

Suspected Acute Coronary Syndrome Patients With Diabetes and Normal Troponin-I Levels Are at Risk for Early and Late Death

Identification of a new high-risk acute coronary syndrome population

STEVEN P. MARSO, MD
DAVID M. SAFLEY, MD
JOHN A. HOUSE, MS

TODD TESSENDORF, MD
KIMBERLY J. REID, MS
JOHN A. SPERTUS, MD, MPH

Clinicians use a variety of methods (1,2) to risk stratify patients with acute coronary syndromes (ACSs). Based on elevated risk, patients are often triaged to an aggressive strategy, including early angiography (3,4) and upstream use of intravenous glycoprotein IIb/IIIa inhibitors (5–7). The current American College of Cardiology (ACC)/American Heart Association (AHA) Guidelines for the Management of Patients with Unstable Angina and Non-ST-segment Elevation Myocardial Infarction do not recognize diabetes as a high-risk ACS indicator. Therefore, we sought to clarify the relative risk of diabetes in early and late death in suspected ACS patients.

RESEARCH DESIGN AND METHODS

In this study, a prospective registry of consecutive ACS patients with and without diabetes ($n = 864$) was used. ACS was diagnosed as either myocardial infarction (8) or unstable angina (9) using standard definitions. Patients with ST-segment elevation myocardial infarction were excluded. All potential unstable angina patients who had a diagnostic angiographic, nuclear, or echocardiographic stress test that excluded obstructive coronary disease or who had an additional diagnostic study

confirming an alternative explanation for presentation were excluded. Diabetes was defined by reported history or new antidiabetic therapy initiated during the index hospitalization. Institutional review board approval was obtained, and all patients provided informed consent.

Continuous data are reported as means \pm SD. Differences between groups were tested using ANOVA and compared using χ^2 or Fisher's exact test. Survival curves were derived by Kaplan-Meier analysis and compared using log-rank tests. Analyses were performed using SAS version 9.1 (SAS Institute, Cary, NC) and R version 1.8.0.

RESULTS— There were 864 patients in this registry. There was a measurable difference in mortality at 30 days for diabetic patients compared with nondiabetic patients (1.7 vs. 0.2%, respectively, $P = 0.02$). Two-year survival rates by diabetes and troponin-I status are illustrated in Fig. 1.

The ACC/AHA high-risk features of ACS that were significant multivariable predictors of death at 2 years included rates (hazard ratio 2.5 [95% CI 1.4–4.3], $P = 0.002$), troponin greater than the upper limit of normal (1.9 [1.1–3.2], $P = 0.013$), previous myocardial infarction

(1.9 [1.2–3.0], $P = 0.004$), age per 10-year increase (1.5 [1.2–1.8], $P < 0.001$), and ejection fraction per 1% decrease (1.04 [1.02–1.06], $P < 0.001$). Diabetes was also a significant predictor (1.8 [1.1–2.7], $P = 0.014$).

In-hospital angiography was performed less frequently in diabetic patients than in nondiabetic patients (74 vs. 79%, respectively, $P = 0.077$). Among diabetic patients, 82% with elevated troponin-I levels underwent in-hospital angiography compared with 66% with normal troponin-I levels ($P < 0.001$). A significantly greater number of diabetic patients with normal troponin-I levels were managed medically (63 vs. 42%, $P < 0.001$). Administration of glycoprotein IIb/IIIa inhibitors was approximately three times more common in diabetic patients with troponin-I elevation compared with diabetic patients with normal levels (49 vs. 16%, respectively, $P < 0.001$).

CONCLUSIONS— In this series of ACS patients, diabetes was associated with increased risk of short- and long-term mortality. This risk persisted following multivariable adjustment, including the contribution of troponin-I levels and other recognized ACC/AHA high-risk features. We believe these findings confirm the prognostic importance of diabetes in ACS patients and suggest that it be included among the high-risk features of suspected ACS patients in clinical guidelines.

It is currently estimated that the prevalence of diabetes among ACS patients is approaching 50% (10). Physicians assess risk among suspected ACS patients in a variety of ways. Current ACC/AHA guidelines provide comprehensive and evidence-based methods to facilitate assessment, risk stratification, and treatment of ACS patients. However, diabetes is not recognized as a high- or intermediate-risk mediator. Our findings are consistent with others (11,12), although our

From the Mid America Heart Institute, University of Missouri-Kansas City, Kansas City, Missouri.

Address correspondence and reprint requests to Steven P. Marso, Associate Professor of Medicine, Mid America Heart Institute, University of Missouri-Kansas City, 4401 Wornall, Kansas City, MO 64111. E-mail: smarso@saint-lukes.org.

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Abbreviations: ACC, American College of Cardiology; ACS, acute coronary syndrome; AHA, American Heart Association.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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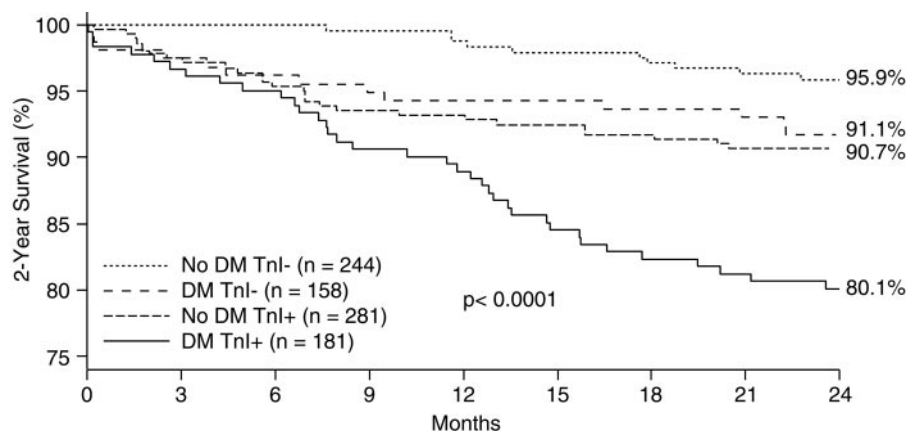


Figure 1—Kaplan-Meier survival rates at 2 years by diabetes status and troponin level. DM, diabetes mellitus; Tn-I+, troponin I greater than the upper limit of normal; Tn-I-, normal troponin I.

data extend the risk to patients with diabetes and normal troponin levels.

While we derived our population using strict inclusion criteria, a potential selection bias may have identified a unique population with normal troponin-I levels. Also, new-onset diabetes patients may have been misclassified as nondiabetic, resulting in an exaggerated difference in mortality if duration of diabetes mediates our observed mortality association. Although previous work is conflicting (13), it is plausible that unrecognized diabetic patients have a lower hazard for mortal events.

In this ACS population, diabetes was associated with increased risk of mortality. This difference was notable 30 days after ACS and persisted through 2 years. Although patients with diabetes and elevated troponin-I levels had a significant risk of 2-year death, patients with diabetes and normal troponin-I levels had a risk of death equivalent to patients without diabetes who had elevated troponin-I levels. Diabetes was also associated with risk estimates similar to the currently identified ACC/AHA high-risk ACS features. Patients with diabetes and normal troponin-I levels were less likely to undergo in-hospital angiography and receive medical treatment known to reduce risk. This study suggests that the risk of diabetes is at least equivalent to that of elevated troponin levels and supports the inclusion of diabetes as a high-risk feature in triaging ACS patients.

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