Renal Function Decline in Latinos With Type 2 Diabetes

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Introduction: Diabetic nephropathy remains a highly prevalent microvascular complication in individuals with type 2 diabetes mellitus (T2DM). Hispanic individuals are at increased risk of metabolic and cardiovascular complications compared with non-Hispanic white individuals. We described the long-term kidney outcomes using a culturally based approach to diabetes management in Hispanic patients implemented by the Joslin Diabetes Center’s Latino Diabetes Initiative.

Methods: Our retrospective study included 594 Hispanic patients evaluated at the Joslin Diabetes Center from July 2002 to July 2015. Demographic and clinical data were collected from the outpatient visits.

Results: Uncontrolled high blood pressure (hazard ratio [HR]: 1.72; 95% confidence interval [CI]: 1.18–2.51; \( P = 0.005 \)), overweight (HR: 2.68; 95% CI: 1.13–6.38; \( P = 0.026 \)), and longstanding T2DM duration (HR: 1.11; 95% CI: 1.08–1.14; \( P < 0.0001 \)) at baseline were significantly associated with increased risk of chronic kidney disease (CKD). Although poor glycemic control (HR: 1.18; 95% CI: 1.099–1.258; \( P < 0.0001 \)), systolic blood pressure (SBP) >140 (HR: 1.01; 95% CI: 1.006–1.02; \( P = 0.0002 \)), and angiotensin-converting enzyme inhibitor/angiotensin receptor blocker use (HR: 1.53; 95% CI: 1.03–2.29; \( P = 0.04 \)) were significantly associated with increased CKD incidence during follow-up. Interestingly, statin use was associated with lower CKD incidence during the follow-up (HR: 0.52; 95% CI: 0.42–0.65; \( P < 0.0001 \)). The annual rate of renal function decline in our cohort was estimated to be –1.39 ml/min per 1.73 m².

Conclusion: Renal function decline in Latinos is associated with expected but modifiable variables, such as uncontrolled diabetes, uncontrolled hypertension, and being overweight. However, the annual rate of renal function decline in our cohort was estimated to be comparatively higher than previous reports in Hispanic individuals without T2DM, and the general US population with T2DM, but lower than expected for this high-risk group. We highlight the importance of a culturally based patient-centered therapeutic approach to improve long-term outcomes in Hispanic patients at high risk of CKD.

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KEYWORDS: chronic kidney disease; culture-based approach; type 2 diabetes mellitus; US Hispanic population

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The prevalence of T2DM continues to increase worldwide. One of every 10 Americans has T2DM, the main cause of CKD and end-stage kidney disease. Approximately 36% of those with T2DM have CKD.¹,² Other risk factors for CKD, including hypertension, obesity, and hyperuricemia, are common in patients with T2DM. Hispanic individuals, the largest ethnic minority in the United States, are at increased risk for both T2DM and CKD.³,⁴ The prevalence of T2DM in Hispanic individuals is approximately 12.1% compared with 7.4% in non-Hispanic white individuals.¹,⁵ CKD progresses faster in Hispanic individuals compared with non-Hispanic white individuals.⁵ Since 2002, the Latino Diabetes Initiative, a culturally appropriate program intended at improving T2DM outcomes in Hispanic individuals at the Joslin Diabetes Center, aims to decrease diabetes complication rates and promote diabetes prevention for future generations. Here we report the kidney outcomes of patients followed for 13 years by the Latino Diabetes Initiative.

METHODS

Population Selection
In this retrospective cohort study, the population consisted of patients with T2DM and Hispanic
background seen at the Joslin Diabetes Center in Boston, MA, between July 2002 and July 2015. A total of 920 patients met the inclusion criteria. Subjects were excluded if they had only 1 medical visit (n = 171), a single creatinine measure (n = 127), or if they had end-stage kidney disease (dialysis or transplant) at baseline (n = 4). The final cohort included 594 participants. The study was approved by the Institutional Review Board at the Joslin Diabetes Center.

Clinical Variables
Demographic, clinical, and biochemical variables were assessed. Glycated hemoglobin (HbA1c), lipid panel (total cholesterol, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol), blood pressure (BP), and kidney function tests (estimated glomerular filtration rate by CKD-Epidemiology Collaboration [eGFR] and urine albumin-creatinine ratio [ACR]) were obtained from clinical. The number of medical appointments with endocrinology and nephrology providers was determined. CKD was defined by either decreased eGFR (<60 ml/min per 1.73 m²) and/or the presence of albuminuria based on spot urine samples using sex-specific cutoffs (urine ACR >17 mg/g in men and >25 mg/g in women). Severe albuminuria was defined as ACR >300 mg/g. The population was stratified according to the rate of glomerular filtration rate loss per year. Annualized based of loss of glomerular filtration rate was defined as the difference between first and last glomerular filtration rate over time (years). Rapid progression was defined as loss of >3 ml/min per year in eGFR. Adequate control was defined as the following: BP when both systolic BP (SBP) <130 mm Hg and diastolic BP <80 mm Hg; whereas diabetes control was defined as HbA1c <7%. lipid control was defined as low-density lipoprotein cholesterol <100 mg/dl, and weight was defined as body mass index between 20 and 25 kg/m².

Statistical Analysis
To assess differences between groups we performed t-test and χ² test as appropriate. Pearson correlation was used to evaluate the relationship between clinical parameters to determine variables to be included in the multivariable models. A mixed linear model was used to assess if eGFR was associated with a number of clinical and anthropometric variables. Cox regressions were used to evaluate risk of developing CKD based on baseline characteristics. This technique also was used to evaluate risk using longitudinal data. In addition, Kaplan-Meier survival analysis was used to depict incident CKD in the population. Analysis was performed using SAS 9.4 (SAS Institute, Inc., Cary, NC).

RESULTS
Table 1 summarizes the demographic and clinical parameters stratified by progression status. More than half of the cohort was female (57.4%). The mean and SD for the following variables at baseline were age 56.6 ± 12.2 years, HbA1c 8.87% ± 2.08%, low-density lipoprotein cholesterol 105.74 ± 37.85 mg/dl, eGFR 86.51 ± 23.44 mL/min per 1.73 m², urine ACR 160.08 ± 655.68 mg/g, SBP 128.54 ± 17.84 mm Hg, diastolic BP 75.26 ± 9.6 mm Hg, and body mass index 32.02 ± 6.46 kg/m². The mean duration of T2DM was 18 ± 9.5 years.

More than a third (35.8%) of participants had eGFR <60 ml/min per 1.73 m² and 28.48% had albuminuria at baseline. Both albuminuria and eGFR <60 ml/min per 1.73 m² were found in 5.28% of our cohort. In patients <50 years old, 26.67% had eGFR <60 ml/min per 1.73 m² and 27.88% had albuminuria. In patients >65 years old, 51.94% had eGFR <60 ml/min per 1.73 m² and 29.46% had albuminuria. In women, 34.9% had eGFR <60 ml/min per 1.73 m² and 24.93% had albuminuria. Moderate and severe albuminuria were found in 39.1% and 8.6%, respectively. Participants with albuminuria at baseline had on average 2.53 ± 1.56 endocrine appointments and 0.52 ± 1.35 nephrology appointments per year. Participants with eGFR<60 ml/min per 1.73 m² had on average 2.58 ± 1.61 endocrine appointments and 0.33 ± 1.04 nephrology appointments per year.

Twenty-five percent of participants had rapid kidney function decline. Participants with rapid CKD progression were more likely to have higher HbA1c, urine ACR, and SBP at baseline. Lipid profiles, smoking history, and eGFR at baseline was not different between rapid and slow progressors.

The mean annual rate of renal function decline in our cohort was −1.39 ml/min ± 14.62. In participants with eGFR<60 ml/min per 1.73 m² or albuminuria at baseline, the decline was −1.26 ± 16.63 ml/min and −0.67 ± 12.83 ml/min, respectively. Participants with severe albuminuria had an annual decline in renal function of −4.95 ± 10.15 ml/min.

Using a mixed linear model, an inverse association was seen between eGFR and age (P < 0.01). Higher SBP and diastolic BP values were associated with higher eGFR at baseline (P < 0.05). Variations in ACR and HbA1c did not affect eGFR throughout the follow-up (P = 0.16 and P = 0.41, respectively).

In a multivariable model, having uncontrolled BP (HR: 1.72; 95% CI: 1.18–2.51; P = 0.005) and being overweight (HR: 2.68; 95% CI: 1.13–6.38; P = 0.026), but not having uncontrolled T2DM (HR: 0.92; 95% CI: 0.55–1.55; P = 0.75) at baseline was associated with
increased risk of incident CKD. Participants with T2DM duration of more than 18 years at baseline (mean diabetes duration) had significantly increased risk of developing CKD (HR: 1.11; 95% CI: 1.08–1.14; P < 0.0001) during follow-up. Female gender and age older than 65 years at baseline increased the risk as well (HR: 1.64; 95% CI: 1.14–2.35; P = 0.008 and HR: 1.03; 95% CI: 1.02–1.05; P < 0.0001, respectively). Interestingly, absence of smoking history increased the risk of developing CKD (HR: 1.54; 95% CI: 1.04–2.28; P = 0.031) (Table 2).

During follow-up, an increased risk of developing CKD was found with higher SBP (HR: 1.01; 95% CI: 1.006–1.02; P = 0.0002), HbA1c (HR: 1.18; 95% CI: 1.099–1.258; P < 0.0001), or older age (HR: 1.03; 95% CI: 1.015–1.037; P < 0.0001). Statin use was associated with reduced risk of developing CKD (HR: 0.52; 95% CI: 0.42–0.65; P < 0.0001), whereas use of angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers was associated with increased incidence of CKD (Table 3).

In patients who did not have CKD at baseline and developed CKD during follow-up, the mean time to development of CKD was 7.8 years (SD 0.12).

Figure 1 shows the predicted eGFR at 25 years of follow-up for different populations (including our

### Table 2. Risk of developing chronic kidney disease during follow-up based on baseline characteristics

| Baseline characteristics | Percentage of total population | Unadjusted | Multivariable model* |
|--------------------------|-------------------------------|------------|----------------------|
|                          |                               | HR (95% CI) | P value              | HR (95% CI) | P value              |
| Uncontrolled T2DM        | 78.5                          | 2.02 (1.86–2.46) | <0.0001              | 0.92 (0.65–1.55) | 0.753               |
| Uncontrolled BP          | 27.9                          | 1.82 (1.51–2.19) | <0.0001              | 1.72 (1.18–2.5)  | 0.005               |
| High LDL                 | 51.5                          | 0.81 (0.69–0.95) | 0.012                | 0.87 (0.62–1.21) | 0.395               |
| Overweight               | 91.8                          | 1.64 (1.61–2.31) | 0.005                | 2.68 (1.13–6.38) | 0.026               |
| No smoking history       | 60.3                          | 1.26 (1.11–1.43) | 0.0004               | 1.54 (1.04–2.28) | 0.031               |
| Age at first visit (>65 yr) | 21.7                        | 1.03 (1.03–1.04) | <0.0001              | 1.03 (1.02–1.05) | <0.0001             |
| Gender (female)          | 57.4                          | 0.67 (0.59–0.77) | <0.0001              | 1.64 (1.14–2.35) | 0.008               |
| T2DM duration (>18 yr)  | 46.3                          | 1.02 (1.01–1.02) | <0.0001              | 1.11 (1.08–1.14) | <0.0001             |

BP, blood pressure; CI, confidence interval; HR, hazard ratio; LDL, low-density lipoprotein; T2DM, type 2 diabetes mellitus.

*Adjusted for all variables included in the table and statin therapy use.
cohort) using previously reported annual rates. There is clear evidence of worse renal outcomes for the Hispanic population compared with the general US population, as well as with those with T2DM.

**DISCUSSION**

We report that Hispanic patients with T2DM have a high prevalence for eGFR $<60 \text{ ml/min per 1.73 m}^2$ and albuminuria. A quarter of participants had rapid kidney function decline. Our study provides support that glucose control and BP control are essential to slow progression of diabetes. We did not find an association among smoking history, lipid profile, and CKD progression, perhaps influenced by survival bias.

T2DM prevalence has been estimated as 9.4% in the United States and it is expected to continue increasing over time.\(^1\) CKD is a common microvascular complication in patients with T2DM, increasing morbidity and mortality as well as costs for health systems worldwide.\(^2\) Hispanic populations are among those with the highest prevalence of T2DM and CKD worldwide. Moreover, prognosis and outcomes tend to be worse in this ethnic group. Prevalence of impaired eGFR and albuminuria in the Hispanic population without T2DM in the United States were estimated as 2.75% and 13.54%, respectively;\(^3\) compared with 35.5% and 28.8%, respectively, in our cohort. Previous reports have shown that Hispanic individuals with T2DM have lower prevalence of albuminuria (structural damage), yet higher prevalence of impaired eGFR (functional damage) compared with non-Hispanic white individuals, leading to higher end-stage kidney disease prevalence.\(^4\)

The mean annual rate of kidney function decline in our Hispanic population with T2DM was $-1.39 \text{ ml/min per 1.73 m}^2$. A mean annual decline in renal function for the US population without T2DM or CKD was estimated to be $-0.3 \text{ ml/min}$; for the Hispanic population without T2DM it was found to be considerably higher ($-1.25 \text{ ml/min}$).\(^5\) Patients with T2DM in the United States, had a mean reported annual decline of $-0.71 \text{ ml/min}$.\(^6\) Of note, higher annual decline of kidney function was expected in our population. Our findings might suggest a benefit from a cultural-approach intervention provided at Joslin with frequent follow-up; however, because no control group was included in our study, this assumption cannot be proven with our findings.

Even though recent studies have described lower cardiovascular events and overall mortality in Hispanic patients with T2DM,\(^10,11\) our findings support the susceptibility of the Hispanic population to worse kidney outcomes. Culturally appropriate treatment programs tailored to the Hispanic community are needed to decrease the kidney disease burden.

**CONCLUSION**

Hispanic individuals with diabetes are at increased risk of developing rapidly progressing CKD. Several modifiable risk factors are associated with rapid CKD progression. Public health measures to improve BP control and obesity, appropriately targeted to this high-risk population, are needed.

**Limitations**

Although our study includes several strengths, including the extensive follow-up, we must acknowledge several

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### Table 3. Chronic kidney disease development risk and clinical characteristics during the follow-up

| Variables during follow-up | Unadjusted | Multivariable model$^a$ |
|----------------------------|------------|-------------------------|
|                            | HR (95% CI) | P value                 | HR (95% CI) | P value                 |
| HbA1C (per %)              | 1.11 (1.05–1.18) | 0.0004                  | 1.17 (1.01–1.26) | $<0.0001$               |
| BP (per mm Hg)             |            |                        |            |                        |
| SBP                        | 1.01 (1.01–1.02) | $<0.0001$              | 1.01 (1.01–1.02) | 0.0002                  |
| DBP                        | 1.00 (0.99–1.01) | 0.881                   | 0.99 (0.97–1.00) | 0.053                   |
| Age at first visit (per yr) | 1.03 (1.03–1.04) | $<0.0001$              | 1.03 (1.02–1.04) | $<0.0001$               |
| Albuminuria use            | 1.77 (1.4–2.24) | $<0.0001$              | 1.53 (1.03–2.29) | 0.0379                  |
| Statin use                 | 0.66 (0.56–0.78) | $<0.0001$              | 0.52 (0.42–0.65) | $<0.0001$               |

$^a$Adjusted for gender in addition to all variables included in the table.
limitations. Our analyses were limited to data collected for clinical purposes. In addition, our center is a multi-specialty referral center for diabetes care, which may not be representative of Hispanic individuals in every community. Last, the Hispanic community in Boston is composed of individuals mostly of Puerto Rican and/or Dominican origin (95% among Hispanic population). Therefore, it may not be representative of all Hispanic individuals in the United States where two-thirds are of Mexican descent.

**DISCLOSURE**

All the authors declared no competing interests.

**SUPPLEMENTARY MATERIAL**

Supplementary File (Word)

STROBE Statement.

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