Racial/Ethnic Differences in Dementia Risk Among Older Type 2 Diabetic Patients: The Diabetes and Aging Study

OBJECTIVE

Although patients with type 2 diabetes have double the risk of dementia, potential racial/ethnic differences in dementia risk have not been explored in this population. We evaluated racial/ethnic differences in dementia and potential explanatory factors among older diabetic patients.

RESEARCH DESIGN AND METHODS

We identified 22,171 diabetic patients without preexisting dementia aged ≥60 years (14,546 non-Hispanic whites, 2,484 African Americans, 2,363 Latinos, 2,262 Asians, 516 Native Americans) from the Kaiser Permanente Northern California Diabetes Registry. We abstracted prevalent medical history (1 January 1996 to 31 December 1997) and dementia incidence (1 January 1998 to 31 December 2007) from medical records and calculated age-adjusted incidence densities. We fit Cox proportional hazards models adjusted for age, sex, education, diabetes duration, and markers of clinical control.

RESULTS

Dementia was diagnosed in 3,796 (17.1%) patients. Age-adjusted dementia incidence densities were highest among Native Americans (34/1,000 person-years) and African Americans (27/1,000 person-years) and lowest among Asians (19/1,000 person-years). In the fully adjusted model, hazard ratios (95% CIs) (relative to Asians) were 1.64 (1.30–2.06) for Native Americans, 1.44 (1.24–1.67) for African Americans, 1.30 (1.15–1.47) for non-Hispanic whites, and 1.19 (1.02–1.40) for Latinos. Adjustment for diabetes-related complications and neighborhood deprivation index did not change the results.

CONCLUSIONS

Among type 2 diabetic patients followed for 10 years, African Americans and Native Americans had a 40–60% greater risk of dementia compared with Asians, and risk was intermediate for non-Hispanic whites and Latinos. Adjustment for sociodemographics, diabetes-related complications, and markers of clinical control did not explain observed differences. Future studies should investigate why these differences exist and ways to reduce them.

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Type 2 diabetes is associated with an approximately twofold greater risk of dementia among older adults (1–3), but it is not clear whether risk of dementia for people with diabetes varies across racial/ethnic groups. In the general population, the prevalence of dementia has been reported to be higher among African Americans and Caribbean Hispanics, lower among Japanese Americans, and similar among Native Americans and Mexican Americans compared with non-Hispanic whites (4,5). A study of community-dwelling older adults in New York City reported that the higher prevalence of type 2 diabetes in African Americans and Hispanics compared with whites partially contributes to the higher observed incidence of dementia and cognitive impairment in these populations (6). To our knowledge, however, racial/ethnic differences in dementia risk have not been investigated among people with type 2 diabetes.

Type 2 diabetes affects >25% of adults aged ≥65 years in the U.S. (7), and the prevalence is highest in some racial/ethnic minorities, including Latinos, African Americans, Native Americans, and some Asian American groups (7,8). Because type 2 diabetes increases the risk of dementia, it is important to understand the risk of dementia among older adults with type 2 diabetes of diverse racial/ethnic backgrounds. With the aging (9) and growing diversity (10) of the U.S. population, the increasing prevalence of type 2 diabetes (11,12), and the national goal of eliminating health disparities (13), understanding racial/ethnic differences in diabetes-related complications, including dementia, among older adults is increasingly important.

The primary goal of this study was to examine whether there are racial/ethnic differences in the 10-year incidence of dementia among patients with type 2 diabetes. Secondarily, we explored whether these differences are explained by diabetes duration, markers of clinical control, and vascular diabetes-related complications in a multiethnic population of older type 2 diabetic patients.

**RESEARCH DESIGN AND METHODS**

**Study Population**

We evaluated patients who were members of the Kaiser Permanente Northern California (KPNC) Diabetes Registry, a well-characterized population of diabetic patients that has been the basis of a wide range of epidemiologic research (14–17). The registry was formed in 1993 and is updated annually to include all KPNC health plan members who are identified as having diabetes on the basis of laboratory results, pharmacy records, and outpatient diagnoses (14). KPNC is a large, integrated health care delivery system that provides comprehensive medical care to >3.3 million members (30% of the geographic region). The KPNC population is generally representative of the overall population of the region, with the exception that individuals at the extreme tails of the income distribution are underrepresented (18,19). Between 1994 and 1996, all noninstitutionalized KPNC Diabetes Registry members ≥19 years of age were sent a self-administered survey (mailed or online) or contacted for a computer-assisted telephone interview on sociodemographic factors and health behaviors. The written and web surveys were in English only, but the computer-assisted telephone interview was available in English, Spanish, Cantonese, Mandarin, and Tagalog through certified translations of an English script and was intended to maximize accessibility to those with language barriers or limited English literacy or fluency. A detailed description of the KPNC Diabetes Registry and survey has been published (14,17). The present study was approved by the Kaiser Foundation Research Institute and University of Chicago institutional review boards.

We included KPNC Diabetes Registry members in this analysis if they completed the 1994–1996 survey, had type 2 diabetes, were ≥60 years of age as of 1 January 1998 (baseline), had no prior diagnosis of dementia, and had no gaps in membership >3 months in the 2 years before baseline (n = 29,956). We excluded patients who reported mixed race or other (n = 139) and Pacific Islanders (n = 183) because of insufficient sample size to support statistical comparisons. We excluded patients missing information on race/ethnicity (n = 301). We also excluded 7,162 patients missing information on the following key covariates: level of education (n = 1,842), glycylated hemoglobin (A1C) (n = 2,976), duration of diabetes (n = 1,745), or more than one of these variables (n = 599). The proportion of patients who were excluded because of missing key covariates was similar across racial/ethnic groups and ranged from 23.0% in non-Hispanic whites to 28.2% in Latinos. The resulting sample size included 22,171 diabetic patients.

**Dementia Diagnosis**

Dementia cases were identified from clinical diagnoses in electronic medical records from inpatient and outpatient encounters between 1 January 1998 and 31 December 2007 based on ICD-9-CM diagnostic codes for Alzheimer disease (331.0); senile dementia, uncomplicated (290.0); presenile dementia (290.1X); senile dementia with delusional or depressive features (290.2X); senile dementia with delirium (290.3); and vascular dementia (290.4X). This method of dementia ascertainment has been used successfully in KPNC health plan members in other publications (15,16,20).

**Other Measures**

**Sociodemographic Characteristics**

Race/ethnicity (non-Hispanic white, African American, Latino, Asian, Pacific Islander, Native American, or mixed race/other) and educational attainment were ascertained by self-report from the survey. Neighborhood deprivation index, based on a validated methodology, was calculated from each patient’s 1996 address and 1990 Census information (21).

**Diabetes Duration and Clinical Control (Baseline)**

Duration of diabetes was estimated from electronic health records according to initial date of diagnosis. Acute metabolic events (severe hyperglycemia or hypoglycemia requiring hospitalization) were identified from electronic hospitalization and emergency department records during the period of 1 January 1996 to 31 December 1997,
using primary ICD-9-CM diagnostic codes (Supplementary Data). A1C levels were abstracted from KPNC electronic laboratory databases, using the most recent measurement during the period of 1 January 1996 to 31 December 1997. The median time from the A1C measurement to baseline (1 January 1998) was 0.34 years (interquartile range 0.16–0.73). Diabetes pharmacotherapy was defined by a ≥30-day supply of glycemia-lowering medication dispensed at a KPNC pharmacy during the 6 months before baseline (1 January 1998).

**Diabetes-Related Complications (Baseline)**

Prevalent diabetes-related microvascular and macrovascular complications were identified from electronic medical records from inpatient and outpatient visits that took place between 1 January 1996 and 31 December 1997, using primary ICD-9-CM diagnostic codes (Supplementary Data). Microvascular complications included end-stage renal disease, diabetic retinal disease, and lower-extremity complications (lower-limb ulcer, gangrene, and lower-extremity amputation). Macrovascular complications included cardiovascular disease (congestive heart failure, peripheral vascular disease, and myocardial infarction) and cerebrovascular disease.

**Other Covariates (Baseline)**

BMI was calculated from self-reported height and weight from the survey. Hypertension was identified from electronic medical records (1 January 1996 to 31 December 1997). As a measure of health care utilization, the average number of clinical visits per year during follow-up for each individual was calculated, resulting in a medical utilization rate.

**Statistical Analyses**

Baseline characteristics were compared across racial/ethnic groups with ANOVA tests for continuous variables and χ² tests for categorical variables. Age-adjusted dementia incidence densities (incidence rates) by racial/ethnic group were estimated after directly standardizing to the 2000 Census population. We specified Cox proportional hazards models to estimate the association between race/ethnicity and risk of dementia. To facilitate comparisons among racial/ethnic groups included in the study, we present hazard ratios for each model, with each racial/ethnic group as the reference group. Because of the strong association between age and dementia incidence, we used age as the time scale in all proportional hazard models to best control for the influence of age on dementia risk. Participants were followed from age as of 1 January 1998 until age at diagnosis of dementia, death, a gap in membership >3 months, or 31 December 2007 (end of study period). We estimated racial/ethnic differences in dementia risk after adjustment for age (as the time scale), sex, and level of education. We evaluated whether the association between race/ethnicity and risk of dementia was explained by racial/ethnic differences in diabetes duration and clinical control (pharmacotherapy, A1C level, acute metabolic events), microvascular complications (end-stage renal disease, diabetic retinopathy, lower-extremity complications), macrovascular complications (cardiovascular disease, cerebrovascular disease, neighborhood deprivation index, BMI, and hypertension. Analyses were performed with SAS versions 9.1 and 9.3 statistical software (SAS Institute Inc., Cary, NC).

**RESULTS**

The study population included 22,171 diabetic patients ≥60 years of age. Approximately 66% were non-Hispanic white, 11% African American, 11% Latino, 10% Asian, and 2% Native American (Table 1). Education levels were lowest among Latinos and highest among Asians, and higher proportions of African Americans and Latinos lived in deprived neighborhoods. Overall, the mean duration of diabetes at baseline was ~6 years, and 82.2% of participants were receiving diabetes pharmacotherapy. A1C levels tended to be highest among African Americans, Latinos, and Asians, and acute metabolic events were more common among African Americans and Native Americans. Individual diabetes-related complications varied by race/ethnicity, but there was no consistent pattern of any one racial/ethnic group consistently having a higher prevalence of diabetes-related complications (microvascular or macrovascular) overall. Among microvascular complications, end-stage renal disease was rare in all groups, the prevalence of lower-extremity complications was lowest among Asians, and diabetic retinopathy was most prevalent among African Americans and Latinos. Among macrovascular complications, peripheral vascular disease was least common among Asians, myocardial infarction was more prevalent among Native Americans and non-Hispanic whites, congestive heart failure was least common among Asians and Latinos, and the prevalence of cerebrovascular disease was highest among non-Hispanic whites and Native Americans.

The average length of follow-up was 6.7 years, and the average age at dementia diagnosis was 79.2 years. The median number of clinical visits per year was similar across race groups but was lowest among Native Americans (median 9.0) and highest among Latinos (median 10.5). During follow-up, there were 10,525 deaths (47% of the cohort).

Over 10 years of follow-up, 3,796 (17.1%) participants were diagnosed with dementia. Among patients with dementia, 676 (17.8%) were diagnosed with Alzheimer disease, 474 (12.5%) with vascular dementia, and 128 (3.4%) with both Alzheimer disease and vascular dementia. The remaining 2,518 (66.3%) dementia cases were unspecified dementia diagnoses made in primary care. Because the majority of dementia diagnoses were for unspecified dementia, we did not evaluate racial/ethnic differences for specific dementia subtypes.

Age-adjusted dementia cumulative incidence and incidence densities were highest among Native Americans and African Americans and lowest among Asians (Table 2). Adjustment for age, sex, and level of education in the Cox proportional hazards models showed consistent patterns (Table 3, model 1). The measures of diabetes control and microvascular and macrovascular complications were significant risk factors for incident dementia in bivariate Cox proportional hazards models (data not shown). However,
adjustment for these measures (Table 3, models 2–4) imparted no substantive change in the association between race/ethnicity and dementia incidence. In all four models, dementia risk was significantly higher among Native Americans and African Americans than among the other racial/ethnic groups, whereas dementia risk was significantly lower among Asians than among all other racial/ethnic groups. Dementia risk was similar for non-Hispanic whites and Latinos, whose risk of dementia was lower than that of Native Americans and African Americans and higher than that of

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**Table 1—Baseline characteristics of the sample by race/ethnicity (1996–1997)**

| Variable                              | Non-Hispanic white | African American | Latino | Asian | Native American | P value |
|---------------------------------------|--------------------|------------------|--------|-------|-----------------|---------|
| Participants, n (%)                   | 14,546 (65.6)      | 2,484 (11.2)     | 2,363 (10.7) | 2,262 (10.2) | 516 (2.3) |         |
| Sociodemographic characteristics     |                    |                  |        |       |                 |         |
| Age (years)                           | 71.4 (6.8)         | 69.5 (6.5)       | 68.9 (5.8) | 68.9 (6) | 70.2 (6.9) | <0.001  |
| Female sex                            | 44.5               | 51.9             | 47.4   | 47.8  | 48.1            | <0.001  |
| Education                             |                    |                  |        |       |                 |         |
| Less than high school graduate        | 15.5               | 25.1             | 44.9   | 19.5  | 22.1           |         |
| High school graduate                  | 31.9               | 27.7             | 27.0   | 23.6  | 32.2           | <0.001  |
| Some college                          | 28.3               | 31.9             | 18.0   | 21.5  | 28.3           |         |
| College graduate                      | 24.3               | 15.4             | 10.1   | 35.4  | 17.5           |         |
| Neighborhood deprivation (4th quartile [poorest]) | 17.0              | 58.3             | 38.2   | 22.2  | 25.0           | <0.001  |
| Diabetes duration and clinical control|                    |                  |        |       |                 |         |
| Diabetes duration (years)             | 6.1 (2.7)          | 6.2 (2.9)        | 6.1 (2.7) | 5.8 (2.5) | 6.1 (2.7) | <0.001  |
| Antidiabetes medication               |                    |                  |        |       |                 | <0.001  |
| None                                  | 18.5               | 14.5             | 17.8   | 16.8  | 19.8           |         |
| Oral only                             | 54.9               | 51.7             | 55.5   | 63.6  | 52.7           |         |
| Insulin only                          | 19.5               | 27.2             | 20.8   | 15.4  | 19.6           |         |
| Insulin and oral                      | 7.1                | 6.5              | 5.9    | 4.2   | 7.9            |         |
| A1C                                   |                    |                  |        |       |                 | <0.001  |
| <6% (42 mmol/mol)                     | 10.9               | 10.9             | 9.1    | 6.0   | 11.0           |         |
| 6–7% (42–53 mmol/mol)                 | 30.6               | 26.7             | 26.2   | 27.4  | 29.7           |         |
| 7–8% (53–64 mmol/mol)                 | 26.7               | 22.9             | 23.7   | 26.3  | 25.4           |         |
| 8–9% (64–75 mmol/mol)                 | 14.1               | 15.3             | 15.3   | 15.3  | 13.2           |         |
| 9–10% (75–86 mmol/mol)                | 7.8                | 8.2              | 9.7    | 10.3  | 8.7            |         |
| ≥10% (86 mmol/mol)                    | 9.7                | 16.1             | 16.0   | 14.7  | 12             | <0.001  |
| Acute metabolic event                 | 3.1                | 7.0              | 3.2    | 2.3   | 5.2            | <0.001  |
| Other health characteristics          |                    |                  |        |       |                 |         |
| BMI (kg/m²)                           | 29.4 (5.6)         | 30 (5.6)         | 29.2 (5.2) | 25.4 (3.7) | 29.9 (5.6) | <0.001  |
| Hypertension                          | 59.8               | 72.6             | 56.4   | 59.9  | 59.1           | <0.001  |
| Microvascular complications           |                    |                  |        |       |                 |         |
| End-stage renal disease               | 0.6                | 1.7              | 1.1    | 1.4   | 1.6            | <0.001  |
| Lower-extremity complications         | 4.6                | 5.2              | 3.9    | 1.3   | 5.0            | <0.001  |
| Diabetic retinopathy                  | 6.1                | 8.3              | 8.2    | 7.4   | 6.8            | <0.001  |
| Macrovascular complications           |                    |                  |        |       |                 |         |
| Peripheral vascular disease           | 6.9                | 6.6              | 4.6    | 2.6   | 6.2            | <0.001  |
| Myocardial infarction                 | 15.9               | 9.9              | 11.3   | 9.6   | 16.5           | <0.001  |
| Congestive heart failure              | 12.6               | 12.4             | 7.6    | 7.8   | 14.7           | <0.001  |
| Cerebrovascular disease               | 7.8                | 6.5              | 5.8    | 5.7   | 7.6            | <0.001  |

Data are mean (SD) or % unless otherwise indicated. P values were calculated with ANOVA tests for continuous variables and χ² tests for categorical variables. All P values are two-sided.

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**Table 2—Dementia incidence densities by race/ethnicity (1998–2007)**

| Race/ethnicity | n     | Cases | Cumulative incidence (%) | Person-years | Age-adjusted incidence density* (95% CI) |
|----------------|-------|-------|--------------------------|--------------|----------------------------------------|
| Non-Hispanic white | 14,546 | 2,586  | 17.78                    | 93,893.03    | 25.33 (24.28, 26.37)                     |
| African American   | 2,484  | 475   | 19.12                    | 17,374.39    | 26.70 (24.20, 29.20)                     |
| Latino             | 2,363  | 354   | 14.98                    | 17,365.58    | 24.33 (21.29, 27.38)                     |
| Asian              | 2,262  | 283   | 12.51                    | 17,072.08    | 19.17 (16.60, 21.74)                     |
| Native American    | 516    | 98    | 18.99                    | 3,165.83     | 33.94 (26.69, 41.19)                     |

*Per 1,000 person-years, using 2000 U.S. Census as the standard.
Asians. The largest observed difference was between Native Americans and Asians. Compared with Asians, Native Americans had a 60% increased risk of dementia in models that accounted for sociodemographic characteristics, diabetes duration, markers of clinical control, and microvascular and macrovascular complications. We also adjusted for BMI, hypertension, and neighborhood deprivation index, but these variables did not change the magnitude of the association between race/ethnicity and risk of dementia (data not shown). The observed trends persisted when we included individuals with missing information on education, A1C, and/or duration of diabetes, when we accounted for the competing risk of death with competing risk regression models (22), and when we stratified by sex (data not shown).

**CONCLUSIONS**

Among older type 2 diabetic patients, 10-year dementia incidence was highest among Native Americans and African Americans, lowest among Asians, and intermediate for non-Hispanic whites and Latinos. The observed differences persisted after accounting for sociodemographic characteristics, diabetes duration, markers of clinical control, and a host of diabetes-related microvascular or macrovascular complications. To our knowledge, this study is the first to examine racial/ethnic differences in dementia incidence among people with diabetes, a group at high-risk for dementia.

Cerebral microvascular and macrocerebrovascular disease are recognized as important risk factors for dementia (23) and are potential pathways that link diabetes and dementia (24,25). Although microvascular complications, macrovascular complications, and markers of clinical control were associated with increased dementia incidence, the observed racial/ethnic differences in dementia risk persisted after adjustment for these factors. Although the prevalence of microvascular and macrovascular complications varied by race/ethnicity in the current study, there was no general pattern of a greater burden of complications in certain racial/ethnic groups. Previous population-based studies reported that among people with diabetes, the rates of microvascular complications, such as end-stage renal disease, tend to be higher and the rates of macrovascular complications lower among racial/ethnic minorities compared with non-Hispanic whites (14,26,27). However, the current finding of no general pattern with respect to race/ethnicity and diabetes-related complications is consistent with earlier research on diabetes-related complications in this population (14).

Unmeasured behavioral or environmental factors may explain the observed differences in dementia risk. Years of education varied across racial/ethnic groups and tended to be lowest among Latinos and highest among Asians. We adjusted for years of education, but this may not account for differences in quality of education, which may partially explain the

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Table 3—Hazard ratios for race/ethnicity and dementia risk (1998–2007)

| Model | Non-Hispanic white | African American | Latino | Asian | Native American |
|-------|--------------------|------------------|--------|-------|----------------|
| 1     | 1.00               | 1.17 (1.06, 1.30) | 0.94 (0.84, 1.06) | 0.77 (0.68, 0.87) | 1.28 (1.05, 1.57) |
| 2     | 1.00               | 1.10 (1.00, 1.22) | 0.92 (0.82, 1.03) | 0.77 (0.68, 0.87) | 1.26 (1.03, 1.54) |
| 3     | 1.00               | 1.15 (1.04, 1.27) | 0.94 (0.84, 1.05) | 0.76 (0.69, 0.88) | 1.28 (1.05, 1.57) |
| 4     | 1.00               | 1.18 (1.07, 1.31) | 0.97 (0.86, 1.09) | 0.79 (0.70, 0.89) | 1.26 (1.03, 1.54) |

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observed racial/ethnic differences in dementia incidence. We adjusted for neighborhood deprivation index, which may have negative effects on health by influencing health behaviors and stress (21). A greater proportion of African American and Latino patients lived in deprived neighborhoods compared with other groups, but adjusting for this variable did not alter observed associations and was not included in final models.

The findings on racial/ethnic difference in dementia risk among older diabetic patients are in accord with previous population-based studies of older adults with and without diabetes, which found that dementia rates were higher among African Americans relative to non-Hispanic whites (4) and similar among Mexican Americans (5) compared with non-Hispanic whites. The current finding that dementia rates are lower among Asian Americans than among non-Hispanic whites is consistent with previous reports among Japanese Americans (4). The literature on dementia among Native Americans is scarce. Although the incidence of dementia was higher among Native Americans than among other racial/ethnic groups in the current study, one small Canadian cross-sectional study reported a similar prevalence of dementia among Native Americans living on two reservations in Manitoba relative to non-Hispanic whites living in Winnipeg (4). The results from the current study may differ from this previous study because the previous study examined dementia prevalence and the current study examined incidence. Another important difference between the two studies is the population source. The previous study comprised Native Americans living on reservations in Canada, and the current study examined Native Americans living in northern California.

To our knowledge, this study is the first to evaluate racial/ethnic differences in dementia risk among older adults with diabetes, a population particularly vulnerable to dementia. Previous studies evaluated racial/ethnic differences in incidence of traditional diabetes-related complications (14,26,27) but provided much fewer data on diabetes-related comorbidities specific to older patients, including dementia. It is important to evaluate possible racial/ethnic differences in dementia incidence as part of the public health effort to eliminate health disparities.

This study has multiple strengths. The KPNC Diabetes Registry is a large, well-characterized, diverse cohort of diabetic patients with detailed information on clinical control and diabetes-related complications. The KPNC Diabetes Registry is an excellent setting in which to examine racial/ethnic differences because health plan members have uniform access to care, so observed racial/ethnic differences in dementia risk should not be attributable to differences in access to care. The long duration of follow-up and generalizability to diabetic patients with access to medical care are also strengths of this study.

This study has some limitations that should be acknowledged. Although study patients had uniform access to care, differences in quality of care may still be present. Dementia diagnosis was based on clinical diagnosis from electronic medical records rather than on standardized assessments administered regularly to all cohort members. It is possible that patients of some racial/ethnic groups are more or less likely to receive a dementia diagnosis from their health care provider. Although our models included adjustment for A1C levels as a measure of glycemic control, evidence from previous studies suggest that A1C levels might not accurately capture average glycemic control across all racial/ethnic groups (28,29).

In conclusion, among older type 2 diabetic patients, African American and Native American patients are at higher risk of dementia than other racial/ethnic groups, and Asian patients are at lower risk of dementia. Somewhat surprising are the observed differences not explained by sociodemographic characteristics or differences in diabetes duration, markers of clinical control, or microvascular or macrovascular complications of diabetes. Given the epidemic of type 2 diabetes and its association with increased risk of dementia, more work is needed to identify factors that may explain these differences in dementia incidence and ways to eliminate them.

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