Journal of Community Hospital Internal Medicine Perspectives

Volume 13 | Issue 2 Article 2

2023

# Clinical And Echocardiographic Predictors Of Recovery Of Moderate-To-Severe Sepsis-Associated Acute Kidney Injury In Critically Ill Patients

Osama MUKHTAR
*Division of Pulmonary and Critical Care Medicine, Mayo Clinic, Rochester, Minnesota, U.S.A*

Amos Lal
*Division of Pulmonary and Critical Care Medicine, Mayo Clinic, Rochester, Minnesota, U.S.A*

Meir Tabi
*Department of Cardiovascular Medicine, Mayo Clinic, Rochester, Minnesota, U.S.A.*

Jacob Jentzer
*Department of Cardiovascular Medicine, Mayo Clinic, Rochester, Minnesota, U.S.A.*

Kianoush Kashani
*Division of Nephrology and Hypertension, Mayo Clinic, Rochester, Minnesota, U.S.A*,
kashani.kianoush@mayo.edu



## Recommended Citation

MUKHTAR, Osama; Lal, Amos; Tabi, Meir; Jentzer, Jacob; and Kashani, Kianoush (2023) "Clinical And Echocardiographic Predictors Of Recovery Of Moderate-To-Severe Sepsis-Associated Acute Kidney Injury In Critically Ill Patients," *Journal of Community Hospital Internal Medicine Perspectives*: Vol. 13: Iss. 2, Article 2.
DOI: 10.55729/2000-9666.1159
Available at: https://scholarlycommons.gbmc.org/jchimp/vol13/iss2/2

# Clinical and Echocardiographic Predictors of Recovery of Moderate-to-severe Sepsis-associated Acute Kidney Injury in Critically Ill Patients

Osama Mukhtar [a], Amos Lal [a], Meir Tabi [b], Jacob Jentzer [b], Kianoush Kashani [c,*]

[a] Division of Pulmonary and Critical Care Medicine, Mayo Clinic, Rochester, MN, USA
[b] Department of Cardiovascular Medicine, Mayo Clinic, Rochester, MN, USA
[c] Division of Nephrology and Hypertension, Mayo Clinic, Rochester, MN, USA

**Abstract**

*Background*: **Acute kidney injury (AKI) is associated with significant short- and long-term morbidity and mortality. In critically ill patients with sepsis, AKI tends to be more severe, more likely to require kidney replacement therapy (KRT), with less chance of recovery. Consequently, critically ill patients with sepsis-associated AKI (SA-AKI) have extended intensive care unit (ICU) stays and higher mortality rates. This study evaluated the predictive value of clinical and transthoracic echocardiographic (TTE) parameters for recovery from moderate-to-severe SA-AKI in critically ill patients.**

*Methods*: **This single-center historical cohort study was conducted at a tertiary academic medical center. We analyzed the data of all adults (age ≥18 years) admitted to the ICU at Mayo Clinic, Rochester, MN, from June 1, 2018, to December 31, 2020. We included all patients who developed sepsis within the initial 24 h of their ICU stay.**

*Results*: **We identified 2919 eligible septic patients with available TTE, among which 1431 patients (49%) had moderate-to-severe SA-AKI. The mean age of the patients was 68 ± 15 years, and the male-to-female ratio was 1.3:1. The most common comorbidities were diabetes mellitus and chronic lung and kidney diseases. Clinical predictors associated with SA-AKI non-recovery were the presence of stage III AKI (*HR* 1.5, 95% *CI* 1.0−2.1, $p = 0.03$) and utilization of kidney replacement therapy (KRT) (*HR* 6.8, 95% *CI* 3.6−12.4, $p = 0.01$). On the other hand, higher TAPSE was the only TTE variable associated with SA-AKI recovery (*HR* 1.1; 95% *CI* 1.08−1.15; $p = 0.01$).**

*Conclusion*: **Our data from a single-center provide new information on the clinical (AKI stage, utilization of KRT, BMI, and peak serum creatinine) and echocardiographic features (TAPSE) associated with improved recovery in SA-AKI. There is a definite knowledge gap in the current literature regarding optimizing recovery in moderate-to-severe SA-AKI. Larger, multi-center studies are required to confirm these findings.**

*Keywords:* Sepsis, Shock, Kidney injury, Critical care, Echocardiogram

## 1. Introduction

Acute kidney injury (AKI) is a common complication in critically ill patients, particularly septic patients. AKI is associated with significant short- and long-term morbidity and mortality.[1,2] In septic patients, AKI tends to be more severe, more likely to require kidney replacement therapy (KRT) and recovers less frequently. Consequently, patients with sepsis who develop AKI have extended intensive care unit (ICU) stays and higher mortality rates.[3]

Sepsis-associated AKI (SA-AKI) is a distinct disease. The pathophysiology of SA-AKI extends far beyond kidney hypoperfusion and ischemia, as SA-AKI can occur in well-resuscitated septic patients despite hyperdynamic circulation and kidney hyperemia.[4] The primary factors contributing to SA-AKI pathophysiology are inflammation, oxidative stress, apoptosis accompanying sepsis syndrome, intra-glomerular hemodynamic changes, and nephrotoxicity.[5] These factors can also lead to sepsis-induced cardiomyopathy (SICM),[6] which further increases the incidence and intensity of SA-

Received 15 August 2022; revised 9 December 2022; accepted 20 December 2022.
Available online 10 March 2023

* Corresponding author at: Division of Nephrology and Hypertension and Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Mayo Clinic, 200 First Street SW, Rochester, MN 55905, USA.
E-mail address: Kashani.Kianoush@mayo.edu (K. Kashani).

https://doi.org/10.55729/2000-9666.1159

AKI. This heart-kidney crosstalk has been well described in multiple prior studies that evaluated cardiac function and its relationship with AKI development in critically ill patients.[7] Sepsis is a well-recognized triggering etiology of type 5 (secondary) cardiorenal syndrome (CRS). Furthermore, when patients with acute or chronic cardiac disease become critically ill with sepsis, AKI often results from typical SA-AKI mechanisms and additional mechanisms that underlie CRS itself.[8]

Various cardiac functional abnormalities have been associated with CRS, and echocardiographic findings can predict AKI development under several conditions.[9-17] In contrast, various clinical and hemodynamic parameters have been evaluated to predict AKI recovery. Ideally, identifying patients at risk of SA-AKI progression and long-term complications would allow early AKI preventive interventions to improve outcomes. However, to our knowledge, no study has explored the utility of transthoracic echocardiography (TTE) in predicting SA-AKI recovery. Accordingly, this study aimed to evaluate the predictive value of clinical and TTE parameters in the recovery of moderate-to-severe SA-AKI among critically ill patients admitted to the ICU at a large academic center in the United States.

## 2. Methods

This was a single-center historical cohort study. The Mayo Clinic Institutional Review Board reviewed and approved the study and waived the need for informed consent owing to the minimal risk and retrospective nature of the study (IRB # 21−004573).

### 2.1. Data extraction

We utilized Structure Query Language (SQL) to extract data from the Mayo Clinic Research Data Marts.[18] The ICU DataMart encompasses a real-time clinical and administrative database of electronic medical records (EMRs) for all patients admitted to ICUs at the Mayo Clinic. In contrast, echocardiographic parameters were extracted from a separate cardiovascular (CV) database, CV DataMart.

### 2.2. Study population and patient selection

We analyzed the data of all adults (age ≥18 years) admitted to an ICU at Mayo Clinic, Rochester, MN, from June 1, 2018, to December 31, 2020. We included all patients admitted to an ICU who developed sepsis within the initial 24 h of their ICU stay. We only considered the first ICU admission for analysis when a patient had multiple ICU encounters during the same hospitalization period.

We utilized Sepsis-3 criteria to identify sepsis patients with a Quick Sequential Organ Failure Assessment (qSOFA) score ≥2 and a suspected or documented source of infection. Initiation of intravenous antibiotics or a positive blood culture ordered within the first 24 h of ICU admission were considered as surrogates for suspected or confirmed infection, respectively. We excluded patients aged <18 years, patients with end-stage kidney disease (ESKD) or dialysis-dependent (peritoneal or hemodialysis), post-kidney/heart transplant patients, and patients with pacemaker/cardiac resynchronization therapy (CRT) devices. In addition, we excluded those with no prior Minnesota Research Authorization or vulnerable adults (e.g., prisoners and patients with known pregnancies).

We stratified our study population into two groups based on AKI development during ICU stay. First, we used the KDIGO criteria to define and stage AKI.[19] We used the average measured serum creatinine level 365 to 7 days before the index hospital admission as the baseline serum creatinine level. For patients with no prior serum creatinine measurements, we back-calculated their baseline creatinine using the Modification of Diet in Renal Disease (MDRD) equation for a glomerular filtration rate (GFR) of 60 mL/min/1.73 $m^2$, instead of 75 mL/min/1.73 $m^2$ to increase the specificity for GFR estimation.[20] We reported the highest AKI stage for each patient during the entire ICU stay. Time zero for every case was defined as the ICU admission time. We calculated and reported the time from ICU admission to AKI development. Second, we assessed kidney function recovery among patients with AKI. Two criteria were examined for AKI recovery among those who did not need or were liberated from KRT, 1) serum creatinine below 1.5 × baseline AND 2) urine output >0.5 mL/kg/hr. AKI recovery was only considered when both criteria were met within seven days of AKI development according to the criteria outlined in the 16th Acute Disease Quality Initiative (ADQI-16) consensus statement.[21] We also identified the time to AKI recovery and reported the timeline from AKI development to recovery. Only candidates with moderate-to-severe AKI (KDIGO stage II or III) were analyzed.

Finally, CV DataMart was used to extract TTEs performed within 48 h following ICU admission. Patients with no qualifying TTE were excluded from the final study group, whereas patients with multiple qualifying examinations had only the initial TTE

considered for analysis. The derived measures were calculated based on the observed TTE parameters (Supplemental 1). A systolic and diastolic dysfunction was defined as outlined in Supplemental 2.

### 2.3. Study variables

Baseline vital signs were obtained from the initial ICU admission and included heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP). Baseline laboratory workup data were extracted from the first 24 h and included WBC count, blood lactate, serum creatinine, blood hemoglobin, serum sodium, and serum potassium. We also reported the SOFA, Acute Physiology Score (APS) III, and Acute Physiology and Chronic Health Evaluation (APACHE) III scores during the first 24 h of ICU stay. Using the International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) codes, we identified comorbidities. Subsequently, comorbidities were assessed individually and combined using the 19-point Charlson Comorbidity Index. In addition, we examined ventilatory support, both invasive and non-invasive. We also evaluated vasopressor use and calculated the Vasoactive-Inotropic Score (VIS) for patients on vasopressor support.[22]

### 2.4. Statistical analyses

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS®), version 27.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were provided for all study variables. Continuous variables are presented as mean ± standard deviation (SD), and categorical variables are expressed as counts (percentage). Statistical tests of significance were conducted (Student's *t*-test for continuous variables and $\chi^2$-test for categorical variables). Variables with a $p \leq 0.2$ in univariate analysis were considered for multivariate analysis. Binary logistic regression using the enter method was used to identify predictors of SA-AKI recovery; the hazard ratio (HR) and 95% confidence interval (CI) were also calculated. A two-tailed $p < 0.05$ was used as a cut-off for statistical significance.

## 3. Results

We screened a total of 2919 eligible patients with sepsis and TTE who met our study criteria (Fig. 1). Among those, 1431 patients (49%) had moderate-to-severe SA-AKI. The baseline demographics and clinical and outcome measures of moderate-to-severe AKI are summarized in Table 1.

### 3.1. Baseline characteristics

The mean age was 68 ± 15 years, and the male-to-female ratio was 1.3:1. The most common comorbidity was diabetes mellitus (19%), followed by chronic pulmonary disease (18%). Chronic kidney disease was the third most common comorbidity, accounting for 16% of the comorbidity burden. Approximately 68% required ventilatory support, which was predominantly invasive (55%), but only 56% required vasopressor support during their ICU stay. The hospital and ICU length of stay (LOS) averages were 13.3 ± 14.3 and 5.8 ± 7.7 days, respectively.

The average time to the moderate-to-severe SA-AKI development was 2.3 ± 4.7 days. The average serum creatinine at baseline for the study group was 1.3 ± 0.8 mg/dL before hospitalization, increased to 1.9 ± 1.5 mg/dL at the time of ICU admission, peaked at 2.8 ± 2.1 mg/dL during the ICU stay, and by the time of discharge, the average serum creatinine decreased to 1.8 ± 1.4 mg/dL. Most patients (52%) developed severe SA-AKI (KDIGO stage III); however, only 27% required KRT. The overall SA-AKI recovery rate was 35%. The average time from AKI to recovery was 3.2 ± 2.8 days; as such, delayed recovery (2–7 days) accounted for the majority of cases (59%), compared to only 41% with early AKI recovery (<48 h). By the end of the first day of ICU admission, the average fluid balance was 871 ± 2372 mL with median 642 mL (IQR: -576-1958).

### 3.2. Characteristics of the recovery group

As shown in Table 1, patients in the recovery group were younger (67 ± 15 *vs.* 69 ± 15 years, $p = 0.010$) and less likely to be overweight or obese (BMI 29.7 ± 7.8 *vs.* 31.5 ± 9.3 kg/m$^2$, $p < 0.001$). The initial ICU mortality scores (SOFA, APS, and APACHE III) were lower in the recovery group than in the non-recovery group. There were no statistically significant differences in sex ($p = 0.673$) or incidence of ventilatory support ($p = 0.940$). In contrast, fewer vasopressors were used in the recovery group (52% *vs.* 58%, $p = 0.020$), and among those requiring vasopressor support, the recovery group had a lower average VIS (9.7 ± 15.6 *vs.* 16.7 ± 25.1, $p < 0.001$). Coronary artery disease was more prevalent in the recovery group (2.6% *vs.* 1%, $p = 0.018$), whereas chronic kidney and liver diseases were more prevalent in the non-recovery group (18% *vs.* 10%, $p < 0.001$ and 13% *vs.* 7%, $p < 0.001$, respectively). Overall, the non-recovery group had a higher

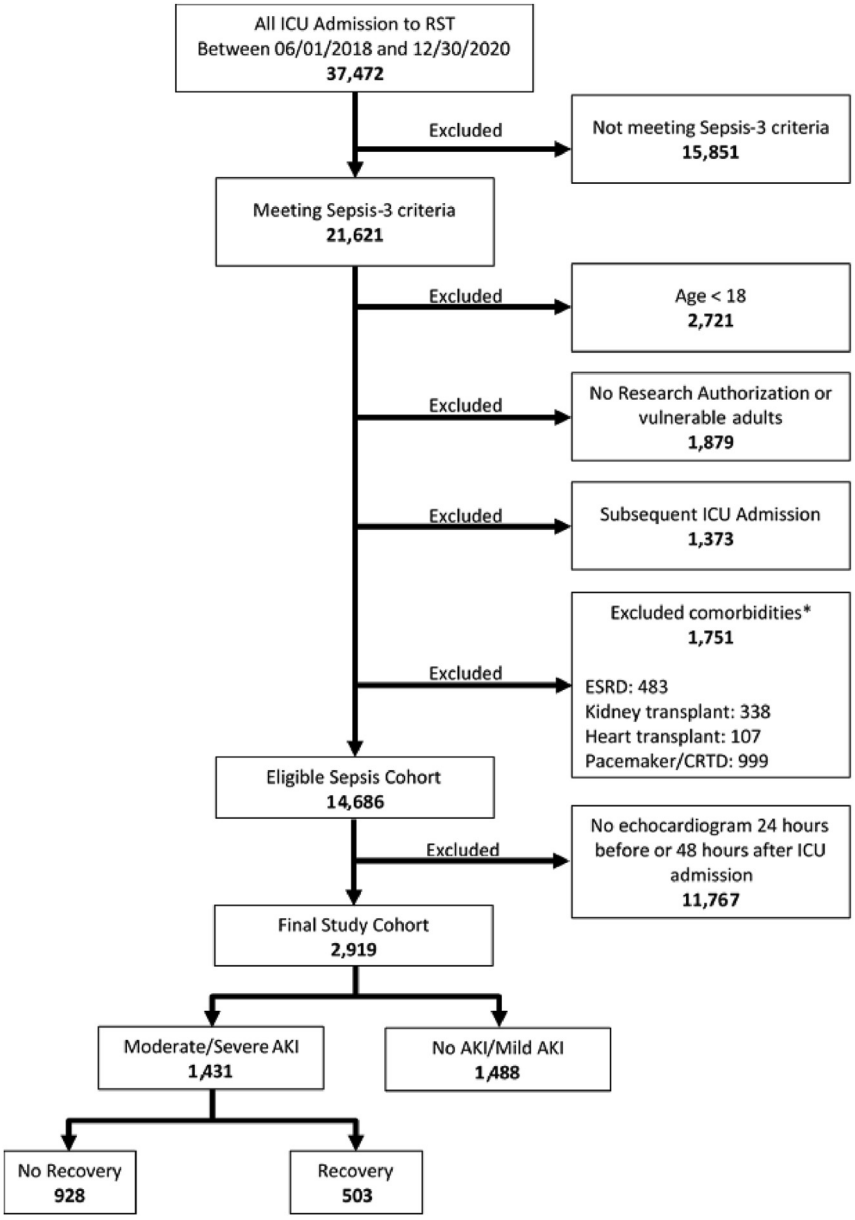



*Fig. 1. Patient Selection Flowchart. * Not mutually exclusive.* ***RST****, Rochester;* ***ICU****, Intensive Care Unit;* ***ESKD****, End-Stage Kidney Disease;* ***CRTD****, Cardiac Resynchronization Therapy;* ***AKI****, Acute Kidney Injury.*

Charlson Comorbidity Index than the recovery group (5.1 ± 2.3 *vs.* 4.5 ± 2.2, $p < 0.001$).

No statistically significant difference was noted in heart rate or systolic blood pressure, but diastolic blood pressure (41.7 ± 11.3 *vs.* 38.8 ± 11.7 mmHg, $p < 0.001$) and mean arterial blood pressure (55.6 ± 12.2 *vs*. 53.4 ± 13.0 mmHg, $p = 0.002$) were higher in the recovery group. The non-recovery group had higher baseline blood lactate, serum creatinine, and serum potassium levels but lower blood hemoglobin and serum sodium ($p$ for all <0.001). The difference in fluid balance on the first day of ICU admission in both groups was not statistically significant. AKI stage III and the need for KRT were more common in the non-recovery group (65% *vs.* 26% and 39% *vs.* 4.2%, respectively; $p < 0.001$). The non-recovery group developed SA-AKI earlier (2.1 ± 3.5 *vs.* 2.7 ± 6.3 days, $p = 0.042$), had higher peak serum creatinine (3.3 ± 2.2 *vs.* 1.8 ± 1.4 mg/dL, $p < 0.001$) and higher serum creatinine at discharge (2.2 ± 1.5 *vs.* 1.0 ± 0.5 mg/dL, $p < 0.001$) than the recovery group. Notably, non-recovery was associated with significantly higher ICU, hospital, and 1-year mortality rates.

*Table 1. Baseline characteristics.*

| Characteristics | Total ($N = 1431$) | SA-AKI | | $p$-Value |
|---|---|---|---|---|
| | | Non-Recovery ($n = 928$) | Recovery ($n = 503$) | |
| **Baseline Characteristics** | | | | |
| **Age** (years) [$] | 68 ± 15 | 69 ± 15 | 67 ± 15 | 0.010* |
| **Gender** | | | | 0.673 |
| Male | 820 (57.3) | 528 (56.9) | 292 (58.1) | |
| Female | 611 (42.7) | 400 (43.1) | 211 (41.9) | |
| **BMI** ($kg/m^2$) [$] | 30.8 ± 8.8 | 31.5 ± 9.3 | 29.7 ± 7.8 | <0.001* |
| **ICU Mortality Scores** | | | | |
| **SOFA Score** - day 1 (points) [$] | 9.1 ± 4.6 | 9.8 ± 4.7 | 8.0 ± 4.2 | <0.001* |
| **APS III Score at 24 h** (points) [$] | 85.3 ± 33.6 | 91.2 ± 34.2 | 74.3 ± 29.7 | <0.001* |
| **APACHE III Score at 24 h** (points) [$] | 99.5 ± 33.5 | 106.1 ± 33.7 | 87.4 ± 29.8 | <0.001* |
| **Ventilatory Support** | 974 (68.1) | 631 (68) | 343 (68.2) | 0.940 |
| Duration (days) | 2.3 ± 4.6 | 2.4 ± 4.9 | 2.1 ± 4.0 | 0.287 |
| **Invasive Ventilation** | 781 (54.6) | 498 (53.7) | 283 (56.3) | 0.346 |
| Duration (days) | 1.9 ± 4.3 | 2.0 ± 4.7 | 1.8 ± 3.6 | 0.284 |
| **Non-invasive Ventilation** | 466 (32.6) | 307 (33.1) | 159 (31.6) | 0.571 |
| Duration (days) | 0.3 ± 0.8 | 0.3 ± 0.8 | 0.3 ± 0.9 | 0.794 |
| **Vasopressor Support**[$] | 799 (55.8) | 539 (58.1) | 260 (51.7) | 0.020* |
| VIS (points) | 14.2 ± 22.5 | 16.7 ± 25.1 | 9.7 ± 15.6 | <0.001* |
| **Comorbidities** | | | | |
| Hypertension | 60 (4.2) | 41 (4.4) | 19 (3.8) | 0.564 |
| Diabetes | 278 (19.4) | 182 (19.6) | 96 (19.1) | 0.810 |
| Coronary Artery Disease[$] | 22 (1.5) | 9 (1) | 13 (2.6) | 0.018* |
| Congestive Heart Failure | 213 (14.9) | 136 (14.7) | 77 (15.3) | 0.740 |
| Chronic Pulmonary Disease | 263 (18.4) | 168 (18.1) | 95 (18.9) | 0.715 |
| Chronic Kidney Disease[$] | 223 (15.6) | 170 (18.3) | 53 (10.5) | <0.001* |
| Chronic Liver Disease[$] | 158 (11) | 123 (13.3) | 35 (7) | <0.001* |
| **Charlson Comorbidity Score** (points) [$] | 4.9 ± 2.2 | 5.1 ± 2.3 | 4.5 ± 2.2 | <0.001* |
| **Vital Signs at Time of ICU Admission** | | | | |
| Heart Rate (beat/min) | 87.9 ± 16.3 | 88.1 ± 16.8 | 87.6 ± 15.4 | 0.641 |
| Systolic Blood Pressure (mmHg) | 75.4 ± 18.9 | 74.9 ± 18.9 | 76.2 ± 18.8 | 0.214 |
| Diastolic Blood Pressure (mmHg) [$] | 39.8 ± 11.6 | 38.8 ± 11.7 | 41.7 ± 11.3 | <0.001* |
| Mean Arterial Pressure (mmHg) [$] | 54.2 ± 12.8 | 53.4 ± 13.0 | 55.6 ± 12.2 | 0.002* |
| **Laboratory Values at Time of ICU Admission** | | | | |
| WBC Count (x $10^9$/L) | 14.0 ± 10.4 | 14.3 ± 11.3 | 13.6 ± 8.3 | 0.218 |
| Blood Lactate (mmol/L) [$] | 4.4 ± 4.0 | 4.7 ± 4.3 | 3.8 ± 3.2 | <0.001* |
| Serum Creatinine (mg/dL) [$] | 1.9 ± 1.5 | 2.2 ± 1.7 | 1.3 ± 0.8 | <0.001* |
| Blood Hemoglobin (g/dL) [$] | 10.6 ± 2.3 | 10.4 ± 2.2 | 11.1 ± 2.3 | <0.001* |
| Serum Sodium (mmol/L) [$] | 136.8 ± 5.0 | 136.4 ± 5.1 | 137.5 ± 4.6 | <0.001* |
| Serum Potassium (mmol/L) [$] | 4.4 ± 0.7 | 4.5 ± 0.8 | 4.3 ± 0.7 | <0.001* |
| **SA-AKI Characteristics** | | | | |
| **KDIGO AKI Stage**[$] | | | | <0.001* |
| Stage II | 693 (48.4) | 319 (34.4) | 374 (74.4) | |
| Stage III | 738 (51.6) | 609 (65.6) | 129 (25.6) | |
| **Time to AKI** (days) [$] | 2.3 ± 4.7 | 2.1 ± 3.5 | 2.7 ± 6.3 | 0.042* |
| **Peak Serum Creatinine** (mg/dL) [$] | 2.8 ± 2.1 | 3.3 ± 2.2 | 1.8 ± 1.4 | <0.001* |
| **Discharge Serum Creatinine** (mg/dL) | 1.8 ± 1.4 | 2.2 ± 1.5 | 1.0 ± 0.5 | <0.001* |
| **KRT**[$] | 384 (26.8) | 363 (39.1) | 21 (4.2) | <0.001* |
| **Fluid Balance Day 1** (mL) [$] | 871 ± 2372 | 938 ± 2484 | 731 ± 2,0299 | 0.099 |
| **Outcome Measures** | | | | |
| **Length of Stay** (days) | | | | |
| Hospital | 13.3 ± 14.3 | 13.2 ± 14.9 | 13.5 ± 13.2 | 0.687 |
| ICU | 5.8 ± 7.7 | 5.7 ± 7.4 | 6.0 ± 8.2 | 0.366 |
| **Survival Analysis** | | | | |
| ICU Mortality | 246 (17.2) | 218 (23.5) | 28 (5.6) | <0.001* |
| Hospital Mortality | 349 (24.4) | 301 (32.4) | 48 (9.5) | <0.001* |
| 1-year Mortality | 703 (49.1) | 535 (57.7) | 168 (33.4) | <0.001* |

* Statistically significant ($p$-value $\leq 0.05$).

[$] Included in multivariate analysis ($p$-value $\leq 0.20$).

**BMI**, Body Mass Index; **SOFA**, Sequential Organ Failure Assessment; **APS III**, Acute Physiology Score III; **APACHE III**, Acute Physiology and Chronic Health Evaluation; **VIS**, Vasoactive-Inotropic Score; **WBC**, White Blood Cells; **KDIGO**, Kidney Disease: Improving Global Outcomes; **AKI**, Acute Kidney Injury; **ICU**, Intensive Care Unit; **KRT**, Kidney Replacement Therapy.

### 3.3. Clinical predictors of SA-AKI recovery

Multivariate logistic regression (Table 2) revealed that a lower BMI (*HR* 0.961, 95% *CI* 0.945–0.977, $p < 0.001$) and a lower peak serum creatinine (*HR* 0.766, 95% *CI* 0.624–0.941, $p = 0.011$) were associated with an increased likelihood of SA-AKI recovery. In addition, a history of coronary artery disease was associated with an increased incidence of recovery (*HR* 0.267, 95% *CI* 0.083–0.855, $p = 0.026$). Conversely, KDIGO AKI stage III (*HR* 1.464, 95% *CI* 1.044–2.054, $p = 0.027$) and the need for KRT (*HR* 6.722, 95% *CI* 3.646–12.395, $p < 0.001$) were associated with a decreased likelihood of recovery.

### 3.4. Echocardiographic characteristics

The mean LV ejection fraction (LVEF) was 51 ± 15%. The mean cardiac output (CO) and cardiac index (CI) were 6.15 ± 1.85 L/min and 3.11 ± 0.87 L/min/m$^2$, respectively (Table 3). On further analysis, 994 patients (70%) had normal cardiac function, 306 patients (21%) had systolic dysfunction and 131 patients (9%) had diastolic dysfunction (Table 4). Overall, there were no significant differences in LV systolic and LV diastolic echocardiographic parameters between the recovery and non-recovery groups, including LVEF, CO, CI, E/A, E/e', CPI, and MCF (Table 3). However, patients with normal cardiac function are more likely to recover (75% *vs.* 67%, $p = 0.001$).

In contrast, several right ventricular parameters were significantly different between the two groups. Patients in the non-recovery group had higher RV systolic pressure (46.7 ± 14.4 *vs.* 44.5 ± 12.9 mmHg, $p = 0.009$) and higher tricuspid regurgitation systolic peak velocity (2.86 ± 0.52 *vs.* 2.80 ± 0.45 m/s, $p = 0.038$) compared to patients in the recovery group. Additionally, patients in the recovery group had higher tricuspid annular plane systolic excursion (20.4 ± 6.6 *vs.* 16.8 ± 5.8 mm, $p < 0.001$) than those in the non-recovery group (Table 3).

### 3.5. Echocardiographic predictors of SA-AKI recovery

Univariate and multivariate logistic regression analyses performed on the echocardiographic parameters are shown in Table 5. Multivariate analysis showed that increased tricuspid annular plane systolic excursion (TAPSE) was associated with SA-AKI recovery (*HR* 1.112, 95% *CI* 1.077–1.148, $p < 0.001$), even after correcting for clinical predictors.

*Table 2. Clinic predictors of SA-AKI recovery.*

| Characteristics | HR (95% CI) | *p*-Value |
|---|---|---|
| **Age** (years) | 0.987 (0.967–1.008) | 0.225 |
| **BMI** (kg/m$^2$) | 0.961 (0.945–0.977) | <0.001* |
| **ICU Mortality Scores** | | |
| **SOFA Score** - day 1 (points) | 1.007 (0.957–1.060) | 0.788 |
| **APS III Score at 24 h** (points) | 1.021 (0.981–1.062) | 0.313 |
| **APACHE III Score at 24 h** (points) | 0.967 (0.930–1.006) | 0.100 |
| **Vasopressor Support** | 0.830 (0.575–1.198) | 0.321 |
| **Comorbidities** | | |
| Coronary Artery Disease | 0.267 (0.083–0.855) | 0.026* |
| Chronic Kidney Disease | 0.893 (0.558–1.430) | 0.638 |
| Chronic Liver Disease | 1.224 (0.691–2.168) | 0.488 |
| **Charlson Comorbidity Score** (points) | 0.951 (0.872–1.037) | 0.256 |
| **Vital Signs at Time of ICU Admission** | | |
| Diastolic Blood Pressure (mmHg) | 1.017 (0.993–1.042) | 0.174 |
| Mean Arterial Pressure (mmHg) | 0.985 (0.963–1.007) | 0.168 |
| **Laboratory Values at Time of ICU Admission** | | |
| Blood Lactate (mmol/L) | 1.011 (0.963–1.062) | 0.660 |
| Serum Creatinine (mg/dL) | 0.801 (0.606–1.056) | 0.120 |
| Blood Hemoglobin (g/dL) | 1.041 (0.974–1.112) | 0.233 |
| Serum Sodium (mmol/L) | 1.015 (0.985–1.046) | 0.324 |
| Serum Potassium (mmol/L) | 1.122 (0.906–1.390) | 0.292 |
| **KDIGO AKI Stage** | | |
| Stage III | 1.464 (1.044–2.054) | 0.027* |
| **Time to AKI** (days) | 1.000 (0.972–1.030) | 0.979 |
| **Peak Serum Creatinine** (mg/dL) | 0.766 (0.624–0.941) | 0.011* |
| **KRT** | 6.722 (3.646–12.395) | <0.001* |
| **Fluid Balance Day 1** (mL) | 1.000 (1.000–1.000) | 0.726 |

* Statistically significant ($p$-value ≤0.05).

BMI, Body Mass Index; **SOFA**, Sequential Organ Failure Assessment; **APS III**, Acute Physiology Score III; **APACHE III**, Acute Physiology and Chronic Health Evaluation; **KDIGO**, Kidney Disease: Improving Global Outcomes; **AKI**, Acute Kidney Injury; **KRT**, Kidney Replacement Therapy.

*Table 3. TTE parameters and characteristics.*

| TTE Parameters | Total | SA-AKI | | *p*-Value |
|---|---|---|---|---|
| | | Non-recovery | Recovery | |
| **Vital Signs at Time of TTE** | | | | |
| Heart Rate (beat/min) [$] | 87 ± 20 | 88 ± 20 | 85 ± 20 | 0.021* |
| Systolic Blood Pressure (mmHg) | 113 ± 21 | 112 ± 21 | 114 ± 20 | 0.229 |
| Diastolic Blood Pressure (mmHg)[$] | 63 ± 14 | 62 ± 15 | 65 ± 14 | 0.002* |
| Mean Arterial Pressure (mmHg)[$] | 80 ± 14 | 79 ± 14 | 81 ± 14 | 0.007* |
| **LV Size and Measurements** | | | | |
| LV Internal End Systolic Diameter (mm) | 35 ± 10 | 35.5 ± 9.5 | 35.2 ± 10.0 | 0.647 |
| LV Internal End Diastolic Diameter (mm) | 50 ± 8 | 50.2 ± 8.0 | 50.0 ± 8.1 | 0.723 |
| LV End Systolic Volume (mL) | 82 ± 55 | 82.2 ± 53.6 | 82.6 ± 57.5 | 0.936 |
| LV End Diastolic Volume (mL) | 150 ± 58 | 151.2 ± 58.1 | 147.2 ± 58.4 | 0.446 |
| IVS Diastolic Thickness (mm) [$] | 11 ± 2 | 10.8 ± 2.2 | 10.5 ± 1.9 | 0.063 |
| LV Mass (g) [$] | 192 ± 67 | 194.3 ± 68.3 | 187.4 ± 63.8 | 0.148 |
| LV Mass Index (g/m$^2$) | 97 ± 30 | 97.5 ± 30.8 | 95.7 ± 29.5 | 0.406 |
| **LV Systolic Function** | | | | |
| LV Ejection Fraction (%) [$] | 51 ± 15 | 50.4 ± 15.6 | 51.6 ± 14.3 | 0.185 |
| LV Outflow Tract Systolic Diameter (cm) | 2.3 ± 0.2 | 2.27 ± 0.20 | 2.26 ± 0.20 | 0.462 |
| LV Outflow Tract Systolic TVI (cm) | 18.1 ± 4.9 | 18.1 ± 5.1 | 18.3 ± 4.6 | 0.431 |
| LV Cardiac Output (L/min) | 6.15 ± 1.85 | 6.17 ± 1.88 | 6.12 ± 1.81 | 0.644 |
| LV Cardiac Index (L/min/m$^2$) | 3.11 ± 0.87 | 3.11 ± 0.88 | 3.12 ± 0.85 | 0.746 |
| LV Stroke Volume (mL) | 71 ± 23 | 71.2 ± 23.8 | 70.2 ± 21.9 | 0.486 |
| LV Systolic Stroke Volume Index (mL/m$^2$) | 36 ± 11 | 35.8 ± 11.0 | 35.7 ± 10.0 | 0.966 |
| LV Wall Motion Score Index[$] | 1.88 ± 0.52 | 1.91 ± 0.52 | 1.83 ± 0.52 | 0.114 |
| MV Lateral Annulus Systolic Velocity (m/sec) | 0.10 ± 0.27 | 0.10 ± 0.34 | 0.08 ± 0.03 | 0.461 |
| MV Medial Annulus Systolic Velocity (m/sec) | 0.08 ± 0.03 | 0.07 ± 0.03 | 0.08 ± 0.03 | 0.589 |
| **LV Diastolic Function** | | | | |
| MV A-Wave Peak Velocity (m/sec) [$] | 0.8 ± 0.3 | 0.79 ± 0.30 | 0.76 ± 0.27 | 0.113 |
| MV E-Wave Peak Velocity (m/sec) [$] | 0.9 ± 0.4 | 0.91 ± 0.37 | 0.85 ± 0.37 | 0.010* |
| MV Deceleration Time (msec) | 189 ± 51 | 189.9 ± 51.5 | 186.3 ± 50.1 | 0.354 |
| MV E to A Ratio | 1.2 ± 0.6 | 1.17 ± 0.58 | 1.14 ± 0.60 | 0.429 |
| MV E to e' Ratio[$] | 13.6 ± 7.2 | 13.99 ± 7.27 | 13.06 ± 6.94 | 0.069 |
| MV Lateral Annulus E to e' Ratio Diastolic PWD | 10.1 ± 5.3 | 10.2 ± 5.2 | 9.9 ± 5.4 | 0.347 |
| MV Lateral Annulus e' Velocity (m/sec) | 0.09 ± 0.03 | 0.092 ± 0.035 | 0.089 ± 0.031 | 0.235 |
| MV Medial Annulus e' Velocity (m/sec) | 0.07 ± 0.03 | 0.066 ± 0.028 | 0.068 ± 0.026 | 0.733 |
| **RV Data** | | | | |
| RV Systolic Pressure (mmHg) [$] | 46 ± 14 | 46.7 ± 14.4 | 44.5 ± 12.9 | 0.009* |
| TV Annulus Systolic Excursion (mm) [$] | 18 ± 6 | 16.8 ± 5.8 | 20.4 ± 6.6 | <0.001* |
| TV Lateral Annulus Systolic Velocity (m/sec) | 0.12 ± 0.04 | 0.12 ± 0.04 | 0.13 ± 0.04 | 0.318 |
| TV Regurgitant Systolic Peak Velocity (m/sec) [$] | 2.84 ± 0.50 | 2.86 ± 0.52 | 2.80 ± 0.45 | 0.038* |
| Estimated RA Pressure (mmHg) | 12 ± 6 | 12.3 ± 5.6 | 12.0 ± 5.6 | 0.374 |
| **Derived Parameters** | | | | |
| Cardiac Power Output (W) | 1.1 ± 0.4 | 1.08 ± 0.39 | 1.10 ± 0.37 | 0.507 |
| Cardiac Power Index (W/m$^2$) [$] | 0.5 ± 0.2 | 0.54 ± 0.19 | 0.56 ± 0.18 | 0.194 |
| LV End Diastolic Pressure (mmHg) [$] | 13 ± 4 | 13.6 ± 4.5 | 13.0 ± 4.3 | 0.069 |
| LV Stroke Work (g.min) | 66 ± 27 | 66 ± 27 | 67 ± 26 | 0.740 |
| LV Stroke Work Index (g.min/m$^2$) | 33 ± 12 | 33 ± 13 | 34 ± 12 | 0.390 |
| Myocardial Contraction Fraction (%) [$] | 23 ± 8 | 24 ± 8 | 23 ± 8 | 0.092 |
| LV Systolic Fractional Shortening (%) | 30 ± 10 | 30 ± 11 | 30 ± 10 | 0.319 |

* Statistically significant (*p*-value ≤0.05).
[$] Included in multivariate analysis (*p*-value ≤0.20).
**LV**, Left Ventricle; **IVS**, Interventricular Septum; **TVI**, Velocity Time Integral; **MV**, Mitral Valve; **PWD**, Pulse Wave Doppler; **LA**, Left Atrium; **RV**, Right Ventricle; **TV**, Tricuspid Valve; **RA**, Right Atrium.

*Table 4. Cardiac function by AKI recovery.*

| Cardiac Function | Total | SA-AKI | | *p*-Value |
|---|---|---|---|---|
| | | Non-recovery | Recovery | |
| Normal | 994 (69.5) | 617 (66.5) | 377 (75) | 0.001* |
| Systolic Dysfunction | 306 (21.4) | 219 (23.6) | 87 (17.3) | 0.212 |
| Diastolic Dysfunction | 131 (9.2) | 92 (9.9) | 39 (7.8) | 0.212 |

* Statistically significant (*p*-value ≤0.05).

*Table 5. TTE predictors of recovery.*

| TTE Parameters | Univariate | | Multivariate | |
|---|---|---|---|---|
| | HR (95% CI) | *p*-Value | HR (95% CI) | *p*-Value |
| **Vital Signs at Time of TTE** | | | | |
| Heart Rate (beat/min) | 0.993 (0.988–0.999) | 0.022* | 0.996 (0.989–1.002) | 0.220 |
| Diastolic Blood Pressure (mmHg) | 1.012 (1.004–1.020) | 0.002* | 1.007 (0.998–1.016) | 0.115 |
| Mean Arterial Pressure (mmHg) | 1.011 (1.003–1.018) | 0.007* | 1.007 (0.998–1.016) | 0.141 |
| **LV Size and Measurements** | | | | |
| IVS Diastolic Thickness (mm) | 0.942 (0.881–1.006) | 0.076 | 0.989 (0.915–1.068) | 0.769 |
| LV Posterior Wall Diastolic Thickness (mm) | 0.890 (0.823–0.962) | 0.003* | 0.951 (0.869–1.041) | 0.278 |
| LV Mass (g) | 0.998 (0.996–1.001) | 0.148 | 1.001 (0.999–1.004) | 0.293 |
| **LV Systolic Function** | | | | |
| LV Ejection Fraction (%) | 1.005 (0.997–1.013) | 0.198 | 1.002 (0.992–1.012) | 0.718 |
| LV Wall Motion Score Index | 0.734 (0.500–1.077) | 0.114 | 0.798 (0.511–1.244) | 0.319 |
| **LV Diastolic Function** | | | | |
| MV A-Wave Peak Velocity (m/sec) | 0.663 (0.399–1.104) | 0.114 | 0.636 (0.357–1.133) | 0.124 |
| MV E-Wave Peak Velocity (m/sec) | 0.625 (0.436–0.895) | 0.010* | 0.827 (0.548–1.246) | 0.364 |
| MV E to e' Ratio | 0.981 (0.961–1.002) | 0.070 | 0.994 (0.970–1.018) | 0.601 |
| LA End Systolic Volume (mL) | 0.994 (0.988–1.000) | 0.037* | 0.995 (0.989–1.001) | 0.108 |
| LA End Systolic Volume Index (mL/m$^2$) | 0.991 (0.980–1.002) | 0.099 | 0.995 (0.989–1.001) | 0.108 |
| **RV Data** | | | | |
| RV End Diastolic Area (cm$^2$) | 0.962 (0.927–0.998) | 0.038* | 0.980 (0.933–1.030) | 0.431 |
| RV Systolic Pressure (mmHg) | 0.988 (0.979–0.997) | 0.012* | 0.991 (0.980–1.001) | 0.091 |
| TV Annulus Systolic Excursion (mm) | 1.099 (1.070–1.128) | <0.001* | 1.112 (1.077–1.148) | <0.001* |
| TV Regurgitant Systolic Peak Velocity (m/sec) | 0.778 (0.607–0.998) | 0.048* | 0.754 (0.561–1.013) | 0.061 |
| **Derived Parameters** | | | | |
| Cardiac Power Index (W/m$^2$) | 1.523 (0.807–2.877) | 0.194 | 1.217 (0.570–2.597) | 0.612 |
| LV End Diastolic Pressure (mmHg) | 0.970 (0.939–1.003) | 0.070 | 0.990 (0.952–1.029) | 0.601 |
| Myocardial Contraction Fraction (%) | 0.984 (0.966–1.003) | 0.092 | 1.009 (0.987–1.031) | 0.428 |

* Statistically significant ($p$-value $\leq$0.05).

**TTE**, transthoracic echocardiogram; **LV**, Left Ventricle; **IVS**, Interventricular Septum; **MV**, Mitral Valve; **LA**, Left Atrium; **RV**, Right Ventricle; **TV**, Tricuspid Valve.

## 4. Discussion

To our knowledge, this is the first study to assess the predictors of moderate-to-severe SA-AKI recovery in critically ill patients and to include echocardiographic data. This study included a large cohort of ICU patients with moderate-to-severe SA-AKI and evaluated the clinical and echocardiographic predictors of recovery. Among the clinical parameters, the strongest predictor of non-recovery was the initiation of a new KRT. Other clinical factors associated with non-recovery from moderate-to-severe SA-AKI were higher peak serum creatinine levels and the presence of KDIGO stage III AKI. In addition, patients with SA-AKI were approximately six times less likely to meet the recovery criteria once KRT was initiated. In contrast, history of CAD was the strongest predictor of recovery. Lower BMI was also an independent predictor of a higher rate of SA-AKI recovery.

The use of echocardiography to guide the management of critically ill patients is becoming increasingly prevalent as the availability of resources increases. Large studies reviewing the utilization of echocardiography (from the MIMIC III database[23]) in ICUs with patients developing AKI have proven its benefit in improving the overall patient-centric outcomes in this patient population (28-day mortality, 1-year mortality, and ventilation-free days).[24] A study by Luo et al. revealed that a 10% increase in cardiac index (CI) after early goal-directed therapy (EGDT) was a protective factor and could predict AKI recovery in septic patients but failed to define a specific CI goal.[25] In addition, poor kidney outcomes were observed in both the high-and low-CI groups.

We found among echocardiogram variables a relatively higher TAPSE to be associated with higher chances of kidney function recovery after moderate-to-severe SA-AKI. Of note, both the recovery and non-recovery groups had TAPSE values in the "normal range" (i.e., 15–25 mm); however, the recovery group had significantly higher TAPSE values when compared to the non-recovery group ($20.4 \pm 6.6$ mm *vs.* $16.8 \pm 5.8$ mm, $p < 0.001$). None of the patients in both groups had documented acute pulmonary embolism at the time of admission. The recovery group TAPSE values probably point towards comparatively robust RV function in response to sepsis. In contrast, the non-recovery group had lower TAPSE values, potentially pointing to a blunted RV response.

Increased pulmonary pressure or systemic volume overload can explain the difference in the

TAPSE ranges between the two groups. In a study by Legrand et al. on hemodynamics in SA-AKI, a high CVP was associated with the development and progression of AKI, regardless of fluid balance and PEEP,[26] supporting the idea that venous congestion plays a role in the pathophysiology of SA-AKI. Therefore, it is plausible that the lower TAPSE in the non-recovery group was due to aggressive fluid resuscitation, leading to RV strain and dysfunction.

### *4.1. Strengths and limitations*

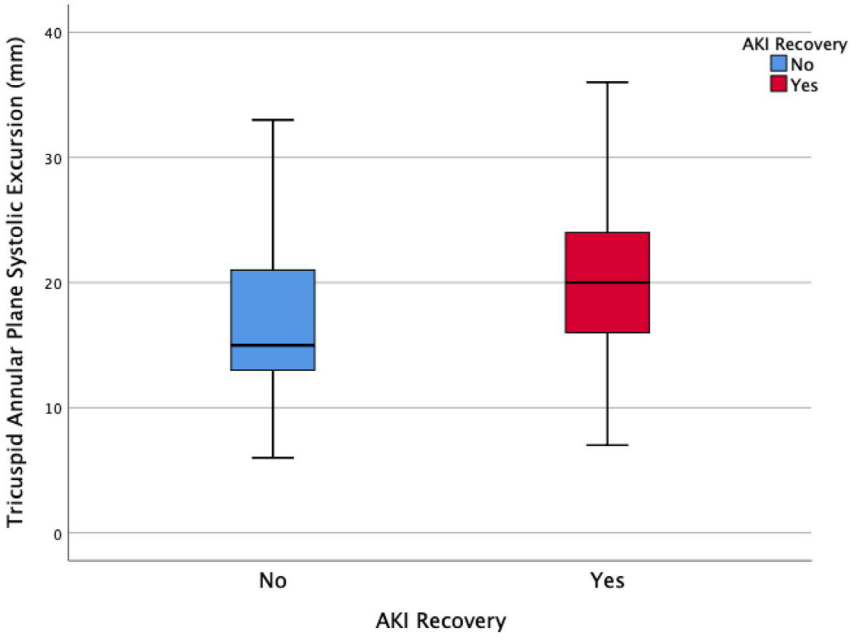
Our study has several strengths. First, to the best of our knowledge, this is the only study to evaluate the clinical and echocardiographic predictors of recovery in moderate-to-severe SA-AKI. Second, the large sample size of the data from our academic center and the validation from previous studies indicate good internal consistency. However, our study is not free from limitations, some of which are inherent in its retrospective design. First, due to the non-availability of echocardiograms within the first 48 h of ICU admission, many patients with SA-AKI were excluded. This was performed deliberately to provide the most accurate temporally associated echocardiographic parameters that could be evaluated for the recovery of moderate-to-severe SA-AKI. Second, although our DataMarts offer a wide range of highly accurate variables, there is always some missingness in the data that cannot be negated in a retrospective study. For example, the rate of missing echocardiographic data in the CV DataMart was approximately 40%. This high rate of missing TTE data could have influenced the results and introduced a bias. Lastly, data from a single large academic center could restrict the generalizability of these results, especially since our sample included approximately 90% whites.

## 5. Conclusion

In conclusion, our data from a large academic center provides nascent information and predictive enrichment regarding the clinical and echocardiographic factors associated with the recovery of moderate-to-severe SA-AKI. There is a definite knowledge gap in the literature regarding management strategies that optimize recovery in moderate-to-severe SA-AKI patients. In our study, we intend to bridge this much-needed deficit. Despite the large sample size and high quality of the data, the retrospective and single-center nature of the study needs further confirmation with more extensive, multicenter, and prospective studies corroborating these findings.

### Conflict of interest

No potential conflict of interest was reported by the authors.



## SUPPLEMENTAL MATERIAL.

*Supplemental 1. Formulas used to calculate derived TTE parameters.*

| Parameter | Formula |
|---|---|
| Body Surface Area (BSA) | BSA (Dubois) = $0.007184 \times \text{Height}^{0.725}$ x $\text{Weight}^{0.425}$ |
| Stroke Volume (SV) | SV = $0.785 \times$ LVOT TVI x $(\text{LVOT Diameter})^2$ |
| Stroke Volume Index (SVI) | SVI = SV/BSA |
| Cardiac Output (CO) | CO = SV/1000 × HR |
| Cardiac Index (CI) | CI = CO/BSA |
| LV Mass Index (LVMI) | LVMI = LV Mass/BSA |
| LA End Systolic Volume Index (LVESVI) | LAESVI = LA ES Volume/BSA |
| Cardiac Power Output (CPO) | CPO = CO x MAP/451 |
| Cardiac Power Index (CPI) | CPI = CI x MAP/451 |
| LV End Diastolic Pressure (LVEDP) | LVEDP = 4.9 + (0.62 × MV E/e' ratio) |
| LV Stroke Work (LVSW) | LVSW = 0.0136 × SV x (MAP - LVEDP) |
| LV Stroke Work Index (LVSWI) | LVSWI = 0.0136 × SVI x (MAP - LVEDP) |
| LV Myocardial Volume (LVMV) | LVMV = $(\text{LVEDD} + \text{PWT} + \text{IVST})^3$ - $\text{LVEDD}^3$ |
| Myocardial Contraction Fraction (MCF) | MCF = SV/LVMV x 100 |
| LV Systolic Fractional Shortening (FS) | FS = (1 - (LVESD/LVEDD)) x 100 |

*Supplemental 2. Definition of systolic and diastolic dysfunction*

| Cardiac Dysfunction | Criteria |
|---|---|
| Systolic Dysfunction | LV EF < 40% |
| Diastolic Dysfunction | LV EF ≥ 40% AND any 3 or more of the following:<br>• MV E to e' Ratio >14<br>• MV Medial Annulus e' Velocity <0.07 (m/sec) OR MV Lateral Annulus e' Velocity <0.10 (m/sec)<br>• TV Regurgitant Systolic Peak Velocity >2.8 (m/sec)<br>• LA End Systolic Volume Index >34 ($\text{mL/m}^2$) |

## References


1. Uchino S, Kellum JA, Bellomo R, et al. Acute renal failure in critically ill patients: a multinational, multicenter study. *JAMA*. 2005;294(7):813−818.
2. Coca SG, Yusuf B, Shlipak MG, Garg AX, Parikh CR. Long-term risk of mortality and other adverse outcomes after acute kidney injury: a systematic review and meta-analysis. *Am J Kidney Dis*. 2009;53(6):961−973.
3. Piccinni P, Cruz DN, Gramaticopolo S, et al. Prospective multicenter study on epidemiology of acute kidney injury in the ICU: a critical care nephrology Italian collaborative effort (NEFROINT). *Minerva Anestesiol*. 2011;77(11):1072−1083.
4. Bougle A, Duranteau J. Pathophysiology of sepsis-induced acute kidney injury: the role of global renal blood flow and renal vascular resistance. *Contrib Nephrol*. 2011;174:89−97.
5. Poston JT, Koyner JL. Sepsis associated acute kidney injury. *BMJ*. 2019;364:k4891.
6. L'Heureux M, Sternberg M, Brath L, Turlington J, Kashiouris MG. Sepsis-induced cardiomyopathy: a comprehensive review. *Curr Cardiol Rep*. 2020;22(5):35.
7. Virzi G, Day S, de Cal M, Vescovo G, Ronco C. Heart-kidney crosstalk and role of humoral signaling in critical illness. *Crit Care*. 2014;18(1):201.
8. Jentzer JC, Bihorac A, Brusca SB, et al. Contemporary management of severe acute kidney injury and refractory cardiorenal syndrome: JACC council perspectives. *J Am Coll Cardiol*. 2020;76(9):1084−1101.
9. Flint N, Kaufman N, Gal-Oz A, et al. Echocardiographic correlates of left ventricular filling pressures and acute cardio-renal syndrome in ST segment elevation myocardial infarction patients. *Clin Res Cardiol*. 2017;106(2):120−126.
10. Choi JS, Baek SH, Chin HJ, et al. Systolic and diastolic dysfunction affects kidney outcomes in hospitalized patients. *BMC Nephrol*. 2018;19(1):292.
11. Wu PS, Wang YW, Tai CC, et al. Early echocardiographic signs of diastolic dysfunction predict acute kidney injury in cirrhotic patients. *J Chin Med Assoc*. 2020;83(11):984−990.
12. Olsson DP, Eck Arvstrand C, Sartipy U, Holzmann MJ. Acute kidney injury after valvular heart surgery and early changes in cardiac function and structure. *Cardiorenal Med*. 2014;4(3−4):201−209.
13. Shacham Y, Gal-Oz A, Topilsky Y, Keren G, Arbel Y. Relation of pulmonary artery pressure and renal impairment in ST segment elevation myocardial infarction patients. *Echocardiography*. 2016;33(7):956−961.
14. Hur M, Nam K, Jo WY, Kim G, Kim WH, Bahk JH. Association between elevated echocardiographic index of left ventricular filling pressure and acute kidney injury after off-pump coronary artery surgery. *Circ J*. 2018;82(3):857−865.
15. Han SS, Park S, Kang SH, et al. Usefulness of preoperative echocardiography to predict acute kidney injury and long-term mortality after coronary artery bypass grafting. *Am J Cardiol*. 2017;119(2):231−236.
16. Chen C, Lee J, Johnson AE, Mark RG, Celi LA, Danziger J. Right ventricular function, peripheral edema, and acute kidney injury in critical illness. *Kidney Int Rep*. 2017;2(6):1059−1065.
17. Lee MJ, Park JS, Kim HH. Diastolic dysfunction is associated with an increased risk of postcontrast acute kidney injury. *Medicine (Baltim)*. 2019;98(48), e17994.
18. Herasevich V, Kor DJ, Li M, Pickering BW. ICU data mart: a non-iT approach. A team of clinicians, researchers and informatics personnel at the Mayo Clinic have taken a homegrown approach to building an ICU data mart. *Healthc Inform*. 2011;28(11):42, 44-45.
19. Kidney Disease: Improving Global Outcomes (KDIGO). Acute kidney injury work group KDIGO clinical practice guideline for acute kidney injury. *Kidney Int Suppl*. 2012;2:1−138.

20. Ahmed A, Vairavan S, Akhoundi A, et al. Development and validation of electronic surveillance tool for acute kidney injury: a retrospective analysis. *J Crit Care*. 2015;30(5): 988−993.
21. Chawla LS, Bellomo R, Bihorac A, et al. Acute kidney disease and renal recovery: consensus report of the Acute Disease Quality Initiative (ADQI) 16 Workgroup. *Nat Rev Nephrol*. 2017;13(4):241−257.
22. Belletti A, Lerose CC, Zangrillo A, Landoni G. Vasoactive-inotropic score: evolution, clinical utility, and pitfalls. *J Cardiothorac Vasc Anesth*. 2021;35(10):3067−3077.
23. Johnson AE, Pollard TJ, Shen L, et al. MIMIC-III, a freely accessible critical care database. *Sci Data*. 2016;3, 160035.
24. Hu Y, Zhou J, Cao Q, et al. Utilization of echocardiography after acute kidney injury was associated with improved outcomes in patients in intensive care Unit. *Int J Gen Med*. 2021; 14:2205−2213.
25. Luo JC, Qiu XH, Pan C, et al. Increased cardiac index attenuates septic acute kidney injury: a prospective observational study. *BMC Anesthesiol*. 2015;15:22.
26. Legrand M, Dupuis C, Simon C, et al. Association between systemic hemodynamics and septic acute kidney injury in critically ill patients: a retrospective observational study. *Crit Care*. 2013;17(6):R278.