

# BNP in Hemodialysis Patients

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The natriuretic peptides comprise at least three molecules (A, B, and C), which play an important role in BP and volume homeostasis, with biologic actions on kidney, heart, and blood vessels (1). ANP is secreted mainly by the right atrium, BNP is produced by the cardiac ventricles, and CNP is produced mainly by endothelial cells. Their biologic effects include increased GFR, natriuresis, and diuresis; vasorelaxation with decreased cardiac preload and afterload; suppression of renin-angiotensin-aldosterone axis, sympathetic outflow, ADH, and endothelin; and inhibition of mitogenesis in vascular smooth muscle cells, growth factor-mediated hypertrophy in cardiac fibroblasts, and cardiac remodeling (1).

Increased left ventricular (LV) volume or pressure overload, such as occurs in congestive heart failure and hypertension, enhance the secretion of BNP from the ventricles. Plasma levels of BNP are elevated in patients with congestive heart failure in proportion to the severity of myocardial systolic and diastolic dysfunction (2). After a myocardial infarct, an increase in level of NT-proBNP may be an important diagnostic tool for the detection and exclusion of impaired LV function, particular in the presence of concomitant LV hypertrophy (LVH) or renal dysfunction (3). However outside of these cardiology clinical contexts, use of BNP tests is of limited diagnostic value because its level is influenced by age, gender, salt intake, and hemodynamic status (1).

The hemodialysis state is a model of LV pressure and volume overload, with salt and water retention, anemia, and the arteriovenous vascular access predisposing to volume overload and with hypertension, arteriosclerosis, and perhaps aortic stenosis predisposing to LV pressure overload (4). In addition, LVH is present in almost 75% of patients who start dialysis, and LV systolic dysfunction is present in approximately 16% (5). LV growth and increase in LV volume is evident over time, and pulmonary edema is a frequent clinical event, which is associated with change in LV structure and function (6).

BNP predicted mortality in hemodialysis patients (7). We recently reported that at baseline in new hemodialysis patients without symptomatic cardiac disease, the only multivariate associations of LV mass index were gender and BNP (8). Independent predictors of subsequent cardiovascular events or death were age, diabetes, systolic BP, and BNP (8); however, it

is unclear whether the BNP relationships are the result of LV volume overload or of underlying cardiac dysfunction.

Booth *et al.* (9) in this issue of *CJASN* report extracellular volume status measured by multifrequency bioimpedance before and after dialysis in 72 stable hemodialysis patients and examine the relationship to NT-pro BNP values. Median age was 55 years, and 76% were on drug treatment for hypertension. Cardiac ejection fraction on echocardiography was normal (59%; interquartile range 55 to 63), as were LV end systolic and diastolic internal diameters; however, intraventricular wall thickness in diastole was elevated ( $1.24 \pm 0.03$  cm), suggesting concentric LVH. The range of postdialysis NT-proBNP was wide and not normally distributed, with a substantial difference between mean ( $932 \pm 230$  pmol/L) and median (242; interquartile range 90 to 688 pmol/L) values. Log-transformed values were not correlated with ejection fraction or degree of LV dilation, although there was a correlation with grade of LV systolic dysfunction; however, multivariate logistic regression modeling indicated that the factor best associated with log BNP was an objective measure of extracellular volume: Extracellular water to total body water measured by bioimpedance. Two indirect potential indicators of volume overload were also independent predictors: Postdialysis mean arterial BP and change in extracellular fluid volume with dialysis corrected for body surface area (comparing values before and after dialysis).

Bioimpedance results may be influenced by loss of cell mass, as occurs in malnutrition. The authors suggest a potential link between NT-proBNP and malnutrition inflammation syndrome because other independent predictors of BNP levels included the use of a higher dialysate calcium (which was restricted to patients with hypokalemia, who are typically malnourished) and postdialysis weight; however, C-reactive protein levels, a marker for inflammation, were not associated with BNP levels.

Although higher BNP levels may be associated with LVH and with systolic dysfunction, it seems reasonable to conclude that in stable hemodialysis patients with normal LV function on echocardiography, high BNP levels are likely the result of blood volume expansion and require reduction in postdialysis dry weight.

## Disclosures

None.

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See related article, “N-terminal proBNP—Marker of Cardiac Dysfunction, Fluid Overload, or Malnutrition in Hemodialysis Patients?” on pages 1036–1040.