Rethinking the Epidemiology of Acute Myocardial Infarction

Challenges and Opportunities

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Background: During the previous decade, many strategies for preventing acute myocardial infarction found to be efficacious in randomized controlled trials have been adopted by physicians in the community. Although evaluations of quality improvement typically focus on process measures at the hospital, practice, or clinician level, assessment of improvements in health outcomes remains the true test for the successful translation of evidence into practice.

Methods: We performed a review of the current literature examining trends in the incidence of myocardial infarction in communities. We focused specifically on the group of population-based studies that have examined trends in myocardial infarction incidence.

Results: Few population-based studies have examined recent temporal trends in the incidence of myocardial infarction, overall and by type. Existing studies have been largely limited by modest sample sizes, limited diversity within the study populations, the use of composite end points that combine disparate outcomes, and the inability to characterize the effect of long-term outpatient medication use on observed trends in incidence and severity of myocardial infarction.

Conclusion: More contemporary assessments of community-wide changes in the epidemiology of myocardial infarction are needed to help assess the effectiveness of primary prevention and to identify areas for potential improvement.

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In recent years, many randomized controlled trials testing therapeutic strategies for the primary and secondary prevention of acute myocardial infarction (MI) have been completed.1-9 As a result, a host of combined medical and interventional strategies have been developed in the community to treat and prevent new and recurrent MIs. However, in the midst of improving practice patterns over time, there have been concurrent detrimental trends in the cardiovascular risk factor profile of the underlying population in the United States, including less physical activity, more obesity and diabetes mellitus, and aging of the population.10-12 Given the high human and economic tolls associated with MI and its sequelae, an accurate assessment of the effect of public health and medical interventions designed to prevent MI in the face of these countervailing forces is of critical importance. Although multiple cardiovascular disease registries have provided important contributions to our understanding of outcomes in acute coronary syndromes, the inability to quantify or characterize the underlying populations from which their patients are drawn limits their usefulness in studying disease incidence and the potential effectiveness of primary prevention efforts.13-15 Population-based studies on trends in MI have thus been the principal source of knowledge in the understanding of MI epidemiology. To date, however, existing literature assessing recent temporal trends in the incidence of MI is relatively sparse, and studies often lack sufficient power and diversity.

In this review, we summarize the current literature examining secular trends in the epidemiology of MI. We focus specifically on the group of population-based studies that have examined trends in MI incidence. We demonstrate that significant gaps remain in our knowledge of whether prevention efforts have led to a true reduction in MI incidence and highlight the need for a reexamination of the traditional distinction between primary and secondary prevention and the common grouping of distinct diseases into the overly broad category of coronary heart disease (CHD). Finally, we discuss briefly how the convergence on a universally accepted definition for MI and the maturation of large electronic health care databases will present opportunities for future studies to assess more accurately trends in disease incidence and prevention.
CURRENT EVIDENCE OF THE EPIDEMIOLOGY OF MI

We searched MEDLINE between 1980 and 2009 using the terms acute myocardial infarction, acute coronary syndrome, unstable angina, coronary heart disease, epidemiology, incidence, prevalence, and trends to find relevant studies. Several identified landmark population-based studies form the basis for what is currently understood about the epidemiology of cardiovascular disease, including temporal trends in incident MI. These studies have generally assembled and followed up moderate-sized samples of patients for the development of CHD, including the Framingham Heart Study (FHS), Minnesota Heart Survey, Worcester Heart Attack Study, and Rochester Epidemiology Project.16-19 Other researchers have studied groups of discrete communities, including the Atherosclerosis Risk in Communities (ARIC) study20 and studies of the Medicare population.21 Examinations of MI incidence within these populations have often yielded different conclusions, depending on the population examined.

STUDIES SUGGESTING NO TEMPORAL DECREASE IN MI INCIDENCE

Framingham Heart Study

Prior studies from the FHS have generally found decreases in overall CHD incidence over time but without corresponding decreases in MI incidence specifically. Sytkowski et al22 observed a significant decrease in the incidence of diagnosed CHD between the FHS 1950 and 1970 cohorts and a 50% reduction in cardiovascular deaths among participants aged 50 to 59 years in 3 successive FHS cohorts followed up for 20 years. On the basis of multivariable analyses, the authors concluded that changes in risk factors accounted for more than half the 51% decrease in deaths attributed to CHD in women between 1950 and 1989 and between one-third and half of the 44% decrease in CHD-related deaths in men during the same period. However, although the incidence of all CHD decreased, the incidence of identified MI did not show a significant change over time, and the proportion of MIs defined as Q-wave MIs remained constant.22,23 In a separate study, Guidry et al24 examined 546 patients aged 28 to 62 years between 1950 and 1989 who presented with initial Q-wave MI. There was a 23% decrease in subsequent all-cause mortality per decade examined and a 30% decrease per decade in CHD-related mortality after adjustment for age, sex, body mass index, diabetes, hypertension, and left ventricular hypertrophy. However, no significant differences were found in the rate of recurrent MI across decades.

ARIC Study

The ARIC study focused on the risk of CHD events among 360,000 residents aged 35 to 74 years in 4 communities: Forsyth County, North Carolina; Jackson, Mississippi; Minneapolis, Minnesota; and Washington County, Maryland.25,26 Between 1987 and 1996, a total of 14,942 hospitalized patients with definite or probable MIs were identified. Black men had the highest age-adjusted incidence of hospitalized MI, whereas white women had the lowest incidence.25,26 The age-adjusted incidence of first MI appeared to be relatively stable between 1987 and 1996, with nonsignificant increases of 1.1% per year in men and 1.7% per year in women. Of note, however, the incidence of first MI in blacks significantly increased by 4.1% per year in men and by 3.9% per year in women. Recurrent MIs decreased 1.9% per year in men and 2.1% per year in women, but the study was underpowered to look for differences across racial/ethnic groups. Case-fatality rates after MI decreased significantly by 6.1% per year in men and 6.2% per year in women between 1987 and 1996. On the basis of observed lower rates of recurrent MI and case-fatality accompanied by increases in incident MI, the authors hypothesized that strategies aimed at secondary prevention rather than primary prevention were largely responsible for improvements in CHD outcomes, although they were unable to directly test this hypothesis.25,26

Worcester Heart Attack Study

The Worcester Heart Attack Study has followed up a community-based cohort of residents of Worcester, Massachusetts, for cardiovascular events.27-29 In a study of patients hospitalized with MI (identified by International Classification of Diseases, Ninth Revision [ICD-9]30 codes and validated by medical record review) between 1975 and 1995, the age-adjusted incidence of first MI increased initially between 1975 and 1981 (to a peak of 272 cases per 100,000 population) then decreased until 1990, before having a slight increase again until 1995 (184 cases per 100,000). Among the trends observed over time were an increase in the median age of patients presenting with MI and an increase in the proportion of patients who were women, had diabetes, or had hypertension. There was no observed decrease in the crude long-term mortality rates after MI during the period studied. However, when adjusted for temporal changes in cardiovascular risk factors, there was a higher 1-year survival rate in the patients presenting in 1993 and 1995 compared with those presenting in 1975 or 1978 (relative risk, 1.56; 95% confidence interval, 1.13-2.16), although the trend was not consistent during the entire period.

STUDIES SUGGESTING A TEMPORAL DECREASE IN MI INCIDENCE

Minnesota Heart Survey

The Minnesota Heart Survey has examined trends in CHD in residents of the Minneapolis/St Paul area between the ages of 30 and 74 years.17 Investigators found a 20% decrease in MI incidence between 1985 and 1990 and again between 1990 and 1995 in men and women; on the other hand, the incidence of diagnosed unstable angina increased by 56% in men and 30% in women across the same period.17 In addition, there was a 50% decrease in CHD-related deaths between 1985 and 1997 (5.5% lower per year) predominantly driven by decreases in out-of-hospital deaths and lower case-fatality rates among patients...
who had been hospitalized for MI. Three-year death rates after MI decreased by 31% in men and 41% in women between 1985 and 1995.

Rochester Epidemiology Project

The Rochester Epidemiology Project examined the incidence of initial coronary artery disease (defined as initial MI), new coronary artery disease diagnosed by coronary angiography, sudden death, or unstable angina in Olmstead County, Minnesota, between 1979 and 1998.31,32 During the study period, 5772 cases of initial coronary disease occurred, including 1991 cases of MI. The incidence of MI remained relatively stable over time, decreasing from 195 cases per 100,000 population to 182 cases per 100,000 population in 1998, with an average yearly decrease of 0.35%, which was not statistically significant. However, in a separate analysis of the same population spanning 1979 to 1994, investigators found that the incidence of MI increased in women and decreased slightly in men (P = .01 for year-sex interaction), and women were found to have a significant age-adjusted increase in MI incidence of 2.1% per year. Mortality at 28 days was stable over time; however, an interaction with age existed, with a significant decrease in mortality in patients younger than 75 years but no significant change in patients 75 years or older.31

METHODOLOGIC CHALLENGES AND UNANSWERED QUESTIONS

The Changing Definition of MI

Published studies examining MI incidence in selected populations have yielded heterogeneous conclusions in assessing changes in the incidence of MI, despite the increasing adoption of strategies for prevention of MI that have been proven efficacious in randomized trials. Although it is possible that trends in the incidence of MI differ greatly by geography and population, closer examination reveals significant limitations in the ability to rely on the existing literature to make valid inferences on MI incidence. The increasing use of cardiac biomarkers for the diagnosis of MI during the past 2 decades and the changing cutoff levels for the laboratory tests used to define myocardial injury or MI are the most obvious complicating factors in many studies of MI trends.33,34 Examining the FHS data, Parikh et al35 recently found that trends in MI incidence were highly dependent on the definition used, with electrocardiography-diagnosed MI incidence decreasing by 50% between 1960 and 1999 but biomarker-diagnosed MI incidence increasing 2-fold. The use of biomarkers has likely improved the ascertainment of MI over time, which would have the dual effects of potentially masking true reductions in disease incidence because of primary prevention efforts and leading to false improvements in MI-related case fatality attributable to inclusion of smaller infarctions that previously would have been clinically unrecognized. The recent formation of a standardized definition of MI and acceptance of troponin I or T as the cardiac biomarker of choice with stably defined cutoff values may allow future inferences about MI incidence trends to be less confounded by changes in the methods of disease ascertainment.34 However, as more sensitive biomarkers or higher sensitivity assays are developed, the difficulties of assessing disease incidence introduced by increasing sensitivity of MI ascertainment will persist.

Limited Population Diversity

The US population is aging and changing quickly with regard to race/ethnicity, with persons of color expected to represent 33% of Americans by the year 2050.35 Yet, existing community- and population-based studies have been almost uniformly limited in the range of racial/ethnic diversity, with the notable exception of the ARIC study,36 and many have not included old-old (ages 85+) persons.37,38,39,40 Prior studies41-44 have highlighted differences in disease incidence, treatment, and outcomes that exist across different racial/ethnic and age groups with regard to cardiovascular disease. Their underrepresentation in clinical trials42 only serves to increase the importance of developing population-based studies in communities that adequately represent the growing sociodemographic diversity in many parts of the United States to provide a more complete and accurate assessment of the current epidemiology of MI.

Use of Combination Cardiovascular End Points

To address limitations in power, combination end points have been used extensively by existing epidemiologic studies. For example, each of the studies described previously have examined the incidence of CHD, typically by using a composite outcome that includes MI, stable angina, angiographically defined coronary disease, and sudden cardiac death, among other cardiac-related diagnoses.10-14 Although the grouping of these individual conditions may be justifiable on the basis of similar pathophysiologic findings, these diseases are often clinically managed in different ways and impose different burdens on patients, physicians, and health care systems. For example, from a health care system perspective, combining these distinct cardiac conditions does not lend necessary insight into the ways that health systems should adapt preventive and therapeutic strategies to changing secular trends in individual disease incidence. Management of stable angina requires a different set of personnel, medications, and other resources than management of acute coronary syndrome, yet these important distinctions can be lost in population-based analyses, which use composite outcomes combining these disparate end points. The pervasive grouping of ST elevation MI and non–ST elevation MI into the single category of MI is another example of the combining of diseases with disparate treatment strategies. Current guidelines have extremely different recommendations for the short-term management of these 2 entities, and ST elevation MI guidelines have led numerous hospitals and communities to establish extensive and costly systems of cardiac catheterization laboratory activation or rapid transfer to facilities with primary percutaneous coronary intervention capability.45-47 A recent study48 has suggested changing secular trends in the relative proportion of ST elevation MI and non–ST elevation MI, and, if confirmed, this would have important implications for the ways that community and health care system resources are organized in the future.

Lack of Data on Longitudinal Medication Use

Many of the published studies have focused on determining whether reductions in CHD are attributable to primary prevention efforts that prevent the first presentation of CHD vs secondary prevention efforts devoted to reducing...
Table. Selected Challenges and Future Directions in the Study of MI Epidemiology

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<tr>
<th>Limitations of Existing Literature</th>
<th>Description</th>
<th>Future Directions</th>
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<tbody>
<tr>
<td>Changing definition of MI</td>
<td>Increased sensitivity of diagnosing MI using cardiac biomarkers has confounded the interpretation of trends in MI incidence and case-fatality rates.</td>
<td>A consistently applied universal definition of MI may reduce drift in ascertainment. The likely introduction of newer and more sensitive biomarkers will necessitate the refinement of techniques to quantify the effect of increasing diagnostic sensitivity on MI incidence and severity over time.</td>
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<td>Limited population diversity</td>
<td>Previously published population-based studies have had limited sociodemographic diversity, reducing the ability to examine important patient subgroups.</td>
<td>The development of population-based studies with broader representation and the use of large administrative databases, including integrated health systems, will provide larger sample size and greater patient diversity.</td>
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<td>Use of combination cardiovascular end points</td>
<td>The grouping of diseases with different clinical and health economic implications in many population-based studies (a decision driven in part by low individual event rates) limits the complete assessment of prevention efforts.</td>
<td>The separation of component end points will require larger studies. Large administrative databases, combined with important clinical data (eg, cardiac enzyme results) and validation studies of coding algorithms, could provide the ability to evaluate individual end-point rates more precisely.</td>
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<td>Lack of data on longitudinal medication use</td>
<td>Most efforts at preventing disease are aimed at treating risk factors in the ambulatory setting. Few studies reliably capture comprehensive, longitudinal outpatient medication use data.</td>
<td>Linkage of pharmacy databases with other clinical data, including within integrated health systems, may enable studying the true effectiveness of prevention in the ambulatory setting.</td>
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<td>Difficulty assessing population denominators</td>
<td>Cardiovascular disease registries have limited clinical information on their underlying source populations.</td>
<td>Population-based studies will remain the gold standard for studies on disease incidence. Ensuring that administrative databases are representative of the populations they cover will be important.</td>
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<td>Separation of primary and secondary prevention</td>
<td>Studies attributing improvements in MI case fatality and morbidity to improvements in hospital care omit the possibility that primary prevention efforts may reduce MI severity.</td>
<td>Future studies of trends in MI-related morbidity and mortality should incorporate measures of presentation severity and prior treatment into their models.</td>
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Abbreviation: MI, myocardial infarction.

postevent morbidity and mortality. However, given that few data exist on population-wide trends in coronary risk factors or longitudinal medication use before an admission for an acute coronary event, the ability to accurately discern the true effect of disease prevention measures is limited. Major methodologic challenges exist in accurately tracking individual outpatient medication use over time and linking these exposures to other relevant patient characteristics and clinical outcomes. New approaches based on populations cared for within more integrated health care systems that routinely capture longitudinal medication exposure and other clinical data (eg, the Cardiovascular Research Network) offer potential cost-efficient ways to overcome many of these limitations.*

Is Prevention the Only Measure of Primary Prevention?

The debate on the relative effect of primary and secondary preventive measures on the overall reduction in CHD-related mortality carries an underlying assumption that the two are, in fact, distinct. Decreases in disease incidence are often seen as the sine qua non of successful primary prevention, whereas decreases in MI case fatalities are generally attributed to initial hospital-based treatment and subsequent postdischarge management. This dichotomy omits the possibility that interventions used as a means of preventing the initial MI may, in fact, also change the case-fatality rate after an MI, should it occur. The grouping of ST elevation MI and non-ST elevation MI is useful in highlighting this problem. The short-term mortality rate after ST elevation MI has been generally found to be higher than that after non–ST elevation MI.13 It is possible that better control of hypertension and dyslipidemia or lower smoking rates in the population would not only prevent an initial MI but also shift the distribution of MIs preferentially toward less severe forms, including non–ST elevation MI, as suggested by a recent ARIC study analysis.20 Thus, associated decreases in short-term mortality after MI that historically would have been attributed to improvements in in-hospital treatment may instead be a function of changes in the natural history of the severity of MI presentation influenced by measures traditionally classified as primary prevention. Conversely, more widespread use and improvement in cardiopulmonary resuscitation may lead to a higher hospitalized MI incidence and higher severity of infarcts. If not properly accounted for, such improvements in community-based cardiopulmonary resuscitation efforts and effectiveness could give the appearance of lower effectiveness of primary prevention and higher in-hospital case-fatality rates.

MOVING FORWARD

The significant limitations of existing studies—underrepresentation of key patient subgroups, reliance on combined disparate end points, lack of information on longitudinal medication use, and potential false dichotomy of effects of primary and secondary prevention—are fundamentally related to the difficulty of studying adequately sized, representative populations with detailed and accurate longitudinal data (Table). Population-based studies will remain the gold standard for characterizing trends in cardiovascular epidemiology and assessing the effect of primary prevention efforts in communities. However, future population-based studies of the epidemiology and outcomes of MI should be larger, have broader age and racial/ethnic diversity, and incorporate...
more detailed longitudinal exposure data on the underlying source population at risk for cardiovascular disease and those who experience an MI event.

Large electronic databases may overcome some of these existing limitations related to sample size and diversity. However, their use is complicated by challenges related to ensuring complete clinical information on patients with MI and the underlying source population, validated diagnoses based primarily on billing and discharge codes, and interoperability to facilitate valid comparisons across systems. We believe that integrated health care systems represent a middle ground between traditional cohort studies and large administrative database studies that will likely play an important role going forward. Integration of results from standardized validation studies of methods to define clinical events and coexisting conditions within cohort studies and large administrative databases, including Medicare data, is needed to support calibration of risk factor prevalence and cardiovascular event rates. These efforts would be useful to increase the validity and acceptance of studies primarily from electronic databases. However, the widespread use of these types of data, generally performed without the acquisition of individual-level informed consent from patients, highlights the need to ensure appropriate protections of patient privacy and the use of personal health information, particularly as increasingly detailed patient-level data are used for more sophisticated analyses.

Finally, the widespread adoption of a commonly accepted definition for MI and uniform use of cardiac troponin as the biomarker of choice may increase the ability of future studies on MI epidemiology to make more valid inferences about improvements in population cardiovascular health in the short term. However, as more sensitive biomarkers are introduced, future studies will need to be designed to account for the effects of changing diagnostic criteria on MI incidence and mortality. These combined efforts will provide the necessary evidence for the continued rigorous examination of quality of care and for supporting rational decision making on future health resource allocation to maximize the nation’s cardiovascular health.

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