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Comparison of Static and Dynamic Baseline Creatinine Surrogates for Defining Acute Kidney Injury

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Abstract

Background: "Dynamic" baseline serum creatinine (sCr), based on a rolling 48-hour window and a static baseline sCr (previous outpatient sCr) were used to define Acute Kidney Injury (AKI).

Methods: Retrospective cohort study of adult admissions to University of Alabama (UAB) Health System hospitals for years 2016 – 2018. Included admissions had >1 and <180-day length of stay, >2 inpatient sCr measurements, and an averaged estimated glomerular filtration rate >15 mL/min/1.73 m^2. The final cohort of 62,380 patients included 100,570 admissions, 3,509 inpatient-deaths and 1,916 admissions with inpatient dialysis. AKI was defined by Kidney Disease Improving Global Outcomes (KDIGO) criteria and a static or dynamic baseline sCr. Discrimination was evaluated with area under receiver-operator curves (AUC), logistic regression, and net reclassification improvement (NRI).

Results: Pre-admission outpatient "static" sCr values were available for 43,433 admissions. The lowest sCr value during a rolling 48-hour window before each inpatient sCr defined a "dynamic" baseline sCr. Using point-wise comparisons, the dynamic baseline sCr performed better than static baseline sCr for inpatient mortality (AUC (0.819 versus 0.741; P<0.001), and NRI ≥ 0.306 (P<0.001)) and inpatient dialysis (AUC (0.903 versus 0.864; P<0.001), and NRI ≥ 0.317 (P<0.001)).

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Author Contributions

All authors contributed to aspects of the study design, analysis and writing of the manuscript. DGW generated the Stata code for analysis and graphical representation. Ayme Miles generated the SQL data extraction files. No one else participated in the analyses, drafting or revision of this manuscript. The authors certify that the results presented in this paper have not been published previously in whole or part, except in abstract format.

Statement of Ethics

This study was approved by the UAB Institutional Review Board (IRB-300000383). The requirement for informed consent was waived due to the use of de-identified data.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Conclusions: The dynamic Baseline sCr is available without reference to pre-admission sCr values, and avoids confounding associated with missing outpatient sCr values. AKI defined with the dynamic baseline sCr significantly improved discrimination of risk for inpatient mortality and dialysis compared to static baseline sCr.

Keywords

serum creatinine; creatinine trajectory; baseline serum creatinine; KDIGO AKI definition

INTRODUCTION

Increases in serum creatinine (sCr) above a pre-specified baseline sCr value is a major criterion for defining acute kidney injury (AKI) according to the Kidney Disease Improving Global Outcomes (KDIGO) criteria [1]. A previous ambulatory sCr value is often used as the baseline sCr surrogate [2-4], but can require imputation of missing values, and was not endorsed in the recent update of the KDIGO AKI Controversies Conference [5]. The minimum sCr value within a rolling 48-hour window before each inpatient sCr value has recently been used as a dynamic baseline sCr surrogate [6, 1, 7, 8], but has not been compared to the previous ambulatory sCr for defining AKI, and risk of associated outcome events.

We hypothesized that a “dynamic” baseline sCr would outperform the static baseline sCr surrogate for assessing the risk associated with AKI for inpatient mortality and provision of inpatient dialysis. Herein, we examined all adult admissions to two hospitals in the University of Alabama (UAB) Health System. Our objectives were to describe the sCr trajectory for each admission; and compare the performance of a dynamic baseline sCr to a static baseline sCr surrogate for defining AKI.

METHODS

Study Setting and Design

The UAB Health System includes UAB Hospital (UABH), Highlands Hospital, and outpatient clinics in and around Birmingham, AL. UABH is a level 1 Trauma Center, with 1,047 inpatient and 206 intensive care unit beds. Highlands Hospital has 110 Inpatient beds (including 12 intensive care unit beds), and is located 1.5 miles from UABH. Both share a single provider number, common laboratory facilities, common coding and billing systems, and professional staff credentialed by the UAB Health System. This study is a retrospective cohort study of all adult admissions to both hospitals during calendar years 2016 – 2018,

Data Collection

Structured Query Language extractions from the electronic healthcare records included demographic data, a de-identified (“dummy”) medical record number, admission and discharge times, admission source, vital status at discharge, and all inpatient and outpatient sCr values (excluding any reported values <0.3 mg/dL) with service location and phlebotomy date-time-stamps. Discharge diagnoses were obtained from International Classification of Diseases, Tenth Revision (ICD-10), and ICD-10 Procedure codes.

Provision of inpatient dialysis was ascertained from ICD-10 Procedure codes, and clinical logs describing inpatient hemodialysis, peritoneal and continuous kidney replacement therapy events during individual admissions.

Cohort Exclusion Criteria

The initial cohort contained 269,601 admissions (139,864 adult patients) with 4,695 inpatient deaths (3.4%) (Figure 1). Admissions were excluded with <3 sCr values (162,382 admissions, 75,008 patients, 684 inpatient deaths (1.1%)). Prolonged admissions (length of stay >180 days) and length of stay <1 day were also excluded (152 admissions, 45 patients, 31 inpatient deaths (69%)). Admissions with average estimated glomerular filtration rate (eGFR)[9] <15 ml/min/1.73 m^2 based on all reported sCr values for that admission were also excluded (6,301 admissions, 2,341 patients, 358 inpatient deaths (15%)).

Previous outpatient sCr values, defined as the most recent sCr obtained >7 days and ≤365 days before the first sCr for any given admission, were available for 43% of the admissions. Additional qualifying admissions for patients with multiple admissions during the 3-year ascertainment period were included. The final cohort with qualifying admissions (Figure 1) included 62,380 patients with 100,570 admissions, and 3,509 inpatient deaths (5.6%). The final cohort from UABH included 53,294 patients with 84,025 admissions, and 3,366 inpatient deaths (6.2%).

Definitions

Primary Exposure—AKI defined by different baseline sCr surrogates.

Primary Outcomes—The primary outcomes were vital status at discharge for each admission, and provision of kidney replacement therapy during that admission.

Other Definitions

sCr trajectories were defined with line graphs that connected all sCr values with elapsed hours after admission for a every admission. AKI was defined for each admission using the KDIGO consensus criteria, with an increase of sCr ≥ 0.3 mg/dL above the baseline sCr within 48 hours, or ≥ 1.5-fold increase in sCr within 7 days for each inpatient sCr value [1], as long as the absolute increase in sCr was >0.3 mg/dL. An AKI event was defined when an individual sCr value met the KDIGO AKI criteria. Because 65% of the patients remained outside the intensive care unit without reliable urine output data, only sCr was used to define AKI [10]. Kidney replacement therapy, including intermittent hemodialysis, peritoneal dialysis and continuous kidney replacement therapy was defined with ICD-10 procedure coding, as well as the daily clinical event logs for each admission in the electronic data warehouse.

AKI categories, based on the timing of the maximal and minimal sCr values during a single admission [11, 12], were used to organize the data for presentation. This approach is similar to the AKI phenotypes (Stable, Improving, Worsening) recent described based with time series analyses [13]. The No-AKI group included admissions with absolute differences between maximal and minimal sCr values <0.3 mg/dL, and no AKI events. The maximal sCr

value occurred before the minimal sCr value, and exceeding the minimal sCr value by ≥0.3 mg/dL for Resolving AKI. In-hospital AKI [10] was defined by sCr trajectories where the maximal sCr occurred after the minimal sCr, and exceeded the minimal sCr value by ≥0.3 mg/dL.

Statistical Analyses

Mean values are presented as ±1 standard deviation (SD), and medians with 25th and 75th-centiles. Baseline characteristics were compared using Chi-squared tests for proportions, multiple comparisons of continuous variables using the Bonferroni correction (Stata routine .**pwmean**), and Wilcoxon rank-sum tests for median values. Odds ratios and incidence rate ratios were derived from Poisson regression analyses, adjusted for binary covariates, including: ± median Age; sex; ethnicity (0, non-black; 1, black); mean eGFR [9] <60 mL/min/1.73 m^2; location (0 Highlands Hospital, 1 UABH); Admission Source (0 community, 1 transfers from another health care facility), and median Charlson Comorbidity Index. A Stata routine (.**roccomp**) was used to generate receiver operator curves and areas under these curves (AUC). Net reclassification improvement (NRI) was carried out as previously described [14, 15]. Pairwise comparisons were made between static and dynamic baseline sCr using the subset of admissions with previous ambulatory sCr values. Receiver-Operator Curves (ROC) were generated with Stata routine .**lroc**. Data analyses and graphics were done with Stata version 16 (Stata Corp, College Station, TX).

RESULTS

Characteristics of the Study Population

Clinical characteristics are shown in Table 1. AKI events were not observed during 38,736 admissions (39%). Resolving AKI was observed during 42,458 admissions (43%), and In-hospital AKI developed during 19,376 admissions (19%). Compared to admissions without AKI, admissions with Resolving AKI and In-hospital AKI included older patients (58 and 59 years versus 54 years, P<0.001); more male patients (56% and 53% versus 46%, P<0.001); and more Black patients (38% and 40% versus 34%, P<0.001).

Resolving AKI develops before admission, and is often described as Community-Acquired AKI. Some of these patients were transferred from other health care facilities, rather than being admitted from the community, and had developed AKI at transfer [11]. Transferred patients accounted for 16% admissions without AKI, 18% of admissions with Resolving AKI, and 21% of admissions with In-hospital AKI.

Compared to No-AKI, admissions with Resolving and In-hospital AKI had lower averaged inpatient eGFR [9] values (76 and 68, versus 100 mL/min/1.73 m^2, P<0.001), higher median Charlson co-morbidity indices (3.0 and 3.0, versus 2.0, P<0.001), and more often received inpatient kidney replacement therapy (2.7% and 3.1%, versus 0.1%, P<0.001). Admissions with Resolving or In-hospital AKI more often required intensive care unit care (37% and 37%, versus 16%, P<0.001), and had more days in an intensive care unit (1.5 days and 1.5 days versus 0.4 days, P<0.001), and longer length of stay (8.7 days and 10 days versus 4.9 days, P<0.001).

Inpatient sCr Values

Admissions with Resolving and In-hospital AKI had more inpatient sCr measurements (7 and 8 values versus 4 values for No-AKI, $P<0.001$); and higher previous outpatient sCr values than admissions without AKI (1.3 and 1.3 mg/dL versus 0.9 mg/dL for No-AKI, $P<0.001$).

The first sCr was significantly higher for Resolving and In-hospital AKI than No-AKI (1.5 and 1.2 mg/dL versus 0.8 mg/dL, $P<0.001$). The last inpatient sCr was higher for Resolving AKI and In-hospital AKI than No-AKI (1.0 and 1.5 versus 0.8 mg/dL, P<0.001). The last inpatient sCr was significantly lower for Resolving AKI (1.0 mg/dL) than In-hospital AKI (1.5 mg/dL, P<0.001), showing better recovery in the Resolving AKI group than the In-hospital AKI group [16, 8, 17]. The median dynamic baseline sCr values [6, 1, 18, 7] were higher for Resolving and In-hospital AKI than the No AKI group (1.0 and 1.0 mg/dL versus 0.8 mg/dL, $P<0.001$).

Outcome Measures

The provision of inpatient dialysis was significantly higher during admissions with Resolving AKI and In-hospital AKI (3.0% and 3.3% versus 0.1% for No-AKI, P<0.001) Table 2. The incidence rate ratios for inpatient dialysis were significantly greater for Resolving AKI (8.61 (95% CI: 3.82 – 8.42)) than Inpatient AKI (6.83 (95% CI: 3.2.70 – 6.02) $P<0.001$).

Inpatient death rates were significantly increased for Resolving AKI and In-hospital AKI (3.4% and 8.6% versus 1.1% for No-AKI, P<0.001); with corresponding increases in the unadjusted inpatient mortality rates (1.40 and 3.07 versus 0.80 deaths per patient-year for No-AKI, $P<0.001$). The incidence rate ratios for inpatient mortality were significantly greater for Inpatient AKI (1.82 (95% CI: 1.62 – 2.04)) than Resolving AKI (0.93 (95% CI: 0.83 – 1.05) $P<0.001$), while the incidence rate ratio for Resolving AKI was the same as No-AKI (Table 2).

sCr Trajectories and AKI Phenotypes

Examples of sCr trajectories for two individual admissions are shown in Figure 2. Resolving AKI had AKI events defined with the static (Figure 2A), but not the dynamic baseline sCr (Figure 2B). In-hospital AKI [10] is shown in Figure 2C, and D. The previous outpatient sCr was 0.5 mg/dL for this particular admission (horizontal dashed line), and AKI (open circles) was defined by sCr values that exceeded the static baseline sCr by 0.3 mg/dL (Figure 2C). Figure 2D illustrates AKI events (open circles) defined by sCr values that exceeded the dynamic baseline sCr (dashed line) by 0.3 mg/dL.

AUC and NRI Analysis Comparing AKI Defined with Static and Dynamic Baseline sCr

Using binary covariates, multi-variable adjusted logistic regression analyses were used to assess the association between AKI and hospital mortality (Table 3), using the most recent outpatient sCr to define AKI for 43,433 admissions (Odds Ratio = 1.64; AUC = 0.741), and the dynamic baseline sCr to define AKI for 100,570 admissions (Odds Ratio = 5.14; AUC = 0.818).

Using the same group of 43,433 admissions for a pairwise comparison, and the previous outpatient sCr as the baseline surrogate to define AKI, the Odds Ratio were significantly greater for AKI defined with the dynamic inpatient baseline sCr, with Odds Ratio (6.57 versus 1.64), and AUC (0.819 versus 0.741). In addition, the NRI was significantly increased (0.306, P<0.001), favoring the dynamic baseline sCr over the previous outpatient sCr for capturing clinically significant changes in sCr that associate with inpatient mortality (Table 3).

Similar results were found when the provision of inpatient dialysis was used as the end-point: The Odds Ratio (7.16 versus 1.27), and AUC (0.770 versus 0.695) were significantly greater using the dynamic baseline compared to the previous outpatient sCr (P<0.001) in the paired comparison of 43,433 admissions. In addition, the NRI was significantly increased (0.317, P<0.001), favoring the dynamic baseline sCr over the previous outpatient sCr for capturing clinically significant changes in sCr that associate with inpatient dialysis (Table 3). The ROC curves for these analyses are presented in Figure 3.

Admission Source as a Source of Residual Confounding

Clinical characteristics and outcomes stratified by admission source and availability of previous outpatient sCr values are shown in Table 4. There were 39,962 community admissions with previous outpatient sCr values, and 42,720 community admissions without previous sCr values. Length of stay and intensive care unit support were significantly increased for the admissions without previous sCr values compared to community admissions with previous sCr values. Crude inpatient mortality rates (7.3% versus 5.6%, $P<0.001$) were significantly higher for AKI in community admissions without previous sCr values compared to those with previous outpatient sCr values. Crude inpatient dialysis was similar for both groups.

There were 3,471 transferred admissions with previous outpatient sCr values, and 14,417 transferred admissions without previous sCr values. Intensive care unit support was significantly increased for the admissions without previous sCr values compared to transferred admissions with previous sCr values. Crude inpatient mortality rates were significantly higher for AKI in transferred admissions without previous sCr values compared to those with previous outpatient sCr values, comparing groups with AKI (18% versus 13%, $P<0.001$), as well as groups without AKI (3.8% versus 2.1%, $P<0.001$).

DISCUSSION

The definition of AKI requires clinically significant changes in sCr compared to a baseline sCr value. Accurate AKI assessment is important for characterizing risk factors associated with specific outcomes, developing risk stratification and prediction tools [19, 20], designing intervention trials [21], assessing inpatient costs attributable to AKI [22, 23], and organizing outpatient follow-up strategies [20, 24]. Assumptions about “the” baseline sCr have been continuing challenges for defining AKI [25-27]. The most recent outpatient sCr is a popular approach for defining the baseline sCr [3, 16], but these analyses excluded admissions without previous outpatient sCr values, and do not consider admission source [2, 3]. Using a previous outpatient sCr as the baseline sCr is not mandated by the original KDIGO

consensus statement [1], nor by the recent update [5], and will require imputation of missing outpatient sCr values for many data sets

We compared the previous outpatient sCr with a dynamic, point-wise baseline value generated in a 48-hour interval before each sCr during an admission. This approach explicitly recognizes that the baseline sCr may vary during the course of an individual admission, and is available for all admissions for which a sCr trajectory is analyzed. Of note, a static baseline sCr based on previous outpatient values was available for 43,433 admissions out of 100,570 admissions (43%) in the current data set. In contrast, the dynamic baseline sCr, based on a 48-hr rolling window of the previous inpatient sCr values for each admission was available for all of the admissions in the current data set. The KDIGO consensus [1] states that "differently ascertained baseline values require further exploration and validation," supporting the recent interest in a 48-hour "sliding" [28] or "rolling" [18] window for defining the baseline sCr. It is important to note that pairwise comparisons of AUC and NRI for static and baseline sCr were carried out with the subset for which previous ambulatory sCr values were available.

Figures 2 illustrates important differences between static and dynamic baseline sCr surrogates, which can affect the detection of AKI events. In Figure 2A, AKI was ascertained using the static baseline sCr, but not with the dynamic baseline sCr (Figure 2B) during an admission with Resolving AKI. This example questions whether Resolving AKI, in which the injury process began before the current hospital admission, should be co-mingled with In-hospital AKI [10]. Based on the differences in admission characteristics (Table 1), and outcomes (Table 2), we believe that these AKI categories are distinct, and should be addressed separately. Another advantage of the dynamic baseline approach is illustrated in Figures 2C and 2D. The previous outpatient sCr was 0.5 mg/dL, which was <0.3 mg/dL below the inpatient sCr values during that admission. Hence, every sCr value during that admission qualified as AKI using the static baseline approach (Figures 2C). In contrast, using the dynamic baseline sCr approach (Figures 2C), AKI was defined on hospital day 24, as a discrete AKI episode.

The potential for residual confounding [29, 30] is an under-appreciated limitation that arises when a previous outpatient sCr is used for the baseline sCr surrogate. We describe significant differences in the patient characteristics and outcomes for admissions without previous sCr values, compared to admissions with previous outpatient sCr values. This effect is especially evident for patients transferred to the referral medical center. These differences reflect the admissions patterns for an academic referral center, and should not be used to make any causal inferences. Nevertheless, admissions with previous outpatient sCr values may not have the same baseline characteristics and outcomes as admissions without previous outpatient sCr values accessible at the time of admission, even when the source of admission is included in multiple imputation approaches for generating missing outpatient sCr values [31]. This potential source of residual confounding should not be a major issue for national or "closed" health care systems [2, 25, 3, 7], because the great majority of patients will have previous outpatient sCr values accessible at the time of admission. Nevertheless, the residual confounding arising with missing ambulatory sCr values was ignored in previous publications that excluded this subset of patients from the analysis [2, 3].

The KDIGO consensus [1] does not address the occurrence of more than one episode of AKI during a single admission [10], or relapsing AKI defined by AKI that is initially resolving, but then complicated by a superimposed episode of In-hospital AKI [10]. A recent Acute Kidney Disease Quality Initiative consensus recognized the possibility of more than one AKI episode during a single hospital admission [16]. Further refinements of the dynamic baseline sCr surrogate are needed to address multiple AKI episodes during a single admission, wherein each episode may have a different baseline sCr defined by point-wise rolling windows during the course of that specific admission.

Our study has several limitations. The number and timing of sCr measurements depends on local clinical practice patterns, and is directly related to the length of stay, and thus, another source of residual confounding [32, 33]. The referral patterns for an academic medical center with availability of intensive care unit care and inpatient kidney replacement therapy may skew the case-mix, severity of illness and outcomes for transferred patients compared to community-based admissions. The current dynamic approach does not define the full extent of the AKI episode because the sCr values after the peak sCr do not exceed the 48-hr rolling average. Thus, definition of the full extent of an AKI episode, as well as recovery from that episode [16, 8] require additional analyses.

We did not determine the AKI etiology, urine output, fluid administration or concomitant medications with the current administrative datasets. Changes in creatinine generation [34-37], and changes in the volume of distribution of creatinine could lead to false-negative ascertainment of AKI events. We have tried to minimize these issues by excluding admissions with averaged inpatient eGFR values below 15 mL/min/1.73 m^2, and length of stay <1 or >180 days.

In conclusion, the performance of two baseline sCr surrogates was evaluated using an inpatient cohort from the UAB Health System. We found that the dynamic approach for defining baseline sCr better reflects the timing, magnitude and duration of changes in sCr during a single hospitalization. This approach defines the baseline inpatient sCr for individual admissions, using a point-wise 48-hour rolling window before every inpatient sCr [6, 1, 7, 8]. The dynamic baseline sCr significantly improved discrimination for assessing the risk of hospital mortality and dialysis requirement associated with AKI compared to the static baseline sCr surrogate. This approach provides a real-time approach for defining baseline sCr, without reference to prior outpatient sCr values or *post-hoc* evaluation following hospital discharge. Finally, the dynamic baseline sCr surrogate avoids imputation, and residual confounding that attends the use of a static baseline sCr surrogate when there are a substantial number of missing outpatient sCr values.

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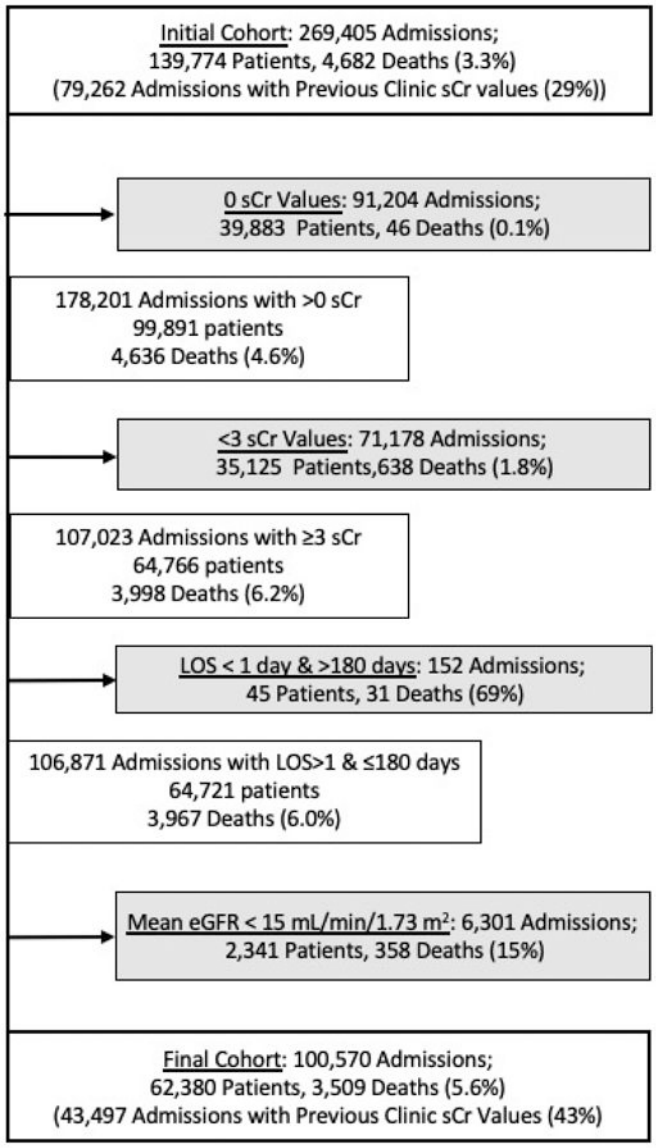

Figure 1. Patient Selection Flow Diagram. Abbreviations: eGFR, estimated glomerular filtration rate (mL/min/1.73 m2); LOS, length of stay (days); sCr, serum Creatinine (mg/dL).

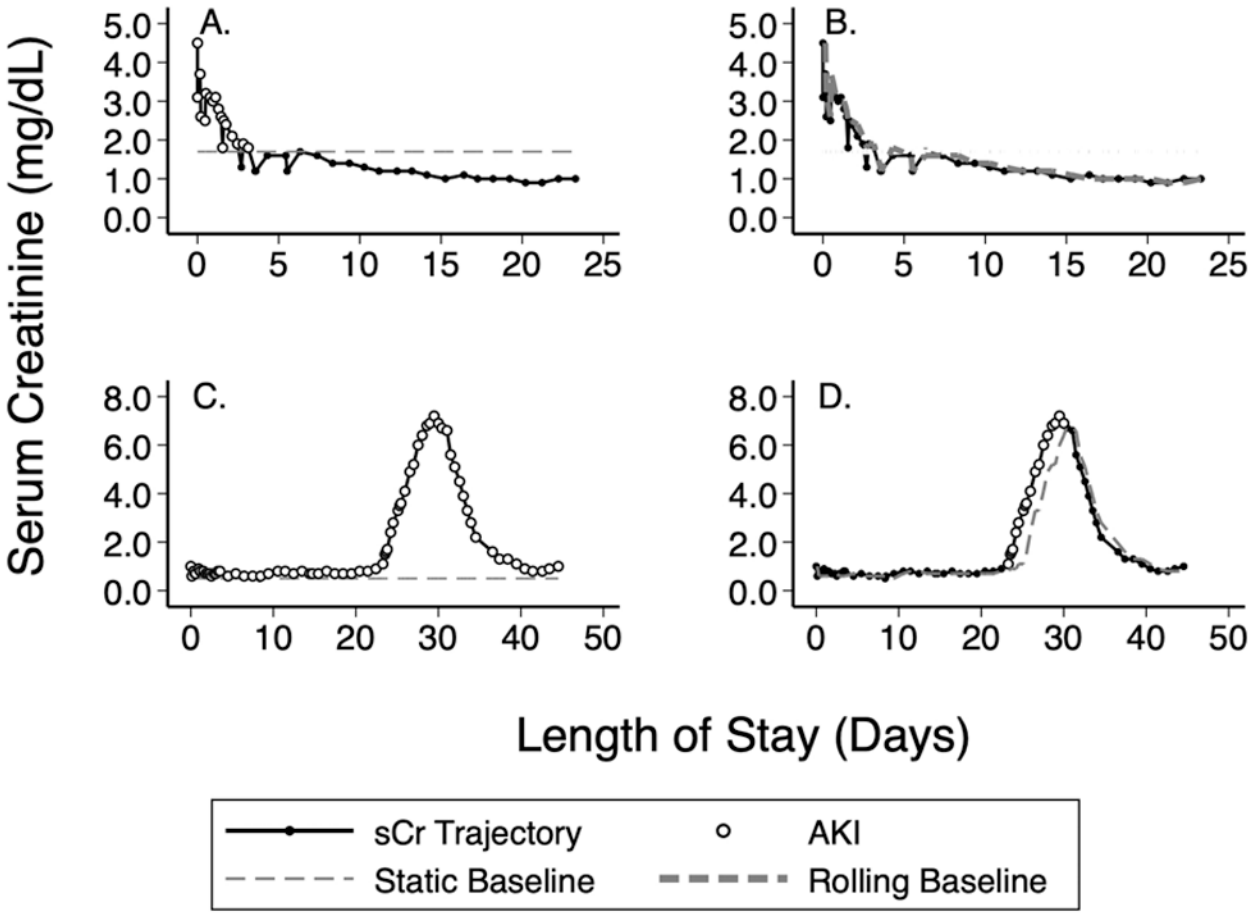

Figure 2. Serum Creatinine Trajectories Illustrating AKI Defined using Static and Dynamic Baseline sCr.

Resolving AKI (Figures 2A and 2B) refers to a sCr trajectory where the maximal sCr occurs before the minimal sCr, and the maximal sCr exceeds the minimal sCr by ≥0.3 mg/d. Figure 2A show the static baseline defined by the previous outpatient sCr for this admission (dash-dot horizontal line at sCr=1.7 mg/dL), and AKI (open circles) defined by 0.3 mg/dL increases above the baseline within 48-hors or 1.5-fold increases within 7 days. Figure 2B show the dynamic, baseline sCr defined by the minimum sCr in a 48-hour window before each sCr (dashed line). There were not any AKI events for this admission when the dynamic baseline sCr was used to define AKI.

In-patient AKI [10] (Figures 2C and 2D) was defined by AKI events that occurred during admission, with the maximal sCr value occurring after the minimal sCr value [11,12], Figure 2C show the static baseline defined by the previous outpatient sCr for this admission (dash-dot horizontal line at sCr=1.0 mg/dL), and AKI (open circles) defined by 0.3 mg/dL increases above the baseline within 48-hours or 1.5-fold increases within 7 days. Figure 2D show the dynamic, point-wise baseline defined by the minimum sCr in a 48-hour window before each sCr (dashed line), and AKI events (open circles) for this admission when the dynamic baseline sCr was used to define AKI. AKI, acute kidney injury; sCr, serum creatinine (mg/dL).

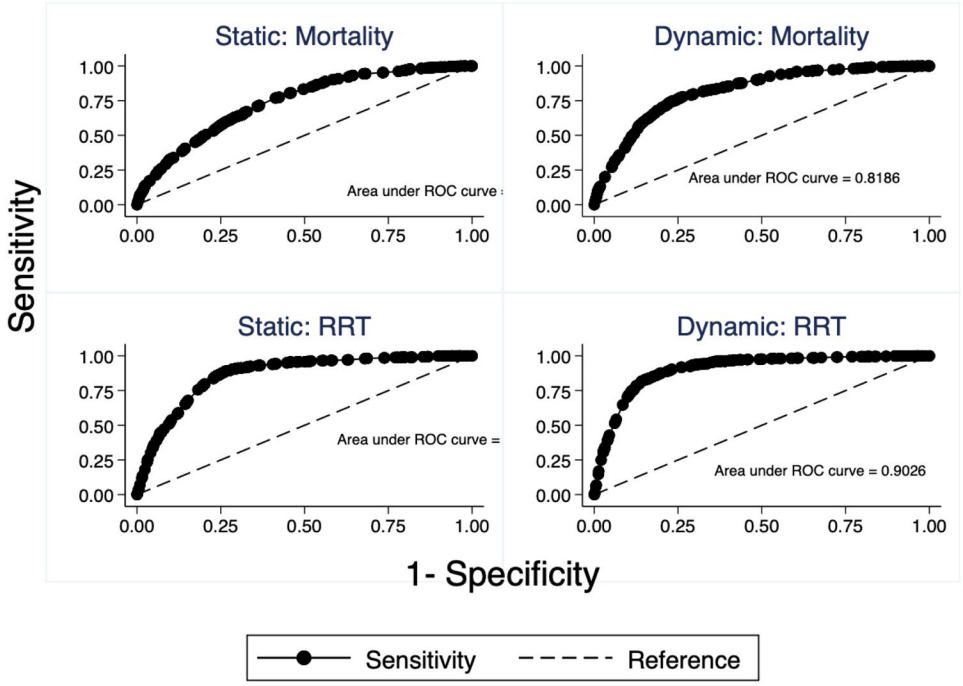

Figure 3. ROC Curves for Static and Dynamic Baseline sCr: Inpatient and Inpatient Renal Replacement Therapy,

Panels show receiver operator curves (ROC) for sensitivity versus (1-specificity) for static baseline sCr (based on previous ambulatory sCr values) compared to dynamic baseline sCr (based on 48-hr rolling average for each individual data point for Inpatient Mortality (Figures 3A and 3B) and Inpatient Renal Replacement Therapy (RRT; Figure 3C and Figure 3D). The solid lines and closed circles denote the ROC curves, and dashed diagonal lines are the reference functions, with reference areas under the curve (AUC) = 0.5). The AUC values are presented in Table 3 and are shown as inserts on each panel.

Table 1:

Baseline Characteristics: 100,570 admissions (62,380 patients; 3,509 Deaths (5.6%))

AKI Status **Admissions (row %)** **Patients (row %)**	**No AKI** **38,736 (39%)** **24,553 (39%)**	**Resolving AKI** **42,458 (43%)** **26,689 (43%)**	**In-hospital AKI** **19,376 (19%)** **11,138 (18%)**
Age, years	54 (18)	**58 (18)** [a]	**59 (17)** [a,b]
Male sex	17,885 (46%)	**23,913 (56%)** [a]	**10,177 (53%)** [a,b]
Black race	13,009 (34%)	**16,036 (38%)** [a]	**7,662 (40%)** [a]
Transferred Admissions	6,113 (16%)	**7,669 (18%)** [a]	**4,106 (21%)** [a,b]
Mean eGFR, mL/min/1.73 m^2	100 (27)	**76 (34)** [a]	**68 (32)** [a,b]
Charlson Index	2 (0 – 4)	**3 (1 – 5)** [a]	**3 (2 – 6)** [a,b]
Kidney Replacement Therapy	16 (0.1%)	**1,158 (2.7%)** [a]	**604 (3.1%)** [a]
ICU Care	6,368 (16%)	**15,508 (37%)** [a]	**7,111 (37%)** [a]
ICU Days	0.4 (1.3)	**1.5 (3.5)** [a]	**1.5 (4.0)** [a,b]
LOS, d	4.9 (5.1)	**8.7 (10)** [a]	**10 (12)** [a,b]
Serum Creatinine Values			
Number of sCr values per Admission	4 (3 – 6)	**7 (4 – 13)** [a]	**8 (5 – 14)** [a]
Static Baseline sCr, mg/dL (43,433 admissions (43%))	0.9 (0.4) 16,634 (43%)	**1.3 (0.9)**[a] **18,021 (45%)**	**1.3 (0.7)**[a,b] **8,778 (45%)**
First IP sCr, mg/dL	0.8 (0.3)	**1.5 (1.0)**	**1.2 (0.6)**
Minimum IP sCr, mg/dL	0.7 (0.3)	**0.9 (0.5)** [a]	**1.0 (0.6)** [a,b]
Maximum IP sCr, mg/dL	0.9 (0.3)	**1.7 (1.1)** [a]	**1.8 (1.11)** [a,b]
Last IP sCr, mg/dL	0.8 (0.3)	**1.0 (0.6)**	**1.5 (0.9)**
Dynamic Baseline sCr, mg/dL (48-hr Rolling Window) (98,864 Admissions (98%))	0.8 (0.6 – 0.9) 38,087 (98%)	**1.0 (0.8 – 1.4)**[a] 41,862 (99%)	**1.0 (0.8 – 1.4)**[a] 18,925 (98%)

Note: Values for continuous variables given as mean ± standard deviation or median [interquartile range]; and as count (percent) for categorical variables. Group characteristics were evaluated by point-wise comparisons with Bonferroni correction, Wilcoxon rank-sum test, and Chi^2 test for proportions.

[a] $P<0.001$, compared to No AKI

[b] $P<0.001$, compared to Resolving AKI

Abbreviations: AKI, acute kidney injury; eGFR, estimated glomerular filtration rate; IP, inpatient; LOS, length of stay; Mean eGFR, eGFR, average of all eGFR calculated for all sCr values for current admission; OP, outpatient; Previous OP sCr, most recent outpatient sCr >7 & <365 days before first IP sCr; sCr, serum creatinine (mg/dL)

Table 2:

Inpatient Mortality and Renal Replacement Therapy by AKI Status

AKI Status Admissions (row %) Patients (row %)	No AKI 38,736 (39%) 24,553 (39%)	Resolving AKI 42,458 (43%) 36,689 (43%)	In-hospital AKI 19,376 (19%) 11,138 (18%)
Inpatient Kidney Replacement Therapy			
Inpatient RRT (1,916)	26 (0.1%)	**1,252 (3.0%)** [a]	**638 (3.3%)** [a,b]
Unadjusted Rate, per patient-year	0.04 (0.02 – 0.06)	**1.03**[a] **(0.97 – 1.09)**	**0.97**[a] **(0.89 – 1.06)**
Incident Rate Ratio	1.00 (reference)	**8.61**[a] **(3.82 – 8.42)**	**6.83**[a,b] **(2.70 – 6.02)**
Inpatient Death			
Inpatient Deaths (3,509)	417 (1.1%)	**1,428 (3.4%)** [a]	**1,664 (8.6%)** [a,b]
Unadjusted Rate, per patient-year	0.80 (0.73 – 0.88)	**1.40**[a] **(1.33 – 1.48)**	**3.07**[a,b] **(2.92 – 3.22)**
Incident Rate Ratio	1.00 (reference)	0.93 (0.83 – 1.05)	**1.82**[a,b] **(1.62 – 2.04)**

Note: Incident Rate Ratios generated with Poisson regression, adjusted with binary covariates based on: median age; male sex; black race; averaged eGFR (calculated using all sCr values for an admission) < 60 ml/min/1.73 m^2; location (Highlands Hospital versus UAB Hospital); Admission Source (community-based admission versus transferred admission); and median Charlson Comorbidity Index

[a] $P<0.001$, compared to No AKI

[b] $P<0.05$, compared to Resolving AKI

Abbreviations: AKI, acute kidney injury; CI, confidence interval; RRT, renal replacement therapy; sCr, serum creatinine (mg/dL).

Table 3.

Comparison of AKI Defined with Static Baseline sCr and Dynamic Baseline sCr (48-hour Rolling Average) for Inpatient Mortality and Renal Replacement Therapy

Inpatient Mortality	**AKI (%)**	**Odds Ratio (± 95% CI)**	**AUC**	**NRI (± 95% CI)**
KDGIO AKI Defined usin g Static Baseline (Most Recent Outpatient sCr before Admission)				
Static Baseline sCr[#]	8,798 (20%) N= 43,433	1.64 (1.43 – 1.88)	0.741 (0.728 – 0.755)	
KDGIO AKI Defined using Dynamic Baseline sCr (48-hr Rolling Average)				
Dynamic Baseline sCr[*]	26,809 (27%) N=100,570	**5.14** [a] **(4.75 – 5.56)**	**0.818** [a] **(0.807 – 0.830)**	
Pairwise Comparison of KDIGO AKI Defined with Static and Dynamic Baseline sCr				
Static Baseline sCr[#]	8,798 (20%) N= 43,433	1.64 (1.43 – 1.88)	0.741 (0.728 – 0.755)	Reference
Dynamic Baseline sCr[#]	11,593 (27%) N=43,433	**6.57** [a] **(6.59– 7.58)**	**0.819** [a] **(0.807 – 0.830)**	**0.306** [a] **(0.263 – 0.349_**

Inpatient Dialysis	**AKI (%)**	**Odds Ratio (± 95% CI)**	**AUC**	**NRI (± 95% CI)**
KDGIO AKI Defined using Static Baseline (Most Recent Outpatient sCr before Admission)				
Static Baseline sCr[#]	408 (4.6%) N= 43,433	1.64 (1.43 – 1.88)	0.741 (0.728 – 0.755)	
KDGIO AKI Defined using Dynamic Baseline sCr (48-hr Rolling Average)				
Dynamic Baseline sCr[*]	1,680 (6.3%) N=100,570	**8.98** [a] **(7.80 – 10.3)**	0.772 (0.764 – 0.780)	
Pairwise Comparison of KDIGO AKI Defined with Static and Dynamic Baseline sCr				
Static Baseline sCr[#]	408 (4.6%) N= 43,433	1.27 (1.10 – 1.46)	0.864 (0.854 – 0.875)	Reference
Dynamic Baseline sCr[#]	742 (6.4%) N=43,433	**7.16** [a] **(5.95 – 8.61)**	**0.903** [a] **(0.839 – 0.911)**	**0.317** [a] **(0.269 – 0.364)**

Note: The Stata command **roctab** was used to generate and test statistical significance between AUCs, which were calculated with multi-variable adjusted logistic regression analyses, using the same adjustments as described in Table 2. NRI analyses were carried out as previously described [2,3]. AUC and NRI pairwise comparisons were carried out on the subset of admissions which has previous ambulatory sCr values.

[a] $P<0.001$ compared to reference

Abbreviations: AKI, acute kidney injury; AUC, area under receiver operator curve; CI, confidence interval; Previous OP sCr, most recent outpatient sCr >7 & <365 days before first Scr for current admission; NRI, net reclassification improvement; sCr, serum creatinine.

[*] These analyses utilized the entire cohort of 100,547 admissions not restricted to availability of previous outpatient sCr values.

[#] These analyses were limited to the sub-cohort of 43,433 admissions for which previous outpatient sCr values were available.

Table 4:

AKI Prevalence and Admission Source Among Patients With, and Without Previous Outpatient sCr

Admission Source: With or Without Previous sCr	**Community: With Previous sCr (39,962 Admissions; 17,387 Patients)**		**Community: Without Previous sCr (42,720 Admissions; 30,974 Patients)**	
AKI Status: row% (Admissions, N)	**No AKI: 66% (15,548)**	**Inpatient AKI: 34% (7,951)**	**No AKI: 70% (17,075)**	**Inpatient AKI: 30% (7,319)**
Age, years (mean)	56 (18)	**60 (17)** [a]	**53 (18)** [b]	**58 (17)** [a,c]
Black, N (%)	5,384 (35%)	**3,263 (41%)** [a]	6,051 (36%)	**3,134 (43%)** [a]
Male, N (%)	6,334 (41%)	**3,596 (45%)** [a]	**8,631 (51%)** [b]	**4,295 (59%)** [a,c]
LOS, days (mean)	4.7 (4.8)	**9.1 (11)** [a]	4.9 (5.4)	**9.8 (11)** [a,c]
ICU, N (%)	1,894 (12%)	**2,212 (28%)** [a]	**2,556 (15%)** [b]	**2,486 (34%)** [a,c]
Outcome Events				
Inpatient dialysis	9 (0.1%)	**240 (3.0%)** [a]	**13 (0.1%)** [b]	**195 (2.7%)** [a]
Inpatient deaths	85 (0.6%)	**446 (5.6%)** [a]	117 (0.7%)	**531 (7.3%)** [a,c]

Admission Source: With or Without Previous sCr	**Transfer: With Previous sCr (3,471 Admissions; 1,438 Patients)**		**Transfer: Without Previous sCr (14,417 Admissions; 12,581 Patients)**	
AKI Status: row% (Admissions. N)	**No AKI: 57% (1,086)**	**Inpatient AKI: 43% (827)**	**No AKI: 61% (5,027)**	**Inpatient AKI: 39% (3,279)**
Age, years (mean)	57 (18)	59 (16)	**54 (19)** [b]	**58 (18)** [a]
Black, N (%)	284 (26%)	**254 (31%)** [a]	1,290 (26%)	**1,011 (31%)** [a]
Male, N (%)	437 (40%)	**398 (48%)** [a]	**2,483 (49%)** [b]	**1,888 (58%)** [a,c]
LOS, days (mean)	5.2 (4.9)	**13 (18)** [a]	5.5 (5.1)	**13 (14)** [a]
ICU, N (%)	241 (22%)	**392 (47%)** [a]	**1,667 (33%)** [b]	**2,021 (62%)** [a,c]
Outcome Events				
Inpatient dialysis	3 (0.3%)	**37 (4.5%)** [a]	1 (0.1%)	**166 (5.1%)** [a]
Inpatient deaths	23 (2.1%)	**107 (13%)** [a]	**192 (3.8%)** [b]	**580 (18%)** [a,c]

[a] $p<0.001$ compared to reference (No AKI)

[b] $p<0.05$ comparing No AKI for both groups

[c] $p<0.01$ comparing Inpatient AKI for both groups.

Abbreviations: AKI, acute kidney injury; ICU, intensive care unit; LOS, length of stay (days).