Mortality Trends for Non–ST-segment Elevation Myocardial Infarction (NSTEMI) in the United States from 1988 to 2004

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ABSTRACT

Background: Non–ST-segment myocardial infarction (NSTEMI) is one of the major causes of hospital admissions. Mortality trend in patients with NSTEMI over the years has not been studied well. The goal of this study is to explore age-adjusted long-term mortality trends from NSTEMI in the United States using a very large database.

Methods: We used the National Inpatient Sample (NIS) database, a component of the Health Care Cost and Utilization (HCUP) project, for this study. International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM) codes were used to identify NSTEMI cases in patients >40 years old. Age-adjusted mortality rates for NSTEMI cases were calculated by multiplying the age-specific mortality rates of NSTEMI by age-specific weights.

Results: A total of 1,400,234 patients above the age of 40 years were identified. The mean age of this cohort was 77.1 ± 10.7 years, with a total of 179,361 deaths being reported over this 16-year period. Among patients who died, 51.2% were men and 48.8% were women. The age-adjusted mortality from NSTEMI declined from 1988 (727 per 100,000) to 2004 (305 per 100,000) until the middle of the decade when mortality from NSTEMI started leveling off. Total mortality decreased from 29.6% in 1988 to 11.3% in 2004.

Conclusions: Our analysis showed a significant reduction in the age-adjusted and total mortality for NSTEMI over the years studied. The cause of this trend is not known but most likely reflects advancement in the treatment of patients with acute coronary syndrome.

Introduction

In 2003, cardiovascular disease accounted for 37.3% of all deaths in the United States, making it the single largest cause of mortality among the US population.¹ Acute coronary syndrome (ACS) is an expression of cardiovascular disease and its occurrence frequently foretells short-term and long-term mortality. ACS is an umbrella term that encompasses unstable angina, non–ST-segment elevation myocardial infarction (NSTEMI), and ST-segment elevation myocardial infarction (STEMI). Of the 1.4 million patients admitted to hospitals in the United States with an ACS, almost 70% tend to have unstable angina or NSTEMI.² The 2000 consensus document defining myocardial infarction (MI), establishes NSTEMI as a substantiated clinical entity and diagnosis.³ NSTEMI patients do not have the typical ST segment elevation characteristic of patients with STEMI, but

still have release of cardiac biomarkers signifying myocardial necrosis secondary to coronary ischemia. Despite repeated guidelines,⁴ the management of NSTEMI has not been as rigorously defined as that of its more easily identifiable counterpart, STEMI. The aggressive revascularization strategies that have been championed for STEMI and have led to a decrease in STEMI mortality have not consistently been extended to patients with NSTEMI. Patients with NSTEMI also tend to be demographically different, when compared to patients who have STEMI.⁵ Secular trends for STEMI have shown a gradual decline in mortality in the United States,⁶ but the trends for mortality of NSTEMI remain imprecise. The goal of this study is to explore age-adjusted long-term mortality trends from NSTEMI in the United States using a very large database of inpatients, the National Inpatient Sample (NIS) database.

Methods

Our data has been obtained from the NIS database, a component of the Health Care Cost and Utilization (HCUP) project,⁷ which is sponsored by the Agency for Healthcare

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Research and Quality (AHRQ). The HCUP databases have been developed as a collective effort between government (both Federal and State) and industry, and serves as the largest collection of longitudinal hospital care data in the United States. The NIS contains data from roughly 8 million hospital stays per year, and is built from submitted payer information from hospital inpatient admissions in the United States, from 1988 through 2004. The database tries to provide a 20% stratified sample that reflects trends from community hospitals in the United States. The database discloses patient demographics, procedures, admission, and discharge status as well as primary and secondary discharge diagnoses. The International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM) coding system was used to identify NSTEMI cases. The specific codes that were utilized for the purposes of this study were: subendocardial infarction (410.71) and acute MI of unspecified site (410.91). We limited our analysis to patients >40 years old in order to exclude the majority of nonatherosclerotic causes of NSTEMI.

Age-adjusted mortality rates for NSTEMI patients were calculated by multiplying NSTEMI age-specific mortalities by age-specific weights. The age-specific mortality rates for NSTEMI patients were obtained from the NIS database. The age-specific weights were calculated from the National Center for Health Statistics recommended standardized US 2000 population. Statistical Package for the Social Sciences (SPSS) (SPSS, Inc., Chicago, IL) software was utilized for statistical analysis. Quantitative variables were expressed as means $\pm$ standard deviation (SD) and independent samples Student *t* test was used for comparative analysis. A *P* value of <0.05 was regarded as statistically significant.

Results

A total of 1,400,234 patients above the age of 40 years were selected from the NIS database based on the aforementioned ICD-9-CM codes. The mean age of this cohort was 77.1 ± 10.7 years, with a total of 179,361 deaths being reported over this 16-year period. Among patients who died, 51.2% were men and 48.8% were women. The age-adjusted mortality from NSTEMI declined from 1988 (727 per 100,000) to 2004 (305 per 100,000) (Table 1). A closer review of the table shows that there was a gradual decline in the mortality until the end of the 1990s when mortality from NSTEMI started leveling off (Figure 1). Total mortality also decreased from 29.6% in 1988 to 11.3% in 2004 (Figure 2).

Discussion

Data from the National Registry of Myocardial Infarction (NORMI) illustrates that from 1990 to 2006, the proportion of patients with NSTEMI increased while the proportion of STEMI declined.⁸ NSTEMI has at present replaced non-Q wave myocardial infarction (NQWMI) as the clinical counterpart to STEMI/Q wave myocardial infarction (QWMI). An STEMI is often associated with an occlusive coronary thrombus,⁹ while the pathological correlate of NSTEMI is less well-defined, likely associated with nonocclusive thrombi, inflammation, and dynamic coronary obstruction.¹⁰ Patients with NSTEMI generally tend to be older and have more extensive coronary disease than patients with

Table 1. NSTEMI Age-Adjusted Mortality from 1988 through 2004

Year	Population	Age-Adjusted Mortality (per 100,000)	Lower CI	Upper CI
1988	20977	727.2793	-256.926	1711.484
1989	31432	556.8362	-58.7623	1172.435
1990	50168	383.0445	47.85385	718.2352
1991	54488	370.5535	59.413	681.6941
1992	59814	359.9600	71.48454	648.4355
1993	63951	351.7327	79.1206	624.3449
1994	64767	322.3853	74.09806	570.6726
1995	71521	309.0036	82.5377	535.4695
1996	75480	295.9795	84.8243	507.1346
1997	86560	291.4456	97.28776	485.6035
1998	93354	291.7703	104.6027	478.9379
1999	103466	304.8158	119.0804	490.5512
2000	117238	298.6814	127.7074	469.6553
2001	120944	291.0755	127.028	455.123
2002	127539	293.6504	132.4874	454.8133
2003	131480	296.4909	136.2263	456.7556
2004	127055	305.2437	137.3993	473.0881

Abbreviations: CI, confidence interval; NSTEMI, non-ST-elevation myocardial infarction.

Figure 1. Trends in NSTEMI mortality from 1988 through 2004. Y-axis is the number of events per 100,000. Abbreviation: NSTEMI, non-ST-segment elevation myocardial infarction.

STEMI.⁵ In comparison to STEMI, patients who experience an NSTEMI have a lower 30-day mortality.¹¹ However, 6-month mortality rates are similar for STEMI and NSTEMI patients.¹²

Our analysis of the secular trends of over a million patients uncovers a significant reduction in age-adjusted mortality for NSTEMI patients over the period extending from 1988 to 2004. This finding is encouraging in the setting of initially increasing and later plateaued incident of NSTEMI.¹³ International registry analyses have also indicated a decrease in NSTEMI mortality, signaling that this is not

Figure 2. Total mortality (%) of patients with NSTEMI who died during the follow-up period. Abbreviation: NSTEMI, non-ST-segment elevation myocardial infarction.

a phenomenon that is exclusive to the United States.¹⁴ In the NRMI database, in-hospital mortality for NSTEMI decreased significantly by 22.6%.⁸ As can be expected, mortality rates from real-world registries are higher than the rates seen in controlled clinical trials. The Global Registry of Acute Coronary Events (GRACE) registry in-hospital mortality rate for NSTEMI was 5.9% and the 6-month mortality rate was 6.2%, with a 6-month rehospitalization rate of about 20%.¹⁵ Mortality from NSTEMI is affected by several factors including demographics such as age, gender, race and comorbidities, and clinical variables such as heart rate, blood pressure, electrocardiographic signs of ischemia, and presence of heart failure.¹⁶ Global risk stratification strategies, such as the GRACE and Thrombolysis in Myocardial Infarction (TIMI) scores, remain an integral component of the management of NSTEMI and assist in identifying patients at risk for recurrent ischemia and death.^{4,17} Higher TIMI scores have been associated with more extensive coronary artery disease¹⁸ as well as impaired epicardial blood flow and presence of visible thrombus.¹⁹

Management of NSTEMI remains hampered by lack of definitive evidence that assures the best outcome in such patients. Guidelines have been published, but the evidence base is nowhere near as robust as the ones for STEMI.^{4,20} Current treatment inclination includes an upfront medical approach followed by a downstream invasive or non-invasive management strategy. A 2010 Cochrane Review verified a 33% reduction in angina and rehospitalization at 6 months with an invasive strategy, along with a 27% reduction in MI at 12 months, albeit with a 2-fold increase in periprocedural MI.²¹ A 2006 meta-analysis of over 8000 patients found an early invasive strategy to have a lower all cause mortality at 24 months.²² In the “Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes with Early Implementation of the ACC/AHA Guidelines” (CRUSADE) registry, an early invasive strategy was associated with a 4.7% risk of death or MI as opposed to 8.9% risk with a conservative strategy.²³ An early invasive strategy was shown to be beneficial by the “Fragmin and fast Revascularization during InStability in Coronary artery disease” (FRISC) II, “Treat Angina with aggrastat and determine Cost of Therapy with Invasive or Conservative Strategy” (TACTICS)-TIMI 18, and “Randomized Intervention Trial of unstable

Angina” (RITA) 3 studies, especially in the subgroup of patients who were at a high risk, such as those patients presenting with an elevated cardiac troponin level. However, the most recent randomized “Invasive versus Conservative Treatment in Unstable Coronary Syndromes” (ICTUS) trial showed that an early invasive strategy was not superior to an early conservative strategy, even for the high risk patients, on the short-term and long-term clinical follow-up.²⁴

The role of an early invasive strategy in NSTEMI has been debated and a consensus continues to elude us, except in patients with high risk markers.^{24,25} Invasive strategies do decrease recurrent angina and MI, but a decrease in mortality has not been definitively or reproducibly documented.²¹ Currently, it is recommended that NSTEMI patients with high-risk features (recurrent ischemia, heart failure, left ventricular dysfunction, hemodynamic or electrical instability, and prior coronary artery bypass grafting [CABG]) undergo an invasive strategy.²⁶

Recently, emphasis has been made to optimize guideline-based medical therapy in patients presenting with ACS. Statins have been repeatedly shown to be effective in reducing recurrent event rates in patients with coronary artery disease. The use of high dose of statin in patients presenting with ACS has lead to lower adverse events. It has lead to improvement in the myocardial flow and lower adverse event²⁷⁻²⁹ and lower long-term event rates.³⁰⁻³² In addition to statin therapy, increases in the utilization of guideline-based therapy in recent years among treating physicians has been documented³³ as an important contributor to lower NSTEMI-related mortality.

Limitations of this analysis include its retrospective nature, which makes it susceptible to significant selection bias. Moreover, patient inclusion was entirely predicated by ICD-9-CM codes, a fact that may have hampered our ability to capture the intended target population. Nevertheless, the extremely large sample size that we have analyzed here intrinsically lends itself to a more robust conclusion. In the GRACE registry, rates of percutaneous coronary intervention (PCI) increased by 18% from 1999 to 2006 and 6-month death rates decreased by 1.6% in NSTEMI patients.³⁴ It would not be a stretch to hypothesize that the advent of a more aggressive and invasive approach to the management of NSTEMI may have contributed to the demonstrated decline in mortality. On the other hand, this remains to be unambiguously established.

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