Elevated Risk of End-Stage Renal Disease, Cardiovascular Events, and Infection Associated With Diabetic Kidney Disease

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Introduction

- Diabetes mellitus (DM) is associated with all-cause and cardiovascular hospitalization and mortality, and is associated with the development of diabetic kidney disease (DKD) (1).
- Of the 120,000 new cases of ESRD in the US annually, 44% are attributable to DM (2).
- However, the association between DKD and non-fatal events including cardiovascular events and infection is not fully characterized.

Methods

- Using the Truven MarketScan database, we identified patients aged 18-64 years with DM and the subset with DKD during 2011-2013 using ICD-9 codes. DKD status was ascertained using chronic kidney disease (CKD) codes, divided into stages 1-2, 3 and 4-5.
- Unadjusted event rates were calculated as number of events per 1,000 patient-years over 3 years of follow-up.
- Adjusted cumulative incidence curves were generated using the method of Cole and Hernán (3).

Methods

- Cox proportional hazards models were used to investigate the association between DKD stage (1-2, 3, and 4-5, compared to no DKD) and five outcomes: ESRD, myocardial infarction (MI), congestive heart failure (CHF), stroke, and infections over a maximum of 3 years of follow-up.
- Models were adjusted for demographics and baseline Elixhauser comorbidities.

Results

- Of 2,213,934 patients with DM, 157,196 (7.1%) had DKD.
- Among patients with DM and DKD, those with higher stage were also older and had higher levels of comorbidity.
- Unadjusted event rates increased dramatically by DKD stage, particularly for ESRD, CHF and infections.
- Adjusted hazard ratios (HRs) similarly showed increasing risk of events by DKD stage (Figure 3):
  - HRs for ESRD were 6.4, 19.1, and 191.8 for stages 1-2, 3, and 4-5, respectively, compared to no DKD.
  - HRs for MI, stroke and infection were of similar magnitude by stage, ranging from 1.2 to 3.0 by increasing stage.
  - CHF HRs were higher, from 1.7 for stage 1-2 to 5.6 for stage 4-5, compared to no DKD.

Table 1. Baseline demographic characteristics and comorbid conditions among diabetes patients by DKD status and stage

	Non-DKD	Stage 1-2	Stage 3	Stage 4-5	Missing Stage
N	2,056,738	21,212	53,074	20,814	62,096
Mean Age (SD)	52.9(9.4)	54.8(8.4)	57.7(6.6)	56.7(7.3)	54.6(8.7)
Age Groups, %					
18-44 years	18.6	13.0	5.7	8.1	13.6
45-54 years	31.5	28.3	20.4	23.4	27.6
55-59 years	24.0	25.8	27.2	26.8	25.6
60-64 years	26.0	32.9	46.7	41.7	33.2
Gender, %					
Male	53.5	59.8	58.9	57.5	58.7
Female	46.5	40.2	41.1	42.5	41.3
Number of Comorbidities, %					
0	17.4	1.9	0.9	1.0	1.8
1	30.4	10.7	6.8	5.5	12.9
2	29.5	22.3	17.9	13.0	23.8
3	13.0	22.6	20.0	15.7	21.2
4+	9.8	42.6	54.4	64.8	40.3
Selected Comorbidities, %					
Congestive heart failure	2.0	6.9	13.5	21.3	9.0
Cardiac arrhythmias	3.8	8.5	12.7	15.0	10.4
Valvular disease	1.4	3.5	5.5	7.7	4.2
Pulmonary circulation disorders	0.6	1.9	3.2	4.2	2.6
Peripheral vascular disorders	1.6	4.8	7.1	9.7	5.3
Hypertension, uncomplicated	44.0	67.2	72.8	72.8	61.5
Hypertension, complicated	1.7	16.2	23.9	34.3	12.2
Paralysis	0.3	0.7	0.9	1.2	1.0
Other neurological disorders	1.2	2.6	3.3	4.9	3.4
Chronic pulmonary disease	5.8	9.7	12.0	13.4	10.5
Hypothyroidism	7.9	9.9	11.6	10.6	10.7
Liver disease	2.1	4.2	4.3	5.9	4.9
Peptic ulcer disease excluding	0.2	0.5	0.5	0.7	0.5
AIDS/HIV	0.2	0.3	0.4	0.4	0.3
Lymphoma	0.3	0.6	0.9	1.2	0.8
Metastatic cancer	0.4	0.7	1.3	1.4	1.3
Solid tumor without metastas	3.0	4.7	6.5	6.0	5.0
Rheumatoid arthritis/collagen	1.8	3.6	4.0	3.7	3.0
Coagulopathy	0.7	1.9	2.8	3.9	2.6
Obesity	6.5	12.8	13.2	12.9	13.2
Weight loss	0.6	1.4	1.9	3.3	2.0
Fluid and electrolyte disorder	2.8	11.4	16.3	25.4	14.6
Blood loss anemia	0.3	0.7	1.0	1.7	0.8
Deficiency anemia	1.6	4.3	5.9	9.0	3.7
Alcohol abuse	0.6	1.1	1.1	1.7	1.5
Drug abuse	0.4	0.8	0.8	1.0	1.1
Psychoses	0.4	0.8	1.2	1.5	1.2
Depression	6.4	8.3	9.3	8.4	9.7
Stroke	1.6	4.1	6.1	7.5	4.8

Figure 1. Unadjusted event rates over three years of follow-up

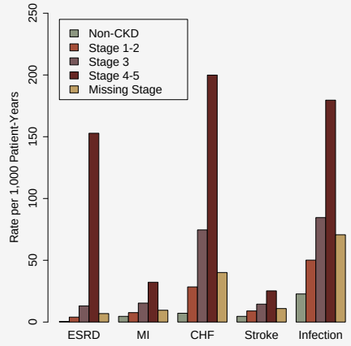


Figure 2. Adjusted Cumulative Incidence

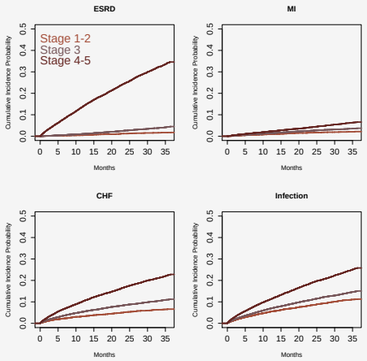
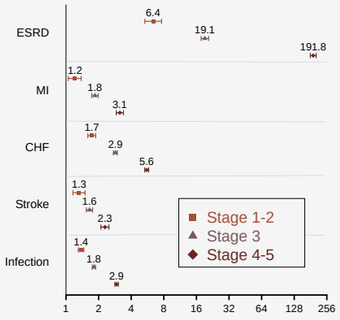


Figure 3. Adjusted Hazard Ratios*



*Reference group is no DKD with HR=1.0; not shown in graph

Conclusions

- Increasingly DKD stage is associated with increasing risks of ESRD, cardiovascular events, and infection.
- Prevention, detection, and reduction of progression is likely critical to reduce the risks of these outcomes, but more research is needed.

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This study was sponsored by Janssen.

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