Elevation of troponin T and N-terminal pro-B-type natriuretic peptide (nt- pro BNP) in heart failure patients with CKD

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Abstract

Elevation of Troponin T and N-Terminal pro-B-type natriuretic peptide (NT-proBNP) are commonly and strongly predictable biomarkers of Heart Failure (HF) patients with CKD. The present study included 150 people with CKD. We examined the association of baseline levels of elevation of TnT and NT-pro BNP with Heart Failure (HF) and CKD patients, after the adjustment for demographic factors, traditional cardiovascular risk factors and biomarkers of Chronic Kidney Disease. Constant medication application and mineral metabolism biomarkers cause Heart Failure and CKD. At base line, elevation of TnT levels ranged from <_5.0 to 1000 pg/ml and NT-proBNP levels ranged from <_5.0 to 35000 pg/ml. Compared to normal controls for TnT <_5.8 – 25.8 pg/ml and NT_proBNP 54 – 340 pg/ml. With this conclusion the elevation of TnT and NT-prBNP were strongly associated with incident of Heart Failure (HF) among with severe

With this conclusion the elevation of ThT and NT-prBNP were strongly associated with incident of Heart Failure (HF) among with severe CKD. Elevations in these biomarkers may indicate subclinical changes in volume and myocardial stress that subsequently contribute to clinical Heart Failure (HF) with CKD.

Keywords: Cardiovascular disease, Heart failure, Kidney disease, Troponin T and N-Terminal pro-B-type natriuretic peptide (NT-proBNP).

Introduction

Raised Troponin T and N - Terminal Pro - B - type Natriuretic Peptide (NT - pro BNP) are more significant in cardiac problems and in chronic renal failure. However in heart attack, they rise and fall but in renal failure the rise is constant. Troponin T regulate heart muscles and tissue contraction. NT - pro BNP is vasopeptide hormones that have major role in regulating blood pressure (BP) and volume through direct effects on the kidney and systemic vasculature and represent a favorable aspects of neurohumoral activation. Troponin is a group of three proteins Troponin C, T, and I Troponin I T are the cardiac markers, they regulate heart muscle and tissue contraction. These proteins are released after the damage of heart muscles. The greater the damage to the heart, the higher the Troponin levels in the blood. Troponin levels may be rise approximately 4 to 6 hours after heart damage. Troponin in blood remain raised upto two weeks. Three different natriuretic peptides have been characterized namely A type (atrial) natriurectic peptide, B type (brain) natriurectic peptide (BN) and C type natriuretic peptide. BNP is synthesized as amino acid precursor protein and undergoes intrcellular modification to a pro hormone (Pro BNP) which comprises 108 amino acids and is secreted from left ventricle (LV) in response to increased myocardial wall stress. It is also found in the kidney glomerular filtration. It has major role in the elimination of BNP. In contrast NT – pro - - BNP is thought to be principally cleared by renal excretion.

Heart Failure (HF) is the most common cardiovascular complication among patients with Chronic Kidney Disease (CKD) and it imposes significant morbidity and mortality. Among people with CKD subclinical cardiac dysfunction e.g early changes in left ventricular structure and function) The cardiac biomarkers high sensitivity Troponin T (hs TnT) and N – terminal pro – B - type natriuretic peptide (NT – pro BNP) have been shown to predict heart failure in the general population. The use of hs TnT and NT – pro BNP to aid in the diagnosis of heart failure among patients with CKD. It has been limited because of concerns that elevated levels may be caused by reduced renal excretion. The elevation in TnT and NT – pro BNP would be independently associated with incident Heart Failure (HF) among patients with mild to severe Chronic Kidney Disease (CKD)

Material and Methods

The present study included 150 patients with end-stage renal failue undergoing chronic hemodialysis, all patients were examined by electrocardiography and two - dimensional echocardiography, at the Departments of Cardiology, Nephrology, Biochemistry and Physiology, Shadan Institue of Medical Sciences, Teaching Hospital & Research Centre, R.R District, Telangana State, India. Based on the examination results patients were found for concentric left ventricular hypertrophy, Acute Myocardial Infarction (AMI) and signs of Coronary Artery Disease (CAD) Heart Failure (HF). Blood was collected from patients before dialysis. Renal Function Test (RFT) was measured in Cobas clinical Analyser and serum electrolytes were measured in ST - 200 PLUS Electrolytes Analyzer Sensa Core. The serum TnT was measured on an ES 700 analyser (Roche Diagnostics) and NT - ProBNP was measured on Mini Vidas (Roche Diagnostics) We have examined the association of baseline levels of elevation of TnT and NT - pro BNP with Heart Failure (HF) and Chronic Kidney Disease (CKD) patients, after adjustment for their demographic facroes, traditional cardiovascular risk factors clinical and biomarkers of Heart Failure (HF) and Chronic Kidney Disease (CKD). The patients for constant medication application and mineral

Characteristics	Patients	Controls	P Value
Age (Years)	40 - 60	30 - 50	< 0.001
Sex (Male%)	50 - 60	40 - 60	
(Female%)	30 - 40	30 - 50	
Body Mass Index kg/m2	35 - 40	30 - 35	
Blood Pressure mm/Hg			
Systolic	120 - 180	110 - 120	
Diastolic	100 - 120	70 - 80	
Renal Function Test (RFT)			
Blood Urea (mg/dl)	80 - 185	15 - 40	< 0.001
Serum Creatinine (mg/dl)	4.5 - 12.5	0.8 - 1.5	
Serum Uric Acid (mg/dl)	8.5 - 10.5	3.5 - 7.0	
Serum Potassium (mEq/L)	5.0 - 8.0	3.5 - 5.0	
GRF (Ru/ml)	150 - 300	110 - 200	
24 Hours Urinary Proteins (g/day)	1.0 - 2.5	0.08 - 0.9	
hs TnT pg/ml	> 10000	5 - 25	
NT – pro BNP pg/ml	> 35000	55 - 340	< 0.001

Table 1: Demographic, Clinical and Physiobiochemical characteristics of Heart Failure (HF) and Chronic Kidney Disease (CKD) patients

P values <0.001 are subject to all the parameters

metabolism biomarkers cause Heart Failue (HF) and Chronic Kidney Disease (CKD). At the base line elevation of TnT levels ranged from <_ 5.0 to 1000 pg/ml and NT – pro BNP levels ranged from <_ 5.0 to 35000 pg/ml. This is compared to normal controls for TnT <_ 5.0 to 25.8 pg/ml and NT – proBNP 54.5 to 340 pg/ml. With this conclusion elevation of TnT and NT- ProBNP were strongly associated with incident of Heart Failure (HF) among with the severe Chronic Kidney Disease (CKD). Elevation in these biomarkers may indicate subclinical changes in volume and myocardial stress that subsequent contributed to clinical Heart Failure (HF) and with Chronic Kidney Disease (CKD).

Results

Among participants in our study for Heart Failure (HF) with Chronic Kidney Disease (CKD) The elevated average mean SD _+ values were found as mean age was 58.5, for both male and female, mean body mass index mean 32.5 kg/m2, mean blood pressure systolic 150mm/Hg, diastolic 110 mm/Hg, renal function test mean blood urea 132.5 mg/dl, mean serum creatinine 8.50 mg/dl, mean serum uric acid 9.5 mg/dl.Mean serum potassium level was 6.5 mEq/L, Mean Glomerular Filtration Rate (GRF) was 225 Ru/ml and Mean 24 hours urinary protein was 1.75 g/day. Beside the above elevated values in Heart Failue (HF) and Chronic Kidney Disease (CKD) patients more significant for hTNT > 10000 pg/ml and NT- pro – BNP > 35000 pg/ml were found.

Conclusion

In conclusion among patients with Chronic Kidney Disease (CKD), elevated levels of hs TNT and NT- proBNP were strongly associated with incident with Heart Failure (HF), even after adjustment for a broad range of demographic, traditional, clinical and physiobiochemical may indicate

early changes in volume and myocardial stress that subsequently contribute to clinical Heart Failure (HF).

Conflict of Interest: None.

References

- Kottgen A, Russell SD, Loehr LR, Crainiceanu CM, Rosamond WD, Chang PP et al, Reduced kidney function as a risk factor for incident heart failure: The atherosclerosis risk in communities (ARIC) study. *J Am Soc Nephrol* 2007;18:1307– 15.
- Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY: Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *N Engl J Med* 2004;351:1296–1305,
- Foley RN, Curtis BM, Randell EW, Parfrey PS: Left ventricular hypertrophy in new hemodialysis patients without symptomatic cardiac disease. *Clin J Am Soc Nephrol* 2010;5:805–13.
- Yamada S, Ishii H, Takahashi H, Aoyama T, Morita Y, Kasuga H et al, Prognostic value of reduced left ventricular ejection fraction at start of hemodialysis therapy on cardiovascular and all-cause mortality in end-stage renal disease patients. *Clin J Am Soc Nephrol* 2010;5:3–1798.
- Saunders JT, Nambi V, de Lemos JA, Chambless LE, Virani SS, Boerwinkle E et al, Cardiac troponin T measured by a highly sensitive assay predicts coronary heart disease, heart failure, and mortality in the Atherosclerosis Risk in Communities Study. *Circ* 123: 1367–1376, 2011
- deFilippi CR, de Lemos JA, Christenson RH, Gottdiener JS, Kop WJ, Zhan M et al, Association of serial measures of cardiac troponin T using a sensitive assay with incident heart failure and cardiovascular mortality in older adults. *JAMA* 304: 2494–2502, 2010
- Yasue H, Yoshimura M, Sumida H, Kikuta K, Kugiyama K, Jougasaki M et al, Localization and mechanism of secretion of B-type natriuretic peptide in comparison with those of A-type natriuretic peptide in normal subjects and patients with heart failure. *Circ* 1994;90:195–203.
- 8. Vickery S, Price CP, John RI, Abbas NA, Webb MC, Kempson ME et al, B-type natriuretic peptide (BNP) and

amino-terminal proBNP in patients with CKD: Relationship to renal function and left ventricular hypertrophy. *Am J Kidney Dis* 2005;46: 610–20.

- Mishra RK, Li Y, Ricardo AC, Yang W, Keane M, Cuevas M et al, Chronic Renal Insufficiency Cohort Investigators: Association of N-terminal pro-B-type natriuretic peptide with left ventricular structure and function in chronic kidney disease (from the Chronic Renal Insufficiency Cohort [CRIC]). Am J Cardiol 2013;111:432–8.
- 10. DeFilippi CR, Fink JC, Nass CM, Chen H, Christenson R: Nterminal pro-B-type natriuretic peptide for predicting coronary disease and left ventricular hypertrophy in asymptomatic CKD not requiring dialysis. *Am J Kidney Dis* 2005;46:35–44.
- 11. de Lemos JA, Drazner MH, Omland T, Ayers CR, Khera A, Rohatgi A et al, Association of troponin T detected with a highly sensitive assay and cardiac structure and mortality risk in the general population. *JAMA* 304: 2503–2512, 2010
- Mishra RK, Li Y, DeFilippi C, Fischer MJ, Yang W, Keane M et al, CRIC Study Investigators: Association of cardiac troponin T with left ventricular structure and function in CKD. Am J Kidney Dis 2013;61:701–9.
- Tsutamoto T, Kawahara C, Yamaji M, Nishiyama K, Fujii M, Yamamoto T et al, Relationship between renal function and serum cardiac troponin T in patients with chronic heart failure. *Eur J Heart Fail* 2009;11: 653–8.
- Wallace TW, Abdullah SM, Drazner MH, Das SR, Khera A, McGuire DK et al, Prevalence and determinants of troponin T elevation in the general population. *Circ* 113: 1958–1965, 2006
- Wiessner R, Hannemann-Pohl K, Ziebig R, Grubitzsch H, Hocher B, Vargas-Hein O et al, Impact of kidney function on plasma troponin concentrations after coronary artery bypass grafting. *Nephrol Dial Transplant* 2008;23:231–8.
- Freda BJ, Tang WH, Van Lente F, Peacock WF, Francis GS: Cardiac troponins in renal insufficiency: Review and clinical implications. J Am Coll Cardiol 2002; 40:2065–71.
- 17. Scheven L, de Jong PE, Hillege HL, Lambers Heerspink HJ, van Pelt LJ, Kootstra JE et al, PREVEND study group: Highsensitive troponin T and N-terminal pro-B type natriuretic peptide are associated with cardiovascular events despite the cross-sectional association with albuminuria and glomerular filtration rate. *Eur Heart J* 2012;33: 2272–81.
- deFilippi C, Seliger SL, Kelley W, Duh SH, Hise M, Christenson RH et al, Interpreting cardiac troponin results from high-sensitivity assays in chronic kidney disease without acute coronary syndrome. *Clin Chem* 2012;58:1342–51.
- Fichtlscherer S, Breuer S, Zeiher AM: Prognostic value of systemic endothelial dysfunction in patients with acute coronary syndromes: Further evidence for the existence of the "vulnerable" patient. *Circ* 110: 1926–1932, 2004
- 20. Ooi DS, Isotalo PA, Veinot JP: Correlation of antemortem serum creatine kinase, creatine kinase-MB, troponin I, and troponin T with cardiac pathology. *Clin Chem* 2000;46: 338–44,
- 21. Korff S, Katus HA, Giannitsis E: Differential diagnosis of elevated troponins. *Heart* 2006;92: 987–93.
- Hasegawa M, Ishii J, Kitagawa F, Kanayama K, Takahashi H, Ozaki Y et al. Prognostic value of highly sensitive troponin T on cardiac events in patients with chronic kidney disease not on dialysis. *Heart Vessels* 2013;28: 473–9.
- deFilippi C, Wasserman S, Rosanio S, Tiblier E, Sperger H, Tocchi M et al, Cardiac troponin T and C-reactive protein for predicting prognosis, coronary atherosclerosis, and cardiomyopathy in patients undergoing long-term hemodialysis. *JAMA* 2003;290: 353–59,
- 24. Madsen LH, Ladefoged S, Corell P, Schou M, Hildebrandt PR, Atar D: N-terminal pro brain natriuretic peptide predicts

mortality in patients with end-stage renal disease in hemodialysis. *Kidney Int* 2007;71:548–54.

- 25. Cleland JG, Taylor J, Freemantle N, Goode KM, Rigby AS, Tendera M: Relationship between plasma concentrations of Nterminal pro brain natriuretic peptide and the characteristics and outcome of patients with a clinical diagnosis of diastolic heart failure: A report from the PEP-CHF study. *Eur J Heart Fail* 2012;14: 487–94.
- Kistorp C, Raymond I, Pedersen F, Gustafsson F, Faber J, Hildebrandt P: N-terminal pro-brain natriuretic peptide, Creactive protein, and urinary albumin levels as predictors of mortality and cardiovascular events in older adults. *JAMA* 2005;293:1609–16.
- 27. Yi S, Contreras G, Miller ER, Appel LJ, Astor BC: Correlates of N-terminal prohormone brain natriuretic peptides in African Americans with hypertensive chronic kidney disease: The African American Study of Kidney Disease and Hypertension. *Am J Nephrol* 2009;29: 292–8.
- Tagore R, Ling LH, Yang H, Daw HY, Chan YH, Sethi SK et al. Natriuretic peptides in chronic kidney disease. *Clin J Am Soc Nephrol* 2008;3:1644–51.
- Takami Y, Horio T, Iwashima Y, Takiuchi S, Kamide K, Yoshihara F et al, Diagnostic and prognostic value of plasma brain natriuretic peptide in non-dialysis-dependent CRF. *Am J Kidney Dis* 2004;44:420–28.
- deFilippi CR, Seliger SL, Maynard S, Christenson RH: Impact of renal disease on natriuretic peptide testing for diagnosing decompensated heart failure and predicting mortality. *Clin Chem* 2007;53: 1511–19.
- 31. Astor BC, Yi S, Hiremath L, Corbin T, Pogue V, Wilkening B, Peterson G, Lewis J, Lash JP, Van Lente F, Gassman J, Wang X, Bakris G, Appel LJ, Contreras G: N-terminal prohormone brain natriuretic peptide as a predictor of cardiovascular disease and mortality in blacks with hypertensive kidney disease: The African American Study of Kidney Disease and Hypertension (AASK). *Circ* 2008; 117: 1685–92.
- 32. Gore MO, Seliger SL, Defilippi CR, Nambi V, Christenson RH, Hashim IA et al, Age- and sex-dependent upper reference limits for the high-sensitivity cardiac troponin T assay. *J Am Coll Cardiol*2014;63:1441–8.
- 33. Apple FS, Quist HE, Doyle PJ, Otto AP, Murakami MM: Plasma 99th percentile reference limits for cardiac troponin and creatine kinase MB mass for use with European Society of Cardiology/American College of Cardiology consensus recommendations. *Clin Chem* 2003;49: 1331–6.
- Fradley MG, Larson MG, Cheng S, McCabe E, Coglianese E, Shah RV et al, Reference limits for N-terminal-pro-B-type natriuretic peptide in healthy individuals (from the Framingham Heart Study). *Am J Cardiol* 2011;108:1341–5.
- Kruger R, Schutte R, Huisman HW, Hindersson P, Olsen MH, Eugen-Olsen J et al, NT-proBNP, C-reactive protein and soluble uPAR in a bi-ethnic male population: The SAfrEIC study. *PLoS ONE*, 2013; 8: e58506
- Choi EY, Bahrami H, Wu CO, Greenland P, Cushman M, Daniels LB et al, N-terminal pro-B-type natriuretic peptide, left ventricular mass, and incident heart failure: Multi-Ethnic Study of Atherosclerosis. *Circ Heart Fail* 2012;5:727–34.
- Paoletti E, Bellino D, Cassottana P, Rolla D, Cannella G: Left ventricular hypertrophy in nondiabetic predialysis CKD. *Am J Kidney Dis* 2005;46: 320–27.
- Wu IW, Hung MJ, Chen YC, Hsu HJ, Cherng WJ, Chang CJ et al, Ventricular function and all-cause mortality in chronic kidney disease patients with angiographic coronary artery disease. *J Nephrol* 2010;23:181–8.
- 39. Isakova T, Xie H, Yang W, Xie D, Anderson AH, Scialla J et al, Chronic Renal Insufficiency Cohort (CRIC) Study Group: Fibroblast growth factor 23 and risks of mortality and

end-stage renal disease in patients with chronic kidney disease. JAMA2011;305:2432–9.

- Feldman HI, Appel LJ, Chertow GM, Cifelli D, Cizman B, Daugirdas J et al, Chronic Renal Insufficiency Cohort (CRIC) Study Investigators: The Chronic Renal Insufficiency Cohort (CRIC) Study: Design and methods. J Am Soc Nephrol 2003;14[2]: S148–S153.
- 41. Lash JP, Go AS, Appel LJ, He J, Ojo A, Rahman M et al, Chronic Renal Insufficiency Cohort (CRIC) Study Group: Chronic Renal Insufficiency Cohort (CRIC) Study: Baseline characteristics and associations with kidney function. *Clin J Am Soc Nephrol* 2009;4:1302–11.
- 42. Giannitsis E, Kurz K, Hallermayer K, Jarausch J, Jaffe AS, Katus HA et al. Analytical validation of a high-sensitivity cardiac troponin T assay. *Clin Chem* 2010;56:254–61,
- Ho KK, Anderson KM, Kannel WB, Grossman W, Levy D: Survival after the onset of congestive heart failure in Framingham Heart Study subjects. *Circ* 1993;88:107–15.
- 44. National Center for Health Statistics (NCHS): National Health and Nutrition Examination Survey Anthropometry Procedures Manual, Centers for Disease Control and Prevention, 2007. Available

at: http://www.cdc.gov/nchs/data/nhanes/nhanes_07_08/manua l_an.pdf. Accessed August 1, 2014

- 45. Joffe M, Hsu CY, Feldman HI, Weir M, Landis JR, Hamm LL, Chronic Renal Insufficiency Cohort (CRIC) Study Group: Variability of creatinine measurements in clinical laboratories: Results from the CRIC study. *Am J Nephrol* 2010;31:426–34.
- 46. Levey AS, Coresh J, Greene T, Marsh J, Stevens LA, Kusek JW et al, Chronic Kidney Disease Epidemiology Collaboration: Expressing the Modification of Diet in Renal Disease Study equation for estimating glomerular filtration rate with standardized serum creatinine values. *Clin Chem* 2007;53:766–72.
- 47. Anderson AH, Yang W, Hsu CY, Joffe MM, Leonard MB, Xie D et al, Feldman HI, CRIC Study Investigators: Estimating

GFR among participants in the Chronic Renal Insufficiency Cohort (CRIC) Study. *Am J Kidney Dis* 2012;60:250–61,

- 48. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA et al, Chamber Quantification Writing Group. American Society of Echocardiography's Guidelines and Standards Committee. European Association of Echocardiography: Recommendations for chamber quantification: A report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. J Am Soc Echocardiogr 2005;18:1440–63.
- Park M, Hsu CY, Li Y, Mishra RK, Keane M, Rosas SE et al, Chronic Renal Insufficiency Cohort (CRIC) Study Group: Associations between kidney function and subclinical cardiac abnormalities in CKD. J Am Soc Nephrol 2012;23:1725–34.
- Bansal N, Keane M, Delafontaine P, Dries D, Foster E, Gadegbeku CA et al, CRIC Study Investigators: A longitudinal study of left ventricular function and structure from CKD to ESRD: The CRIC study. *Clin J Am Soc Nephrol* 2013;8: 355– 62.
- 51. Schiller NB, Shah PM, Crawford M, DeMaria A, Devereux R, Feigenbaum H et al, Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. American Society of Echocardiography Committee on Standards, Subcommittee on Quantitation of Two-Dimensional Echocardiograms. J Am Soc Echocardiogr 1989;2:358–67.

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