Furosemide responsiveness as a predictor of occurrence of acute kidney injury (AKI), AKI progression and need for kidney replacement therapy (KRT) among critically-ill hospitalized patients: A single center study
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Introduction

- The presence and severity of AKI are associated with increased duration of hospital stay, increased resource utilization, increased risk of adverse outcomes and increased risk for subsequent CKD.
- The advent of the development of new therapeutic strategies highlights the parallel need to identify accurate assessment tools for AKI progression and severity that may help identify high-risk patients that will likely benefit from such interventions.
- From the limitations of biomarkers (ie. limited availability, inconsistency among laboratory assays, cost, and dynamic changes over time) arises the need for investigation on functional markers such as furosemide stress test.
- Furosemide is widely available, inexpensive, and has the advantage on its therapeutic role on fluid balance and blood pressure control.

Methods and Materials

The study is a retrospective cohort of all adult patients admitted in the critical care units of St. Luke's Medical Center- Quezon City, Philippines from March 1, 2016 to February 28, 2021. Eligible patients are those referred to Nephrology service, with or without apparent AKI as defined and staged using KDIGO criteria, and who received intravenous bolus of furosemide regardless of dose.

Exclusion criteria included age <18 years, pregnant women, previous kidney transplantation, evidence of obstructive uropathy, baseline eGFR <30 mL/min, necessitating dialysis within 24 hours of admission, moribund patients, volume depletion, known hypersensitivity to loop diuretic, furosemide dose ≥ 120 mg, and administration of additional furosemide dose (infusion or IV bolus) within 24 hours from initial furosemide dose.
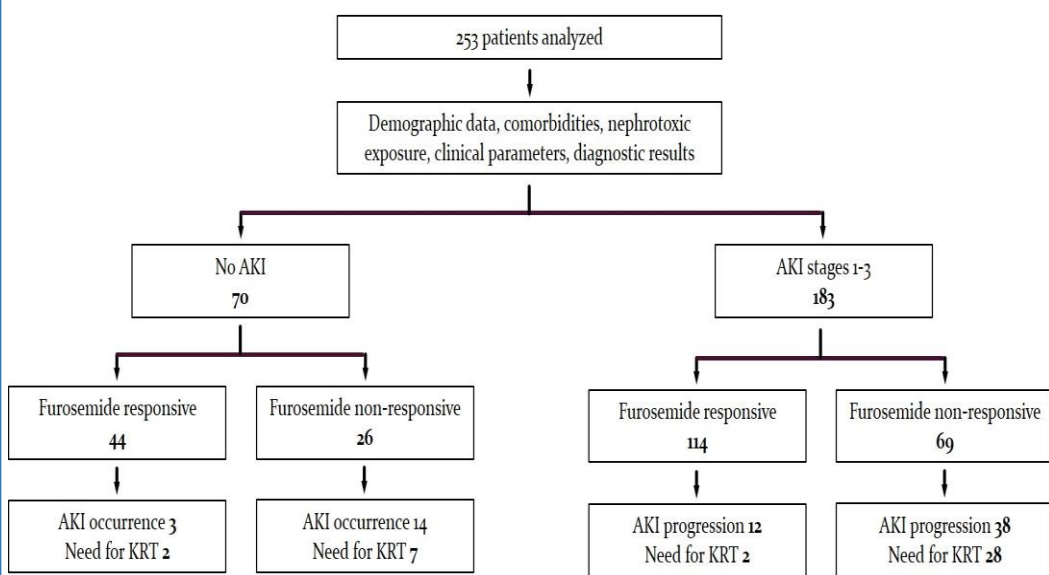

Figure 1. Patient flow

Results

We analyzed a total of 253 adult critically-ill patients—70 with no AKI and 183 with AKI at the time of furosemide administration. Receiver operating curve analysis revealed that among patients with no AKI, FR was able to predict the occurrence of AKI and eventual need for KRT within 7 days with an area under the curve (AUC) values of 0.8. The best cutoff values identified were 33 mL/mg/4h for occurrence of AKI and 24 mL/mg/4h for eventual need for KRT.
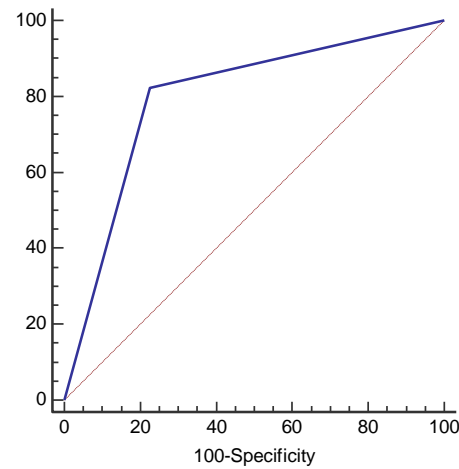

Fig 1. ROC of furosemide responsiveness (cutoff 33 mL/mg/4h) in predicting occurrence of AKI
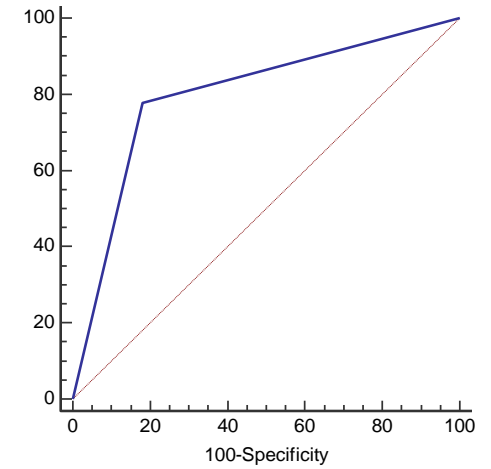

Fig 2. ROC of furosemide responsiveness (cutoff 24 mL/mg/4h) in predicting need for KRT among those with no AKI at baseline

Furthermore, FR was able to predict AKI progression and eventual need for KRT within 7 days among critically-ill patients with AKI with AUC values of 0.76 and 0.77, respectively. The best cutoff values identified were 27 mL/mg/6h for AKI progression and 26.5 mL/mg/6h for eventual need for KRT.
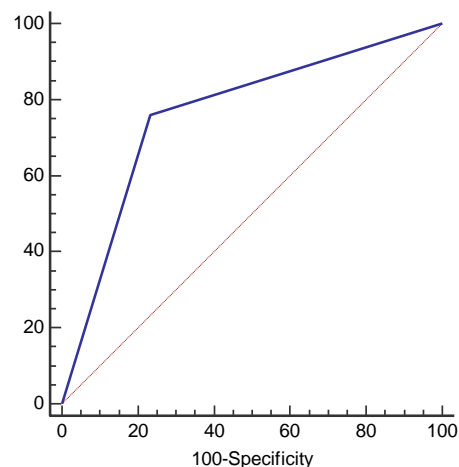

Fig 3. ROC of furosemide responsiveness (cutoff 27 mL/mg/6h) in predicting AKI progression
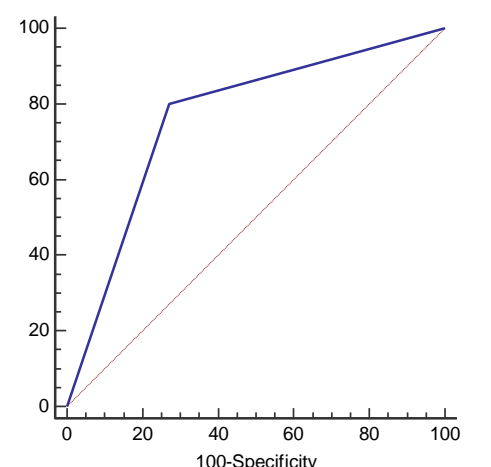

Fig 4. ROC of furosemide responsiveness (cutoff 26.5mL/mg/6h) in predicting need for KRT among those with AKI at baseline

The predictive factor of FR was maintained when adjusted for several factors such as the presence and stage of CKD, heart failure, various nephrotoxic exposure, prior use of loop diuretic or other diuretics, need for pressor and/or inotrope, urine output in the prior 12 hours, creatinine clearance <20 mL/min and hypoalbuminemia.

Conclusions

Despite the use of varying doses of furosemide, FR has a good predictive ability in identifying critically-ill patients who are likely to have eventual occurrence of AKI, AKI progression, and/or need for KRT.