Health Care Resource Utilization Following Hyperkalemia in Adults With and Without Chronic Kidney Disease in the UK

Lei Qin,[1] Laura Horne,[2] Akhtar Ashfaq,[2*] Sharon MacLachlan,[3] Marvin Sinsakul,[2] Robert LoCasale[2]

[1]Health Economics, AstraZeneca, Gaithersburg, MD, USA; [2]Global Medical Affairs, AstraZeneca, Gaithersburg, MD, USA; [3]Real World Evidence, Evidera, London, UK

*At the time of the study

Introduction

- Hyperkalemia (HiK) is a potentially life-threatening electrolyte abnormality characterized by elevated serum potassium (K^+) concentrations[1]
- The severity of HiK increases as the serum K^+ concentration increases above normal[2,3]
- HiK frequently occurs in patients with progressive renal disease and is often associated with adverse clinical outcomes, including cardiac arrhythmias and mortality[2,3]
- Little is known about the impact of HiK and its severity and concurrence with chronic kidney disease (CKD) on health care resource utilization
- Here, we report results from a retrospective, population-based analysis characterizing health care resource utilization in patients with HiK in the overall population and in those with prior CKD among patients obtaining health care in England

Methods

- Retrospective cohort analyses were conducted using patient data from the Clinical Practice Research Datalink (CPRD) database linked to the Hospital Episode Statistics (HES) database
  - CPRD is an electronic primary care database of >11 million anonymous longitudinal medical records across the UK and has established linkages to HES.[4] HES provides information on hospital/emergency department admissions and outpatient appointments at National Health Service hospitals in England[5]

Table 1. Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
• Aged ≥18 years • Record in linked CPRD/HES dataset • Incident HiK event (first occurrence of HiK event) defined as READ diagnosis code or a serum K^+ laboratory result ≥5.0 mmol/L in CPRD or ICD-10 codes for HiK in HES between 1/1/2009 and 12/31/2013 **Additional criteria for CKD analyses:** • Diagnostic code or eGFR <60 mL/min/1.73 m^2 on ≥2 occasions (>90 days apart) before or on date of incident HiK event	• Serum K^+ laboratory value ≥10.0 mmol/L • <365 days of observation time between the incident HiK event date and the current registration or up to standard dates • History of HiK before 1/1/2009 • Active cancer • Recent history of volume depletion/dehydration

CKD, chronic kidney disease; CPRD, Clinical Practice Research Datalink; eGFR, estimated glomerular filtration rate; HES, Hospital Episode Statistics; HiK, hyperkalemia; ICD-10, International Classification of Diseases, 10th Revision; K^+, potassium.

- CKD was defined as a diagnostic code or estimated glomerular filtration rate <60 mL/min/1.73 m^2 on ≥2 occasions (>90 days apart) before or on the date of incident HiK event
- Incident HiK events were stratified by severity and defined as:
  - K 5.0–≤5.5: serum K^+ concentration 5.0–≤5.5 mmol/L or CPRD diagnosis code for HiK with no laboratory results
  - K >5.5–≤6.0: serum K^+ concentration >5.5–≤6.0 mmol/L
  - K >6.0: serum K^+ concentration >6.0 mmol/L or HES diagnosis code for HiK, regardless of K^+ concentration
- A cohort analysis was used to determine health care resource utilization
- Statistical analyses:
  - Incidence of initial HiK event was determined for the overall population and was stratified by incident event serum K^+ concentration
  - Descriptive analysis was performed to evaluate health care resource utilization outcomes at 3, 7, 30, 90, 180, and 365 days after an initial HiK event for the overall population, for the CKD subgroup, and by HiK severity strata. One inpatient admission, 1 outpatient visit, all laboratory measurements, and all prescriptions filled could be included per day. Health care resource utilization outcomes were cumulative, not adjusted for covariates, and are presented as crude frequencies

Results

- A total of 195,178 patients with an incident HiK event were included and stratified by severity at time of event: K 5.0–≤5.5 (n = 177,945; 91.2%); K >5.5–≤6.0 (n = 14,020; 7.2%); and K >6.0 (n = 3213; 1.6%)
- Of the 195,178 patients with HiK, 17.9% had CKD (**Table 2**)
  - Relative to the overall population of patients with HiK, patients in the CKD subgroup were older, included more females, and greater proportions had prespecified baseline comorbidities and reported use of renin–angiotensin–aldosterone system inhibitors compared with the overall cohort of patients

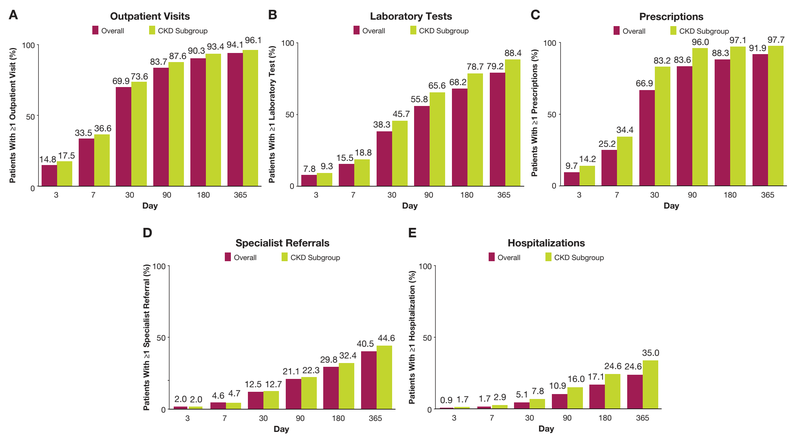
Table 2. Patient Demographics and Baseline Characteristics

	Overall (N = 195,178)	CKD Subgroup (n = 34,912)	Severity of Incident HiK Event		
			K 5.0–≤5.5 (n = 177,945)	K >5.5–≤6.0 (n = 14,020)	K >6.0 (n = 3213)
Age, years, mean (SD)	60.6 (16.6)	75.5 (11.9)	60.5 (16.5)	60.7 (17.0)	63.7 (18.7)
Female, %	52.1	63.1	52.2	51.2	52.3
BMI, kg/m², mean (SD)	28.3 (6.1)	28.3 (5.9)	28.4 (6.1)	27.9 (6.1)	27.8 (6.7)
eGFR, mL/min/1.73 m², mean (SD)	80.5 (21.1)	56.3 (13.7)	80.6 (20.9)	79.7 (22.0)	78.2 (23.9)
Comorbidities, %					
Hypertension	50.7	81.5	50.7	48.8	58.1
Hyperlipidemia	19.6	34.1	19.7	18.0	22.1
Obstructive lung disease	18.3	21.3	18.2	18.6	22.5
CKD	17.9	100.0	17.7	17.5	27.9
Ischemic heart disease	12.8	27.8	12.6	12.4	20.7
Diabetes (types 1 and 2)	12.5	20.2	12.5	11.8	14.7
Arrhythmia (including AF)	9.5	20.9	9.3	9.7	18.6
AF	6.8	16.9	6.6	7.4	15.4
Cerebrovascular disease	6.5	14.8	6.3	6.9	12.9
Myocardial infarction	5.2	11.0	5.1	5.0	9.3
Liver disease	3.8	3.5	3.7	4.2	9.2
Heart failure	2.2	6.5	2.1	2.5	9.0
Peripheral arterial disease	1.8	4.3	1.8	1.9	3.5
RAASi use, %					
Never	64.8	30.9	64.8	67.1	57.7
Current	30.5	59.2	30.7	28.6	28.9
Former	4.7	9.9	4.6	4.4	13.4
Concomitant medication, %					
ACE inhibitors	22.5	40.9	22.7	21.3	20.0
NSAIDs	9.3	8.4	9.3	9.3	7.7
ARBs	7.9	18.4	8.0	7.1	7.8
Thiazide diuretics	7.3	16.5	7.3	6.6	8.4
Bendroflumethiazide	5.9	13.1	5.9	5.4	6.3
Indapamide	0.7	1.6	0.7	0.6	1.1
Hydrochlorothiazide	0.5	1.2	0.5	0.4	0.6
Chlorthalidone	0.2	0.4	0.1	0.2	0.2
Loop diuretics	5.9	18.5	5.7	6.9	12.6
MRAs	2.0	5.8	1.9	2.8	5.5
Antibiotics	1.6	3.0	1.5	2.2	3.3

ACE, angiotensin-converting enzyme; AF, atrial fibrillation; ARBs, angiotensin receptor blockers; BMI, body mass index; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; HiK, hyperkalemia; MRAs, mineralocorticoid receptor antagonists; NSAIDs, nonsteroidal anti-inflammatory drugs; RAASi, renin–angiotensin–aldosterone system inhibitor; SD, standard deviation.

- In the overall and CKD populations with HiK, the proportion of patients with ≥1 health care resource utilization event increased by >70% between 3 and 7 days post-HiK event for all outcomes (**Figure 1**)

Figure 1. Proportions of Patients in the Overall Population and CKD Subgroup With ≥1 Health Care Resource Utilization



CKD, chronic kidney disease.

- The mean number of health care resource utilizations was greater for patients with HiK and CKD versus those without CKD (**Table 3**). The greatest difference over time was observed for utilization of laboratory tests

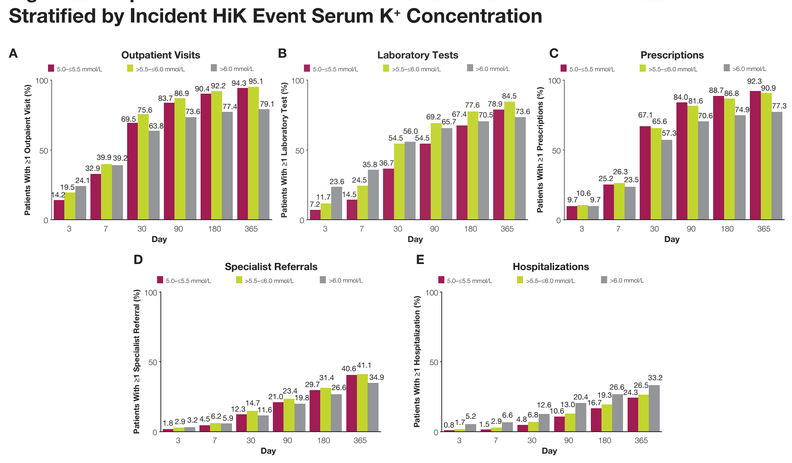
Table 3. Mean[a] Number of Health Care Resource Utilizations Over Time in the Overall Population and CKD Subgroup With HiK

	Outpatient Visits		Laboratory Tests		Prescriptions		Specialist Referrals		Hospitalizations	
Days	Overall	CKD	Overall	CKD	Overall	CKD	Overall	CKD	Overall	CKD
3	1.1	1.1	4.3	4.8	2.5	3.2	1.1	1.1	1.0	1.0
7	1.2	1.3	5.4	6.1	2.7	3.5	1.1	1.1	1.1	1.1
30	1.9	2.1	8.8	10.3	3.7	5.1	1.2	1.2	1.2	1.4
90	3.4	4.0	14.6	18.1	4.7	6.7	1.4	1.4	1.5	1.7
180	5.4	6.6	22.4	28.9	5.4	7.8	1.5	1.6	1.7	2.1
365	8.8	11.4	36.2	48.3	6.5	9.3	1.8	2.0	2.1	2.7

[a]Mean was calculated among patients who had experienced ≥1 health care resource utilization.
CKD, chronic kidney disease; HiK, hyperkalemia.

- In general, within 1 week of the incident HiK event, numerically greater proportions of patients with incident HiK of K >6.0 utilized health care resources over time versus patients with less severe HiK (**Figure 2**). One exception was the proportions of patients who filled any prescriptions through 7 days after the event; these were similar across HiK severity strata (25.2%, 26.3%, and 23.5% for K 5.0–≤5.5, K >5.5–≤6.0, and K >6.0, respectively)
- Overall, through day 365, more patients with an incident HiK event of K >5.5–≤6.0 utilized health care resources than those with an event of K 5.0–≤5.5. There were fewer proportions of patients with an incident HiK event of K >6.0 utilizing all health care resources examined, with the exception of hospitalizations at days 30 through 365 (**Figure 2**)

Figure 2. Proportions of Patients With ≥1 Health Care Resource Utilization as Stratified by Incident HiK Event Serum K^+ Concentration



CKD, chronic kidney disease.

- Despite the low proportion of patients reporting an incident HiK event of K >6.0, these patients utilized more health care resources on average than patients with an HiK event of K 5.0–≤5.5 or K >5.5–≤6.0 over time (**Table 4**)

Table 4. Mean[a] Number of Health Care Resource Utilizations Over Time as Stratified by Severity of Incident HiK Event

	Outpatient Visits			Laboratory Tests			Prescriptions			Specialist Referrals			Hospitalizations		
Days	K 5.0–≤5.5	K >5.5–≤6.0	K >6.0	K 5.0–≤5.5	K >5.5–≤6.0	K >6.0	K 5.0–≤5.5	K >5.5–≤6.0	K >6.0	K 5.0–≤5.5	K >5.5–≤6.0	K >6.0	K 5.0–≤5.5	K >5.5–≤6.0	K >6.0
3	1.1	1.1	1.1	4.0	5.6	7.5	2.5	2.5	3.0	1.1	1.1	1.2	1.0	1.0	1.1
7	1.2	1.3	1.5	5.0	7.0	9.1	2.7	2.7	3.1	1.1	1.1	1.2	1.1	1.1	1.2
30	1.9	2.1	2.4	8.5	10.5	13.4	3.7	3.7	4.3	1.2	1.3	1.3	1.2	1.3	1.8
90	3.4	3.7	4.3	14.3	16.1	21.0	4.6	4.7	5.7	1.4	1.4	1.5	1.4	1.6	2.6
180	5.3	5.6	6.7	22.2	23.4	30.9	5.4	5.5	6.7	1.5	1.6	1.7	1.7	1.9	3.8
365	8.8	9.0	10.7	36.0	36.2	46.4	6.5	6.5	7.9	1.8	1.8	2.0	2.0	2.3	5.0

[a]Mean was calculated among patients who had experienced ≥1 health care resource utilization.
CKD, chronic kidney disease; HiK, hyperkalemia.

Limitations

- Analysis was limited to available data in the linked CPRD/HES dataset and primarily captures HiK in the outpatient setting, as laboratory data are not available in HES
- The dataset may not reflect the totality of patients hospitalized for or with HiK as the HES only provides diagnosis codes (no laboratory values); clinical diagnoses were not adjudicated; and transient HiK cases may not have been captured if laboratory testing was done only during periods of normal serum K^+ levels
- The data were not adjusted for differences in baseline characteristics across subgroups
- This analysis cannot determine whether HiK is the main cause of health care use or whether management of HiK would reduce associated resource utilization

Conclusions

- A trend towards increasing utilization of health care resources was observed among patients with HiK and CKD versus those with HiK but without CKD
- Health care resource utilization appeared to depend on the severity of HiK as patients with K >6.0 utilized more health care resources over time versus patients with less severe HiK
- Because only one-quarter of patients filled prescriptions within 7 days of diagnosis, it seems that no direct treatment for HiK is used routinely in England. It is possible that the high costs associated with HiK are related to lack of a rapid, effective treatment for HiK

References

1. Kovesdy CP. *Am J Med.* 2015;128(12):1281–1287.
2. Kovesdy CP. *Nat Rev Nephrol.* 2014;10(11):653–662.
3. National Kidney Foundation. https://www.kidney.org/content/clinical-update-hyperkalemia-chronic-risk-ckd-patients-and-potential-barrier-recommended-ckd. Accessed May 8, 2017.
4. Herrett E, et al. *Int J Epidemiol.* 2015;44(3):827–836.
5. Hospital Episode Statistics. http://www.hscic.gov.uk/hes. Accessed April 6, 2017.

Acknowledgements

This analysis of the UK CPRD/HES linked dataset was supported by AstraZeneca. Jessica Deckman, PhD, CMPP, of inScience Communications, Springer Healthcare (Philadelphia, PA, USA), provided medical writing support funded by AstraZeneca. The authors acknowledge valuable input received from Robin Mukherjee of AstraZeneca.

Supported by: AstraZeneca

Presented at the European Renal Association–European Dialysis and Transplant Association (ERA–EDTA) 54th Annual Congress, June 3–6, 2017, Madrid, Spain.