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Original Article

Continuous Urine Output-Based Alert Identifies Cardiac Surgery–associated Acute Kidney Injury Earlier Than Serum Creatinine: A Prospective and Retrospective Observational Study

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Objective(s): Acute kidney injury (AKI) is defined and staged by reduced urine output (UO) and increased serum creatinine (SCr). UO is typically measured manually and documented in the electronic health record, making early and reliable detection of oliguria-based AKI and electronic data extraction challenging. The authors investigated the diagnostic performance of continuous UO, enabled by active drain line clearance–based alerts (Accuryn AKI Alert), compared with AKI stage 2 SCr criteria and their associations with length of stay, need for continuous renal replacement therapy, and 30-day mortality.
Design: This study was a prospective and retrospective observational study.
Setting: Nine tertiary centers participated.
Participants: Cardiac surgery patients were enrolled.
Interventions: None.

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Measurements and Main Results: A total of 522 patients were analyzed. AKI stages 1, 2, and 3 were diagnosed in 32.18%, 30.46%, and 3.64% of patients based on UO, compared with 33.72%, 4.60%, and 3.26% of patients using SCr, respectively. Continuous UO-based alerts diagnosed stage ≥1 AKI 33.6 (IQR =15.43, 95.68) hours before stage ≥2 identified by SCr criteria. A SCr-based diagnosis of AKI stage ≥2 has been designated a Hospital Harm by the Centers for Medicare & Medicaid Services. Using this criterion as a benchmark, AKI alerts had a discriminative power of 0.78. The AKI Alert for stage 1 was significantly associated with increased intensive care unit and hospital length of stay and continuous renal replacement therapy, and stage ≥2 alerts were associated with mortality.

Conclusions: AKI Alert, based on continuous UO and enabled by active drain line clearance, detected AKI stages 1 and 2 before SCr criteria. Early AKI detection allows for early kidney optimization, potentially improving patient outcomes.

Key Words: urine output; acute kidney injury; cardiac surgery; cardiac surgery−associated acute kidney injury; intensive care unit; serum creatinine; KDIGO; active drain line clearance

CARDIAC SURGERY−ASSOCIATED ACUTE KIDNEY INJURY (CSA-AKI) is a common postoperative complication affecting 5% to 42% of cardiac surgery patients.[1-3] CSA-AKI is also associated with higher perioperative and long-term mortality, prolonged intensive care unit (ICU) and hospital length of stay (LOS), and increased healthcare costs.[4-6] Surviving patients remain at risk for premature chronic kidney disease (CKD), even if renal function initially recovers.[7] Up to 5% of patients subsequently require ongoing kidney replacement therapy.[8,9] However, early detection of patients with developing AKI allows for the implementation of aggressive early preventive care measures, including a Kidney Disease Improving Global Outcomes (KDIGO) kidney care bundle, to avoid injury progression and complications.[10-12]

AKI is identified by a rise in serum creatinine (SCr) and/or reduction in urinary output (UO) as surrogate markers of reduced glomerular filtration rate (GFR). AKI is defined and staged for severity using criteria from KDIGO guidelines.[13] UO has been suggested as a sensitive and early marker of AKI,[14,15] and oliguria has been described as an independent predictor of poor patient outcomes.[16-18]

The value of using UO to detect AKI depends on the measurement method, with UO values differing according to how UO is measured and recorded (urinary catheter *v* no catheter, hourly measurements *v* continuous real-time measurements, etc.).[19] KDIGO does not define whether UO should be measured using consecutive hourly readings or mean output over a fixed period of time, but the method of measurement used can affect the reported incidence of AKI and sensitivity and/or specificity of UO as a diagnostic test.[19] While UO is routinely used in clinical practice to guide care, real-time continuous UO, enabled by active drain line clearance,[20,21] is an innovation that has the potential to advance clinical care.

The authors hypothesized that an automated alert system (Accuryn AKI Alert) based on continuous UO could diagnose AKI faster than the KDIGO AKI stage 2 criteria based on routine laboratory SCr measurements. The primary outcome was the diagnostic performance of Accuryn AKI Alert compared with AKI stage 2 SCr criteria. Secondary outcomes were the associations between initial Accuryn AKI Alert and ICU and hospital LOS, the need for continuous renal replacement therapy (CRRT), and 30-day mortality.

Methods

Study Design and Ethics

The current study represents a subanalysis of a large observational multicenter trial (NCT04669548). The primary objective of the Accuryn Registry study was to analyze data streams (intra-abdominal pressure [IAP], UO, temperature) recorded by the Accuryn Monitoring System and correlate these values with the occurrence of AKI following cardiac surgery. The secondary objective was to assess the incidence of intraoperative and/or postoperative intra-abdominal hypertension (IAH), analyze factors contributing to IAH development, and examine associations between IAH and organ dysfunctions, including AKI and other clinical outcomes, such as LOS, use of hemodialysis, and readmission.

This study received approval from all nine participating sites (IRB00099580, IRB00069008, IRB00004989, IRB00000209, IRB00000533, IRB00000251, IRB00000536). Informed written consent was obtained and verified for patients at all institutions except Emory University School of Medicine and Cedar Sinai, which granted waivers of consent.

Elective and emergent adult cardiac surgery patients at nine medical centers in the United States undergoing various on- and off-pump cardiac surgical procedures requiring open sternotomy were prospectively and retrospectively enrolled. Data were collected between March 25 and October 1, 2019 (Emory) and between December 16, 2020, and May 3, 2023, for all other sites. One site (Mission Hospital, Ashville, NC, USA) could not provide electronic health record (her) data in time for this analysis.

The urinary catheter of the Accuryn Monitoring System was inserted after anesthesia induction and remained in place until the patient left the ICU or no longer required a urinary catheter (whichever came first).

Data Collection

Accuryn Monitoring System

The Accuryn Monitoring System consists of the Accuryn Monitor and Accuryn SmartFoley catheter that continuously measures UO, IAP, and bladder temperature. The Accuryn Monitoring System incorporates Active Drain Line Clearance

technology, which automatically clears urine from the Foley drain line. The Accuryn SmartFoley catheter contains two anti-backflow valves that prevent urine from flowing back into the bladder.[20,21] These features help eliminate standing urine in the bladder and drain line (due to airlocks), reduce false and missed oliguria due to incorrect time attribution of urine production, and enable real-time, accurate, and continuous UO.

Collected data included high-resolution UO from the Accuryn Monitoring System. Demographics, surgical characteristics, and clinical data were obtained by clinicians and entered into an electronic data capture (EDC) system, while other data was collected from the EHR. All data was deidentified on-site. Accuryn Monitoring System data were linked to EHR and EDC data using a deidentified subject number.

Definition of AKI

AKI was diagnosed according to KDIGO criteria.[13] Patients with SCr increases of ≥0.3 mg/dL within 48 hours or 1.5- to 1.9-times baseline were diagnosed with AKI stage 1, patients with SCr increases of 2- to 2.9-times baseline were diagnosed with AKI stage 2, and patients with SCr increases of ≥3 times baseline or ≥4 mg/dL were diagnosed with AKI stage 3. Further, using the Accuryn AKI Alert system, patients with a UO <0.5 mL/kg/h for ≥6 hours were diagnosed with AKI stage 1, those with UO <0.5 mL/kg/h for ≥12 h were diagnosed with AKI stage 2, and those with <0.3 mL/kg/h for ≥24 hours or anuria for ≥12 hours were diagnosed with AKI stage 3.

Outcomes

The primary objective of this study was to evaluate the sensitivity, specificity, and advanced diagnosis time for AKI provided by the Accuryn AKI Alert system compared with AKI stage 2 diagnosis based on routine SCr measurements. The secondary objective was to evaluate the associations between Accuryn AKI Alert and outcome variables, including ICU and hospital LOS, need for CRRT, and 30-day mortality.

Statistical Analysis

Accuryn data, EHR data, and manually captured data (RedCap[22,23] EDC), were combined into a single sqlite[24] database. If a patient had multiple surgeries, the earliest surgery was used. Measurements of each patient's SCr and UO from Accuryn were both terminated at the time of their last SCr measurement, 3 days after the last Accuryn measurement, or 30 days after the end of surgery, whichever came first. Analysis was carried out in Python[25] with the aid of the following industry standard, open-source packages: numpy,[26] pandas,[27] sqlalchemy,[28] matplotlib,[29] seaborn,[30] scikit-learn,[31] scipy,[32] graphviz,[33] and statsmodels.[34] Packages and environments were managed using the Anaconda Python distribution.[35] Source control was provided by Git.[36,37]

UO from the Accuryn monitor was sampled directly after active drain line clearance events and computed as the numerical derivative between these events. Importantly, without active drain line clearance, a substantial amount of urine may be in the catheter drainage line due to airlock, potentially underestimating the true amount of urine produced.[20,38] Urine that is delayed in the drain line could artificially depress several hourly measurements, creating a false-positive AKI signal, or urine could build up in the drain line and create an inrush that artificially increases an hourly measurement, resulting in a false-negative, or missed, AKI.[20]

Accuryn AKI Alerts were defined as whether the patient meets each stage of the UO AKI criteria, and diagnoses based on SCr were made following KDIGO guidelines.[13] The time of meeting AKI criteria based on either SCr values or UO (ie, Accuryn AKI Alert) was calculated relative to the end of surgery. Accuryn AKI Alert was not displayed on the monitors, so it was assumed that clinician behavior was not modified.

The Accuryn AKI Alert was compared with SCr AKI stage 2 using the median time to diagnose, area under the receiver operating characteristic curve (AUROC), and associations with LOS, use of CRRT, and 30-day mortality. For continuous variables, the median, interquartile range (IQR), and difference between the medians are reported, whereas for proportions, the percentages, total count, and percentage difference are reported. Continuous variables were tested for associations using the Mann-Whitney U test,[39] while proportions were tested for associations using the Fisher exact test.[40] Using the Benjamini-Hochberg procedure,[41] p-values were adjusted for false discovery rate. The Wilcoxon sign rank test[42] was used to determine the significance of the difference in time to diagnose between the Accuryn AKI Alert operating points and KDIGO stage ≥2 SCr criteria.

Results

Patient Population

The Accuryn Registry database includes 1,139 patients from 9 sites. After exclusion for missing Accuryn UO or SCr data and for preoperative AKI, 522 patients were included in this study (Fig 1). The number of patients included per study site is shown in Supplementary Table 1. The median age of the final cohort was 65, and 65.5% were males. Patient demographics and clinical characteristics can be found in Table 1.

AKI Outcomes

Of the 522 patients in the cohort, the Accuryn AKI Alert identified AKI stages 1, 2, and 3 in 32.18% (168), 30.46% (159), and 3.64% (19) compared with 33.72% (176), 4.60% (24), and 3.26% (17) detected by SCr criteria, respectively. Assessment of AKI based on UO (Accuryn AKI Alert) diagnoses additional patients at higher stages relative to SCr (Fig 2).

Analytics for Accuryn AKI Alert Scores

The Accuryn AKI Alert stage 1+ (AKI stage 1 or higher, 6 hours) score was defined as the maximum hourly UO, as

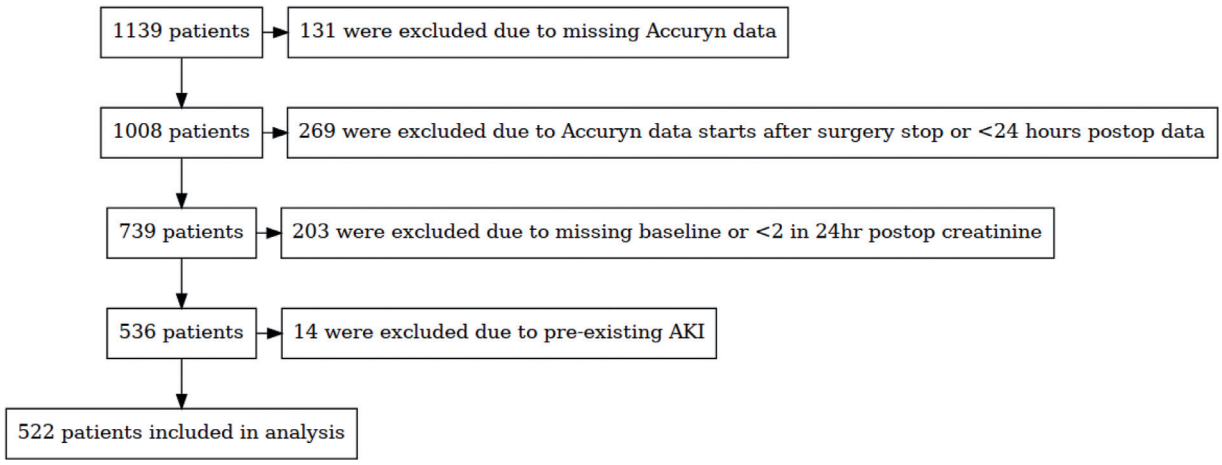

Fig 1. Standards for the reporting of diagnostic accuracy studies (STARD) diagram. Details patient exclusion from the study due to missing data and pre-existing AKI. AKI, acute kidney injury.

measured by Accuryn, over 6 consecutive hours and, when it falls below the 0.5 mL/kg/h threshold, the patient has met the Accuryn AKI Alert stage 1 criteria. Similarly, for the Accuryn AKI Alert stage 2+ (AKI stage 2 or higher, 12 hours) score, UO <0.5 mL/kg/h met the criteria for AKI stage 2. For the Accuryn AKI Alert stage 3a (24 hours) score at 24 hours with UO <0.3 mL/kg/h or for the Accuryn AKI Alert 3b (12 hours) score of UO = 0 mL/kg/h met the criteria for AKI stage 3. The Accuryn AKI Alert scores and, thus, the Accuryn AKI Alert stages, update every minute based on the past 6, 12, and 24 hours of UO data, respectively.

Table 1
Patient Demographics and Clinical Characteristics

Demographics	Total Patients (N = 522)
Age, median (IQR)	65.0 (57.0, 72.0)
BMI, kg/m^2, median (IQR)	27.25 (24.22, 31.2)
Male sex, % (N)	65.52% (342)
Race: White, % (N)	76.82% (401)
Race: Black or African American, % (N)	11.11% (58)
Race: Other, % (N)	5.75% (30)
Race: Asian, % (N)	5.36% (28)
Hispanic or Latinx, % (N)	12.64% (66)
Surgery characteristics	
CABG surgery, % (N)	42.53% (222)
Valve surgery, % (N)	49.62% (259)
CABG plus valve surgery, % (N)	10.92% (57)
Off-pump CABG surgery, % (N)	5.75% (30)
Heart transplants, % (N)	4.98% (26)
Lung transplants, % (N)	3.26% (17)
Other cardiac surgery, % (N)	10.54% (55)
Redo cardiac surgery, % (N)	2.3% (12)
Aortic clamp, % (N)	88.31% (461)
Procedures with cardiopulmonary bypass, % (N)	89.46% (467)
Cardiopulmonary bypass duration, min, median (IQR)	132.0 (103.0, 168.0)
Surgery duration, h, median (IQR)	4.93 (3.97, 6.25)
Foley duration, h, median (IQR)	74.29 (51.33, 113.71)
Patient risk scores and comorbidities	
Max ASA score, median (IQR)	4.0 (4.0, 4.0)
Euroscore, median (IQR)	1.99 (1.09, 3.8)
Baseline SCr, mg/dL, median (IQR)	0.95 (0.82, 1.17)
Chronic kidney disease, % (N)	12.45% (65/522)
Chronic kidney disease stage, median (IQR)	3.0 (1.25, 3.0)
Chronic obstructive pulmonary disease, % (N)	4.6% (24)
Congestive heart failure, % (N)	19.54% (102)
Hypertension, % (N)	70.69% (369)
Type 1 diabetes, % (N)	0.96% (5)
Type 2 diabetes, % (N)	29.31% (153)

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; CABG, coronary artery bypass graft; IQR, interquartile range.

Comparison of Accuryn AKI Stage 1, 2, and 3 Alerts

The Accuryn AKI Alert scores are continuous values used to determine Accuryn AKI Alert status; thus, an AUROC curve (Fig 3) can be used to compare their discriminative power. The Centers for Medicare & Medicaid Services (CMS) recently designated AKI stage 2 by SCr as a reportable Hospital Harm, and the Society of Thoracic Surgeons (STS) includes SCr AKI stage 2 in its reporting database.[43,44] Therefore, AKI stage 2 diagnosed by SCr was utilized as the benchmark for Accuryn AKI Alert comparison.

The Accuryn AKI Alert stage 1+ score performed similarly to the Accuryn AKI Alert scores for stages 2+ and 3 when discriminating between patients that meet the SCr criteria for AKI stage ≥2. Respective AUROCs show a delta of 0.04 (0.78, 0.74, and 0.76, respectively) (Supplementary Figs 1 and 2). At the operating point corresponding to the Accuryn AKI Alert stage 1, the sensitivity was 0.90, the specificity was 0.36, and the median prognosis time was 33.6 (IQR = 15.43, 95.68) hours before SCr AKI stage ≥2 diagnosis (Fig 3). AUROCs for different UO and SCr AKI stages can be found in the supplementary materials. ROC curves for Accuryn AKI Alerts stages 2 and 3 and comparisons against AKI stages ≥1 and 3 can be found in Supplementary Figures 3, 4, and 5.

Primary Outcome: Time to Diagnosis Using Accuryn AKI Alert

Accuryn AKI Alert diagnosed any stage of AKI (≥stage 1) earlier than SCr, with a median time to diagnosis of 17.9

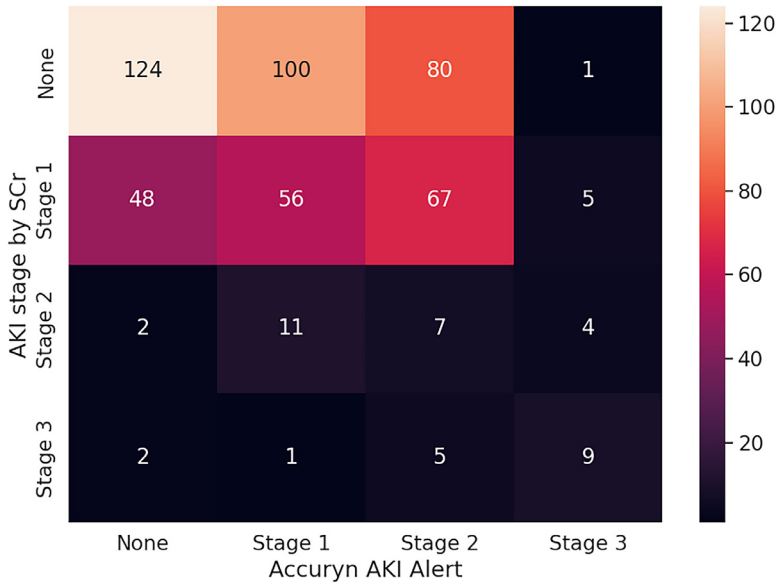

Fig 2. Confusion matrix shows the number of patients meeting each AKI stage (1-3) according to SCr and UO (Accuryn AKI Alert). AKI, acute kidney injury; SCr, serum creatinine; UO, urine output.

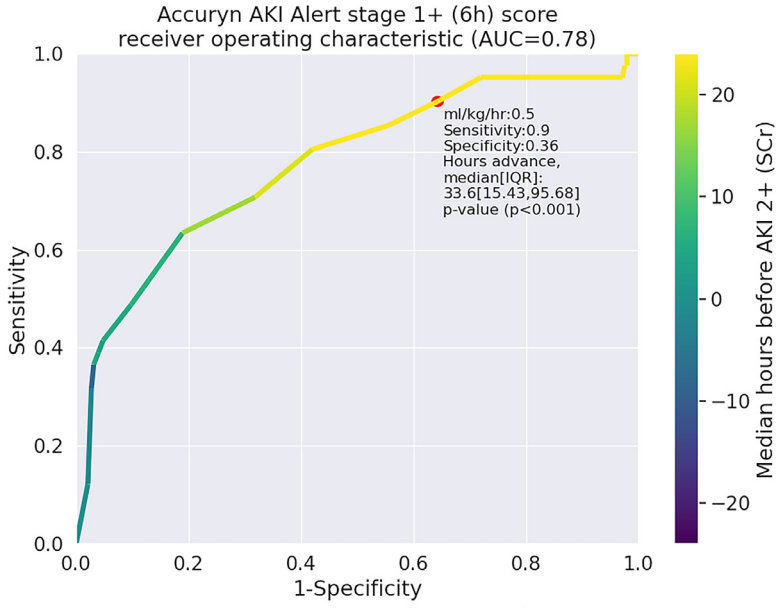

Fig 3. Receiver operating characteristic curve for the Accuryn AKI Alert stage 1 score is colored by the median hours before the AKI by SCr stage 2+. The Accuryn AKI Alert stage 1 operating point using UO <0.5 mL/kg/h is shown in *red*. AKI, acute kidney injury; SCr, serum creatinine; UO, urine output.

(IQR = 12.5, 25.8) hours after the end of surgery for Accuryn AKI Alert compared to 30.2 (IQR = 16.7, 40.4) hours after the end of surgery for AKI stage 1 diagnosed by SCr. For AKI ≥ stage 2, Accuryn AKI Alert shows a median time to diagnosis of 23.0 (IQR = 18.0, 30.25) hours after the end of surgery compared to SCr at 56.4 (IQR = 29.7, 96.1) hours after the end of surgery. Contrarily, Accuryn AKI Alert stage 3 diagnoses later than SCr, with a median of 96.6 (IQR = 29.4, 171.4) hours after the end of surgery compared to 38.9 (IQR = 28.2, 96.7) hours after the end of surgery, respectively (Fig 4).

Secondary Outcome

Patients with Accuryn AKI Alerts of any stage (stage ≥1) show a significant increase in the length of ICU and hospital stays ($p < 0.001$) and significantly increased rates of CRRT ($p = 0.0308$, $p < 0.001$, and $p < 0.001$ for stages 1, 2, and 3, respectively). Patients with an Accuryn AKI Alert stage 2 or 3 had significantly higher mortality compared with patients without Accuryn AKI Alerts ($p = 0.0115$ and $p < 0.001$, respectively) (Table 2).

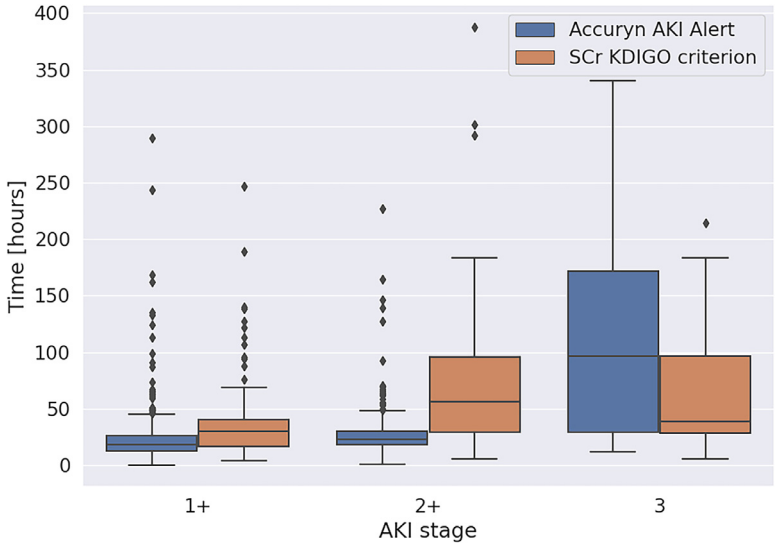

Fig. 4. Time in hours needed to diagnose AKI after the end of surgery for Accuryn AKI Alert and SCr criteria for each AKI. AKI, acute kidney injury; KDIGO, Kidney Disease Improving Global Outcomes; SCr, serum creatinine.

Patients with AKI stages 1 to 3 according to SCr criteria also displayed significant increases in LOS outcomes, utilization of CRRT, and mortality in all AKI stages compared with patients who did not meet SCr criteria (Supplementary Table 2). Even in patients who were not diagnosed with AKI ≥2 by SCr, Accuryn AKI Alert stage 1 showed a significant increase in their ICU ($p < 0.001$) and hospital stays ($p = 0.001$), whereas Accuryn AKI Alert stage 2 showed an additional significant increase in CRRT ($p < 0.05$) and Accuryn AKI Alert stage 3 showed significant increases in mortality ($p < 0.001$) (Supplementary Table 3).

Discussion

Using data from a multicenter observational study of 522 patients, the current authors analyzed whether AKI Alert, an alert based on continuous UO enabled by active drain line clearance, could determine AKI status earlier than SCr stage 2 criteria. Confirming previous studies, AKI defined by oliguria was common, with any stage AKI occurring in 66.28% (346/522) of patients. Compared with SCr, AKI Alert had median lead times to diagnose AKI stages 1 and 2 of 12.32 hours and 33.43 hours, respectively. Patients with Accuryn AKI Alerts

Table 2
Comparison of Outcomes of Patients With Accuryn AKI Alerts Versus No Accuryn AKI Alerts

Outcome variable	NO Accuryn AKI Alert Stage 1+ (n = 176)	Accuryn AKI Alert Stage 1+ (n = 346)	Difference	p-value	p-adjusted
ICU LOS, h, median (IQR)	66.18 (33.48, 105.82)	92.67 (51.8, 143.49)	26.48	$p < 0.001$	$p < 0.001$
Hospital LOS, h, median (IQR)	178.73 (130.48, 257.17)	229.94 (153.63, 347.42)	51.21	$p < 0.001$	$p < 0.001$
Treated with CRRT	1.14% (2/176)	4.62% (16/346)	3.49%	0.0283	0.0308
Mortality	1.14% (2/176)	2.6% (9/346)	1.46%	0.223	0.223
	No Accuryn AKI Alert Stage 2+ (n = 344)	Accuryn AKI Alert Stage 2+ (n = 178)			
ICU LOS, h, median (IQR)	72.53 (46.05, 122.62)	95.41 (54.24, 151.05)	22.88	$p < 0.001$	$p < 0.001$
Hospital LOS, h, median (IQR)	193.68 (138.73, 290.56)	248.82 (160.33, 415.43)	55.13	$p < 0.001$	$p < 0.001$
Treated with CRRT	1.16% (4/344)	7.87% (14/178)	6.7%	$p < 0.001$	$p < 0.001$
Mortality	0.87% (3/344)	4.49% (8/178)	3.62%	0.00959	0.0115
	No Accuryn AKI Alert Stage 3 (n = 503)	Accuryn AKI Alert Stage 3 (n = 19)			
ICU LOS, h, median (IQR)	76.97 (48.17, 124.42)	547.33 (319.93, 703.19)	470.37	$p < 0.001$	$p < 0.001$
Hospital LOS, h, median (IQR)	202.15 (148.92, 320.67)	756.37 (302.4, 1042.32)	554.22	$p < 0.001$	$p < 0.001$
Treated with CRRT	1.59% (8/503)	52.63% (10/19)	51.04%	$p < 0.001$	$p < 0.001$
Mortality	1.19% (6/503)	26.32% (5/19)	25.12%	$p < 0.001$	$p < 0.001$

NOTE. Length of ICU and hospital stay, CRRT, and 30-day mortality in patients with Accuryn AKI Alerts compared with those without. Stage 1+ corresponds to AKI stages 1 or higher. Stage 2+ corresponds to AKI stages 2 or higher.
Abbreviations: AKI, acute kidney injury; CRRT, continuous renal replacement therapy; ICU, intensive care unit; IQR, interquartile range; LOS, length of stay.

displayed significantly longer lengths of ICU and hospital stays, and patients with Accuryn AKI Alerts of stage ≥2 had significantly higher mortality than those without active Accuryn AKI Alerts. The lead time to diagnose AKI based on continuous UO technology has not been reported previously.

In the past, most researchers have primarily relied on SCr due to its discrete data field in the EHR and its singular validated measured value. In contrast, assessing UO requires a dynamic evaluation of change over time, with values measured against time intervals. Accurate UO monitoring has previously been difficult as it relies on manual UO measurements from urinary catheters and subsequent documentation in the EHR. Additionally, most automated urimeters fail to clear the drain line, producing inaccurate real-time UO measurements. Continuous UO monitoring with an automatic flow of data alleviates this limitation.

Recent findings suggest that oliguria may be strongly correlated with patient outcomes. Kellum et al. examined the UO and SCr AKI criteria in 32,000 adults in a single health system. They investigated associations between morbidity and mortality in patients who met SCr or UO output criteria for AKI, either alone or combined. Their findings revealed significant increases in hospital LOS, provision of renal replacement therapy, and mortality at 30 days, 90 days, and 1 year among patients who experienced AKI according to either criterion. Notably, the occurrence of these adverse outcomes nearly doubled in patients who developed AKI according to both criteria combined compared with those meeting either of the single criteria.[17] Neglecting to consider UO in defining AKI could result in failure to recognize many affected patients. UO can detect AKI earlier than SCr, as SCr is a late biomarker of AKI.

While SCr is a reliable indicator of glomerular filtration rate under normal kidney function, its accuracy diminishes in non-steady-state conditions. Postoperative cardiac surgery and other critically ill patients receiving aggressive fluid resuscitation experience an increased volume of distribution, leading to SCr dilution.[43] This dilution delays diagnosis and underestimates the severity of AKI. Continuous UO and other AKI-related biomarkers may facilitate earlier detection relative to SCr criteria. Moreover, Accuryn AKI Alert provides a more accurate prediction of CSA-AKI compared with relying solely on clinical and surgical risk factors in this patient population. With prediction and early diagnosis of AKI, kidney care bundles and future novel therapies can prevent the incidence and progression of AKI. Early prediction and diagnosis of AKI is vital to implement timely strategies to reduce the progression.

KDIGO guidelines for AKI recommend initiating various supportive measures known as the kidney care bundle (volume management, maintenance of adequate blood pressure, and judicious avoidance of nephrotoxins, contrast agents, and hyperglycemia) in patients at high risk for or in AKI. However, only a minority of high-risk patients or patients in AKI are treated with complete bundle care.[44] Early implementation of the KDIGO kidney care bundle effectively reduces AKI in cardiac surgery patients.[10,11,45] The Accuryn AKI Alert diagnoses AKI a median of 33.6 (IQR = 15.43, 95.68) hours in advance of SCr criteria for AKI stage 2, compared with standard of care based on hourly UO, which diagnoses AKI 11 hours earlier than SCr as previously described.[15,46] Oliguria is also an independent predictor of adverse clinical outcomes,[16,47] which this study confirms with increased LOS metrics and mortality.

CMS recently acknowledged the importance of AKI prevention and early treatment. CMS now considers AKI stage 2 a Hospital Harm, with inclusion in the Electronic Clinical Quality Measures. AKI stage 2 by SCr will be a reportable event starting in 2025, with financial repercussions for healthcare systems in 2027.[48] Due to this CMS ruling and the fact that STS[49] only collects AKI stage 2 data, we defined the SCr AKI stage 2 criterion was defined as the benchmark or "gold standard" to compare the stage 1, 2, and 3 Accuryn AKI Alert scores.

The Accuryn AKI Alerts depend on the KDIGO UO criteria.[13] The 6-hour Accuryn AKI Alert (for AKI stage 1) score demonstrates similar performance to the 12-hour (for AKI stage 2) and 24-hour (for AKI stage 3) scores in discriminating between patients meeting the SCr AKI stage 2 criteria. Their respective AUROCs are comparable, with only marginal differences (0.78, 0.74, and 0.76, respectively) (Supplementary Fig 1). This suggests that 6 hours of low UO may be as informative as 12 and 24 hours of oliguria.

The only US Food and Drug Administration–approved biomarker for early clinical AKI prediction currently is the product of the urinary concentrations of tissue inhibitor of metalloproteinase and insulin-like growth factor-binding protein (NephroCheck). This test calculates the AKI Risk Index, which, if >0.3 (mg/L),[2] predicts the development of AKI stage 2 to 3 within 12 hours, with a reported sensitivity of 92% and specificity of 46%.[50,51] Accuryn AKI Alert's sensitivity and specificity are comparable to NephroCheck's. At the operating point corresponding to AKI stage 1 by UO, the sensitivity and specificity are 0.9 and 0.36, respectively.

Study Limitations

First, while this data includes multiple academic centers in the United States, the sample size remains relatively small. Due to financial and time constraints, this study was done before the assembly and cleaning of all available data was finalized. The results may not be generalizable to all cardiac surgery patients worldwide. However, the overall event rates and outcomes concord with recently published studies in cardiac surgery patients.[10,52] Second, the association between AKI and adverse outcomes could be confounded by different factors not captured. The data used were not recorded specifically for this study, thus potentially limiting the strength of inferences. Third, although the sensitivity of the Accuryn AKI Alert is high, the specificity is not. However, due to the impact of AKI on patients' immediate and long-term outcomes (and healthcare costs), false negatives carry more risks than false positives. Therefore, sensitivity was prioritized over specificity, thus, focusing on the AKI stage 1 alert. Fourth, while UO was reliably measured for all patients included in this analysis, the frequency of SCr measurements was not consistent for all

patients, which could contribute to the lower diagnosis rate compared with Accuryn AKI Alert. Fifth, the Accuryn AKI Alert presented in this study is specific to the Accuryn Monitoring System. Lastly, many factors might influence UO during cardiac surgery, especially cardiopulmonary bypass, volume status, and diuretics. The authors plan to consider these confounding factors when using Accuryn AKI Alert in predicting AKI with the final dataset.

Conclusions

Patients undergoing cardiac surgery experience high rates of AKI, which dramatically worsens their prognosis. Early identification of AKI with the Accuryn AKI Alert allows clinicians to implement the KDIGO kidney care bundle and optimize treatment early, potentially improving patient outcomes and lowering healthcare costs.

Declaration of competing interest

V. Moll is a paid consultant for Acccuryn Medical. M. Zhao, S. Minear, A. Kurz, and M. Swaminathan declare no support from any organization for the submitted work, no financial relationships with any organizations that might have an interest in the submitted work in the previous three years, and no other relationships or activities that could appear to have influenced the submitted work. A. K. Khanna is a paid consultant for and chairs the steering committee for the Predict AKI Group for Accuryn Medical and consults for Edwards Lifesciences, Medtronic, Philips North America, GE Healthcare, Retia Medical, Pharmazz Inc., Hill-Rom, and Caretaker Medical. His institution has grant funding from Caretaker Medical for ongoing investigations on portable hemodynamic monitoring. A. K. Khanna is on the executive advisory board for Medtronic, Philips Hemodynamics Safety, and Retia Medical and receives support from the Wake Forest CTSI via NIH/NCATS KL2 for a trial of continuous portable hemodynamic and saturation monitoring in hospital wards. K. Stanton is employed by Accuryn Medical, Hayward, CA, USA. J. Huang received research funding from Acccuryn Medical, Mespere LifeSciences, and GE Healthcare and is a consultant for GE Healthcare and Medtronic. K. G. Parr is a paid consultant for FlexiCare and NorthGauge.

CRediT authorship contribution statement

Vanessa Moll: Conceptualization, Investigation, Writing – original draft, Writing – review & editing. **Manxu Zhao:** Writing – review & editing, Investigation. **Steven Minear:** Investigation, Writing – review & editing. **Madhav Swaminathan:** Investigation, Writing – review & editing. **Andrea Kurz:** Investigation, Writing – review & editing. **Jiapeng Huang:** Investigation, Writing – review & editing. **K. Gage Parr:** Investigation, Writing – review & editing. **Kelly Stanton:** Formal analysis, Methodology, Writing – review & editing. **Ashish K. Khanna:** Investigation, Writing – review & editing.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1053/j.jvca.2024.06.021.

References

1 Nadim MK, Forni LG, Bihorac A, et al. Cardiac and vascular surgery-associated acute kidney injury: The 20th International Consensus Conference of the ADQI (Acute Disease Quality Initiative) Group. J Am Heart Assoc 2018;7:e008834. https://doi.org/10.1161/JAHA.118.008834.

2 Ostermann M, Cennamo A, Meersch M, et al. A narrative review of the impact of surgery and anaesthesia on acute kidney injury. Anaesthesia 2020;75. https://doi.org/10.1111/anae.14932;e121-33.

3 Wu B, Chen J, Yang Y. Biomarkers of acute kidney injury after cardiac surgery: A narrative review. Biomed Res Int 2019;2019:7298635. https://doi.org/10.1155/2019/7298635.

4 Hobson CE, Yavas S, Segal MS, et al. Acute kidney injury is associated with increased long-term mortality after cardiothoracic surgery. Circulation 2009;119:2444–53. https://doi.org/10.1161/CIRCULATIONAHA.108.800011.

5 Ortega-Loubon C, Fernández-Molina M, Carrascal-Hinojal Y, et al. Cardiac surgery-associated acute kidney injury. Ann Card Anaesth 2016;19:687–98.

6 Srivastava V, D'Silva C, Tang A, et al. The impact of major perioperative renal insult on long-term renal function and survival after cardiac surgery. Interact Cardiovasc Thorac Surg 2012;15:14–7. https://doi.org/10.1093/icvts/ivs106.

7 Haines RW, Powell-Tuck J, Leonard H, et al. Long-term kidney function of patients discharged from hospital after an intensive care admission: Observational cohort study. Sci Rep 2021;11:9928. https://doi.org/10.1038/s41598-021-89454-3.

8 Vandenberghe W, Gevaert S, Kellum JA, et al. Acute kidney injury in cardiorenal syndrome type 1 patients: A systematic review and meta-analysis. Cardiorenal Med 2016;6:116–28. https://doi.org/10.1159/000442300.

9 Machado MN, Nakazone MA, Maia LN. Prognostic value of acute kidney injury after cardiac surgery according to Kidney Disease: Improving Global Outcomes definition and staging (KDIGO) criteria. PLoS One 2014;9:e98028. https://doi.org/10.1371/journal.pone.0098028.

10 Zarbock A, Küllmar M, Ostermann M, et al. Prevention of cardiac surgery-associated acute kidney injury by implementing the KDIGO guidelines in high-risk patients identified by biomarkers: The PrevAKI-multicenter randomized controlled trial. Anesth Analg 2021;133:292–302. https://doi.org/10.1213/ANE.0000000000005458.

11 Meersch M, Schmidt C, Hoffmeier A, et al. Prevention of cardiac surgery-associated AKI by implementing the KDIGO guidelines in high risk patients identified by biomarkers: The PrevAKI randomized controlled trial. Intensive Care Med 2017;43:1551–61. https://doi.org/10.1007/s00134-016-4670-3.

12 Göcze I, Jauch D, Götz M, et al. Biomarker-guided intervention to prevent acute kidney injury after major surgery: The prospective randomized BigpAK study. Ann Surg 2018;267:1013–20. https://doi.org/10.1097/SLA.0000000000002485.

13 Kellum JA, Lameire N, Guideline Work Group KDIGO AKI. Diagnosis, evaluation, and management of acute kidney injury: A KDIGO summary (Part 1). Crit Care 2013;17:204. https://doi.org/10.1186/cc11454.

14 Leedahl DD, Frazee EN, Schramm GE, et al. Derivation of urine output thresholds that identify a very high risk of AKI in patients with septic

shock. Clin J Am Soc Nephrol 2014;9:1168–74. https://doi.org/10.2215/CJN.09360913.
15 Koeze J, Keus F, Dieperink W, et al. Incidence, timing and outcome of AKI in critically ill patients varies with the definition used and the addition of urine output criteria. BMC Nephrol 2017;18:70. https://doi.org/10.1186/s12882-017-0487-8.
16 Macedo E, Malhotra R, Bouchard J, et al. Oliguria is an early predictor of higher mortality in critically ill patients. Kidney Int 2011;80:760–7. https://doi.org/10.1038/ki.2011.150.
17 Kellum JA, Sileanu FE, Murugan R, et al. Classifying AKI by urine output versus serum creatinine level. J Am Soc Nephrol 2015;26:2231–8. https://doi.org/10.1681/ASN.2014070724.
18 Goldstein SL. Urine output assessment in acute kidney injury: The cheapest and most impactful biomarker. Front Pediatr 2019;7:565. https://doi.org/10.3389/fped.2019.00565.
19 Macedo E, Malhotra R, Claure-Del Granado R, et al. Defining urine output criterion for acute kidney injury in critically ill patients. Nephrol Dial Transplant 2011;26:509–15. https://doi.org/10.1093/ndt/gfq332.
20 Kramer GC, Luxon E, Wolf J, et al. Inaccuracy of urine output measurements due to urinary retention in catheterized patients in the burn ICU. J Burn Care Res 2017;38:e409–17. https://doi.org/10.1097/BCR.0000000000000405.
21 Brockway P, Hill DM, Moll V, et al. A retrospective, observational study of catheter-associated urinary tract infection events post-implementation of a novel urinary catheter system with active drain line clearance and automated intra-abdominal pressure monitoring. Life 2022;12. https://doi.org/10.3390/life12121950.
22 Harris PA, Taylor R, Minor BL, et al. The REDCap consortium: Building an international community of software platform partners. J Biomed Inform 2019;95:103208. https://doi.org/10.1016/j.jbi.2019.103208.
23 Harris PA, Taylor R, Thielke R, et al. Research electronic data capture (REDCap)—A metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009;42:377–81. https://doi.org/10.1016/j.jbi.2008.08.010.
24 Owens M. The definitive guide to SQLite. Apress. Available at: https://link.springer.com/book/10.1007/978-1-4302-0172-4. Accessed April 2, 2024.
25 Van Rossum G, Drake FL. Python 3 reference manual: (Python documentation manual part 2). CreateSpace Independent Publishing Platform; 2009.Available at: https://play.google.com/store/books/details?id=KIybQQAACAAJ.
26 Harris CR, Millman KJ, van der Walt SJ, et al. Array programming with NumPy. Nature 2020;585:357–62. https://doi.org/10.1038/s41586-020-2649-2.
27 McKinney W. Data structures for statistical computing in Python. In: Proceedings of the 9th Python in Science Conference. SciPy, 2010. Available at: https://conference.scipy.org/proceedings/scipy2010/pdfs/mckinney.pdf. Accessed October 4, 2021.
28 Brown A, Wilson G. The architecture of open source applications structure, scale, and a few more fearless hacks. Volume II. [S.L.]. Brown & Wilson; 2012.Available at: http://aosabook.org/en/index.html.
29 Hunter JD. Matplotlib: A 2D graphics environment. Comput Sci Eng 2007;9:90–5. https://doi.org/10.1109/MCSE.2007.55.
30 Waskom M. Seaborn: Statistical data visualization. J Open Source Softw 2021;6:3021 https://joss.theoj.org/papers/10.21105/joss.03021.
31 Pedregosa F, Varoquaux G, Gramfort A, et al. Scikit-learn: Machine learning in Python. arXiv; 2012. Available at: http://arxiv.org/abs/1201.0490.
32 Virtanen P, Gommers R, Oliphant TE, et al. SciPy 1.0: Fundamental algorithms for scientific computing in Python. Nat Methods 2020;17:261–72. https://doi.org/10.1038/s41592-019-0686-2.
33 Gansner ER, Koutsofios E, North SC, et al. A technique for drawing directed graphs. IEEE Trans Software Eng 1993;19:214–30. https://doi.org/10.1109/32.221135.
34 Seabold S, Perktold J. Statsmodels: Econometric and statistical modeling with Python. In: Proceedings of the 9th Python in Science Conference. SciPy; 2010. Available at: http://conference.scipy.org.s3-website-us-east-1.amazonaws.com/proceedings/scipy2010/seabold.html. Accessed October 4, 2021.
35 Rolon-Mérette D, Ross M, Rolon-Mérette T, et al. Introduction to Anaconda and Python: Installation and setup. Quant Methods Psychol 2020;16;S3–11. https://www.tqmp.org/SpecialIssues/vol16-5/S003/S003.pdf.
36 Chacon S, Straub B. Pro Git. Apress; 2009.Available at: https://link.springer.com/book/10.1007/978-1-4842-0076-6.
37 Spinellis D. Git. IEEE Softw 2012;29:100-1. https://doi.org/10.1109/MS.2012.61.
38 Garcia MM, Gulati S, Liepmann D, et al. Traditional Foley drainage systems—Do they drain the bladder? J Urol 2007;177:203–7;discussion 207. https://www.auajournals.org/doi/abs/10.1016/j.juro.2006.08.101.
39 Mann HB, Whitney DR. On a test of whether one of two random variables is stochastically larger than the other. Ann Math Stat 1947;18:50–60 http://www.jstor.org/stable/2236101.
40 Fisher RA. Statistical methods for research workers. Springer series in statistics. New York, NY: Springer New York; 1992. p. 66–70https://link.springer.com/chapter/10.1007/978-1-4612-4380-9_6.
41 Benjamini Y, Hochberg Y. Controlling the false discovery rate: A practical and powerful approach to multiple testing. J R Stat Soc 1995;57:289–300 https://rss.onlinelibrary.wiley.com/doi/10.1111/j.2517-6161.1995.tb02031.x.
42 Conover WJ. Practical nonparametric statistics. 3rd Ed Wiley India Pvt. Limited; 2006.Available at: https://play.google.com/store/books/details?id=UBV2VwCxrMcC.
43 Macedo E, Bouchard J, Soroko SH, et al. Program to improve care in acute renal disease study. Fluid accumulation, recognition and staging of acute kidney injury in critically-ill patients. Crit Care 2010;14:R82. https://doi.org/10.1186/cc9004.
44 Küllmar M, Weiß R, Ostermann M, et al. A multinational observational study exploring adherence with the kidney disease: Improving global outcomes recommendations for prevention of acute kidney injury after cardiac surgery. Anesth Analg 2020;130:910–6. https://doi.org/10.1213/ANE.0000000000004642.
45 Engelman DT, Crisafi C, Germain M, et al. Using urinary biomarkers to reduce acute kidney injury following cardiac surgery. J Thorac Cardiovasc Surg 2020;160:1235–1246.e2. https://doi.org/10.1016/j.jtcvs.2019.10.034.
46 Dennen P, Parikh CR. Biomarkers of acute kidney injury: Can we replace serum creatinine? Clin Nephrol 2007;68:269–78. https://doi.org/10.5414/cnp68269.
47 Priyanka P, Zarbock A, Izawa J, et al. The impact of acute kidney injury by serum creatinine or urine output criteria on major adverse kidney events in cardiac surgery patients. J Thorac Cardiovasc Surg 2021;162:143–51. https://doi.org/10.1016/j.jtcvs.2019.11.137;.e7..
48 Centers for Medicare & Medicaid Services. Hospital harm-Acute kidney injury (HH-AKI). 2023. Available at: https://ecqi.healthit.gov/measure-data-elements/179056.
49 Society of Thoracic Surgeons. STS Performance Measure Descriptions. Available at: https://www.sts.org/quality-safety/performance-measures/descriptions. Accessed October 11, 2023.
50 Bihorac A, Chawla LS, Shaw AD, et al. Validation of cell-cycle arrest biomarkers for acute kidney injury using clinical adjudication. Am J Respir Crit Care Med 2014;189:932–9. https://doi.org/10.1164/rccm.201401-0077OC.
51 Ilaria G, Kianoush K, Ruxandra B, et al. Clinical adoption of NephroCheck in the early detection of acute kidney injury. Ann Clin Biochem 2021;58:6–15. https://doi.org/10.1177/0004563220970032.
52 Hu J, Chen R, Liu S, et al. Global incidence and outcomes of adult patients with acute kidney injury after cardiac surgery: A systematic review and meta-analysis. J Cardiothorac Vasc Anesth 2016;30:82–9. https://doi.org/10.1053/j.jvca.2015.06.017.