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Impact of comorbidities by age on symptom presentation for suspected acute coronary syndromes in the emergency department

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Abstract

Background—It is estimated half of acute coronary syndrome (ACS) patients have one or more associated comorbid conditions.

Aims—Aims were to: 1) examine the prevalence of comorbid conditions in patients presenting to the emergency department with symptoms suggestive of ACS; 2) determine if comorbid conditions influence ACS symptoms; and 3) determine if comorbid conditions predict the likelihood of receiving an ACS diagnosis.

Methods—A total of 1064 patients admitted to five emergency departments were enrolled in this prospective study. Symptoms were measured on presentation to the emergency department. The Charlson Comorbidity Index (CCI) was used to evaluate group differences in comorbidity burden across demographic traits, risk factors, clinical presentation, and diagnosis.

Results—The most prominent comorbid conditions were prior myocardial infarction, diabetes without target organ damage, and chronic lung disease. In younger ACS patients, higher CCI predicted less chest pain, chest discomfort, unusual fatigue and a lower number of symptoms. In older ACS patients, higher CCI predicted more chest discomfort, upper back pain, abrupt symptom onset, and greater symptom distress. For younger non-ACS patients, higher CCI predicted less chest pain and symptom distress. Higher CCI was associated with a greater likelihood of receiving an ACS diagnosis for younger but not older patients with suspected ACS.

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Conflict of interest

The authors declare that there is no conflict of interest.

Conclusions—Younger patients with ACS and higher number of comorbidities report less chest pain, putting them at higher risk for delayed diagnosis and treatment since chest pain is a hallmark symptom for ACS.

Keywords

Acute coronary syndrome; comorbidities; symptoms; age; cardiovascular conditions; emergency medicine

Introduction

It is estimated that nearly half of patients with acute coronary syndrome (ACS) have one or more comorbid conditions such as history of myocardial infarction (MI), diabetes, chronic lung disease, chronic kidney disease, peripheral vascular disease, and cerebrovascular disease.[1,2] However, clinical practice guidelines for patients with coronary heart disease (CHD) were developed for the treatment of a single chronic condition and may not be successful for the management of CHD in the presence of multiple comorbidities.[3] In addition, individuals with multiple comorbid conditions are often excluded from randomized clinical trial populations,[4,5] reducing the pragmatic application of research findings into clinical practice.

Comorbid conditions have been linked to demographic and clinical characteristics of ACS patients. Fassa et al.[6] assessed data from 19,496 ACS patients in the Acute Myocardial Infarction in Switzerland (AMIS) Plus registry and found higher Charlson Comorbidity Index (CCI) scores were associated with increased age, female sex, hypertension, dyslipidemia, obesity, and lower current cigarette use. Higher CCI scores were also associated with fewer “typical symptoms” of chest pain and dyspnea. In a study of 2972 American patients hospitalized with acute MI, Chen et al.[7] examined both cardiovascular and non-cardiovascular comorbid conditions. The most common cardiac comorbidity was hypertension (75%). Chronic kidney disease (22%) was the most common noncardiac comorbid condition. Patients with multiple comorbid conditions were significantly more likely to be older, female, unmarried, have a history of prior MI, and present with a non-ST elevation MI.

The complexity of clinical decision-making in the presence of multiple comorbidities and the lack of explicit guidelines has been linked to poorer adherence to treatment protocols and worse outcomes for ACS patients.[3,4,6,8] Under-usage of medication and standard-of-care procedures due to the unknown effects of certain therapies for patients with multiple comorbidities has been reported (e.g. percutaneous coronary interventions, dual antiplatelet therapy).[3,4,6,8] Worse in-hospital and one year outcomes as well as increased mortality rates have also been reported in ACS patients with multiple co-morbidites.[2,4,6,7,9,10]

Limited research has investigated the relationships between multiple comorbid conditions, CHD risk factors, clinical presentation, and diagnosis among patients presenting to the emergency department (ED) with symptoms prompting an evaluation for ACS. Available data are insufficient to provide scientific support for evidence-based care of patients afflicted by multiple comorbidities. Therefore, the aims of this study were to: 1) examine the

prevalence of CHD risk factors and comorbid conditions in a sample of patients presenting to the ED with symptoms suggestive of ACS; 2) determine if comorbid conditions influence symptoms; and 3) determine if comorbid conditions predict the likelihood of receiving an ACS diagnosis.

Methods

Study design

The study was a descriptive, prospective study whose main aim was to explore the influence of sex on symptoms suggestive of ACS.[11] The investigation conforms with the principles outlined in the Declaration of Helsinki.[12] The Institutional Review Board (IRB) from the sponsoring institution and each clinical data collection site gave approval for the study prior to launch. Each IRB approved a waiver of initial consent for electronic screening of patients and to collect initial symptom data prior to enrollment. A waiver of initial consent was granted since the main study aim was to evaluate symptoms on presentation to the ED and because the emergent nature of patients presenting with possible ACS precluded the provision of immediate informed consent.[13] All patients gave written, informed consent prior to enrollment in the study when they were stable and had been transferred to a private examination room.

Study setting and population

Individuals presenting to the ED with symptoms triggering a cardiac evaluation, ≥21 years old, fluent in English, and who arrived by private transportation or emergency medical services were eligible. Patients were excluded if they had an exacerbation of heart failure (brain natriuretic peptide >500pg/ml), were transferred from a hemodialysis facility, were referred for evaluation of a dysrhythmia, or had cognitive impairment, defined as the inability to understand and provide written informed consent. Enrollment occurred between January 2011 and December 2014 in five EDs in the Midwest, West, and Pacific Northwest regions of the USA. The centers included four academic medical centers and a large, referral community medical center.[14]

Study protocol

Study research staff completed the ACS Symptom Checklist shortly after the patient was evaluated in triage. The symptom checklist was completed by the patient if they were able or by research staff if the patient could not read or was otherwise unable to complete the checklist. Research staff were blinded to the patient's final diagnosis. Symptoms were assessed within 15 min of ED presentation in most cases and enrollment occurred between 07:00 h and 23:00 h every day of the week. Research staff were unavailable between the hours of 23:00 and 07:00. Patients triggering a cardiac workup were approached by the research staff for enrollment after they were deemed stable by the primary nurse or physician and had been transferred to a private examination room in either the ED or hospital unit. The study purpose was explained, and once the patient provided written informed consent, additional clinical and individual characteristics were recorded by research staff. Initial symptom data were destroyed if the patient declined to participate. Of eligible patients, 28.7% declined to participate, citing fatigue, anxiety, or lack of interest.

Measures

CCI—Comorbid conditions were measured with the CCI, a 19-item weighted index which has been used extensively to quantify illness risk and risk of mortality associated with comorbid conditions.[15,16] Higher scores represent a greater burden of disease. Studies have demonstrated that the CCI is a valid measure for predicting disability and death following ischemic stroke and heart disease.[16] Correlations with mortality, disability, hospital readmission and length of stay have ranged from 0.35 to 0.93 (p<0.001).[17,18]

ACS Symptom Checklist—Symptoms were measured with the validated 13-item ACS Symptom Checklist. The checklist was derived from the Symptoms of Acute Coronary Syndromes Index (SACSI). The SACSI, a reliable (Cronbach's α=0.81)[19] and valid (content validity indexes of 0.88 and 0.94) instrument, was tested in previous studies.[20,21] Participants indicate whether the symptom is present or absent on presentation to triage. Symptoms not appearing on the checklist can be recorded in a blank space marked "other". For this study, symptoms were measured dichotomously on ED admission (yes/no). Each symptom is analyzed individually and there is no summary score.

ACS Patient Information Questionnaire—The questionnaire includes patient-reported information on demographic and clinical variables including CHD risk factors. The questionnaire was designed using the standardized reporting guidelines for studies evaluating ED patients with potential ACS.[22] The criteria were established by the Multidisciplinary Standardized Reporting Criteria Task Force and are supported by the Society for Academic Medicine, the American College of Emergency Physicians, the American Heart Association, and the American College of Cardiology. The purpose of the questionnaire is to establish standardized ED reporting criteria that will facilitate study comparisons and meta-analyses. CHD risk factors included on the tool are high blood pressure, family history of heart disease or sudden cardiac death, diabetes, tobacco use, hypercholesterolemia, cocaine or amphetamine use, kidney disease, and obesity.

Duke Activity Status Index—Functional status was measured with the Duke Activity Status Index (DASI), a 12-item instrument that measures functional capacity.[23] Scores range from 0 to 58.2, with higher scores representing better physical functioning. Items are weighted to reflect metabolic energy expenditure and correlate highly with peak VO_2 (r = 0.80, p < 0.0001)[23] in patients with ACS,[24] ischemic heart disease,[25] heart failure,[26] and revascularization procedures.[27]

Data analyses

Data analyses were performed using SPSS, Version 22.0 (IBM Corp, Armonk, NY, USA) and SAS, Version 9.4 (SAS®, Cary, NC, USA). Significance was set at p<0.05 for all statistical procedures. Frequency distributions were assessed for all variables. Fisher's exact tests were used to test differences in the frequencies of individual comorbid conditions between ACS and non-ACS diagnosed patients. After stratifying by ACS diagnosis, general linear modeling was used to test the differences in mean CCI scores by demographic, clinical characteristics, and CHD risk factors while adjusting for age. General (for continuous variables) and generalized linear modeling with a logit link function (for

categorical variables) were used to determine if comorbidity scores could predict an ACS diagnosis and ACS symptom characteristics controlling for age, sex, race, tobacco use (never, former, current user), DASI score, high blood pressure (yes/no), and recruitment site. Type of ACS diagnosis was included as a covariate for models predicting symptoms among ACS patients. Covariates were selected for the model based on whether they were significantly related to CCI scores in the bivariate models and/or if the variables were significantly related to the outcome measure in multivariate models. Interaction terms between age and comorbidity score were included in all models to produce age-specific estimates. Age and comorbidity scores were included in the models as continuous variables and odds ratios (for dichotomous variables) or unstandardized beta coefficients (for continuous variables) and were calculated at 10 year intervals (40, 50, 60, 70, and 80 years old) representing the effect of a one unit change in CCI score on the outcome for a person of that age. Comorbidity data were missing for three participants, therefore the final sample size for the analyses was 1061.

Results

Demographic and clinical characteristics of the sample by diagnosis

Demographic and clinical characteristics for patients discharged with an ACS or non-ACS diagnosis are summarized in Table 1. The sample was predominately male (*n*=662, 62.4%) and non-Hispanic White (*n*=737, 69.5%). The majority of patients had private insurance through an employer (*n*=330, 31.1%) or Medicare (*n*=348, 32.8%). There was a range of education and income levels; patients most frequently reported having some college education or higher (*n*=700, 66%) and lower or middle income levels (*n*=632, 59.6%). The mean age was 61.7 ±11.9 years for ACS patients and 59.0±15.4 years for non-ACS patients. The most common ACS diagnosis was non-ST elevation MI (NSTEMI; *n*=251, 53.1%), followed by ST elevation MI (STEMI; *n*=118, 24.9%) and unstable angina (UA; *n*=104, 22%). The majority of patients had multiple risk factors and some functional limitations.

Prevalence of CCI conditions by diagnosis

The most prominent comorbid conditions in patients presenting to the ED with potential ACS were previous history of MI, diabetes without target organ damage, and chronic lung disease (Table 2 and Figure 1). Eighteen of the 19 conditions listed on the CCI occurred in <25% of patients. The exception was a previous history of MI. Only three conditions varied by diagnosis; patients with ACS were more likely to have a history of prior MI and peripheral vascular disease. Non-ACS patients were more likely to have renal disease. The mean CCI score differed by diagnosis only for patients less than 50 years old.

Comorbid conditions and demographic and clinical characteristics

As expected, the mean number of comorbid conditions increased with age (Table 1). CCI scores differed by type of insurance for patients with and without ACS. Patients with government sources of health insurance (Medicare, Medicaid, Social Security Disability, and Veterans Affairs) had more comorbid conditions compared with those with private insurance or those who were uninsured. For those ruled-out for ACS, patients with less than a high school diploma and with a reported income less than US$20,000 per year had higher mean

CCI scores. Mean CCI scores were highest for patients with NSTEMI and unstable angina compared with STEMI. For both ACS and non-ACS patients, higher CCI scores were associated with hypertension and functional limitations. Notably, former tobacco users had higher CCI scores compared with current users. Obesity was associated with a higher CCI score in patients with ACS.

Comorbidity score predicts ACS diagnosis in younger patients

A multivariate model was constructed to determine if CCI scores would predict an ACS diagnosis while controlling for age and other established CHD risk factors (Table 3 and Figure 2). Using the regression model, odds ratios were calculated to show how a one unit change in CCI score affected the odds of an ACS diagnosis when a patient was either 40, 50, 60, 70, or 80 years old. CCI scores were found to be predictive of an ACS diagnosis for younger patients only (40–50 years old). Thus, the presence of comorbid conditions increased the likelihood that younger patients (under age 60) presenting to the ED with ACS symptoms would receive a final ACS diagnosis.

Predicting symptoms for ACS patients by comorbidity scores

Multivariate modeling was conducted to assess the impact of CCI scores on symptom presentation for ACS and non-ACS patients (Table 3 and Figure 2). Odds ratios for dichotomous outcomes and unstandardized beta coefficients (b) for continuous outcomes are presented to show how a one unit change in CCI score affected the odds or changed the mean score of the outcome when a patient was either 40, 50, 60, 70, or 80 years old. For younger ACS patients, more comorbid conditions meant that several symptoms were less likely to be reported. Younger patients with ACS were less likely to present with chest discomfort, chest pain, and unusual fatigue as comorbidity scores increased. Greater comorbidity burden also meant that younger ACS patients reported fewer symptoms overall. For middle-aged ACS patients, more comorbid conditions meant that arm pain and indigestion were reported less. For older patients with ACS, more comorbid conditions were linked to more reports of chest discomfort and upper back pain. Also, having more comorbid conditions was related to a greater likelihood of having an abrupt onset of symptoms and greater distress from symptoms for older patients.

Predicting symptoms for non-ACS patients by comorbidity score

For patients who received a non-ACS diagnosis, greater comorbidity burden was only linked to two symptom characteristics. For younger patients ruled-out for ACS, greater comorbidity burden was linked to less chest pain. More comorbidities were also connected to less distress from symptoms for younger non-ACS patients (Table 3 and Figure 2).

Discussion

There were few differences (three of 19) in the number of comorbid conditions between those ruled-in versus those ruled-out for ACS. Presence of comorbid conditions as measured by the CCI in this study provided little additional information that could contribute to risk stratification on arrival to the ED. Traditional risk factors have also performed poorly in prior ED studies, leading clinicians to perform 12-lead electrocardiograms and cardiac

biomarkers on all potential ACS patients.[28,29] Consistent with prior research, the CCI appears to be a valid measure of the impact of comorbid conditions on mortality but unfortunately does not appear to be a robust measure of the impact of comorbid conditions on ACS risk stratification, incidence of disease, or clinical presentation. The finding that a previous history of MI was the most prevalent comorbid condition in this population was not surprising. Prior findings have also supported rates of prior MI in the 60% range.[7] Diabetes was reported by almost a quarter of patients. In addition to being a comorbid condition, diabetes is also a strong CHD risk factor and so these findings add additional evidence from a large heterogeneous population to what is already known about the risks of this disease. The finding that chronic obstructive pulmonary disease (COPD) was the third highest reported comorbidity for patients with and without ACS is noteworthy and may be related to smoking since smoking is an important risk factor for both CHD and COPD.

Those in a lower socioeconomic class had more comorbid conditions, which is consistent with prior reports[30] and may reflect reduced access to health care. Patients with NSTEMI and UA had a higher number of comorbid conditions and CHD risk factors (tobacco use, hypertension, hypercholesterolemia) than those with STEMI. This was not explained by age since even those patients with NSTEMI and UA under age 50 had more comorbid conditions. Obese patients with ACS (but not those without ACS) had significantly higher mean CCI scores. This adds more evidence of the CHD risk that has been linked to obesity in the last decade. Patients receiving government sponsored health insurance and older patients had higher mean CCI scores as expected given that these individuals are eligible for Medicare and that older individuals have more comorbid conditions. The finding that an ACS diagnosis was more likely with higher comorbidities in younger but not older patients is noteworthy, particularly for males who develop ACS at an earlier age compared with women.[31] Finally, consistent with our findings, Scheuermeyer et al.[32] found that many symptoms were less likely for younger ACS patients with comorbidities, which could increase risk of pre-hospital delay and complicate patient triage.

The prevalence of multiple comorbid conditions is increasing in the American population due to improvements in acute care and primary prevention strategies that have increased life expectancy.[33] In addition, multiple comorbidities are associated with higher mortality rates and health care utilization.[7] In a cohort of Danish patients, Schmidt et al.[34] found that the odds of death at 30 days post MI increased from 1.96 (95% confidence interval (CI), 1.83–2.11) to 3.89 (95% CI, 3.58–4.24) for those with “normal” comorbid conditions compared with those with “severe” comorbid conditions. A portion of the increase in death rates with older age may be explained by less aggressive treatment or palliative care approaches,[35] but comorbidities still pose a threat to patients with ACS.

Strengths

Much of the data published on comorbid conditions in patients with ACS have been collected in Europe.[1,2,6,36] Far fewer studies have been completed in the USA, where it appears that rates of multiple comorbidities are higher. In addition, symptoms reported directly by patients were recorded soon after presentation to the ED. The availability of self-report of active symptoms eliminated recall bias, enhancing the internal validity of the

findings. The inclusion of a large heterogeneous sample of patients resulted in a well-powered study facilitating the detection of small effects. Our sample (30.1% minority members) was representative of the US population and there were minimal baseline differences between patients with and without ACS. Finally, we adjusted for factors well-known to affect symptoms and comorbidity burden such as age and functional status.

Limitations

Sampling bias is a potential limitation to the study. Patients whom ED nurses and physicians deemed to be at risk for ACS were included in the study. Hence, we may have missed patients if the patient was not evaluated for ACS. In order to include enough patients who ruled-in for ACS, we targeted patients with an elevated troponin level and therefore the sample may not be representative of all those presenting to triage with possible ACS symptoms. Patients were only enrolled from 07:00 h to 23:00 h. Therefore, findings may not be generalizable to patients arriving at the ED from 23:00 h to 07:00 h. There was potential selection bias as 28.7% of patients approached declined to participate in the study. This is not surprising due to the high acuity rates in the ED setting.

Conclusions

Comorbidities affect symptoms for patients presenting to the ED with suspected ACS and this relationship varies by age. Comorbidities may present a unique challenge in younger patients because they are less likely to report chest symptoms. More studies are needed to better understand the impact of comorbidities on ACS symptom presentation and risk stratification in the ED. Awareness of these findings could help in getting more individuals screened for CHD and risk stratified accurately, potentially reducing the incidence of ACS.

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Implications for practice

- Our research did not support use of the Charlson Comorbidity Index for assessing acute coronary syndrome risk stratification, incidence of disease, or clinical presentation in the emergency department.
- Nurses should be alert to the risk of acute coronary events among patients with chronic obstructive pulmonary disease and diabetes as nearly 20% and 30% (respectively) of patients in our sample had these conditions.
- Nurses should be aware of a potentially higher number of comorbid conditions among patients with non-ST elevation myocardial infarction and unstable angina compared with ST elevation myocardial infarction. There may be a propensity to delay evaluation or treatment of non-ST elevation myocardial infarction/unstable angina patients since both these conditions are considered to be less life-threatening than ST elevation myocardial infarction.
- Emergency department nurses and nurses evaluating patients with suspected acute coronary syndrome should be aware that *younger* patients with *comorbid conditions* may have a higher likelihood of receiving an acute coronary syndrome diagnosis.
- Emergency department nurses and nurses evaluating patients with suspected acute coronary syndrome should know that *younger* patients with *comorbid conditions* may be less likely to present with classic acute coronary syndrome symptoms and may present with fewer acute coronary syndrome symptoms overall.

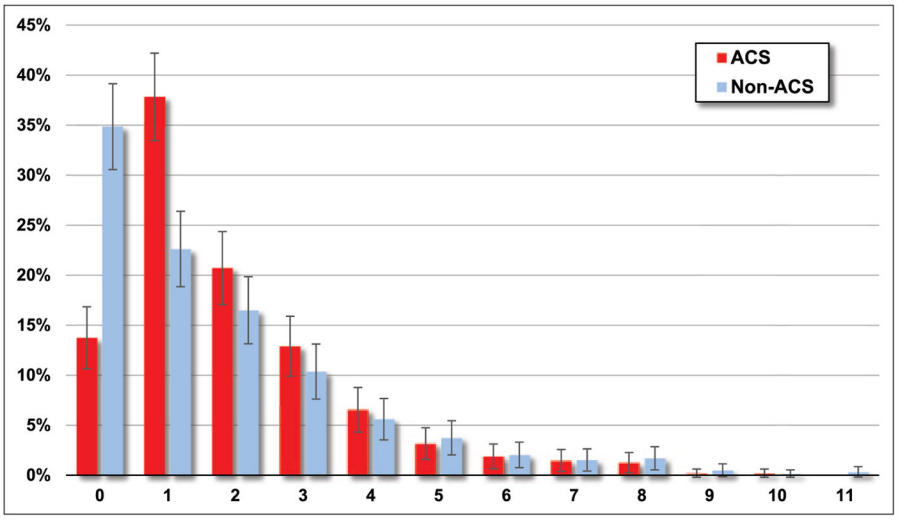

Figure 1.

Frequency of Charlson Comorbidity Index scores by diagnosis.

ACS: acute coronary syndrome.

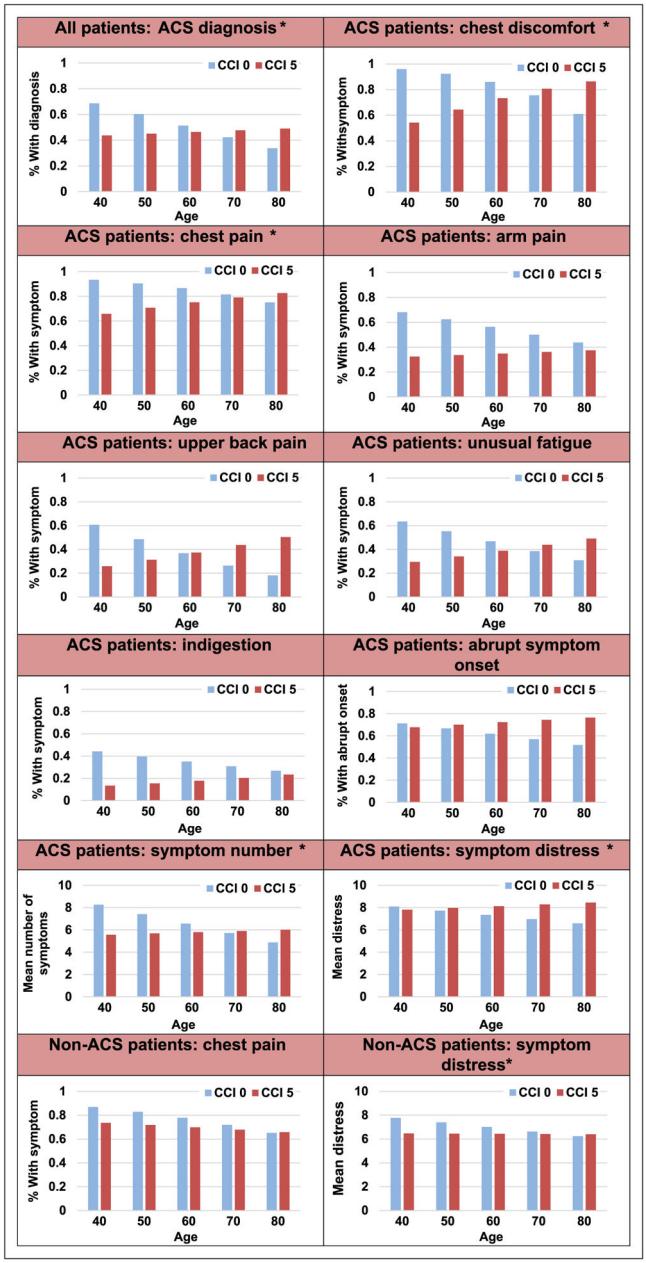

Figure 2.

Predicted percentages and means of ACS diagnosis and type, number, and distress of symptoms by comorbidity scores for given ages. Example CCI scores of 0 and 5 were selected to represent the likelihood of the outcome for an example patient with either a low or high comorbidity score. Results are listed by age group due to significant interactions between CCI scores and age. Models adjusted for gender, race, functional status, tobacco use, hypertension and recruitment site. ACS models were adjusted for type of ACS diagnosis.

*Denotes key findings.

ACS: acute coronary syndrome; CCI: Charlson Comorbidity Index.

Table 1

Age-adjusted mean CCI score by clinical characteristics and discharge diagnosis.

Characteristic category			ACS (*n*=473)		Non-ACS (*n*=588)	
			***n* (%)**	**CCI Mean (95% CI)**	***n* (%)**	**CCI Mean (95% CI)**
Age	<50 years old	1	70 (14.8)	**1.5 (1.1, 1.9)$^{(3,4)}$**	162 (27.5)	**1.0 (0.7, 1.3)$^{(2,3,4)}$**
	50 to <60 years old	2	148 (31.3)	**1.7 (1.4, 2.0)$^{(3,4)}$**	134 (22.8)	**1.7 (1.3, 2.0)$^{(1,4)}$**
	60 to <70 years old	3	137 (29.0)	**2.1 (1.9, 2.4)$^{(1,2)}$**	138 (23.5)	**1.8 (1.5, 2.1)$^{(1,4)}$**
	≥70 years old	4	118 (24.9)	**2.3 (2.0, 2.6)$^{(1,2)}$**	154 (26.2)	**2.5 (2.2, 2.8)$^{(1,2,3)}$**
Sex	Female	1	130 (27.5)	1.9 (1.6, 2.1)	269 (45.7)	1.7 (1.4, 1.9)
	Male	2	343 (72.5)	2.0 (1.8, 2.2)	319 (54.2)	1.8 (1.6, 2.0)
Race	White-non Hispanic	1	324 (68.5)	1.9 (1.7, 2.1)	413 (70.2)	1.7 (1.5, 1.9)
	African-American	2	56 (11.8)	2.3 (1.8, 2.7)	78 (13.3)	1.6 (1.2, 2.1)
	Hispanic	3	45 (9.5)	2.0 (1.5, 2.5)	36 (6.1)	2.0 (1.3, 2.6)
	Other	4	45 (9.5)	1.9 (1.4, 2.4)	59 (10.0)	1.8 (1.3, 2.3)
Insurance	Private – employer	1	150 (31.7)	**1.6 (1.4, 1.9)$^{(3,4)}$**	180 (30.6)	**1.3 (1.0, 1.6)$^{(3,4)}$**
	Private – self	2	45 (9.5)	1.9 (1.4, 2.4)	61 (10.4)	1.7 (1.2, 2.1)
	Medicare	3	142 (30.0)	**2.4 (2.1, 2.7)$^{(1,5)}$**	206 (35.0)	**2.1 (1.8, 2.4)$^{(1,5}$**
	Government – other	4	55 (11.6)	**2.4 (2.0, 2.9)$^{(1,5)}$**	66 (11.2)	**2.3 (1.8, 2.7)$^{(1,5)}$**
	Not insured	5	70 (14.8)	**1.5 (1.1, 1.9)$^{(3,4)}$**	68 (11.6)	**1.3 (0.8, 1.7)$^{(3,4)}$**
Education	<High school diploma	1	60 (12.7)	2.2 (1.8, 2.6)	64 (10.9)	**2.2 (1.8, 2.7)$^{(4,5)}$**
	High school diploma	2	112 (23.7)	2.1 (1.8, 2.4)	122 (20.7)	**1.5 (1.1, 1.8)$^{(5)}$**
	Some college	3	154 (32.6)	2.0 (1.7, 2.2)	190 (32.3)	**1.4 (1.0, 1.8)$^{(5)}$**
	College graduate/graduate work	4	88 (18.6)	1.9 (1.5, 2.2)	127 (21.6)	**2.0 (1.6, 2.3)$^{(1)}$**
	Graduate degree	5	58 (12.3)	1.5 (1.1, 2.0)	83 (14.1)	**1.7 (1.4, 2.0)$^{(1,2)}$**
Income	<US$20,000	1	120 (25.4)	2.2 (1.9, 2.5)	195 (33.2)	**2.2 (1.9, 2.4)$^{(3,4)}$**
	US$20,000–49,999	2	139 (29.4)	2.0 (1.7, 2.3)	178 (30.3)	**1.8 (1.5, 2.1)$^{(4)}$**
	US$50,000–99,999	3	103 (21.8)	1.7 (1.4, 2.0)	86 (14.6)	**1.4 (1.0, 1.8)$^{(1)}$**
	≥US$100,000	4	56 (11.8)	1.6 (1.2, 2.1)	79 (13.4)	**1.0 (0.6, 1.5)$^{(1,2)}$**
Diagnosis	UA	1	104 (22.0)	**2.0 (1.7, 2.4)$^{(3)}$**		

Characteristic category			ACS (*n*=473)		Non-ACS (*n*=588)	
			***n* (%)**	**CCI Mean (95% CI)**	***n* (%)**	**CCI Mean (95% CI)**
	NSTEMI	2	251 (53.1)	**2.1 (2.0, 2.3)[3]**		
	STEMI	3	118 (24.9)	**1.6 (1.2, 1.9)[1,2]**		
Hypertension	Yes	1	323 (68.3)	**2.2 (2.0, 2.3)[2]**	362 (61.6)	**2.0 (1.8, 2.2)[2]**
	No	2	147 (31.1)	**1.4 (1.2, 1.7)[1]**	221 (37.6)	**1.3 (1.0, 1.5)[1]**
Tobacco use	Never	1	227 (48.0)	**1.9 (1.7, 2.1)[2]**	339 (57.6)	**1.5 (1.3, 1.7)[2]**
	Former	2	119 (25.2)	**2.3 (2.0, 2.7)[1,3]**	135 (22.9)	**2.0 (1.7, 2.4)[1]**
	Current	3	114 (24.1)	**1.8 (1.4, 2.1)[2]**	102 (17.3)	1.9 (1.6, 2.3)
Hyper-cholesterolemia	Yes	1	291 (61.5)	2.1 (1.9, 2.3)	274 (46.6)	1.9 (1.7, 2.2)
	No	2	171 (36.1)	1.8 (1.5, 2.0)	296 (50.3)	1.6 (1.4, 1.8)
Obesity	Yes	1	183 (38.7)	**2.2 (2.0, 2.5)[2]**	262 (44.6)	1.9 (1.7, 2.1)
	No	2	287 (60.7)	**1.8 (1.6, 2.0)[1]**	325 (55.3)	1.6 (1.4, 1.8)
Functional limitations	Yes	1	350 (74.0)	**2.2 (2.0, 2.4)[2]**	454 (77.2)	**2.0 (1.8, 2.2)[2]**
	No	2	123 (26.0)	**1.2 (0.9, 1.5)[1]**	134 (22.8)	**0.8 (0.4, 1.1)[1]**

Sex, race, insurance, education, income, diagnosis, hypertension, tobacco use, hypercholesterolemia, obesity, and functional limitations categories adjusted for age. Superscripts in parentheses with bold text represent statistically significant differences between categories.

CCI: Charlson Comorbidity Index; ACS: acute coronary syndrome; CI: confidence interval; UA: unstable angina; NSTEMI: non-ST elevation myocardial infarction; STEMI: ST-elevation myocardial infarction.

Table 2

Prevalence of CCI conditions and total CCI score by final ACS diagnosis.

CCI conditions	Weight	ACS (*n*=473)	Non-ACS (*n*=588)	*p*-value
		***n* (%)**	***n* (%)**	
History of prior myocardial infarction	1	323 (68.4)	153 (26.1)	**<0.001**
Diabetes without target organ damage	1	119 (25.2)	130 (22.1)	0.244
Chronic lung disease – asthma	1	88 (18.6)	137 (23.3)	0.070
Peripheral vascular disease	1	45 (9.5)	30 (5.1)	**0.008**
Cerebrovascular disease –stroke	1	37 (7.8)	55 (9.4)	0.443
Connective tissue disease – lupus	1	31 (6.6)	36 (6.1)	0.801
Dyspnea	1	24 (5.1)	24 (4.1)	0.460
Mild liver disease	1	15 (3.2)	24 (4.1)	0.513
Peptic ulcer disease	1	13 (2.8)	27 (4.6)	0.144
Dementia	1	4 (0.8)	13 (2.2)	0.089
Malignant neoplasm	2	36 (7.6)	53 (9.0)	0.437
Diabetes with target organ damage	2	26 (5.5)	37 (6.3)	0.604
Moderate to severe renal disease	2	14 (3.0)	34 (5.8)	**0.037**
Lymphoma	2	6 (1.3)	6 (1.0)	0.775
Hemiplegia	2	4 (0.8)	4 (0.7)	1.000
Leukemia	2	3 (0.6)	6 (1.0)	0.739
Moderate to severe liver disease	3	1 (0.2)	3 (0.5)	0.633
Metastatic solid tumor	6	6 (1.3)	15 (2.6)	0.183
Acquired immunodeficiency syndrome	6	2 (0.4)	3 (0.5)	1.000
		***M* (SD)**	***M* (SD)**	***p*-value**
Mean score		2.0 (1.7)	1.7 (2.0)	**0.049**
	< 50 years old	1.5 (1.5)	1.0 (1.8)	**0.034**
	50–59 years old	1.7 (1.7)	1.7 (1.9)	0.812
	60–69 years old	2.2 (1.7)	1.8 (1.8)	0.080
	70+ years old	2.3 (1.8)	2.5 (2.2)	0.377

Bold *p*-values are statistically significant. Fisher's exact tests used for categorical variables and *t*-tests used for comparisons of means.

CCI: Charlson Comorbidity Index; ACS: acute coronary syndrome.

Table 3

Prediction of ACS diagnosis and type, number, and distress of symptoms by comorbidity score for patients of a given age.

Characteristic	40 years old	50 years old	60 years old	70 years old	80 years old
All Patients (n=1019)					
ACS diagnosis, OR (95% CI)	**1.23 (1.06, 1.42)** **	**1.13 (1.02, 1.25)** *	1.04 (0.96, 1.13)	0.96 (0.87, 1.05)	0.88 (0.77, 1.00)
ACS (n=451)					
Chest discomfort, OR (95% CI)	**0.54 (0.40, 0.73)** ***	**0.68 (0.55, 0.83)** **	**0.85 (0.74, 0.97)** *	1.06 (0.90, 1.24)	**1.32 (1.03, 1.69)** *
Chest pain, OR (95% CI)	**0.69 (0.52, 0.91)** **	**0.78 (0.64, 0.94)** **	0.88 (0.76, 1.00)	0.99 (0.84, 1.16)	1.12 (0.88, 1.42)
Arm pain, OR (95% CI)	0.76 (0.57, 1.02)	**0.81 (0.66, 0.99)** *	**0.86 (0.75, 0.99)** *	0.92 (0.78, 1.07)	0.97 (0.77, 1.23)
Upper back pain	0.73 (0.53, 1.01)	0.85 (0.68, 1.07)	0.99 (0.85, 1.16)	1.15 (0.97, 1.37)	**1.34 (1.04, 1.72)** *
Unusual fatigue, OR (95% CI)	**0.75 (0.57, 0.98)** *	0.83 (0.69, 1.00)	0.93 (0.81, 1.06)	1.04 (0.89, 1.21)	1.16 (0.92, 1.46)
Indigestion, OR (95% CI)	0.73 (0.51, 1.03)	**0.78 (0.61, 1.00)** *	**0.84 (0.71, 1.00)** *	0.90 (0.75, 1.08)	0.97 (0.75, 1.26)
Abrupt onset, OR (95% CI)	0.97 (0.76, 1.25)	1.04 (0.88, 1.23)	1.11 (0.98, 1.25)	**1.18 (1.01, 1.37)** *	**1.26 (1.01, 1.57)** *
No. of symptoms, b (95% CI)	**−0.54 (−0.86, −0.22)** **	**−0.35 (−0.57, −0.13)** **	−0.16 (−0.32, 0.01)	0.04 (−0.15, 0.23)	0.23 (−0.05, 0.51)
Symptom distress, b (95% CI)	−0.06 (−0.35, 0.23)	0.05 (−0.15, 0.25)	**0.16 (0.01, 0.30)** *	**0.26 (0.09, 0.44)** **	**0.37 (0.11, 0.63)** **
Non-ACS (n=568)					
Chest pain, OR (95% CI)	**0.84 (0.72, 0.99)** *	**0.88 (0.78, 0.99)** *	0.92 (0.83, 1.01)	0.96 (0.86, 1.07)	1.01 (0.87, 1.16)
Symptom distress, b (95% CI)	**−0.26 (−0.44, −0.08)** **	**−0.19 (−0.32, −0.06)** **	**−0.12 (−0.23, −0.01)** *	−0.04 (−0.17, 0.08)	0.03 (−0.13, 0.19)

Results show change in likelihood of the variable of interest for a one unit increase in comorbidity score. Odds ratios are reported for categorical variables. Unstandardized beta coefficients (b) are listed for continuous variables. Results are listed by age due to significant interactions between CCI scores and age. Models adjusted for gender, race, functional status, tobacco use, hypertension and recruitment site. ACS models were adjusted for type of ACS diagnosis.

* $p<0.05$

** $p<0.01$

*** $p<0.001$

ACS: acute coronary syndrome; OR: odds ratio; CI: confidence interval; CCI: Charlson Comorbidity Index.