

Cardiovascular Risk Attributable to Diabetes in Southern Brazil

A population-based cohort study

LEILA B. MOREIRA, MD, PHD¹
SANDRA C. FUCHS, MD, PHD²
MÁRIO WIEHE, MD, PHD³
JERUZA L. NEYELOFF³

RAFAEL V. PICON³
MARINA B. MOREIRA³
MIGUEL GUS, MD, PHD³
FLÁVIO D. FUCHS, MD, PHD³

OBJECTIVE — To analyze the effect of diabetes on general and cardiovascular disease (CVD) mortality and morbidity in southern Brazil.

RESEARCH DESIGN AND METHODS — A population-based cohort study of 1,091 individuals was conducted. Diabetes was ascertained by medical history. The vital status of 982 individuals and the incidence of events were ascertained during another visit and through hospital records, death certificates, and verbal necropsy with relatives.

RESULTS — The mean \pm SD age of participants was 43.1 ± 17 years, and 55.7% were women. The prevalence of diabetes was 4.2%, and the mean follow-up time was 5.3 ± 0.07 years. Mortality was 36.3% and 6.6% in participants with or without diabetes, respectively; the incidence of CVD was 20.8% and 3.0%, with an adjusted hazard ratio of 4.4 (95% CI 2.4–7.9). Diabetic population-attributable risk (PAR) for CVD mortality was 10.1% and 13.1% for total CVD.

CONCLUSIONS — Diabetes is responsible for a large PAR for overall mortality and cardiovascular events in Brazil.

Diabetes Care 32:854–856, 2009

Approximately 2.2 million deaths worldwide from ischemic heart disease and stroke were attributed to high levels of blood glucose in 2001 (1). We describe the effect of diabetes on cardiovascular disease (CVD) morbidity and mortality in southern Brazil.

RESEARCH DESIGN AND METHODS

The baseline data of this cohort study were collected from 1989 and have previously been described in detail (2,3). In brief, 1,091 participants aged ≥ 18 years, identified through a population-based multistage probability sampling, were interviewed at home after they had given informed consent. Diabetes was established for partic-

ipants who self-reported a physician diagnosis or who were using drugs for diabetes.

Incident CVD was adjudicated if a participant reported the occurrence of a cardiovascular event since the baseline visit, and a detailed history was obtained or the cause of death was identified through medical records and verbal necropsy with relatives. The final ascertainment of the cause of death and incident CVD (myocardial infarction, stroke, heart failure, and sudden death) was done by two clinicians based on interview records, death certificates, and hospital records.

Data were analyzed using the complex sample module in SPSS (version 16). Hazard ratios (HRs) were computed using

the survival analysis and the time frame from baseline to the second visit as time to event, adjusting for age, sex, skin color, smoking habits, alcohol consumption, blood pressure, and BMI. Diabetic population-attributable risk (PAR), adjusted for the same confounders, was computed with the Interactive Risk Assessment Program (version 2.2; National Cancer Institute, Bethesda, MD).

RESULTS — The mean \pm SD age of the 982 individuals was 43.1 ± 17 years (range 18–81), and 55.7% were women. Overall prevalence of diabetes was 4.2% (95% CI 3.0–5.8) and increased to 7.3% (5.4–10.0) among participants aged ≥ 40 years, as only three individuals aged < 40 years reported diabetes. The mean follow-up time was 5.3 ± 1.5 years, being 5.4 ± 1.5 years for nondiabetic individuals and 4.1 ± 2.1 years for diabetic individuals ($P < 0.001$). Participants who reported diabetes were older (62.8 ± 14.7 vs. 55.5 ± 16.7 years; $P < 0.001$) and had higher BMI (28.4 ± 4.9 vs. 26.2 ± 4.6 kg/m²; $P < 0.001$) and systolic blood pressure (149.2 ± 26.9 vs. 135.2 ± 22.2 mmHg; $P < 0.001$). Table 1 shows that the medical diagnosis of diabetes was a strong risk factor for overall mortality and fatal plus nonfatal CVD events. In the analysis stratified by skin color, the HRs were significant for white participants for overall mortality (4.2 [95% CI 2.1–8.4]), fatal CVD events (2.0 [1.1–3.6]), and fatal plus nonfatal CVD events (5.0 [2.4–10.0]). In nonwhite participants, the estimates remained at the risk side but were significant only for fatal plus nonfatal CVD events: 2.8 (95% CI 0.7–11.3) for overall mortality, 1.1 (0.3–3.4) for fatal CVD events, and 5.5 (1.2–24.7) for fatal plus nonfatal CVD events.

Diabetes explained about 9% of overall mortality, 10% of CVD mortality, and 13% of fatal plus nonfatal cardiovascular events in this population, with an adjusted PAR of 9.8 (95% CI 3.8–22.9), 10.1 (1.9–39.2), and 13.1 (5.8–26.9), respectively.

From the ¹Department of Pharmacology, School of Medicine, Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil; the ²Department of Social Medicine, School of Medicine, Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil; and the ³Division of Cardiology, Hospital de Clínicas de Porto Alegre, Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil.

Corresponding author: Leila B. Moreira, lbmoreira@hcpa.ufrgs.br.

Received 28 October 2008 and accepted 10 February 2009.

Published ahead of print at <http://care.diabetesjournals.org> on 19 February 2009. DOI: 10.2337/dc08-1948.

© 2009 by the American Diabetes Association. Readers may use this article as long as the work is properly cited, the use is educational and not for profit, and the work is not altered. See <http://creativecommons.org/licenses/by-nc-nd/3.0/> for details.

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked "advertisement" in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

Table 1—Incidence and HRs for overall mortality, CVD mortality, and fatal plus nonfatal CVD in diabetic and nondiabetic individuals

	Event rate % (95% CI)	Events (1,000 person-years)	HR (95% CI)*	P
Overall mortality	7.9 (5.7–7.8)	14.1		0.001
No diabetes	6.6 (4.6–9.4)	12.2	1.0	
Diabetes	36.3 (20.2–56.3)	88.5	3.6 (1.8–7.2)	
CVD mortality	2.7 (1.7–4.3)	4.8		0.16
No diabetes	2.2 (1.2–3.6)	4.1	1.0	
Diabetes	14.0 (5.1–32.9)	34.2	1.5 (0.8–2.5)	
Fatal/nonfatal CVD†	3.7 (2.7–5.2)	6.6		<0.001
No diabetes	3.0 (2.0–4.3)	5.6	1.0	
Diabetes	20.8 (11.3–35.0)	50.7	4.4 (2.4–7.9)	

*Cox regression analysis: HR adjusted for age, sex, skin color, smoking habits, alcoholic beverage consumption, systolic blood pressure, and obesity. †Sudden death, congestive heart failure, myocardial infarction, and stroke.

CONCLUSIONS— This population-based cohort study confirmed that diabetes is a major risk factor for overall mortality and fatal and nonfatal cardiovascular events in southern Brazil, demonstrating that Brazilian populations had already experienced the epidemiological transition and are presenting with risks for chronic diseases similar to those in developed countries. The risks were not substantially different in white and non-white individuals.

The baseline prevalence of diabetes (4.2%) was somewhat lower than that reported in another recent survey in Brazil (6.3%) (4) and in the National Health and Nutrition Examination Surveys (NHANESs) of 1988–1994 (5.1%) and 1999–2002 (6.5%) (5) and may be secondary to an underreporting.

Overall mortality incidence in diabetic participants accounted for 19.2% of the deaths, which is more than the 10.6% reported in NHANES I (6). The high incidence of cerebrovascular disease in the southern regions of Brazil (7) may explain this higher prevalence because diabetes has been associated with increased risk of incident stroke (8,9). The risks for cardiovascular events were almost restricted to individuals aged >40 years because only three individuals reported diabetes at a younger age.

The adjusted HR for fatal and nonfatal CVD in our study (4.4 [95% CI 2.4–7.9]) is similar to the odds ratio of 4.2 (95% CI 2.5–7.1) for acute myocardial infarction reported in the INTERHEART study in Brazil (10). The PAR of fatal/nonfatal CVD associated with self-reported diabetes (13.1%) is close to the 12.7% (9.4–17.0) reported in South America and to the data

reported in the Brazilian participants of the INTERHEART study (17.0% [95% CI 12.2–23.1]) (11).

The major limitation of our study is the small sample size and, therefore, the small number of incident events. This explains the wide CIs and precluded stratification of the analysis by sex. Other studies (11–13) suggested that the risk of fatal or nonfatal coronary heart disease associated with diabetes is higher in women than in men. Otherwise, a cohort of Brazilian type 2 diabetic patients (14) did not demonstrate any differences in diabetes-related mortality risk between sexes. The diagnosis of diabetes—based on medical history without screening by blood glucose sampling—may explain the lower prevalence of diabetes in our study than in other Brazilian surveys (15), but it probably did not substantially influence the risk estimates as shown by Huxley et al. (13). The PAR, however, is influenced by the prevalence rates and therefore may be higher than our estimates. The population-based sample and the control for other risk factors for CVD are strengths of our study.

In conclusion, diabetes has a high PAR for cardiovascular events in Brazil. As such, interventions aiming to prevent and control diabetes should warrant high priority among the public health strategies to lower the incidence of CVD in Brazil.

Acknowledgments— This study was funded by the National Council for Scientific and Technological Development (CNPq), the Research Foundation of the State of Rio Grande do Sul (FAPERGS), and Hospital de Clínicas-FIPE, Brazil.

No potential conflicts of interest relevant to this article were reported.

References

- Danaei G, Lawes CM, Vander Hoorn S, Murray CJ, Ezzati M. Global and regional mortality from ischaemic heart disease and stroke attributable to higher-than-optimum blood glucose concentration: comparative risk assessment. *Lancet* 2006;368:1651–1659
- Moreira LB, Fuchs FD, Moraes RS, Brede-meier M, Cardozo S, Fuchs SC, Victora CG. Alcoholic beverage consumption and associated factors in Porto Alegre, a southern Brazilian city: a population-based survey. *J Stud Alcohol* 1996;57:253–259
- Moraes RS, Fuchs FD, Moreira LB, Wiehe M, Pereira GM, Fuchs SC. Risk factors for cardiovascular disease in a Brazilian population-based cohort study. *Int J Cardiol* 2003;90:205–211
- Capilheira MF, Santos IS, Azevedo MR Jr, Reichert FF. Risk factors for chronic non-communicable diseases and the CARMEN Initiative: a population-based study in the South of Brazil. *Cad Saude Publica* 2008;24:2767–2774
- Cowie CC, Rust KF, Byrd-Holt DD, Eberhardt MS, Flegal KM, Engelgau MM, Saydah SH, Williams DE, Geiss LS, Gregg EW. Prevalence of diabetes and impaired fasting glucose in adults in the U.S. population: National Health and Nutrition Examination Survey 1999–2002. *Diabetes Care* 2006;29:1263–1268
- Gu K, Cowie CC, Harris MI. Mortality in adults with and without diabetes in a national cohort of the U.S. population, 1971–1993. *Diabetes Care* 1998;21:1138–1145
- Marinho de Souza MF, Timerman A, Serrano CV Jr, Santos RD, de Pádua Mansur A. Trends in the risk of mortality due to cardiovascular diseases in five Brazilian geographic regions from 1979 to 1996. *Arq Bras Cardiol* 2001;77:562–575
- Ho JE, Paultre F, Mosca L; Women's Pooling Project. Is diabetes mellitus a cardiovascular disease risk equivalent for fatal stroke in women? Data from the Women's Pooling Project. *Stroke* 2003;34:2812–2816
- Kuller LH, Velentgas P, Barzilay J, Beauchamp NJ, O'Leary DH, Savage PJ. Diabetes mellitus: subclinical cardiovascular disease and risk of incident cardiovascular disease and all-cause mortality. *Arterioscler Thromb Vasc Biol* 2000;20:823–829
- Lanas F, Avezum A, Bautista LE, Diaz R, Luna M, Islam S, Yusuf S; INTERHEART Investigators in Latin America. Risk factors for acute myocardial infarction in

- Latin America: the INTERHEART Latin American study. *Circulation* 2007;115:1067–1074
11. Yusuf S, Hawken S, Ôunpuu S, Dans T, Avezum A, Lanas F, McQueen M, Budaj A, Pais P, Varigos J, Lisheng L; INTERHEART Study Investigators. *Lancet* 2004;364:937–952
 12. Hu FB, Stampfer MJ, Solomon CG, Liu S, Willett WC, Speizer FE, Nathan DM, Manson JE. The impact of diabetes mellitus on mortality from all causes and coronary heart disease in women: 20 years of follow-up. *Arch Intern Med* 2001;161:1717–1723
 13. Huxley R, Barzi F, Woodward M. Excess risk of fatal coronary heart disease associated with diabetes in men and women: meta-analysis of 37 prospective cohort studies. *BMJ* 2006;332:73–78
 14. Salles GF, Bloch KV, Cardoso CR. Mortality and predictors of mortality in a cohort of Brazilian type 2 diabetic patients. *Diabetes Care* 2004;27:1299–1305
 15. Oliveira JE, Milech A, Franco LJ, the Cooperative Group for the Study of Diabetes Prevalence in Rio De Janeiro. The prevalence of diabetes in Rio de Janeiro, Brazil. *Diabetes Care* 1996;19:663–666