Changes in Kidney Disease: Improving Global Outcomes (KDIGO) Risk Categories in Patients with Type 2 Diabetes and Chronic Kidney Disease

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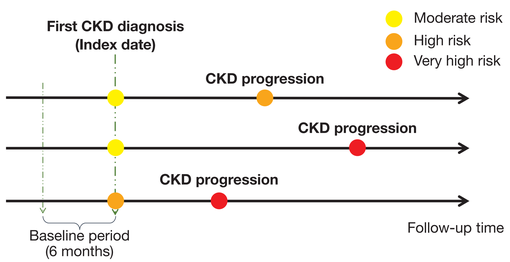
BACKGROUND & OBJECTIVE

- Although progression of chronic kidney disease (CKD) is commonly defined by a decline in estimated glomerular filtration rate (eGFR), elevated urine albumin-to-creatinine ratio (UACR) is also an important early disease marker in patients with CKD associated with type 2 diabetes (T2D)[1]
- Despite the KDIGO guideline recommendations to characterize the disease risk categories using both UACR (A1-A3 stages) and estimated glomerular filtration rate (eGFR, G1-G5 stages),[2] studies of CKD progression continue to rely heavily on eGFR changes
- This study aimed to describe CKD progression patterns based on changes in KDIGO risk categories in patients with CKD associated with T2D; this information will help clinicians better understand the course of CKD

METHODS

- Data from the Optum electronic healthcare records (EHR) database (January 2007 to December 2019) were used
- Patients with CKD and T2D who were of moderate (G3a-A1 and G1/2-A2) or high risk (G3b-A1, G3a-A2, G1/2-A3) based on the KDIGO heat map were included
- The index date was defined as the earliest record indicating CKD of moderate or high risk after T2D diagnosis and patients were followed until the end of continuous eligibility (**Figure 1**)
- Statistical analyses
  - The probability of advancing to a higher KDIGO risk category (i.e., moving from moderate to high/very high risk or from high to very high risk) within 5 years was estimated using Kaplan-Meier analysis for each risk category. Only the most severe KDIGO risk category within 5 years was considered for each patient
  - Changes in kidney function over time were assessed using the trajectories of eGFR, which were depicted by line charts using mean eGFR values at index date and at 1, 2, 3, 4, and 5 years after index date by index KDIGO risk category

Figure 1. Study design diagram for assessing CKD progression patterns



RESULTS

- A total of 269,187 patients with CKD and T2D of moderate (81.3%) or high risk (18.7%) at index date were included in the study (**Table 1**)

Table 1. Baseline KDIGO prognosis risk categories among patients with CKD and T2D of moderate or high risk

		Albuminuria Categories (mg/g)		
		A1: <30	A2: 30-300	A3: >300
eGFR Categories (ml/min/1.73m²)	G1: ≥90		66,754 (24.8%)	6,085 (2.3%)
	G2: 60-90		86,379 (32.1%)	8,989 (3.3%)
	G3a: 45-59	65,558 (24.4%)	18,354 (6.8%)	
	G3b: 30-44	17,068 (6.3%)		
	G4: 15-29			
	G5: <15			

- The majority of patients were 65 years or older (55.3%), female (51.6%), and had hypertension (67.5%) or hyperlipidemia (62.5%)
  - Patients in the high-risk category were older, had lower eGFR, higher UACR, and higher prevalence of hypertension, ischemic heart disease, and chronic pulmonary disease (**Table 2**)

Table 2. Baseline characteristics of patients with CKD and T2D of moderate or high risk (2007-2019)

	All patients N = 269,187	Index KDIGO Risk Category	
		Moderate risk N = 218,691	High risk N = 50,496
Demographics, n (%)			
Age ≥ 65	148,824 (55.3%)	113,879 (52.1%)	34,945 (69.2%) *
Male	130,171 (48.4%)	106,306 (48.6%)	23,865 (47.3%) *
Race			
African American	27,583 (10.2%)	22,422 (10.3%)	5,161 (10.2%)
Asian	5,642 (2.1%)	4,780 (2.2%)	862 (1.7%)
Caucasian	221,580 (82.3%)	179,687 (82.2%)	41,893 (83.0%)
Other/Unknown	14,382 (5.3%)	11,802 (5.4%)	2,580 (5.1%)
Lab tests, mean ± SD			
Index eGFR	73.7 ± 22.6	77.4 ± 21.1	57.9 ± 22.2 *
Index UACR	102.1 ± 365.4	52.7 ± 51.9	316.2 ± 802.4 *
HbA1c	7.3 ± 1.5	7.3 ± 1.5	7.3 ± 1.5
Comorbidities, n (%)			
Hypertension	181,780 (67.5%)	145,182 (66.4%)	36,598 (72.5%) *
Hyperlipidemia	168,375 (62.5%)	136,787 (62.5%)	31,588 (62.6%)
Obesity	47,159 (17.5%)	38,971 (17.8%)	8,188 (16.2%) *
Ischemic heart disease	44,198 (16.4%)	33,227 (15.2%)	10,971 (21.7%) *
Chronic pulmonary disease	39,250 (14.6%)	30,928 (14.1%)	8,322 (16.5%) *

* indicates significant difference ($p < 0.05$) comparing the high-risk category with the moderate-risk category.

- The majority of patients with T2D and CKD of moderate or high risk on the index date moved to a higher risk category within 5 years. (**Table 3**)
  - Patients with CKD of high risk were more likely to move to a higher risk category than patients with CKD of moderate risk
  - However, even for patients with moderate risk at baseline, the probability of moving to a higher risk category was high (G1-A2, 18.8%; G2-A2, 53.9%; G3a-A1, 83.7%)
  - For patients in the same index eGFR stage, higher UACR stage was associated with higher risk of moving to very high risk (e.g., G2-A2 vs. G2-A3: 16.1% vs. 71.6%; G3a-A1 vs. G3a-A2: 27.4% vs. 88.0%)

Table 3. Five-years probabilities of progression based on the index KDIGO risk categories

		Albuminuria Categories (mg/g)		
		A1: <30	A2: 30-300	A3: >300
eGFR Categories (ml/min/1.73m²)	G1: ≥90		To high risk: 16.7% **To very high risk: 2.1%**	- **12.8%**
	G2: 60-90		37.8% **16.1%**	- **71.6%**
	G3a: 45-59	56.3% **27.4%**	- **88.0%**	
	G3b: 30-44	- **87.1%**		
	G4: 15-29			
	G5: <15			

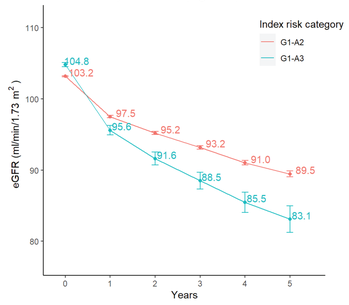
- Among patients with the same index eGFR stage, patients with higher UACR values experienced a faster decline in eGFR (e.g., a steeper slope of decreasing in eGFR was seen in patients with G3a-A2 compared to those with G3a-A1) (**Figure 2**)

LIMITATIONS

- As with all EHR database analyses, medical services and lab tests obtained outside of the healthcare network were not captured; coding inaccuracy and errors may have led to misclassifications of T2D patients identified based on ICD codes
- Highly variable measures of eGFR may have caused misclassification of CKD risk categories; infrequent lab testing, especially of UACR, may have caused lags in the identification of disease progression

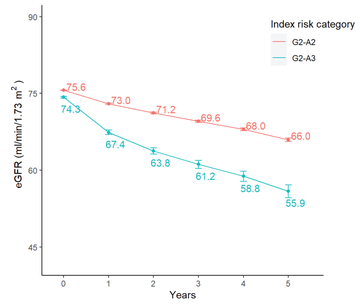
Figure 2. Five-year eGFR trajectories by index KDIGO risk category

a) G1-A2 (moderate risk) and G1-A3 (high risk) at index date



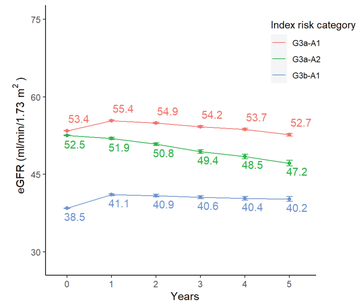
Years	0	1	2	3	4	5
N: G1-A2	66754	34241	23504	15949	10643	6655
N: G1-A3	6085	2980	2046	1344	939	647

b) G2-A2 (moderate risk) and G2-A3 (high risk) at index date



Years	0	1	2	3	4	5
N: G2-A2	86379	49490	34601	24018	16432	10664
N: G2-A3	8989	4968	3383	2310	1540	992

c) G3a-A1 (moderate risk), G3a-A2 and G3b-A1 (high risk) at index date



Years	0	1	2	3	4	5
N: G3a-A1	65558	39990	29054	21429	15256	10243
N: G3a-A2	18354	10817	7659	5409	3731	2431
N: G3b-A1	17068	10475	7625	5621	4095	2754

Note: Error bars represent 95% confidence intervals.

CONCLUSIONS

- This study described CKD progression patterns in terms of KDIGO risk categories based on both eGFR and UACR, and demonstrated the clinical value of UACR in assessing disease progression
- The majority of T2D patients with CKD of moderate to high risk moved to a higher risk category within five years
- Patients with more impaired UACR had faster declines in eGFR, which confirms the importance of UACR in detecting CKD progression and highlights its value in CKD management

References

1. Persson F, Rossing P. Diagnosis of diabetic kidney disease: state of the art and future perspective. Kidney international supplements. 2018;8(1):2-7.
2. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney International Supplements Volume 3 Issue 1 Jan 2013. URL: https://kdigo.org/wp-content/uploads/2017/02/KDIGO_2012_CKD_GL.pdf

Conflict of Interest:

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