PLASMA RENALASE AS A BIOMARKER OF ACUTE RENAL INJURY AFTER CARDIAC SURGERY

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BACKGROUND/OBJECTIVE

- Renal ischemia/reperfusion injury (IRI) is a frequent potentially reversible cause of acute kidney injury (AKI)[1,2]. Ischemic AKI is a major cause of morbidity and mortality after cardiac surgery[3].
- The scarcity of early biomarkers and validated risk models for predicting acute kidney injury (AKI) has hindered our ability to launch potentially preventive and therapeutic measures in a timely manner[4].
- Renalase, a key player in catecholamine equilibrium was shown to protect against ischemic AKI in animal models[5].
- We **tested** the hypothesis that plasma renalase is an early biomarker for ischaemic renal injury after cardiac surgery.

METHODS

- This **prospective cohort** study included 40 adult patients undergoing cardiac surgery at Cairo University Hospital (Cairo, Egypt). All patients undergoing cardiopulmonary bypass for cardiac surgery between January, 2015, and December, 2015, were enrolled.
- **Exclusion** criteria included pre-existing renal insufficiency, renal transplant patients, peripheral vascular disease, and use of nephrotoxic drugs before or during the study period.
- Demographic, clinical, laboratory, operative and postoperative **variables** were evaluated (Table 1). Plasma renalase levels (ELISA) were measured before surgery and 18 - 24 hours after surgery. NGAL levels (ELISA) were measured 18 - 24 hours after surgery.
- The **primary outcome** measure was AKI diagnosed by the Acute Kidney Injury Network (AKIN) criteria defined as a 50% or greater increase in serum creatinine from baseline **or** more than 0.3 mg/dL within 72 hours after surgery

RESULTS

Table (1): Clinical and laboratory characteristics of study population

	Total (N = 40)	AKI (n = 25)	No AKI (n = 15)	*P*
Male Gender	27 (67.5 %)	14 (56 %)	13 (86.6 %)	0.4
Age (y)	47.67 ± 12.8	47.64 ± 12.7	47.7 ± 13.4	0.98
Serum creatinine (mg/dL)	0.901 ± 0.22	0.9 ± 0.238	0.9 ± 0.19	0.73
eGFR (ml/min)	89.17 ± 27.9	88.96 ± 32.62	89.5 ± 18.8	0.95
Cardiopulmonary bypass (CPB) time (min)	85 ± 19.39	91.08 ± 21.34	75.06 ± 9.7	0.01*
Aortic cross-clamp time (AXT) (min)	66.1 ± 16.96	71.4 ± 18.35	57.3 ± 9.5	0.009*
Vasopressor/ inotropic support (No - %)	21 (52.5 %)	15 (60 %)	6 (40 %)	0.009*
Length of ICU stay (d)	4.95 ± 1.98	5.6 ± 1.9	3.8 ± 1.56	0.004*
Length of hospital stay (d)	14.675 ± 4.8	16.04 ± 5.2	12.4 ± 3	0.018*
Peak serum creatinine (mg/dL)	1.35 ± 0.84	1.5 ± 1.04	1.12 ± 0.18	0.17
Δ Serum creatinine (mg/dL)	0.45 ± 0.733	0.6 ± 0.9	0.2 ± 0.07	0.09
% change serum creatinine	47.7 ± 49.2	62.3 ± 57.3	23.3 ± 9.7	0.001*
Continuous hemodialysis (No - %)	1 (2.5 %)	1 (4 %)	0 (0%)	0.07
ICU Mortality (No - %)	3 (7.5 %)	2 (8%)	1 (6.6 %)	0.127
Preop renalase (ng/ml)	1.18 ± 0.44	1.204 ± 0.46	1.14 ± 0.41	0.675
Postop renalase (24 hours)(ng/ml)	0.95 ± 0.4	0.89 ± 0.42	1.04 ± 0.35	0.27
Δ Renalase (ng/ml)	0.23 ± 0.19	0.3 ± 0.18	0.1 ± 0.11	0.0003*
Percent of Δ Renalase	19.8 ± 15.67	26.9 ± 14.8	7.92 ± 8.08	< 0.0001*
Postop NGAL (24 hours)(ng/ml)	1.78 ± 0.3	1.84 ± 0.33	1.69 ± 0.24	

Values expressed as mean ± SD or number (percent).

- The demographic, clinical, laboratory and perioperative features of patients are shown in table (1). Of 40 patients, 25 patients (62.5 %) developed AKI after surgery. Plasma concentrations of renalase decreased significantly from a mean of 1.2 0.46 ng/ml at baseline to 0.9 0.42 ng/ml 18 - 24 hours after cardiopulmonary bypass, with a mean % change of 27 14.8 in the AKI group (Fig 1,2).
- In patients with AKI, univariete linear regression analysis showed that percent of Δ renalase correlated positively with peak Cr, change in Cr, % change in Cr, Δ renalase, NGAL, CPB time, AXT, ICU and hospital stay durations; while correlated negatively with EF, and postoperative renalase (Fig 3).

RESULTS (cont'd)

- Receiver operating characteristic (ROC) analysis revealed that for % change in plasma renalase concentrations at 18 - 24 h, the AUC was 0·9, sensitivity 0.92, specificity 0·87, PPV was 0.92, NPV was 0.87 and likelihood ratio of 7.07 for a cutoff value of 9 % change (Fig 4).

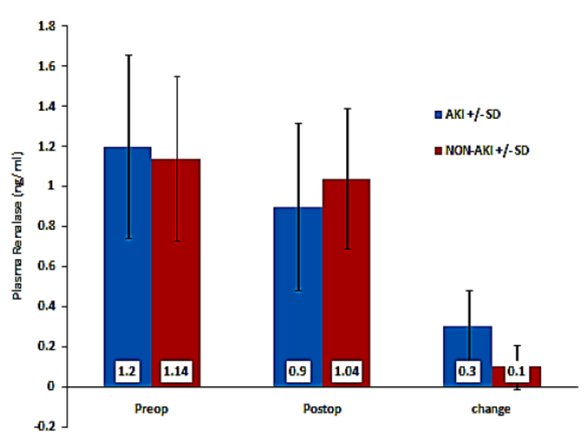

Fig 1. Plasma renalase levels before (PreOP) and after (PostOP) cardiac surgery (hours) in patients with or without acute kidney injury

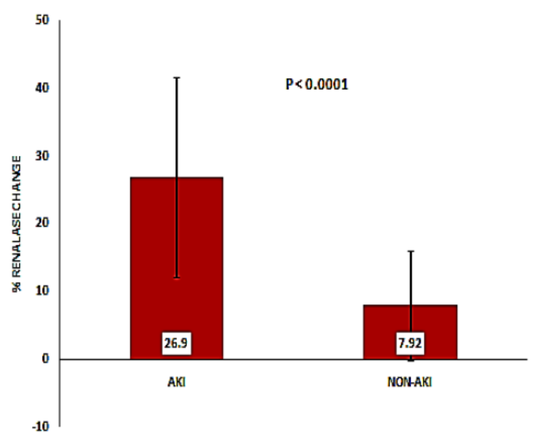

Fig 2. Percent change in plasma renalase levels after cardiac surgery (hours) in patients with or without acute kidney injury

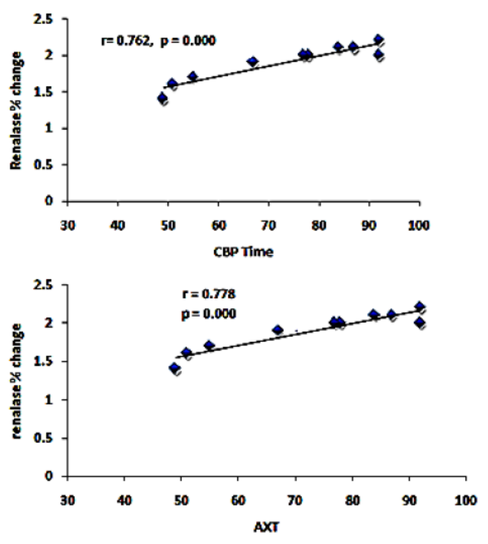

Fig 3. Correlation Between CBP Time or AXT and plasma renalase percent change.

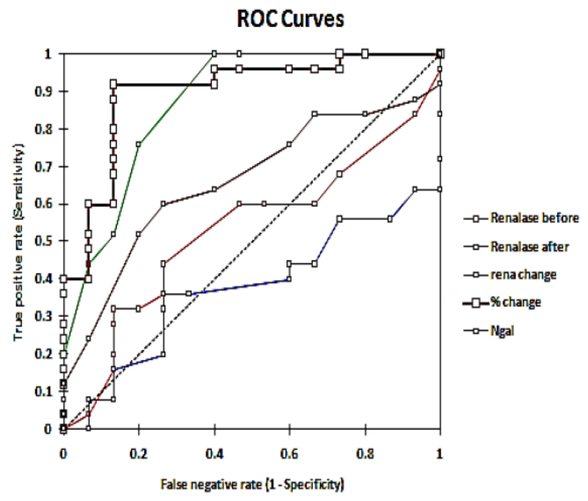

Fig 4. Receiver operating characteristic curves for plasma renalase and urinary NGAL as predictors of acute kidney injury (AKI).

DISCUSSION

- This study showed that plasma renalase may serve as a novel and sensitive biomarker for the early detection of ischemic AKI post-cardiac surgery. Our results compare favourably with those obtained for several other biomarkers of ischaemic renal injury[6].
- As far as we know, this is the first study investigating the possible role of plasma renalase for the early diagnosis of ischaemic renal injury.
- Our **limitations** in this study include being a single-centre study, small sample size, observational nature of the study, postoperative measurement of biomarkers at single timepoint, and finally, we did not simultaneously study both urine and serum samples.

CONCLUSION

- Our hypothesis that plasma renalase might represent an early biomarker of ischaemic renal injury in patients undergoing cardiac surgery was confirmed in a prospective cohort study.
- The rate of change of plasma renalase from baseline was more accurate predictor of AKI than absolute values.
- Our findings provide a conceptual framework for further larger randomized studies in AKI in sepsis and drug nephrotoxicity.

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