To the Editor

With great interest we read the article by Srisawasdi et al. They found that the ratio between N-terminal (NT)-pro-B-natriuretic peptide (BNP) and BNP increases exponentially with the stage of renal disease. van Kimmenade et al., however, suggested the NT-proBNP/BNP ratio increases only slightly and shows a linear trend. Their findings are used to support the hypothesis that BNP and NT-proBNP concentrations rely equally on the glomerular filtration rate and predominantly on cardiac diseases, rather than on renal clearance. The findings by Srisawasdi et al suggest otherwise, and they rightly advocate that renal dysfunction should be taken into account when interpreting the diagnostic and prognostic potential of NT-proBNP and BNP.

Missing in the data from Srisawasdi et al are the ratios in the patients with end-stage renal disease who were treated with hemodialysis. On reading the article by Srisawasdi et al, we decided to take a look at the NT-proBNP/BNP ratios in a population of patients receiving long-term hemodialysis for whom we recently described cardiac biomarker concentrations and their relationship with volume status.

The population consisted of 44 patients receiving long-term hemodialysis from whom blood samples were obtained before dialysis at the start of the study and subsequently every 2 months for a period of 6 months. To better compare our results with those in the aforementioned study, we give the results for patients who were in clinically stable condition during the study period (eg, with no acute worsening in condition). After exclusion of hospitalized patients, our population consisted of 21 men and 11 women with an average age of 66 years and average time of receiving dialysis of 33 months. The patients were divided into groups without (n = 15) and with (n = 17) a history of cardiovascular disease, which was considered present when the patient had a previous myocardial infarction, had required coronary intervention (eg, percutaneous transluminal coronary angioplasty or coronary artery bypass grafting), or had congestive cardiac failure. More details about the population can be found elsewhere.

In Figure 1, we summarize the NT-proBNP/BNP ratios measured during the 6-month study for each of the 32 patients (patients 16-32 have a history of cardiovascular disease). To clarify the results in Figure 1 and to foster understanding of the magnitude of the NT-proBNP/BNP ratios in this population, we mention that even patients with the lowest ratios, ie, patients 9, 12, and 13, had ratios of more than 5 on at least 1 occasion. It is interesting to note that although the within-patient variations could be quite large, the median (interquartile

![Figure 1](image-url)
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NT-proBNP ratios. More in general, it would be prudent to investigate the reasons behind the strongly elevated NT-proBNP/BNP ratios before using NT-proBNP and BNP measurements as a means of assessing changes in a patient’s condition or as a means to therapeutically guide the treatment for patients with substantially reduced renal functions.

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The values found in the dialysis population are, therefore, much higher than those found in patients with end-stage renal disease (chronic kidney disease stage 5) not receiving dialysis. Summarizing the preceding information seems to reveal that the relative amount of NT-proBNP (vs BNP) increases exponentially with a decrease in renal function and that this increase continues in patients receiving hemodialysis treatment. These findings are in agreement with those of Srisawasdi et al and suggest large differences in the clearance or production of BNP and/or NT-proBNP in patients with chronic kidney disease. Future research is needed to identify the underlying mechanisms behind the strongly elevated NT-proBNP ratios.

References

The Authors’ Reply

The letter by Jacobs et al broadens our study to include more patients with end-stage renal disease. Their results extend our observations into end-stage renal disease with hemodialysis. As we found, they observed an exponential relationship between the NT-proBNP/BNP ratio and renal disease stage.

In regard to the comments on the study by van Kimmenade et al in which they observed only a slight linear relationship between the NT-proBNP/BNP ratio and the estimated glomerular filtration rate (eGFR), further reflection shows that the majority of their patients had an eGFR of more than 60 mL/min/1.73 m², placing them at most in stage I or stage II. Thus, their results were weighted toward mildly affected renal function. The exponential change is observed with more severe renal disease. In fact, they commented that they observed an inverse correlation between the NT-proBNP/BNP ratio and the GFR at the lower extreme of renal function.

They noted, as well, that the concentrations of BNP and NT-proBNP are higher in patients with heart failure than in hypertensive patients for the same range of GFR. They concluded that in heart failure there is an increased secretion of the peptides. Furthermore, we agree with Jacobs et al that future studies are needed to understand the mechanism or mechanisms that dictate the observed values for the NT-proBNP/BNP ratio. These investigations should include empirical and theoretical studies to account for potential differences in secretion and clearance that may occur in different disease states.

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