ARIC Manuscript Proposal #725

PC Reviewed: 05/23/00 Status: A Priority: 1
SC Reviewed: 06/07/00 Status: A Priority: 1

1.a. Full Title: Prognosis of hospitalized myocardial infarction according to degree of myocardial injury assessed by biochemical markers and other risk indicators

1.b. Abbreviate Title (Length 26 characters): Prognosis of MI by Severity

2. Writing Group: (list the individual with lead responsibility first)
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3. Timeline: Analysis using closed 1987-1997 data can begin immediately. Final analyses for publication may require additional years of events to ensure sufficient cases with troponin values.

4. Rationale:
The case fatality for hospitalized myocardial infarction is decreasing. It is unknown whether this decrease differs according to MI severity, i.e., whether the decrease in case fatality is mostly among those with less severe MI. The case fatality among “suspect” MIs – cases with elevated cardiac enzymes but less than 2 x ULN – is unknown; these case do not contribute to calculated CHD incidence rates in ARIC but may contribute to CHD mortality. Assays for troponin T and troponin I, structural proteins that serve as markers for myocardial damage, were developed in the late 1980s. The ARIC diagnostic criteria for myocardial infarction have been revised to include these new cardiac markers. Results from clinical trials have shown that elevated troponin levels among cases of suspected MI are associated with increased risk of subsequent cardiac events (i.e., MI, death, unstable angina). However, these studies have taken place under controlled settings with specific patient exclusion criteria so the generalizability of these findings are limited. Analysis using ARIC data would allow for the assessment of the utility of cardiac biomarkers as indicators of severity of myocardial injury among all hospitalized cases of MI in the community-based surveillance population. Another marker of severity using items recorded in the medical record (PREDICT score) has recently been reported to predict long term prognosis after hospitalized MI.

5. Main Hypothesis:
   (1) Risk of mortality increases monotonically with increasing MI severity (PREDICT score and levels of cardiac enzymes, troponin I, and troponin T)
   (2) Trends in MI case fatality over time differ according to MI severity (PREDICT score and levels of cardiac enzymes, troponin I, and troponin T) after adjustment for treatment medications and procedures.
   (3) For a given level of severity, women are at higher risk of death than men, after adjustment for treatment.
6. **Data (variables, time window, source, inclusions/exclusions):**
Hospitalization in the ARIC community surveillance database including case fatality files. The PREDICT score uses information from the medical record including shock, heart failure, ECG findings, CVD history, kidney function, and age. Modifications to the PREDICT score will be investigated due to the fact that ARIC does not collect detailed data on kidney function. Peak levels for CK, CK-MB, troponin I, troponin T, LDH1, and LDH2 recorded during the hospitalization will be used. Survival analysis (Cox regression) will be used to assess the relationship between increasing MI severity and mortality risk, whether the relationship has changed over time, and whether these relationships differ for men and women. The management, including medications and procedures, of patients according to MI severity and gender will be compared.