A Model to Predict Risk of Hyperkalemia in CKD Patients

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PUK23

BACKGROUND

- Limited published models exist to predict which patients will develop hyperkalemia (HK).
- HK is one of the major reasons that guideline-directed medications such as angiotensin-converting enzyme inhibitors (ACEis) and angiotensin-receptor blockers (ARBs) are discontinued or fail to reach guideline-recommended dosing for patients with heart failure (HF) and/or chronic kidney disease (CKD).[1,2]
- The ultimate goal of developing a predictive model for HK is to identify patients at risk for HK and better manage them so that guideline-recommended therapies are not discontinued.

OBJECTIVE

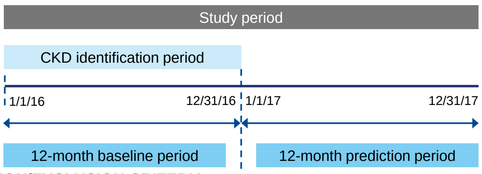
- Develop and validate a predictive model to identify patients at risk of developing HK using administrative claims data in order to facilitate appropriate care-management programs.

METHODS

STUDY DESIGN

- Retrospective study using a large administrative claims database from 1/1/16 to 12/31/17 to develop and validate a model to predict patients at risk for developing HK (**Figure 1**).
  - HK was defined by two labs >5.0 or 2 ICD HK codes or one of each or a binder Rx (patiromer/SPS).

FIGURE 1. STUDY DESIGN



INCLUSION/EXCLUSION CRITERIA

- Inclusion
  - Aetna fully insured commercial health plan and Medicare Advantage individuals with medical and pharmacy health insurance benefits for at least 24 months during the study periods.
  - Age ≥18
  - Medical/pharmacy claims and laboratory results with service dates 1/1/16 to 12/31/16 used to identify CKD population.
  - Qualifying criteria: patients with at least one estimated glomerular filtration rate value indicating CKD by the modification of diet in renal disease (MDRD) equation or one claim with ICD-9-CM/ICD-10-CM codes (585.x, N18.x) for CKD.
- Exclusion
  - Individuals with HK during the baseline period; individuals who had a dialysis procedure during the baseline period; individuals enrolled in the Aetna Compassionate Care Program and/or on hospice during the study.

METHODS: MODEL DEVELOPMENT

- Machine learning techniques
  - Multiple machine learning techniques were evaluated, including neural network, decision tree, and multivariate logistic regression.
  - Multivariate logistic regression was chosen due to similar area under the curve (AUC) performance to neural network technique.
- Variable selection
  - Demographic, CKD stage, comorbidities, drugs, labs, and healthcare resource utilization (HRU) were all included in this multivariate logistic regression model.
  - In univariate logistic regression models, variables not associated with HK (P>0.05) were excluded from further analyses.
- Multivariate logistic regression
  - Logistic regression (stepwise, α=0.05 of entry and exit)
  - Multicollinearity was checked using Pearson correlation coefficient.
  - Two-way interaction term was checked, such as optimal dose and proportion of days covered (PDC) ≥0.8
  - Goodness-of-fit tests: deviance, Hosmer-Lemeshow, and log likelihood
- Data partition
  - Training, validation, test
- Performance measures
  - AUC, calibration plots, gain chart, lift chart

RESULTS AND DISCUSSION

TABLE 1. BASELINE PATIENT CHARACTERISTICS AND COMORBIDITIES

Characteristics	Overall N=435,512	Patients with HK n=6235	Patients without HK n=429,277
Mean age, years (SD)	61.25 (16.3)	69.32 (11.8)	61.13 (16.3)
Male, n (%)	186,261 (42.8)	3281 (52.6)	182,980 (42.6)
Geographic region, n (%)			
Midwest	77,548 (17.8)	853 (13.7)	76,695 (17.9)
Northeast	132,504 (30.4)	1703 (27.3)	130,801 (30.5)
South	185,599 (42.6)	3302 (53.0)	182,297 (42.5)
West	39,613 (9.1)	377 (6.1)	39,236 (9.2)
Insurance type, n (%)			
Commercial	199,155 (45.7)	1293 (20.7)	197,862 (46.1)
Medicare Advantage	236,357 (54.3)	4942 (79.3)	231,415 (53.9)
Retrospective ERG risk scores			
Mean (SD)	3.44 (3.7)	5.05 (4.5)	3.41 (3.7)
Comorbidities, n (%)			
Hyperlipidemia	276,289 (63.4)	5365 (86.0)	270,917 (63.1)
Hypertension	278,336 (63.9)	5270 (84.5)	273,063 (63.6)
Diabetes	110,881 (25.5)	3139 (50.4)	109,294 (25.5)
Obesity	89,324 (20.5)	1708 (27.4)	87,615 (20.4)
Chronic heart failure	40,067 (9.2)	1327 (21.3)	38,764 (9.0)

ERG, episode risk group.

TABLE 2. BASELINE MEDICATIONS

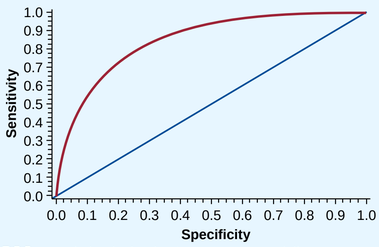
Medications, n (%)	Overall N=435,512	Patients with HK n=6235	Patients without HK n=429,277
RAASis			
MRAs	10,339 (2.4)	281 (4.5)	10,058 (2.3)
ACEis	108,269 (24.9)	2532 (40.6)	105,737 (24.6)
ARBs	83,325 (19.1)	1536 (24.6)	81,789 (19.1)
Other RAASis	528 (0.1)	19 (0.3)	509 (0.1)
NSAIDs	90,124 (20.7)	1335 (21.4)	88,789 (20.7)
Calcineurin inhibitors	917 (0.2)	48 (0.8)	869 (0.2)
Beta-blockers	98,485 (22.6)	2058 (33.0)	96,427 (22.5)

MRA, mineralocorticoid receptor antagonist; NSAID, non-steroidal anti-inflammatory drug; RAASi, renin-angiotensin-aldosterone system inhibitor.

TABLE 3. BASELINE TOTAL MEAN COSTS PER PATIENT: HK OBSERVED VS NORMOKALEMIA COHORTS (2016)

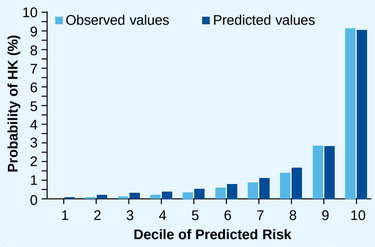
Resource costs, $ (mean SD)	Overall N=435,512	Patients with HK n=6235	Patients without HK n=429,277
Medical costs	7673 (19,314)	9868 (23,493)	7641 (19,246)
Pharmacy costs	3063 (10,250)	4396 (11,221)	3044 (10,235)
Total allowed costs	10,736 (22,792)	14,265 (26,938)	10,685 (22,723)

FIGURE 2. MODEL VALIDATION IN TEST DATASET: RECEIVER OPERATING CURVE (ROC)



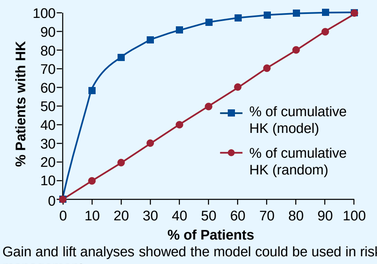
ROC curve in the test data showed good predictive accuracy (AUC=0.836).

FIGURE 3. MODEL VALIDATION: CALIBRATION PLOT



Calibration plot showed the predicted and observed HK rates were very consistent in each decile of patients in the test dataset, and observed good calibration.

FIGURE 4. MODEL VALIDATION: GAIN CHART



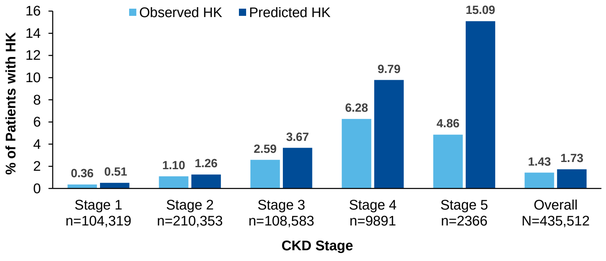
Gain and lift analyses showed the model could be used in risk management.

TABLE 4. PATIENT CHARACTERISTIC PREDICTORS OF HK

Patient characteristics	Adjusted odds ratios (95% CI)
CKD stage 5 vs 1	11.6 (7.9–17.1)
Potassium, per 0.1 mmol/L higher	8.6 (7.9–9.4)
CKD stage 4 vs 1	7.5 (6.0–9.3)
Calcineurin inhibitors use	4.4 (3.0–7.0)
CKD stage 3 vs 1	3.3 (2.8–4.0)
CKD stage 2 vs 1	1.7 (1.4–2.0)
South vs Midwest	1.6 (1.4–1.8)
Diabetes	1.5 (1.4–1.6)
Hyperlipidemia	1.5 (1.3–1.7)
Osteoporosis	1.3 (1.1–1.5)
MRA use	1.3 (1.0–1.5)
ACEi use	1.3 (1.2–1.4)
Peripheral artery disease	1.2 (1.1–1.3)
Cancer	1.2 (1.0–1.3)
COPD	1.1 (1.0–1.2)
Number of comorbid conditions	1.1 (1.1–1.0)

COPD, chronic obstructive pulmonary disease.

FIGURE 5. HK OBSERVED VS PREDICTED FROM THE MODEL



- In a study population of 435,512, the model predicted 1.73% and the actual observed HK incidence was 1.43% (6235). HK prevalence prior to exclusion of previous HK and dialysis was 6.25% (baseline [2016]) and 6.35% (predicted [2017]).

LIMITATIONS

- This study is subject to all limitations inherent to a claims-based analysis (missing data, incorrect values, coding errors).
- Results may not be generalizable to populations younger than 18 years of age or populations with a different mix of comorbidities.
- No causal inference can be made from these data.

CONCLUSIONS

- This model observed good predictive accuracy with ROC (AUC=0.836) and good calibration.
- HK was predicted in 1.73% of the study population and actually observed in 1.43%.
- Baseline total mean costs per patient were higher for the HK cohort vs the no HK cohort.
- Increasing CKD severity and incremental baseline potassium level were the strongest predictors of HK.
- Further validation in other populations is needed before the model is ready to use in clinical practice.
- Using only claims data, patients at high risk of HK could be identified up to 1 year in advance.
- The findings support the use of predictive models to better target intervention.

REFERENCES

1. Yildirim T, et al. *Ren Fail*. 2012;34:1095-1099.
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