had >1 hospitalization for the same disease category, the first one was selected. We excluded CCS hospitalizations that occurred at a frequency <1% to avoid counting hospitalizations for less frequent diseases in the Medicare population.

Statistical Analysis

We divided patients into 2 samples, 2009–2011 and 2012–2014. We used the first sample to conduct the main analysis and the second to confirm the findings. We compared baseline characteristics between patients who had a recurrent AMI and those who did not have a recurrent AMI using the chi-squared test for categorical variables and the t test for continuous variables. Using the 2009–2011 sample, for each patient, we estimated the baseline risk at the time of discharge of having a recurrent AMI within 1 year after discharge by fitting a Cox proportional hazards model with Markov Chain Monte Carlo simulations that modeled time to first recurrent AMI as a function of a patient's baseline characteristics described above. The model also included in-hospital treatments (percutaneous coronary intervention, coronary artery bypass grafting, and cardiac catheterization), length of stay, and discharge to home (yes/no) because these variables may be associated with the outcome. We retained a variable in the model if the posterior probability of its nonzero coefficient was >0.95. We used the regression coefficients estimated from this model to calculate a baseline risk score for recurrent AMI for each patient. We standardized the score through the *Z* score method and stratified patients into 1 of 3 risk groups based on the risk score distribution: low (<10th percentile), average (10th–90th percentile), and high (>90th percentile). The baseline risk group represented a patient's risk of recurrent AMI at discharge. We used variables selected using the 2009–2011 data to calculate the score for patients in the 2012–2014 data as well.

We fit a single-variable Cox regression model to describe the observed relationship between 1-year recurrent AMI and a CCS-specific condition-related subsequent hospitalization, without accounting for patient baseline risk of recurrence. The time a hospitalization occurred was used as a time-varying variable in the analysis. We repeated this analysis for each of the potential subsequent hospitalizations. To further assess the association between rehospitalizations and 1-year recurrent AMI, we fit the Cox regression model with Markov Chain Monte Carlo simulations that modeled recurrent AMI as a function of all potential subsequent hospitalizations (event, yes/no, and time) as time-varying variables, adjusted for the patient baseline risk score for recurrent AMI. We retained a rehospitalization in the model if the posterior probability of its nonzero coefficient was >0.95. To further assess the change in risk of recurrent AMI between patients with and without at least 1 subsequent rehospitalization, we fit the Cox model with a binary time-varying indicator (1=had ≤1 subsequent CCS-specific condition-related rehospitalizations; 0=no rehospitalization), stratified by baseline risk group and further by age group. If a patient had >1 CCS-specific condition-related rehospitalization, the time that the first event occurred was used for the model.

Analyses were conducted using SAS version 9.4, 64-bit Windows (SAS Institute Inc., Cary, NC). As

Table 1. Patient Baseline Characteristics by Study Sample

	Fiscal Year 2009–2011			Fiscal Year 2012–2014		
	Aggregated (n=447 690)	Without Recurrent AMI (n=426 426)	With Recurrent AMI (n=21 264)	Aggregated (n=437 241)	Without Recurrent AMI (n=419 120)	With Recurrent AMI (n=18 121)
Demographics, n (%)						
Age, mean (SD)	78.3 (8.6)	78.2 (8.5)	79.1 (9.0)	77.8 (8.6)	77.8 (8.6)	78.3 (9.0)
Female	218 034 (48.7)	207 463 (48.7)	10 571 (49.7)	204 361 (46.7)	195 846 (46.7)	8515 (47.0)
White	391 029 (87.3)	373 133 (87.5)	17 896 (84.2)	378 338 (86.5)	363 327 (86.7)	15 011 (82.8)
Black	35 049 (7.8)	32 874 (7.7)	2175 (10.2)	35 158 (8.0)	33 234 (7.9)	1924 (10.6)
Other	21 612 (4.8)	20 419 (4.8)	1193 (5.6)	23 745 (5.4)	22 559 (5.4)	1186 (6.5)
Prior cardiovascular events, n (%)						
Heart failure	57 891 (12.9)	53 063 (12.4)	4828 (22.7)	52 783 (12.1)	48 970 (11.7)	3813 (21.0)
AMI	18 926 (4.2)	16 607 (3.9)	2319 (10.9)	17 917 (4.1)	15 946 (3.8)	1971 (10.9)
Unstable angina	11 499 (2.6)	10 219 (2.4)	1280 (6.0)	10 356 (2.4)	9375 (2.2)	981 (5.4)
Chronic atherosclerosis	326 924 (73.0)	310 783 (72.9)	16 141 (75.9)	322 038 (73.7)	308 135 (73.5)	13 903 (76.7)
Cardiopulmonary respiratory failure or shock	20 232 (4.5)	18 717 (4.4)	1515 (7.1)	21 444 (4.9)	20 102 (4.8)	1342 (7.4)
Anterior MI (*ICD-9* 410.00–410.19)	40 964 (9.2)	39 685 (9.3)	1279 (6.0)	36 106 (8.3)	35 157 (8.4)	949 (5.2)
Inferior/lateral/posterior MI (*ICD-9* 410.20–410.69)	60 244 (13.5)	58 556 (13.7)	1688 (7.9)	56 186 (12.9)	54 903 (13.1)	1283 (7.1)
Comorbidities, n (%)						
Hypertension	299 244 (66.8)	284 380 (66.7)	14 864 (69.9)	301 284 (68.9)	288 320 (68.8)	12 964 (71.5)
Stroke	17 964 (1.8)	16 798 (1.8)	1166 (2.3)	16 651 (1.7)	15 600 (1.7)	1051 (2.3)
Cerebrovascular disease	57 891 (4.0)	53 063 (3.9)	4828 (5.5)	52 783 (3.8)	48 970 (3.7)	3813 (5.8)
Renal failure	52 288 (11.7)	47 971 (11.2)	4317 (20.3)	54 285 (12.4)	50 429 (12.0)	3856 (21.3)
COPD	88 711 (19.8)	83 582 (19.6)	5129 (24.1)	85 379 (19.5)	81 060 (19.3)	4319 (23.8)
Pneumonia	64 817 (14.5)	61 108 (14.3)	3709 (17.4)	58 620 (13.4)	55 605 (13.3)	3015 (16.6)
Protein-calorie malnutrition	21 010 (4.7)	20 090 (4.7)	920 (4.3)	21 924 (5.0)	21 057 (5.0)	867 (4.8)
Dementia	48 997 (10.9)	46 521 (10.9)	2476 (11.6)	24 691 (5.6)	23 583 (5.6)	1108 (6.1)
Functional disability	10 927 (2.4)	10 182 (2.4)	745 (3.5)	10 552 (2.4)	9908 (2.4)	644 (3.6)
Peripheral vascular disease	27 609 (6.2)	25 358 (5.9)	2251 (10.6)	24 431 (5.6)	22 712 (5.4)	1719 (9.5)
Metastatic cancer	29 141 (6.5)	27 664 (6.5)	1477 (6.9)	27 341 (6.3)	26 094 (6.2)	1247 (6.9)
Major trauma in past year	26 039 (5.8)	24 762 (5.8)	1277 (6.0)	22 871 (5.2)	21 951 (5.2)	920 (5.1)
Major psychiatric disorder	9417 (2.1)	8867 (2.1)	550 (2.6)	9679 (2.2)	9210 (2.2)	469 (2.6)
Chronic liver disease	3009 (0.7)	2835 (0.7)	174 (0.8)	3446 (0.8)	3282 (0.8)	164 (0.9)
Depression	25 098 (5.6)	23 821 (5.6)	1277 (6.0)	26 353 (6.0)	25 187 (6.0)	1166 (6.4)
Diabetes mellitus	139 047 (31.1)	130 064 (30.5)	8983 (42.2)	144 787 (33.1)	136 443 (32.6)	8344 (46.0)
Parkinson or Huntington disease	6186 (1.4)	5845 (1.4)	341 (1.6)	6045 (1.4)	5771 (1.4)	274 (1.5)
Anemia	11 0791 (24.7)	104 398 (24.5)	6393 (30.1)	112 477 (25.7)	106 785 (25.5)	5692 (31.4)
Asthma	10 699 (2.4)	10 178 (2.4)	521 (2.5)	11 153 (2.6)	10 681 (2.5)	472 (2.6)
In-hospital procedures, n (%)						
Percutaneous coronary intervention	181 125 (40.5)	174 586 (40.9)	6539 (30.8)	192 090 (43.9)	185 794 (44.3)	6296 (34.7)
Coronary artery bypass grafting	41 365 (9.2)	40 676 (9.5)	689 (3.2)	39 558 (9.0)	38 948 (9.3)	610 (3.4)
Cardiac catheterization	260 515 (58.2)	250 689 (58.8)	9826 (46.2)	263 534 (60.3)	254 605 (60.7)	8929 (49.3)
Discharge disposition, n (%)						
Home	253 528 (56.6)	241 745 (56.7)	11 783 (55.4)	255 527 (58.4)	245 028 (58.5)	10 499 (57.9)
Home with care	69 802 (15.6)	65 712 (15.4)	4090 (19.2)	66 388 (15.2)	63 034 (15.0)	3354 (18.5)
Skilled nursing facility or intermediate care facility	84 997 (19.0)	80 767 (18.9)	4230 (19.9)	76 120 (17.4)	72 897 (17.4)	3223 (17.8)

(*Continued*)

Table 1. Continued

	Fiscal Year 2009–2011			Fiscal Year 2012–2014		
	Aggregated (n=447 690)	Without Recurrent AMI (n=426 426)	With Recurrent AMI (n=21 264)	Aggregated (n=437 241)	Without Recurrent AMI (n=419 120)	With Recurrent AMI (n=18 121)
Outcome						
Length of stay, mean (SD) days	6 (5.4)	6 (5.5)	5 (4.6)	5 (5.1)	5 (5.1)	5 (4.2)
Medicare payment, median (IQR), $1000	10.8 (8.3–16.1)	10.8 (8.4–16.2)	10.3 (7.1–14.2)	11.1 (8.5–16.7)	11.1 (8.5–16.8)	10.4 (7.1–14.8)
30-day mortality after discharge, n (%)	23 061 (5.2)	22 487 (5.3)	574 (2.7)	21 743 (5.0)	21 240 (5.1)	503 (2.8)
1-year mortality after discharge, n (%)	86 692 (19.4)	81 729 (19.2)	4963 (23.3)	76 542 (17.5)	72 639 (17.3)	3903 (21.5)
30-day all-cause readmission after discharge, n (%)	85 234 (19.0)	76 967 (18.1)	8270 (38.9)	72 910 (16.7)	65 913 (15.7)	6997 (38.6)

AMI indicates acute myocardial infarction; COPD, chronic obstructive pulmonary disease; *ICD-9*, *International Classification of Diseases, Ninth Revision;* IQR, interquartile range; and MI, myocardial infarction.

of 2019, the data were 5 years old. Analyses were repeated using the 2012–2014 data. Deaths before recurrent AMI were addressed using the Fine and Gray[20] method for competing risks. The Lee, Wei, and Amato method[21] of robust sandwich variance matrix estimation was used to adjust for within-hospital clustering of patients. All statistical testing was 2-sided, and $P<0.05$ was considered statistically significant. The study followed the guidelines for cohort studies described in the Strengthening the Reporting of Observational Studies in Epidemiology Statement: Guidelines for Reporting Observational Studies.[22] The Yale University Institutional Review Board reviewed the study protocol and granted a waiver of informed consent for the use of the deidentified database.

RESULTS

Study Sample and Patient Baseline Characteristics

The study included 884 931 (447 690 in 2009–2011 and 437 241 in 2012–2014) unique patients who were discharged alive after AMI, were not transferred to another acute-care hospital, and were hospitalized for >1 day during their index admission. Overall, patients had a mean age of 78.0 (SD, 8.6) years, and 47.7% were female. The most common comorbidities were chronic atherosclerosis (73.3%), hypertension (67.9%), diabetes mellitus (32.1%), and anemia (25.2%). During the index AMI hospitalization, 42.2% of patients had a percutaneous coronary intervention, 9.1% underwent coronary artery bypass grafting, and 58.2% had cardiac catheterization. The median length of stay was 4 (interquartile range [IQR], 2–7) days, and 57.5% of patients were discharged to home. Patient characteristics were no different between the 2009–2011 and 2012–2014 samples (Table 1).

Outcome

For the 2009–2011 and 2012–2014 samples, the rates of 1-year recurrent AMI were 5.3% (95% CI, 5.27–5.41) and 4.6% (95% CI, 4.54–4.67), respectively ($P<0.001$). Among these patients who had a recurrent AMI, the median (IQR) days from discharge to a recurrent AMI was 115 (34–230) for the 2009–2011 sample and 106 (31–217) for the 2012–2014 sample. In the 2009–2011 and 2012–2014 samples, respectively, the median (IQR) survived days among patients who died within 1 year without a recurrent AMI were 56 (20–128) and 53 (19–121), and the median (IQR) survived days among patients who died with a recurrent AMI were 105 (49–188) and 97 (48–179).

All-cause mortality rates after the index AMI and before a recurrent AMI were 17.5% (95% CI, 17.4–17.6) and 15.7% (95% CI, 15.6–15.8) for the 2009–2011 and 2012–2014 samples, respectively. Compared with patients without a recurrent AMI, patients with a recurrent AMI had a higher 30-day postdischarge all-cause mortality rate (5.3% versus 2.7%; $P<0.001$), higher 30-day all-cause readmission rate (38.9% versus 18.1%; $P<0.001$), higher 1-year all-cause mortality rate (23.3% versus 19.2%; $P<0.001$), lower median Medicare payment ($10 300 versus $10 500), and shorter mean (SD) length of stay (5 [4.6] days versus 6 [5.5] days). These observed outcomes were similar in the 2009–2011 and 2012–2014 samples (Table 1).

Association Between Patient Baseline Characteristics and Recurrent AMI

In the 2009–2011 sample, the 5 baseline characteristics most strongly associated with 1-year

recurrent AMI were AMI before the index admission (hazard ratio [HR], 1.8 [95% CI, 1.76–1.93]), unstable angina (HR, 1.5 [95% CI, 1.41–1.59]), diabetes mellitus (HR, 1.4 [95% CI, 1.39–1.47]), chronic atherosclerosis (HR, 1.3 [95% CI, 1.26–1.35]), and renal failure (HR, 1.2 [95% CI, 1.14–1.23]; Figure 1). Patients with a standardized risk <–1.2 times the SD, between –1.2 and 1.2, and >1.2 were stratified into low-, average-, and high-risk groups, respectively (Figure 2). The mean (SD) estimated rates of 1-year recurrent AMI were 1.7% (0.47) for the low-risk group, 5.1% (2.03) for average risk, and 14.3% (5.31) for high risk. Within a risk group, the rate of recurrence increased with patient age (Figure 3, top panel). Results were similar for the 2012–2014 sample (Figure 3, bottom panel).

Subsequent Hospitalizations

Among 285 CCS-specific conditions, 19 occurred in at least 1% of patients and were included in the model for the 2009–2011 sample (Table 2). The median (IQR) tetrachoric correlations among parts of these conditions were low (0.11 [95% CI, 0.08–0.16] in 2009–2011 and 0.12 [95% CI, 0.09–0.18] in 2012–2014). The highest correlation occurred between chronic obstructive pulmonary disease and bronchiectasis (CCS-127) and respiratory failure/insufficiency/arrest (CCS-131), which was 0.40 in 2009–2011 and 0.41 in 2012–2014. Among 447 690 patients in the 2009–2011 sample, 36.0% (n=161 327) had at least 1 rehospitalization for 1 of these 19 CCS-specific conditions before a recurrent AMI within 1 year. The 5 most common rehospitalization events were congestive heart failure (CCS-108,

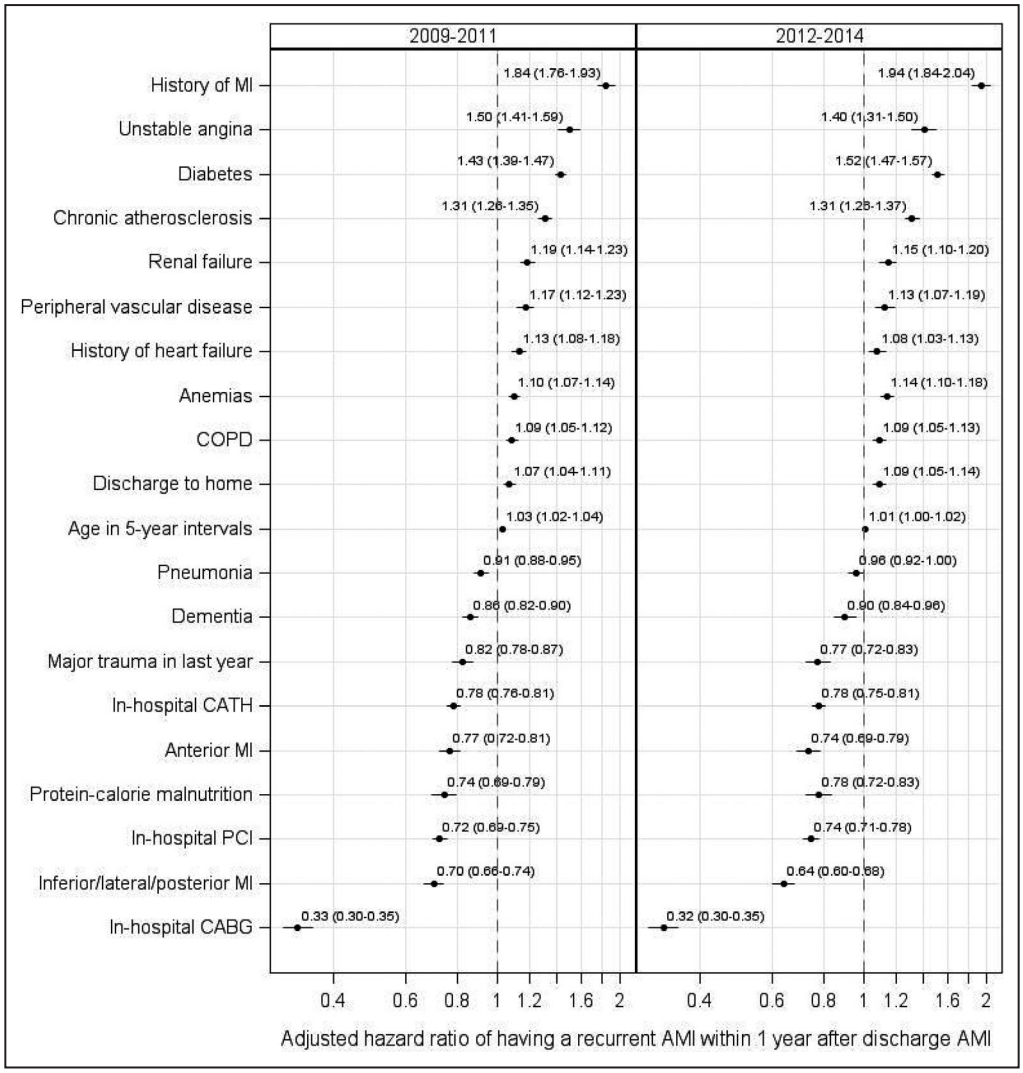

Figure 1. Patient baseline characteristics associated with recurrent AMI within 1 year after the initial AMI.

AMI indicates acute myocardial infarction; CABG, coronary artery bypass grafting; CATH, cardiac catheterization; COPD, chronic obstructive pulmonary disease; and PCI, percutaneous coronary intervention.

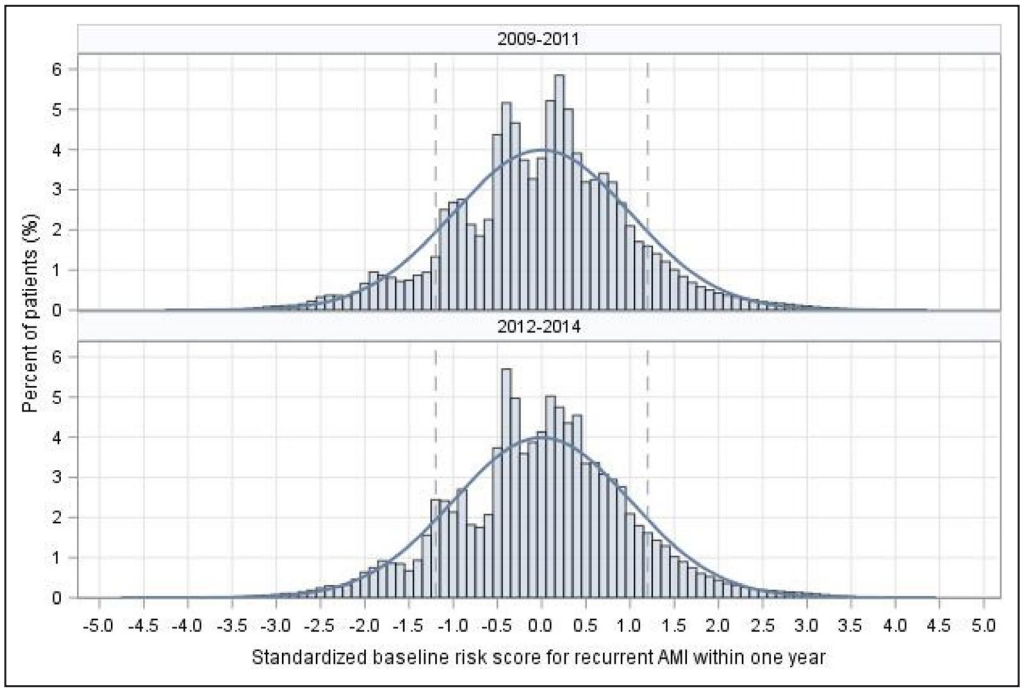

Figure 2. Distribution of baseline risk of recurrent acute myocardial infarction within 1 year after discharge for AMI.
AMI indicates acute myocardial infarction.

9.8%), coronary atherosclerosis and other heart disease (CCS-101, 6.6%), septicemia (CCS-2, 4.0%), cardiac dysrhythmias (CCS-106, 3.7%), and pneumonia (CCS-122, 3.4%). The 5 events that occurred soonest after discharge were complications of surgical procedures or medical care (CCS-238; median, 53 [IQR, 12–165] days), coronary atherosclerosis and other heart disease (CCS-101; median, 54 [IQR, 19–154]

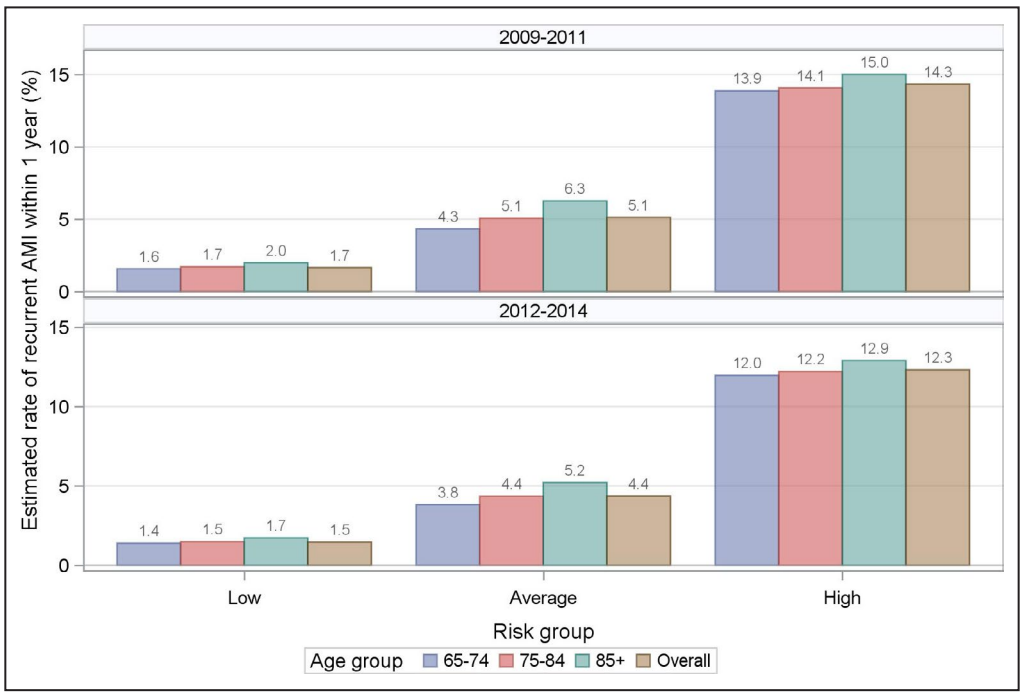

Figure 3. Baseline risk groups of recurrent acute myocardial infarction within 1 year after discharge for AMI.
AMI indicates acute myocardial infarction.

Table 2. Occurrence of 19 Targeted Types of CCS-Specific Condition-Related Subsequent Hospitalizations

Rehospitalization, N (%)	FY 2009–2011 N=447,690	FY 2012–2014 N=437,241
Septicemia (CCS-2; except in labor)	18 582 (4.2)	19 333 (4.4)
Diabetes mellitus with complications (CCS-50)	5445 (1.2)	4462 (1.0)
Fluid and electrolyte disorders (CCS-55)	7210 (1.6)	5407 (1.2)
Deficiency and other anemia (CCS-59)	5159 (1.2)	3971 (0.9)
Hypertension with complications and secondary hypertension (CCS-99)	6305 (1.4)	6216 (1.4)
Coronary atherosclerosis and other heart disease (CCS-101)	31 034 (6.9)	21 222 (4.9)
Nonspecific chest pain (CCS-102)	10 046 (2.2)	6855 (1.6)
Cardiac dysrhythmias (CCS-106)	17 167 (3.8)	14 521 (3.3)
Congestive heart failure (CCS-108; non-hypertensive)	46 340 (10.4)	37 766 (8.6)
Acute cerebrovascular disease (CCS-109)	8825 (2.0)	7837 (1.8)
Pneumonia (CCS-122; except that caused by tuberculosis or sexually transmitted disease)	15 762 (3.5)	12 688 (2.9)
Chronic obstructive pulmonary disease and bronchiectasis (CCS-127)	9949 (2.2)	8012 (1.8)
Respiratory failure; insufficiency; arrest (CCS-131; adult)	8397 (1.9)	7288 (1.7)
Gastrointestinal hemorrhage (CCS-153)	9592 (2.1)	8825 (2.0)
Acute and unspecified renal failure (CCS-157)	11 172 (2.5)	10 684 (2.4)
Urinary tract infections (CCS-159)	9389 (2.1)	7232 (1.7)
Fracture of neck of femur (CCS-226; hip)	4804 (1.1)	4002 (0.9)
Complication of device; implant or graft (CCS-237)	10 109 (2.3)	8191 (1.9)
Complications of surgical procedures or medical care (CCS-238)	7680 (1.7)	6306 (1.4)

AMI indicates acute myocardial infarction; CCS, Clinical Classifications Software; and FY, fiscal years.

days), congestive heart failure (CCS-108; median, 62 [IQR, 18–161] days), respiratory failure/insufficiency/arrest (CCS-131; median, 88 [IQR, 28–198] days), and cardiac dysrhythmias (CCS-106; median, 90 [IQR, 25–204] days; Figure 4, top panel). The findings were similar for the 2012–2014 sample (Figure 4, bottom panel). In-hospital mortality for these CCS-specific hospitalizations ranged from 0.3% (nonspecific chest pain, CCS-102) to 21.9% (septicemia, CCS-2).

Association Between Subsequent Hospitalizations and Recurrent AMI

Most of the 19 subsequent hospitalizations were associated with an increased recurrent AMI risk in the descriptive analysis without accounting for patient baseline risk of recurrent AMI (Table 3). The Cox model based on the 2009–2011 data identified 12 CCS-specific subsequent hospitalizations significantly associated to recurrent AMI risk (Figure 5). These hospitalizations were septicemia (CCS-2), diabetes mellitus with complications (CCS-50), deficiency and other anemia (CCS-59), hypertension with complications and secondary hypertension (CCS-99), coronary atherosclerosis and other heart disease (CCS-101), nonspecific chest pain (CCS-102), congestive heart failure (CCS-108), pneumonia (CCS-122), chronic obstructive pulmonary disease and bronchiectasis (CCS-127), gastrointestinal hemorrhage (CCS-153), acute and unspecified renal failure (CCS-157), and complication of device (implant or graft; CCS-237). All these rehospitalizations except septicemia (CCS-2) were associated with increased risk of recurrent AMI; septicemia (CCS-2) was associated with a lower risk of recurrent AMI (Figure 5). The HRs ranged from 1.6 (95% CI, 1.55–1.70, heart failure [CCS-108]) to 1.1 (95% CI, 1.04–1.25, pneumonia [CCS-122]); the HR for septicemia (CCS-2) was 0.6 (95% CI, 0.58–0.71; Figure 5).

Overall, 26.9% of patients in 2009–2011 and 22.5% of patients in 2012–2014 had at least 1 of the identified subsequent CCS-specific hospitalizations significantly associated with increased risk of recurrent AMI. For the low-, average-, and high-risk groups in the 2009–2011 sample, having at least 1 CCS-specific hospitalization was associated with an increase in the risk of recurrent AMI by 210% (95% CI, 77%–149%), 73% (95% CI 66%–79%), and 43% (95% CI 34%–52%), respectively. The younger age group (65–74 years) in the average-risk strata was most likely to have a recurrence with at least 1 CCS-specific hospitalization (Figure 6, left panel). The findings were similar for the 2012–2014 cohort (Figure 6, right panel).

DISCUSSION

In this study, we demonstrated that hospitalizations after AMI were associated with the risk of a subsequent AMI. Although patient baseline characteristics

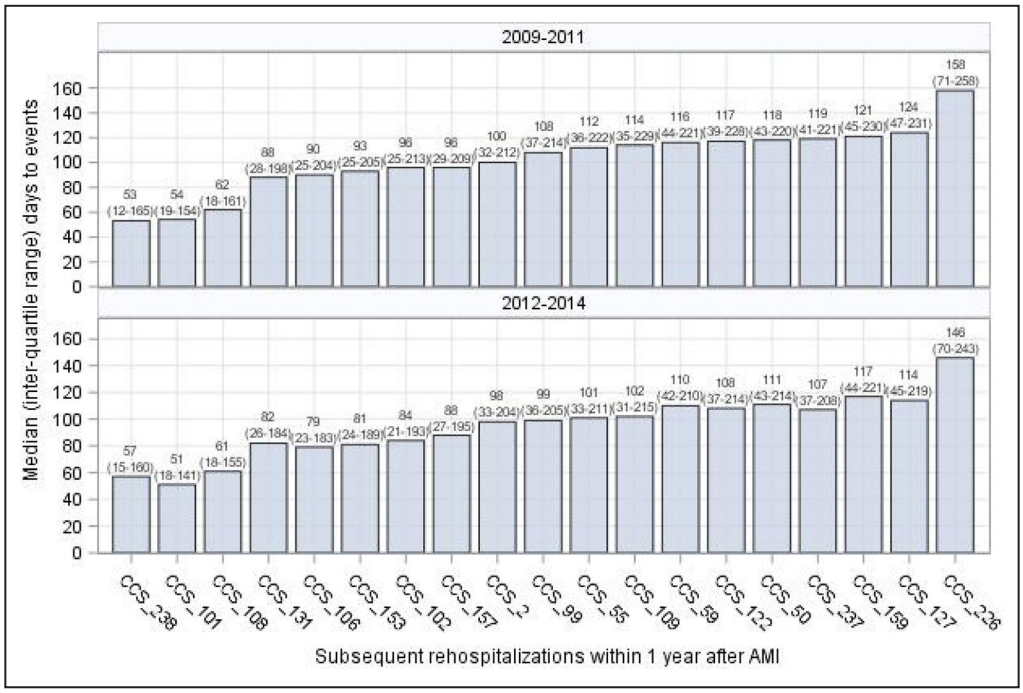

Figure 4. Median (interquartile range [IQR]) days to subsequent rehospitalizations within 1 year after discharge for index AMI.

The median (IQR) days to recurrent AMI were 115 (34–230) in the 2009–2011 sample and 106 (31–217) in the 2012 to 2014 sample. AMI indicates acute myocardial infarction; CAD, coronary artery disease; CCS_101, Coronary atherosclerosis and other heart disease; CCS_102, Nonspecific chest pain; CCS_106, Cardiac dysrhythmias; CCS_108, Congestive heart failure; CCS_109, Acute cerebrovascular disease; CCS_122, Pneumonia; CCS_131, Respiratory failure; insufficiency; arrest; CCS_153, Gastrointestinal hemorrhage; CCS_157, Acute and unspecified renal failure; CCS_159, Urinary tract infections; CCS_2, Septicemia; CCS_226, Fracture of neck of femur; CCS_237, Complication of device; implant or graft; CCS_238, Complications of surgical procedures or medical care; CCS_50, Diabetes mellitus with complications; CCS_55, Fluid and electrolyte disorders; CCS_59, Deficiency and other anemia; CCS_99, Hypertension with complications and secondary hypertension; CCS, Clinical Classifications Software; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; HTN, hypertension; and UTI, urinary tract infection

were also associated with the risk of a recurrent AMI, we showed that patient risk of recurrence was influenced by hospitalizations that occurred after discharge. Among the 12 rehospitalization categories identified in this study, 11 were associated with increased risk of recurrent AMI, with the increase in risk ranging from 14% (pneumonia) to 62% (heart failure). We found that patients who survived a hospitalization for septicemia had a lower risk of a recurrent AMI.

There are several potential explanations for the associations between subsequent hospitalizations and increased patient risk of recurrent AMI. It is possible that the hospitalization is a marker for the presence and severity of comorbidities. Sick patients tend to have more comorbidities[23] and are more likely to be rehospitalized after AMI.[24] We adjusted for baseline comorbidities, but information about the severity does not reside within the administrative codes in our Medicare database. Additionally, the hospitalizations may be a marker for postdischarge quality of care. Postdischarge care factors, such as continuity of care, type of care, and care providers, could impact AMI patient outcomes.[25–27] Studies have identified associations between poor postdischarge care and subsequent hospitalizations,[28–30] including recurrent AMI. Many subsequent hospitalizations identified by our study, including those for diabetes mellitus, anemia, hypertension, coronary atherosclerosis, chest pain, heart failure, pneumonia, chronic obstructive pulmonary disease and bronchiectasis, respiratory failure, gastrointestinal hemorrhage, renal failure, and complications of an implant or graft, have been individually identified as potential risk markers for recurrent AMI or major cardiovascular events in previous studies.[6,8,31] Another possible explanation for our findings is that the hospitalization itself increased the risk. The reason for the hospitalization may have been associated with inflammation, a known contributor to AMI risk, or to other factors associated with AMI, such as stress or depression. It is also possible that the hospitalization

Table 3. Observed Association Between a Targeted CCS-Specific Condition-Related Subsequent Hospitalization and 1-Year Recurrent AMI Based on a Single-Variable Cox Regression Model

Rehospitalization	FY 2009–2011	FY 2012–2014
	HR (95% CI)	HR (95% CI)
Septicemia (CCS-2; except in labor)	0.80 (0.72–0.89)	0.87 (0.78–0.97)
Diabetes mellitus with complications (CCS-50)	2.10 (1.85–2.37)	2.50 (2.18–2.86)
Fluid and electrolyte disorders (CCS-55)	1.49 (1.31–1.68)	1.74 (1.51–2.01)
Deficiency and other anemia (CCS-59)	1.87 (1.64–2.14)	1.97 (1.68–2.31)
Hypertension with complications and secondary hypertension (CCS-99)	2.35 (2.11–2.62)	2.39 (2.13–2.69)
Coronary atherosclerosis and other heart disease (CCS-101)	1.70 (1.61–1.80)	1.94 (1.82–2.08)
Nonspecific chest pain (CCS-102)	1.79 (1.63–1.97)	1.89 (1.68–2.13)
Cardiac dysrhythmias (CCS-106)	1.26 (1.16–1.37)	1.25 (1.13–1.38)
Congestive heart failure (CCS-108; non-hypertensive)	2.12 (2.03–2.21)	2.00 (1.90–2.11)
Acute cerebrovascular disease (CCS-109)	1.03 (0.90–1.18)	1.00 (0.86–1.17)
Pneumonia (CCS-122; except that caused by tuberculosis or sexually transmitted disease)	1.46 (1.33–1.59)	1.57 (1.42–1.73)
Chronic obstructive pulmonary disease and bronchiectasis (CCS-127)	1.93 (1.75–2.13)	1.75 (1.55–1.97)
Respiratory failure; insufficiency; arrest (CCS-131; adult)	1.54 (1.38–1.73)	1.28 (1.11–1.47)
Gastrointestinal hemorrhage (CCS-153)	1.42 (1.28–1.58)	1.48 (1.32–1.67)
Acute and unspecified renal failure (CCS-157)	1.60 (1.45–1.76)	1.47 (1.31–1.63)
Urinary tract infections (CCS-159)	1.37 (1.22–1.54)	1.35 (1.17–1.56)
Fracture of neck of femur (CCS-226; hip)	1.40 (1.18–1.66)	1.26 (1.02–1.56)
Complication of device; implant or graft (CCS-237)	1.98 (1.80–2.17)	2.13 (1.91–2.37)
Complications of surgical procedures or medical care (CCS-238)	0.90 (0.79–1.04)	1.03 (0.88–1.20)

AMI indicates acute myocardial infarction; CCS, Clinical Classifications Software; FY, fiscal years; and HR, hazard ratio.

led to the discontinuation of secondary preventive medications or the addition of medications to a patient's regimen, which may have resulted in nonadherence to the regimen.

The negative association of septicemia with recurrent AMI may represent a survivorship bias because patients who survived sepsis may have been healthier than those who died with sepsis and were therefore

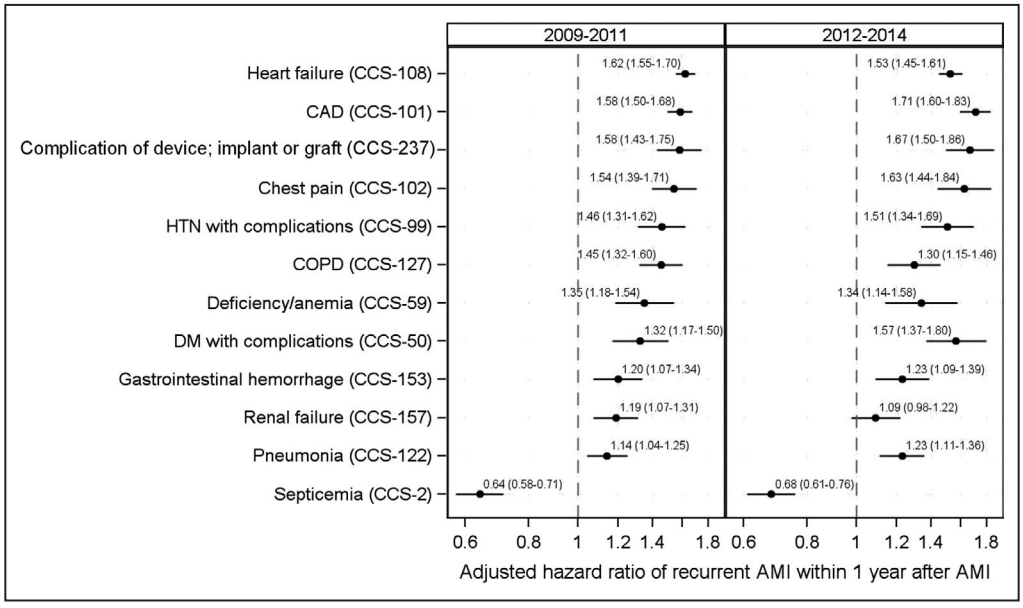

Figure 5. Association between subsequent rehospitalizations and recurrent AMI after discharge for index AMI, accounting for baseline risk of recurrence.
AMI indicates acute myocardial infarction; CAD, coronary artery disease; CCS, Clinical Classifications Software; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; and HTN, hypertension.

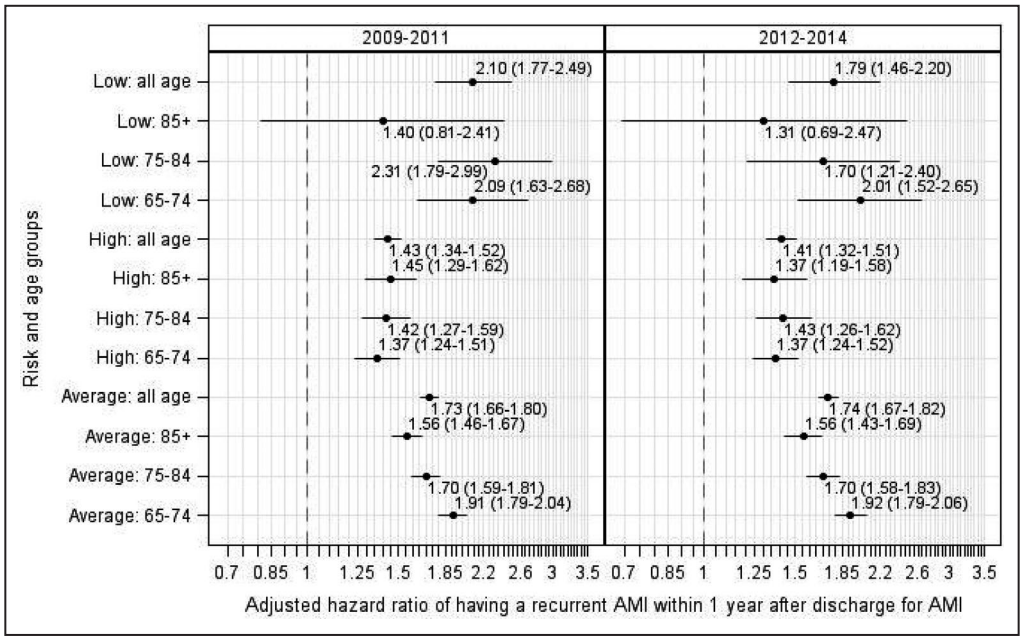

Figure 6. Association between at least 1 subsequent hospitalization and risk of recurrent AMI by patient baseline risk and age groups.
AMI indicates acute myocardial infarction.

less likely to have a recurrent AMI. Our data showed that approximately 22% of AMI survivors rehospitalized for sepsis died during the sepsis hospitalization.

Our study, based on real-world data, has several important characteristics. We focused on the first year after an initial AMI, a period that has the highest risk of recurrent AMI.[4] Our findings provide real-world empirical evidence of the importance of accounting for postdischarge rehospitalizations to help ensure better long-term outcomes. We showed that patient risk stratification for recurrent AMI was a dynamic measure that could change immediately after discharge. The CCS categories allowed the grouping of similar medical conditions to provide hospitals and physicians a parsimonious, clinically meaningful, and practically useful composite measure of rehospitalizations. Such a composite measure could be used more easily than a traditional approach based on individual *ICD* diagnosis codes. The 12 subsequent hospitalizations identified in the study were based on the 285 CCS categories, which represent all principal diagnosis codes for rehospitalizations. These CCS categories are easy to collect and readily available at the time of discharge for the rehospitalization.

A model that combines rehospitalizations with patient baseline characteristics would allow hospitals and physicians to reevaluate patient risk for recurrent AMI throughout the first year and may help patients understand that their risk of recurrence depends not only on their baseline characteristics but also the sequence of rehospitalizations that occur after their initial AMI. The ability to identify individuals with the highest risk of recurrent AMI after a rehospitalization may aid in the provision of targeted, intensive, and higher-quality longitudinal care after discharge. Additionally, insight regarding the long-term risk of subsequent hospitalizations associated with recurrent AMI is important from a patient perspective as educating patients regarding their long-term risk might provide an even stronger incentive to follow-up and adhere to medications. Our study also provides evidence that hospitals and primary care physicians caring for patients with a history of AMI should be aware that subsequent hospitalizations can change patient risk of recurrent AMI.

Our study has several limitations. We considered only the first recurrent AMI and acknowledge that patients may experience multiple recurrent events, in which a recurrent event model can be fit. The subsequent hospitalizations identified in our study were based on the CCS categories, which represent multiple principal discharge diagnosis codes, while an individual rehospitalization only represents a single principal diagnosis code that could be more clinically important. We accounted for only inpatient rehospitalizations and did not consider outpatient care, observation stays, or emergency department visits. We treated subsequent rehospitalizations independently and acknowledge that some hospitalizations may have been related. Nevertheless, we found that the median tetrachoric correlation among these rehospitalizations was not high, indicating these rehospitalizations were not strongly related to each other. We

did not address whether the association between a subsequent hospitalization and a recurrent AMI depended on the hospitalization-free duration from an index AMI discharge to a rehospitalization, which could be clinically important. We restricted the 2011–2015 data to the first 10 diagnosis codes to align with the 2009–2010 data, which only contained 10 diagnosis codes. Accordingly, we may have missed some comorbidity information carried by the additional codes. Our study was limited by the availability of data resources, and therefore it did not incorporate information on medication adherence, nursing home stays, and home health services, which were associated with rehospitalizations and recurrent AMI in prior work.[32–34] Moreover, we used comorbidity information from administrative data. These data lack detailed clinical information on patient functional status, left ventricular function, non–ST-segment–elevation myocardial infarction, and ST-segment elevation myocardial infarction, which could be important for assessing risk of recurrence and reducing measurement error.

In conclusion, patient risk of recurrent AMI changed on the basis of the occurrence of subsequent hospitalizations. Improving post–acute care to prevent unplanned rehospitalizations, especially those for chronic diseases, and extending the current focus on all-cause 30-day rehospitalizations to condition-specific rehospitalizations beyond the 30-day period are important for the secondary prevention of AMI. Moreover, there should be strong efforts to ensure that patients who experience these events have optimal secondary prevention strategies.

ARTICLE INFORMATION

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Disclosures

Dr Krumholz was a recipient of a research grant, through Yale, from Medtronic and the US Food and Drug Administration to develop methods for postmarket surveillance of medical devices; is a recipient of research agreements with Medtronic and Johnson & Johnson (Janssen), through Yale, to develop methods of clinical trial data sharing; was a recipient of a research agreement, through Yale, from the Shenzhen Center for Health Information for work to advance intelligent disease prevention and health promotion; collaborates with the National Center for Cardiovascular Diseases in Beijing; chairs a Cardiac Scientific Advisory Board for UnitedHealth; is a participant/participant representative of the IBM Watson Health Life Sciences Board; is a member of the Advisory Board for Element Science and the Physician Advisory Board for Aetna; received payment from the Arnold & Porter Law Firm for work related to the Sanofi clopidogrel litigation and from the Ben C. Martin Law Firm for work related to the Cook inferior vena cava filter litigation; and is the founder of Hugo, a personal health information platform. Drs Krumholz and Normand work under contract to the Centers for Medicare & Medicaid Services to develop and maintain performance measures that are publicly reported. The remaining authors have no disclosures to report.

Supplementary Material

Table S1

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SUPPLEMENTAL MATERIAL

Table S1. Clinical Classifications Software categories.

CCS ID	Disease category
1	Tuberculosis
2	Septicemia (except in labor)
3	Bacterial infection; unspecified site
4	Mycoses
5	HIV infection
6	Hepatitis
7	Viral infection
8	Other infections; including parasitic
9	Sexually transmitted infections (not HIV or hepatitis)
10	Immunizations and screening for infectious disease
11	Cancer of head and neck
12	Cancer of esophagus
13	Cancer of stomach
14	Cancer of colon
15	Cancer of rectum and anus
16	Cancer of liver and intrahepatic bile duct
17	Cancer of pancreas
18	Cancer of other GI organs; peritoneum
19	Cancer of bronchus; lung
20	Cancer; other respiratory and intrathoracic
21	Cancer of bone and connective tissue
22	Melanomas of skin
23	Other non-epithelial cancer of skin
24	Cancer of breast
25	Cancer of uterus
26	Cancer of cervix
27	Cancer of ovary
28	Cancer of other female genital organs
29	Cancer of prostate
30	Cancer of testis
31	Cancer of other male genital organs
32	Cancer of bladder
33	Cancer of kidney and renal pelvis
34	Cancer of other urinary organs
35	Cancer of brain and nervous system
36	Cancer of thyroid
37	Hodgkin`s disease
38	Non-Hodgkin`s lymphoma
39	Leukemias
40	Multiple myeloma
41	Cancer; other and unspecified primary
42	Secondary malignancies
43	Malignant neoplasm without specification of site

44	Neoplasms of unspecified nature or uncertain behavior
45	Maintenance chemotherapy; radiotherapy
46	Benign neoplasm of uterus
47	Other and unspecified benign neoplasm
48	Thyroid disorders
49	Diabetes mellitus without complication
50	Diabetes mellitus with complications
51	Other endocrine disorders
52	Nutritional deficiencies
53	Disorders of lipid metabolism
54	Gout and other crystal arthropathies
55	Fluid and electrolyte disorders
56	Cystic fibrosis
57	Immunity disorders
58	Other nutritional; endocrine; and metabolic disorders
59	Deficiency and other anemia
60	Acute posthemorrhagic anemia
61	Sickle cell anemia
62	Coagulation and hemorrhagic disorders
63	Diseases of white blood cells
64	Other hematologic conditions
650	Adjustment disorders
651	Anxiety disorders
652	Attention-deficit, conduct, and disruptive behavior disorders
653	Delirium, dementia, and amnestic and other cognitive disorders
654	Developmental disorders
655	Disorders usually diagnosed in infancy, childhood, or adolescence
656	Impulse control disorders, NEC
657	Mood disorders
658	Personality disorders
659	Schizophrenia and other psychotic disorders
660	Alcohol-related disorders
661	Substance-related disorders
662	Suicide and intentional self-inflicted injury
663	Screening and history of mental health and substance abuse codes
670	Miscellaneous disorders
76	Meningitis (except that caused by tuberculosis or sexually transmitted disease)
77	Encephalitis (except that caused by tuberculosis or sexually transmitted disease)
78	Other CNS infection and poliomyelitis
79	Parkinson`s disease
80	Multiple sclerosis
81	Other hereditary and degenerative nervous system conditions
82	Paralysis
83	Epilepsy; convulsions
84	Headache; including migraine
85	Coma; stupor; and brain damage

86	Cataract
87	Retinal detachments; defects; vascular occlusion; and retinopathy
88	Glaucoma
89	Blindness and vision defects
90	Inflammation; infection of eye (except that caused by tuberculosis or sexually transmitted disease)
91	Other eye disorders
92	Otitis media and related conditions
93	Conditions associated with dizziness or vertigo
94	Other ear and sense organ disorders
95	Other nervous system disorders
96	Heart valve disorders
97	Peri-; endo-; and myocarditis; cardiomyopathy (except that caused by tuberculosis or sexually transmitted disease)
98	Essential hypertension
99	Hypertension with complications and secondary hypertension
100	Acute myocardial infarction
101	Coronary atherosclerosis and other heart disease
102	Nonspecific chest pain
103	Pulmonary heart disease
104	Other and ill-defined heart disease
105	Conduction disorders
106	Cardiac dysrhythmias
107	Cardiac arrest and ventricular fibrillation
108	Congestive heart failure; nonhypertensive
109	Acute cerebrovascular disease
110	Occlusion or stenosis of precerebral arteries
111	Other and ill-defined cerebrovascular disease
112	Transient cerebral ischemia
113	Late effects of cerebrovascular disease
114	Peripheral and visceral atherosclerosis
115	Aortic; peripheral; and visceral artery aneurysms
116	Aortic and peripheral arterial embolism or thrombosis
117	Other circulatory disease
118	Phlebitis; thrombophlebitis and thromboembolism
119	Varicose veins of lower extremity
120	Hemorrhoids
121	Other diseases of veins and lymphatics
122	Pneumonia (except that caused by tuberculosis or sexually transmitted disease)
123	Influenza
124	Acute and chronic tonsillitis
125	Acute bronchitis
126	Other upper respiratory infections
127	Chronic obstructive pulmonary disease and bronchiectasis
128	Asthma
129	Aspiration pneumonitis; food/vomitus

130 Pleurisy; pneumothorax; pulmonary collapse
131 Respiratory failure; insufficiency; arrest (adult)
132 Lung disease due to external agents
133 Other lower respiratory disease
134 Other upper respiratory disease
135 Intestinal infection
136 Disorders of teeth and jaw
137 Diseases of mouth; excluding dental
138 Esophageal disorders
139 Gastroduodenal ulcer (except hemorrhage)
140 Gastritis and duodenitis
141 Other disorders of stomach and duodenum
142 Appendicitis and other appendiceal conditions
143 Abdominal hernia
144 Regional enteritis and ulcerative colitis
145 Intestinal obstruction without hernia
146 Diverticulosis and diverticulitis
147 Anal and rectal conditions
148 Peritonitis and intestinal abscess
149 Biliary tract disease
150 Liver disease; alcohol-related
151 Other liver diseases
152 Pancreatic disorders (not diabetes)
153 Gastrointestinal hemorrhage
154 Noninfectious gastroenteritis
155 Other gastrointestinal disorders
156 Nephritis; nephrosis; renal sclerosis
157 Acute and unspecified renal failure
158 Chronic kidney disease
159 Urinary tract infections
160 Calculus of urinary tract
161 Other diseases of kidney and ureters
162 Other diseases of bladder and urethra
163 Genitourinary symptoms and ill-defined conditions
164 Hyperplasia of prostate
165 Inflammatory conditions of male genital organs
166 Other male genital disorders
167 Nonmalignant breast conditions
168 Inflammatory diseases of female pelvic organs
169 Endometriosis
170 Prolapse of female genital organs
171 Menstrual disorders
172 Ovarian cyst
173 Menopausal disorders
174 Female infertility
175 Other female genital disorders

176 Contraceptive and procreative management
177 Spontaneous abortion
178 Induced abortion
179 Postabortion complications
180 Ectopic pregnancy
181 Other complications of pregnancy
182 Hemorrhage during pregnancy; abruptio placenta; placenta previa
183 Hypertension complicating pregnancy; childbirth and the puerperium
184 Early or threatened labor
185 Prolonged pregnancy
186 Diabetes or abnormal glucose tolerance complicating pregnancy; childbirth; or the puerperium
187 Malposition; malpresentation
188 Fetopelvic disproportion; obstruction
189 Previous C-section
190 Fetal distress and abnormal forces of labor
191 Polyhydramnios and other problems of amniotic cavity
192 Umbilical cord complication
193 OB-related trauma to perineum and vulva
194 Forceps delivery
195 Other complications of birth; puerperium affecting management of mother
196 Normal pregnancy and/or delivery
197 Skin and subcutaneous tissue infections
198 Other inflammatory condition of skin
199 Chronic ulcer of skin
200 Other skin disorders
201 Infective arthritis and osteomyelitis (except that caused by tuberculosis or sexually transmitted disease)
202 Rheumatoid arthritis and related disease
203 Osteoarthritis
204 Other non-traumatic joint disorders
205 Spondylosis; intervertebral disc disorders; other back problems
206 Osteoporosis
207 Pathological fracture
208 Acquired foot deformities
209 Other acquired deformities
210 Systemic lupus erythematosus and connective tissue disorders
211 Other connective tissue disease
212 Other bone disease and musculoskeletal deformities
213 Cardiac and circulatory congenital anomalies
214 Digestive congenital anomalies
215 Genitourinary congenital anomalies
216 Nervous system congenital anomalies
217 Other congenital anomalies
218 Liveborn
219 Short gestation; low birth weight; and fetal growth retardation

220	Intrauterine hypoxia and birth asphyxia
221	Respiratory distress syndrome
222	Hemolytic jaundice and perinatal jaundice
223	Birth trauma
224	Other perinatal conditions
225	Joint disorders and dislocations; trauma-related
226	Fracture of neck of femur (hip)
227	Spinal cord injury
228	Skull and face fractures
229	Fracture of upper limb
230	Fracture of lower limb
231	Other fractures
232	Sprains and strains
233	Intracranial injury
234	Crushing injury or internal injury
235	Open wounds of head; neck; and trunk
236	Open wounds of extremities
237	Complication of device; implant or graft
238	Complications of surgical procedures or medical care
239	Superficial injury; contusion
240	Burns
241	Poisoning by psychotropic agents
242	Poisoning by other medications and drugs
243	Poisoning by nonmedicinal substances
244	Other injuries and conditions due to external causes
245	Syncope
246	Fever of unknown origin
247	Lymphadenitis
248	Gangrene
249	Shock
250	Nausea and vomiting
251	Abdominal pain
252	Malaise and fatigue
253	Allergic reactions
254	Rehabilitation care; fitting of prostheses; and adjustment of devices
255	Administrative/social admission
256	Medical examination/evaluation
257	Other aftercare
258	Other screening for suspected conditions (not mental disorders or infectious disease)
259	Residual codes; unclassified
260	E Codes: All (external causes of injury and poisoning)
2601	E Codes: Cut/pierceb
2602	E Codes: Drowning/submersion
2603	E Codes: Fall
2604	E Codes: Fire/burn
2605	E Codes: Firearm

2606	E Codes: Machinery
2607	E Codes: Motor vehicle traffic (MVT)
2608	E Codes: Pedal cyclist; not MVT
2609	E Codes: Pedestrian; not MVT
2610	E Codes: Transport; not MVT
2611	E Codes: Natural/environment
2612	E Codes: Overexertion
2613	E Codes: Poisoning
2614	E Codes: Struck by; against
2615	E Codes: Suffocation
2616	E Codes: Adverse effects of medical care
2617	E Codes: Adverse effects of medical drugs
2618	E Codes: Other specified and classifiable
2619	E Codes: Other specified; NEC
2620	E Codes: Unspecified
2621	E Codes: Place of occurrence