THE BURDEN OF HYPERKALEMIA IN GERMANY – A CLAIMS DATABASE ANALYSIS

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BACKGROUND

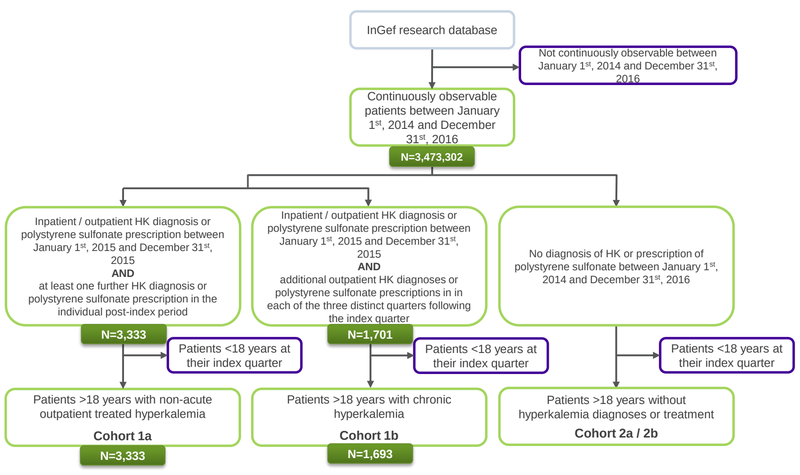
- Hyperkalemia (HK) refers to an increased serum potassium concentration in the blood, due to the disabled excretion of potassium in the kidney. [1,2]
- Hyperkalemia can lead to muscle weakness. Furthermore, critical effects on cardiac conduction, arrhythmias or sudden death are also possible. [3]
- It commonly occurs in patients with chronic kidney disease (CKD), heart failure (HF) or diabetes mellitus (DM). HK can be amplified by medications, e.g. inhibitors of the renin-angiotensin-aldosterone system (RAAS).
- There are deviating treatment options for HK, which depend on if HK is considered as acute or chronic. Acute – often live threatening - HK is associated with serious adverse effects and is mostly treated inpatient. Chronic HK creates the necessity of continuous treatment and monitoring and in turn is associated with outpatient treatment.
- The aims of this study were to assess health-relevant outcomes of non-acute outpatient treated HK patients and in particular chronic HK patients and to compare healthcare costs as well as dialysis initiation between HK patients and non-HK patients. Additionally, specified underlying comorbidities and treatment patterns of HK patients were assessed.

METHODS

- A retrospective study design was applied using claims from the "Institut für angewandte Gesundheitsforschung, Berlin" (InGef) research database, which includes approximately 4 million covered lives structured to represent the German population in terms of age and gender (structure of age and gender according to the Federal Office of Statistics (DESTATIS)).
- For this analysis, data from January 1st, 2014 through December 31st, 2016 was used. The enrollment period for the patient selection spanned from January 1st, 2015 through December 31st, 2015, to allow for an individual pre-index period of 4 quarters (Q1/2014 to Q3/2015) as well as an individual post-index period including the index quarter (defined as the first observable HK diagnosis or prescription of polystyrene sulfonate in 2015) and 3 consecutive quarters (Q1/2015 to Q3/2016).
- Two cohorts of HK patients, those with non-acute outpatient treated HK (cohort 1a) and with chronic HK (cohort 1b), were identified in the database based on ICD-10-GM (International Statistical Classification of Diseases and Related Health Problems, 10th revision, German Modification) diagnoses codes of E87.5 "Hyperkalemia" or prescriptions of polystyrene sulfonate (Anatomical-therapeutic-chemical classification system (ATC) code: V03AE01), which indicates necessary HK treatment. Due to the strongly deviating treatment options of acute life-threatening and chronic hyperkalemia, solely inpatient treated hyperkalemia considered as life-threatening, was excluded from the analysis.
- Assignment of patients to cohort 1a and 1b is displayed in **Figure 1**.
- Each identified hyperkalemia patient of cohort 1a and cohort 1b was matched 1:1 to a patient without hyperkalemia.
- Patient characteristics of both HK cohorts were assessed by including demographics in the index quarter. Specified underlying comorbidities, such as CKD, HF and diabetes mellitus type 2 (T2DM) as well as the updated Charlson Comorbidity Index (CCI) were assessed in the pre-index period.
- All-cause and HK-related hospitalizations were analyzed in the 3 quarters following the index quarter in terms of number of patients with hospitalizations and length of inpatient stays. The index quarter was not taken into account as the number of hospitalizations in the index quarter was used as matching parameter.
- Concomitant treatment was identified by ATC codes. Additionally, prescriptions were analyzed in terms of mean number of prescriptions for SPS/CPS.
- Healthcare costs in the post-index period were assessed in total and stratified by different healthcare sectors. The cost assessment was conducted for all HK patients of cohort 1a and 1b with the respective comparison groups.
- Time to dialysis initiation was assessed for all HK patients suffering from CKD (all stages) who did not have dialysis in the pre-index period and was analyzed using the Kaplan-Meier method.

Figure 1. Patient flowchart

Steps performed to identify HK patients



RESULTS

Descriptive Analysis Results

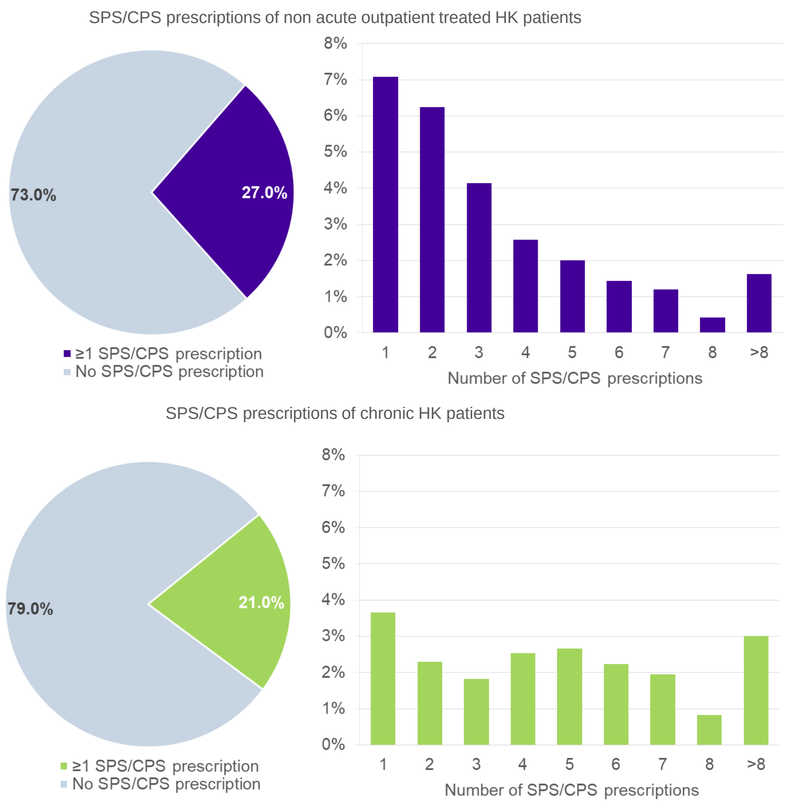
- In total, 3,333 patients with non-acute outpatient treated HK and 1,693 chronic HK patients who were at least 18 years of age were identified in the database in 2015.
- Non-acute outpatient treated HK patients (1a) were 70.6 years old on average (SD: 13.3, range: 18-102) and chronic HK patients (1b) were 71.2 years old on average (SD: 12.7, range: 21-101). 42.6% of the non-acute HK patients and 43.9% of the chronic HK patients were female.
- CKD had the highest prevalence of the specified underlying comorbidities with 52.1% among outpatient treated (1a) and 50.8% among chronic HK patients (1b). When considering patients with CKD, most patients in cohort 1a (19.3%) and cohort 1b (18.7%) had CKD stage 5. Of these patients with CKD stage 5, 81,7% (1a) and 80,1% (1b) received dialysis treatment, indicated by the respective dialysis treatment coding.
- HF had the lowest prevalence of the specified underlying comorbidities with 20.4% in the outpatient HK cohort (1a) and 18.9% in the chronic HK cohort (1b), respectively.
- Most patients in both cohorts presented with CKD and T2DM and no HF (17.5% and 17.4%) when considering different combinations of distinct comorbidities (see **Table 1**).

Table 1. Specified underlying comorbidities

Disease (ICD-10-GM code)	Non-acute outpatient treated HK patients (cohort 1a)		Chronic HK patients (cohort 1b)	
	N=3,333	%	N=1,693	%
None of the specified underlying comorbidities	943	28.3	483	28.5
CKD				
CKD total (all stages N18.1-N18.5)	1,737	52.1	860	50.8
CKD stage 1+2 (N18.1+N18.2)	114	3.4	55	3.2
CKD stage 3 (N18.3)	534	16.0	252	14.9
CKD stage 4 (N18.4)	443	13.3	236	13.9
CKD stage 5 w/o dialysis (N18.5)	118	3.5	63	3.7
CKD stage 5 with dialysis (N18.5 plus OPS/EBM code)	528	15.8	254	15.0
HF				
Heart failure total (all NYHA classes I50.11-I50.19)	681	20.4	320	18.9
Heart failure NYHA class I (I50.11)	40	1.2	21	1.2
Heart failure NYHA class II (I50.12)	159	4.8	82	4.8
Heart failure NYHA class III (I50.13)	206	6.1	104	6.1
Heart failure NYHA class IV (I50.14)	199	6.0	83	4.9
Heart failure, unspecified (I50.19)	77	2.3	30	1.8
T2DM				
Diabetes mellitus, type 2 (E11.-)	1,481	44.4	753	44.5
Distinct comorbidity groups				
CKD only				
CKD stage 1+2 (N18.1+N18.2)	39	1.2	24	1.4
CKD stage 3 (N18.3)	160	4.8	79	4.7
CKD stage 4 (N18.4)	159	4.8	88	5.2
CKD stage 5 w/o dialysis (N18.5)	49	1.5	25	1.5
CKD stage 5 with dialysis (N18.5 plus OPS/EBM code)	233	7.0	115	6.8
HF only				
Heart failure NYHA class I (I50.11)	8	0.2	6	0.4
Heart failure NYHA class II (I50.12)	28	0.8	13	0.8
Heart failure NYHA class III (I50.13)	19	0.6	10	0.6
Heart failure NYHA class IV (I50.14)	10	0.3	5	0.3
Heart failure, unspecified (I50.19)	12	0.4	<5	NA
T2DM only				
Diabetes mellitus, type 2 (E11.-)	486	14.6	264	15.6
Combination of specified underlying comorbidities				
CKD and HF (no T2DM)	192	5.8	88	5.2
CKD and T2DM (no HF)	583	17.5	295	17.4
HF and T2DM (no CKD)	90	2.7	48	2.8
CKD and HF and T2DM	322	9.7	146	8.6

- The assessment of SPS/CPS prescriptions, indicated for the treatment of hyperkalemia, showed that 73.3% of the outpatient treated and 79.0% of the chronic HK patients did not receive specific HK related treatment. Patients who were treated with SPS/CPS had on average 3.4 prescriptions (1a) and 5.1 prescriptions (1b) (see **Figure 2**).

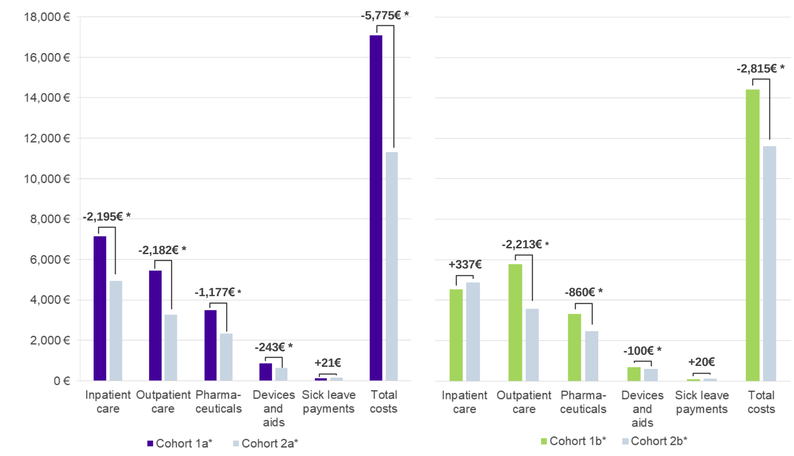
Figure 2. Patients with and without SPS/CPS prescriptions



Matching Results

- After matching the cohort of non-acute outpatient treated HK patients (1a*) to a non-HK cohort (2a*) and also matching the chronic HK patients (1b*) to a non-HK cohort (2b*), a study population of n=3,191 patients with non-acute outpatient treated HK and n=1,664 patients with chronic HK with respective control groups without HK remained for the analysis.
- After the exact matching, the aforementioned matching parameters were completely balanced with standardized differences of 0 and p-values of 1 for all factors.
- Comparing the healthcare costs for the matched cohorts 1a* and 2a* as well as 1b* and 2b*, the analysis revealed that mean total healthcare costs were significantly higher in the post-index period for patients with outpatient treated HK and chronic HK when compared to their non-HK control groups (cohorts a*: 17,076€ vs. 11,301€, p<0.001/ cohorts b*: 14,421€ vs. 11,606€, p<0.001).
- A significant difference in mean costs between cohort 1a* and 2a* was observed in the inpatient and outpatient care setting, as well as for pharmaceuticals and devices and aids with differences in the mean costs of 2,195€, 2,182€, 1,177€, and 243€, respectively (see **Figure 3**).

Figure 3. Mean healthcare costs



- The number of dialysis events were assessed in the post-index period for those individuals with CKD and no dialysis in the pre-index period for the respective cohorts. The dialysis initiation events were highest in cohort 1a* with 1,134,294 events (326,224 cohort 2a*), whereas cohort 1b* had 633,224 events (170,209 cohort 2b*).
- The proportion of patients with dialysis initiation events was over twofold higher for both cohorts 1a* and 1b* with 118 (10.5%) and 51 (8.7%) in comparison to their matched controls 62 (4.8%) and 28 (4.2%), respectively.
- However, the average time until dialysis initiation was significantly higher for individuals for both hyperkalemia cohorts in comparison to their matched counterparts (1a* mean in quarters 1.3 vs. 2a* mean in quarters 1.0; p≤0.001 and 1b* mean in quarters 1.0 vs. 2b* mean in quarters 0.8; p≤0.001) (see **Table 2**).

Table 2. Time-to-dialysis initiation event

	Number of patients with dialysis initiation events		Average length of observation time until dialysis initiation event (in quarters)				
	n	%	Mean	STD	Median	Min	Max
Patients with outpatient hyperkalemia (group 1a*)	118	10.5	1.3	1.2	1.0	0.0	3.0
Patients without hyperkalemia (group 2a*)	62	4.8	1.0	1.1	1.0	0.0	3.0
Patients with chronic hyperkalemia (group 1b*)	51	8.7	1.0	1.2	1.0	0.0	3.0
Patients without hyperkalemia (group 2b*)	28	4.2	0.8	1.0	0.0	0.0	3.0

CONCLUSIONS

- To our knowledge, this is the first study in Germany assessing the burden of hyperkalemia irrespective of the concomitant diseases. However, it should be noted that, similar to previous analyses, HK patients are multi-morbid and present with an increased prevalence of CKD, HF and diabetes.
- The disease burden of patients with outpatient treated or chronic hyperkalemia was significantly higher than in their matched controls, suggesting a necessity for treatment improvement.
- Only a minority of patients suffering from HK receive specific potassium lowering medication as CPS or SPS
- In the respective patient population, HK is a risk factor for early onset of dialysis

LIMITATIONS

- In general, claims data analyses are subject to limitations as they are primarily collected for accounting purposes, and therefore clinical parameters (e.g. severity grades, laboratory results), dosage and intake of medication, or additional information (e.g. quality of life) are not covered.

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