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Hospital Treatment Practices, 30-Day Hospital Readmissions, and Long-Term Prognosis in Patients Hospitalized with Acute Myocardial Infarction: A Dissertation

Han-Yang Chen
University of Massachusetts Medical School

HOSPITAL TREATMENT PRACTICES, 30-DAY HOSPITAL READMISSIONS, AND LONG-TERM PROGNOSIS IN PATIENTS HOSPITALIZED WITH ACUTE MYOCARDIAL INFARCTION: A DISSERTATION

A Dissertation Presented

By

Han-Yang Chen, M.S.

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The signatures of the Dissertation Defense Committee signify completion and approval as to style and content of the Dissertation

Robert J. Goldberg, Ph.D., Thesis Advisor

Catarina I. Kiefe, M.D., Ph.D., Member of Committee

Sharina D. Person, Ph.D., Member of Committee

Eric Mick, Sc.D., Member of Committee

Charles B. Eaton, M.D., M.S., Member of Committee

The signature of the Chair of the Committee signifies that the written dissertation meets the requirements of the Dissertation Committee

Kate L. Lapane, Ph.D., Chair of Committee

The signature of the Dean of the Graduate School of Biomedical Sciences signifies that the student has met all graduation requirements of the school.

Anthony Carruthers, Ph.D.,
Dean of the Graduate School of Biomedical Sciences

Clinical & Population Health Research Program

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DEDICATION

This dissertation is dedicated to my beloved family whose support and belief in me never wavered on this journey.

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ABSTRACT

Background

Cardiovascular disease (CVD) remains the leading cause of morbidity and mortality in the U.S. Acute myocardial infarction (AMI), with or without ST-segment elevation, is a common presentation of coronary heart disease and affected more than 800,000 American adults in 2010. The overall goal of this dissertation was to examine decade-long trends in the extent of delay in the receipt of a primary percutaneous coronary intervention (PCI) among patients hospitalized with ST-segment elevation myocardial infarction (STEMI), 30-day hospital readmission rates in patients having survived an AMI, and multiple decade long trends in 1-year post-hospital all-cause mortality, as well as factors associated with these outcomes, among patients hospitalized with AMI.

Methods

Data from the Worcester Heart Attack Study, a population-based chronic disease surveillance project that has been carried out among adult residents of the Worcester, MA, metropolitan area, hospitalized with AMI on a biennial basis from 1975 through 2009 at all medical centers in central MA, were used for this dissertation.

Results

Between 1999 and 2009, among patients hospitalized with STEMI, the likelihood of receiving a primary PCI within 90 minutes after emergency department arrival increased dramatically from 1999/2001 (11.6%) to 2007/2009 (70.5%). Between 1999 and 2009, among hospital survivors of an AMI, the 30-day all-cause rehospitalization rates decreased from 1999/2001 (20.3%) to 2007/2009 (16.7%). The overall cause-specific 30-day rehospitalization rates due to CVD, non-CVD, and AMI were 10.1%, 7.1%, and 1.8%, respectively, during the years under study. Between 1975 and 2009, among hospital survivors for a first AMI, the 1-year post-discharge mortality rates remained relatively stable from 1975-1984 (12.9%) to 1986-1997 (12.5%), but increased during 1999-2009 (15.8%). We identified several demographic, clinical and in-hospital treatment factors associated with an increased risk of failing to receive a primary PCI within 90 minutes after emergency department arrival, 30-day readmissions, and 1-year post-discharge mortality.

Conclusions

Our findings can hopefully lead to the enhanced development of innovative, patient-centered, intervention strategies which can further improve the treatment and transitions of care, as well as short and long-term prognosis, of men and women hospitalized with AMI.

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Chen H-Y, Tisminetzky M, Lapane KL, Yarzebski J, Person SD, Kiefe CI, Gore JM, Goldberg RJ. Decade-long trends in 30-day rehospitalization rates after acute myocardial infarction. (Currently under review)

CHAPTER 1 : INTRODUCTION

1.1 Specific Aims

Cardiovascular disease (CVD) remains the leading cause of morbidity and mortality in the United States.[1] Acute myocardial infarction (AMI), with or without ST-segment elevation, is a common presentation of coronary heart disease (CHD) and affected more than 800,000 American adults in 2010.[1]

The prompt administration of coronary reperfusion therapy for patients with an evolving AMI is crucial in reducing mortality and the risk of serious clinical complications in these patients. In the past decade, primary percutaneous coronary intervention (PCI) has gradually replaced thrombolysis as the main revascularization strategy for most patients presenting with ST-segment elevation myocardial infarction (STEMI).[2] Although clinical guidelines recommend that patients with STEMI receive a primary PCI within 90 minutes after hospital presentation,[3] there are little population-based data describing contemporary trends in the proportion of patients with STEMI who receive a primary PCI and the characteristics of those experiencing delay from hospital presentation to the initiation of a primary PCI.[4–6]

Thirty-day hospital readmission rates have become a quality performance measure for patients hospitalized with AMI,[7] and nearly 1 in 5 Medicare patients hospitalized with AMI are readmitted within 30 days of discharge.[8] There is a great deal of interest from hospitals and clinicians to better understand and improve modifiable factors associated with 30-day hospital readmissions, which are increasingly being linked to hospital reimbursement.[9] However, we have limited contemporary data that describe trends in 30-day readmission rates as well as demographic, clinical, and treatment related factors associated with 30-day readmissions among patients surviving an AMI, particularly from a more generalizable population-based perspective. Finally, although several studies have reported improvements in long-term survival among patients after hospital discharge for AMI,[10,11] there are little data describing post discharge death rates after a first AMI and changes over time therein. Moreover, scarce population-based data have characterized contemporary trends in long-term survival, and prognostic factors associated with long-term mortality, among patients who survived a first AMI.

The overall goal of this dissertation was to examine the extent of delay in the receipt of a primary PCI, 30-day hospital readmission rates, and 1-year post-hospital all-cause mortality, as well as factors associated with these outcomes, among patients hospitalized with AMI. These objectives were accomplished from the perspective of a population-based investigation among adult residents of the Worcester, MA, metropolitan area, hospitalized with AMI at all medical centers in central MA (Worcester Heart Attack Study: WHAS).[12–15] The WHAS is an ongoing coronary disease surveillance project that has collected data about patient's demographics, medical history, clinical and laboratory findings, receipt of cardiac treatments and revascularization procedures, and post-discharge survival status over 3 decades (1975-2009). The WHAS offers a unique opportunity to study changing trends in patient characteristics and treatment practices, as well as short and long-term outcomes, in patients hospitalized with an independently confirmed AMI.

The specific aims and accompanying hypotheses of this proposal were as follows:

Aim 1: To examine decade long trends in the extent of delay from hospital emergency department presentation to the initiation of a primary PCI over time, and associated factors, among patients hospitalized for STEMI in the WHAS on a biennial basis between 1999 and 2009.

Hypothesis: Among patients hospitalized with STEMI who underwent a primary PCI, the proportion of patients receiving this intervention in a timely manner (≤90 minutes) after hospital emergency department arrival increased during the most recent compared with earlier study years. Older age, history of several comorbidities, and in-hospital factors were associated with a higher risk of prolonged delay in receiving a primary PCI among patients with STEMI.

Aim 2: To examine decade long trends in 30-day readmission rates, and associated factors, among patients hospitalized for AMI in the WHAS between 1999 and 2009.

Hypothesis: The 30-day readmission rates of patients discharged after AMI decreased during the most recent compared with earlier study years. Older age, history of several comorbidities, and development of in-hospital clinical complications were associated with a higher risk of 30-day readmission.

Aim 3: To examine trends in long-term prognosis, and hospital treatment practices associated with post-hospital 1-year all-cause mortality rates, among patients who survived a first AMI in the WHAS from 1975 to 2009.

Hypothesis: The 1-year all-cause mortality rates of patients discharged after a first AMI decreased during the most recent compared with earlier years. Hospital treatment practices were associated with improved survival during the first year after hospital discharge for an initial AMI.

1.2 Background

Acute myocardial infarction among U.S. adults

Cardiovascular disease (CVD) remains the leading cause of morbidity and mortality in the United States.[1] In 2010, CVD accounted for nearly one third (787,650) of all deaths occurring in the U.S. Coronary heart disease (CHD) is the most common type of heart disease. It has been estimated that 15.4 million adult Americans have CHD (prevalence: 6.4%).[1] Beginning in the early part of the 20th century, death rates from CHD in the U.S. increased dramatically reaching epidemic proportions by the mid to late 1960's.[16] Between 1968 and 2008, the death rate from CHD declined and there has been an approximate 5% average annual decline in the age-adjusted mortality from CHD in the U.S. between 1999 and 2008.[17] However, CHD continues to be the major cause of mortality in American men and women. In 2010, CHD death rates (per 100, 000) were 152 for white males, 169 for black males, 84 for white females, and 105 for black females.[1]

Acute myocardial infarction (AMI) is the acute and life-threatening form of CHD that accounts for most CHD related hospitalizations. The two principal clinical manifestations of AMI based on serial ECG findings are ST-segment elevation myocardial infarction (STEMI) and non-ST-segment elevation myocardial infarction (NSTEMI). These disease entities share common pathophysiological origins related to coronary plaque progression, instability, or rupture with or without luminal thrombosis and vasospasm.[1] In 2010, there were more than 800,000 hospital discharges for AMI (including primary and secondary discharge diagnoses).[1] Approximately one third of patients with STEMI die within 24 hours of acute symptom onset, emphasizing the need for prompt and effective treatment.[18] The 30-day all-cause hospital readmission rate is nearly 20% for Medicare patients hospitalized with AMI.[8] There is great interest in understanding and improving modifiable factors associated with 30-day readmission rates due to ongoing and planned changes in reimbursement policies.[9] Moreover, about 1 in 5 men and 1 in 4 women may die within the first year after hospital discharge after a first AMI.[1] Given present trends of an increasingly older patient population with a greater prevalence of comorbidities,[11,19,20] the management of patients hospitalized with a first AMI presents significant challenges to health care providers.

Aim 1: Delay in the receipt of a primary PCI in patients hospitalized with STEMI

The prompt seeking of medical care after the onset of symptoms suggestive of AMI has been associated with the receipt of coronary reperfusion therapy and effective cardiac medications in hospitalized patients. Timely medical care is crucial to reducing mortality and the risk of serious clinical complications in patients with AMI, since it can maximize benefits of evidence-based treatments, and possibly reduce sudden cardiac deaths and the eventual size of the infarct. Early administration of coronary reperfusion therapy improves survival in patients hospitalized with STEMI by reestablishing coronary blood flow within the occluded infarct-related artery.[21] In the past decade, clinical guidelines have emphasized the importance of rapid reperfusion of patients with STEMI and specify a maximum delay of 30 minutes for the use of fibrinolytic therapy and 90 minutes for administration of a primary PCI in these patients.[3] Reperfusion therapy administered beyond guideline-recommend times has been associated with significantly increased 30-day death rates.[22] In contrast, among patients with AMI without ST-segment elevation (NSTEMI), the culprit artery is often patent and the patient typically has a good response to initial medical treatment.[23] Among initially stabilized patients with NSTEMI for whom an early invasive strategy of coronary angiography is chosen, optimal timing of angiography has not been well defined.[24] It is thus important that AMI patients are diagnosed rapidly for early risk stratification to assign appropriate treatments and improve their in-hospital and more long-term outcomes.[3,24]

In the past decade, primary PCI has gradually replaced fibrinolytic therapy as the main revascularization strategy for many patients presenting with STEMI,[2] since primary PCI has been found to be superior to fibrinolytic therapy when performed rapidly by expert teams.[2] Data from the National Hospital Discharge Survey (NHDS) examined hospitalizations with a first-listed diagnosis of AMI over the period 1979 to 2005 and showed that PCI was performed in 2.9% of cases from 1985-1987 and increased to 30% by 2003-2005.[20] Data from the Register of Information and Knowledge about Swedish Heart Intensive Care Admission (RIKS-HIA) examined 61,238 patients with a first-time diagnosis of STEMI between 1996 and 2007; the use of primary PCI increased from 12% in 1996 to 61% in 2007 ($p<.001$).[25]

Although primary PCI has been shown to improve outcomes in patients with STEMI, its effectiveness may be limited by delays in its more timely delivery.[3] Data from the National Registry of Myocardial Infarction (NRMI) has demonstrated a strong relationship between door-to-balloon time and in-hospital mortality among 29,222 patients with STEMI; after multivariable adjustment for several patient characteristics, each 15-minute reduction in door-to-balloon time from 150 to less than 90 minutes was associated with 6.3 fewer deaths per 1,000 treated patients.[26] Currently available data, however, have shown mixed results of improvement in door-to-balloon times. Data from the NRMI study examined patients admitted with STEMI who received a primary PCI (n=33,647) between 1999 and 2002; only 35% of patients were treated within the recommended 90 minutes after arrival at the hospital. Meaningful improvements in these times to reperfusion over the 4-year study period were not observed.[5] Findings from the Blue Cross Blue Shield of Michigan Cardiovascular Consortium of 8,771 patients with STEMI who underwent a primary PCI between 2003 and 2008 showed that the median door-to-balloon time had decreased annually from 113 minutes in 2003 to 76 minutes in 2008 ($p<.001$). In addition, the percentage of patients revascularized with a door-to-balloon time of less than 90 minutes significantly increased from 29% to 67% over this period ($p<.001$).[6]

Although several studies have reported increasing use of primary PCI[20,25] over time, there have been mixed findings in the extent of delay in receiving a primary PCI among patients hospitalized with STEMI,[4–6] and only limited population-based studies have examined potential risk factors[5,6,27,28] for delay in receiving a primary PCI using multivariable regression analyses. Inasmuch, there are few contemporary data that describe long-term trends in the extent of delay from hospital presentation to initiation of a primary PCI, and factors, such as patient demographics, history of comorbid conditions, and in-hospital factors, associated with the failure to receive a primary PCI within the guideline-recommended time frame among patients with STEMI, particularly from a population-based perspective.

In my first study aim, relatively contemporary data from the WHAS,[12–15] were used to examine possible trends in the extent of delay from hospital presentation to initiation of a primary PCI over time (1999-2009), and factors associated with failure to receive a primary PCI within the guideline-recommended time frame, among patients hospitalized with STEMI at the 3 PCI capable hospitals in central MA on a biennial basis between 1999 and 2009.

Aim 2: Thirty-day hospital readmission rates among patients who survived hospitalization for AMI

Reducing hospital readmission rates is a national priority, as hospital readmission rates have become an indicator of poor health care quality and efficiency.[29] Nearly one fifth of the 11,855,702 Medicare beneficiaries who had been discharged for any condition from a hospital were rehospitalized within 30 days in 2003-2004.[30] The Patient Protection Affordable Care Act of 2010 has created new incentives to reduce readmissions because hospitals with high readmission rates can lose ≤3% of their Medicare reimbursement by 2015.[9] There is a great deal of interest from hospitals and clinicians to better understand and improve modifiable factors associated with 30-day readmission rates due to ongoing and planned changes in these reimbursement policies.[9]

With advances in medical treatment, in-hospital survival after AMI has dramatically improved.[20] Thus, many AMI survivors are being discharged from the hospital into the community who are at risk for hospital readmission. Approximately 20% of Medicare fee-for-service beneficiaries were readmitted for all causes within 30 days of discharge following hospitalization for AMI between 2007 and 2009.[8] Thirty-day hospital readmission rates have become a quality performance measure for patients hospitalized with AMI,[7,29] since the Centers for Medicare & Medicaid Services (CMS) began publicly reporting 30-day risk-standardized readmission rates (RSRRs) for heart failure (HF), AMI, and pneumonia as performance measures after these measures were endorsed by the National Quality Forum.[29]

A systematic review[31] of patient-level predictors of hospital readmission (ranging from 30 days to 1 year post-discharge) after AMI found that all-cause readmission rates at 30 days ranged from approximately 11% to 28% across 7 studies that were carried out between 1991 and 1999. A recent retrospective cohort study,[32] conducted in 3 hospitals in Olmsted County, MN, found that 30-day all-cause readmission rates among patients who survived their hospitalization for a first AMI were 23% during the period 1987 to 1992, 22% between 1993 and 1998, 22% between 1999 and 2004, and 19% during the most recent 5 year period under study (2005 to 2010); comorbid conditions, longer length of the original hospital stay, and complications of angiography and revascularization or reperfusion were associated with increased risk of 30-day readmissions after a first AMI.

Although several studies have reported 30-day readmission rates among patients surviving an AMI,[31,32] and few have examined potential risk factors for 30-day readmissions using multivariable regression analyses, there are very little contemporary data that describe long-term trends in all-cause and cause specific 30-day readmission rates. Moreover, few studies have examined factors such as patient demographics, comorbid conditions, in-hospital development of complications, and treatment practices during hospitalization that may be associated with 30-day readmissions among patients surviving an AMI in the US, particularly from a more broad population-based perspective.

In study Aim 2, we used data from the WHAS[12–15] to examine contemporary trends in all-cause and cause-specific (e.g., AMI, CVD-related (except AMI), non CVD-related) 30-day readmission rates among residents of central Massachusetts discharged from three major medical centers in central MA after an AMI over a decade long period (1999-2009). This study also described patient characteristics, treatment practices, and prognostic factors associated with an increased risk of all-cause 30-day readmissions in patients surviving hospitalization for an AMI.

Aim 3: Long-term all-cause mortality rates among patients after a first AMI

Although CVD remains a leading cause of death and disability, and a major burden on health care systems in the US,[1,33] there have been ongoing improvements in hospital and long-term survival among patients after AMI during the past several decades.[11,19] The encouraging declines in long-term mortality among patients hospitalized with AMI are attributable to a number of factors including improvements in the primary prevention of AMI and more widespread use of coronary reperfusion and revascularization procedures and effective cardiac medications.[11,19] Despite these encouraging trends, approximately 1 in every 7 patients discharged from the hospital after an AMI will die during the next year.[34]

Several studies have reported improvements in long-term survival after hospital discharge for AMI;[11,19] however, there are little data describing post-hospital discharge death rates among patients hospitalized with a first AMI, especially from the more generalizable perspective of a population-based investigation. It has been estimated that approximately 620,000 Americans will develop a first AMI annually.[1] Given present trends of an increasingly older patient population with a greater prevalence of comorbidities,[11,19,20] the management of patients hospitalized with a first AMI presents significant challenges to health care providers. Inasmuch, the need for contemporary monitoring of long-term prognosis of this patient population remains important, and the identification of factors associated with an increased risk of dying after hospital discharge for an initial AMI.

There are very little population-based data that have examined contemporary trends in long-term survival, and factors associated with long-term mortality, among patients discharged from the hospital after a first AMI in the U.S.[35] In addition, although previous studies have observed that patients discharged from the hospital after NSTEMI have a worse long-term prognosis than those with STEMI,[36,37] very little population-based analysis has been performed to examine the association between STEMI/NSTEMI and long-term mortality among patients who survived a first AMI. A Spanish study conducted in 6 public hospitals has shown that patients with NSTEMI experienced a worse 7-year mortality rate than patients with STEMI.[37] A recent Danish nationwide population-based study examined 25 year trends in first time hospitalizations for AMI and showed that the 1-year overall mortality declined from 42.1% (during 1984–1988 to 24.2% during 2004–2008; comorbidity burden was a strong predictor of 1-year mortality.[38] In addition, it remains of importance to examine whether the increased use of effective cardiac medications and intervention approaches during recent years has resulted in an improved outlook for hospital survivors of a first AMI.

In study Aim 3, we examined changing trends in long-term prognosis among residents of central Massachusetts discharged from all central MA medical centers after a first AMI over an approximate 35-year period (1975-2009). Although limited by the nonrandomized nature of this study, we examined the impact of various treatment regimens (i.e., effective cardiac medications, and coronary diagnostic and interventional procedures) on the 1-year post-discharge mortality patterns observed during the years under study. Data from the WHAS were used for this investigation.[12–15]

1.3 Research Design and Methods

The aims of this dissertation were to examine trends in the extent of delay in the receipt of a primary PCI in patients hospitalized with STEMI, and factors associated with failure to receive a primary PCI within the current guideline-recommended time frame; to examine trends in 30-day hospital readmission rates from all causes, and specific causes, over time and factors associated with readmission among patients hospitalized with AMI; to examine trends in long-term prognosis, and hospital treatment practices associated with all-cause 1-year mortality post-hospitalization, among patients hospitalized for a first AMI. This dissertation will analyze secondary data collected in the WHAS.[12–15]

1.3.1 Study Designs, Participating Hospitals, and Patient Populations

The Worcester Heart Attack Study (WHAS)

The WHAS[12–15] is one of the largest ongoing population-based investigations of CHD in the world. This observational study is examining long-term trends in the descriptive epidemiology of AMI in residents of the Worcester, MA, metropolitan area (2000 census= 478,000) hospitalized at all 16 greater Worcester medical centers in Central Massachusetts. Data have been collected on an approximately biennial basis during 1975, 1978, 1981, 1984, 1986, 1988, 1990, 1991, 1993, 1995, 1997, 1999, 2001, 2003, 2005, 2007, 2009, and recently 2011, which presently includes a total of 18 cohorts.[12–15] In 2000, the median age of residents of the Worcester Standard Metropolitan Statistical Area was 37 years, 49% were men, 89% were white, and approximately 25% had a bachelor's degree or higher.[15] Due to hospital closures, mergers, or conversion to long-term care or rehabilitation facilities, fewer hospitals (n=11) have been providing care to greater Worcester residents during more recent study years. The 11 acute care general hospitals include 2 in the city of Worcester (UMass Memorial Health Care and St. Vincent/Worcester Medical Center), and 9 hospitals in the Worcester metropolitan area (Clinton, Harrington Memorial, Health Alliance, Henry Heywood, Hubbard, Marlboro, Metrowest, Milford-Regional and Wing). A particular strength of the WHAS is the ability to examine contemporary and long-term trends in the clinical epidemiology of AMI among residents of the Worcester metropolitan area hospitalized at all greater Worcester, MA, medical centers.

Methods for identifying cases of AMI

Computerized printouts of primary and secondary discharge diagnoses of AMI and related acute and chronic coronary disease rubrics were obtained from all participating greater Worcester medical centers for purposes of identifying possible cases of AMI occurring during the periods under study. The PI and the project director of the WHAS reviewed the appropriate (9th and/or 10th) International Classification of Disease (ICD) codes for CHD at participating metropolitan Worcester hospitals. The 9th revision ICD codes included codes 410-414 and 786.5 and the corresponding 10th revision codes of I20-I25 and R07. The vast majority of validated cases of AMI came from ICD-9 diagnostic rubric 410 (AMI), followed by a small number of cases from ICD rubric 411 (other acute and sub-acute forms of CHD). An extremely low yield of cases of definite AMI have come from ICD rubrics 412 (old MI), 413 (angina pectoris), 414 (other forms of chronic CHD), and 786.5 (chest pain); these latter disease categories primarily included patients with chronic manifestations of CHD or nonspecific chest pain.

Diagnostic criteria for validating AMI

Cases of possible AMI treated at all greater Worcester medical centers were validated according to predefined criteria for AMI. This diagnosis was made on the basis of the well accepted criteria developed by the World Health Organization which includes a supportive clinical history, increases in serum enzyme levels, and serial electrocardiographic findings; these criteria have been utilized in a number of clinical and epidemiological investigations including the MONICA study.[39] These diagnostic criteria included:

- a suggestive clinical history (i.e., a typical history of prolonged chest pain suggestive of AMI that is not relieved by rest and/or use of nitrates)
- increases in several serum biomarkers (e.g., creatine kinase (CK), CK-MB, and troponin values)
- serial electrocardiographic findings during hospitalization consistent with the presence of AMI

Study inclusion and exclusion criteria

Patients who satisfied at least 2 of these 3 diagnostic criteria, and were residents of the Worcester metropolitan area, were included in this study. Patients who developed AMI secondary to an interventional procedure or surgery were excluded from the study sample. Additional exclusion criteria were set for each of the 3 aims.

Aim 1: We restricted our study population to those who were hospitalized with STEMI and received a primary PCI during 1999-2009, since our goal was to examine contemporary trends in door-to-balloon time and in-hospital delay to a primary PCI based on a guideline recommended time interval initiated in 1999.[40]

Aim 2: We restricted our study population to those who survived their hospitalization for AMI during 1999-2009, since our goal was to examine 30-day readmission rates among hospital survivors; 30-day readmission rates, and reasons for these hospital readmissions, were also only collected between 1999 and 2009.

Aim 3: We restricted our study population to those who were hospitalized for a first AMI and survived their hospitalization between 1975 and 2009. Patients with an initial AMI were identified by either mention in the review of the hospital charts that this was the patient's first admission for an AMI or through the review of previous hospital records and electrocardiograms that failed to indicate the occurrence of a previous AMI. The approaches used to ascertain survival status after hospital discharge included a review of records for additional hospitalizations and a statewide and national search of death certificates for residents of the Worcester metropolitan area, which resulted in a high follow-up rate of greater than 99%.

Data collection

Trained nurses and physicians abstracted information on patients' demographic characteristics, medical history, clinical data, and treatment practices through the review of hospital medical records. These factors included patient's socio-demographic characteristics (e.g., age, sex, race, marital status), year of hospitalization, hospital length of stay, time of hospital admission (time of day, day of week), history of previously diagnosed comorbidities (e.g., hypertension, stroke, diabetes, and heart failure), AMI order (initial vs. recurrent), AMI type (STEMI vs. NSTEMI), and the development of important in-hospital complications (e.g., atrial fibrillation, cardiogenic shock, heart failure, and stroke). Data on several coronary diagnostic and interventional procedures [cardiac catheterization, PCI, and coronary artery bypass grafting (CABG)] during hospitalization, and medications during hospitalization and at the time of hospital discharge, including the prescribing of several effective cardiac medications [angiotensin converting inhibitors (ACE-I)/angiotensin receptor blockers (ARBs), anticoagulants, lipid lowering agents, beta blockers, channel blockers, and aspirin], were obtained. Data on time interval from hospital emergency department presentation to receiving a primary PCI, mode of transportation to the hospital, 1-year post-hospital discharge all-cause death rates, and all-cause, and cause-specific, hospitalizations which occurred within 30 days after hospital discharge were also collected.

Characteristics of the WHAS Population over Time

Table 1-1 describes changes in the WHAS population over time (1975-2009). There have been relatively significant increases in the age profile of greater Worcester residents hospitalized with AMI as well as in the proportion of patients presenting with previously diagnosed diabetes, heart failure, hypertension, and stroke. In terms of clinical complications, although the proportion of patients developing atrial fibrillation increased, the proportions of patients developing heart failure and cardiogenic shock decreased over the years under study. The proportion of patients hospitalized with an initial AMI remained relatively stable. Despite the presence of an increasingly older patient population with a greater prevalence of comorbidities, in-hospital mortality rates declined appreciably over time. The hospital length of stay also declined significantly during the years under study.

Table 1-1 Characteristics of the Worcester Heart Attack Study Population, 1975-2009

Characteristics	1975-1984 (n=3,338)	1986-1997 (n=5,998)	1999-2009 (n=6,018)
Age (mean, years)	66.5	68.9	70.3
Male (%)	62.2	58.3	56.4
White (%)	97.6	96.4	93.5
Married (%)	64.0	60.8	53.7
Q-Wave (%)	61.1	42.5	22.3
ST-segment myocardial infarction (%)	N/A	N/A	34.9
Initial AMI (%)	65.2	65.4	64.4
In-hospital case-fatality rates (CFR)	19.0	14.3	10.1
Medical history (%)			
Heart failure	14.9	17.0	24.4
Hypertension	45.7	54.9	72.0
Stroke	6.9	9.8	11.8
Diabetes	22.4	27.8	33.7
In-hospital complication (%)			
Atrial fibrillation	15.7	15.6	19.9
Cardiogenic shock	7.2	7.1	5.5
Stroke	N/A	1.3	1.8
Heart failure	43.2	38.3	37.8
Hospital length of stay (mean, days)	15.7	9.5	5.6

Human subjects

The Worcester Heart Attack Study (WHAS) protocol was reviewed and approved by the Institutional Review Board at the University of Massachusetts Medical School (UMMS). There was no additional data collection for the proposed study. All the analyses proposed in this study were conducted using secondary data sets from the WHAS. All identifiers were removed from the study data sets by the WHAS data coordinating center, so none of the investigators on this study had access to identifiers that can link data to subjects.

1.3.2 Measures

Aim 1: Association between time period of hospitalization and failure to receive a primary PCI within 90 minutes after hospital presentation

Data source: WHAS 1999-2009

Outcome variable

The main outcome variable was delay to receipt of a primary PCI, which was defined as the time interval from hospital emergency department presentation to receipt of a primary PCI. Data abstractors were instructed to use time of first balloon inflation as the time of primary PCI. Delay to receipt of a primary PCI was categorized into ≤90 vs. >90 minutes, based on clinical guidelines that patients with STEMI receive a primary PCI within 90 minutes after emergency department presentation.[3]

Key exploratory variable

The main exploratory variable was year of hospitalization. For ease of analysis and interpretation, we aggregated the 6 individual study years (1999, 2001, 2003, 2005, 2007, and 2009) into approximate 3 time strata (1999/2001, earliest; 2003/2005, middle; and 2007/2009, most recent) for purposes of examining changing trends in our primary and secondary study outcomes.

Covariate Measures

Candidate variables considered as potential confounders/predictors were chosen based on findings from prior studies. These potential confounding variables included socio-demographic and clinical characteristics (Table 1-2).

Table 1-2 Covariate measures for Aim 1

Type	Variables
socio-demographic	self-reported age (<55, 55-64, 65-74, and ≥75 years), sex, race (white vs. non-white), marital status
history of previously diagnosed comorbidities	angina, atrial fibrillation, heart failure, hypertension, peripheral vascular disease, stroke, diabetes, chronic obstructive pulmonary disease, depression, and chronic kidney disease, and prior coronary revascularization (PCI or CABG surgery)
AMI order	initial or prior
clinical presentation at hospital admission	heart rate (beats/min), systolic blood pressure (mmHg) diastolic blood pressure (mmHg)

laboratory findings at hospital admission	glucose (mg/dl), creatinine (mg/dl)
hospital emergency department arrival	time of day (12 am-5:59 am; 6 am-11:59 am; 12 pm-5:59 pm and 6 pm-11:59 pm), day of week (weekday vs. weekend); mode of transportation

Aim 2: Association between time period of hospitalization and 30-day all-cause hospital readmissions

Data source: WHAS 1999-2009

Outcome variable

The main outcome variable was 30-day all-cause hospital readmissions among patients discharged from 3 major greater Worcester medical centers after AMI. We analyzed available data from medical record abstractions on all-cause, and cause-specfiic, hospitalizations occurring within 30 days after hospital discharge for AMI between 1999 and 2009.

Key exploratory variable

The main exploratory variable was year of hospitalization. For ease of analysis and interpretation, we aggregated the 6 individual study years (1999, 2001, 2003, 2005, 2007, and 2009) into approximate 3 time strata (1999-2001, earliest; 2003-2005, middle; and 2007-2009, most recent) for purposes of examining changing trends in our primary study outcomes.

Covariate Measures

Candidate variables considered as potential confounders/predictors were chosen based on findings from prior studies. These potential confounding variables included socio-demographic and clinical determinants (Table 1-3).

Table 1-3 Covariate measures for Aim 2

Type	Variables
socio-demographic	self-reported age (<55, 55-64, 65-74, 75-84, and ≥85 years), sex, race (white vs. non-white), marital status
history of previously diagnosed comorbidities	angina, atrial fibrillation, heart failure, hypertension, peripheral vascular disease, stroke, diabetes, chronic obstructive pulmonary disease, depression, and chronic kidney disease
hospital length of stay	days of hospitalization
AMI type	STEMI, NSTEMI
AMI order	initial or prior
development of important in-hospital complications	atrial fibrillation, cardiogenic shock, heart failure, stroke
clinical presentation at hospital admission	heart rate (beats/min), systolic blood pressure (mmHg) diastolic blood pressure (mmHg)
laboratory findings at hospital admission	glucose (mg/dl), creatinine (mg/dl)
in-hospital management	thrombolytic therapy, cardiac catheterization, PCI, and coronary artery bypass grafting (CABG)

medication at hospital discharge	angiotensin converting inhibitors (ACE-I)/angiotensin receptor blockers (ARBs), aspirin, beta blockers, and lipid lowering agents

Aim 3: Association between time period of hospitalization and 1-year post-hospital discharge all-cause mortality after a first AMI

Data source: WHAS 1975-2009

Outcome variable

The main outcome variable was 1-year post-hospital discharge all-cause mortality among patients hospitalized for a first AMI. Patients with an initial AMI were identified by either mention in the review of the hospital charts that this was the patient's first admission for an AMI or through the review of previous hospital records and electrocardiograms that failed to indicate the occurrence of a previous AMI. The approaches used to ascertain survival status after hospital discharge included a review of medical records for additional hospitalizations and a statewide and national search of death certificates using the Social Security Death Index Records for residents of the Worcester metropolitan area; follow-up was available through the end of 2012.

Key exploratory variable

The main exploratory variable was year of hospitalization. For ease of analysis and interpretation, we aggregated the 17 individual study years (1975, 1978, 1981, 1984, 1986, 1988, 1990, 1991, 1993, 1995, 1997, 1999, 2001, 2003, 2005, 2007, and 2009) into approximate 3 decade-long time strata (1975-1984, earliest; 1986-1997, middle; and

1999-2009, most recent) for purposes of examining changing trends in our primary study outcomes.

Covariate Measures

Candidate variables considered as potential confounders/predictors were chosen based on findings from prior studies. These potential confounding variables included socio-demographic and clinical factors (Table 1-4).

Table 1-4 Covariate measures for Aim 3

Type	Variables
socio-demographic	self-reported age (<55, 55-64, 65-74, 75-84, and ≥85 years), sex, race (white vs. non-white), marital status
history of previously diagnosed comorbidities	angina, atrial fibrillation, heart failure, hypertension, peripheral vascular disease, stroke, diabetes, chronic obstructive pulmonary disease, depression, and chronic kidney disease
hospital length of stay	days of hospitalization
AMI type	Q-wave, non-Q-wave; STEMI, NSTEMI
development of important in-hospital complications	atrial fibrillation, cardiogenic shock, heart failure, stroke
clinical presentation at admission	heart rate (beats/min), systolic blood pressure (mmHg) diastolic blood pressure (mmHg)
laboratory findings at admission	glucose (mg/dl), creatinine (mg/dl)

in-hospital management	thrombolytic therapy, cardiac catheterization, PCI, and coronary artery bypass grafting (CABG)
medication at hospital discharge	angiotensin converting inhibitors (ACE-I)/angiotensin receptor blockers (ARBs), aspirin, beta blockers, and lipid lowering agents

1.3.3 Statistical Analyses

Similar analytic approaches were used to address each of the 3 study aims. These approaches included descriptive analyses of the study sample characteristics, and simple regression analysis followed by multivariable-adjusted regression modeling, which was carried out to examine the three aims of this dissertation. Comparisons between various patient groups were carried out using the chi-square tests for categorical variables, and the ANOVA tests for continuous variables. The Cochran-Armitage tests and linear regression models were used to test for linear trends over time among categorical and continuous variables, respectively. All analyses were performed using SAS 9.3.

Aim 1: Association between time period of hospitalization and failure to receive a primary PCI within 90 minutes after hospital presentation: WHAS 1999-2009

Poisson regression models with robust error variance[41] were used to examine the association between the 3 time strata (1999/2001, earliest; 2003/2005, middle; and 2007/2009, most recent) and failure to receive a primary PCI within 90 minutes (≤90 vs.>90 minutes) of hospital arrival, and to determine factors associated with this outcome.

In each analysis, a series of regression models were used to adjust for the potentially confounding influence of socio-demographic characteristics, comorbidities, and in-hospital factors on the association between time and failure to receive a primary PCI within 90 minutes after hospital emergency department arrival for patients hospitalized with STEMI. For model building, potential confounders/predictors were selected based on a review of the published literature; other analytic approaches including forward selection and backward elimination were considered and compared. The unadjusted model included only time of hospitalization. Multivariable-adjusted regression models further adjusted for factors, such as socio-demographics, medical history of various cardiovascular diseases, and comorbidities and in-hospital factors.

Aim 2: Association between time period of hospitalization and 30-day all-cause hospital readmissions: WHAS 1999-2009

Logistic regression analyses[42] were used to examine the association between the 3 time strata (1999/2001, earliest; 2003/2005, middle; and 2007/2009, most recent) and 30-day all-cause hospital readmissions (yes vs. no), and to determine factors associated with 30-day all-cause readmission. Similar simple regression analyses followed by multivariable regression modeling adjusting for several potentially confounding/predictor variables of prognostic importance as described previously in aim 1 were performed. We also examined the specific causes of 30-day hospital readmissions by time period of hospitalization.

Aim 3: Association between time period of hospitalization and 1-year post-hospital discharge all-cause mortality: WHAS 1975-2009

Logistic regression analyses[42] were performed to examine the association between the 3 time strata (1975-1984, earliest; 1986-1997, middle; and 1999-2009, most recent) and 1-year post-hospital discharge all-cause mortality (dead vs. alive) and to determine factors associated with these outcomes. Similar simple regression analyses followed by multivariable regression modeling adjusting for several potentially confounding variables of prognostic importance as described previously in aim 1 were performed.

1.4 Summary

In summary, AMI remains a significant public health and clinical concern. There is a need for contemporary epidemiologic research that examines treatment practices with regards to the extent of delay in door-to-balloon time, 30-day hospital readmission rates, long-term post-hospital all-cause mortality, and factors associated with these outcomes among patients hospitalized for an AMI.

This study would contribute to the current literature in the management of patients hospitalized with AMI for several reasons. First, our investigation provided relatively contemporary and long-term trends into the changing magnitude of prognostic factors and outcomes and identified at-risk patients for 30-day hospital readmissions, which will be valuable to help evaluate current health policy and management guideline and inform necessary policy change. Second, our study benefited from the ability to track long-term trends in predictors and outcomes among patients hospitalized for an AMI, as these trends remain particularly important to monitor from a community-wide perspective, where the characteristics of patients studied have been shown to differ from those enrolled in clinical trials where more restrictive inclusion/exclusion criteria may be applied and generalizability has been limited.[43] Finally, the findings of the proposed research provided useful information that can inform the design of novel public health interventions and clinical guidelines to improve the short and long-term prognosis of men and women hospitalized with AMI.

Aim 1: our results could be used to identify at-risk patients hospitalized with STEMI for failure to receive a primary PCI within the current guideline recommended time frame and lead to the design of interventions to improve door-to-balloon time.

Aim 2: our results highlighted contemporary population-based trends in 30-day readmission rates and specific reasons for 30-day readmissions among patients discharged with AMI. Our results also helped to identify patient and clinical factors that place patients at higher risk for 30-day hospital readmissions, which can be used to design patient-centered post-discharge care to prevent subsequent readmissions and improve long-term outcomes.

Aim 3: our results provided insights into the changing characteristics, management practices, long-term outcomes, and potential impact of effective cardiac treatment approaches during the patient's index hospitalization in association with changes in long-term mortality among patients who survived their hospitalization for a first AMI. These results can hopefully lead to the development of innovative, patient-centered, intervention strategies which can improve the long-term outcomes among patients after a first AMI.

CHAPTER 2 : DECADE-LONG TRENDS IN DELAY TO THE RECEIPT OF A PRIMARY PERCUTANEOUS CORONARY INTERVENTION IN PATIENTS HOSPITALIZED WITH ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION

Abstract

Background

There are limited data available describing contemporary trends in door-to-balloon time among patients hospitalized with ST-segment elevation myocardial infarction (STEMI) who receive a primary percutaneous coronary intervention (PCI) in the broader community setting. We examined decade-long trends (1999-2009) in, and factors associated with, door-to-balloon time within 90 minutes among patients hospitalized with STEMI.

Methods

Residents of the Worcester, MA, metropolitan area hospitalized with STEMI and receiving a primary PCI at 3 PCI-capable medical centers on a biennial basis (1999-2009) comprised the study population (n=548). Multivariable Poisson regression analyses were used to examine the factors of failing to receive a primary PCI within 90 minutes after emergency department (ED) arrival.

Results

The average age of this population was 61.8 years, 31.2% were women, and 92.0% were white. During the years under study, 43.2% of patients received a primary PCI within 90 minutes of ED arrival; this proportion increased dramatically from 1999/2001 (11.6%) to 2007/2009 (70.5%) in crude as well as multivariable adjusted analyses. Older age, having previously diagnosed diabetes and chronic kidney disease, prior CABG surgery, and arriving at the ED by car/walked-in and during off-hours were significantly associated with a higher risk of failing to receive a primary PCI within 90 minutes.

Conclusions

The likelihood of receiving a timely primary PCI in patients hospitalized with STEMI increased dramatically during the years under study. Several high risk groups were identified for purposes of heightened surveillance and intervention efforts to reduce the likelihood of failing to receive a timely primary.

2.1 Introduction

The prompt administration of coronary reperfusion therapy for patients with an evolving acute myocardial infarction (AMI) is crucial in reducing mortality and the risk of serious clinical complications in these patients.[3] During the past decade, primary percutaneous coronary intervention (PCI) has gradually replaced thrombolysis as the main revascularization strategy for patients presenting with ST-segment elevation myocardial infarction (STEMI), since primary PCI has been found to be superior to thrombolytic therapy when performed rapidly by expert teams.[2] Because the effectiveness of a primary PCI may be limited by delays in its prompt delivery, current clinical guidelines have recommend a door-to-balloon time of 90 minutes or less for patients hospitalized with STEMI who undergo a primary PCI.[3]

To date, there are little population-based data available describing contemporary trends in the magnitude of, and factors associated with, door-to-balloon times in patients experiencing an STEMI;[5,6,27,28] the limited studies in this area have shown mixed results of improvement in door-to-balloon time during varying study years and an inconsistent profile of patients who fail to be treated within recommended guidelines.[5,6,27,28] Inasmuch, there is a need to describe relatively contemporary long-term trends in the extent of, and potential risk factors associated with, delays in door-to-balloon time among patients hospitalized with STEMI, particularly from the more generalizable perspective of a population-based investigation.

The primary objective of our observational study was to describe decade-long (1999-2009) trends in the extent of delay from hospital emergency department presentation to initiation of a primary PCI among patients hospitalized with STEMI. Our secondary objective was to examine factors associated with the failure to receive a primary PCI within 90 minutes among patients hospitalized with STEMI. Data from the Worcester Heart Attack Study were used for purposes of this investigation.[12–15]

2.2 Methods

Described elsewhere in detail,[12–15] the Worcester Heart Attack Study is an ongoing population-based investigation examining long-term trends in the descriptive epidemiology of AMI in residents of the Worcester, MA, metropolitan area (2000 census= 478,000) hospitalized at all 16 medical centers in Central Massachusetts on an approximate biennial basis between 1975 and 2009.[12–15] Due to hospital closures, mergers, or conversion to long-term care or rehabilitation facilities, fewer hospitals (n=11) have been providing care to greater Worcester residents during the most recent years under study.

Computerized printouts of patients discharged from all greater Worcester hospitals with possible AMI [International Classification of Disease (ICD) 9 codes: 410-414, 786.5] were identified. Cases of possible AMI were independently validated using predefined criteria for AMI;[12–15] these criteria included a suggestive clinical history, increases in several serum biomarkers (e.g., creatine kinase (CK), CK-MB, and troponin values), and serial electrocardiographic findings during hospitalization consistent with the presence of AMI. Patients who satisfied at least 2 of these 3 criteria, and were residents of the Worcester metropolitan area since this study is population-based, were included. A diagnosis of STEMI was made when new ST-segment elevation was present at the J point in 2 or more contiguous leads.[44]

For purposes of the present study, we restricted our sample to adult residents of the Worcester metropolitan area who were hospitalized with STEMI and received a primary PCI between 1999 and 2009. Patients who received thrombolytic therapy during hospitalization were excluded since they did not meet the criteria for receiving a primary PCI. Door-to-balloon time was defined as the time interval from the patient's arrival at the hospital emergency department to inflation of the balloon to restore coronary flow. Patients who were transferred from another hospital were excluded, since the clinical guidelines of door-to-balloon time within 90 minutes were recommended for those who were initially seen at a PCI-capable hospital. To increase the likelihood that we were assessing patients who received a primary PCI, we excluded patients with delay times which exceeded 6 hours.[27,45] Patients who did not have door-to-balloon times documented were also excluded. This study was approved by the Institutional Review Board at the University of Massachusetts Medical School.

Data Collection

Trained nurses and physicians abstracted information on patients' demographic characteristics, medical history, clinical data, and treatment practices through the review of hospital medical records. Information on patient's socio-demographic characteristics (e.g., age, sex, race, marital status), year of hospitalization, history of previously diagnosed comorbidities (e.g., stroke, diabetes, heart failure), prior coronary revascularization [PCI or coronary artery bypass graft surgery (CABG)], AMI order (initial vs. prior), hospital emergency department arrival day and time, mode of transportation (car/walked-in vs. ambulance), and door-to-balloon time were collected.

Data Analysis

For ease of analysis and interpretation, we aggregated the 6 individual study years into 3 two-year strata (1999/2001, earliest; 2003/2005, middle; and 2007/2009, most recent) for purposes of examining trends in our principal study outcomes. Door-to-balloon time was further dichotomized as ≤90 vs. >90 minutes, based on current clinical guidelines recommendations.[3] Differences in the distribution of patient demographic and clinical characteristics between patients hospitalized during the 3 time periods were examined using the ANOVA test for continuous variables and the chi-square test for categorical variables. The Cochran-Armitage tests and linear regression models were used to test for linear trends over time among categorical and continuous variables, respectively.

Delay to the receipt of a primary PCI was examined by calculating mean and median door-to-balloon time, and the frequency of receipt of a primary PCI within 90 minutes among patients hospitalized with STEMI during the years under study. Due to the common nature of the primary outcome (i.e., >10%) and the advantage of providing relative risk estimates, multivariable adjusted Poisson regression models with robust error variance[41] were used to examine the association between the main explanatory variable of time period of hospitalization (1999-2001, earliest; 2003-2005, middle; and 2007-2009, most recent) and the outcome of whether or not patients failed to receive a primary PCI within 90 minutes after hospital emergency department arrival (i.e., door-to-balloon time: >90 vs. ≤90 minutes) while adjusting for several potentially confounding variables of prognostic importance; hospital dummy variables were included as fixed effects in our regression models. Since a linear relationship between the 3 time periods of hospitalization and the outcome of failure to receive a primary PCI within 90 minutes was not assumed, we dummy coded this variable with the earliest study years (1999/2001) serving as the reference group.

Several covariates associated with delay to the receipt of a primary PCI in patients hospitalized with STEMI in prior studies were examined[4–6,46] These factors included age, sex, race (white vs. non-white), marital status (married vs. not married), previously diagnosed comorbid conditions (angina, atrial fibrillation, heart failure, hypertension, peripheral vascular disease, stroke, diabetes, chronic obstructive pulmonary disease, depression, and chronic kidney disease), prior coronary revascularization (PCI or CABG surgery), AMI order (initial vs. prior), and hospital emergency department arrival time (regular hours: 8 am-6 pm, weekday vs. off-hours: before 8 am or after 6 pm, weekday and weekend) and mode of transportation (car/walked-in vs. ambulance). We repeated these same analyses restricted to patients hospitalized in 2007/2009 to examine factors associated with failure to receive a primary PCI within 90 minutes in the most recent study cohorts.

The results of our Poisson regression models with robust error variance were presented as multivariable adjusted risk ratios (RR) and accompanying 95% confidence intervals (CI). All statistical analyses were conducted using SAS version 9.3 (SAS Institute, Inc, Cary, North Carolina).

2.3 Results

Study population characteristics

The study population consisted of 548 adult residents of the Worcester metropolitan area who were hospitalized with STEMI and received a primary PCI at 3 PCI-capable hospitals in central Massachusetts between 1999 and 2009. Overall, the average age of this population was 61.8 years, 31.2% were women, the majority were white (92.0 %), and 62.3% were married. In addition, 76.3% of our study sample was hospitalized for an initial AMI, 22.0% arrived at participating hospitals either by car/walked-in, and 56.8% arrived at the emergency departments during off-hours. There was a significant increase in the proportion of patients who presented at the emergency departments during off-hours during the years under study (Table 2-1).

During the most recent years under study, patients who were hospitalized with STEMI and received a primary PCI were more likely to have a history of peripheral vascular disease, or depression, compared to those hospitalized with STEMI during earlier study periods (Table 2-1).

Trends in door-to-balloon time

The average delay time from the patient's arrival at the hospital emergency department to inflation of the balloon to restore coronary flow during the years under study was 110 minutes. There was a marked decrease in this mean delay time from

1999/2001 (146 minutes) to 2007/2009 (82 minutes) (Figure 2-1). The median delay time from the patient's arrival at the hospital emergency department to balloon inflation during the years under study was 91 minutes. There was also a significant decrease in the median duration of delay from 1999/2001 (143 minutes) to 2007/2009 (71 minutes) (Figure 2-1).

Among all study patients who underwent a primary PCI, 43.2% of these patients received the intervention within 90 minutes after their emergency department arrival. There was a dramatic increase in the proportion of STEMI patients who received a primary PCI within guideline-recommended 90 minutes between 1999/2001 (11.6%) and 2007/2009 (70.5%) (p for trend <0.001) (Figure 2-1). Among all study patients who received a primary PCI within 90 minutes, 46.0% were treated during the first hour after hospital emergency department arrival; this proportion significantly increased from 18.2% in 1999/2001 to 53.7% in 2007/2009.

In examining changing trends in the failure to receive a primary PCI within 90 minutes, after adjusting for several demographic characteristics and clinical factors, there was a significant reduction in the risk of failing to receive a primary PCI within 90 minutes among patients hospitalized in 2003/2005 (RR=0.82, 95% CI=0.71-0.96) and in 2007/2009 (RR=0.33, 95% CI=0.26-0.41), compared with those hospitalized in 1999/2001 (Table 2-2).

Factors associated with failure to receive a primary PCI within 90 minutes

Using multivariable adjusted regression analyses, we examined the role of various prognostic factors associated with failure to receive a primary PCI within 90 minutes in all study patients (Table 2-2). Older age (>75 years), having previously diagnosed diabetes and chronic kidney disease, having previously undergone CABG surgery, and arriving at the emergency department by car/walked-in and during off-hours were significantly associated with a higher risk of failing to receive a primary PCI within 90 minutes (Table 2-3). When we examined factors associated with failure to receive a primary PCI within 90 minutes in the most recent patient populations (2007/2009), having previously diagnosed diabetes, and arriving at the emergency department by car/walked-in and during off-hours were significantly associated with a higher risk of failing to receive a timely primary PCI.

2.4 Discussion

The results of this observational study suggest that, among greater Worcester residents who were hospitalized for an STEMI and received a primary PCI at 3 PCI-capable hospitals in central MA between 1999 and 2009, there was a 6 fold increase in the proportion of patients who received a primary PCI within guideline-recommended 90 minutes during the years under study. Older age, having previously diagnosed diabetes and chronic kidney disease, having previously undergone CABG surgery, and arriving at the emergency department by car/walked-in and during off-hours were significantly associated with a higher likelihood of failing to receive a primary PCI within 90 minutes at participating study hospitals.

Trends in, and magnitude of, door-to-balloon time

Timely medical care is crucial to reducing mortality and the risk of serious clinical complications in patients with AMI. This is because it can maximize the benefits of evidence-based treatments and possibly reduce the likelihood of sudden cardiac deaths and the eventual size of the infarct. Although primary PCI has been shown to improve outcomes in patients with STEMI, its effectiveness may be limited by delays in its more timely delivery.[3]

Since 1999, clinical practice guidelines for the management of patients with STEMI have recommended door-to-balloon times of 90 minutes or less.[3,40,47] However, earlier data from the National Registry of Myocardial Infarction (NRMI), which examined 33,647 patients hospitalized with STEMI who received a primary PCI between 1999 and 2002 at 421 U.S. hospitals, reported that only 35% of patients were treated within the recommended 90 minutes after arrival at the hospital; meaningful improvements in door-to-balloon times over the study period were not observed.[5]

These discouraging findings have led to several national efforts dedicated to reducing door-to-balloon time in patients hospitalized with STEMI. The Centers for Medicare and Medicaid Services (CMS) and the Joint Commission began using door-to-balloon time as a performance measure in 2002.[48] In 2006, the CMS began publicly reporting hospital achievement of door-to-balloon times of 90 minutes or less. In November 2006, the American College of Cardiology (ACC), the American Heart Association (AHA), and several other organizations launched the "Door to Balloon

(D2B): An Alliance for Quality" campaign, with the goal of increasing the percentage of STEMI patients who would receive a primary PCI within 90 minutes of presentation at a PCI-capable hospital to 75%.[49] In May 2007, the AHA launched Mission: Lifeline, another national initiative designed to educate patients and providers about the importance of rapid response to STEMI and to help hospitals create coordinated STEMI diagnostic and treatment systems.[50]

Several studies in the U.S. have shown reductions in door-to-balloon times since these national efforts have been employed.[6,27,28] Findings from the Blue Cross Blue Shield of Michigan Cardiovascular Consortium of 8,771 patients with STEMI who underwent a primary PCI between 2003 and 2008 showed that the median door-to-balloon time had decreased from 113 minutes in 2003 to 76 minutes in 2008 ($p<.001$). In addition, the percentage of patients who were revascularized with a door-to-balloon time of less than 90 minutes significantly increased from 29% in 2003 to 67% in 2008 ($p<.001$).[6] A prior study which examined data from more than 300,000 Medicare patients at 900 U.S. hospitals found that door-to-balloon times declined from a median of 96 minutes in 2005 to 64 minutes in 2010. There were corresponding increases in the percentage of patients who had door-to-balloon times <90 minutes (44.2% to 91.4%).[27] A recent study analyzed data from 96,738 admissions for patients with STEMI who underwent a primary PCI from July, 2005 through June, 2009 at 515 U.S. hospitals participating in the CathPCI Registry. Median door-to-balloon times declined significantly from 83 minutes in the first year to 67 minutes in the most recent study year, and the percentage of patients for whom the door-to-balloon time was 90 minutes or less increased from 59.7% to 83.1% during the years under study ($p<.001$).[28] Consistent with the timeline of national efforts in reducing door-to-balloon time and prior research results, our current study observed, particularly in 2007/2009, a substantial decrease in the median door-to-balloon time and a dramatic increase in the proportion of patients who received a primary PCI within the guideline-recommended 90 minutes.

While reducing door-to-balloon times has shown considerable improvements in U.S. hospitals over time, some unintended consequences of these efforts merit attention. Corresponding to the national effort initiated by the ACC in 2006 to reduce door-to-balloon times, several strategies and organizational factors associated with shorter door-to-balloon time have been identified and promoted.[51–53] These efforts including encouraging emergency medical service providers and emergency department physicians to activate the cardiac catheterization laboratory prior to consultation with a staff cardiologist, which may have achieved a significant reduction in door-to-balloon time, while increasing the rate of "false activations" (defined as emergent cardiac catheterization laboratory activation when the patient was determined to not require emergent transfer from the emergency department to the cardiac catheterization laboratory for a primary PCI). Indeed, a prior study of all adult patients with a suspected STEMI between 2007 and 2011 at the University of Michigan Hospital noted that the median door-to-balloon time decreased from 67 minutes in 2007 to 55 minutes in 2011, but the false activation rates increased from 15% to 40% of all cases.[54] When the cardiac catheterization laboratory is activated emergently, resources must be collected to prepare for a potential patient. During off-hours, this often requires bringing in a full team to begin preparing the cardiac catheterization laboratory. These false cardiac catheterization laboratory activations can be a drain on staff and a poor use of resources. Therefore, future studies of healthcare system interventions to decrease the rates of false cardiac catheterization laboratory activations while maintaining short door-to-balloon times remain warranted.

Factors associated with failure to receive a primary PCI within 90 minutes after emergency department arrival

A recent systematic review and meta-analysis examining the association between off-hour presentation and outcomes in patients with AMI has suggested that patients with STEMI presenting during off-hours have longer door to balloon times.[55] A prior study examined data from the Get With the Guidelines–Coronary Artery Disease databases between 2000 and 2005 found that among the 5,454 patients with STEMI who received a primary PCI, those arriving during off-hours were less likely to achieve door-to-balloon times ≤90 minutes compared with those arriving during regular-hours.[56] In the NRMI study of 33,647 patients with STEMI treated with a primary PCI from 1999 to 2002,[46] 54% of patients were treated during off-hours; door-to-balloon times were substantially longer during off-hours (116 minutes) than regular hours (95 minutes). Longer door-to-balloon times during off-hours were primarily due to a longer interval between obtaining the electrocardiogram and patient arrival at the cardiac catheterization laboratory. Similarly, our study observed that patients with STEMI admitted to the emergency department during off-hours were more likely to fail to receive a timely primary PCI, compared with those admitted during regular hours. Approaches to provide onsite staffing of the cardiac catheterization laboratory and rapid access to interventional cardiologists during off-hours, including consideration of the costs of providing such coverage, would be beneficial.

In the current investigation, we found that patients with STEMI who arrived at the emergency department by car/walked-in were more likely to fail to receive a primary PCI within 90 minutes, compared with those who arrived at the emergency department by ambulance. Pre-hospital electrocardiograms (ECGs) have been recommended and are increasingly used in the management of patients with chest pain transported by emergency medical services (EMS),[3] such that paramedics can rapidly diagnose and triage patients with a suspected STEMI before hospital arrival. Since hospitals can use the pre-hospital ECG results to activate the cardiac catheterization lab while the patient is en route to the hospital, door-to-balloon times are shorter than when activation is initiated after the patient's arrival to the emergency department. Several studies have shown that the use of pre-hospital ECGs is associated with shorter door-to-balloon times.[57,58] A prior study analyzed data from the NCDR (National Cardiovascular Data Registry) ACTION (Acute Coronary Treatment and Intervention Outcomes Network) registry of 12,097 patients hospitalized with STEMI in 2007 reported that median door-to-balloon times for patients undergoing a primary PCI were significantly shorter for patients with a pre-hospital ECG .[58]

Although our study identified several patient related factors, such as older age, history of previously diagnosed diabetes and chronic kidney disease, and having previously undergone CABG surgery, to be significantly associated with failing to receive a primary PCI within the guideline-recommended time frame, a prior systematic review of various factors associated with door to balloon time in patients with STEMI treated with PCI has found mixed findings with regards to the strength of association of these factors between studies.[59] While these differences in study results may be due to differences in study design, definitions of key covariates, patient populations under study, and sample size considerations, our study identified several patient groups at high risk for failing to be treated in a timely manner in whom further surveillance and/or hospital/provider educational efforts might be directed.

Although several studies, including ours, have suggested encouraging reductions in door-to-balloon times over the years, healthcare providers should continue their efforts to educate patients about the symptoms of AMI and importance of calling 911 to facilitate EMS triage, treatment, and transport to reduce not only in-hospital but also prehospital treatment delays. Indeed, delays in patient's medical care seeking behavior following the development of acute coronary symptoms continue to remain unduly long and have improved little over time.[60,61]

Study strengths and imitations

The strengths of the present community-based study include the examination of relatively contemporary decade-long trends in, and factors associated with, door-to-balloon time among patients hospitalized with STEMI. Several limitations need to be acknowledged, however, in the interpretation of the present findings. Since our study population included only patients who had been hospitalized at 3 PCI-capable hospitals in central MA, one needs to be careful in extrapolating our findings to those who reside in other geographic areas. Because study patients were predominantly white, the generalizability of our findings to other race/ethnic groups may be limited. In addition there is the potential for unmeasured confounding in any of our observed associations since we did not have information available on several patient-associated characteristics, such as education, psychosocial factors, and treatment preference, as well as healthcare system level factors, which may have affected door-to-balloon times.

Conclusions

The results of the present investigation provide insights into contemporary trends in door-to-balloon time, and potential factors associated with an increased risk of failing to receive a primary PCI within guideline-recommended 90 minutes, among patients who were hospitalized with STEMI on an alternating yearly basis between 1999 and 2009. The likelihood of receiving a primary PCI within guideline-recommended 90 minutes in these patients has increased remarkably during the years under study. Although most of the identified risk factors for the less than optimal timely receipt of a primary PCI were not modifiable, our findings can hopefully lead to better development of innovative, patient-centered, intervention strategies which can further reduce the door-to-balloon times of patients hospitalized with STEMI.

Table 2-1 Characteristics of patients who were hospitalized with an ST-segment elevation myocardial infarction (STEMI) and received a primary percutaneous coronary intervention (PCI): Worcester Heart Attack Study, 1999-2009

	1999-2001 (N=95)	2003-2005 (N=202)	2007-2009 (N=215)	P Value*	P for trend†
Age, mean, years	61.2	62.3	61.6	0.75	0.77
Age, %, years				0.24	
<55	30.5	33.7	31.8		
55-64	28.4	23.8	32.2		
65-74	24.2	19.3	14.7		
75+	16.8	23.3	21.2		
Female, %	33.7	30.7	30.7	0.84	0.65
White, %	91.9	92.9	91.5	0.86	0.78
Married, %	72.5	56.9	63.0	0.04	0.35
Initial AMI, %	73.7	77.7	76.1	0.74	0.79

Emergency department off-hours arrival, %	43.2	57.9	61.0	0.011	0.006
Transport to hospital by car/walked-in, %	13.6	25.5	21.9	0.09	0.34
Medical history					
Angina, %	18.9	11.4	3.6	<.0001	<.0001
Atrial fibrillation, %	5.3	4.0	3.2	0.66	0.37
Heart failure, %	5.3	7.9	5.2	0.44	0.69
Hypertension, %	60.0	60.4	60.6	0.99	0.93
Peripheral vascular disease, %	4.2	8.9	14.3	0.015	0.004
Stroke, %	6.3	6.4	2.0	0.043	0.028
Diabetes, %	32.6	21.3	24.7	0.11	0.30
Chronic obstructive pulmonary disease, %	8.4	11.9	9.6	0.59	0.99
Depression, %	5.3	13.9	17.9	0.011	0.003
Chronic kidney disease, %	5.3	8.9	10.4	0.33	0.15
Prior percutaneous coronary intervention, %	14.7	18.8	21.9	0.30	0.13
Prior coronary artery bypass graft surgery, %	5.3	4.0	4.4	0.88	0.81

Physiological parameters on admission					
Initial heart rate, mean, beats/min	78.8	78.6	79.2	0.95	0.86
Systolic blood pressure, mean, mmHg	133.5	135.5	138.4	0.35	0.19
Diastolic blood pressure, mean, mmHg	81.0	78.4	81.7	0.21	0.79
Serum glucose, mean, mg/dL	175.9	166.2	162.8	0.31	0.13
Estimated glomerular filtration rate, mean, mL/min per 1.73 m^2	72.1	68.4	62.1	<.0001	<.0001

* P-values derived from ANOVA tests for continuous variables and chi-square tests for categorical variables.

† P-values derived from Cochran-Armitage tests for categorical variables and linear regression models for continuous variables.

Table 2-2 Association between time period of hospitalization and failure to receive a primary percutaneous coronary intervention (PCI) within 90 minutes among patients who were hospitalized with an ST-segment elevation myocardial infarction (STEMI): Worcester Heart Attack Study, 1999-2009

	Failure to receive a primary PCI within 90 minutes	Adjusted for sociodemographics, comorbidities, prior revascularization *	Further adjusted for in-hospital factors†
Study Period	%	Adjusted RR (95% CI)	
1999/2001	88.4	1.00	1.00
2003/2005	75.7	0.90 (0.79-1.01)	0.82 (0.71-0.96)
2007/2009	29.5	0.35 (0.28-0.44)	0.33 (0.26-0.41)

RR: risk ratios; CI: confidence intervals

* Adjusted for sociodemographics, previously diagnosed comorbid conditions, prior coronary revascularization (PCI or CABG surgery), and participating hospitals.

† Adjusted for sociodemographics, previously diagnosed comorbid conditions, prior coronary revascularization (PCI or CABG surgery), AMI order, emergency department arrival time and mode of transportation, and participating hospitals.

Table 2-3 Association between various prognostic factors and failure to receive a primary percutaneous coronary intervention (PCI) within 90 minutes among patients who were hospitalized with an ST-segment elevation myocardial infarction (STEMI): Worcester Heart Attack Study, 1999-2009

	Adjusted for sociodemographics, comorbidities, prior revascularization*	Further adjusted for in-hospital factors†
Factors	Adjusted RR (95% CI)	
Age <55	1.00	1.00
Age 55-64	0.96 (0.78-1.17)	0.93 (0.75-1.14)
Age 65-74	1.07 (0.86-1.32)	1.04 (0.83-1.30)
Age 75	1.29 (1.05-1.58)	1.34 (1.09-1.65)
Female (vs. Male)	1.05 (0.90-1.22)	1.08 (0.92-1.26)
White (vs. non-White)	0.87 (0.66-1.15)	0.84 (0.62-1.14)

Married (vs. not Married)	1.01 (0.88-1.18)	1.02 (0.88-1.19)
<u>Comorbid condition</u>		
Angina	1.10 (0.91-1.31)	1.19 (0.97-1.45)
Atrial fibrillation	1.12 (0.84-1.49)	1.20 (0.93-1.56)
Heart failure	0.97 (0.75-1.26)	0.98 (0.75-1.28)
Hypertension	0.85 (0.73-0.98)	0.85 (0.74-0.99)
Peripheral vascular disease	0.85 (0.65-1.10)	0.83 (0.64-1.07)
Stroke	0.84 (0.60-1.17)	0.82 (0.60-1.13)
Diabetes	1.23 (1.05-1.44)	1.27 (1.07-1.50)
Chronic obstructive pulmonary disease	1.10 (0.89-1.35)	1.06 (0.86-1.30)
Depression	0.86 (0.67-1.10)	0.84 (0.65-1.08)
Chronic kidney disease	1.16 (0.96-1.40)	1.25 (1.02-1.54)
Prior PCI	0.98 (0.81-1.19)	0.87 (0.70-1.07)
Prior CABG surgery	1.53 (1.18-1.99)	1.62 (1.20-2.19)
Initial AMI (vs. Prior AMI)		0.86 (0.72-1.04)

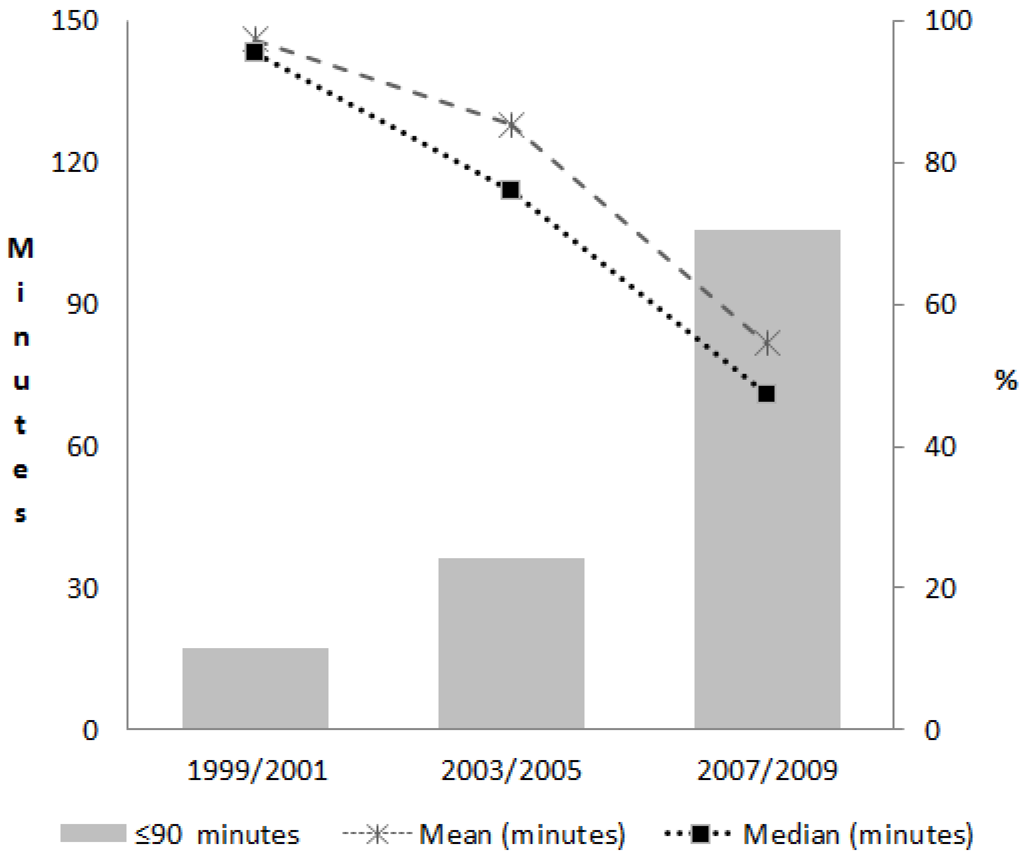
Arrival at emergency department during off-hours (vs. regular hours)	1.49 (1.28-1.73)
Arrival at emergency department by car/walked-in (vs. ambulance)	1.52 (1.29-1.80)

RR: risk ratios; CI: confidence intervals

* Adjusted for study period, sociodemographics, previously diagnosed comorbid conditions, prior coronary revascularization (PCI or CABG surgery), and participating hospitals.

† Adjusted for study period, sociodemographics, previously diagnosed comorbid conditions, prior coronary revascularization (PCI or CABG surgery), AMI order, emergency department arrival time and mode of transportation, and participating hospitals.

Figure 2-1 Trends in door-to-balloon time among patients hospitalized with ST-segment elevation myocardial infarction (STEMI): Worcester Heart Attack Study, 1999-2009



CHAPTER 3 : DECADE-LONG TRENDS IN 30-DAY REHOSPITALIZATION RATES AFTER ACUTE MYOCARDIAL INFARCTION

Abstract

Background

There are limited data available describing relatively contemporary trends in 30-day rehospitalizations among patients who survive hospitalization after an acute myocardial infarction (AMI) in the community setting. We examined decade-long (1999-2009) trends in, and factors associated with, 30-day rehospitalizations in patients discharged from two central Massachusetts (MA) hospitals after AMI.

Methods

Residents of the Worcester, MA, metropolitan area discharged after AMI from two central MA hospitals on a biennial basis between 1999 and 2009 comprised the study population (n=4,911). Logistic regression analyses were used to examine the association between selected factors and 30-day rehospitalizations.

Results

The average age of this population was 69 years, 42% were women, and 93% were white. During the years under study, 19.1% of patients were rehospitalized within 30 days after hospital discharge. Crude 30-day rehospitalization rates decreased from 20.1% in 1999/2001 to 16.7% in 2007/2009. After adjusting for several patient characteristics, there was a trend toward a reduced odds of being rehospitalized in 2007/2009 (OR=0.79, 95% CI=0.62-1.00) compared with 1999/2001; this trend was slightly attenuated after further adjustment for hospital treatment practices. Female sex, having previously diagnosed diabetes and chronic kidney disease, in-hospital heart failure, and having a ST-segment elevation MI were associated with an increased odds of being rehospitalized.

Conclusions

The likelihood of being rehospitalized during the first month after hospital discharge for AMI remained relatively high during the years under study. Several high risk groups were identified for purposes of heightened surveillance and/or intervention efforts to reduce the likelihood of being readmitted.

3.1 Introduction

Cardiovascular disease remains the leading cause of morbidity and mortality in the United States.[1] Acute myocardial infarction (AMI) is a common manifestation of underlying coronary heart disease which affected more than 800,000 adults in the U.S. in 2010.[1] Concomitant with advances in pre-hospital and hospital treatment, in-hospital survival after AMI has dramatically improved.[20] Inasmuch, many patients are being discharged from the hospital into the community who are at risk for being readmitted to the hospital due to a variety of contributory factors and reasons.[31,32] Although not all hospital readmissions can be prevented, excess readmissions within a short time frame can be a marker of poor quality of care and efficiency. Since the Centers for Medicare and Medicaid Services (CMS) began publicly reporting 30-day risk-standardized readmission rates for heart failure, AMI, and pneumonia as performance measures,[29] 30-day hospital readmission rates have become a quality performance measure for patients hospitalized with AMI[7,29]

There has been considerable interest from hospitals and clinicians to better understand and improve modifiable factors associated with 30-day hospital readmissions, which are increasingly being linked to hospital reimbursement.[9] Although several studies have reported 30-day rehospitalization rates among patients surviving hospitalization for AMI,[8,32,62] few have examined risk factors for being readmitted to the hospital during the following month using multivariable regression analyses. Moreover, there are little contemporary data that describe long-term trends in 30-day rehospitalization rates, the reasons for rehospitalization, as well as sociodemographic, clinical, and treatment related factors that may affect 30-day rehospitalization rates among patients surviving an AMI.

Our primary study objective was to describe relatively contemporary decade long (1999-2009) trends in the frequency of 30-day rehospitalizations among patients surviving hospitalization for an AMI. Our secondary study objective was to describe patient characteristics, treatment practices, and clinical factors associated with an increased risk of 30-day rehospitalizations among residents of central Massachusetts (MA) discharged from the three principal medical centers in central MA after an AMI. Data from the Worcester Heart Attack Study were used in this study.[12–15]

3.2 Methods

Described elsewhere in detail,[12–15] the Worcester Heart Attack Study is an ongoing population-based investigation examining long-term trends in the descriptive epidemiology of AMI in residents of the Worcester, MA, metropolitan area (2010 census=518,000) hospitalized at all 16 medical centers in Central MA on an approximate biennial basis between 1975 and 2009. [12–15] Due to hospital closures, mergers, or conversion to long-term care or rehabilitation facilities, fewer hospitals (n=11) have been providing care to greater Worcester residents during more recent years.

Computerized printouts of patients discharged from all greater Worcester hospitals with possible AMI [International Classification of Disease (ICD) 9 codes: 410-414, 786.5] were identified and cases of possible AMI were independently validated using predefined criteria for AMI.[12–15] These criteria included a suggestive clinical history, increases in several serum biomarkers (e.g., creatine kinase (CK), CK-MB, and troponin values), and serial electrocardiographic findings during hospitalization consistent with the presence of AMI. Patients who satisfied at least 2 of these 3 criteria, and were residents of the Worcester metropolitan area since this study is population-based, were included.

Because the focus of the current study was rehospitalization after hospital discharge for AMI, we included adult residents of the Worcester metropolitan area who survived their index hospitalization for AMI on a biennial basis between 1999 and 2009. This time period was selected due to its contemporary nature and data availability. We further restricted our study population to patients hospitalized at the three largest tertiary care and community medical centers in central MA. This was done since the majority (approximately 90%) of patients hospitalized for AMI in central MA was discharged from these facilities, which also have excellent electronic medical records. The patient' index hospitalization occurred in either of the three participating hospitals as did any subsequent rehospitalization. Patients who had their index hospitalization or the rehospitalization outside of these three major medical centers were not included in this study. This study was approved by the Institutional Review Board at the University of Massachusetts Medical School.

Data Collection

Trained nurses and physicians abstracted information on patient's demographic characteristics, medical history, clinical data, and treatment practices through the review of hospital medical records. These factors included patient's socio-demographic characteristics (e.g., age, sex, race, marital status), year of hospitalization, hospital length of stay, history of previously diagnosed comorbidities (e.g., stroke, diabetes, heart failure), AMI order (initial vs. prior) and AMI type [ST-segment elevation myocardial infarction (STEMI) vs. non-ST-segment elevation myocardial infarction (NSTEMI)].[3,24] Information on the development of important in-hospital complications including atrial fibrillation,[63] cardiogenic shock,[64] heart failure,[65] and stroke[66] was also collected.

Data on the receipt of thrombolytic therapy and 3 coronary diagnostic and interventional procedures [cardiac catheterization, percutaneous coronary intervention (PCI), and coronary artery bypass grafting (CABG)] during hospitalization, and pharmacotherapies at the time of hospital discharge, including the prescribing of 4 effective cardiac medications [angiotensin converting inhibitors (ACE-I)/angiotensin receptor blockers (ARBs), aspirin, beta blockers, and lipid lowering agents], were obtained.

A rehospitalization was defined as the patient's first admission to a study hospital within 30 days of discharge after their index hospitalization for AMI during the years under study. The principal reason for being rehospitalized was further categorized into either AMI, cardiovascular disease (CVD) (excluding AMI) related, or non-CVD related. Indications for CVD related hospitalizations included unstable angina, heart failure, type II diabetes mellitus, and chronic ischemic heart disease. Examples of non-CVD related hospitalizations included urinary tract infections, hemorrhage, osteoarthritis, and bone fractures.

Data Analysis

For ease of analysis and interpretation, we aggregated the 6 individual study years into 3 two-year strata (1999/2001, earliest; 2003/2005, middle; and 2007/2009, most recent) for purposes of examining trends in our principal study outcomes. Differences in the distribution of various patient demographic and clinical characteristics between patients hospitalized during the 3 aggregated time periods were examined using the ANOVA test for continuous variables and the chi-square test for categorical variables. The Cochran-Armitage tests and linear regression models were used to assess for linear trends over time among categorical variables and continuous variables, respectively.

Thirty-day rehospitalization rates were examined by calculating the frequency of having a first rehospitalization within 30 days among patients discharged from the hospital after their index AMI during the years under study. We examined the reasons for being rehospitalized during this period and calculated the cause-specific 30-day rehospitalization rates. Multivariable adjusted logistic regression analyses were performed to examine the association between the main explanatory variable of time period of hospitalization (1999-2001, earliest; 2003-2005, middle; and 2007-2009, most recent) and the outcome of whether or not the patient was rehospitalized during the following 30 days while adjusting for several potentially confounding variables of prognostic importance. Since a linear relationship between the 3 time periods and the outcome of 30-day rehospitalizations was not assumed, we dummy coded this variable with the earliest period (1999/2001) serving as the reference group.

Several covariates associated with rehospitalization after AMI in prior studies[31,32] were examined including age, sex, race (white vs. non-white), marital status (married vs. not-married), AMI order (initial vs. prior), AMI type (STEMI vs. NSTEMI), previously diagnosed comorbid conditions (angina, atrial fibrillation, heart failure, hypertension, peripheral vascular disease, stroke, diabetes, chronic obstructive pulmonary disease, depression, and chronic kidney disease), hospital clinical complications (atrial fibrillation, heart failure, cardiogenic shock, and stroke), and hospital length of stay. We further adjusted for hospital treatment practices, including the receipt of thrombolytic therapy and 3 coronary diagnostic and interventional procedures (cardiac catheterization, PCI, and CABG), and the prescribing of 4 guideline recommended cardiac medications (ACE-I/ARBs, aspirin, beta blockers, and lipid lowering agents) at the time of hospital discharge during the patient's index hospitalization in our regression analyses to examine the potential effects of hospital treatment practices on 30-day rehospitalization trends. We repeated the same analyses after excluding patients (n=157) who were not rehospitalized but died within the 30-day post-discharge period. To examine factors associated with 30-day rehospitalization in the most recent study cohorts, we carried out these regression analyses restricted to patients hospitalized in 2007/2009.

The results of our logistic regression analyses were presented as multivariable adjusted odds ratios (OR) and accompanying 95% confidence intervals (CI), which were calculated based on standard errors clustered at the hospital level to account for potential within-hospital correlation with variance adjustment through the use of Morel's small sample bias correction.[67] All statistical analyses were conducted using SAS version 9.3 (SAS Institute, Inc, Cary, North Carolina).

3.3 Results

Study population characteristics

The study population consisted of 4,911 adult residents of the Worcester metropolitan area who survived their hospitalization for AMI at the three major central MA medical centers between 1999 and 2009 (Table 3-1). Overall, the average age of this population was 69.3 years, 42.0% were women, the majority were white (93.2 %), and 55.1% were married.

During the most recent years under study, patients who survived an AMI were more likely to be younger and have a history of hypertension, peripheral vascular disease, depression or chronic kidney disease than patients hospitalized during earlier study periods (Table 3-1). Between 1999 and 2009, 35.3% of our study sample was diagnosed with a STEMI, which declined from 41.7% in 1999/2001 to 30.7% in 2007/2009. The average hospital length of stay in this study population was 5.8 days, which declined over time from 6.7 days in 1999/2001 to 4.9 days in 2007/2009 (Table 3-1). In addition, the likelihood of developing cardiogenic shock and stroke during hospitalization remained relatively low (3.4% and 1.3% overall, respectively) whereas the incidence rates of in-hospital heart failure and atrial fibrillation were considerably higher (35.3% and 18.7% , respectively) over the years under study (Table 3-1).

Thirty-day rehospitalization rates

The overall 30-day rehospitalization rate for patients who survived their index AMI during the years under study was 19.1%. The average post-discharge 30-day rehospitalization rates decreased from 1999/2001 (20.3%) to 2003/2005 (19.9%) and 2007/2009 (16.7%) (p for trend=0.013) (Table 3-2). The proportion of patients who were rehospitalized was the highest (7.2%) during the first week (0-7 days) after hospital discharge, and continued to decrease as the length of post-discharge time increased (Figure 3-1). Rehospitalizations which occurred during the first week after hospital discharge accounted for 37.7% of all 30-day rehospitalizations; this proportion decreased from 39.6% in 1999/2001 to 31.0% in 2007/2009.

In examining the specific causes of 30-day rehospitalizations, 53.2% of the identified rehospitalizations were CVD related (excluding AMI), 37.4% were non-CVD related, and 9.4% were due to a recurrent AMI during the years under study. The overall cause-specific 30-day rehospitalization rates due to CVD, non-CVD, and AMI were 10.1%, 7.1%, and 1.8%, respectively, during the years under study (Figure 3-2). The average post-discharge 30-day rehospitalization rates due to CVD (excluding AMI) (p for trend=0.03) or non-CVD (p for trend=0.03) related reasons decreased during the most recent years under study, while no significant differences in 30-day rehospitalization rates due to AMI were observed (Figure 3-2).

In examining changing trends in 30-day rehospitalizations, after adjusting for several demographic characteristics, comorbidities and in-hospital clinical factors, there was no significant difference in the odds of having a 30-day rehospitalization in

2003/2005 (OR=0.93, 95% CI=0.69-1.24), but a borderline significant trend toward a reduced odds of being rehospitalized during the subsequent 30 days (OR=0.79, 95% CI=0.62-1.00) among patients who survived an AMI in 2007/2009, in comparison with those discharged in 1999/2001 (Table 3-2). However, after further adjustment for medical procedures and treatments received during hospitalization, there were no significant differences in the odds of having a 30-day rehospitalization in 2003/2005 and in 2007/2009 compared with those discharged from the hospital in 1999/2001 (Table 3-2). We observed similar results after excluding patients who were not rehospitalized but died during the 30-day post-discharge period.

Factors associated with all-cause 30-day rehospitalizations

Using multivariable adjusted regression analyses, we examined the role of various prognostic factors associated with 30-day rehospitalizations in all study patients (Table 3-3). Female sex, a history of previously diagnosed diabetes or chronic kidney disease, development of in-hospital heart failure and a STEMI, and increased hospital length of stay were significantly associated with an increased odds of being rehospitalized for any reason within 30 days after hospital discharge. On the other hand, patients who received various coronary diagnostic and interventional procedures (cardiac catheterization and PCI or/and CABG) had a reduced odds for being rehospitalized within 30 days after hospital discharge compared with those who did not undergo these procedures (Table 3-3). Similar factors (with the exception of diabetes) were significantly associated with 30-

day rehospitalizations after excluding patients who were not rehospitalized but died during the 30-day post-discharge period.

When we examined factors associated with 30-day rehospitalization in the most recently discharged patient cohort (2007/2009), patients who developed heart failure during their index hospiatlization were at increased odds, while those who received various coronary diagnostic and interventional procedures had a reduced odds, for being rehospitalized during the following month after hospital discharge.

3.4 Discussion

The results of this large observational study suggest that, among greater Worcester residents who survived hospitalization for an AMI at the three major medical centers in central MA between 1999 and 2009, nearly 1 in 5 patients remained at risk for being rehospitalized within 30 days and 38% of all 30-day rehospitalizations occurred during the first week after hospital discharge during the years under study. Our findings suggest a slight decline in the odds of being rehospitalized during the first 30 days after hospital discharge over time though this odds was slightly attenuated after further adjustment for hospital treatment practices. In addition, we identified several demographic and clinical factors associated with an increased odds for being rehospitalized during the first month after hospital discharge for AMI that included female sex, having previously diagnosed diabetes and chronic kidney disease, in-hospital heart failure, and having a STEMI.

Trends in, and magnitude of, 30-day rehospitalization rates

Reducing hospital readmissions is a national priority to improve the quality of patient care and lower healthcare spending.[9,29,68] This is because excess hospital readmissions indicate potentially poor health care quality or inadequate coordination of post-discharge care, represent a significant burden to both patients and the healthcare system, and are costly.[9,29,68]

Several prior studies have examined 30-day rehospitalization rates after AMI.[8,32,62] Between 2007 and 2009, nearly 1 in every 5 Medicare fee-for-service patients discharged from all acute care hospitals in the U.S. after AMI was readmitted within 30 days after hospital discharge.[8] In a recent study utilizing an all-payer administrative dataset from California, which consisted of 107,256 hospitalizations for AMI among adults less than 65 years old between 2007 and 2009, the 30-day rehospitalization rate was 15%.[62] A retrospective cohort study[32] conducted in 3 hospitals in Olmsted County, MN, from 1987 to 2010 found that the 30-day readmission rates among adult patients who survived their hospitalization for a first AMI were approximately 23% during the period 1987 to 1992, 22% between 1993 and 1998, 22% between 1999 and 2004, and 19% during the most recent 5 year period under study (2005 to 2010). In our study, we found similar results in that nearly one fifth of adult greater Worcester residents who survived their hospitalization for an AMI on a biennial basis between 1999 and 2009 were readmitted to the hospital within 30 days after hospital discharge. In addition, consistent with the results of the Olmsted County, MN, study,[32] our findings suggested no significant changes in the odds of having a 30-day rehospitalization during the years under study after adjustment for several potentially confounding variables of prognostic importance.

Since June, 2009, the Centers for Medicare and Medicaid Services (CMS) began publicly reporting 30-day risk-standardized readmission rates for AMI as one of the major hospital performance measures.[29] Furthermore, the Patient Protection Affordable Care Act of 2010, through the establishment of the Medicare Hospital Readmissions Reduction Program (HRRP), has created new financial incentives to reduce readmissions because hospitals with excess readmissions can lose up to 3% of their Medicare reimbursement by 2015.[9] Although some early evidence suggests that the Medicare HRRP has had a positive impact on reducing the rates of 30-day rehospitalization among Medicare beneficiaries,[69] there remains no clear consensus on how many hospital readmissions may in all actuality be preventable. Moreover, there are also concerns about potential flaws in the methodology for determining excess readmissions and computation of the penalty to hospitals.[68] Thus, it remains of considerable public health and clinical importance to continue monitoring changing trends in 30-day rehospitalization rates after AMI given ongoing refinement of the methodological approach by CMS.

With regards to the timing of hospital readmissions, a recent study which analyzed Medicare fee-for-service claims data (2007-2009) on 30-day readmissions after hospitalization for AMI showed that approximately 40% of all 30-day readmissions occurred during the first week after hospital discharge.[8] Another recent study using 2007–2009 administrative data from the state of California found that 19% of readmissions occurred within 0–3 days, and 21% occurred during 4–7 days, after hospital discharge for AMI.[62] Similar to these results, our study found that 38% of all 30-day rehospitalizations occurred during the first week after hospital discharge for AMI. These findings suggest that proper arrangement of transitional care, and continuing follow up with patients during the first several days to first week post hospital discharge, can be beneficial in reducing 30-day readmission rates among these patients. Encouragingly, we also observed a decline in the proportion of patients who were readmitted during this particularly high risk period during the years under study which may suggest that efforts at reducing hospital readmissions may be paying dividends in reducing short-term hospital readmissions.

Causes and predictors for 30-day rehospitalizations

A retrospective cohort study of adult patients in Olmsted County, MN[32] who were discharged from the hospital after a first AMI found that 43% of 30-day rehospitalizations after AMI were related to the incident AMI, 30% were unrelated, and 27% had an unclear relationship. The investigators also reported that about 8% of all 30-day rehospitalizations were due to a recurrent AMI.[32] A recent study of Medicare fee-for-service beneficiaries hospitalized for AMI at all acute care hospitals in the U.S. between 2007 and 2009 showed that 10% of patients were readmitted for the same condition after their index AMI hospitalization.[8] We observed similar results in that nearly 10% of all 30-day rehospitalizations were due to AMI, and a significant proportion (37%) of all 30-day rehospitalizations was non-CVD related. As the prevalence of comorbid conditions and aging of the American population increase over time, and efforts continue to be focused on the enhanced use of effective secondary prevention strategies to improve the post-discharge outcomes of patients with AMI, 30-day rehospitalizations after AMI due to non-CVD causes need further attention.

For example, recent research has suggested that patients discharged from the hospital may be vulnerable to "post-hospitalization syndrome," which puts them at risk for rehospitalization for conditions unrelated to their initial hospitalization.[70] Further research is needed to confirm the association between this syndrome and other hospital and post-discharge factors that may place patients at risk for non-CVD related hospital readmissions, and identify effective strategies for reducing readmissions.

Although efforts remain ongoing to find strategies that hospitals can employ to prevent many readmissions, there is an ongoing debate on whether the hospital is the appropriate entity to be held accountable for all readmissions, particularly when many of the events and circumstances that are associated with readmission may take place outside of the hospital setting and after the administration of effective acute care. These factors include patients' lifestyle behaviors and practices, employment, marital, and financial status, adherence to discharge instructions and medications, and the availability and quality of post-discharge care. Thus, reducing the frequency of hospital readmissions requires considerable collaborations, not only from hospitals, but also from patients and their caregivers and other community professionals and providers across the continuum of health.

Due to ongoing and planned changes in national reimbursement policies,[9] there has been great interest from healthcare providers to better understand and improve modifiable factors associated with 30-day rehospitalizations. A recent study in Olmsted County, MN examined factors associated with 30-day rehospitalizations after an incident AMI.[32] The investigators found that certain comorbid conditions (i.e., diabetes, anemia, COPD), a longer hospital stay, and complications of coronary angiography and revascularization or reperfusion were associated with an increased risk of being rehospitalized.[32] Our study also observed similar results in that patients with a history of previously diagnosed diabetes and chronic kidney disease, development of in-hospital heart failure, and increased hospital length of stay were significantly associated with an increased odds of being rehospitalized during the first month after hospital discharge for an AMI. Although most of these factors are not modifiable, these findings suggest that healthcare providers should pay extra attention to these high risk groups of patients to prevent potential early readmissions when planning hospital discharge and post discharge management.

Despite the potential for confounding by indication given the nonrandomized nature of the present investigation, our multivariable regression analyses adjusting for the use of various hospital treatment practices showed that the use of invasive coronary interventions was associated with a reduced odds of being rehospitalized among patients hospitalized with AMI during the decade-long period under study. Furthermore, encouraging declines in 30 day rehospitalizations during the years under study were attenuated after adjustment for hospital treatment practices, suggesting the beneficial effects of various cardiac medications on 30 day readmission rates. A recent study examining rehospitalizations after an acute coronary syndrome among 5,219 patients enrolled in the Australian and New Zealand populations of the Global Registry of Acute Coronary Events (GRACE) between 1999 and 2007 also observed similar results in that hospital revascularization was associated with a reduced odds of being rehospitalized during the next month.[71]

To date, interventions designed to reduce readmission after hospitalization for AMI have primarily focused on improving transitional care from the hospital back to the community. However, few studies have specifically examined the impact of transitional care strategies on 30-day readmission.[72] A recent analysis of data from the CRUSADE Registry of 25,872 older (≥65 years of age) patients with NSTEMI in 228 hospitals from 2003 to 2006 found wide variation among hospitals in early physician follow-up (i.e., a physician visit within 7 days after discharge) and hospitals with higher early follow-up rates did not have lower 30-day readmission rates.[73] Future studies examining the post-discharge transitions of care in higher-risk patients, including those with multiple comorbid conditions and hospital clinical complications, remain needed to achieve greater declines in 30-day rehospitalizations in this patient population.

Study strengths and limitations

The strengths of the present study include its large population of residents of all ages and both sexes from a major central MA metropolitan area who were hospitalized with a confirmed AMI and examination of relatively contemporary decade-long trends in 30-day rehospitalization rates among hospital survivors of an AMI. Several limitations need to be acknowledged, however, in the interpretation of the present findings. Since our study population included only patients who had been hospitalized and discharged at two central MA medical centers, one needs to be careful in extrapolating our findings to those who reside in other geographic areas. If a rehospitalization occurred outside of the Worcester metropolitan area, it was not captured. Since study patients were predominantly white, the generalizability of our findings to other race/ethnic groups may be limited. There is also the potential for unmeasured confounding in our observed associations since we did not have information available on several patient-associated characteristics, such as income, education, psychosocial factors, and treatment preference which may have affected the outcomes examined. We were unable to collect information on other factors that have been shown to affect 30-day rehospitalization after AMI, including transitions of care and patients' adherence to various post-discharge treatment regimens. Finally, since our study included patients hospitalized for AMI between 1999 and 2009, future studies remain warranted to evaluate possible changes in 30-day rehospitalization rates after public reporting of 30-day risk-standardized readmission rates initiated in 2009 and the implement of financial penalties to hospitals due to excess readmissions in 2012.[9,29]

Conclusions

The results of this large observational investigation provide insights into trends and causes of 30-day rehospitalizations, and factors associated with an increased risk of 30-day rehospitalizations, among patients who survived hospitalization for an AMI between 1999 and 2009. The likelihood of subsequent rehospitalizations during the following month remained frequent. Although most of the identified risk factors were not modifiable, our findings can hopefully lead to better development of innovative, patient-centered, intervention strategies which can improve in-hospital management and follow-up care that will further reduce the 30-day rehospitalization rates of patients discharged from the hospital after an AMI

Table 3-1 Characteristics of patients who survived an acute myocardial infarction (AMI): Worcester Heart Attack Study, 1999-2009

	1999/2001 (n=1,737)	2003/2005 (n=1,719)	2007/2009 (n=1,455)	P-value*	P for trend†
Age (mean, years)	70.2	70.5	66.6	<0.001	<.0001
Age (%, years)				<0.001	
<55	16.6	15.8	22.0		
55-64	16.9	18.7	22.0		
65-74	22.0	20.5	21.3		
75-84	28.3	26.7	25.4		
85+	16.1	18.3	9.3		
Female, %	41.2	44.0	40.5	0.10	0.76
White, %	94.7	92.7	92.0	0.007	0.003
Married, %	57.2	52.1	56.1	0.009	0.44

Hospital length of stay (mean, days)	6.7	5.6	4.9	<0.001	<.0001
Medical history					
Angina, %	22.6	18.9	7.7	<0.001	<0.001
Atrial fibrillation, %	13.1	13.2	13.3	0.99	0.91
Heart failure, %	22.5	24.4	21.1	0.09	0.42
Hypertension, %	67.4	74.6	74.8	<.0001	<.0001
Peripheral vascular disease, %	12.2	18.7	18.8	<.0001	<.0001
Stroke, %	11.6	11.2	10.5	0.61	0.32
Diabetes, %	31.7	33.9	34.6	0.18	0.08
Chronic obstructive pulmonary disease, %	16.7	17.7	16.8	0.70	0.92
Depression, %	11.1	17.6	18.6	<.0001	<.0001
Chronic kidney disease, %	12.0	19.4	23.1	<.0001	<.0001
ST-segment myocardial infarction, %	41.7	32.8	30.7	<.0001	<.0001
Initial myocardial infarction, %	64.8	64.8	64.0	0.86	0.63
In-hospital clinical complications					

Atrial fibrillation, %	17.8	21.1	17.0	0.006	0.67
Cardiogenic shock, %	3.6	3.0	3.6	0.60	0.96
Stroke, %	1.5	1.3	1.0	0.51	0.25
Heart failure, %	35.6	36.9	33.2	0.09	0.18
Physiological factors on hospital admission					
Initial heart rate (mean, beats/min)	86.0	85.9	83.7	0.003	0.002
Systolic blood pressure (mean, mmHg)	144.7	143.9	140.6	0.001	<0.001
Diastolic blood pressure (mean, mmHg)	78.6	77.1	78.2	0.06	0.51
Serum glucose (mean, mg/dL)	169.8	170.3	162.0	0.004	0.005
Estimated glomerular filtration rate (mean, mL/min per 1.73 $m^{2)}$	60.9	59.6	57.0	<.0001	<.0001

* P-values derived from ANOVA tests for continuous variables and chi-square tests for categorical variables.

† P-values derived from Cochran-Armitage tests for categorical variables and linear regression models for continuous variables.

Table 3-2 Association between time period of hospitalization and 30-day all-cause rehospitalizations among patients who survived an acute myocardial infarction (AMI): Worcester Heart Attack Study, 1999-2009

	Frequency of 30-day rehospitalization	Adjusted for sociodemographics and comorbidities*	Further adjusted for in-hospital factors†	Further adjusted for in-hospital management‡	Further adjusted for discharge medications§
Study Period	%			Adjusted OR (95% CI)	
1999-2001	20.3	1.00	1.00	1.00	1.00
2003-2005	19.9	0.91 (0.69-1.19)	0.93 (0.69-1.24)	0.99 (0.73-1.34)	0.98 (0.71-1.36)
2007-2009	16.7	0.76 (0.61-0.94)	0.79 (0.62-1.00)	0.86 (0.67-1.09)	0.85 (0.66-1.10)

OR: odds ratios (OR); CI: confidence intervals

* Adjusted for age, sex, race, marital status, and previously diagnosed comorbid conditions.

† Adjusted for sociodemographics, comorbid conditions, AMI order, AMI type, in-hospital complications, and hospital length of stay.

‡ Adjusted for sociodemographics, comorbid conditions, in-hospital factors, and in-hospital management as represented by thrombolytic therapy and receipt of 3 coronary interventional procedures (cardiac catheterization, PCI, and CABG).

§Adjusted for sociodemographics, comorbid conditions, in-hospital factors, in-hospital management, and prescribing of 4 guideline-recommended cardiac medications (ACE-I/ARBs, lipid lowering agents, beta blockers, and aspirin) at the time of hospital discharge.

Table 3-3 Association between various prognostic factors and 30-day all-cause rehospitalizations among patients who survived an acute myocardial infarction (AMI): Worcester Heart Attack Study, 1999-2009

	Adjusted for sociodemographics and comorbidities*	Further adjusted for in-hospital factors†	Further adjusted for in-hospital management‡	Further adjusted for discharge medications§
Factors				Adjusted OR (95% CI)
Age <55	1.00	1.00	1.00	1.00
Age 55-64	1.17 (0.68-2.01)	1.12 (0.66-1.90)	1.11 (0.66-1.87)	1.11 (0.66-1.86)
Age 65-74	1.31 (0.88-1.96)	1.19 (0.83-1.72)	1.17 (0.81-1.68)	1.17 (0.83-1.66)
Age 75-84	1.62 (1.01-2.60)	1.46 (0.92-2.33)	1.38 (0.89-2.15)	1.38 (0.89-2.16)
Age 85+	1.27 (0.67-2.42)	1.14 (0.62-2.08)	1.00 (0.56-1.79)	1.00 (0.56-1.80)
Female (vs. Male)	1.25 (1.09-1.43)	1.26 (1.11-1.44)	1.24 (1.09-1.42)	1.24 (1.09-1.42)
White (vs. non-White)	0.76 (0.49-1.16)	0.75 (0.46-1.21)	0.76 (0.47-1.24)	0.76 (0.46-1.24)
Married (vs. not Married)	1.08 (0.87-1.33)	1.09 (0.89-1.32)	1.10 (0.90-1.34)	1.10 (0.91-1.34)

Comorbidity				
Angina	1.10 (0.92-1.32)	1.09 (0.92-1.30)	1.11 (0.93-1.33)	1.11 (0.92-1.33)
Atrial fibrillation	1.28 (0.99-1.65)	1.21 (0.87-1.67)	1.19 (0.87-1.61)	1.19 (0.88-1.62)
Heart failure	1.38 (1.14-1.69)	1.24 (1.00-1.53)	1.20 (0.97-1.48)	1.20 (0.97-1.48)
Hypertension	0.91 (0.76-1.07)	0.91 (0.77-1.07)	0.92 (0.78-1.08)	0.92 (0.78-1.09)
Peripheral vascular disease	1.15 (0.85-1.54)	1.12 (0.83-1.50)	1.13 (0.85-1.49)	1.13 (0.86-1.49)
Stroke	1.07 (0.76-1.51)	1.08 (0.76-1.53)	1.05 (0.74-1.48)	1.05 (0.74-1.48)
Diabetes	1.20 (1.04-1.39)	1.16 (1.00-1.33)	1.15 (1.01-1.32)	1.15 (1.00-1.32)
Chronic obstructive pulmonary disease	1.12 (0.94-1.35)	1.08 (0.88-1.32)	1.06 (0.88-1.27)	1.06 (0.88-1.27)
Depression	1.08 (0.89-1.32)	1.09 (0.88-1.35)	1.08 (0.88-1.33)	1.08 (0.88-1.34)
Chronic kidney disease	1.52 (1.19-1.95)	1.45 (1.13-1.86)	1.40 (1.11-1.77)	1.40 (1.12-1.74)
Initial AMI (vs. Prior AMI)		0.89 (0.76-1.04)	0.89 (0.76-1.04)	0.90 (0.77-1.04)
ST-segment myocardial infarction		1.12 (0.98-1.28)	1.17 (1.01-1.35)	1.17 (1.01-1.36)
Hospital Length of Stay (per day)		1.01 (1.00-1.03)	1.02 (1.00-1.03)	1.02 (1.00-1.03)
In-hospital clinical complication				

Atrial fibrillation	1.20 (0.87-1.65)	1.20 (0.87-1.65)	1.20 (0.88-1.65)
Cardiogenic shock	1.23 (0.84-1.80)	1.28 (0.90-1.84)	1.28 (0.87-1.87)
Stroke	0.71 (0.25-2.01)	0.68 (0.24-1.93)	0.70 (0.26-1.89)
Heart failure	1.39 (1.20-1.61)	1.36 (1.18-1.57)	1.36 (1.18-1.57)
<u>Coronary diagnostic/interventional procedure</u>			
No coronary procedure		1.00	1.00
Cardiac catheterization		0.80 (0.62-1.04)	0.79 (0.60-1.04)
Cardiac catheterization and PCI and/or CABG		0.75 (0.61-0.91)	0.74 (0.60-0.91)
Thrombolytic therapy		1.03 (0.65-1.62)	1.03 (0.65-1.62)
<u>Medication at hospital discharge</u>			
ACEI/ARBs			0.99 (0.73-1.34)
Aspirins			1.11 (0.85-1.45)
Beta blockers			0.99 (0.80-1.24)

Lipid-lowering agents	1.01 (0.80-1.28)

OR: odds ratios (OR); CI: confidence intervals

* Adjusted for study period, sociodemographics, and comorbidities.

† Adjusted for study period, sociodemographics, comorbid conditions, AMI order, AMI type, in-hospital clinical complications, and hospital length of stay.

‡ Adjusted for study period, sociodemographics, comorbid conditions, in-hospital factors, and in-hospital management as represented by thrombolytic therapy and receipt of 3 coronary interventional procedures (cardiac catheterization, PCI, and CABG).

§Adjusted for study period, sociodemographics, comorbid conditions, in-hospital factors, in-hospital management, and prescribing of 4 guideline-recommended cardiac medications (ACE-I/ARBs, lipid lowering agents, beta blockers, and aspirin) at the time of hospital discharge

Figure 3-1 Rates of rehospitalizations within 30 days after hospital discharge among patients who survived an acute myocardial infarction (AMI): Worcester Heart Attack Study, 1999-2009

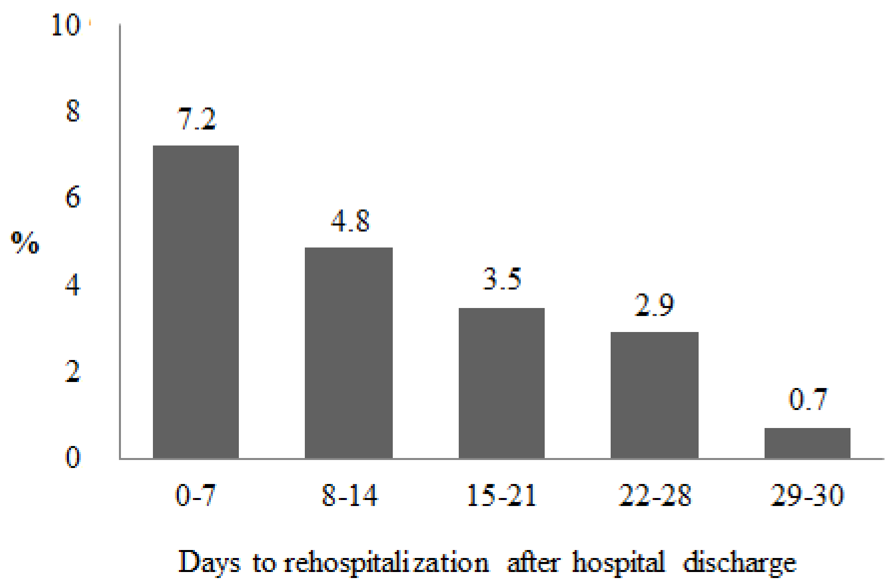
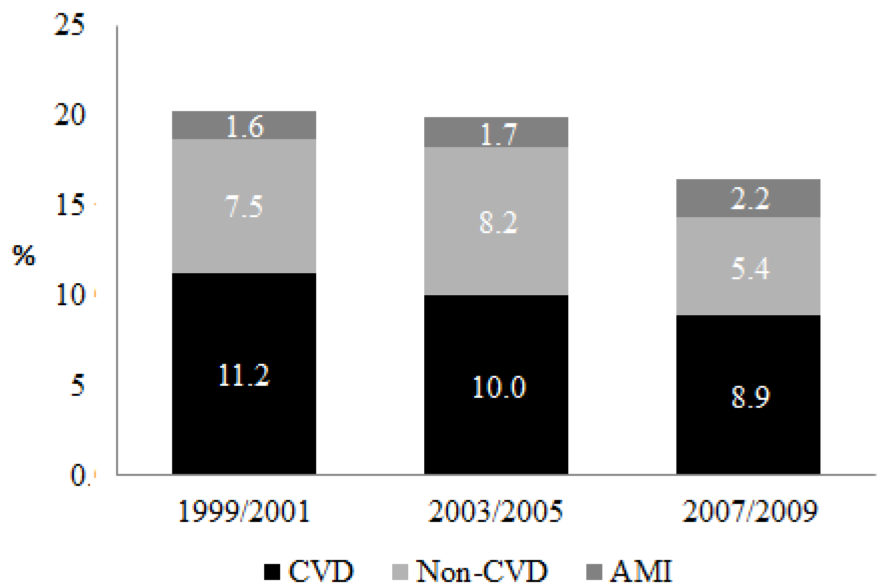


Figure 3-2 Cause-specific 30-day rehospitalization rates after hospital discharge among patients who survived an acute myocardial infarction (AMI): Worcester Heart Attack Study, 1999-2009



*CVD: Cardiovascular diseases exclude AMI

CHAPTER 4 : A 35-YEAR PERSPECTIVE (1975-2009) INTO THE LONG-TERM PROGNOSIS AND HOSPITAL MANAGEMENT OF PATIENTS DISCHARGED FROM THE HOSPITAL AFTER A FIRST ACUTE MYOCARDIAL INFARCTION

Abstract

Background

There are limited population-based data available describing trends in the long-term prognosis of patients discharged from the hospital after an initial acute myocardial infarction (AMI). Our objectives were to describe multi-decade (1975-2009) trends in post-discharge mortality, and their association with hospital management practices, among patients discharged from all central Massachusetts medical centers after a first AMI.

Methods

Residents of the Worcester, MA, metropolitan area discharged from 11 central Massachusetts hospitals after a first AMI between 1975 and 2009 comprised the study population (n=8,728). Multivariable-adjusted logistic regression analyses were used to examine the association between year of hospitalization and 1-year post-discharge mortality.

Results

The average age of this population was 66 years and 40% were women. Patients hospitalized in 1999-2009, as compared with those discharged in 1975-1984, were older, more likely to be women, and have multiple previously-diagnosed comorbidities. Hospital use of invasive cardiac interventions and medications increased markedly over time. Unadjusted 1-year mortality rates were 12.9%, 12.5%, and 15.8% for patients discharged during 1975-1984, 1986-1997, and 1999-2009, respectively. After adjusting for several demographic characteristics, clinical factors, and in-hospital complications,

there were no significant differences in the odds of dying at 1 year post-discharge during the years under study. After further adjustment for hospital treatment practices, the odds of dying at 1 year post-discharge was 2.43 (95% confidence intervals: 1.83-3.23) times higher in patients hospitalized in1999-2009 than in 1975-1984.

Conclusions

The increased use of invasive cardiac interventions and pharmacotherapies was associated with enhanced long-term survival among patients hospitalized for a first AMI.

4.1 Introduction

Although coronary heart disease remains a leading cause of death and disability, and a major burden on health care systems in the U.S.,[1] there have been continuous improvements in the in- hospital and 30-day survival of American adults hospitalized with acute myocardial infarction (AMI) during the past several decades.[19,20,34,74] The encouraging increases in short-term survival among patients hospitalized with AMI are associated with a number of factors including improvements in the primary prevention of AMI, patient education, and more widespread use of coronary reperfusion and revascularization procedures and effective cardiac medications.[75–78] Despite these encouraging trends in short-term survival, approximately 1 in every 7 patients discharged from the hospital after an AMI will die during the next year.[34] Moreover, some studies have shown either no change over time, or actual worsening survival, among patients discharged from the hospital after an AMI.[34,79]

While a limited number of studies in the U.S. have examined long-term survival after hospital discharge for AMI,[11,34,79] data describing relatively contemporary, and potentially changing, trends in the post-hospital discharge mortality rates of patients after a first AMI are sparse.[34,79] Moreover, it is unclear whether and how much changes in hospital treatment practices are associated with the risk of dying post-hospital discharge, particularly from the more generalizable perspective of a population-based investigation.

The primary objective of our large community-based study was to examine changing trends in long-term prognosis among residents of central Massachusetts discharged from all central Massachusetts medical centers after a first AMI over an approximate 35-year period (1975 - 2009). A secondary study goal was to understand whether, and to what extent, increases in the use of effective cardiac treatment approaches during the patient's index hospitalization were associated with changes in long-term mortality. Data from the population-based Worcester Heart Attack Study were used for purposes of this investigation.[3,12–15]

4.2 Methods

Described elsewhere in detail,[12–15] the Worcester Heart Attack Study is an ongoing population-based investigation describing long-term trends in the epidemiology of AMI in residents of the Worcester, Massachusetts, metropolitan area (2000 census= 478,000) hospitalized at all 16 medical centers in Central Massachusetts on an approximate biennial basis during 1975, 1978, 1981, 1984, 1986, 1988, 1990, 1991, 1993, 1995, 1997, 1999, 2001, 2003, 2005, 2007, and 2009.[12–15] In 2000, the median age of residents of the Worcester metropolitan area was 37 years, 49% were men, 89% were white, and approximately 25% had a bachelor's degree or higher.[15] Due to hospital closures, mergers, or conversion to long-term care or rehabilitation facilities, fewer hospitals (n=11) have been providing care to greater Worcester residents during the most recent years of this community-wide investigation.

Computerized printouts of patients discharged from all greater Worcester hospitals with possible AMI [International Classification of Disease (ICD) 9 codes: 410-414, 786.5] were identified. Cases of possible AMI were independently validated using predefined criteria for AMI;[12–15] these criteria included a suggestive clinical history, increases in several serum biomarkers (e.g., creatine kinase (CK), CK-MB, and troponin values), and serial electrocardiographic findings during hospitalization consistent with the presence of AMI. Patients who satisfied at least 2 of these 3 criteria, and were residents of the Worcester metropolitan area, were included.

For purposes of the present study, we restricted our sample to adult residents of the Worcester metropolitan area who survived their index hospitalization for a first AMI between 1975 and 2009. Patients with an initial AMI were identified by either mention in the review of hospital charts that this was the patient's first admission for an AMI or through the review of previous hospital records and electrocardiograms that failed to indicate the occurrence of a previous AMI. This study was approved by the Institutional Review Board at the University of Massachusetts Medical School.

Data Collection

Trained nurses and physicians abstracted information on patients' demographic characteristics, medical history, clinical data, and treatment practices through the review of hospital medical records. These factors included patient's socio-demographic characteristics (age, sex, race, marital status), year of hospitalization, hospital length of stay, history of previously diagnosed comorbidities (e.g., stroke, diabetes, heart failure), and AMI type [Q-wave vs. non-Q-wave; ST-segment elevation myocardial infarction (STEMI) vs. non-ST-segment elevation myocardial infarction (NSTEMI)].[3,24] Information on the development of important in-hospital complications including atrial fibrillation,[63] cardiogenic shock,[64] heart failure,[65] and stroke[66] was also collected.

Data on the receipt of thrombolytic therapy and 3 coronary diagnostic and interventional procedures [cardiac catheterization, percutaneous coronary intervention (PCI), and coronary artery bypass grafting (CABG) surgery] during hospitalization, and pharmacotherapies at the time of hospital discharge, including the prescribing of 6 effective cardiac medications [angiotensin converting inhibitors (ACE-I)/angiotensin receptor blockers (ARBs), anticoagulants, aspirin, beta blockers, calcium channel blockers, and lipid lowering agents], were obtained. While we collected follow-up information on all study patients through 2012, we examined trends in 1-year post-hospital discharge all-cause mortality rates. This time point was chosen since a number of prior investigations[80,81] have shown this follow-up point to be a particularly high-risk period for dying among patients discharged from the hospital after an AMI. The approaches used to ascertain survival status after hospital discharge included a review of medical records for additional hospitalizations and a statewide and national search of death certificates for residents of the Worcester metropolitan area.

Data Analysis

For ease of analysis and interpretation, we aggregated the 17 individual study years into approximate 3 decade-long time periods (1975-1984, earliest; 1986-1997, middle; and 1999-2009, most recent) for purposes of examining changing trends in 1 year post-discharge mortality rates. Furthermore, these time period categorizations reflect major changes in the management of patients hospitalized with AMI that have occurred over time from the use of mainstay therapies, such as aspirin and beta blockers during the earliest years under study, to the use of thrombolytic therapy in the mid-1980s, to the use of more aggressive and invasive interventions including PCI and lipid lowering therapy during the most recent decade under study. Differences in the distribution of various patient demographic and clinical characteristics, development of in-hospital clinical complications, receipt of in-hospital interventional procedures and thrombolytic therapy, and prescribing of cardiac medications at the time of hospital discharge between patients hospitalized during the 3 time periods were examined using the ANOVA test for continuous variables and the chi-square test for categorical variables. The Cochran-Armitage tests and linear regression models were used to test for linear trends over time among categorical variables and continuous variables, respectively.

Long-term mortality after hospital discharge was examined by calculating 1 year all-cause mortality rates. Multivariable-adjusted logistic regression analyses were performed to examine the association between the main explanatory variable of time period of hospitalization (1975-1984, earliest; 1986-1997, middle; and 1999-2009, most recent) and the outcome of 1-year post-discharge all-cause mortality (dead vs. alive) while adjusting for several potentially confounding variables of prognostic importance. Since the 3 time periods reflect changes in the management of patients hospitalized with AMI, and a linear relationship with the outcome of total mortality was not assumed, we dummy coded this variable with the earliest period (1975-1984) serving as the reference group. Several covariates associated with long-term mortality in patients discharged from the hospital after AMI in prior studies[11,34,76–78] were examined sequentially in 4 blocks. The first block included age, sex, race (white vs. non-white), marital status (married vs.

not-married), and previously diagnosed comorbid conditions (i.e., angina, diabetes, heart failure, hypertension, and stroke). The second block included AMI type (Q-wave vs. non-Q-wave), in-hospital clinical complications (atrial fibrillation, heart failure, cardiogenic shock), and hospital length of stay. The third block included in-hospital management practices as represented by the receipt of thrombolytic therapy and 3 coronary interventional procedures (e.g., cardiac catheterization, PCI, and CABG). The fourth block included the prescribing of 4 guideline-recommended cardiac medications (ACE-I/ARBs, lipid lowering agents, beta blockers, and aspirin) at the time of hospital discharge. Based on their clinical relevance and preliminary univariate associations, all potential covariates were retained and fitted into multivariable logistic regression models by adding the blocks of variables sequentially.

We also repeated our multivariable-adjusted logistic regression analyses restricted to patients hospitalized during the most recent decade under study (1999-2009) for purposes of providing a relatively contemporary perspective into the association between year of hospitalization and 1-year all-cause mortality. For this analysis, we also adjusted for type of AMI (STEMI and NSTEMI) since information about whether the patient's ECG showed changes in ST segment elevation or otherwise was only obtained from 1999 on. Our results were presented as multivariable adjusted odds ratios (OR) and accompanying 95% confidence intervals (CI), which were calculated based on standard errors clustered at the hospital level to account for potential within-hospital correlation with variance adjustment through the use of Morel's small sample bias correction.[67] All statistical analyses were conducted using SAS version 9.3 (SAS Institute, Inc, Cary, North Carolina).

4.3 Results

Study population characteristics

The study population consisted of 8,728 adult residents of the Worcester metropolitan area who survived their hospitalization for an independently confirmed first AMI at all central Massachusetts medical centers between 1975 and 2009 (Table 1). Overall, the average age of this patient population was 66.4 years, 60.0% were men, the majority were white (95.4%), and 61.0% were married.

Patients discharged from all greater Worcester hospitals after a first AMI during recent, as compared with earlier, study years were significantly older, were more likely to be women, and were less likely to be married (Table 4-1). The proportion of patients with a Q-wave MI declined over time and, between 1999 and 2009, 40.0% of our study sample was diagnosed with an STEMI.

During the most recent years under study, patients who survived their initial AMI were more likely to have a history of heart failure, hypertension, diabetes, or stroke than patients hospitalized during earlier study periods (Table 1). The proportion of patients with multiple (≥2) comorbid conditions increased from 24.2% in 1975-1984 to 36.6% in 1999-2009 (p for trend <0.001). The average hospital length stay declined markedly over time from an average of 16.8 days in 1975-1984 to 5.5 days in 1999-2009 (Table 4-1).

Overall, the likelihood of developing cardiogenic shock or a stroke during the patient's index hospitalization remained relatively low (2.7% and 1.0% overall, respectively) whereas the incidence rates of in-hospital heart failure and atrial fibrillation were considerably higher (30.5% and 15.2% overall, respectively). In general, there was an upward trend in the proportion of patients who developed cardiogenic shock (p for trend <0.0001) and atrial fibrillation (p for trend=0.0003) during their index hospitalization, but a downward trend in the development of acute heart failure (p for trend =0.043) was observed from the earliest to the most recent years under study; the development of acute stoke remained low and stable throughout the years under study (p=0.67) (Figure 4-1).

Receipt of coronary procedures, thrombolytic therapy, and cardiac medications

The use of cardiac catheterization and PCI has increased markedly over time whereas the proportion of patients undergoing CABG surgery during their index hospitalization has significantly increased but remained relatively low during the years under study (all p values for trend <0.001). The use of thrombolytic therapy increased during the 1990's but markedly decreased thereafter (Figure 4-2a). Cardiac catheterization, PCI, CABG surgery, and thrombolytic therapy were used in 78.2%, 60.8%, 6.7%, and 0.2% respectively, of patients who survived a first AMI in 2009 (Figure 4-2a).

Marked increases in the prescribing of aspirin, ACEI/ARBs, beta blockers, and lipid-lowering medications at the time of hospital discharge were observed during the years under study (p for trend <0.001) (Figure 4-2b). On the other hand, use of calcium channel blockers has declined markedly during recent years (p for trend <0.001). The use of anticoagulants among patients who survived a first AMI increased through the mid-1990's, declined in the late 1990's, and remained stable during the 2000's (Figure 4-2b). Aspirin, ACEI/ARBs, beta blockers, and lipid-lowering medications were prescribed at the time of hospital discharge in 94.0%, 64.4%, 90.7%, and 90.1% of patients who survived a first AMI in 2009.

Post-hospital discharge 1-year all-cause mortality rates

The overall (1975-2009) all-cause death rates for patients who survived a first AMI were 13.9% at 1 year after hospital discharge. The average 1-year all-cause mortality rates remained relatively stable from 1975-1984 (12.9%) to 1986-1997 (12.5%), but increased during 1999-2009 (15.8%).

In examining changing trends in all-cause mortality during the first year after hospital discharge, our unadjusted analyses showed that, compared with patients surviving an initial AMI in 1975-1984, there were no significant differences in the odds of dying at 1 year post discharge among patients discharged from all central MA medic al centers after a first AMI in 1986-1997 (OR=0.96, 95% CI=0.64-1.45) and in 1999-2009 (OR=1.27, 95% CI=0.80-2.02) (Table 4-2).

After sequentially adjusting for several demographic characteristics, clinical factors, and in-hospital clinical complications, there were no significant differences in the odds of dying at 1 year post discharge among patients discharged from all metropolitan

Worcester hospitals in 1986-1997 (OR=0.80, 95% CI=0.60-1.08) and 1999-2009 (OR=0.82, 95% CI=0.59-1.15), compared with those hospitalized in 1975-1984. However, after further adjustment for medical treatment during hospitalization, and the prescribing of evidence-based medications at hospital discharge, there was a borderline significant trend (p=0.08) toward an increased risk of dying at 1 year post discharge among patients hospitalized in 1986-1997; the odds of dying from all causes at 1 year post discharge was approximately 2.4 times higher in patients discharged from the hospital in 1999-2009 compared with those discharged during 1975-1984 (Table 4-2).

We repeated these crude and multivariable adjusted analyses in patients who were hospitalized during the most recent decade under study (1999-2009) to reflect more recent trends in long-term prognosis. The unadjusted analyses showed that, compared with patients discharged after an initial AMI in 1999/2001 (referent group), there was no significant difference in the odds of dying at 1 year post discharge among patients hospitalized in 2003/2005 and in 2007/2009 (Table 4-2). After controlling for several demographic characteristics, clinical factors, and in-hospital complications, the odds of dying at 1 year post discharge was significantly decreased among patients hospitalized in 2003/2005 (OR=0.68, 95% CI=0.48-0.97) and 2007/2009 (OR=0.62, 95% CI=0.47-0.83), compared with those hospitalized in 1999/2001. However, after further adjustment for the receipt of medical interventions during hospitalization, and the prescribing of evidence-based medication at the time of hospital discharge, there was no significant difference in the odds of dying at 1 year post discharge among patients hospitalized in 2003/2005 and in 2007/2009, in comparison with those hospitalized in 1999/2001 (Table 4-2).

4.4 Discussion

The results of this community-wide study suggest that there have been considerable changes in the demographic, clinical, and treatment profile of greater Worcester residents who survived hospitalization for a first AMI at all central Massachusetts medical centers between 1975 and 2009. The hospital use of invasive coronary interventions and effective cardiac medications increased markedly over time. The average post-discharge 1-year all-cause mortality rates remained relatively stable from 1975-1984 to 1986-1997, but increased slightly during 1999-2009. Using multivariable-adjusted regression analyses, after adjustment for demographic characteristics, clinical factors, and in-hospital complications, no significant differences in the odds of dying at 1 year after hospital discharge were observed during the years under study. Once we adjusted for the receipt of various hospital treatment practices during hospitalization, however, the odds of dying at 1 year post discharge among patients hospitalized during the most recent years under study actually increased, suggesting the beneficial impact of these treatment modalities on the long-term prognosis of discharged patients.

Changing profile of hospital survivors after a first AMI

Consistent with the findings from a prior population-based study conducted at nonfederal acute care hospitals in New Jersey,[34] we found that residents of the Worcester metropolitan area who survived their hospitalization for a first AMI during the most recent years under study were significantly older, were more likely to be women, and had multiple comorbidities previously diagnosed than patients who were hospitalized during earlier study years.

Prior studies have suggested that reductions in the primary risk factors for coronary heart disease (e.g., smoking, blood lipids, and blood pressure) and improvements in the management of patients with acute coronary disease account for the majority of the decline in CHD mortality and incidence observed in developed countries during the past several decades.[75,82] Although only speculative, several factors may have contributed to delaying the onset of a first AMI to an older age as observed in our investigation. These factors include the healthier aging of the American population, improvements in the medical and clinical management of patients with pre-existing coronary disease, and the increasing adoption of healthy lifestyle practices and other primary preventive modalities in the general population and in various at-risk groups. However, it is worth noting that survivors of a first AMI during our most recent study years (1999-2009) were much more likely to have had diabetes previously diagnosed compared with those hospitalized during the earliest years under study (1975-1984). These trends likely reflect the ongoing epidemic of obesity and diabetes in the U.S.[1]

The current trends of increasing age and prevalence of multiple comorbidities in patients hospitalized with a first AMI present significant challenges to healthcare providers involved in the management of these high risk patients. Indeed, several population-based investigations, including our own, have demonstrated that, compared with younger patients hospitalized with AMI, older patients are more likely to develop important hospital clinical complications and have a worse in-hospital and long-term survival.[20,34,83,84] Previous studies have also demonstrated a poorer long-term prognosis for patients hospitalized with AMI who had previously diagnosed comorbidities, such as diabetes, heart failure, and stroke.[11,34,85] Therefore, continued surveillance remains needed to monitor these and other ongoing trends in patients hospitalized with a first AMI in central Massachusetts as well as in other geographic settings throughout the U.S.

Post-hospital discharge mortality rates and hospital treatment practices

Although several population-based studies[34,79] have reported encouraging declines in the in-hospital and 30 day mortality rates in patients hospitalized with a first AMI, there are data to suggest that favorable short-term trends in mortality may not extend to patient's long-term prognosis after hospital discharge.[34,79] The current investigation and several prior studies[34,79] have shown that the 1 year death rate among patients discharged after a first AMI remains relatively high, emphasizing the need for continued surveillance and optimization of the medical care of these patients.

Our study showed that the unadjusted 1-year all-cause mortality rates among patients discharged from all central Massachusetts medical centers after a first AMI have actually increased in the most recently hospitalized patient cohort (1999-2009), which likely reflects the increasingly older patient population with a greater prevalence of multiple comorbidities. A previously published study of more than 285,000 patients hospitalized with a first AMI at nonfederal acute care hospitals in New Jersey between 1986 and 2007 found that the 1-year post-discharge mortality rates also increased over time, from 12.1% in 1986 to 13.9% in 2007;[34] the increased risk of dying over time was most evident in the oldest patients and were primarily due to non-cardiovascular causes of death.[34] In a study of 2,816 residents of Olmsted County, MN, hospitalized with an incident AMI between 1987 and 2006, there were no changes in 1 year post-discharge mortality during the years under study.[79]

These findings suggest that improving the long-term outcomes of patients discharged from the hospital after a first AMI will likely require expanding the use of existing, and novel, preventive and/or therapeutic strategies in these patients after hospital discharge, and these treatment plans need to take into account the age and presence of other comorbid conditions in these patients. To effectively implement these strategies, collaboration of care management between patients and their providers, and strong partnership between cardiologists and primary care physicians, remain crucial to the success of effective post-discharge care transitions.

Consistent with the results of several population-based investigations, we showed that the use of coronary interventional procedures and effective cardiac medications has increased markedly over the past several decades.[19,20,25] Despite the potential for confounding by indication given the nonrandomized nature of the present community-based investigation, our multivariable regression analyses adjusting for the use of various hospital treatment practices showed that the increased use of invasive interventions and evidence-based pharmacotherapies was associated with increased post discharge survival among patients hospitalized for a first AMI during the most recent decade under study.

Several prior studies have used similar multivariable regression analyses to examine the effects of hospital treatment practices on patient's long-term prognosis.[77,78] In a study of 4,451 patients aged 35-64 years with a first AMI from the population-based Perth MONICA (Multinational MONItoring of trends and determinants in CArdiovascular disease) cohort (1984-2005), improving trends in 1 year and longer survival were observed and were associated with an increased use of evidence-based treatments during hospitalization and in the 12 months after the index event.[78] A recent population-based study examined the use of treatment approaches and outcomes in a random sample of 1,226 patients 75 years and older who were hospitalized for AMI in Minneapolis/St. Paul, and Goteborg, Sweden in 2001-2002. The investigators demonstrated that the use of PCI was markedly higher in Minneapolis/St. Paul than in Goteborg, and the long-term survival at 1, 3, and 5 years was greater among elderly patients in Minneapolis/St. Paul compared with those from Goteborg, Sweden, likely related to the greater utilization of PCI.[77]

Although clinical trials remain the gold standard for examining treatment efficacy, data from observational studies can provide important complementary insights into the effectiveness of treatments in the broader community setting. These studies, however, have several limitations including the lack of data on patients' post-discharge cognitive status, changes in healthy lifestyle practices, and long-term adherence to evidence-based treatment after hospital discharge for AMI. Current data suggests less than optimal patient adherence to evidence-based therapies after AMI,[86] and non-adherence to these effective medications has been associated with an increased risk of cardiovascular mortality.[87] Inasmuch, ongoing dialogues between patients and their providers about the importance of adhering to effective secondary prevention approaches on a long-term basis remain important. Future studies examining the increasing use of conventional and more novel treatment strategies, and post-discharge transitions of care, in higher-risk patients, including the elderly and those with multiple comorbid conditions, remain needed to achieve greater declines in long-term mortality in this patient population.

Study strengths and imitations

The strengths of the present study include its community-based design and examination of multiple decade long trends in long-term mortality rates and hospital treatment practices among hospital survivors of an initial AMI. Several limitations need to be acknowledged, however, in the interpretation of the present findings. First, since our study only included patients who had been hospitalized for an initial AMI at all central Massachusetts medical centers, one needs to be careful in extrapolating our findings to persons who died before hospitalization, or to those who reside in other geographic areas. Second, since our study patients were predominantly white, the generalizability of our findings to other race/ethnic groups may be limited. Our study examined pharmacotherapies prescribed at the time of hospital discharge. However, patients might have been prescribed these medications as outpatients. Lastly, there is the potential for unmeasured confounding in our observed associations since we did not have information available on several patient-associated characteristics, such as income, education, psychological factors, and treatment preference, and we were unable to collect information on other factors that have been shown to affect long-term prognosis after AMI, including the severity of the AMI, and patients' adherence to various post-discharge treatment regimens after being discharged from the hospital after a first AMI.

Conclusions

The results of this community-wide investigation provide insights into the changing characteristics, management practices, and long-term prognosis of patients who survived hospitalization for a first AMI over a 35-year period of investigation. The increased use of invasive cardiac interventions and pharmacotherapies during the patient's index hospitalization was associated with a reduced risk for dying at 1 year in this patient population based on observed mortality findings after adjustment for these treatment approaches. Our findings reinforce the importance of expanding the scope of care from the acute treatment of AMI to effective post-discharge care management strategies, including education of the patient's caregivers, to improve the long-term outlook of patients after a first AMI. Future studies examining the impact of individual and combined evidence-based treatments on patient's long-term survival, and the effects of medication adherence on endpoints of clinical and public health importance, including hospital readmissions, the development of recurrent coronary events, and quality of life remain warranted.

Table 4-1 Characteristics of patients who survived a first acute myocardial infarction (AMI) according to time period of hospitalization: Worcester Heart Attack Study, 1975-2009

	1975-1984 (n=1,820)	1986-1997 (n=3,407)	1999-2009 (n=3,501)
Age (mean, years)	63.8	66.3	67.9
Age (%, years)			
<55	24.7	21.0	21.5
55-64	27.8	20.7	19.9
65-74	15.5	21.9	25.1
75-84	15.5	21.9	25.1
≥85	6.2	8.4	13.4
Male (%)	64.3	59.5	58.2
White (%)	97.2	96.1	93.7
Married (%)	67.1	62.2	56.6

ST-segment myocardial infarction (%)	N/A	N/A	40.0
Q-wave (%)	64.7	51.3	27.6
Hospital length of stay (mean, days)	16.8	9.5	5.5
Medical History (%)			
Angina	18.4	19.0	12.8
Heart failure	6.5	7.8	13.8
Hypertension	44.1	51.7	65.5
Stroke	4.6	6.7	8.3
Diabetes	18.5	23.2	27.1

* P-values derived from ANOVA tests for continuous variables and chi-square tests for categorical variables were all <0.001.

**P-values derived from Cochran-Armitage tests for categorical variables and linear regression models for continuous variables were all <0.001.

Table 4-2 Crude and multivariable adjusted odds of dying at 1-year after hospital discharge for patients who survived a first acute myocardial infarction (AMI): Worcester Heart Attack Study, 1975-2009

	Unadjusted	Adjusted for sociodemographics and comorbidities*	Further adjusted for in-hospital factors†	Further adjusted for in-hospital management‡	Further adjusted for discharge medications§
	Crude OR (95% CI)	Adjusted OR (95% CI)			
1975-1984	1.00	1.00	1.00	1.00	1.00
1986-1997	0.96 (0.64-1.45)	0.72 (0.53-0.97)	0.80 (0.60-1.08)	1.13 (0.85-1.51)	1.30 (0.97-1.74)
1999-2009	1.27 (0.80-2.02)	0.73 (0.51-1.04)	0.82 (0.59-1.15)	1.65 (1.25-2.17)	2.43 (1.83-3.23)
1999/2001	1.00	1.00	1.00	1.00	1.00
2003/2005	0.84 (0.56-1.25)	0.69 (0.50-0.96)	0.68 (0.48-0.97)	0.84 (0.60-1.17)	0.96 (0.67-1.35)
2007/2009	0.71 (0.46-1.08)	0.62 (0.44-0.86)	0.62 (0.47-0.83)	0.89 (0.70-1.15)	1.13 (0.86-1.48)

OR: odds ratios (OR); CI: confidence intervals

*Adjusted for age, sex, race, marital status, and comorbid conditions (angina, diabetes, heart failure, hypertension, and stroke).

[†] Adjusted for sociodemographics, comorbid conditions, AMI type, in-hospital clinical complications (atrial fibrillation, heart failure, cardiogenic shock), and hospital length of stay.

[‡] Adjusted for sociodemographics, comorbid conditions, in-hospital factors, and in-hospital management as represented by thrombolytic therapy and receipt of 3 coronary interventional procedures (cardiac catheterization, PCI, and CABG).

[§]Adjusted for sociodemographics, comorbid conditions, in-hospital factors, in-hospital management, and prescribing of 4 guideline-recommended cardiac medications (ACE-I/ARBs, lipid lowering agents, beta blockers, and aspirin) at the time of hospital discharge.

Figure 4-1 In-hospital clinical complications among patients who survived a first acute myocardial infarction (AMI): Worcester Heart Attack Study, 1975-2009

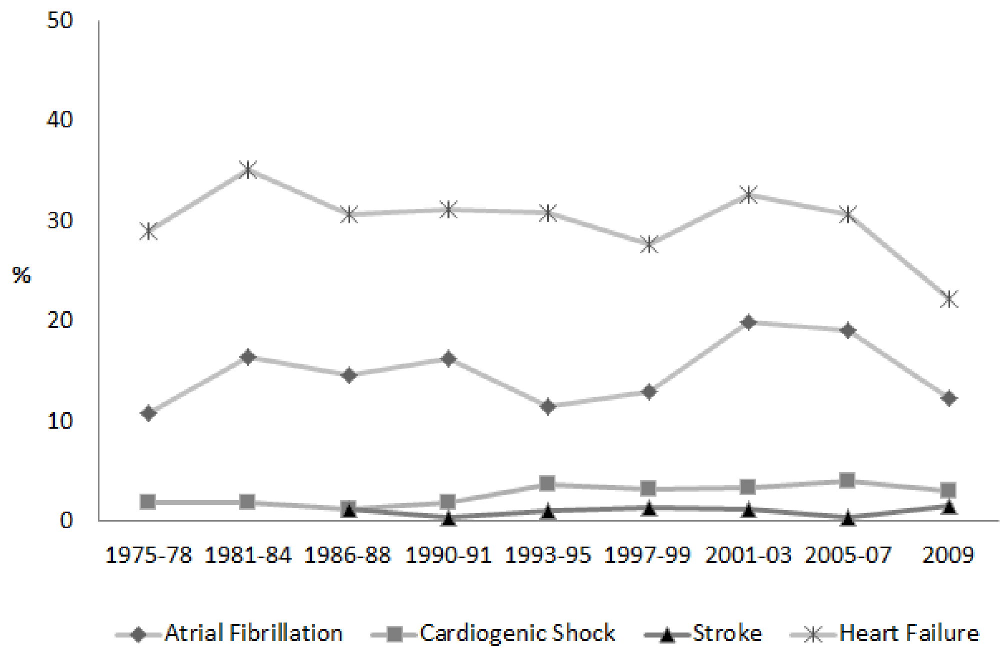
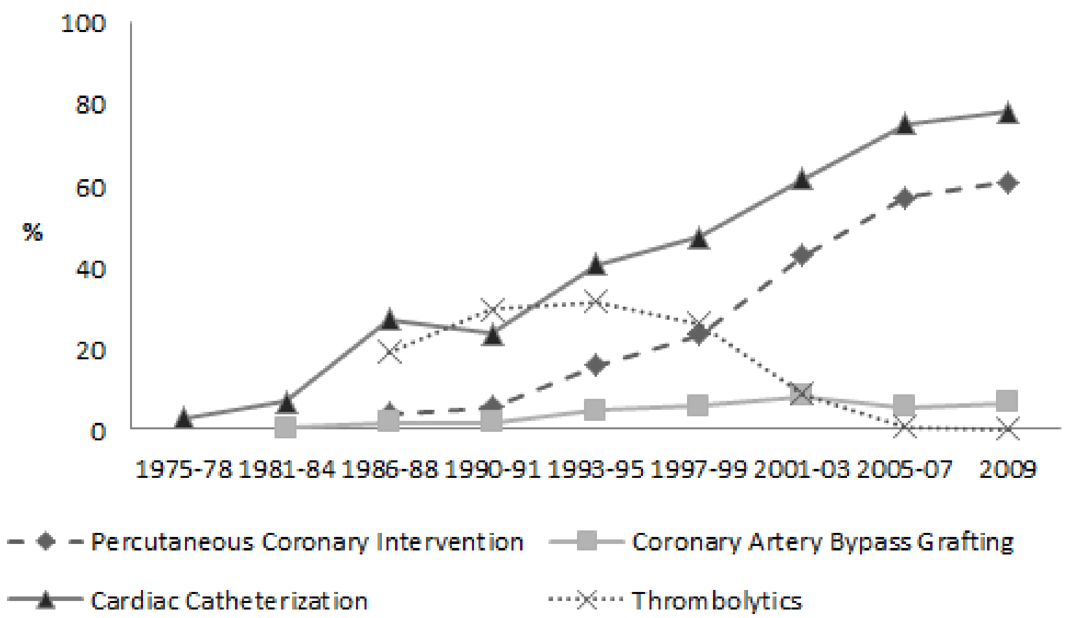
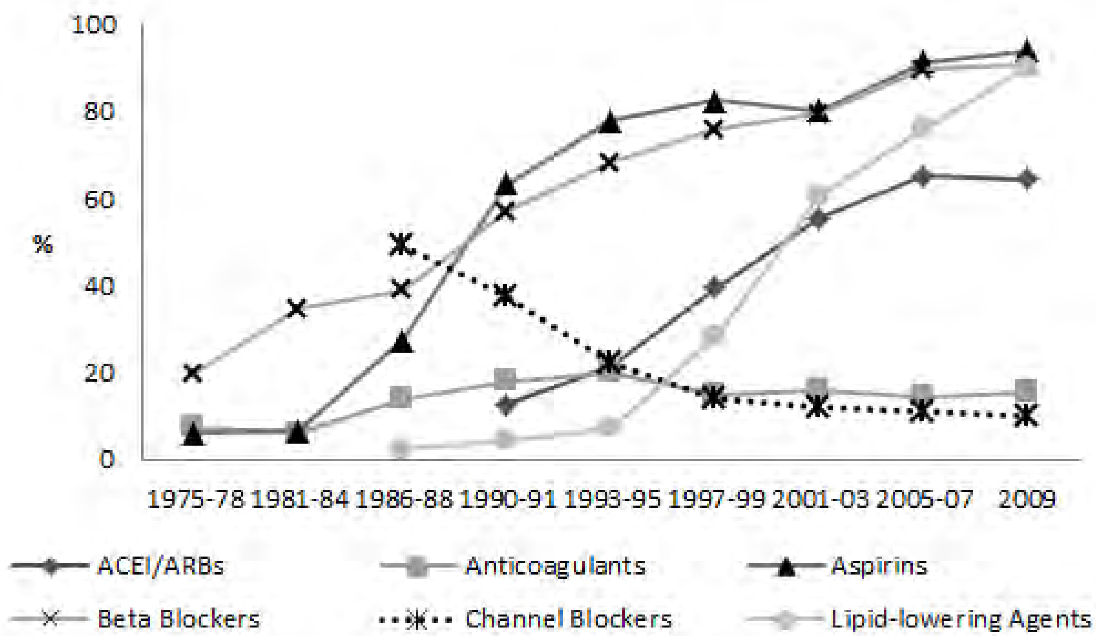


Figure 4-2 In-hospital coronary procedures and thrombolytic therapy, and cardiac medications at the time of hospital discharge among patients who survived a first acute myocardial infarction (AMI): Worcester Heart Attack Study, 1975-2009

(a) In-hospital coronary procedures and thrombolytic therapy



(b) Cardiac medications at hospital discharge



CHAPTER 5 : CONCLUSIONS

5.1 Summary of Findings

The objectives of this dissertation were to examine changing trends in the extent of delay in the receipt of a primary PCI among patients who were hospitalized with STEMI, 30-day hospital readmission rates among patients who were hospitalized for AMI, and 1-year post-hospital mortality rates among patients who survived their hospitalization for a first AMI, and factors associated with these outcomes, among patients hospitalized with AMI at all or select medical centers in central Massachusetts (MA) over a multi-decade long period.

In my first study aim, the primary objective was to describe decade-long (1999-2009) trends in the extent of delay from hospital emergency department presentation to initiation of a primary PCI among patients hospitalized with STEMI. The secondary objective was to examine factors associated with the failure to receive a primary PCI within 90 minutes of hospital arrival among patients hospitalized with STEMI. The results suggested that, among greater Worcester residents who were hospitalized for STEMI and received a primary PCI at the 3 PCI-capable hospitals in central MA between 1999 and 2009, there was a nearly 6 fold increase in the proportion of patients who received a timely primary PCI during the years under study. Older age, having previously diagnosed diabetes and chronic kidney disease, prior CABG surgery, and arriving at the emergency department by car/walked-in and during off-hours were significantly associated with a higher risk of failing to receive a primary PCI within 90 minutes of hospital arrival.

In my second study aim, the primary objective was to describe relatively contemporary decade long (1999-2009) trends in the frequency of 30-day all-cause and cause specific rehospitalizations among patients surviving hospitalization for an AMI. The secondary objective was to examine patient characteristics, treatment practices, and clinical factors associated with an increased risk of 30-day rehospitalizations among residents of central MA discharged from the 3 principal medical centers in central MA after an AMI. The results suggested that, among greater Worcester residents who survived their hospitalization for an AMI at the 3 major medical centers in central MA between 1999 and 2009, nearly 1 in 5 patients remained at risk for being rehospitalized within 30 days and 38% of all 30-day rehospitalizations occurred during the first week after hospital discharge during the years under study. The overall cause-specific 30-day rehospitalization rates due to CVD, non-CVD, and AMI were 10.1%, 7.1%, and 1.8%, respectively, during the years under study. Our findings suggested a slight decline in the odds of being rehospitalized during the first 30 days after hospital discharge over time though this odds was slightly attenuated after further adjustment for hospital treatment practices. In addition, we identified several demographic and clinical factors associated with an increased odds for being rehospitalized during the first month after hospital discharge for AMI that included female sex, having previously diagnosed diabetes and chronic kidney disease, development of heart failure during the patient's index hospital admission, and having developed a STEMI during their index admission.

In my third study aim, the primary objective was to examine changing trends in long-term prognosis among residents of central MA discharged from all 16 central MA medical centers after a first AMI over an approximate 35-year period (1975-2009). A secondary study goal was to understand whether, and to what extent, increases in the use of effective cardiac treatment approaches during the patient's index hospitalization were associated with changes in long-term mortality. Our findings suggested that there have been considerable changes in the demographic, clinical, and treatment profile of greater Worcester residents who survived their hospitalization for a first AMI at all central MA medical centers between 1975 and 2009. The hospital use of invasive coronary interventions and effective cardiac medications increased markedly over time. The average post-discharge 1-year all-cause mortality rates remained relatively stable from 1975-1984 to 1986-1997, but increased slightly during 1999-2009. Using multivariable-adjusted regression analyses, after adjustment for demographic characteristics, clinical factors, and in-hospital complications, no significant differences in the odds of dying during the first year after hospital discharge were observed during the years under study. Once we adjusted for the receipt of various hospital treatment practices during hospitalization, however, the odds of dying at 1 year post discharge among patients hospitalized during the most recent years under study actually increased, suggesting the beneficial impact of these treatment modalities on the long-term prognosis of discharged patients.

5.2 Study Strengths and Limitations

Several strengths of this dissertation are worth noting. We used data from a large, federally funded, population-based investigation among adult residents of the Worcester, MA, metropolitan area hospitalized with a confirmed AMI at all medical centers in central MA (Worcester Heart Attack Study: WHAS).[12–15] In addition, we examined multi-decade long and contemporary trends in patient characteristics, treatment practices, as well as short and long-term outcomes in patients hospitalized with AMI. Several limitations need to be acknowledged, however, in the interpretation of the present findings. Since our study population included only patients who had been hospitalized at all or selected hospitals in central MA, one needs to be careful in extrapolating our findings to those who died before hospitalization, or to those who reside in other geographic areas of the U.S. Because study patients were predominantly white, the generalizability of our findings to other race/ethnic groups may be limited. If a rehospitalization occurred outside of the Worcester metropolitan area, it was not captured. Our study examined pharmacotherapies prescribed at the time of hospital discharge. However, patients might have been prescribed these medications as outpatients. There is also the potential for unmeasured confounding in our observed associations since we did not have information available on several patient-associated characteristics, such as income, education, psychosocial factors, and treatment preference, as well as healthcare system level factors, which may have affected the outcomes examined. We were unable to collect information on other factors that have been shown to affect readmission or long-term prognosis after AMI, such as the severity of the AMI, transitions of care, and patients' adherence to various post-discharge treatment regimens.

5.3 Study Implications and Future Research Directions

Our results demonstrated a dramatic increase in the proportion of STEMI patients who received a primary PCI within the guideline-recommended 90 minutes after hospital arrival, particularly in 2007/2009, which was consistent with national efforts to reduce door-to-balloon times among patients hospitalized with STEMI and prior research results. We found that patients with STEMI admitted to the emergency department during off-hours were more likely to fail to receive a timely primary PCI, compared with those admitted during regular hours. Approaches to provide onsite staffing of the cardiac catheterization laboratory and rapid access to interventional cardiologists during off-hours, including consideration of the costs of providing such coverage, would be beneficial. Although several studies, including our current investigation, have suggested encouraging findings in reducing door-to-balloon times over the years, reducing door-to-balloon time remains important in the care of patients hospitalized with STEMI. Healthcare providers should continue their efforts to educate patients about the symptoms of AMI and importance of calling 911 to facilitate EMS triage, treatment, and hospital transport to reduce not only in-hospital but also prehospital treatment delays.

Between 1999 and 2009, we found that nearly 1 in 5 patients who survived an AMI remained at risk for being rehospitalized within 30 days after hospital discharge, and 38% of all 30-day rehospitalizations occurred during the first week after hospital discharge. These findings suggest that proper arrangement of transitional care, and continuing follow up with patients during the first several days to first week post hospital discharge could be beneficial in reducing 30-day readmission rates among these patients.

In addition, we observed that a significant proportion (37%) of all 30-day hospital readmissions were non-CVD related. As the prevalence of comorbid conditions and aging of the American population increase over time, and efforts continue to be focused on the enhanced use of effective secondary prevention strategies to improve the post-discharge outcomes of patients with AMI, 30-day rehospitalizations after AMI due to non-CVD causes need further attention. Further research is needed to look into the "post-hospitalization syndrome," [70] and confirm the association between this syndrome and other hospital and post-discharge factors that may place patients at risk for non-CVD related hospital readmissions, and develop effective strategies for reducing readmissions due to these factors. Since our study population consisted of patients hospitalized for AMI between 1999 and 2009, future studies remain warranted to evaluate possible changes in 30-day rehospitalization rates after the public reporting of 30-day risk-standardized readmission rates in 2009 and the implementation of financial penalties to hospitals due to excess readmissions in 2012.[9,29]

Our current investigation showed that the 1-year all-cause mortality rate among central MA residents discharged from all area medical centers after a first AMI remains relatively high, emphasizing the need for continued surveillance and optimization of the medical care of these patients. We also observed that the unadjusted 1-year mortality rates among patients discharged after a first AMI have actually increased in the most recently hospitalized patient cohort (1999-2009), which likely reflects the increasingly older patient population with a greater prevalence of multiple comorbidities. These findings suggest that improving the long-term outcomes of patients discharged from the hospital after a first AMI will likely require expanding the use of existing, and novel, preventive and/or therapeutic strategies in these patients after hospital discharge, and these treatment plans need to take into account the age and presence of other comorbid conditions in these patients. To effectively implement these strategies, collaboration of care management between patients and their providers, and strong partnership between cardiologists and primary care physicians, remain crucial to the success of effective post-discharge care transitions. Future studies examining the increasing use of conventional and more novel treatment strategies, and post-discharge transitions of care, in higher-risk patients, including the elderly and those with multiple comorbid conditions, remain needed to achieve greater declines in long-term mortality in this patient population.

In conclusion, the findings of this dissertation provide useful and contemporary information regarding changing trends in the extent of delay in the receipt of a primary PCI, 30-day hospital readmission rates, and 1-year post-hospital mortality, as well as factors associated with these outcomes, among patients hospitalized with AMI in the Worcester metropolitan area. These data can hopefully lead to better development of innovative, patient-centered, intervention strategies which can further improve the short and long-term prognosis of men and women hospitalized with AMI.

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