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Impact of cardiac- and noncardiac-related conditions on adverse outcomes in patients hospitalized with acute myocardial infarction

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Abstract

Background: To examine the impact of cardiac- and noncardiac-related conditions on the risk of hospital complications and 7- and 30-day rehospitalizations in older adult patients with an acute myocardial infarction (AMI).

Methods and Results: The study population consisted of 3863 adults aged 65 years and older hospitalized with AMI in Worcester, Massachusetts, during six annual periods between 2001 and 2011. Individuals were categorized into four groups based on the presence of 11 previously diagnosed cardiac and noncardiac conditions. The median age of the study population was 79 years and 49% were men. Twenty-eight percent of patients had two or less cardiac- and no noncardiacrelated conditions, 21% had two or less cardiac and one or more noncardiac conditions, 20% had three or more cardiac and no noncardiac conditions, and 31% had three or more cardiac and one or more noncardiac conditions. Individuals who presented with one or more noncardiac-related conditions were less likely to have been prescribed evidence-based medications and/or to have undergone coronary revascularization procedures than patients without any noncardiac condition. After multivariable adjustment, individuals with three or more cardiac and one or more noncardiac conditions were at greatest risk for all adverse outcomes.

Conclusions: Older patients hospitalized with AMI carry a significant burden of cardiac- and noncardiac-related conditions. Older adults who presented with multiple cardiac and noncardiac conditions experienced the worse short-term outcomes and treatment strategies should be developed to improve their in-hospital and post-discharge care and outcomes.

Keywords

Chronic conditions, myocardial infarction

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Introduction

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Cardiovascular disease (CVD) adversely impacts patient's quality of life and is the leading cause of morbidity and mortality in American adults.¹ As the US population continues to age, the prevalence of CVD has correspondingly increased, together with other chronic conditions.^{2–4} There is increasing recognition that individuals with CVD and multiple chronic conditions (MCCs) experience higher levels of health-care use and poorer outcomes than patients without MCCs.^{4–10} Despite the high prevalence of MCCs in patients with CVD, there remains uncertainty as to how different combinations and burdens of cardiac and noncardiac conditions impact their in-hospital and post-discharge outcomes, especially in older adults aged 65 years and older.

There is considerable heterogeneity with existing measures of MCCs and none of these are considered to represent a gold standard of disease classification. Some examples of the most commonly used measures include the Charlson and Elixhauser indices, and simple unweighted counts of diagnoses of chronic conditions.^{9–11} Since clinicians treat individual patients and not measures of MCCs,¹² clinicians need simple and efficient approaches/ methodologies on how to best assess, manage, and intervene in patients with MCCs and enhance the short- and long-term outcomes of this vulnerable population.

The two major objectives of this large observational study were to (1) describe the magnitude of previously diagnosed cardiac- and noncardiac-related conditions, and hospital management practices, among older adults hospitalized with an independently validated acute myocardial infarction (AMI); and (2) examine the association between the burden of cardiac and noncardiac conditions and the occurrence of clinically significant in-hospital complications and being readmitted to the hospital. Our overarching study hypothesis was that older adults hospitalized with AMI who present with a greater burden of cardiac and noncardiac conditions will be at greater risk for adverse outcomes than those with a lower burden of previously diagnosed chronic conditions. A secondary hypothesis was that patients who presented with one or more noncardiac conditions, in addition to the cardiac-related conditions examined, would be at increased risk for developing adverse outcomes as compared with those who presented with only cardiac-related conditions. Data from the Worcester Heart Attack Study were used for purposes of this investigation.13-16

Methods

The Worcester Heart Attack Study is an ongoing population-based investigation that is examining long-term trends in the clinical epidemiology of AMI among residents of the Worcester, Massachusetts, metropolitan area hospitalized at all medical centers in Central Massachusetts on an approximate biennial basis.^{13–17}

Computerized printouts of residents of Central Massachusetts admitted to the three largest teaching and community hospitals in the city of Worcester with possible AMI (International Classification of Disease (ICD, see Appendix) 9 codes 410–414, and 786.5) on a biennial basis between 2001 and 2011 were identified. Cases of possible AMI were independently validated using predefined criteria for AMI, including diagnoses of ST segment elevation myocardial infarction (STEMI) and non-ST segment elevation myocardial infarction (NSTEMI).^{18,19} This study was approved by the Institutional Review Board at the University of Massachusetts Medical School.

Trained nurses and physicians abstracted information on patient's demographic and clinical characteristics, hospital treatment practices, and short-term outcomes through the review of hospital medical records. These characteristics included patient's age, sex, race/ethnicity, hospital length of stay, and 11 previously diagnosed chronic conditions. These 11 previously diagnosed chronic conditions were selected based on their high prevalence in our study cohort. These conditions were defined as those with a frequency equal to or greater than 3% and were further classified into two groups $^{20-22}$; seven cardiac-related conditions: atrial fibrillation, diabetes mellitus, heart failure, hyperlipidemia, hypertension, myocardial infarction, and stroke, and four noncardiac-related conditions: anemia, asthma/chronic pulmonary disease, chronic kidney disease (CKD), and depression. Information on the development of clinically significant in-hospital complications including atrial fibrillation,²³ cardiogenic shock,²⁴ heart failure,²⁵ stroke,²⁶ and dying was collected through the review of hospital medical records. Data on the receipt of three coronary diagnostic and interventional procedures (cardiac catheterization, percutaneous coronary intervention (PCI), and coronary artery bypass graft surgery (CABG)) during hospitalization, and evidence-based pharmacotherapies during hospitalization,^{19,27,28} namely angiotensin converting enzyme inhibitors (ACE-I)/angiotensin receptor blockers (ARBs), aspirin, beta-blockers, and lipid-lowering agents, were also collected.

For the present study, a rehospitalization was defined as the patient's first admission to a study hospital for any reason within 7 or 30 days of discharge after their index hospitalization for AMI during the years under study. Two of the study investigators adjudicated whether the principal reason for readmission was due to either an AMI, CVD (excluding AMI)-related, or non-CVD-related readmission based on the review of information contained in hospital medical records. For the present investigation, and due to sample size limitations and ease of data interpretation, we have focused on all-cause hospitalizations. The composite endpoint was defined as the risk of dying or developing any of the examined important clinical complications (heart failure, stroke, cardiogenic shock, or atrial fibrillation) during hospitalization for AMI.

Data analysis

Based on the sample distribution, we stratified our study population into four groups according to the presence of cardiac- or noncardiac-related conditions for purposes of analysis, namely those with two or less cardiac- and no noncardiac-related condition (group 1), two or less cardiacand one or more noncardiac-related condition (group 2), three or more cardiac- and no noncardiac-related condition (group 3), and three or more cardiac- and one or more noncardiac-related conditions (group 4). We compared differences in the baseline demographic and clinical characteristics, hospital management practices, and development of in-hospital complications and post-discharge hospital readmissions between each of these four groups using χ^2 tests for categorical variables and the analysis of variance test for continuous variables.

For purposes of more systematically examining the association between the number of cardiac and noncardiac conditions previously diagnosed with the risk of dying in hospital, developing clinically important in-hospital complications, or being rehospitalized within 7 or 30 days after the patient's index hospitalization for AMI, we used logistic regression modeling, adjusting for several potentially confounding demographic and clinical factors of prognostic importance in these models.^{29,30} These factors were chosen based on findings from prior studies and on their clinical significance. The variables we controlled for included patient's age, sex, type of AMI (STEMI vs. NSTEMI), hospital length of stay, receipt of evidencebased cardiac medications during the index hospitalization (ACE-I/ARBs, aspirin, beta-blockers, and lipid-lowering medications), and the receipt of any of the three coronary diagnostic and interventional procedures examined (cardiac catheterization, PCI, and CABG) during the patient's index hospitalization for AMI. We performed post hoc pairwise comparisons with Bonferroni corrections to examine differences between the four groups included in this study.

Results

A total of 3863 residents of Central Massachusetts 65 years and older were hospitalized with an independently validated AMI at the three largest medical centers in Worcester, Massachusetts, during the six study years between 2001 and 2011. The median age of this patient population was 79 years and 48.9% were men. The four comparison groups in our study included 1084 (28%) patients in group 1, 806 (21%) patients in group 2, 784 (20%) patients in group 3, and 1189 (31%) patients in group 4, respectively.

Baseline patient characteristics according to the presence of cardiac and noncardiac conditions

Patients in group 2 were the oldest (median age 81 years) and were more likely to be female as compared with those in group 1 (Table 1). Patients in group 3 had the lowest proportion of individuals older than 75 years and had the second highest prevalence of patients who developed an NSTEMI as compared with those in group 1 (Table 1). Patients in group 4 were slightly older and were more likely to be female as compared with patients in group 1 (Table 1). Patients in group 4 had the highest prevalence of NSTEMI

	Cardiac-/noncardiac-related conditions			
		Group 2 (n = 806)		Group 4 (n = 1189)
Characteristic				
Age (years, median)	78	81	78	79 ^ь
65–74	34.7	25.7	33.3	28.8 ^b
75–84	37.2	38.6	43.I	41.0 ^b
85 and older	28.1	35.7	23.6	30.2 ^b
Male	51.7	42.8	50.I	49.7 ^b
White race	91.5	93.3	92.2	91.1
NSTEMI	65.0	71.0	76.8	83.1°
Length of stay	4	5	4	5 ^b
(days, median)				
Medical history				
AMI	24.5	31.3	45.5	55.5°
Anemia	0	21.0	0	30.8 ^c
Atrial fibrillation	6.7	9.1	28.7	32.7°
CKD	0	34.7	0	56.6°
Chronic obstructive	0	42.4	0	38.8 ^b
pulmonary disease				
Depression	0	35.6	0	28.9 ^c
Diabetes	10.8	13.7	62.8	62.2 ^c
Heart failure	6.0	13.5	38.4	59.4 ^c
Hyperlipidemia	41.1	32.5	79.9	75.7°
Hypertension	64.0	67.9	95.6	94.1°
Stroke	3.8	4.7	22.5	25.9°
Complications during				
hospitalization				
Atrial fibrillation	20.9	25.1	29.1	30.8 ^c
Cardiogenic shock	5.4	6.3	6.5	5.9
Heart failure	40.6	51.1	55.2	68.0 ^c
Stroke	1.6	2.5	3.2	2.0
Death	9.1	14.0	11.2	13.9 ^b
Readmission to the				
hospital				
7 days	4.6	6.5	5.9	6.8
30 days	14.5	15.8	17.1	21.5

NSTEMI: non-ST segment elevation myocardial infarction; AMI: acute myocardial infarction; CKD: chronic kidney disease.

^aGroup 1: two or less cardiac diseases and no noncardiac disease; group 2: two or less cardiac diseases and one or more noncardiac disease; group 3: three or more cardiac diseases and no noncardiac disease; and group 4: three or more cardiac diseases and one or more noncardiac disease. ^bp < 0.01.

^cp < 0.001.

as compared to the other three groups and together with those in group 2 had the longest length of stay as compared to groups 1 and 3.

Frequency of previously diagnosed chronic conditions

The most prevalent chronic conditions among patients in group 1 were hypertension (64%), hyperlipidemia (41%), previous myocardial infarction (25%), and diabetes mellitus (11%) (Table 1). Among patients in group 2, the most

prevalent conditions were hypertension (68%), chronic pulmonary disease (42%), depression (36%), and CKD (35%) (Table 1). For those in group 3, the most prevalent conditions were hypertension (96%), hyperlipidemia (80%), diabetes mellitus (63%), and previous myocardial infarction (45%) (Table 1). Among patients in group 4, the most prevalent conditions were hypertension (94%), hyperlipidemia (76%), diabetes mellitus (62%), and heart failure (59%) (Table 1).

In-hospital clinical complications

In the overall study population, heart failure and atrial fibrillation were the most common hospital clinical complications, with the highest incidence in group 4. Approximately one in every two patients, and one in every four patients in group 2, developed heart failure and atrial fibrillation, respectively (Table 1). Similarly, approximately one in every two patients, and one in every three patients in group 3, developed heart failure and atrial fibrillation, respectively, during their index hospitalization (Table 1). Patients in group 4 were at the greatest risk for developing heart failure (68%) and atrial fibrillation (31%) during their index hospitalization for AMI. Groups 2 and 4 had the highest death rate as compared with the other two groups.

Hospital management practices

Patients in group 2 had the lowest proportion of individuals who were treated with ACE-I/ARBs as compared with patients in the other three groups. Patients in group 3 were more likely to have been treated with ACE-I/ARBs and lipid-lowering medications as compared with patients in group 1. Patients in group 4, together with those in group 2, were slightly less likely to have been treated with aspirin and beta-blockers during their acute hospitalization as compared with patients in the other two groups (Table 2).

The proportion of patients in groups 2 and 4 who received any diagnostic/interventional procedure was significantly lower as compared with the other two patient groups (Table 2).

Risk of adverse hospital and post-discharge outcomes

After controlling for several potentially confounding demographic and clinical factors of prognostic importance, patients in groups 2, 3, and 4 had an increased risk of dying during hospitalization as compared with those in group 1; the greatest risk for dying was observed among patients in group 4 (Table 3). After performing pairwise comparisons with Bonferroni corrections, these important differences were statistically significant between group 2 and group 1 and between group 4 and group 1 (p < 0.05).

The risk of developing any clinically significant inhospital complication was increased across all comparison groups, with an increasing trend from group 2 through

	Cardiac-/noncardiac-related conditions			
	Group I (n = 1084)	Group 2 (n = 806)		•
Diagnostic/intervention	al			
procedure				
Cardiac	59.9	41.7	56.6	42.2 ^b
catheterization				
Coronary artery	7.7	4.5	7.0	4.8 ^c
bypass surgery				
PCI	42.5	27.7	35.7	23.9 ^b
Medications				
ACE-I/ARBs	65.I	58.8	74.0	68.1 ^b
Aspirin	92.8	90.0	92.6	90.2 ^c
Beta-blockers	90.5	86. I	90.1	89.6 ^c
Lipid-lowering medications	70.5	63.2	77.9	75.3 [⊾]

AMI: acute myocardial infarction; PCI: percutaneous coronary intervention; ACE-I: angiotensin converting enzyme inhibitors; ARBs: angiotensin receptor blockers.

^aGroup 1: two or less cardiac diseases and no noncardiac disease; group 2: two or less cardiac diseases and one or more noncardiac disease; group 3: three or more cardiac diseases and no noncardiac disease; and group 4: three or more cardiac diseases and one or more noncardiac disease. ^bb < 0.001.

 $c_{p}^{c} < 0.01$.

group 4 (Table 3). After running pairwise comparisons with Bonferroni corrections, our findings suggest that these comparisons were statistically significant between group 2 and group 1, group 3 and group 1, group 4 and group 1, group 4 and group 2, and for patients in group 4 and group 3 (p < 0.05).

The risk for being readmitted to the hospital within 7 days after the patient's index hospitalization for AMI, according to the presence of cardiac and noncardiac conditions, was slightly higher during this period among patients in groups 2 and 4 as compared with those in group 1, with the highest risk of being readmitted during the subsequent 7 days noted for patients in group 4. Similar trends were found with regard to the risk of readmission within 30 days, with the highest risk noted among patients in group 4 (Table 3). After running pairwise comparisons with Bonferroni corrections, there were no differences between groups in the risk of having a 7-day readmission. On the other hand, when examining 30-day readmissions, the comparisons were statistically significant between group 3 and group 1 and group 4 and group 1 (p < 0.05).

Discussion

In this investigation of more than 3800 patients 65 years and older hospitalized with a confirmed AMI at the three largest tertiary care and community medical centers in Central Massachusetts between 2001 and 2011,

Adverse events	Cardiac-/noncardiac-related conditions			
	$\overline{\text{Group I } (n = 1084)}$	Group 2 (n = 806)	Group 3 (n = 784)	Group 4 ($n = 1189$)
In-hospital death OR 95% CI				
Unadjusted model	Reference	1.62 (1.22; 2.16)	1.26 (0.93; 1.70)	1.60 (1.23; 2.09)
Adjusted by age and sex model	Reference	1.53 (1.13; 2.06)	1.26 (0.92; 1.72)	1.52 (1.15; 1.99)
Full adjusted model	Reference	I.3I (0.95; I.8I)	1.59 (1.14; 2.22)	1.78 (1.32; 2.39)
Composite outcome			· · · · ·	
Unadjusted model	Reference	1.53 (1.27; 1.84)	1.81 (1.50; 2.17)	3.10 (2.61; 3.69)
Adjusted by age and sex model	Reference	1.56 (1.28; 1.89)	1.94 (1.60; 2.36)	3.32 (2.77; 3.97)
Full adjusted model	Reference	1.43 (1.17; 1.75)	1.81 (1.48; 2.21)	2.82 (2.33; 3.42)
7-day any cause rehospitalization OR 95% C				
Unadjusted model	Reference	1.49 (0.99; 2.22)	1.32 (0.88; 2.00)	1.58 (1.10; 2.28)
Adjusted by age and sex model	Reference	1.44 (0.95; 2.19)	1.31 (0.86; 2.00)	1.56 (1.07; 2.26)
Full adjusted model	Reference	1.49 (0.98; 2.27)	1.32 (0.86; 2.01)	1.62 (1.10; 2.37)
30-day any cause rehospitalization OR 95%	CI			
Unadjusted model	Reference	1.17 (0.91; 1.52)	1.26 (0.97; 1.62)	1.75 (1.40; 2.18)
Adjusted by age and sex model	Reference	1.15 (0.88; 1.51)	1.23 (0.95; 1.60)	1.74 (1.38; 2.18)
Full adjusted model	Reference	1.14 (0.87; 1.50)	1.18 (0.91; 1.54)	1.67 (1.32; 2.11)

Table 3. Crude and multivariable adjusted risk of adverse events according to categories of cardiac- and noncardiac-related conditions.^a

CI: confidence interval; NSTEMI: non-ST segment elevation myocardial infarction; AMI: acute myocardial infarction; STEMI: ST segment elevation myocardial infarction; PCI: percutaneous coronary intervention; ACE-I: angiotensin converting enzyme inhibitors; ARBs: angiotensin receptor blockers; CABG: coronary artery bypass graft surgery.

^aFully adjusted models controlled for age, sex, type of AMI (STEMI/NSTEMI), length of stay, receipt of any of the four medications examined (ACE-I/ ARBs, aspirin, beta-blockers, and lipid-lowering medications), and the receipt of any of the three coronary diagnostic and interventional procedures (cardiac catheterization, PCI, and CABG) during the index hospitalization for AMI. Group 1: two or less cardiac diseases and no noncardiac disease; group 2: two or less cardiac diseases and one or more noncardiac disease; group 3: three or more cardiac diseases and no noncardiac disease; and group 4: three or more cardiac diseases and one or more noncardiac disease.

patients presented to these hospitals with a considerable burden of cardiac- and noncardiac-related conditions. Moreover, after multivariable adjustment, patients in group 4 (those with the greatest burden of MCCs) had a greater risk for developing each of the adverse outcomes examined compared with patients in the other three groups. Of note, our findings suggest that individuals who presented with a higher burden of cardiac- and noncardiacrelated conditions were at greater risk for dying or developing clinically significant complications during their index admission for AMI whereas individuals who presented with any noncardiac-related conditions were at a slightly higher risk of being readmitted to the hospital within 7 days of their index AMI event.

Frequency of individual chronic conditions

Among patients in group 4 (31% of the study cohort), hypertension, hyperlipidemia, diabetes, heart failure, and CKD were highly prevalent; a relatively similar profile of these conditions was observed among patients in group 2 though these individuals also presented with a high prevalence of chronic pulmonary disease and depression.

Our findings share similar patterns to the results of a previous analysis from the Worcester Heart Attack Study which showed a high prevalence of hypertension and diabetes among patients with two or more cardiac comorbidities while the most prevalent noncardiacrelated condition was CKD.³¹ The present results are also consistent with findings from other contemporary investigations that have studied patients hospitalized with AMI, including a community-based study from Kaiser Permanente Northern California that demonstrated a high burden of hypertension and diabetes in this large HMO population.³²

Differences in hospital management practices according to the presence of previously diagnosed cardiac and noncardiac conditions

We observed relatively small differences across the four groups with regard to the prescribing of in-hospital cardiac medications. Clinical trials of treatments for CVD have usually excluded older adults with a high burden of multimorbidity, which has led to evidence gaps in how to best treat this medically complex, vulnerable population.10 We also found that patients in groups 2 and 4, who were slightly older and sicker than the other comparison groups, were less likely to have undergone coronary revascularization procedures. Thus, there is a clear need for developing evidence-based data to help clinicians care for this group of patients given their MCCs and high risk for adverse clinical outcomes.

Risk of adverse hospital outcomes according to the presence of previously diagnosed cardiac and noncardiac conditions

The individual effects of cardiac- and noncardiac-related conditions on in-hospital complications and 7- and 30-day rehospitalizations in individuals hospitalized with AMI have been studied in a number of prior investigations.^{5,9,31,33} In a large study in two major hospitals in Spain of more than 5000 patients hospitalized with AMI between 2003 and 2009, those who presented with heart failure and/or various cardiac arrhythmias were at higher risk for dying during their index hospital admission as compared to those without these chronic conditions.³³ In a prior publication from the Worcester Heart Attack Study, patients with an increasing number of cardiac-related conditions were at greater risk for dying at 30 days and 1 year than those with none or one previously diagnosed cardiac condition.⁹

Patients with noncardiac-related conditions have also been shown to be at increased risk for developing adverse outcomes in persons hospitalized with AMI, including patients previously studied in the Worcester Heart Attack Study.³¹ Similarly, in a prior publication from the Worcester Heart Attack Study, patients presenting with noncardiac-related conditions were at increased risk for developing adverse outcomes during the index hospitalization for AMI. In a study of more than 3900 patients admitted with AMI to 19 US medical centers between 2003 and 2004, the presence of any noncardiac condition was associated with a five times greater risk of dying during hospitalization as compared to those without any noncardiac condition.⁵

The combined effects of cardiac- and noncardiac-related conditions on short-term hospital and post-discharge outcomes in individuals hospitalized with AMI are less well known. In our study of Central Massachusetts residents hospitalized with AMI, individuals who presented with three or more cardiac- and one or more noncardiacrelated condition were at the greatest risk for dying during their acute hospitalization, developing clinically significant complications, and for being rehospitalized during the next 30 days. The Swiss AMIS Plus registry of more than 29,600 patients with an acute coronary syndrome examined the burden of multimorbidity, as assessed by the Charlson Comorbidity Index, in relation to the risk of dying during the patient's index hospitalization. The study investigators reported a two times greater risk of dying during the index hospitalization in individuals with three or more chronic conditions as compared to those without any of the examined chronic conditions.³⁴ A study of more than 3000 patients who were hospitalized in Olmsted County, Minnesota, with a first-ever AMI between 1987 and 2010 and who presented with diabetes, chronic obstructive pulmonary disease, or anemia were at higher risk for being readmitted to the hospital within 30 days as compared to those without these chronic conditions. In a study of more than 3000 patients admitted to the hospital with an incident AMI in Olmsted County, Minnesota, between 1987 and 2010, researchers reported that the presence of diabetes, chronic pulmonary disease or anemia was associated with higher risk for being readmitted to the hospital within 30 days as compared to those without these chronic conditions.³⁵

We found that individuals with one or more noncardiacrelated condition (groups 2 and 4), in addition to any cardiac condition, experienced a slightly higher risk of being rehospitalized over the subsequent 7 days as compared with patients in group 1. These findings provide further supportive evidence that the presence of noncardiac-related conditions including CKD, chronic pulmonary disease, anemia, and depression should be carefully considered and monitored when managing patients recently admitted to the hospital with an AMI.

Clinical implications

The present study expands upon previous work by studying not only the individual but also the combined effects of several previously diagnosed cardiac and noncardiac conditions in patients hospitalized with an AMI. Our results indicate that cardiac and noncardiac conditions are common in individuals hospitalized with AMI and have important prognostic implications. The presence of these cardiac- and noncardiac-related conditions increases the challenges for health-care providers due to the complexity of the interaction between diseases, diseases and medical treatments, and between various cardiac and noncardiac medications.25 Since clinical guidelines and disease management programs typically focus on patients with single conditions, and clinical research often excludes persons with MCCs, our observation that patients with several cardiac or noncardiac conditions were significantly more likely to have experienced adverse hospital and post-discharge outcomes suggests that current clinical guidelines need to take into consideration these high-risk patients.

Study strengths and limitations

The strengths of the present study include its communitybased design, its large sample of patients hospitalized with AMI, and its relatively contemporary perspective in examining clinically relevant outcomes and hospital treatment practices according to the frequency of a number of important cardiac and noncardiac conditions. There was comprehensive ascertainment of cardiac- and noncardiac-related conditions, death, in-hospital complications, and postdischarge hospitalizations. Several limitations need to be acknowledged, however, in the interpretation of the present findings. First, since our study population included only patients who had been hospitalized in the Worcester metropolitan area, one needs to be careful to extrapolate our findings to those who reside in other geographic areas. Second, since the majority of the study patients were White, the generalizability of our findings to other race/ ethnic groups may be limited. There is the potential for unmeasured confounding since we did not have information available on several patient-associated characteristics, such as income, education, psychosocial factors, body mass index, or smoking status, that may have affected several of the endpoints examined. Finally, detailed information about the duration or severity of the chronic conditions studied was unavailable.

Conclusions

The findings of our investigation suggest that cardiac- and noncardiac-related conditions are highly prevalent in patients 65 years of age and older hospitalized with AMI and individuals presenting with both types of chronic conditions are at greatest risk for developing adverse in-hospital and short-term outcomes. We observed that individuals who presented with one or more noncardiacrelated condition were less likely to have been prescribed evidence-based medications and/or undergone coronary revascularization procedures than patients without any noncardiac condition. Due to the extremely limited published evidence that exists to guide the treatment of this vulnerable population, there is a clear need for developing guidelines that might help health-care providers caring for these patients. Future research should also examine the impact of cardiac- and noncardiac-related conditions on important long-term clinical and patient-centered outcomes in patients hospitalized with AMI that will help clinicians, caregivers, and patients in discussions about the management and prognosis of patients with these chronic conditions.

Declaration of conflicting interests

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References

1. FASTSTATS. Heart Disease, http://www.cdc.gov/nchs/fas tats/heart.htm (accessed 21 October 2018).

- Saczynski JS, Go AS, Magid DJ, et al. Patterns of comorbidity in older adults with heart failure: the cardiovascular research network PRESERVE study. J Am Geriatr Soc 2013; 61(1): 26–33.
- Ather S, Chan W, Bozkurt B, et al. Impact of noncardiac comorbidities on morbidity and mortality in a predominantly male population with heart failure and preserved versus reduced ejection fraction. *J Am Coll Cardiol* 2012; 59(11): 998–1005.
- Vogeli C, Shields AE, Lee TA, et al. Multiple chronic conditions: prevalence, health consequences, and implications for quality, care management, and costs. *J Gen Intern Med* 2007; 22(Suppl 3): 391–395.
- Lichtman JH, Spertus JA, Reid KJ, et al. Acute noncardiac conditions and in-hospital mortality in patients with acute myocardial infarction. *Circulation* 2007; 116(17): 1925–1930.
- Ani C, Pan D, Martins D, et al. Age- and sex-specific inhospital mortality after myocardial infarction in routine clinical practice. *Cardiol Res Pract* 2010; 2010: 752–765.
- Braunstein JB, Anderson GF, Gerstenblith G, et al. Noncardiac comorbidity increases preventable hospitalizations and mortality among Medicare beneficiaries with chronic heart failure. *J Am Coll Cardiol* 2003; 42(7): 1226–1233.
- Sachdev M, Sun JL, Tsiatis AA, et al. The prognostic importance of comorbidity for mortality in patients with stable coronary artery disease. *J Am Coll Cardiol* 2004; 43(4): 576–582.
- McManus DD, Nguyen HL, Saczynski JS, et al. Multiple cardiovascular comorbidities and acute myocardial infarction: temporal trends (1990–2007) and impact on death rates at 30 days and 1 year. *Clin Epidemiol* 2012; 4: 115–123.
- Boyd CM, Leff B, Wolff JL, et al. Informing clinical practice guideline development and implementation: prevalence of coexisting conditions among adults with coronary heart disease. J Am Geriatr Soc 2011; 59(5): 797–805.
- Huntley AL, Johnson R, Purdy S, et al. Measures of multimorbidity and morbidity burden for use in primary care and community settings: a systematic review and guide. *Ann Fam Med* 2012; 10(2): 134–141.
- Green AR, Leff B, Wang Y, et al. Geriatric conditions in patients undergoing defibrillator implantation for prevention of sudden cardiac death: prevalence and impact on mortality. *Circ Cardiovasc Qual Outcomes* 2016; 9(1): 23–30.
- Goldberg RJ, Gore JM, Alpert JS, et al. Recent changes in attack and survival rates of acute myocardial infarction (1975 through 1981): the Worcester Heart Attack Study. *JAMA* 1986; 255(20): 2774–2779.
- Goldberg RJ, Gore JM, Alpert JS, et al. Incidence and case fatality rates of acute myocardial infarction (1975–1984): The Worcester Heart Attack Study. *Am Heart J* 1988; 115(4): 761–767.
- 15. Goldberg RJ, Yarzebski J, Lessard D, et al. A two-decade (1975 to 1995) long experience in the incidence, in-hospital and long-term case-fatality rates of acute myocardial

infarction: a community-wide perspective. *J Am Coll Cardiol* 1999; 33(6): 1533–1539.

- Floyd KC, Yarzebski J, Spencer FA, et al. A 30-year perspective (1975–2005) into the changing landscape of patients hospitalized with initial acute myocardial infarction: Worcester Heart Attack Study. *Circ Cardiovasc Qual Outcomes* 2009; 2(2): 88–95.
- McManus DD, Gore J, Yarzebski J, et al. Recent trends in the incidence, treatment, and outcomes of patients with STEMI and NSTEMI. *Am J Med* 2011; 124(1): 40–47.
- 18. Jneid H, Anderson JL, Wright RS, et al. 2012 ACCF/AHA focused update of the guideline for the management of patients with unstable angina/non-ST-elevation myocardial infarction (updating the 2007 guideline and replacing the 2011 focused update): a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 2012; 60(7): 645–681.
- O'Gara PT, Kushner FG, Ascheim DD, et al. 2013 ACCF/ AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation* 2013; 127(4): e362–e425.
- Marengoni A, Winblad B, Karp A, et al. Prevalence of chronic diseases and multimorbidity among the elderly population in Sweden. *Am J Public Health* 2008; 98(7): 1198–1200.
- Marengoni A, Rizzuto D, Wang HX, et al. Patterns of chronic multimorbidity in the elderly population. *J Am Geriatr Soc* 2009; 57(2): 225–230.
- 22. Tisminetzky M, Gurwitz J, McManus DD, et al. Multiple chronic conditions and psychosocial limitations in patients hospitalized with an acute coronary syndrome. *Am J Med* 2016; 129(6): 608–614.
- Goldberg RJ, Yarzebski J, Lessard D, et al. Recent trends in the incidence rates of and death rates from atrial fibrillation complicating initial acute myocardial infarction: a community-wide perspective. *Am Heart J* 2002; 143(3): 519–527.
- 24. Goldberg RJ, Spencer F, Gore JM, et al. Thirty-year trends (1975 to 2005) in the magnitude of, management of, and hospital death rates associated with cardiogenic shock in patients with acute myocardial infarction: a population-based perspective. *Circulation* 2009; 119(9): 1211–1219.

- 25. McManus DD, Chinali M, Saczynski JS, et al. 30-year trends in heart failure in patients hospitalized with acute myocardial infarction. *Am J Cardiol* 2011; 107(3): 353–359.
- Saczynski JS, Spencer FA, Gore JM, et al. Twenty-year trends in the incidence of stroke complicating acute myocardial infarction: Worcester Heart Attack Study. *Arch Intern Med* 2008; 168(19): 2104–2110.
- 27. Makam RC, Erskine N, McManus DD, et al. Decade-long trends (2001 to 2011) in the use of evidence-based medical therapies at the time of hospital discharge for patients surviving acute myocardial infarction. *Am J Cardiol* 2016; 118(12): 1792–1797.
- Amsterdam EA, Wenger NK, Brindis RG, et al. 2014 AHA/ ACC guideline for the management of patients with non-STelevation acute coronary syndromes: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation* 2014; 130(25): 2354–2394.
- 29. Tisminetzky M, Nguyen HL, Gurwitz JH, et al. Magnitude and impact of multiple chronic conditions with advancing age in older adults hospitalized with acute myocardial infarction. *Int J Cardiol* 2018; 272: 341–345.
- 30. Tisminetzky M, Chen HY, McManus DD, et al. Trends in the magnitude of, and patient characteristics associated with, multiple hospital readmissions after acute myocardial infarction. Am J Cardiol 2016; 118(8): 1117–1122.
- Chen HY, Saczynski JS, McManus DD, et al. The impact of cardiac and noncardiac comorbidities on the short-term outcomes of patients hospitalized with acute myocardial infarction: a population-based perspective. *Clin Epidemiol* 2013; 5: 439–448.
- Yeh RW, Sidney S, Chandra M, et al. Population trends in the incidence and outcomes of acute myocardial infarction. N Engl J Med 2010; 362(23): 2155–2165.
- Gili M, Sala J, López J, et al. Impact of comorbidities on inhospital mortality from acute myocardial infarction, 2003– 2009. *Rev Esp Cardiol* 2011; 64(12): 1130–1137.
- Radovanovic D, Seifert B, Urban P, et al. Validity of Charlson Comorbidity Index in patients hospitalized with acute coronary syndrome. Insights from the nationwide AMIS Plus registry 2002–2012. *Heart* 2014; 100(4): 288–294.
- Dunlay SM, Weston SA, Killian JM, et al. Thirty-day rehospitalizations after acute myocardial infarction: a cohort study. *Ann Intern Med* 2012; 157(1): 11–18.

Appendix: ICD-9 Chronic Conditions Codes

Chronic Condition	ICD-9		
Acute myocardial infarction	410-414, and 786.5		
Anemia	280-285		
Atrial fibrillation	427.31; 427.32		
Chronic kidney disease	016.00, 016.01, 016.02, 016.03, 016.04, 016.05, 016.06, 095.4, 189.0, 189.9, 223.0, 236.91, 249.40, 249.41, 250.40, 250.41, 250.42, 250.43, 271.4, 274.10, 283.11, 403.01, 403.11, 403.91, 404.02, 404.03, 404.12, 404.13, 404.92, 404.93, 440.1, 442.1, 572.4, 580.0, 580.4, 580.81, 580.89, 580.9, 581.0, 581.1, 581.2, 581.3, 581.81, 581.89, 581.9, 582.0, 582.1, 582.2, 582.4, 582.81, 582.89, 582.9, 583.0, 583.1, 583.2, 583.4, 583.6, 583.7, 583.81, 583.89, 583.9, 584.5, 584.6, 584.7, 584.8, 584.9, 585.1, 585.2, 585.3, 585.4, 585.5, 585.6, 585.9, 586, 587, 588.0, 588.1, 588.81, 588.89, 588.9, 591, 753.12, 753.13, 753.14, 753.15, 753.16, 753.17, 753.19, 753.20, 753.21, 753.22, 753.23, 753.29, 794.4		
Chronic pulmonary disease	490, 491.0, 491.1, 491.20, 491.21, 491.22, 491.8, 491.9, 492.0, 492.8, 494.0, 494.1, 496		
Depression	296.20, 296.21, 296.22, 296.23, 296.24, 296.25, 296.26, 296.30, 296.31, 296.32, 296.33, 296.34, 296.35, 296.36, 296.51, 296.52, 296.53, 296.54, 296.55, 296.56, 296.60, 296.61, 296.62, 296.63, 296.64, 296.65, 296.66, 296.89, 298.0, 300.4, 309.1, 311		
Diabetes	249.00, 249.01, 249.10, 249.11, 249.20, 249.21, 249.30, 249.31, 249.40, 249.41, 249.50, 249.51, 249.60, 249.61, 249.70, 249.71, 249.80, 249.81, 249.90, 249.91, 250.00, 250.01, 250.02, 250.03, 250.10, 250.11, 250.12, 250.13, 250.20, 250.21, 250.22, 250.23, 250.30, 250.31, 250.32, 250.33, 250.40, 250.41, 250.42, 250.43, 250.50, 250.51, 250.52, 250.53, 250.60, 250.61, 250.62, 250.63, 250.70, 250.71, 250.72, 250.73, 250.80, 250.81, 250.82, 250.83, 250.90, 250.91, 250.92, 250.93, 357.2, 362.01, 362.02, 362.03, 362.04, 362.05, 362.06, 366.41		
Heart Failure	398.91, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, 428.0, 428.1, 428.20, 428.21, 428.22, 428.23, 428.30, 428.31, 428.32, 428.33, 428.40, 428.41, 428.42,		
Hyperlipidemia	272.0, 272.1, 272.2, 272.3, 272.4		
Hypertension	401.0, 401.1, 401.9, 402.00, 402.01, 402.10, 402.11, 402.90, 402.91, 403.00, 403.01, 403.10, 403.11, 403.90, 403.91, 404.00, 404.01, 404.02, 404.03, 404.10, 404.11, 404.12, 404.13, 404.90, 404.91, 404.92, 404.93, 405.01, 405.09, 405.11, 405.19, 405.91, 405.99, 362.11, 437.2		
Stroke/CVA	430, 431, 433.01, 433.11, 433.21, 433.31, 433.81, 433.91,434.00, 434.01,434.10, 434.11, 434.90, 434.91, 435.0, 435.1, 435.3, 435.8, 435.9, 436, 997.02		