Female Advantage in AMI Mortality Is Reversed in Patients With Type 2 Diabetes in the Skaraborg Project

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Abbreviations: AMI, acute myocardial infarction; CHD, coronary heart disease.

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

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Two major risk factors for acute myocardial infarction (AMI) are hypertension and type 2 diabetes (1). Men are also recognized as having a higher incidence of AMI than women (1); however, in subjects with type 2 diabetes, the female advantage is known to disappear. In fact, a Finnish study recently presented a significant interaction between female sex and type 2 diabetes in the risk of coronary heart disease (CHD) (2). The current study was therefore designed to explore further the potential interaction between sex and type 2 diabetes in the risk of AMI in patients treated within primary care. Since previous studies in patients with type 2 diabetes have shown that hypertension has stronger macrovascular implications than type 2 diabetes itself, the analyses also include hypertension (3,4).

RESEARCH DESIGN AND METHODS — In the Skaraborg county in southwestern Sweden, including the small community of Skara, patients with hypertension and/or diabetes have been treated at special outpatient clinics within primary care since the 1970s (the Skaraborg Hypertension and Diabetes Project) (5). From 1992 to 1993, all 1,149 patients with hypertension and/or diabetes who completed an annual check-up at the hypertension and diabetes clinic in Skara were consecutively surveyed for cardiovascular risk factors (5–10). From 1993 to 1994, a population survey using the same protocol as the patient survey was conducted with a randomized sample from the population census register, stratified by age and sex (11). Of 1,400 invited subjects ≥40 years of age, 1,109 (80%) completed the study visit. The ethics committee at Gothenburg University, Gothenburg, Sweden, approved both surveys.

After excluding 33 patients with type 1 diabetes, 1,116 patients of all ages remained from the patient survey. From the 1,109 subjects in the population survey, 824 remained after excluding 285 subjects with hypertension and/or diabetes. In both samples, all cases ≥85 years of age at baseline were excluded, leaving 1,085 subjects in the patient sample and 804 in the population sample. Those who reached 85 years of age during the follow-up period were then censored. The patient sample was divided into two categories according to diagnoses of hypertension and type 2 diabetes. All 804 remaining subjects in the population sample served as reference. Information on the end points, fatal AMI events, and all fatal events in this observational cohort study was ascertained according to a valid method (12,13) by record linkage with the national inpatient and mortality registers from baseline through 2002.

SPSS Base System for Macintosh 11.0 (SPSS, Chicago, IL) was used for data analyses. Mortality rates were age standardized in ten-year intervals using the whole Skara population ≥40 years old as standard. After controlling for proportionality, hazard ratios were examined, and confounders were accounted for by Cox proportional hazard model and expressed with 95% CIs. Two-way interaction terms were used to explore the association of sex, type 2 diabetes, and hypertension on AMI risk. All tests were two-sided and statistical significance assumed at \( P < 0.05 \).

RESULTS — While there were no obvious differences in risk factor levels between men and women at baseline, patients generally had more dyslipidemia and higher blood pressure and glucose than the reference population. The mean age for women was 67 years in patients and 59 years in the population, whereas corresponding means in men were 66 and 60 years. The majority of women were postmenopausal (92% of patients and 73% of the population were ≥50 years old).

After a mean follow-up of 8.1 years, there were 52 events of fatal AMI in men and 29 in women. Mortality rates were considerably lower in women (2/10,000 person-years) than in men (39/10,000) in subjects without type 2 diabetes, whereas they were higher in women (116/10,000) than in men (95/10,000) in patients with type 2 diabetes. The age-adjusted hazard ratios for patients with type 2 diabetes compared with the population were 5.0 (2.4–10.8) in women and 1.9 (1.1–3.2) in men. The only significant interaction was revealed between sex and type 2 diabetes showing, with a female disadvantage, a triple risk of fatal AMI (Table 1). All results remained when also adjusting for smoking, total cholesterol, BMI, and leisure-time physical activity.

CONCLUSIONS — Whereas the overall incidence of AMI is lower in women, the female advantage is known to disappear in subjects with type 2 diabetes, and the risk is sometimes even considered
the type 2 diabetic group includes all patients with type 2 diabetes, with or without hypertension. *Women compared with men.

Table 1—Two-way interactions between sex, hypertension, and type 2 diabetes

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<thead>
<tr>
<th>Sex</th>
<th>Hypertension</th>
<th>Type 2 diabetes</th>
<th>Hypertension and sex*</th>
<th>Hypertension and type 2 diabetes</th>
<th>Hypertension and type 2 diabetes and sex*</th>
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<td>Male</td>
<td>Prevalence</td>
<td>HR (95% CI)</td>
<td>NCI</td>
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Female AMI risk is reversed in type 2 diabetes


