Premature mortality in individuals living with type 2 diabetes in Jalisco, Mexico, 2011-2019

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Abstract

Objective. To estimate survival outcomes in a population living with diabetes, screened for chronic kidney disease (CKD) and to describe characteristics associated with premature mortality using data from an administrative cohort in Jalisco, Mexico. **Materials and methods.** Using and administrative cohort design, we investigated the 8-year cumulative mortality associated with CKD.We linked screening with mortality data and described population characteristics by CKD stage, computed years of life lost (YLL), and performed Kaplan-Meier curves and Cox proportional hazard models to analyze survival and mortality risk factors. **Results.** At screening, 44% of the cohort exhibited impaired renal function. The mortality rate stood at 14%, 2.5% linked to CKD; 8.7% were premature deaths, accumulating 8 036 YLL. Eight-year survival was 93% for individuals with normal renal function at screening, decreasing to 41% for those with

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Resumen

Objetivo. Estimar la supervivencia en una población que vive con diabetes y que participó en un tamizaje de enfermedad renal crónica (ERC) y describir las características asociadas con mortalidad prematura en Jalisco, México. **Material y métodos.** Utilizando un diseño de cohorte administrativa, se estimó la mortalidad asociada con ERC, acumulada a 8 años. Se vincularon los datos del tamizaje con datos de mortalidad y se describieron las características de la población por estadio de ERC, se calcularon los años de vida perdidos (AVP), curvas de Kaplan-Meier y modelos de riesgos proporcionales de Cox para analizar los factores de riesgo de supervivencia y mortalidad. **Resultados.** En el tamizaje, 44% de la cohorte presentaba función renal deteriorada. La tasa de mortalidad fue de 14%, 2.5% vinculada con ERC; 8.7% fueron muertes prematuras, acumulando 8 036 AVP. La supervivencia a ocho años fue de 93% para

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glomerular filtration rate below 30 mL/min/1.73m². Albumin-creatinine ratio >300 mg/dl, increased years since diabetes diagnosis, hypertension, amputations, retinopathy, and smoking were associated with higher mortality risk; female sex and obesity with a lower risk. **Conclusion.** The high prevalence of renal impairment in this cohort and its association with high mortality underscores the critical importance of timely detection and protocolized intervention for CKD to mitigate this burden.

Keywords: chronic kidney disease; diabetes mellitus type 2; premature mortality; survival analysis; database linkage

individuos con función renal normal, disminuyendo a 41% para aquellos con tasa de filtración glomerular menor de 30 mL/min/1.73 m². Una relación albúmina-creatinina >300 mg/dl, más años con diabetes, hipertensión, amputaciones, retinopatía y tabaquismo se asociaron con mayor riesgo de mortalidad, sexo femenino y obesidad con riesgo menor. **Conclusión.** La alta prevalencia de deterioro renal en esta cohorte y su asociación con una alta mortalidad subrayan la importancia crítica de la detección oportuna y la intervención protocolizada en la ERC para mitigar esta carga.

Palabras clave: enfermedad renal crónica; diabetes mellitus tipo 2; mortalidad prematura; análisis de supervivencia; vinculación de bases de datos

Chronic kidney disease (CKD) is increasing worldwide. In 2017, global prevalence reached 9.1% with a 29.3% increase since 1990.[1] In Mexico, CKD prevalence was estimated at 11.5% in the general population and 38% among individuals with diabetes in 2019.[2,3]

Diabetes mortality rates increased by 7.4% from 2017 to 2020 in Mexico.[4] Type 2 diabetes (T2D) is the leading cause of CKD-related deaths, accounting for 29.1%. In 2017, the years of life lost (YLL) rate for diabetes-related CKD was 335.4 per 100 000, a 134.6% increase since 1990.[5]

A cohort study in Uruguay with a 5.5-year median follow-up revealed a 37.7% mortality rate among CKD patients. Mortality risk factors included diabetes, cardiovascular comorbidity, high blood pressure, and proteinuria.[6] A study using the third National Health and Nutrition Examination Survey (NHANES III) data linked to the US national death index found a 31.1% all-cause 10-year cumulative mortality among people with CKD and diabetes in 2013.[7]

There is a need to strengthen evidence concerning the viability and effectiveness of CKD detection campaigns to inform public policies related to the treatment and control of CKD.[8]

This study aims to analyze survival outcomes and describe clinical and demographic characteristics linked to premature mortality in an uninsured population with T2D screened for CKD. Our objective is to demonstrate the need for protocolized interventions for early detection, treatment, and follow-up of CKD in high-risk populations. We designed an administrative cohort by linking mortality records with data from a CKD screening campaign using a probabilistic linkage algorithm.[9]

Materials and methods

Data sources

We linked data from 7 693 individuals with T2D who participated in a CKD screening program to national mortality data from 2011 to 2019. This administrative cohort represented 4.03% of the target adult population without social security living with diabetes in Jalisco, reflecting the reported diabetes prevalence and estimated target population.[10]

T2D-CKD database

This database includes data from 7 693 people with T2D who responded to an open invitation from Jalisco State Health Services (SESAJ) for a CKD screening between September 2011 and March 2012. Participants needed a T2D diagnosis, no prior CKD diagnosis, and willingness to participate. The screening was free and conducted across four jurisdictions in Jalisco, targeting individuals affiliated with *Seguro Popular*.

We accessed the data through a confidentiality agreement with SESAJ, the Mexican Kidney Foundation (MKF), and the *Instituto Nacional de Salud Pública* (INSP). Details of the screening are described in the supplementary material, section 1.[11]

Epidemiological and Statistical Death System (SEED) mortality databases 2008-2019

The Epidemiological and Statistical Death System (SEED) mortality databases (national death index for

Mexico),[12] administered by the Ministry of Health (MoH), include information about medical attention received, place of death, sociodemographic characteristics of the deceased, and the ICD-10 classification of cause of death. We had access to SEED databases with personal identifiers through existing confidentiality agreements between the MoH and the INSP. These variables were needed for database linkage. Linked databases were anonymized before analysis.

Procedures

The screened population suspected CKD stage was defined according to the Kidney Disease: Improving Global Outcomes 2022 (KDIGO 2022) clinical practice guideline for diabetes management in CKD patients.[13] For risk comparison, screened population was reclassified into four CKD groups, named according to the stage that would correspond if functional abnormalities were confirmed.

1. Normal estimated glomerular filtration rate (eGFR) - urine albumin to creatinine ratio (ACR) group (eGFR ≥90 mL/min/1.73 m² and ACR <30 mg/g).
2. Early stage group (eGFR ≥60 mL/min/1.73 m² and ACR ≥30 mg/g, KDIGO stages 1 or 2).
3. Intermediate stage group (eGFR 30 to 59 mL/min/1.73 m², KDIGO stages 3a and 3b).
4. Advanced stage group (eGFR <30 mL/min/1.73 m², KDIGO stages 4 or 5).

Outcome variables were obtained by probabilistic linkage with the SEED for 2011-2019 using an algorithm based on the Fellegi-Sunter method, as described by Quezada-Sánchez and colleagues.[9] This algorithm uses name, birth date and place, and sex, showing good performance with 90.72% sensitivity and 97.1% positive predictive value. Figure 1 shows details of the linkage procedure used for this work.

Causes of death were grouped into five categories based on the primary cause recorded in the mortality database: diabetes, CKD, cardiovascular, cancer, and other causes (excluding external causes such as injuries). Deaths were assigned to each group according to ICD-10 codes mapped to the list of causes of the Global Burden of Disease study 2019.[14]

We estimated survival after screening and YLL,[15] a metric for premature mortality considering both the frequency and age of deaths.[16] Premature deaths were defined as those occurring before 75 years, according to Mexican life expectancy in 2019.[17]

Statistical analysis

We described clinical and demographic characteristics of the population in the T2D-CKD database as percentages and proportions for categorical variables and mean and standard deviation for quantitative variables.

To assess differences between the four CKD groups, X^2 or t-tests were used as appropriate. Variables with a $p < 0.05$ were deemed statistically significant.

We computed total and average YLL for each CKD group and cause of death. To calculate YLL, we subtracted from 75 the age at death for individuals who died prematurely.[15] Then, we summed the years lost in each CKD group and death-cause category. Finally, we calculated cause-specific YLL per 100 000 person/years for the eight-year period.

To compare survival among CKD groups, we performed Kaplan-Meier curves with Wilcoxon rank sum test. The starting point for this analysis was the date of the screening (September 2011 and March 2012). Each screened individual was searched in the mortality database from the date of the screening until December 31, 2019 (mortality 2020-2022 was not included in the study due to the pandemic disruption); the date of death of those individuals found in the database was recorded. This administrative cohort assumes no individuals lost to follow up, and the only censored data are individuals alive at the end of the study period.

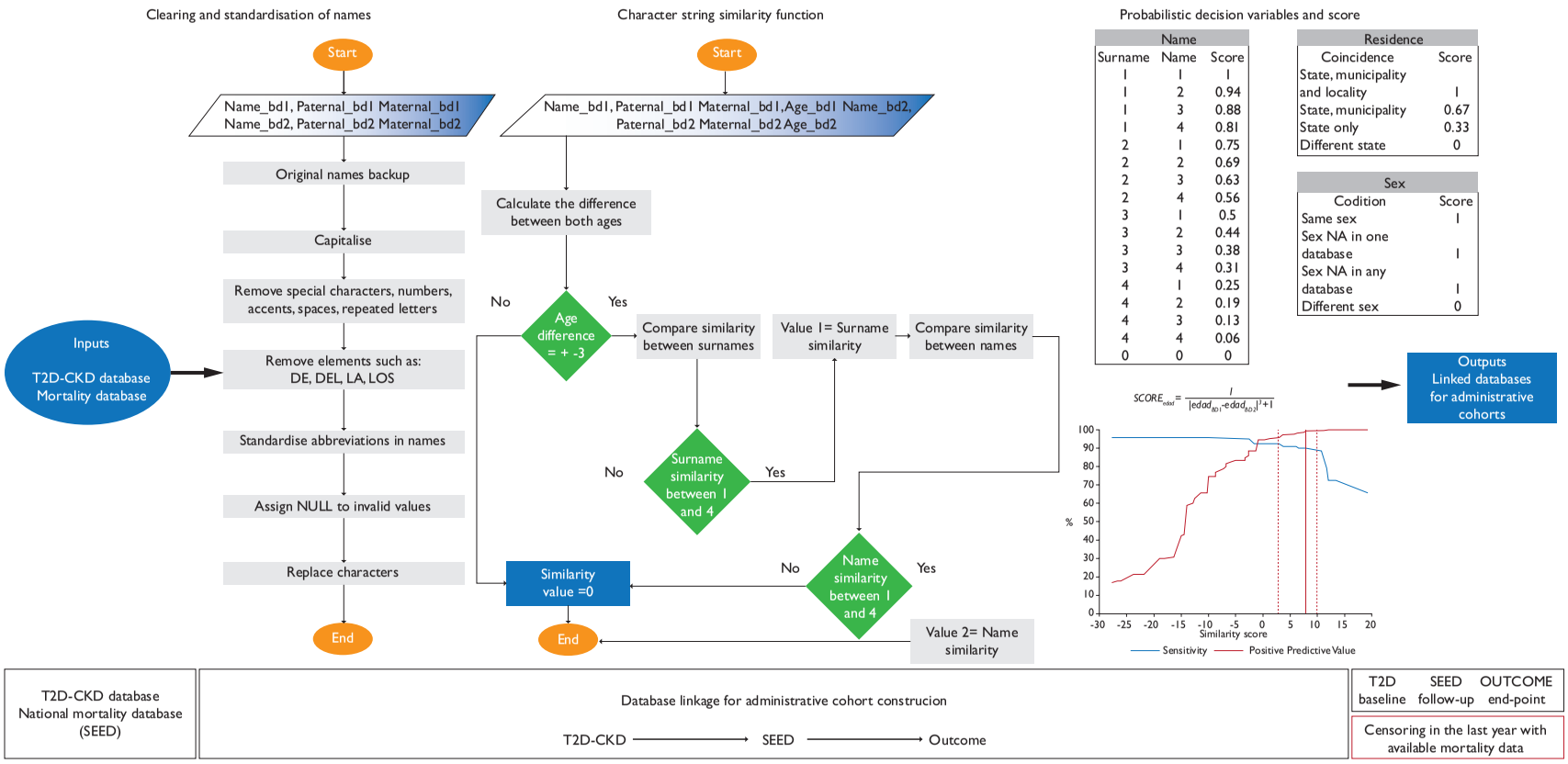
We calculated Cox proportional hazard models with clinical and demographic characteristics at screening time as covariates; all-cause, CKD-related, and all-cause premature mortality were modeled as outcome variables, as shown in equation 1. A detailed specification of all the models is presented in the supplementary material, section 2.[11]

Equation 1

$$^{h}all\ caurse\ mortality\ (t) = h_0(t) \times exp(b_1x_1 + b_2x_2 + \ldots b_px_p)$$

where,
t represents the survival time
$^{h}all\ caurse\ mortality\ (t)$ is the hazard function with death from any cause at any age as outcome variable
h_0 is the baseline hazard
b_1 are the coefficients that measure the impact of covariates
x_1 are the covariates included in the model

Hazard ratios and their confidence intervals were estimated for each CKD group and covariate. Proportional



T2D: type 2 diabetes; CKD: chronic kidney disease

Figure 1. Probabilistic linkage of databases without identification variables

hazard assumptions were tested with the Schoenfeld residuals versus transformed time test to ensure the adequacy of the models used.[18] Analyses were performed using R version 4.3.2.* The research protocol was approved by the Research Ethics Committee of the INSP.

Results

CKD staging and prevalence

We analyzed 7 693 records. Thirty were excluded due to data inconsistencies. Among the remaining 7 663, we found a probable CKD prevalence of 44% (3 371 cases), with 35.3% (2 704) assigned to the early stage group, 7.7% (588) to the intermediate, and 1% (79) to the advanced stage group (table I).

Clinical and sociodemographic characteristics at screening

Women accounted for 72% (5 532) of the screened population. The average age was 58.4 years (SD 12.2); 6 408 individuals (83.6%) reported to be affiliated to *Seguro Popular*. The mean time after T2D diagnosis was 9.5 years (SD 7.7). For the normal eGFR-ACR group it was 7.9 (SD 6.6), 10.8 (SD 7.9) for the early stage, 14.3

* R Foundation for Statistical Computing. https://www.r-project.org

Table I

Clinical and demographic characteristics of a type 2 diabetes population screened for CKD in Jalisco, Mexico, 2011-2012

Variables at baseline	*N*	*Normal eGFR-ACR group*		*Early stage group (1-2)*		*Intermediate stage group (3a-3b)*		*Advanced stage group (4-5)*		*P*
	7 663	*n = 4 292*		*n = 2 704*		*n = 588*		*n = 79*		
	n (category %)	*n*	*row %*	*n*	*row %*	*n*	*row %*	*n*	*row %*	
Sex										0.035
Male	2 131 (27.8)	1 153	54.1	776	36.4	171	8	31	1.5	
Female	5 532 (72.2)	3 139	56.7	1 928	34.9	417	7.5	48	0.9	
Smoked >100 cigarettes						*				0.006
No	4 883 (63.7)	2 796	57.3	1 696	34.7	345	7.1	46	0.9	
Yes	2 780 (36.3)	1 496	53.8	1 008	36.3	243	8.7	33	1.2	
BMI category				*		*				<.001
Underweight	26 (0.3)	9	34.6	11	42.3	6	23.1	0	0	
Normal weight	1 213 (15.8)	590	48.6	479	39.5	124	10.2	20	1.6	
Overweight	2 937 (38.3)	1 654	56.3	1 021	34.8	230	7.8	32	1.1	
Obese	3 487 (45.5)	2 039	58.5	1 193	34.2	228	6.5	27	0.8	
Albumin/Creatinine ratio				*		*		*		<.001
<30 mg/g	4 492 (58.6)	4 292	95.5	0	0	191	4.3	9	0.2	
30-300 mg/g	2 638 (34.4)	0	0	2 328	88.2	278	10.5	32	1.2	
>300 mg/g	533 (7.0)	0	0	376	70.5	119	22.3	38	7.1	
Social security										0.21
SP	6 408 (83.6)	3 565	55.6	2 277	35.5	497	7.8	69	1.1	
No institution	647 (8.4)	397	61.4	208	32.1	35	5.4	7	1.1	
IMSS	470 (6.1)	256	54.5	168	35.7	43	9.1	3	0.6	
ISSSTE	68 (0.9)	36	52.9	28	41.2	4	5.9	0	0	
MoH	40 (0.5)	22	55	15	37.5	3	7.5	0	0	
Banks	22 (0.3)	12	54.5	5	22.7	5	22.7	0	0	
Other	8 (0.1)	4	50	3	37.5	1	12.5	0	0	

(continues...)

(continuation)										
Hypertension						*		*		<.001
No	3 438 (44.9)	2 054	59.7	1 226	35.7	144	4.2	14	0.4	
Yes	4 225 (55.1)	2 238	53.0	1 478	35.0	444	10.5	65	1.5	
Hypercholesterolemia										0.23
No	4 738 (61.8)	2 644	55.8	1 702	35.9	344	7.3	48	1.0	
Yes	2 925 (38.2)	1 648	56.3	1 002	34.3	244	8.3	31	1.1	
Myocardial infarction						*				<.001
No	7 455 (97.3)	4 200	56.3	2 627	35.2	554	7.4	74	1.0	
Yes	208 (2.7)	92	44.2	77	37.0	34	16.3	5	2.4	
Cardiac bypass										<.001
No	7 611 (99.3)	4 270	56.1	2 687	35.3	576	7.6	78	1.0	
Yes	52 (0.7)	22	42.3	17	32.7	12	23.1	1	1.9	
Stroke										0.227
No	7 581 (98.9)	4 254	56.1	2 670	35.2	580	7.7	77	1.0	
Yes	82 (1.1)	38	46.3	34	41.5	8	9.8	2	2.4	
Heart failure						*		*		<.001
No	7 425 (96.9)	4 181	56.3	2 621	35.3	551	7.4	72	1.0	
Yes	238 (3.1)	111	46.6	83	34.9	37	15.5	7	2.9	
Atherosclerosis										0.399
No	7 482 (97.6)	4 196	56.1	2 638	35.3	573	7.7	75	1.0	
Yes	181 (2.4)	96	53.0	66	36.5	15	8.3	4	2.2	
Anemia						*		*		<.001
No	6 868 (89.6)	3 910	56.9	2 412	35.1	483	7.0	63	0.9	
Yes	795 (10.4)	382	48.1	292	36.7	105	13.2	16	2.0	
Retinopathy				*		*		*		<.001
No	6 805 (88.8)	3 922	57.6	2 352	34.6	471	6.9	60	0.9	
Yes	858 (11.2)	370	43.1	352	41.0	117	13.6	19	2.2	
Glaucoma						*				<.001
No	7 369 (96.2)	4 154	56.4	2 593	35.2	547	7.4	75	1.0	
Yes	294 (3.8)	138	46.9	111	37.8	41	13.9	4	1.4	
Neuropathy				*		*				<.001
No	4 493 (58.6)	2 629	58.5	1 510	33.6	311	6.9	43	1.0	
Yes	3 170 (41.4)	1 663	52.5	1 194	37.7	277	8.7	36	1.1	
	n (SD)	*n*	*SD*	*n*	*SD*	*n*	*SD*	*n*	*SD*	
Age	58.4 (12.2)	56.6	11.8	58.9*	12.2	68.3*	10.2	65.7*	10.4	<.001
Years with diabetes	9.5 (7.7)	7.9	6.6	10.8*	7.9	14.3*	9.9	16.2*	10.5	<.001
Abdominal circumference	100.7 (12.1)	101	12.2	100.4	12.1	100.4	11.9	100.3	11.1	0.265

Data sources: T2D-CKD database (description provided in the supplementary material)
* Indicates statistical significance in tests of frequency distribution between normal eGFR and ACR group and each CKD group
T2D: type 2 diabetes; CKD: chronic kidney disease; eGFR: estimated glomerular filtration rate; ACR: albumin to creatinine ratio; BMI: body mass index
SP: National Health Protection Commission *(Seguro Popular)*
IMSS: *Instituto Mexicano del Seguro Social*
ISSSTE: I*nstituto de Seguridad y Servicios Sociales de los Trabajadores del Estado*
MoH: Ministry of Health of Mexico

(SD 9.9) for the intermediate, and 16.2 (SD 10.5) for the advanced CKD stage group (p <0.001) (table I).

No significant sex differences were found in the normal eGFR-ACR, early, and intermediate CKD stage groups. However, the proportion of men in the advanced stage was 1.7 times higher than women (p= 0.035). Thirty-six percent (2 780) of participants had smoked over 100 cigarettes in their lives. Smokers were 1.2 times more likely to be in the intermediate stage group than non-smokers (p= 0.006).

Body mass index (BMI) indicated 38.3% (2 937) of patients were overweight and 45.5% (3 487) were obese, with fewer obese patients in advanced CKD stages (p <0.001). Abdominal circumference showed no significant differences among groups, averaging 101 cm (SD 12.1) (table I).

Fifty-eight percent of the cohort had an ACR <30 mg/g, 34.4% had 30-300 mg/g, and 7% had >300 mg/g. The likelihood of an ACR >300 mg/g was 5.2 times higher in the intermediate stage and 35 times higher in the advanced stage compared to normal ACR. There were 191 individuals in the intermediate stage and nine in the advanced stage with ACR <30 mg/g. Hypertension was the predominant comorbidity, reported by 55.1% (4 225) of individuals, with a higher prevalence in groups with lower eGFR (p <0.001). Other prevalent comorbidities included neuropathy (41.4%, 3 170), hypercholesterolemia (38.2%, 2 925), and retinopathy (11.2%, 858).

Table I shows significant variations in comorbidities across CKD groups. The prevalence of myocardial infarction, heart failure, anemia, retinopathy, glaucoma, and neuropathy were higher in the intermediate or advanced CKD groups.

Premature mortality and associated clinical and demographic characteristics at screening

As of December 2019, 1 071 individuals from the cohort were found in the mortality database, excluding 26 cases attributed to injuries. This corresponds to 14% of the screened individuals. According to CKD groups at baseline, we found 327/4 292 (7.6%) deaths in the normal eGFR-ACR group, 496/2 704 (18.3%) in the early stage, 204/588 (34.7%) in the intermediate, and 44/79 (55.7%) in the advanced stage group. CKD was the cause of 191 deaths (17.8% of total deaths and 2.5% of the overall population); 159 of them (83.3%) were diagnosed with probable CKD at baseline.

Within the cohort, 61.9% of deaths (663) occurred in individuals under 75 years, representing an estimated premature mortality of 8.7%. The average age at death was 66.1, contributing to 8 036 YLL, with 1 730 (21.5%) attributed to CKD.

Diabetes was the main cause of death in the early stage group, and CKD in the intermediate and advanced stage groups. In the normal eGFR-ACR group, the proportion of cancer deaths was higher than in any other group (table II).

The YLL rate per 100 000 person-years due to CKD is higher in groups with lower baseline renal function: 717.1 in the normal group, 4 010.3 in the early stage, 9 307.0 in the intermediate stage, and 29 817.4 in the advanced stage. The all-cause YLL rate is also higher in advanced CKD groups, while YLL due to cancer is lower. The proportion of cardiovascular-related deaths is similar across groups (table II).

The 8-year survival probability revealed statistically significant differences between CKD groups (p <0.0001). For the normal eGFR-ACR group it was 93% (95%CI: 92,94); 83% (95%CI: 82,85) for the early stage, 67% (95%CI: 63,71) for the intermediate, and 42% (95%CI: 32,55) for the advanced stage group (figure 2).

Belonging to the intermediate or advanced stage group significantly heightened the risk of CKD mortality (HR 5.8 [95%CI: 2.8,11.7] and HR 8.6 [95%CI: 3.6,20.9] respectively). Likewise, an ACR exceeding 300 mg/g increased all-cause mortality (HR 3.2 [95%CI: 2.3,4.5]), premature mortality (HR 3.9 [95%CI: 2.3,6.6]), and CKD-specific mortality risk (HR 5.3 [95%CI: 2.7,10.4]) compared with an ACR <30 mg/dl (figure 3 and supplementary material, section 3[11]).

Other factors contributing to increased risks of all-cause, premature, and CKD-specific mortality include time since diabetes diagnosis, history of amputations, and retinopathy. Hypertension and smoking over 100 cigarettes in a lifetime were linked to higher all-cause mortality risk but not CKD-specific mortality (figure 3). Women had lower risk of all-cause (HR 0.7 [95%CI: 0.6,0.74]), premature (HR 0.6 [95%CI: 0.5,0.8]), and CKD-specific mortality (HR 0.6 [95%CI: 0.5,0.8]) compared with men. Obesity significantly reduced the risk of all-cause (HR 0.8 [95%CI: 0.7,0.96]), premature (HR 0.8 [95%CI: 0.6,0.97]), and CKD-specific mortality (HR 0.8 [95%CI: 0.6,0.97]). Hazard ratios for all the variables in unadjusted and adjusted models are provided in supplementary material, section 3.[11]

Discussion

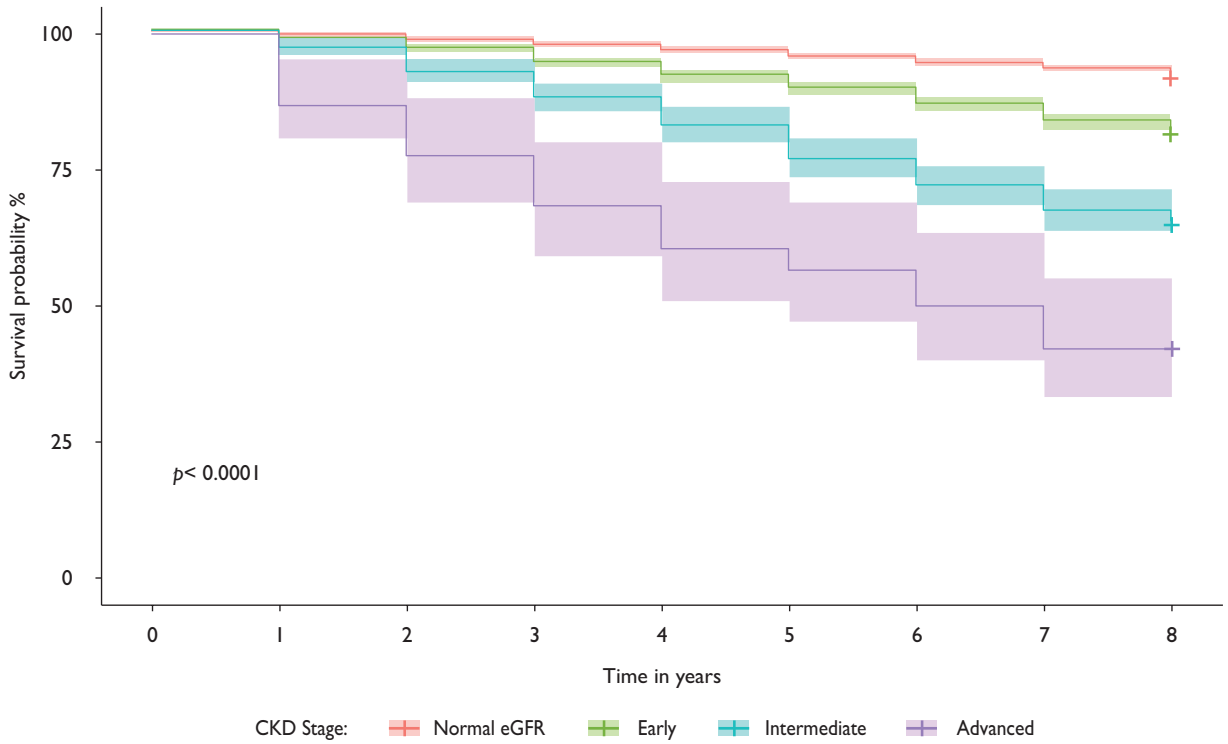
We analyzed data of 7 663 subjects with T2D screened for CKD. Eight-year mortality outcomes were obtained by probabilistic linkage of screening and mortality databases. The high mortality highlights the critical importance of timely CKD detection and intervention to reduce renal

Table II

Premature deaths and YLL by cause group and CKD group in a type 2 diabetes population screened for CKD in Jalisco, Mexico, 2011-2019

CKD group	Population at screening	Person years of follow-up	Death causes	Total deaths per cause and CKD group		Cause specific death rate per 100 000 person/years	Premature deaths per cause and CKD group		Average age at death	Total YLL per cause and CKD group	Average YLL per cause and CKD group	Cause specific YLL per 100 000 person/years	
				n	%		n	%				years	%
Normal eGFR-ACR	4 292	37 371	CKD	32	9.8	85.6	23	10.7	63.3	268	11.7	717.1	10.5
			Diabetes	71	21.7	190.0	37	17.3	62.9	447	12.1	1 196.1	17.4
			Cardio	60	18.3	160.6	36	16.8	63.6	411	11.4	1 099.8	16.0
			Cancer	66	20.2	176.6	55	25.7	62.0	714	13	1 910.6	27.9
			Other	98	30.0	262.2	63	29.4	63.5	723	11.5	1 934.7	28.2
			Total	327	100.0	875.0	214	100.0	63.1	2 563	11.9	6 858.3	100.0
Early stage	2 704	22 467	CKD	79	15.9	351.6	65	20.4	61.1	901	13.9	4 010.3	21.5
			Diabetes	151	30.4	672.1	93	29.2	61.2	1 282	13.8	5 706.1	30.6
			Cardio	98	19.8	436.2	55	17.2	64.1	598	10.9	2 661.7	14.3
			Cancer	44	8.9	195.8	35	11.0	63.2	412	11.8	1 833.8	9.8
			Other	124	25.0	551.9	71	22.3	61.0	993	14	4 419.8	23.7
			Total	496	100.0	2 207.7	319	100.0	62.1	4 186	12.88	18 631.8	100.0
Intermediate stage	588	4 448	CKD	63	30.9	1 416.4	42	41.6	65.1	414	9.9	9 307.6	44.2
			Diabetes	60	29.4	1 348.9	25	24.8	66.8	204	8.2	4 586.3	21.8
			Cardio	36	17.6	809.4	14	13.9	65.6	131	9.4	2 945.1	14.0
			Cancer	7	3.4	157.4	3	3.0	68.0	21	7	472.1	2.2
			Other	38	18.6	854.3	17	16.8	65.2	167	9.8	3 754.5	17.8
			Total	204	100.0	4 586.3	101	100.0	66.2	937	8.86	21 065.6	100.0
Advanced stage	79	493	CKD	17	38.6	3 448.3	13	44.8	63.7	147	11.3	29 817.4	42.0
			Diabetes	9	20.5	1 825.6	5	17.2	65.8	46	9.2	9 330.6	13.1
			Cardio	7	15.9	1 419.9	4	13.8	61.8	53	13.3	10 750.5	15.1
			Cancer	0	0	0	0	0	..	0	0	0	0
			Other	11	25.0	2 231.2	7	24.1	60.1	104	14.9	21 095.3	29.7
			Total	44	100.0	8 924.9	29	100.0	62.8	350	9.74	70 993.9	100.0

Data sources: T2D-CKD database (description provided in the supplementary material); Epidemiological and Statistical Death System (SEED) mortality databases 2011-2019.
T2D: type 2 diabetes
YLL: Years of life lost
CKD: chronic kidney disease
eGFR: estimated glomerular filtration rate
ACR: albumin/creatinine ratio



Data sources: T2D-CKD database (description provided in the supplementary material); Epidemiological and Statistical Death System (SEED) mortality databases 2011-2019.
$p < 0.0001$ for Wilcoxon Rank sum test
CKD: chronic kidney disease
eGFR: estimated glomerular filtration rate

Figure 2. Survival curves of a type 2 diabetes population screened for CKD in Jalisco, Mexico, by CKD stage group at screening, 2011-2019

complications and premature mortality. We found that 44% of the screened population likely had CKD per the Kidney Early Evaluation Program (KEEP) methodology, with 8.7% in intermediate or advanced stages. This aligns with previous findings, such as a 2008 study showing CKD prevalence of 38% in Mexico City and 35% in Jalisco among individuals with diabetes.[3]

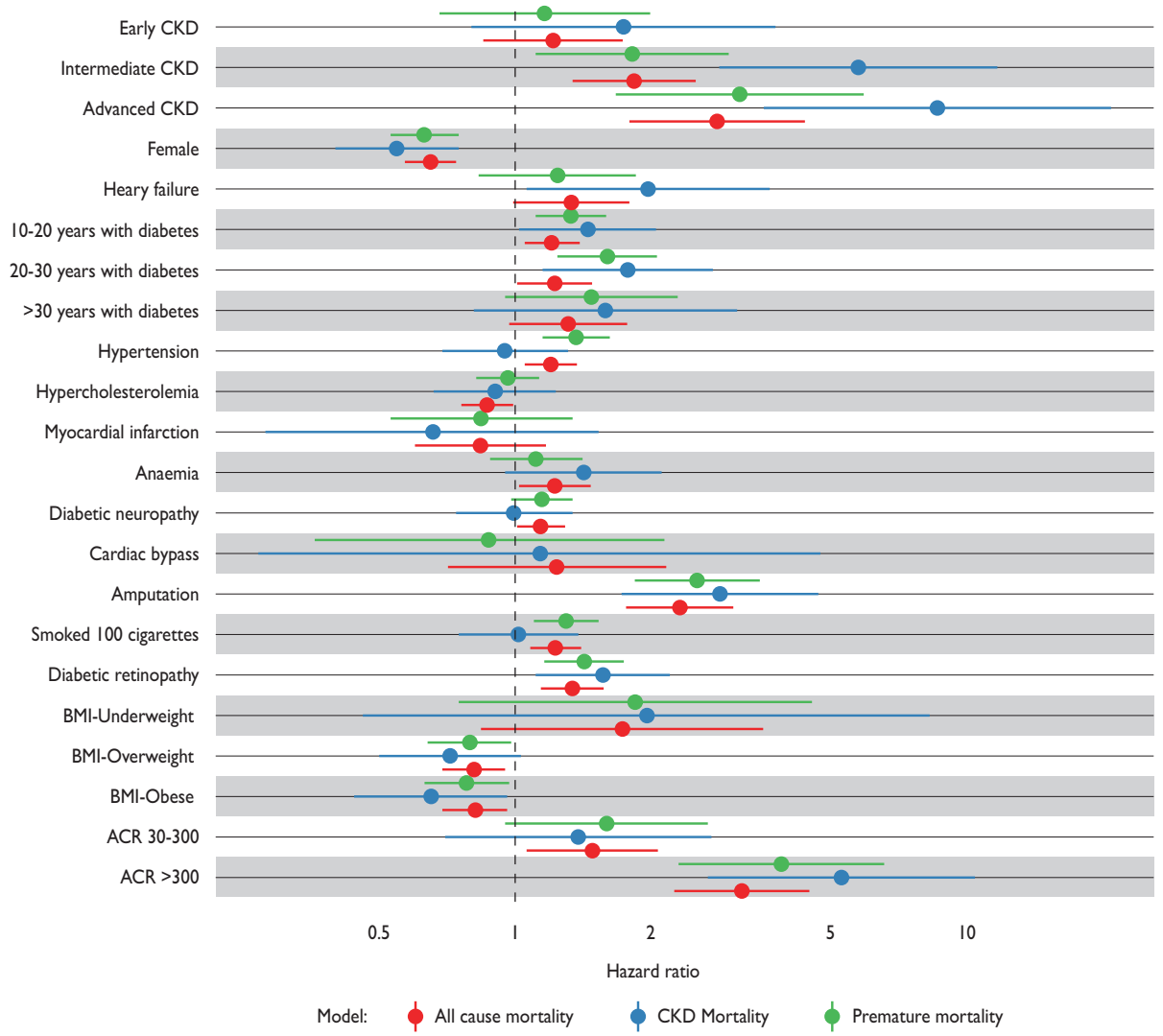
Our study revealed that 2.5% of the cohort died due to CKD over an 8-year period. As a precedent, a report based on the GBD 2019 study informed that CKD attributable to T2D accounted for 2.58% of total mortality in Mexico. This figure marks a 285% increase from the 1990 rate of 0.67%.[2]

After an 8-year follow-up, our sample experienced 191 CKD-related deaths, accumulating 1 730 YLL. The CKD-specific YLL rate per 100 000 person/years is 42 times higher in the advanced stage group when compared with the normal eGFR-ACR group, and 7 times higher than the early stage group.

CKD survival analyses in other countries also show significant losses in life expectancy. In Uruguay, a 17-year follow-up of people with CKD stages 3b and 4 with a median follow-up of 5.5 years found a 37.7% mortality rate. Similarly, in our cohort, 39% of people in intermediate stages died after a 5-year follow-up. Afkarian and colleagues found a 31.1% cumulative 10-year mortality in a US study linking NHANES III and mortality data. Our results are even more alarming.[7]

Participants in the screening were predominantly women; this is possibly a result of men delaying medical care.[19] Additionally, screenings were conducted during typical working hours, and in Mexico employment rates are higher in men. However, the proportion of men is higher in intermediate and advanced stage groups and mortality rates were lower in women. A higher morbidity and mortality burden in men has been previously suggested.[20,21]

We found a high prevalence of overweight and obesity with visceral fat accumulation in both sexes, aligning with Mexico's 75% prevalence rate.[22] Despite a strong association between high BMI and CKD risk,[23,24]



Data sources: T2D-CKD database (description provided in the supplementary material); Epidemiological and Statistical Death System (SEED) mortality databases 2011-2019.
Reference categories are normal eGFR-ACR, for the CKD group; male, for sex; less than 10 years, for years with diabetes; not having reported the condition, for heart failure, hypertension, hypercholesterolemia, myocardial infarction, stroke, anemia, diabetic neuropathy, cardiac bypass, amputations, smoked 100 cigarettes, and diabetic retinopathy; normal weight, for BMI.
T2D: type 2 diabetes
CKD: chronic kidney disease
eGFR: estimated glomerular filtration rate
ACR: albumin to creatinine ratio
BMI: body mass index

FIGURE 3. CLINICAL AND DEMOGRAPHIC CHARACTERISTICS ASSOCIATED WITH SURVIVAL IN A T2D POPULATION SCREENED FOR CKD IN JALISCO, MEXICO, 2011-2019. COX PROPORTIONAL HAZARDS MODELS

our study showed lower BMIs in advanced CKD stages, likely due to increased malnutrition risk. Notably, obesity was significantly associated with reduced mortality risk. These results align with previous observations of increased mortality with decreasing BMI in advanced CKD patients.[25]

In our study, a high proportion of subjects reported comorbidities. Over half reported hypertension, and

over a third reported hypercholesterolemia or neuropathy at screening. Comorbidities were more prevalent in advanced CKD stages. Amputations and retinopathy were associated with shorter survival, reflecting their association with diabetes duration.

It should be noted that individuals identified with possible CKD during the screening were referred to receive standard medical care because state health services have not protocolized management after screening. Consequently, the CKD burden is much higher than expected.

The earlier the strategies to slow CKD progression are implemented, the better their efficacy;[26] therefore, screening high risk populations has been found to be cost-effective.[27,28] CKD screening including ACR and eGFR measurement has been recommended for T2D population at the time of diabetes diagnosis and annually thereafter, and it should be implemented in primary health care settings.[29,30]

Protocolized treatment might have prevented renal damage progression in our cohort. Unfortunately, over a decade since the screening, the MoH has not established a model linking timely detection with a care pathway for CKD stages. We hope this study informs public policy and supports implementing relevant initiatives.

Beyond high CKD mortality rates, there is a significant financial burden on the health system. In 2021, the *Instituto Mexicano del Seguro Social* (IMSS) reported that diabetes, hypertension, and kidney failure were the top three diseases in healthcare costs. The expenditure per patient was 7 002 pesos for hypertension, 14 567 for diabetes, and 245 493 for kidney failure,[31] 16.9 times higher than diabetes without kidney failure.

Our study has limitations. The screened individuals were self-selected, possibly indicating specific health concerns. Comorbidities and time since diagnoses, except for overweight and obesity, were self-reported, relying on individuals' memory and understanding, likely leading to underdiagnosis. Probabilistic linkage is effective for longitudinal analysis, but the algorithm's 90.7% sensitivity means about 9.3% of deceased subjects may not have been identified in the mortality database.

Conclusions

Our results underscore the urgent need for early CKD screening and targeted interventions as a routine strategy among people living with T2D in Mexico. The huge burden of diabetes in Mexico and limited screening resources mean that CKD screening is underperformed. Consequently, patients often have a late diagnosis. Community interventions and protocolized treatment have the potential to improve quality of life, extend life expectancy, and reduce the economic burden on the population and the health systems. This remains a challenge for Mexico and other LMICs. It is imperative that healthcare systems develop protocolized interventions spanning early detection, diagnosis, treatment, and follow-up to reduce this burden.

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