POTENTIALLY MODIFIABLE METABOLIC FACTORS AND THE RISK OF CARDIOVASCULAR DISEASE HOSPITALIZATIONS IN URBAN AFRICAN AMERICANS WITH DIABETES

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Objective: Diabetes and cardiovascular disease (CVD) are frequent causes of hospitalization in African Americans but have rarely been studied as coexisting diagnoses. We analyzed data from an urban African American diabetes patient population to identify variables associated with CVD hospitalizations.

Design: Demographic, disease, and metabolic characteristics of patients seen from 1991 to 1997 were extracted from an electronic patient tracking system. Data were linked to a statewide hospital discharge dataset to establish who was hospitalized between 1998 and 2001. Patients with a CVD hospitalization were compared to patients without a CVD hospitalization.

Results: 3397 diabetes patients (average age, 56 years; 65% women; 92% African American) were included in the analysis; 24% had hospitalizations primarily due to CVD. Persons with CVD hospitalizations were older and had diabetes longer, and fewer were women. Mean systolic blood pressure (SBP), low-density lipoprotein (LDL) cholesterol, triglyceride, and total cholesterol levels and urinary albumin/creatinine ratio were all higher among persons with CVD hospitalizations. In adjusted analyses, women had lower odds of experiencing a CVD hospitalization, but advancing age, diabetes duration, SBP, and LDL cholesterol were all associated with greater odds.

Conclusions: In this predominantly African American patient sample with diabetes, specific factors (age, sex, diabetes duration, LDL cholesterol, SBP) were associated with CVD hospitalizations. Additional studies are needed to determine whether management of metabolic risk factors in outpatient settings will translate into lower hospitalization rates due to CVD in this population. (*Ethn Dis*. 2006;16:852–858)

Key Words: Cardiovascular Disease, Diabetes, Hospitalizations

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INTRODUCTION

Cardiovascular disease (CVD) is a chief contributor to the morbidity and mortality experienced by patients with diabetes mellitus.[1–3] Moreover, diabetes worsens outcomes from heart disease.[4–7] Diabetes is associated with multiple metabolic abnormalities that predispose to development of CVD.[8] Some variables, such as hypertension and hyperlipidemia, are potentially modifiable, and their treatment can decrease the risk of CVD events among persons with established diabetes.[9–11]

CVD and diabetes each account for a large number of hospitalizations annually in the United States.[12,13] CVD is the most common principal cause of hospitalization among persons with diabetes, and the risks for CVD hospitalization are increased more than two-fold among persons with diabetes than among persons hospitalized for CVD without a diabetes diagnosis.[13,14] Moreover, diabetes increases the length of stay and leads to higher hospital charges among patients hospitalized for CVD.[14] Disparities exist in diabetes and CVD-related hospitalizations. We have recently shown that non-Hispanic Blacks with diabetes have more than a two-fold greater risk of being hospitalized than do Whites with diabetes.[15] Other studies have demonstrated that, compared with Whites, African Americans have more hospitalizations attributable to diabetes and to such CVD conditions as angina and congestive heart failure.[16]

To identify which characteristics are associated with a CVD hospitalization, we analyzed data from a large cohort of African Americans with diabetes who were receiving care through an urban outpatient clinic.

Although diabetes and CVD individually are frequent causes of hospitalization in African Americans, these two diseases have seldom been studied in situations where both conditions are present as coexisting diagnoses.[17] However, if effective risk assessment and prevention strategies are to be developed for African Americans with diabetes, more information is needed about the demographic, disease, or metabolic variables that might increase the risk of a CVD-related hospitalization in this group. To identify which characteristics are associated with a CVD hospitalization, we analyzed data from a large cohort of African Americans with diabetes who were receiving care through an urban outpatient clinic.

METHODS

Patient Population

Patients selected for analysis were adults who received care through an

outpatient diabetes clinic affiliated with a county hospital system located in metropolitan Atlanta, Georgia. Prior inpatient studies and analyses from various clinical sites from within the system showed that this diabetes population typically lacks health insurance, is low income, mostly has type 2 diabetes, and is predominantly African American.[18–23]

Beginning in 1991, a longitudinal electronic diabetes patient tracking system (DPTS) was established to record demographic, pharmacologic, and metabolic parameters on all diabetes patients who received care at the clinic. The DPTS has been used in numerous analyses, and its validity is well established.[20,24–27] During a 10-year period (1992–2001), the racial/ethnic mix of the diabetes patient population has remained 90% African American.[28]

Data Abstraction

The study population was the cohort of diabetes patients seen in the clinic between 1991 and 1997. To include discharge data from hospitalizations that occurred both within and outside the public hospital system, we abstracted data from the DPTS on patients who visited the clinic between 1991 and 1997 and linked this file with the discharge dataset of the Georgia Hospital Association (GHA) for the calendar years 1998 to 2001. The GHA did not start accruing full calendar-year discharge information until January 1, 1998, which is why our hospitalization data begin with that year. Federal hospitals (Veterans Affairs and military) do not report data to the GHA. All nonfederal hospitals, however (including private, academic, and public), are required by state law to report discharge information to the GHA. The DPTS provided the demographic variables, disease characteristics, and metabolic factors that were included in the analysis to assess the risk of a CVD hospitalization.

The electronic file returned from the GHA contained data on which patients had a hospital discharge between 1998 and 2001. Discharges principally due to CVD were identified by using the *International Classification of Diseases, 9th Revision, Clinical Modification* codes 390–459; if a patient had more than one CVD hospitalization, the date of the first CVD-related discharge was used to classify the patient as having a CVD hospitalization. Thus, the DPTS patients were stratified into two categories: those who had a CVD hospitalization (cases) and patients who had no CVD hospitalization (controls). The cases included the subset of patients who had only a CVD discharge plus persons who had a CVD discharge but who also may have had a discharge for some other reason between 1998 and 2001. The controls consisted of patients who had no hospitalizations plus persons who had no record of a CVD discharge diagnosis but had a hospitalization for some other reason.

Data Analysis

The diabetes clinic began recording metabolic data in the DPTS in 1991. Hospitalizations throughout the state of Georgia were recorded in the GHA discharge database starting in 1998. Therefore, we evaluated how well data between 1991 and 1997 (baseline exposure period) could predict whether a patient was hospitalized primarily because of CVD between 1998 and 2001 (follow-up period). Thus, all patients had known diabetes before the follow-up period, and the baseline period represents the time when patients would have been exposed to the metabolic factors that might predispose to CVD. To be included in the analysis, the DPTS had to show that the patient was present in the health system both during the baseline exposure period and the study period. The analysis was further limited to patients who had type 2 diabetes. During the baseline exposure period, no changes were made in laboratory techniques to determine hemoglobin A1C (HbA1C), lipids, or urinary albumin/creatinine ratio.[29–31]

The following characteristics were assessed: age, sex, race/ethnicity, diabetes duration (self-reported), body mass index, systolic blood pressure (SBP), HbA1C, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides, total cholesterol (TC), and urinary albumin/creatinine ratio. Age was the patient's age on December 31, 1997. Duration of diabetes was from the time of reported diagnosis to December 31, 1997. Body mass index (BMI) was calculated by using the height from the first visit at the diabetes clinic between 1991 and 1997. Weight, systolic blood pressure, HbA1C, LDL cholesterol, HDL cholesterol, triglycerides, TC, and urinary albumin/creatinine ratio levels for the analysis were from the most recent annual average before 1998. We calculated the absolute and annual rates of change in metabolic markers from the first annual average to the most recent annual average for persons who had data available for at least two years.

The prevalence of characteristics and mean levels was compared between the "CVD hospitalization" patients and the "no CVD hospitalization" patients. Statistical significance was calculated by using the Pearson χ^2 statistic or the 2-sample t statistic. In addition, multiple logistic regression was used to create a multivariable model. A forward selection strategy was used because of the large number of variables. Terms were included in the model if the nominal adjusted level of significance was $<.001$. Terms were also tested for all pairwise interactions among factors that were nominally significant at the $\alpha=.05$ level in the univariable comparisons. Interaction terms were included in the model if the nominal adjusted significance level was $<.0001$. Models resulting from other inclusion criteria were also explored, and these models were compared by using the Akaike information criterion. No other modeling

Table 1. General characteristics of 3397 diabetes patients

Characteristic	No.	Value*
Age, years	3397	56 (13)
Female sex, %	2213	65
African American race, %	3113	92
Diabetes duration, years	3397	8.4 (7.7)
BMI, kg/m^2	3393	32.5 (7.8)
HbA1C, %	3377	8.5 (2.4)
Systolic blood pressure, mm Hg	3381	128 (19)
Urinary albumin/creatinine ratio, mg/g	303	2.0 (1.6)
Lipids, mg/dL		
Low-density lipoprotein cholesterol	3295	134 (40)
High-density lipoprotein cholesterol	3389	47 (15)
Triglycerides	3389	170 (190)
Total cholesterol	3391	204 (49)

BMI=body mass index, HbA1C=hemoglobin A1C.
* Data are mean (SD) or percentage.

Table 2. Differences between patients with or without cardiovascular disease hospitalizations

Characteristic	CVD hospitalization (n=810)		No CVD hospitalization (n=2,587)		P value
	Value*	No.	Value*	No.	
Age, years	60 (11)	810	55 (13)	2587	<.001
Diabetes duration, years	11.1 (8.7)	810	7.5 (7.1)	2587	<.001
Female sex, %	61	491	67	1722	.002
African American race, %	88	715	93	2398	<.001
BMI, kg/m^2	32.5 (7.9)	809	32.6 (7.8)	2584	.90
HbA1C, %	8.6 (2.4)	802	8.4 (2.5)	2575	.13
Systolic blood pressure, mm Hg	133 (20)	806	127 (19)	2575	<.001
Lipids, mg/dL					
Low-density lipoprotein cholesterol	142 (41)	780	132 (39)	2515	<.001
High-density lipoprotein cholesterol	46 (16)	809	47 (15)	2580	.46
Triglycerides	180 (230)	808	160 (180)	2581	.001
Total cholesterol	213 (56)	809	202 (46)	2582	<.001
Urinary albumin/creatinine ratio, mg/g	2.3 (1.8)	134	1.7 (1.3)	169	.003

* Data are mean (SD) or percentage.
BMI=body mass index; CVD=cardiovascular disease; HbA1C=hemoglobin A1C.

strategy produced a model that improved the statistic for model fit. The diagnostic power for predicting CVD hospitalization with the multivariable model was calculated by using the jackknife method. We used receiver-operating characteristics analysis to determine the cutoff score that yielded the highest likelihood ratio.[32] Analyses and procedures were approved by the institutional review boards of the participating institutions.

RESULTS

General Patient Characteristics

We included 3397 patients with type 2 diabetes in the analysis (Table 1). Of these, 24% had evidence of a hospitalization with a principal CVD diagnosis.

Characteristics of CVD vs No CVD Discharges

Persons with CVD discharges were significantly older and had had diabetes longer than did persons hospitalized without a CVD cause (Table 2). Fewer patients with a CVD discharge were women, and a smaller percentage were African American. Mean systolic blood pressure, LDL cholesterol, triglyceride, and TC levels were all significantly higher among persons with than without a CVD hospitalization. Finally, average urinary albumin/creatinine ratio was higher among patients with a CVD discharge (Table 2). No significant differences were observed in HbA1C, BMI, or HDL cholesterol.

Changes in Variables

To assess the magnitude of changes in metabolic variables occurring over time, we calculated the change from the first annual average level to the most recent average annual level for persons who had data available for at least two years. During the baseline exposure period, BMI (n=2082) increased overall an average (±SD) of .5 ± 3.0 kg/m^2, HbA1C (n=2020) declined by .5% ± 2.7%, and SBP (n=2085) increased 5 ± 20 mm Hg. Low-density lipoprotein (LDL) cholesterol (n=1191), triglycerides (n=1241), and TC (n=1694) decreased an average of 13 ± 36, 5 ± 200, and 9 ± 46 mg/dL, respectively, and HDL cholesterol (n=1,238) and urinary albumin/creatinine ratio (n=52) increased by 4 ± 11 mg/dL and .5 ± 1.7 mg/g, respectively. No significant differences were seen in the magnitude of changes in these variables between patients with CVD hospitalizations and those without CVD hospitalizations. In addition, with the exception of TC, no differences were seen in annual rates of change in any of the metabolic markers between the two groups. For TC, the value decreased an average 6 mg/dL per year in the CVD hospitalization group but only 2 mg/dL per year in those without a CVD hospitalization (P=.02) (not shown).

Variables Associated With a Risk of CVD Hospitalization

A regression model (Table 3) was constructed to determine which variables were predictive of CVD hospitalization. The risk of hospitalization primarily because of CVD was lower among women but increased with age and diabetes duration. Additionally, the risk of a CVD hospitalization rose with increasing SBP and higher LDL cholesterol (Table 3).

The regression model yielded a score that evaluated the likelihood of having a CVD hospitalization in this popula-

Table 3. Results of multiple logistic regression model and variables significantly associated with a CVD discharge*

Factor	OR	95% CI	*P* value
Female sex	.64	.53–.76	<.001
Age, per 20-year increase	1.46	1.27–1.69	<.001
Diabetes duration, per 10-year increase	1.59	1.43–1.76	<.001
Systolic blood pressure, per 20-mm Hg increase	1.23	1.13–1.35	<.001
LDL cholesterol, per 50-mg/dL increase	1.33	1.20–1.48	<.001

* Compared with ''no CVD hospitalization'' group; HbA1C, race/ethnicity (African American vs non-African American), body mass index, high density-lipoprotein cholesterol, total cholesterol, urinary albumin/creatinine ratio, and rates of change in metabolic variables were all not significant.

CI=confidence interval; CVD=cardiovascular disease; LDL=low-density lipoprotein; OR=odds ratio.

tion. The equation to calculate the score is:

$$\begin{aligned}\text{Score} = {} & -4.7799 - .2264 \times \textit{female} \\ & + .0190 \times \textit{patient age (years)} \\ & + .0461 \times \textit{diabetes duration (years)} \\ & + .0105 \times \textit{systolic blood pressure (mm Hg)} \\ & + .0058 \times \textit{LDL level (mg/dL)}\end{aligned}$$

A score >.08 predicted a CVD hospitalization. The model had a 52% positive predictive value and a 77% negative predictive value. A patient with a high score (>.08) was 2.3 times as likely to have a hospitalization primarily because of CVD compared to a patient with a lower score.

DISCUSSION

Minority populations, particularly African Americans, have a high prevalence of diabetes,[33] poorer glycemic control,[34,35] and more disease-related complications[36] than do Whites. Disparities also are present in hospital discharge data; African Americans have more hospitalizations attributable either to diabetes or CVD,[15,16] but studies rarely have focused on patients who have both diseases.[17] We have previously reported on the higher rates of CVD-related discharges in diabetes patients, including non-Hispanic Blacks,[14] and we wanted to examine more closely the variables in this group that might be associated with the risk of a CVD hospitalization.

We used a large, well-established clinical database to assess variables associated with a CVD hospitalization in what historically has been a disadvantaged African American patient population with known diabetes. The patients in our sample obtained care through the outpatient diabetes program but could have been hospitalized outside the affiliated public hospital. The ability to link our clinical data with a larger, state-level discharge data warehouse permitted us to include the CVD-related discharges that occurred both within and outside the county health system.

Differences were seen between CVD hospitalization groups in age, sex, race/ethnicity, duration of diabetes, systolic blood pressure, LDL cholesterol, triglycerides, TC, and urinary albumin/creatinine ratio. However, in the adjusted analysis, only female sex, age, diabetes duration, systolic blood pressure, and LDL cholesterol were significantly associated with the likelihood of having a hospitalization principally for CVD. Race was not statistically significant after accounting for other variables, but this finding may have been due to the underrepresentation of other racial/ethnic categories in the dataset. The equation that describes the relationship between female sex, age, diabetes duration, systolic blood pressure, and LDL cholesterol with CVD hospitalization may be useful to assess risk in the outpatient setting for this study population and thus requires prospective evaluation.

A recent analysis of an ethnically diverse urban diabetes patient population found that men had a higher incidence of several CVD conditions than did women, although hospitalization rates were not examined.[37] The observation that women had a lower risk than men for CVD hospitalization may simply reflect a possible lower prevalence of cardiovascular-related disease. The lower odds of a CVD hospitalization among women, however, could also be caused by a greater out-of-hospital mortality—a possibility that cannot be assessed from this dataset. Another possible explanation for the difference is that women in this population have more exposure to medical services. Historically, most (approximately two thirds) patients attending the outpatient diabetes clinic have been women.[20,23–25] Therefore, women in our sample may have had more opportunities to receive outpatient education and therapeutic interventions during the baseline study period that would have decreased their risk for a CVD hospitalization. Further study is needed to determine the basis for these sex-related differences.

Both advancing age and increased diabetes duration were associated with a greater risk of experiencing a hospitalization principally due to CVD. Age and diabetes duration have been correlated with a higher incidence of CVD,[37] although to our knowledge our data are the first to link these variables to hospitalization risk. Older patients with a longer duration of diabetes could be identified in the outpatient setting as being at particular risk for experiencing a future admission for CVD and could be targeted for aggressive control of the risk factors that predispose to macrovascular disease.

In our study, patient characteristics such as sex, age, and diabetes duration can help identify a patient at high risk for a CVD-related hospitalization; these factors cannot be modified. On the other hand, the two variables we identified—SBP and LDL cholesterol—are amenable to pharmacologic intervention. Treatment of hypertension and LDL cholesterol in the outpatient setting can reduce the risk for CVD events.[9–11] Appropriate treatment of these metabolic abnormalities could therefore translate into fewer hospital admissions for CVD events. However, our retrospective data do not allow us to test this hypothesis.

Although SBP and LDL cholesterol are potential targets of outpatient treatment, our data also suggest a need to improve the management of hypertension and hyperlipidemia. Our analysis demonstrated that no significant reductions occurred in either SBP or LDL cholesterol during the baseline exposure period. Racial/ethnic differences in hospitalizations for various CVD conditions, which have been regarded as potentially preventable with appropriate outpatient care, have been attributed to disparities in income and access to health care,[16,38–41] but insufficient therapy of key metabolic risk factors could be another variable that has an impact on the risk of hospitalization. We previously demonstrated that significant changes in LDL cholesterol do not occur in this patient population without pharmacologic therapy.[24] A quality improvement program directed at overcoming clinical inertia in blood pressure and lipid management—as was done for treatment of hyperglycemia[25]—may be needed to effectively reduce the risk of CVD in these patients.

The degree of albuminuria differed significantly between patients with or without CVD hospitalizations, but in the adjusted analysis it was not statistically important. Albuminuria is a known risk factor for CVD in patients with diabetes. In a longitudinal study of patients with type 2 diabetes, preexisting albuminuria increased the risk for hospitalization related to congestive heart failure.[42] Thus, albuminuria may be more predictive of hospitalization for specific CVD diagnoses—an effect that might not have been detected in our aggregate analyses of CVD hospitalizations. Alternatively, the number of cases with a recorded albumin/creatinine ratio in our final data set was small and may have impeded detection of a significant association.

Although SBP and LDL cholesterol are potential targets of outpatient treatment, our data also suggest a need to improve the management of hypertension and hyperlipidemia.

Our retrospective study design and the structure of the DPTS dataset imposed some limitations on our analysis. We cannot tell from our hospital discharge data which patients had preexisting CVD or whether a patient's hospital encounter represented the first diagnosed CVD event. The DPTS does not contain data on tobacco use or information on demographic variables, such as household income and size. Although the DPTS does contain pharmacotherapy data, numerous medication classes exist to treat diabetes, hypertension, and dyslipidemia, and changes in the types of medications and their doses that most likely occurred during the baseline exposure period preclude incorporating them into a retrospective study design. Finally, the patients we studied received care from a specialty outpatient diabetes program with extensive experience in caring for urban African Americans. Therefore, the variables found to be associated with CVD hospitalization in this group, and the associated equation derived from the regression model, may not apply to other types of clinical settings or to other racial/ethnic populations.

Despite these limitations, our study provides insight on variables that increase the risk for CVD hospitalization in a largely African American diabetes patient population. These variables can be incorporated into a model that may be useful in assessing outpatients at risk for a CVD-related hospitalization. Some characteristics (sex, age, and diabetes duration) cannot be modified, but their presence should alert practitioners to evaluate diabetes patients more aggressively for CVD and to provide intensive risk-reduction education. Other characteristics (SBP and LDL cholesterol) are potentially modifiable. Additional studies are needed to determine whether management of these metabolic risk factors translates into lower rates of hospitalization in African Americans with diabetes.

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