



**University of Dundee**

## **The Relationship between AKI and CKD in Patients with Type 2 Diabetes**

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*Published in:*  
Journal of the American Society of Nephrology

*DOI:*  
[10.1681/ASN.2020030323](https://doi.org/10.1681/ASN.2020030323)

*Publication date:*  
2021

*Document Version*  
Publisher's PDF, also known as Version of record

[Link to publication in Discovery Research Portal](#)

*Citation for published version (APA):*  
Hapca, S., Siddiqui, M. K., Kwan, R. S. Y., Lim, M., Matthew, S., Doney, A. S. F., Pearson, E. R., Palmer, C. N. A., Bell, S. (2021). The Relationship between AKI and CKD in Patients with Type 2 Diabetes: An Observational Cohort Study. *Journal of the American Society of Nephrology*, 32(1), 138-150.  
<https://doi.org/10.1681/ASN.2020030323>

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Number of serum creatinine tests flagged as AKI	All patients (N=16700)	T2DM (N=9417)	Control (N=7283)
Old algorithm ( retrospective tests)	28306	24257	4049
SCr $\geq 1.5$ x median SCr 365 to 8 days prior to index	20608	17671	2937
SCr $\geq 1.5$ x lowest SCr in the 7 days prior to index	10170	8536	1634
SCr > 26 $\mu\text{mol/L}$ higher than lowest SCr in the 48 hrs prior to index.	12569	10856	1713
Modified algorithm (retrospective and prospective tests)	40567	34469	6098
SCr $\geq 1.5$ x median SCr 365 to 8 days prior to index	20608	17671	2937
SCr $\geq 1.5$ x lowest SCr in the 7 days prior/post index	21205	17782	3423
SCr > 26 $\mu\text{mol/L}$ higher than lowest SCr in the 48 hrs prior/post to index.	24577	21220	3357
SCr $\geq 1.5$ x median SCr 365 to 8 days post to index	16156	13662	2494

Table S1: Number of AKI cases identified using the NHS England algorithm and the modified algorithm broken down by the different criteria used in the definition of the AKI case.

## Sensitivity analysis tables

Patients' groups	AKI patients N (%)	Number of AKI episodes	AKI episodes per 1000 person-years			
			Un-adjusted		Adjusted for age and sex	
			Mean rate (95%CI)	Rate ratio (95%CI)	Mean rate (95% CI)	Rate ratio (95% CI)
All patients (N=16700)	2404 (14.4)	3295	27.7 (26.3-29.2)	-	25.5 (24.1-26.9)	-
Control (N=7282)	436 (6.0)	543	8.3 (7.6-9.2)	1.0	9.1 (8.2-10.0)	1.0
Type 2 diabetes (N=9417)	1968 (20.9)	2752	43.5 (41.0-46.0)	5.2 (4.7-5.8)	39.5 (37.1-42.0)	4.4 (3.9-4.9)
No CKD (N=11090)	854 (7.7)	1083	13.8 (12.6-15.2)	-	16.3 (14.4-18.5)	-
Control (N=6032)	195 (3.2)	228	4.1 (3.6-4.8)	1.0	5.5 (4.7-6.5)	1.0
Type 2 diabetes (N=5058)	659 (13.0)	855	26.2 (23.6-29.2)	6.4 (5.3-7.6)	30.6 (26.7-35.0)	5.5 (4.6-6.6)
CKD (N=5610)	1550 (27.6)	2212	55.7 (52.4-59.1)	-	56.2 (51.8-61.0)	-
Control (N=1251)	241 (19.3)	315	32.1 (27.9-36.8)	1.0	29.7 (25.5-34.6)	1.0
Type 2 diabetes (N=4359)	1309 (30.0)	1897	62.7 (58.7-66.9)	2.0 (1.7-2.3)	62.8 (57.8-68.2)	2.1 (1.8-2.5)
Prior to CKD diagnosis (N=2442)	187 (7.7)	233	22.6 (19.3-26.5)	-	24.2 (19.7-29.7)	-
Control (N=587)	23 (3.9)	24	8.8 (5.7-13.7)	1.0	9.6 (6.1-15.2)	1.0
Type 2 diabetes (N=1855)	164 (8.8)	209	27.3 (23.1-32.3)	3.1 (1.9-4.9)	29.6 (23.9-36.6)	3.1 (1.9-4.9)
Post CKD diagnosis (N=5610)	1415 (25.2)	1979	68.1 (63.9-72.7)	-	69.9 (61.4-79.7)	-
Control (N=1251)	224 (17.9)	291	41.3 (35.6-47.8)	1.0	38.9 (32.2-47.1)	1.0
Type 2 diabetes (N=4359)	1201 (27.6)	1688	75.9 (70.7-81.4)	1.8 (1.6-2.2)	76.5 (67.2-87.2)	2.0 (1.7-2.3)

Table S2. Incidence rates of stage 2 and 3 AKI episode and rate ratios in the diabetic and non-diabetic groups depending on the CKD status.

Patients' groups	AKI patients N (%)	Number of AKI episodes	AKI episodes per 1000 person-years			
			Un-adjusted		Adjusted for age and sex	
			Mean rate (95%CI)	Rate ratio (95%CI)	Mean rate (95% CI)	Rate ratio (95% CI)
All patients (N=16700)	3550	6384	58.4 (55.8-61.2)	-	49.3 (46.9-51.7)	-
Control (N=7282)	660	974	15.6 (14.5-16.9)	1.0	15.9 (14.6-17.2)	1.0
Type 2 diabetes (N=9417)	2890	5410	92.3 (87.6-97.2)	5.9 (5.4-6.5)	77.9 (73.8-82.2)	4.9 (4.5-5.4)
No CKD (N=11090)	1091	1572	21.5 (19.7-23.4)	-	24.4 (21.8-27.3)	-
Control (N=6032)	273	350	6.5 (5.7-7.4)	1.0	8.7 (7.5-10.0)	1.0
Type 2 diabetes (N=5058)	818	1222	40.7 (36.8-45.1)	6.3 (5.4-7.4)	45.9 (40.5-52.1)	5.3 (4.5-5.4)
CKD (N=5610)	2459	4812	129.6 (123.3-136.1)	-	125.8 (117.3-134.9)	-
Control (N=1251)	387	1026	67.5 (60.3-75.5)	1.0	59.2 (52.2-67.2)	1.0
Type 2 diabetes (N=4359)	2072	3780	147.5 (139.8-155.6)	2.2 (1.9-2.5)	141.8 (132.1-152.2)	2.4 (2.1-2.7)
Prior to CKD diagnosis (N=2442)	304	422	42.0 (36.9-47.8)	-	41.9 (34.8-50.4)	-
Control (N=587)	40	52	19.9 (14.5-27.4)	1.0	20.8 (14.8-29.3)	1.0
Type 2 diabetes (N=1855)	264	370	49.4 (43.0-56.7)	2.5 (1.8-3.5)	49.7 (41.0-60.4)	2.4 (1.7-3.4)
Post CKD diagnosis (N=5610)	2296	4390	160.1 (152.0-168.6)	-	169.8 (152.9-188.6)	-
Control (N=1251)	361	974	85.2 (75.6-96.1)	1.0	83.2 (71.4-97.1)	1.0
Type 2 diabetes (N=4359)	1935	3410	181.2 (171.2-191.7)	2.1 (1.9-2.4)	187.4 (168.8-207.9)	2.3 (2.0-2.6)

Table S3. AKI episode incidence rates and rate ratios for AKIs lasting more than 48hrs in the diabetic and non-diabetic groups depending on the CKD status.

Patients' groups	AKI patients N (%)	Number of AKI episodes	AKI episodes per 1000 person-years			
			Un-adjusted		Adjusted for age and sex	
			Mean rate (95%CI)	Rate ratio (95%CI)	Mean rate (95% CI)	Rate ratio (95% CI)
All patients (N=16700)	4620 (27.7)	4800	32.6 (31.7-33.5)	-	31.2 (30.2-32.3)	-
Non diabetic (N=7282)	952 (13.1)	977	13.9 (13.1-14.8)	1.0	15.9 (15.0-17.0)	1.0
Type II diabetes (N=9417)	3668 (39.0)	3823	49.6 (48.0-51.2)	3.6 (3.3-3.9)	44.5 (42.8-46.3)	2.8 (2.6-3.0)
No CKD (N=11090)	1736 (15.7)	1782	17.5 (16.7-18.3)	-	22.0 (20.8-23.3)	-
Non diabetic (N=6032)	481 (8.0)	495	8.3 (7.6-9.1)	1.0	11.7 (10.7-12.8)	1.0
Type II diabetes (N=5058)	1255 (24.8)	1287	30.4 (28.8-32.1)	3.7 (3.3-4.0)	35.6 (33.3-38.1)	3.0 (2.7-3.4)
CKD (N=5610)	2884 (51.4)	3018	66.2 (63.9-68.6)	-	60.5 (57.2-64.1)	-
Non diabetic (N=1251)	471 (37.6)	482	44.5 (40.7-48.7)	1.0	36.6 (33.0-40.5)	1.0
Type II diabetes (N=4359)	2413 (55.4)	2536	73.0 (70.2-75.8)	1.6 (1.5-1.8)	67.0 (63.2-71.1)	1.8 (1.7-2.0)
Prior to CKD diagnosis (N=2442)	156 (6.4)	163	15.1 (12.9-17.6)	-	12.6 (9.5-16.7)	-
Non diabetic (N=587)	25 (4.3)	26	9.5 (6.4-13.9)	1.0	8.2 (5.2-12.8)	1.0
Type II diabetes (N=1855)	131 (7.1)	137	17.0 (14.4-20.1)	1.8 (1.2-2.7)	14.4 (10.7-19.4)	1.8 (1.1-2.7)
Post CKD diagnosis (N=5610)	2744 (48.9)	2855	88.2 (79.1-105.1)	-	77.5 (71.5-84.1)	-
Non diabetic (N=1251)	448 (35.8)	356	56.4 (51.5-61.9)	1.0	48.6 (43.1-54.8)	1.0
Type II diabetes (N=4359)	2296 (53.7)	2399	89.8 (86.3-93.5)	1.6 (1.4-1.8)	84.5 (77.8-91.7)	1.7 (1.6-1.9)

Table S4. AKI episode incidence rates and rate ratios for AKIs during a hospital admission in the diabetic and non-diabetic groups

depending on the CKD status.

	All patients (N=16700) IRR (95% CI)	No CKD (N=11090) <sup>a</sup> IRR (95%CI)	CKD (N=5610) <sup>b</sup> IRR (95%)
T2DM vs Control	3.54 (3.30-3.80)	3.85 (3.44-4.32)	2.01 (1.82-2.22)
Sex: Female vs Male	0.98 (0.92-1.05)	0.96 (0.87-1.07)	0.92 (0.86-0.99)
Age at recruitment: (per 20 year increase)	1.71(1.66-1.76)	1.76 (1.67-1.84)	1.21 (1.16-1.26)
Comorbidities at recruitment			
Coronary Artery Disease (CAD)	1.34 (1.24-1.45)	1.28 (1.11-1.47)	1.26 (1.16-1.38)
Congestive Heart Failure (CHF)	2.07 (1.80-2.39)	2.24 (1.60-3.14)	1.85 (1.61-2.13)
Peripheral Vascular Disease (PVD)	1.88 (1.63-2.17)	2.37 (1.73-3.23)	1.50 (1.30-1.72)
Cerebrovascular Disease (CD)	1.63 (1.43-1.85)	1.76 (1.35-2.29)	1.44 (1.26-1.64)
Hypertension:	1.45 (1.34-1.56)	1.41 (1.26-1.58)	1.01 (0.91-1.12)
Liver Disease (CD)	3.41 (2.60-4.49)	4.58 (2.87-7.31)	2.17 (1.59-2.96)

<sup>a</sup> No CKD at recruitment or during follow-up

<sup>b</sup> CKD at recruitment or during follow-up

Table S5. AKI episode incidence rate ratios adjusted for sex, age and comorbidities at recruitment depending on CKD status.

Model variable (Fixed Effects)	No CKD at recruitment (N=9460; No Scr =222564)					
	T2D (N=4618; No Scr=147698)		No diabetes (N=4842; No Scr=74866)		Difference	
	Estimate	P-value	Estimate	P-value	Estimate	P-value
Reference group*: intercept	103.69 (102.65 to 104.72)	<0.001	98.38 (97.66 to 99.10)	<0.001	5.30 (4.04 to 6.56)	<0.001
Time: slope per 1year	-0.20 (-0.33 to -0.07)	<0.001	-0.33 (-0.42 to -0.23)	<0.001	0.13 (-0.03 to 0.29)	0.123
AKI intercept: pre AKI vs no AKI	-1.03 (-1.73 to -0.32)	0.004	-1.98 (-3.08 to -0.88)	<0.001	0.95 (-0.35 to 2.26)	0.152
post AKI vs pre AKI	2.68 (0.81 to 4.55)	0.005	5.20 (1.86 to 8.54)	0.002	-2.52 (-6.35 to 1.31)	0.197
AKI slope : pre AKI vs no AKI	-1.14 (-1.24 to -1.03)	<0.001	-0.29 (-0.46 to -0.11)	0.001	-0.85 (-1.05 to -0.65)	<0.001
post AKI vs pre AKI	-0.29 (-0.59 to 0.01)	0.056	-0.55 (-1.08 to -0.03)	0.038	0.26 (-0.34 to 0.86)	0.396
Sex intercept only: M vs F	1.32 (0.7 to 1.94)	<0.001	-1.04 (-1.65 to -0.42)	0.001	2.36 (1.48 to 3.24)	<0.001
Age intercept: 50 to 64 vs 49 and under	-12.85 (-13.87 to -11.84)	<0.001	-9.5 (-10.33 to -8.66)	<0.001	-3.36 (-4.68 to -2.04)	<0.001
65 to 79 vs 49 and under	-23.71 (-24.74 to -22.68)	<0.001	-18.73 (-19.67 to -17.8)	<0.001	-4.98 (-6.38 to -3.59)	<0.001
80 and above vs 49 and under	-29.09 (-30.97 to -27.21)	<0.001	-25.80 (-27.5 to -24.11)	<0.001	-3.29 (-5.82 to -0.76)	0.011
Age slope: 50 to 64 vs 49 and under	-0.32 (-0.46 to -0.18)	<0.001	0.05 (-0.06 to 0.17)	0.362	-0.38 (-0.56 to -0.2)	<0.001
65 to 79 vs 49 and under	-0.37 (-0.51 to -0.23)	<0.001	-0.04 (-0.17 to 0.09)	0.549	-0.33 (-0.52 to -0.14)	<0.001
80 and above vs 49 and under	0.01 (-0.28 to 0.3)	0.925	-0.17 (-0.42 to 0.07)	0.162	0.19 (-0.19 to 0.56)	0.331
Coronary Artery Disease: intercept	-1.02 (-1.83 to -0.21)	0.013	-0.29 (-1.37 to 0.8)	0.607	-0.73 (-2.09 to 0.62)	0.288
Congestive Heart Failure: intercept	-2.05 (-4.23 to 0.13)	0.066	0.78 (-3.3 to 4.85)	0.71	-2.83 (-7.45 to 1.8)	0.231
Peripheral Vascular Disease: intercept	-0.07 (-2.15 to 2.01)	0.948	-2.04 (-5.44 to 1.36)	0.24	1.97 (-2.02 to 5.96)	0.332
Peripheral Vascular Disease: slope	-0.73 (-1.03 to -0.42)	<0.001	-0.13 (-0.61 to 0.34)	0.584	-0.59 (-1.16 to -0.03)	0.04
Cerebrovascular Disease: intercept	-2.34 (-3.96 to -0.72)	0.005	0.12 (-2.78 to 3.01)	0.937	-2.45 (-5.77 to 0.86)	0.147
Hypertension: intercept	-1.64 (-2.35 to -0.93)	<0.001	-1.05 (-1.77 to -0.33)	0.004	-0.59 (-1.6 to 0.42)	0.251
Hypertension: slope	-0.19 (-0.29 to -0.09)	<0.001	0.01 (-0.08 to 0.11)	0.786	-0.21 (-0.34 to -0.07)	0.004

\*Reference group includes: No AKI during follow-up, female, 49 and below, no cardiovascular disease

Table S6: Parameter estimates of the longitudinal eGFR data analysis for people with and without T2D and no CKD at recruitment



Model variable (Fixed Effects)	CKD at recruitment (N=1432; No Scr =56827)					
	T2D (N=1047; No SCr=44299)		No diabetes (N=385; No SCr=12528)		Difference	
	Estimate	P-value	Estimate	P-value	Estimate	P-value
Reference group <sup>a</sup> : intercept	59.63 (56.53 to 62.74)	<0.001	63.99 (58.63 to 69.35)	<0.001	-4.35 (-10.55 to 1.84)	0.168
Time: slope per 1year	-0.71 (-1.12 to -0.30)	<0.001	0.01 (-0.81 to 0.82)	0.99	-0.71 (-0.20 to 1.63)	0.125
AKI intercept: pre AKI vs no AKI	-3.85 (-5.27 to -2.43)	<0.001	-0.99 (-3.45 to -1.46)	0.427	-2.85 (-5.59 to -0.02)	0.049
post AKI vs pre AKI	2.29 (-0.15 to 4.74)	0.066	9.08 (4.35 to 13.8)	<0.001	-6.78 (-12.1 to -1.46)	0.013
AKI slope : pre AKI vs no AKI	-0.79 (-1.05 to -0.52)	<0.001	-0.4 (-0.85 to 0.05)	0.079	-0.38 (-0.90 to 0.14)	0.148
post AKI vs pre AKI	0.23 (-0.24 to 0.71)	0.329	-0.84 (-1.73 to 0.06)	0.066	1.07 (0.06 to 2.08)	0.038
Sex intercept only: M vs F	-0.64 (-2.06 to 0.79)	0.381	-2.13 (-4.49 to 0.23)	0.076	1.5 (-1.26 to 4.25)	0.287
Age intercept: 49 and under vs 50 to 64	-9.11 (-19.6 to 1.38)	0.089	-	-	-	-
65 to 79 vs 50 to 64	-4.91 (-7.33 to -2.49)	<0.001	-4.78 (-9.85 to 0.3)	0.065	-0.13 (-5.75 to 5.49)	0.963
80 and above vs 50 to 64	-8.17 (-10.82 to -5.52)	<0.001	-9.04 (-14.29 to -3.79)	<0.001	0.87 (-5.02 to 6.75)	0.772
Age slope: 49 and under vs 50 to 64	1 (-0.88 to 2.88)	0.297	-	-	-	-
65 to 79 vs 50 to 64	0.37 (-0.05 to 0.79)	0.085	-0.09 (-0.95 to 0.76)	0.831	0.46 (-0.49 to 1.42)	0.339
80 and above vs 50 to 64	0.58 (0.11 to 1.05)	0.017	0.06 (-0.83 to 0.95)	0.892	0.51 (-0.49 to 1.52)	0.316
Coronary Artery Disease: intercept	0.04 (-1.64 to 1.72)	0.962	1.42 (-1.56 to 4.39)	0.35	-1.38 (-4.79 to 2.04)	0.429
Congestive Heart Failure: intercept	1.48 (-2.02 to 4.99)	0.407	-5.5 (-14.56 to 3.57)	0.235	6.98 (-2.74 to 16.7)	0.159
Congestive Heart Failure: slope	-0.86 (-1.49 to -0.22)	0.008	0.01 (-1.62 to 1.63)	0.996	-0.86 (-2.61 to 0.88)	0.332
Peripheral Vascular Disease: intercept	-3.83 (-7.37 to -0.29)	0.034	-0.62 (-7.57 to 6.33)	0.863	-3.21 (-11.01 to 4.59)	0.419
Peripheral Vascular Disease: slope	0.14 (-0.55 to 0.83)	0.697	0.64 (-0.58 to 1.87)	0.304	-0.5 (-1.91 to 0.9)	0.481
Cerebrovascular Disease: intercept	-0.78 (-3.4 to 1.83)	0.556	-0.28 (-5.09 to 4.54)	0.911	-0.51 (-5.99 to 4.97)	0.855
Cerebrovascular Disease: slope	-0.12 (-0.6 to 0.36)	0.62	-0.7 (-1.6 to 0.2)	0.128	0.58 (-0.44 to 1.59)	0.266
Hypertension: intercept	0.99 (-1.2 to 3.18)	0.377	-4.61 (-7.86 to -1.35)	0.006	5.59 (1.67 to 9.52)	0.005

\*Reference group includes: No AKI during follow-up, female, 50 to 64, no cardiovascular disease

Table S7: Parameter estimates of the longitudinal eGFR data analysis for people with and without T2D and no CKD at recruitment.

**Figure S1:** Identifying AKI episodes (red circles) from longitudinal serum creatinine test (a1-d1). The different trajectories of AKI episodes (red) during the course of the disease (a2-d2) ranging from rapid recovery within seven days (a2) to longer recovery more than seven days and/or multiple AKI insults leading to AKD (b2-c2), or irreversible AKI leading to AKD and CKD (d2). Cleaning of the eGFR longitudinal data to ascertain CKD status (a3-d3): first AKI flagged eGFR values are removed (red circles), then median eGFR is calculated based on the remaining eGFR values (black line), which is used to determine the date of CKD onset.

