

GLUTAMYL AMINOPEPTIDASE ACTIVITY IN MICROSOMAL FRACTION OF URINE IS AN EARLY BIOMARKER OF AKI IN PATIENTS UNDERGONE TO CARDIAC SURGERY

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OBJECTIVES

The aim of this work is to analyze if glutamyl aminopeptidase (GluAp) activity measured in microsomal fraction of urine is an early marker of acute kidney injury (AKI) in patients undergone to cardiac surgery.

	No AKI (n=27)	AKI (n=33)
Proteinuria (mg/mg Cr)	11.4 ± 1.89	17.3 ± 2.37
Microalbuminuria (mg/mg Cr)	0.58 ± 0.09	0.69 ± 0.09
NAG (mU/mg Cr)	110 ± 22.1	165 ± 31.3
NGAL (NG/MG Cr)	14.6 ± 1.97	32.0 ± 7.79
β2-microglobuline	85.8 ± 13.1	85.2 ± 13.0
AlaAp (nmol/min/mg Cr)	7.54 ± 0.98	10.3 ± 3.14
GluAp (nmol/min/mg Cr)	3.60 ± 0.42	5.18 ± 0.95
Microsomal AlaAp (nmol/min/mg Cr)	1.01 ± 0.30	1.34 ± 0.29
Microsomal GluAp (pmol/min/mg Cr)	90.3 ± 23.3	152 ± 28.0*

Table 1. Urinary markers measured at income in ICU in patients that developed AKI within 48 hours after surgery AKI and patients that did not develop AKI. * p<0.05 vs no AKI patients.

	AUC	Sensitivity (%)
Proteinuria (mg/mg Cr)	0.6355	15.3
Microalbuminuria (mg/mg Cr)	0.5360	11.6
NAG (mU/mg Cr)	0.5697	15.0
NGAL (NG/MG Cr)	0.6064	21.8
β2-microglobuline	0.4712	9.58
AlaAp (nmol/min/mg Cr)	0.4856	11.6
GluAp (nmol/min/mg Cr)	0.5546	13.2
Microsomal AlaAp (nmol/min/mg Cr)	0.6203	8.22
Microsomal GluAp (pmol/min/mg Cr)	0.6598	12.2

Table 2. ROC-AUC and sensitivity at 95 % of specificity of urinary markers to distinguish AKI from no AKI patients at income in ICU.

METHODS

60 patients were selected for the study.

Blood and urine samples were taken before surgery, and at income in Intensity Care Unit (ICU), 12, 24 and 48 hours after surgery.

Proteinuria, microalbuminuria, NAG, NGAL, β2-microglobuline, alanyl aminopeptidase (AlaAp) and GluAp were measured in all urine samples at income in ICU.

Urines were subjected to two serial centrifugation steps at 400 g 5 minutes, obtaining a sediment that contained whole cells and debris, and at 17.000 g in order to obtain a microsomal fraction containing microvesicles, ectosomes and large membrane fragments. These fractions were redissolved in 10 mM HCl-Tris, pH 8.6. AlaAp and GluAp activity were measured in both fractions of urine.

Serum creatinine (SCr) value determined at income, 12, 24 or 48 hours after surgery was used to classify patients in:

- AKI (increased creatinine of ≥ 0.3 mg/dl or increase to $\geq 150\%$ from baseline, n=33) or
- No AKI (n=27).

ROC-AUC curves were built in order to analyze sensitivity and specificity of the different markers to differentiate between AKI and No AKI.

RESULTS

At income in ICU, GluAp activity in microsomal fraction of urine was the only urinary marker that was significantly higher in patients that developed AKI vs patients that did not develop AKI (Table 1). Microsomal GluAp exhibited a larger ROC-AUC to distinguish patients that developed AKI than the rest of urinary markers (Table 2). A simultaneous criterium of SCr and microsomal GluAp increased sensitivity from 15.2 (SCr ≥ 0.3) to 39.4 % (SCr ≥ 0.3 or GluAp ≥ 191).

CONCLUSIONS

We conclude that GluAp activity in microsomal fraction of urine is an early biomarker of AKI development after cardiac surgery. Microsomal fraction of urine is a promising source of biomarkers for AKI and other renal pathologies.

