ACUTE AND CHRONIC COMPLICATION PROFILES AMONG PATIENTS IDENTIFIED WITH CHRONIC KIDNEY DISEASE IN ALBERTA, CANADA

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1 Introduction & Objective

- Chronic kidney disease (CKD) poses a substantial burden to patients and the healthcare system.
- CKD is associated with 10-30x higher risk of cardiovascular (CV) morbidity and mortality compared to general population.[1]
- When compared to earlier stages, more advanced stages of CKD are associated with higher rates of both acute and chronic adverse events, mortality, and healthcare costs.[2-4]
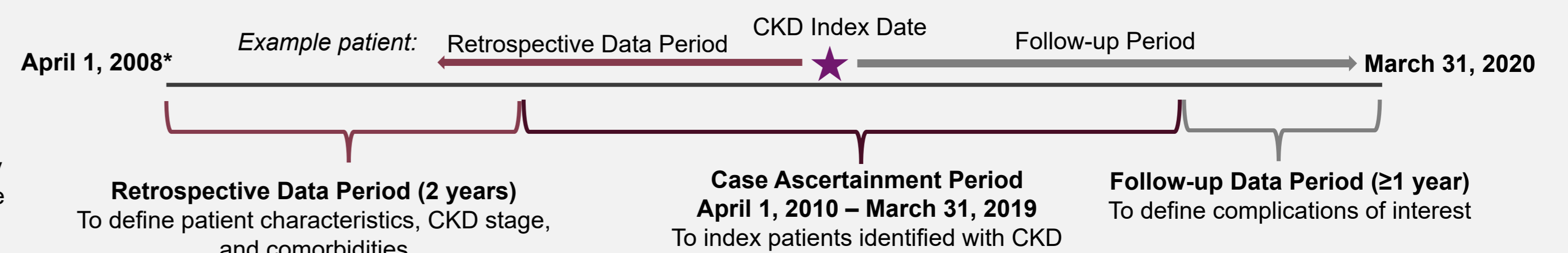
Objective: To describe comorbidities and complication profiles in patients identified with CKD in Alberta, Canada.

2 Methods

- This was a population-based retrospective study linking Alberta's administrative health databases
- Included adult patients (≥18 years of age) with newly identified CKD and at least 1 year of follow-up data, between April 1, 2010 to March 31, 2019, based on a published algorithm incorporating International Classification of Disease (ICD) diagnostic codes (ICD-9-CM/ICD-10-CA) and laboratory values (estimated glomerular filtration rate [eGFR] and/or albuminuria) (**Figure 1**). CKD stage was determined by eGFR/albuminuria cut-off values from the published 2012 Kidney Disease Improving Global Outcomes (KDIGO) Guidelines.[5]

Figure 1: Study timeline

Abbreviations: CKD: chronic kidney disease.
* Laboratory data (used to stage CKD) was only available within 18 months of the first index date (April 1, 2010)

Example patient: April 1, 2008* — Retrospective Data Period — CKD Index Date — Follow-up Period — March 31, 2020

Retrospective Data Period (2 years): To define patient characteristics, CKD stage, and comorbidities
Case Ascertainment Period April 1, 2010 – March 31, 2019: To index patients identified with CKD
Follow-up Data Period (≥1 year): To define complications of interest

- **Comorbidities** were described as frequencies (n (%)) in the two years prior to CKD index date.
- **Complications** were described as acute (rates based on the number of events occurring after the CKD index date per 100 person-years) and chronic (rates based on the first event occurring after the CKD index date per 100 person-years) and were further stratified by CKD stage (1-5) at CKD index date.

3 Results

- The study cohort included 588,170 patients (**Table 1**).
- Most patients (75.8%) could not be staged due to the absence of albuminuria values or a lack of specificity in eGFR values.

Table 1: Patient characteristics at CKD index date

Characteristics	CKD Cohort (n=588,170)
Age (years), n (%)	
<45	80,084 (14.3)
45-<55	96,208 (17.2)
55-<65	148,590 (26.6)
65-<75	131,567 (23.6)
≥75	101,721 (18.2)
Mean (SD)	60.7 (15.3)
Sex, n (%)	
Female	277,578 (49.7)
Male	280,592 (50.3)
CCI score[a], n (%)	
0	382,874 (68.9)
1-2	86,085 (15.5)
3+	86,691 (15.6)
Mean (SD)	1.0 (2.0)
ASCVD at CKD index date, n (%)	63,786 (11.4)
T2DM at baseline, n (%)	134,439 (24.1)
CKD stage, n (%)	
No stage	446,010 (75.8)
Stage 1	3,739 (0.6)
Stage 2	11,706 (2.0)
Stage 3a	80,095 (13.6)
Stage 3b	14,770 (2.5)
Stage 4	1,775 (0.3)
Stage 5	75 (0.0)

Abbreviations: ASCVD: atherosclerotic cardiovascular disease; CCI: Charlson Comorbidity Index; SD: standard deviation; T2DM: type 2 diabetes mellitus.
[a] The Charlson Comorbidity Index score was derived based on hospitalizations and physician visits in the one year prior to the CKD index date

- The most frequently identified comorbidities in the two years prior to CKD index date were hypertension, any infection, and dyslipidemia (**Table 2**).

Table 2: Comorbidity profiles (n (%))

	2 years prior to index date (n (%))		2 years prior to index date (n (%))
Cardiovascular		**Kidney**	
Atrial fibrillation	15287 (2.7)	Acute kidney injury	9269 (1.7)
Cardiovascular hospitalization	45689 (8.2)	Acute kidney injury with dialysis	9520 (1.7)
Chronic heart failure	14505 (2.6)	Albuminuria	12503 (25.8)
Coronary artery disease	8985 (1.6)	CRRT	1842 (0.3)
Dyslipidemia	102619 (18.4)	Dialysis Initiation	494 (0.1)
HHF broad	23661 (4.2)	ESKD	1659 (0.3)
HHF specific	3162 (0.6)	Fast eGFR decline	78545 (37.8)
Hypertension	206146 (36.9)	Hematuria	16468 (3.0)
Myocardial infarction	6965 (1.2)	Hyperkalemia	4886 (0.9)
Peripheral artery disease	3930 (0.7)	Kidney Transplantation	753 (0.1)
Stroke/TIA	18594 (3.3)	**Other Comorbidities**	
Fracture		Anemia	40530 (7.3)
Any fracture	32094 (5.7)	Any other infection	161378 (28.9)
Diabetes Related		Bacteremia	1271 (0.2)
Diabetic ketoacidosis	1036 (0.2)	Cellulitis abscess	28847 (5.2)
Hypoglycemia	1703 (0.3)	Gangrene	4900 (0.9)
Lower limb amputations	501 (0.1)	Hospital infection	11098 (2.0)
		Pneumonia	31964 (5.7)
		Ulcer before gangrene	6560 (1.2)
		UTI	119221 (21.4)

Proportion (%) 0.10 — 36.90

Abbreviations: CRRT: continuous renal replacement therapy; eGFR: estimated glomerular filtration rate; ESKD: end-stage kidney disease; HHF: hospitalization for heart failure; TIA: transient ischemic attack; UTI: urinary tract infection.

Table 3: Complication profiles and rates (per 100 person-years) for the incident CKD study cohort by stage across the study follow-up[a]

Rate per 100 person-years 0.03 — 65.90

Complication	No Stage	Overall	Stage 1	Stage 2	Stage 3a	Stage 3b	Stage 4	Stage 5
Acute								
Cardiovascular								
Cardiovascular hospitalization	90,212 (20.2)	136,208 (24.4)	637 (17.0)	3,054 (26.1)	32,838 (41.0)	8,270 (56.0)	1,147 (64.6)	50 (66.7)
HHF – broad	47,897 (10.7)	76,887 (13.8)	350 (9.4)	1,703 (14.5)	20,303 (25.3)	5,751 (38.9)	855 (48.2)	28 (37.3)
Myocardial infarction	14,206 (3.2)	21,016 (3.8)	97 (2.6)	448 (3.8)	4,898 (6.1)	1,200 (8.1)	160 (9.0)	7 (9.3)
Stroke/transient ischemic attack	36,882 (8.3)	55,207 (9.9)	191 (5.1)	1,147 (9.8)	13,515 (16.9)	3,096 (21.0)	365 (20.6)	11 (14.7)
Diabetes Related								
Diabetic ketoacidosis	2,308 (0.5)	3,137 (0.6)	78 (2.1)	151 (1.3)	430 (0.5)	135 (0.9)	33 (1.9)	<5
Hypoglycemia	4,982 (1.1)	7,291 (1.3)	92 (2.5)	311 (2.7)	1,437 (1.8)	405 (2.7)	61 (3.4)	<5
Lower limb amputations	1,734 (0.4)	2,588 (0.5)	51 (1.4)	136 (1.2)	488 (0.6)	145 (1.0)	30 (1.7)	<5
Kidney								
Acute kidney injury	35,769 (8.0)	56,292 (10.1)	254 (6.8)	951 (8.1)	13,716 (17.1)	4,783 (32.4)	781 (44.0)	38 (50.7)
Acute kidney injury with dialysis	36,149 (8.1)	56,826 (10.2)	257 (6.9)	959 (8.2)	13,821 (17.3)	48,10 (32.6)	786 (44.3)	44 (58.7)
Hyperkalemia	13,753 (3.1)	23,450 (4.2)	142 (3.8)	652 (5.6)	6,094 (7.6)	2,273 (15.4)	510 (28.7)	26 (34.7)
Other								
Any fracture	67,508 (15.1)	91,863 (16.5)	398 (10.6)	1,486 (12.7)	18,031 (22.5)	3,966 (26.8)	456 (25.7)	21 (28.0)
Any infection	249,864 (56.0)	325,079 (58.2)	1,941 (51.9)	6,090 (52.0)	54,625 (68.2)	11,076 (75.0)	1421 (80.1)	62 (82.7)
Cellulitis abscess	61773 (13.8)	82654 (14.8)	610 (16.3)	1781 (15.2)	14943 (18.7)	3086 (20.9)	440 (24.8)	21 (28.0)
Gangrene	12372 (2.8)	18781 (3.4)	192 (5.1)	657 (5.6)	4313 (5.4)	1062 (7.2)	172 (9.7)	13 (17.3)
Hospitalization for infection	35,198 (7.9)	53,294 (9.5)	306 (8.2)	1,051 (9.0)	12,662 (15.8)	3,524 (23.9)	532 (30.0)	21 (28.0)
UTI	196969 (44.2)	255962 (45.9)	1484 (39.7)	4336 (37.0)	43068 (53.8)	8890 (60.2)	1162 (65.5)	53 (70.7)
Chronic								
Cardiovascular								
Atrial fibrillation	18,088 (4.1)	28,605 (5.1)	80 (2.1)	582 (5.0)	7,853 (9.8)	1,769 (12.0)	224 (12.6)	9 (12.0)
Chronic heart failure	22,695 (5.1)	38,447 (6.9)	180 (4.8)	896 (7.7)	11,038 (13.8)	3,111 (21.1)	510 (28.7)	17 (22.7)
Coronary artery disease	15,794 (3.5)	23,493 (4.2)	115 (3.1)	568 (4.9)	5,598 (7.0)	1,248 (8.4)	162 (9.1)	8 (10.7)
Dyslipidemia	74,176 (16.6)	96,739 (17.3)	535 (14.3)	2,043 (17.5)	16,850 (21.0)	2,804 (19.0)	323 (18.2)	8 (10.7)
Hypertension	51,850 (11.6)	66,311 (11.9)	493 (13.2)	1,188 (10.1)	10,643 (13.3)	1,869 (12.7)	250 (14.1)	18 (24.0)
Peripheral artery disease	7,785 (1.7)	12,089 (2.2)	67 (1.8)	322 (2.8)	3,041 (3.8)	734 (5.0)	129 (7.3)	11 (14.7)
Kidney								
CKD progression	24,510 (5.8)	43,498 (8.2)	282 (7.7)	1,192 (10.2)	12,398 (15.5)	4,302 (29.1)	772 (43.5)	42 (56.0)
Dialysis initiation	4,155 (0.9)	5,983 (1.1)	47 (1.3)	92 (0.8)	971 (1.2)	464 (3.1)	222 (12.5)	32 (42.7)
ESKD	15,260 (3.4)	34,170 (6.1)	338 (9.0)	742 (6.3)	12,380 (15.5)	4,485 (30.4)	893 (50.3)	72 (96.0)
Hematuria	37,708 (8.5)	48,348 (8.7)	249 (6.7)	934 (8.0)	7,924 (9.9)	1,375 (9.3)	154 (8.7)	<5
Kidney transplantation	1,341 (0.3)	2,023 (0.4)	10 (0.3)	16 (0.1)	390 (0.5)	166 (1.1)	89 (5.0)	11 (14.7)
Other								
Anemia	56,647 (12.7)	82,227 (14.7)	418 (11.2)	1,776 (15.2)	18,214 (22.7)	4,458 (30.2)	674 (38.0)	40 (53.3)
Mortality[b]								
All-cause mortality	35,821 (8.0)	61,857 (11.1)	136 (3.6)	1,054 (9.0)	17,988 (22.5)	5,883 (39.8)	935 (52.7)	40 (53.3)
Cardiovascular death	9,717 (2.2)	19,075 (3.4)	38 (1.0)	355 (3.0)	6,241 (7.8)	2,322 (15.7)	384 (21.6)	18 (24.0)
Death from infection	671 (0.2)	1,299 (0.2)	5 (0.1)	26 (0.2)	407 (0.5)	167 (1.1)	20 (1.1)	<5

Abbreviations: CKD: chronic kidney disease; ESKD: end-stage kidney disease; HHF: hospitalization for heart failure; UTI: urinary tract infection.
[a] Numeric values in each cell represent the n (%) for the complication profiles, while shading in the cells represents the rate per 100 person-years.
[b] Mortality outcomes were calculated as chronic event rates (based on the event occurring after CKD index date per 100 person-years).

- Dyslipidemia, anemia, and hypertension were the most common chronic complications, corresponding to rates (95% CI) of 11.9 (11.7-12.1), 4.76 (4.69-4.83), and 13.0 (12.8-13.3) per 100 person-years, respectively (**Table 3**)
- Urinary tract infections and hospitalization for cardiovascular disease were the most common acute complications, corresponding to rates (95% CI) of 20.6 (20.5-20.7) and 8.37 (8.32-8.42) per 100 person-years, respectively.
- Higher stages of CKD at index demonstrated higher rates of complications.

4 Limitations

- The CKD index date was an approximate for diagnosis date however, due to the study timeframe and algorithm used, patients may have been diagnosed earlier than indexed.
  - The lack of CKD staging results may limit the interpretation of complications stratified by stage
- Potential misclassification bias of the CKD cohort and complication outcome definitions due to incorrect or unavailable diagnostic codes or laboratory values may be present.

5 Conclusion

- This study revealed **over two-thirds of patients experienced an acute or chronic complication** after CKD index.
- Strategies to mitigate complications following CKD diagnosis would be helpful to reduce the burden of CKD on patients and healthcare systems.

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