

URINARY NETRIN-1 PREDICT EARLY ISCHEMIC ACUTE KIDNEY INJURY AFTER CARDIOPULMONARY BYPASS

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Objectives:

- Acute kidney injury is a common and serious postoperative complication of cardiac surgery requiring cardiopulmonary bypass (CPB). Several studies reported that even mild increases in serum creatinine levels following cardiac surgery were associated with significant effects on mortality (2), long-term survival was depending AKI duration (3), and early recovery of renal function was associated with improved long-term survival after CSA-AKI. Experimental studies have identified interventions that may prevent or treat AKI if instituted early in the disease process, well before the serum creatinine rises. The lack of early predictive biomarkers has impaired our ability to translate these promising findings to human AKI.
- The netrins are laminin-related proteins, which was discovered as a kidney injury marker during spatial and temporal expression studies in the kidney after ischemia followed by reperfusion (4). This study was designed to test urinary netrin-1 as marker of early kidney injury post cardiac surgery.

Methods:

- All patients who underwent to cardiac surgery using Cardio-Pulmonary Bypass (CPB) were included in the study except those who were excluded by exclusion criteria then division of total subjects into two main groups (AKI and NON-AKI groups) according to their post-operative rise of serum creatinine depending on KDIGO definition of AKI as increase in serum creatinine by > 0.3 mg/dl within 48 hours (KDIGO 2012). All subjects were selected to be free from chronic kidney disease, hypertension (BP > 140/90), diabetes mellitus, liver diseases, collagen diseases, sepsis and malignancy. All subjects were subjected to: full medical history and complete clinical examination, Complete blood picture, fasting plasma glucose level, Liver function. Measurement of basal serum creatinine and urinary netrin-1 by ELISA then 6 hours and 24 hours after Cardiac surgery. Calculation of glomerular filtration rate using MDRD equation basal, 6 hours and 24 hours after Cardiac surgery.

Validity of the studied biomarker as predictor for AKI 6 hours after CPB	Biomarker	Sensitivity	specificity	PPV	NPV	P
	Urinary netrin-1 6hours after CPB (pg/ml)	86.7%	91.7%	86.6%	91.6%	< 0.001**
	Serum creatinine (mg/dl)	53.3%	66.7%	50%	69.5%	0.21
	Combined Urinary netrin and Serum creatinine	86.7%	91.7%	86.6%	91.6%	< 0.001**

Results:

14 patient developed AKI after cardiac surgery. A statistically significant elevation urinary netrin-1 at 6 and 24 hours after CPB surgery in the AKI group while serum creatinine failed to show any statistically significant elevation at 6 hours after CPB in the same group. No statistically significant change in level of creatinine or urinary netrin-1 at 6 and 24 hours after CPB surgery in the non AKI group. The sensitivity and specificity of urinary netrin-1 to detect AKI at 6 h after CPB surgery was 86.7% and 91.7% respectively at a cutoff value of 107.3 pg/ml. Combined urinary netrin-1 and serum creatinine have the same sensitivity and specificity.

- In conclusion, urinary netrin-1 may be considered as early sensitive and specific biomarker of acute kidney injury at 6 hours after cardiac surgery requiring cardiopulmonary bypass instead of rise in serum creatinine that delayed 24-48 hours after surgery in cardiac surgery associated- acute kidney injury patients.

Conclusions:

- Mao H, Katz N, Ariyanon W, Blanca-Martos L, Adýbelli Z, et al (2013): Cardiac Surgery-Associated Acute Kidney Injury. *Cardiorenal Med J.* (3):178-99.
- Ramesh G, Krawczeski C, Woo J, Wang Y, Devarajan P (2010): Urinary netrin-1 is an early predictive biomarker of acute kidney injury after cardiac surgery. *Clin JAm Soc Nephrol.*;5:395-401.
- .Brown JR, Kramer RS, Coca SG, Parikh CR (2010): Duration of acute kidney injury impacts long-term survival after cardiac surgery. *Ann Thorac Surg* 43: 993-9.
- Wang W, Brian RW, Ramesh G (2008): Netrin-1 and kidney injury. I. Netrin-1 protects against ischemia reperfusion injury of the kidney. *Am J Physiol Renal Physiol*; 294(4):F739-47.

References: