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Coronary Atherosclerosis in Diabetes Mellitus

A Population-Based Autopsy Study

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OBJECTIVES The study was conducted to test the hypothesis that the prevalence of coronary atherosclerosis is greater among diabetic than among nondiabetic individuals and is similar for diabetic individuals without clinical coronary artery disease (CAD) and nondiabetics with clinical CAD.

BACKGROUND Persons with diabetes but without clinical CAD encounter cardiovascular mortality similar to nondiabetic individuals with clinical CAD. This excess mortality is not fully explained. We examined the association between diabetes and coronary atherosclerosis in a geographically defined autopsied population, while capitalizing on the autopsy rate and medical record linkage system available via the Rochester Epidemiology Project, which allows rigorous ascertainment of coronary atherosclerosis, clinical CAD, and diabetes.

METHODS Using two measures, namely a global coronary score and high-grade stenoses, the prevalence of atherosclerosis was analyzed in a cohort of autopsied residents of Rochester, Minnesota, age 30 years or older at death, while stratifying on diabetes, clinical CAD diagnosis, age, and gender.

RESULTS In this cohort, diabetes was associated with a higher prevalence of atherosclerosis. Among diabetic decedents without clinical CAD, almost three-fourths had high-grade coronary atherosclerosis and more than half had multivessel disease. Without diabetes, women had less atherosclerosis than men, but this female advantage was lost with diabetes. Among those without clinical CAD, diabetes was associated with a global coronary disease burden and a prevalence of high-grade atherosclerosis similar to that observed among nondiabetic subjects with clinical CAD.

CONCLUSIONS These findings provide mechanistic insights into the excess risk of clinical CAD among diabetic individuals, thereby supporting the need for aggressive prevention of atherosclerosis in all diabetic individuals, irrespective of clinical CAD symptoms. (J Am Coll Cardiol 2002; 40:946–53) © 2002 by the American College of Cardiology Foundation

Individuals with diabetes have an increased risk of coronary artery disease (CAD) morbidity and mortality (1–3). People with type 2 diabetes experience higher rates of ischemic events and death after a first myocardial infarction (MI) (4–9); and in the absence of established CAD, they experience the burden of CAD at a rate equal to that of nondiabetic individuals with established CAD (10,11). This implies that prevention measures for asymptomatic diabetic individuals should be similar to secondary prevention measures among nondiabetic individuals, a position recently adopted by the American Diabetes Association and the Joint National Committee VI (12,13). Whereas the clustering of other cardiac risk factors with diabetes suggests an increased prevalence of atherosclerosis (4,7,14–16), the mechanisms for increased clinical CAD burden in diabetes are not fully defined. To this end, contrasting and speculative reports point toward more severe anatomic CAD or increased frequency of clinical events due to microvascular disease or coagulation disturbances (17–20); yet the argument for aggressive preventive measures in diabetics is based on the assumption of higher prevalence of atherosclerosis among diabetic individuals even in the absence of clinical CAD, despite the lack of anatomic data supporting this approach. Angiographic case series, which include patients referred to angiography with most often symptoms of CAD, cannot, by design, define the burden of anatomic CAD in asymptomatic subjects (21).

Prior autopsy studies in diabetics were subject to referral bias owing to their hospital-based nature or to exceedingly low autopsy rates in the source population (18), whereas other studies were limited by small sample size (17–19,22–24).

Higher autopsy rates in Rochester, Minnesota, combined with detailed ascertainment of antemortem CAD and diabetes, offer a unique opportunity to examine the anatomic atherosclerotic burden according to the presence or absence of diabetes among autopsied decedents in the community. We tested the hypothesis that the prevalence of coronary atherosclerosis was greater among diabetic than among nondiabetic individuals and that the prevalence of coronary atherosclerosis among diabetic individuals without

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Abbreviations and Acronyms

CAD = coronary artery disease
CI = confidence interval
MI = myocardial infarction
NDDG = National Diabetes Data Group
OR = odds ratio
PR = prevalence ratio

antemortem CAD was similar to that among nondiabetics with clinical antemortem CAD.

METHODS

Study setting and population. The environment in Olmsted County, Minnesota, provides a unique setting to assess anatomic aspects of clinical diseases because its population is served by a unified medical care system that has accumulated comprehensive records over a long period of time and has relatively high autopsy rates (25,26). Each care provider in the county uses a unit medical record system whereby all data are assembled in one place. These are easily retrievable as the Rochester Epidemiology Project (AR-30582) developed extensive indices based on clinical and histologic diagnoses and surgical procedures, resulting in the linkage of all inpatient and outpatient medical records including death certificates and autopsy reports for the entire county population. For this study, all residents of Rochester who had an autopsy between 1979 and 1994 and were age 30 years or older at time of death were included. Except for coroner's cases, the decision to perform an autopsy is made on a case-by-case basis with the attending physician and the family.

Conduct of the autopsy. All autopsies of persons dying in hospitals or nursing homes and of coroner's cases in Olmsted County are performed in the Medical Sciences Department of Pathology at the Mayo Clinic, using uniform, comprehensive, and standardized techniques (27). Both its validity and its reproducibility were prospectively examined and reported as all specimens are archived as part of the Rochester Epidemiology Project Autopsy Registry (26).

The major extramural coronary arteries are examined by serial transverse sectioning at 5-mm intervals. Arteries with extensive calcification are dissected out intact and decalcified before sectioning. The left main, left anterior descending, left circumflex, and right coronary arteries are graded in ascending order of reduction in cross-sectional luminal area by visual inspection by each prosector at the time of autopsy. The semi-quantitative grading system reports on the degree of reduction in luminal area including: grade 1, up to 25% reduction; grade 2, 26% to 50% reduction; grade 3, 51% to 75% reduction; grade 4, 76% to 99% reduction; and grade 5, complete occlusion. This standardized system was consistently used during the study period (28,29).

Ascertainment of baseline characteristics and data collection. The Rochester Epidemiology Project diagnostic index was used to identify all Rochester decedents with diabetes or diabetes-like condition (e.g., hyperglycemia, elevated blood glucose, impaired glucose tolerance, diabetic nephropathy) from the date of first contact with any care provider until death. The median duration of medical history available for review was 43 years (first-quartile–third quartile = 24 to 58 years). For autopsied decedents, abstractors reviewed all medical records (including all laboratory glucose values) to validate the diagnosis of diabetes, using the criteria of the National Diabetes Data Group (NDDG). These require two consecutive fasting glucose levels of 140 mg/dl or more or 1- to 2-h levels of 200 mg/dl or more obtained using a standard oral glucose tolerance test (30). Published methods were used to adjust for temporal changes in laboratory methods to measure glucose (31). Several Rochester Epidemiology Project studies on diabetes used these criteria (32–34). To select adult-onset diabetes, only those decedents older than 30 years of age when they first met NDDG criteria were included. In previous studies, 94% of diabetics in this age group were categorized as type 2 diabetes using an algorithm based on age, body mass index, treatment, and evidence of ketosis (35). The abstractors collected demographic and autopsy data. Antemortem diagnosis of CAD was ascertained with the Rochester Epidemiology Project diagnostic index using all clinical codes for angina, MI, and other forms of coronary disease. Because autopsy data are used to assign the cause of death in Olmsted County, only diagnoses made prior to death or autopsy were included as clinical diagnosis. Deaths were ascribed to CAD if the underlying cause of death on the death certificate was coded as codes 410 through 414 of the International Classification of Disease–9th revision.

Data analysis. Descriptive statistics used chi-square tests for categorical variables and *t* tests or rank-sum tests for continuous variables. Coronary atherosclerosis was analyzed using two complementary methods focusing on four predefined arterial segments including the left main, right, circumflex, and left anterior descending coronary arteries. First, for each patient we generated a summary coronary score by summing the grades for each artery such that the scores could take values ranging from 4 for grade 1 in each segment to a maximum of 20 for grade 5 in each segment. Three coronary score strata were constructed (4 to 9, 10 to 15, and 16 to 20). Second, we defined high-grade coronary atherosclerosis as the presence of grade 3 or higher disease in the left main, or grade 4 or higher disease in any of the other three segments, using customary thresholds (36). Multivessel disease was defined as the presence of high-grade coronary atherosclerosis in either the left main or two or more major coronary arteries. The prevalence of high-grade atherosclerosis and the summary coronary scores were compared between diabetic and nondiabetic individuals, while stratifying on antemortem diagnosis of CAD, age, and gender. Prevalence rates were compared using preva-

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Table 1. Demographic and Clinical Characteristics of Decedents Undergoing Autopsy by Diabetes Status

	Diabetes (n = 293)	No Diabetes (n = 1,763)	p Value
Decedent characteristics			
Male gender (%)	51	48	0.34
Mean age ± SD	75 ± 11	73 ± 15	0.14
Out-of-hospital deaths (%)	54	56	0.52
Coroner's cases (%)	44	47	0.41
Antemortem CAD (%)	49	33	< 0.001
Body mass index (kg/m^2)	27 ± 20	23 ± 8	< 0.001
Autopsy results			
Cardiac hypertrophy (%)	57	45	< 0.001
MI by autopsy (%)	49	35	< 0.001
LV dilation (%)	26	21	0.06

CAD = coronary artery disease; LV = left ventricle; MI = myocardial infarction.

lence ratios with standard errors obtained using published approaches (37). Each individual was classified into one of four categories according to diabetes and antemortem CAD statuses. Analysis of variance with Bonferroni correction for multiple comparisons was used to compare the summary coronary scores among groups. Logistic regression examined the association between high coronary score (defined as 10 or higher) and the categories representing diabetes/antemortem CAD status while adjusting for age and gender. To examine the generalizability to nonautopsied decedents, referral to autopsy by diabetic status, age, gender, and location of death of all decedents was examined. All aspects of the study were approved by the Mayo Clinic Institutional Review Board.

RESULTS

Baseline characteristics. The demographic and clinical characteristics of 293 diabetic and 1,736 nondiabetic autopsied residents of Rochester are shown in Table 1. Age and gender distributions were similar. Diabetic individuals had a higher body mass index, were more likely to have clinical CAD and to have left ventricular dilation, hypertrophy, and evidence of MI.

Global atherosclerosis burden and high-grade atherosclerosis. The summary coronary score, an indicator of the *global atherosclerosis burden*, had a mean value of 11.3 ± 3.4 in diabetics, significantly higher than the mean of 9.8 ± 3.6 among nondiabetics ($p < 0.0001$). A greater percentage of diabetics had higher scores in the upper two strata of the scores as compared to nondiabetics (74% vs. 55%, $p < 0.001$).

The prevalence of *high-grade atherosclerosis* according to diabetes, age, and gender is shown in Table 2. Among diabetic decedents, 75% had high-grade coronary atherosclerosis versus only 55% among nondiabetic decedents (prevalence ratio [PR], 1.3; 95%CI [confidence interval], 1.2 to 1.5, $p < 0.001$). Among nondiabetics, the prevalence of high-grade coronary atherosclerosis was higher in men (62%) than in women (49%) (PR, 1.3; 95%CI, 1.2 to 1.4, $p < 0.001$). However, no gender difference was detected

Table 2. Prevalence of Any High-Grade and Multivessel Coronary Atherosclerosis by Age and Gender

	Any High-Grade Coronary Atherosclerosis			Multivessel High-Grade Coronary Atherosclerosis		
	Diabetes (n/total)†	No Diabetes (n/total)†	PR (95%CI), p Value	Diabetes (n/total)†	No Diabetes (n/total)†	PR (95%CI), p Value
Overall	75% (219/293)	55% (962/1736)	1.4 (1.2–1.5), p < 0.001	58% (171/293)	41% (718/1736)	1.4 (1.2–1.6), p < 0.001
Men	79% (118/149)	62% (519/831)	1.3 (1.1–1.4), p < 0.001	62% (92/149)	48% (399/831)	1.3 (1.1–1.5), p = 0.002
Women	70% (101/144)	49% (443/905)	1.4 (1.2–1.7), p < 0.001	55% (79/144)	35% (319/905)	1.6 (1.3–1.9), p < 0.001
PR men vs. women (95%CI), p value	1.1 (1.0–1.3), p = 0.07	1.3 (1.2–1.4), p < 0.001		1.1 (0.9–1.4), p = 0.23	1.4 (1.2–1.5), p < 0.001	
Age 30–64 yrs						
Men	58% (18/31)	52% (153/293)	1.1 (0.8–1.6), p = 0.54	45% (14/31)	37% (107/293)	1.2 (0.8–1.9), p = 0.34
Women	64% (14/22)	35% (43/170)	2.5 (1.5–4.1), p < 0.001	50% (11/22)	18% (30/170)	2.8 (1.6–5.1), p < 0.001
PR men vs. women (95%CI), p value	0.9 (0.6–1.4), p = 0.68	2.1 (1.6–2.7), p < 0.001		0.9 (0.5–1.6), p = 0.73	2.1 (1.5–2.9), p < 0.001	
Age ≥ 65 yrs						
Men	85% (100/118)	68% (366/538)	1.3 (1.1–1.4), p < 0.001	66% (78/118)	54% (292/538)	1.2 (1.0–1.4), p = 0.019
Women	71% (87/122)	54% (400/735)	1.3 (1.1–1.5), p < 0.001	56% (68/122)	39% (289/735)	1.4 (1.2–1.7), p < 0.001
PR men vs. women (95%CI), p value	1.2 (1.0–1.4), p < 0.01	1.3 (1.1–1.4), p < 0.001		1.2 (1.0–1.5), p = 0.10	1.4 (1.2–1.6), p < 0.001	

†n = number with high-grade coronary atherosclerosis; total = total number of decedents within each category; CI = confidence interval; PR = prevalence ratio.

between diabetic men (79%) and diabetic women (70%) (PR, 1.1; 95%CI, 1.0 to 1.3, p = 0.07). The effect of diabetes was most salient in younger women, with a PR for diabetics versus nondiabetics of 2.5 (95%CI, 1.5 to 4.1). The difference was not significant for young diabetic men (PR, 1.1; 95%CI, 0.8 to 1.6, p = 0.54).

Among older decedents, a modest increase in the prevalence of high-grade coronary atherosclerosis was observed among both diabetic men and diabetic women relative to their nondiabetic counterparts. The prevalence of multivessel high-grade atherosclerosis among diabetics and nondiabetics by age and gender categories is presented in Table 2. Multivessel high-grade CAD was present in 58% of the diabetic decedents and 41% of nondiabetic decedents ($p < 0.001$). It was more prevalent in nondiabetic men than among women, but no gender difference was detected in diabetic persons. The effect of diabetes on the prevalence of multivessel disease was greater in younger women (PR for diabetes, 2.8; 95%CI, 1.6 to 5.1, $p < 0.001$) than for younger men (PR, 1.2; 95%CI, 0.8 to 1.9, p = 0.34). Thus, among younger women, the prevalence of multivessel disease increased from 18% in nondiabetic individuals to 50% in diabetic individuals, thereby equating the prevalence of 45% in younger diabetic men (p = 0.73).

Diabetes as an equivalent of clinical CAD. This analysis examined whether diabetes was associated with an anatomic coronary disease burden equivalent to that of individuals with clinical CAD. Both indicators of atherosclerosis, namely global coronary score and prevalence of high-grade atherosclerosis, were examined in four strata defined by the presence or absence of diabetes and clinical CAD, while focusing on the contrast between individuals with diabetes but without CAD and those with clinical CAD but no diabetes.

The mean value of the coronary scores is shown in Figure 1. The scores were different between all groups except between those with clinical CAD in whom the mean scores were similar irrespective of diabetes status. With regards to the contrast between diabetics without CAD and individuals with clinical CAD, the global anatomic disease burden was higher in persons with clinical CAD (11.6 ± 3.1) as compared to diabetics without clinical CAD (10.6 ± 3.4, p = 0.001). After adjusting for age and gender, the relative odds of having a higher coronary score increased stepwise from diabetes without CAD (OR [odds ratio], 2.3; 95%CI, 1.7 to 3.5) to clinical CAD and no diabetes (OR, 3.1; 95%CI, 2.5 to 3.9) to clinical CAD and diabetes (OR, 4.6; 95%CI, 3.0 to 7.1). The OR for diabetes without CAD compared to that of CAD with no diabetes was 0.78 (95%CI, 0.52 to 1.16), indicative of a nonsignificant difference in global anatomic disease burden between diabetes alone and clinical CAD alone.

The prevalence of *high-grade atherosclerosis*, stratified by age and gender, is presented in Figure 2.

Diabetic decedents (68%) were more likely than their nondiabetic counterparts (46%) to have high-grade atherosclerosis (PR, 1.5; 95%CI, 1.3 to 1.7, $p < 0.001$). Among persons with clinical CAD during life, high-grade atherosclerosis was common irrespective of diabetes status (82% and 75% in diabetics and nondiabetics, respectively, p = 0.10). Without antemortem CAD, 50% of the younger diabetic men and 81% of the older diabetic men had high-grade atherosclerosis at autopsy (Fig. 2A). Notably, among older men, the prevalence of high-grade coronary atherosclerosis was similar among diabetic individuals without an antemortem CAD (81%) and nondiabetic individuals with antemortem CAD (84%) (p = 0.51). Thus, among older men, diabetes is equivalent to clinical CAD, for the prevalence of high-grade atherosclerosis.

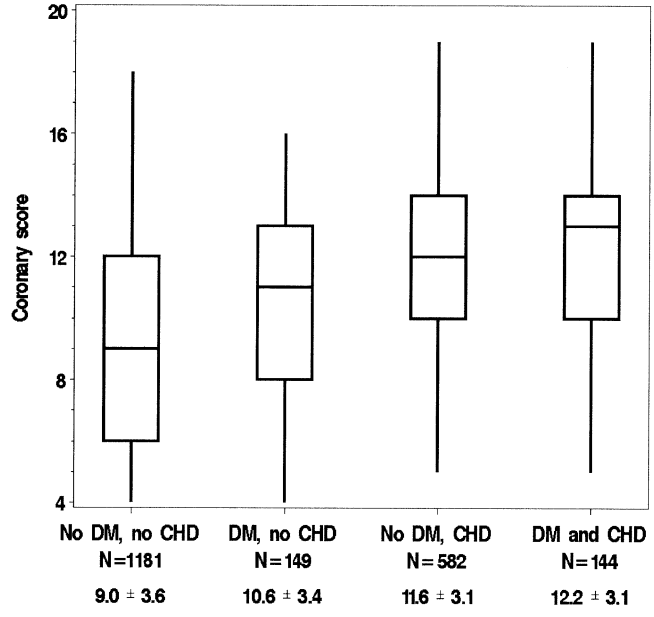

Figure 1. Distribution of global coronary scores by diabetes and clinical coronary disease status. CHD = coronary heart disease; DM = diabetes mellitus.

In younger women without antemortem diagnosis of CAD, the prevalence of high-grade coronary atherosclerosis was 19% among nondiabetics, contrasted with 50% among diabetic individuals (PR, 2.6; 95%CI, 1.3 to 5.1, $p < 0.001$) (Fig. 2B). Irrespective of age, diabetic women without clinical CAD had a prevalence of high-grade coronary atherosclerosis similar to that of nondiabetic women with antemortem CAD. This implies that, in women of all ages, diabetes is equivalent to clinical CAD for the prevalence of high-grade atherosclerosis.

Multivessel disease was highly prevalent in the presence of clinical CAD irrespective of diabetes status (67% in diabetic and 63% in nondiabetic decedents, p = 0.39). However, among those without clinical CAD, 50% of diabetics had multivessel CAD, versus only 31% among nondiabetics (PR for diabetes, 1.6; 95%CI, 1.3 to 2.0, $p < 0.001$). These results, shown in Figures 2C and 2D, are similar to the findings noted for the presence of any high-grade coronary atherosclerosis. Analogous results were also noted when the

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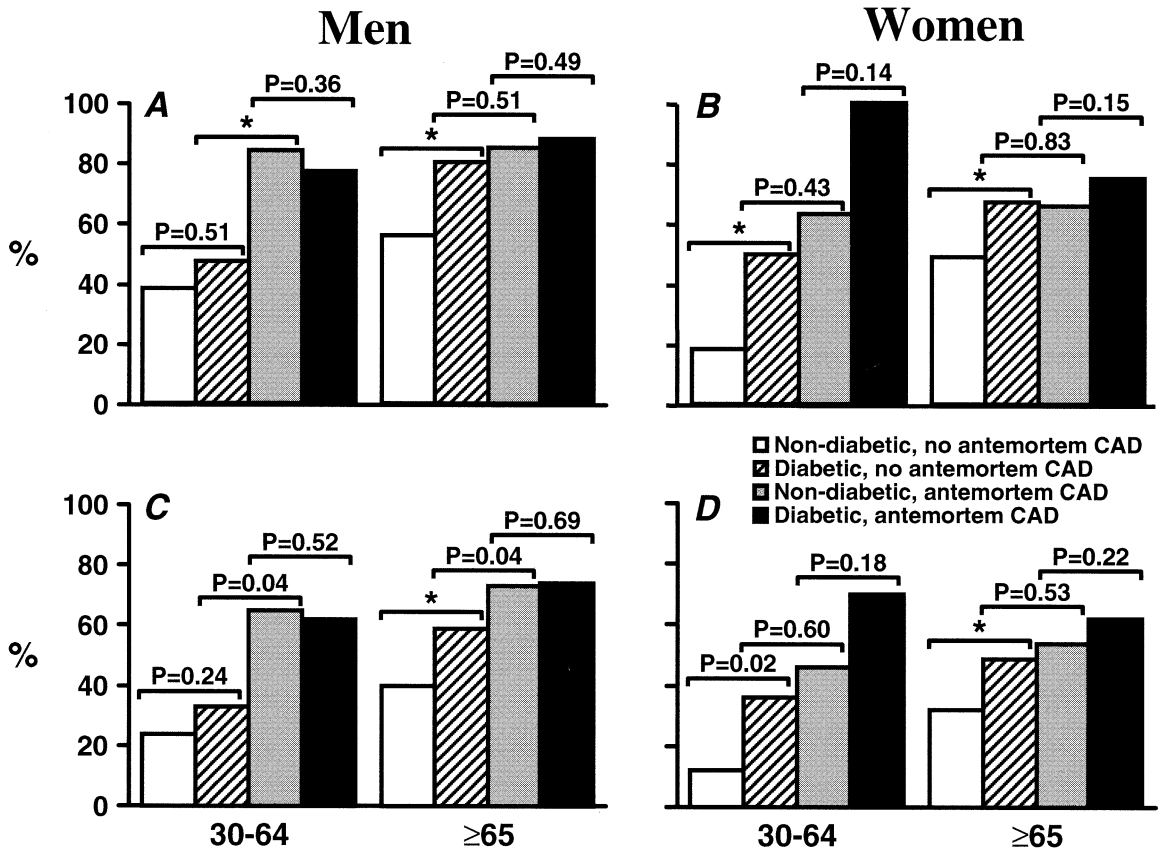

Figure 2. Prevalence of any high-grade or multivessel coronary atherosclerosis at autopsy by diabetes and clinical coronary disease status. Data are presented by age and gender categories. **(Top)** Prevalence of any high-grade coronary atherosclerosis for **(A)** men and **(B)** women. **(Bottom)** Prevalence of multivessel disease for **(C)** men and **(D)** women. The p values are for results of test for equality between groups, indicated by horizontal brackets. *$p < 0.01$. CAD = coronary artery disease.

presence of disease in the left anterior descending artery was examined as a separate end point.

Referral to autopsy by diabetes status. Autopsy rates were similar for diabetic (29%, n = 293) and nondiabetic decedents (28%, n = 1736; p = 0.36). Associations among age, gender, location of death, antemortem diagnosis of CAD, MI, or cerebrovascular disease and referral to autopsy did not differ according to diabetes.

DISCUSSION

In this geographically defined autopsy cohort, the prevalence of coronary atherosclerosis was higher among diabetic than among nondiabetic individuals. Among diabetic decedents without clinical CAD, almost three-fourths had high-grade coronary atherosclerosis and more than half had multivessel coronary disease. In the absence of diabetes, women had less atherosclerosis than men did, but this female advantage was lost with diabetes. Diabetes among persons without clinical CAD was associated with a global coronary disease burden and a prevalence of high-grade atherosclerosis similar to that observed among nondiabetic persons with clinical CAD.

Diabetes and anatomic coronary disease. Whereas diabetes is commonly thought of as associated with increased atherosclerosis, anatomic data supporting this perception are relatively scarce. Several (38) but not all angiographic case series showed that coronary atherosclerosis was more severe among patients with diabetes. However, these reports include patients referred to angiography with most often clinical symptoms of CAD, and they do not, by design, define the burden of anatomic CAD in asymptomatic persons (21). Prior autopsy studies indicated that coronary atherosclerosis was more prevalent among diabetic than among nondiabetic decedents (39), but their generalizability was often limited by exceedingly low autopsy rates in the source population, small sample size (17–19,22–24), or referral bias (18). Autopsy data of several epidemiologic cohorts, including the Framingham Heart Study and the Honolulu Heart Program, detected univariate associations between diabetes and coronary atherosclerosis, which were, however (17,19,22–24), not confirmed after adjustment for other risk factors. This led some to hypothesize the role of nonatherosclerotic processes, such as microvascular disease (20,40) or clotting disorders, to explain cardiovascular events in diabetic persons. However, both small sample size and the low use of autopsy in the source population hinder the generalizability of these data.

The present study extends these observations by showing,

in a large autopsy cohort within a geographically defined community with higher autopsy rates, that diabetic subjects have increased coronary atherosclerosis relative to nondiabetic subjects. Because there was no detectable difference in referral to autopsy by diabetes status, these data provide insight into the burden of coronary atherosclerosis among all diabetics. This study does not address the etiologic link between diabetes and atherosclerosis; rather, it addresses from a public health perspective the population burden of coronary disease among people with diabetes.

Diabetic women in the Framingham Heart Study exhibited a greater vulnerability to cardiovascular complications than did diabetic men (41). The Rancho Bernardo investigators identified a similar gender effect with a higher adjusted diabetes-associated relative risk for women than for men (2), and they hypothesized that the higher risk of diabetes in women was largely a function of their lower cardiac mortality in the absence of diabetes (42). The anatomic basis for this clinical observation was not clear, however, as studies of subclinical atherosclerosis had not identified an increased prevalence of atherosclerosis among diabetic women (43,44). The findings presented herein address this question by indicating that, among younger women, the prevalence of coronary atherosclerosis in the absence of diabetes was lower than among men. With diabetes, however, the prevalence of atherosclerosis in women increased to the level of men in all age groups, thereby providing anatomic support for the clinical observation of the equalization of cardiac risk between men and women with diabetes.

Diabetes as a clinical CAD equivalent and clinical implications. Several studies including those from the Rochester Epidemiology Project provide compelling evidence that diabetes increases the risk of both fatal and nonfatal cardiac events (8,9,11,45), and that, in the absence of clinical CAD, people with diabetes experience cardiac events at a rate equal to that of nondiabetics with established CAD (10,11). This indicates that, in diabetic subjects, aggressive prevention should precede the clinical onset of CAD. Key to the implementation of this strategy is the determination of the mechanisms for this increased risk and whether diabetic subjects without clinical CAD have similar extent of atherosclerosis compared with nondiabetic subjects with clinical CAD. If this is true, this supports similar risk-factor modification in both groups.

Few studies examined the prevalence of coronary atherosclerosis among diabetics according to the presence or absence of clinical CAD. Using carotid ultrasound, the Insulin Resistance Atherosclerosis Study showed similar severity of atherosclerosis among diabetic subjects without clinical CAD and nondiabetic subjects with clinical CAD (46). As noted by the investigators, however, the relatively small number of cases with clinical CAD limited their ability to analyze results by gender, and the cohort design is subject to the *healthy participant effect* (47). The study by Waller et al. (18) reported that the prevalence of atherosclerosis at autopsy was similar among subjects with clinical CAD and among those with diabetes. However, its design, which is akin to case-control with its inherent biases, its selection criteria (also a source of bias), and the referral bias inherent in the restriction to subjects seen in a diabetes clinic and who conceivably have more severe diabetes than subjects followed in the primary care setting, all limit the inference that can be drawn from these data. These methodological concerns do not apply to the present population-based study, which greatly enhances its robustness. It provides a mechanistic explanation for the observed similarity of cardiac events between diabetics without clinical CAD and nondiabetics with clinical CAD by indicating that the extent of anatomic atherosclerosis in these two groups is similar. These indicate, in turn, that risk-factor modification should be pursued as aggressively in asymptomatic diabetic patients as in their nondiabetic counterparts with clinical CAD. Because the prevalence of other cardiac risk factors, such as hypertension, hypercholesterolemia, and obesity, is high in people with diabetes (4,7,14–16), preventive approaches should be addressed toward all existing risk factors in any patient with diabetes (6,13,48–50).

Study strengths and limitations. These results provide important insights into the relation between diabetes and coronary atherosclerosis, and some points should be kept in mind to assist in the interpretation of the data.

Although the population of Rochester, Minnesota, is becoming more diverse, its racial and ethnic composition limits the generalization of these data to ethnic groups not adequately represented in this population. Conversely, quasi-complete insurance coverage in the county reduces confounding by access to care (51). Whereas autopsy reports were used to ascertain atherosclerosis, the classification was used consistently over time. Moreover, a prospective review of specimen, all archived as part of the Rochester Epidemiology Project Autopsy Registry, indicated good to excellent agreement between the report and the specimen review (26). Death certificates are not reliable to ascertain diabetes (33,52). In the present study, diabetes was determined via a complete review of the medical records using rigorous definitions (30), which excluded individuals who did not meet NDDG criteria. Redefining diabetes to include all decedents ever assigned a clinical diagnosis of diabetes yielded similar results.

CONCLUSIONS

In this geographically defined autopsy cohort, the prevalence of coronary atherosclerosis was higher among diabetic than among nondiabetic individuals. Among diabetic decedents without clinical CAD, almost three-fourths had high-grade coronary atherosclerosis and more than half had multivessel disease. In the absence of diabetes, women had less coronary atherosclerosis than did men, but this female advantage was lost with diabetes. Among individuals with-

out clinical CAD, diabetes was associated with a global coronary disease burden and a prevalence of high-grade atherosclerosis similar to that observed among nondiabetic persons with clinical CAD. These data provide anatomic support for approaching diabetes as "CAD risk equivalent" in terms of risk-factor management.

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