Acute Kidney Injury (AKI)
Phenotype Algorithm Pseudo Code

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2022/11/29 (V1)

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Updates:
Initial commit

I. Background and Significance:

- **Acute kidney injury (AKI)** is characterized by a rapid decline in kidney function, but causes of AKI are highly heterogeneous. These can be divided into three general categories: pre-renal causes due to reduced blood flow to the kidneys (e.g., shock or volume depletion), intra-renal causes due to tissue injury (e.g., toxic drug exposure), and post-renal causes due to urinary tract obstruction. While the detection of distal obstruction is typically achieved by sonographic imaging, the distinction between pre-renal and intra-renal causes can be difficult and is frequently based on the response to intravenous fluids. AKI can lead to serious complications, including electrolyte imbalances, fluid overload, and even death. Early detection and proper management of AKI are important for preventing further kidney damage and improving clinical outcomes. This provides strong motivation for the design and implementation of electronic algorithms for the detection, staging, and subtyping of AKI.
- **Our AKI algorithm** follows the KDIGO (Kidney Disease: Improving Global Outcomes) classification of AKI based on temporal changes in serum creatinine levels and urine output[1]. Despite well-known limitations of serum creatinine, such as poor sensitivity and delayed rise after injury[2,3], the KDIGO AKI definitions provide a standardized framework to diagnose AKI and guide treatment decisions in hospitalized patients. While serum creatinine is available in electronic health records (EHR), urine output is not recorded for most patients outside the intensive care units (ICUs). Therefore, a simplified KDIGO stage definition without urine output criteria is typically considered when implementing electronic AKI detection algorithms[4,5].
- **Staging and subtyping AKI**
    - AKI severity: AKIN (Acute Kidney Injury Network) stage is used to evaluate the severity of the acute rise in serum creatinine within 48 hours.
    - AKI subtype: Considering that the KDIGO criteria do not differentiate intrinsic AKI from pre-renal causes that are often reversible. This can, however, be accounted for by electronic subtyping of AKI that distinguishes reversible AKI from a sustained form of AKI based on the improvement or further loss of renal function over the period of 24-48 hours after hospital admission. The subtype of

sustained AKI has previously been reported to be associated with worse clinical outcomes[6,7].

In this study, we designed and validated a new electronic phenotype for detecting, staging, and characterizing of AKI.

II. Development:

- AKI, no AKI, and AKI Stages and AKI subtypes are developed using structured EHR data using domain knowledge and standards
- Validation is performed against expert opinion on curated dataset

III. Algorithm Definitions (flowchart Figure 1)

1. AKI unknown
    - No diagnosis and procedure of kidney transplant or dialysis.
    - No baseline SCr or no available SCr during the potential AKI presentation time window
2. No AKI (No AKI on the flowchart, AKI control)?
    - No diagnosis and procedure of kidney transplant or dialysis.
    - Baseline SCr is available.
    - All daily kidney excretory function during the potential AKI presentation time window is normal.
3. AKI
    - No diagnosis and procedure of kidney transplant or dialysis.
    - Baseline SCr is available.
    - At least one daily kidney excretory function during the potential AKI presentation time window is abnormal.
4. Staging and subtyping AKI

4.1 AKI Blocks: consecutive days with at least one SCr higher than 50% baseline are defined as one AKI block. There may have one or more AKI blocks in the potential AKI presentation time window. There are at least two days without SCr between AKI blocks.

4.2 AKI Recurrence: After defining the first AKI event, the algorithm also assesses the AKI recurrence and counts the number of AKI occurrences during a given hospitalization. Recurrence of AKI was defined as another increase in SCr 1.5-times over baseline more than two days after resolution of the previous AKI event.

4.3 Phenotyping AKI blocks: the severity and subtype are determined for each AKI occurrence/block.

4.3.1 AKI severity was staged using the AKIN classification system (stages 1-3)[4,5] using the ratio of maximum SCr to baseline SCr.

- AKIN Stage 1: ≥ 1.5- to 2-fold increase
- AKIN Stage 2: 2- to 3-fold increase
- AKIN Stage 3: > 3-fold increase

4.3.2 AKI subtype was defined based on AKI duration by adopting the definitions by Stevens et al.[6].

- Transient AKI (tAKI, lasting less than 48 hours)
- Sustained AKI (sAKI, lasting more than 48 hours)

4.4 The first AKI block's AKI severity and AKI subtype are used to characterizing AKI overall.

IV. AKI Implementation

1. AKI algorithm related variables (coding see Table 1 and file AKIalgorithm_V1_coding.txt)

1.1 Patient diagnosis: kidney transplant, dialysis.
1.2 Patient procedure: kidney transplant, dialysis
1.3 Patient lab test: serum creatinine

2. Baseline SCr calculation

- 1st Line: Median SCr in 7-365 days before the presentation
- 2nd Line: Minimum SCr between 0-7 days before the presentation
- 2rd Line: Minimum SCr from the presentation to the SCr under consideration

3. AKI and AKI characterization implementation (see AKIalgorithm_V1_queryTemplate_omop.sql)

The query implementation is based on OMOP V5 for identifying AKI for the emergency visit. This implementation can not only be customized to another clinical database with customization on database schema and vocabulary mapping; but also be customized to different event related AKI.

3. The algorithm output

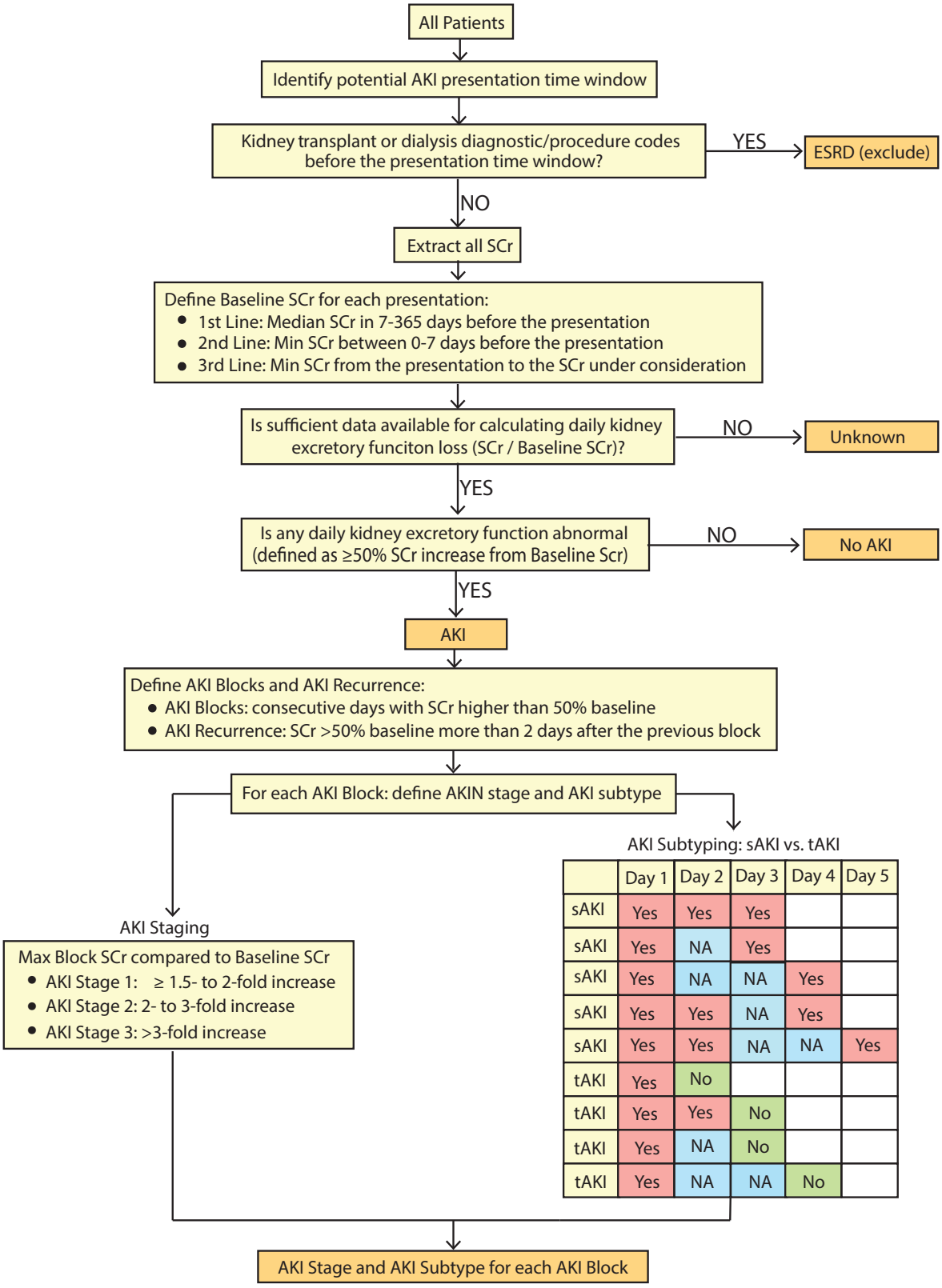
AKI presentation time window, AKI (Yes/No), ESRD (Yes, No)
For each AKI presentation time window, AKIN and AKI subtype for all identified AKI blocks and overall.

VI. Evaluation

MIMIC-III evaluation set is provided.

VII. Publication

Under review.



	Day 1	Day 2	Day 3	Day 4	Day 5
sAKI	Yes	Yes	Yes		
sAKI	Yes	NA	Yes		
sAKI	Yes	NA	NA	Yes	
sAKI	Yes	Yes	NA	Yes	
sAKI	Yes	Yes	NA	NA	Yes
tAKI	Yes	No			
tAKI	Yes	Yes	No		
tAKI	Yes	NA	No		
tAKI	Yes	NA	NA	No	

Figure 1. Acute Kidney Injury (AKI) Electronic Phenotype Algorithm Summary. This rule-based algorithm first pre-filters patient records based on pre-existing ESRD and available SCr

data. Next, “Baseline SCr” is defined using ordered priority rules based on available retrospective EHR kidney function data. Once the first instance of SCr >50% baseline is detected, an “AKI Block” is defined as a number of consecutive days with SCr >50% baseline; the block is terminated on the day that SCr returns below 50% baseline. Recurrent AKI is defined by a subsequent elevation of SCr >50% baseline more than 2 days after the previous block. For each block, AKI stage and subtype are defined. AKIN stage is defined based on the maximum SCr per block. AKI subtype is defined based on the rules depicted in the table, with “YES” (red) indicating a day with SCr exceeding 50% baseline, “NA” (blue) indicating a day with missing kidney function data, and “No” indicating a day with SCr below 50% baseline. We use average SCr for the days with multiple SCr measurements. The algorithm’s outputs are depicted in orange. The algorithm’s outputs are depicted in orange. The staging and subtyping for only block 1 (first AKI event after admission) was used for representing the AKI stage and subtype for the potential AKI presentation window.

Table 1 Codes used in the algorithm*

Data Element	Coding Variable Name (used in AKIalgorithm_V1_coding.txt)
Dialysis diagnosis	dx.CkdEsrd_Dialysis.icd10, dx.CkdEsrd_Dialysis.icd9
Dialysis procedure	proc.CkdEsrd_Dialysis.cpt4, proc.CkdEsrd_Dialysis.icd10, proc.CkdEsrd_Dialysis.icd9
Kidney transplant diagnosis	dx.CkdEsrd_kidneyTransplant.icd10, dx.CkdEsrd_kidneyTransplant.icd9
Kidney transplant procedure	proc.CkdEsrd_kidneyTransplant.cpt4, proc.CkdEsrd_kidneyTransplant.icd10, proc.CkdEsrd_kidneyTransplant.icd9
Serum creatinine test	lab.serumCreatinine.loinc

* All codes’ corresponding OMOP standard concept_id are provided

Reference

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3. Nickolas, T.L.*, et al.* Diagnostic and prognostic stratification in the emergency department using urinary biomarkers of nephron damage: a multicenter prospective cohort study. *J Am Coll Cardiol* **59**, 246-255 (2012).
4. Bellomo, R.*, et al.* Acute renal failure – definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. *Critical Care* **8**, R204 (2004).
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