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Long-Term Prognostic Importance of Diabetes After a Myocardial Infarction Depends on Left Ventricular Systolic Function

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OBJECTIVE—This study was performed to understand how left ventricular function modulates the prognostic importance of diabetes after myocardial infarction (MI).

RESEARCH DESIGN AND METHODS—Consecutively hospitalized MI patients screened for three clinical trials were followed for a median of 7 years. Multivariable Cox regression models were used to assess the risk of mortality associated with diabetes, and the importance of diabetes was evaluated independently within defined left ventricular ejection fraction (LVEF) subgroups.

RESULTS—A total of 16,912 patients were included; 1,819 (11%) had diabetes. Diabetes and 15% unit depression in LVEF were of similar prognostic importance; hazard ratios (HRs) were 1.45 (95% CI 1.37–1.54) and 1.41 (1.37–1.45) for diabetes and LVEF depression, respectively. LVEF modified the outcomes associated with diabetes, with HRs being 1.29 (1.19–1.40) and 1.61 (1.40–1.74) in patients with LVEF <40% and LVEF ≥40%, respectively (P = 0.03).

CONCLUSIONS—Patients within the higher LVEF categories have a greater mortality risk attributable to diabetes than patients within the lower LVEF categories.

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During a median observational time of 2,609 days (interquartile range 820–3,937), 1,396 (77%) patients with diabetes and 8,985 (60%) patients without diabetes died, respectively. Figure 1 presents the unadjusted mortality rates for some given intervals of LVEF in patients with and without diabetes. Decreasing LVEF subgroup was associated with increasing hazard ratios (HRs) (adjusted for age, sex, wall motion index analysis method, and calendar year): 1.02 (0.81–1.27), 1.46 (1.34–1.60), 1.84 (1.64–2.06), and 1.61 (1.44–1.80) in the LVEF <25%, LVEF 25–35%, LVEF 36–50%, and LVEF >50% subgroups, respectively. In multivariable Cox analysis, diabetes and a 15% unit depression in LVEF were found to be of similar prognostic importance: HRs 1.45 (95% CI 1.37–1.54) and 1.41 (1.37–1.45) for diabetes and LVEF depression, respectively. The prognostic importance of diabetes was modulated by LVEF; P for interaction between diabetes and LVEF = 0.03. Among patients with low LVEF (<40%), diabetes was associated with HR 1.29 (1.19–1.40), which corresponded to the importance of having 10% unit depression in LVEF (HR 1.26 [1.24–1.28] in the overall analysis). Among patients with a high LVEF (≥40%), diabetes was associated with HR of 1.61 (1.49–1.74) and was of similar prognostic importance as 20% unit depression in LVEF (HR 1.58 [1.53–1.64]).

CONCLUSIONS—This study demonstrated that the prognostic importance of diabetes depends on left ventricular function, with diabetes having a stronger negative influence with preserved ventricular function. This result was also found in another study (3) and may appear counterintuitive given the detrimental influence of diabetes in patients with heart failure (9). However, the relationship between diabetes and heart failure is bidirectional, which may not always contribute causally to the adverse prognosis. For example, it is known that a great proportion of patients with severe heart failure will develop diabetes over time (10).

Other studies have in accordance with our finding reported the risk of dying from diabetes after MI to be greatest among patients with lowest baseline mortality risk (11) and among patients with mildest coronary artery lesions (12). In our study, diabetes was associated with a 60% increase in relative risk of mortality among patients with preserved LVEF. Although in the current study it was impossible to investigate what exactly may have driven this increase in risk, complications such as incident heart failure are common over time and are associated with a poor prognosis (13,14).

Finally, as previously reported (3), the protective effect on mortality associated with good left ventricular function after MI was found to be attenuated by diabetes, with diabetes conferring a risk equivalent to 10–20% unit depression in LVEF. With regards to prognostic stratification, this is clinically important because predischarge assessment of LVEF should be interpreted differently in patients with diabetes.

Limitations
The diagnosis of diabetes relied on patient history, and oral glucose tolerance tests were not performed on a routine basis. LVEF was estimated by wall motion index, which is observer-dependent and an approximation of LVEF. The current study did not have information on diabetes duration, HbA1c values, incident diabetes, use of glucose-lowering agents, or diastolic function, which may have influenced outcomes. Finally, the subgroup of patients with LVEF <25% was small; therefore, a small true increase in HR associated with diabetes cannot be excluded.

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C.A. wrote the initial draft of the manuscript and participated in data analysis. Study design came from S.D.S., C.T.-P., and L.K., who also analyzed data. All authors contributed equally to discussion and critical review of the manuscript.

References
1. Haffner SM, Lehto S, Ronnemaa T, Pyörälä K, Laakso M. Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. N Engl J Med 1998;339:229–234
2. Norgaard ML, Andersen SS, Schramm TK, et al. Changes in short- and long-term cardiovascular risk of incident diabetes

Figure 1.—Mortality rates per 100 person-years according to LVEF in patients with and without diabetes. Error bars represent 95% CIs. *P < 0.0001 for differences between patients with and without diabetes (obtained from unadjusted Cox analyses); LVEF <25% subgroup P for difference = 0.6.
and incident myocardial infarction: a nationwide study. Diabetologia 2010;53:1612–1619
3. Shah AM, Uno H, Køber L, et al. The inter-relationship of diabetes and left ventricular systolic function on outcome after high-risk myocardial infarction. Eur J Heart Fail 2010;12:1229–1237
4. Køber L, Torp-Pedersen C, Carlsen JE, et al. A clinical trial of the angiotensin-converting-enzyme inhibitor trandolapril in patients with left ventricular dysfunction after myocardial infarction. N Engl J Med 1995;333:1670–1676
5. Køber L, Bloch Thomsen PE, Møller M, et al. Effect of dofetilide in patients with recent myocardial infarction and left-ventricular dysfunction: a randomised trial. Lancet 2000;356:2052–2058
6. Torp-Pedersen C, Køber L, Ball S, et al. The incomplete bucindolol evaluation in acute myocardial infarction Trial (BEAT). Eur J Heart Fail 2002;4:495–499
7. Køber L, Torp-Pedersen C, Carlsen J, Videbaek R, Egeblad H. An echocardiographic method for selecting high risk patients shortly after acute myocardial infarction, for inclusion in multi-centre studies (as used in the TRACE study): TRAndolapril Cardiac Evaluation. Eur Heart J 1994;15:1616–1620
8. Berning J, Steensgaard-Hansen F. Early estimation of risk by echocardiographic determination of wall motion index in an unselected population with acute myocardial infarction. Am J Cardiol 1990;65:567–576
9. Gustafsson I, Brendorp B, Seibæk M, et al. Influence of diabetes and diabetes-gender interaction on the risk of death in patients hospitalized with congestive heart failure. J Am Coll Cardiol 2004;43:771–777
10. Andersson C, Norgaard ML, Hansen PR, et al. Heart failure severity, as determined by loop diuretic dosages, predicts the risk of developing diabetes after myocardial infarction: a nationwide cohort study. Eur J Heart Fail 2010;12:1333–1338
11. Singer DE, Moulton AW, Nathan DM. Diabetic myocardial infarction: interaction of diabetes with other preinfarction risk factors. Diabetes 1989;38:350–357
12. Ishihara M, Sato H, Kawagoe T, et al. Impact of diabetes mellitus on long term survival after acute myocardial infarction in patients with single vessel disease. Heart 2001;86:133–138
13. Gottlieiner JS, Arnold AM, Aurigemma GP, et al. Predictors of congestive heart failure in the elderly: the Cardiovascular Health Study. J Am Coll Cardiol 2000;35:1628–1637
14. de Simone G, Devereux RB, Chinali M, et al. Diabetes and incident heart failure in hypertensive and normotensive participants of the Strong Heart Study. J Hypertens 2010;28:353–360