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Two Problems With Analyzing Natriuretic Peptide Levels: Obesity and Acute Myocardial Infarction

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Numerous reports show the value of plasma measurements of the B-type natriuretic peptide (BNP) or N-terminal pro-BNP (NT-proBNP) to assist in the diagnosis of symptomatic heart failure (HF) and to provide independent prediction of death and later cardiovascular events in both acute and chronic HF.[1)2)] And, NPs (BNP and NT-proBNP) are strong predictors of adverse events in acute coronary syndrome.[3)] Recent studies have shown that obese and overweight individuals have considerably lower circulating natriuretic peptide levels compared with individuals that have a normal body mass index (BMI).[4)] Also, the serum BNP level changes dynamically after the onset of an acute myocardial infarction (AMI). Alteration of the BNP level can show a biphasic peak pattern for one month after the onset of an AMI.[5)] Choi et al.[6)] addressed the relationship between obesity and NT-proBNP levels as a prognostic value after AMI.[7)] Many variables, such as age, sex, renal diseases and their related drug therapies, as well as assay methods have been found to affect or confound the interpretation of blood NP concentrations.[1)] In this study, we faced 2 problems for analyzing NP levels, obesity and AMI.

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Low Levels of Natriuretic Peptides in Obesity

Circulating levels of NPs are significantly lower in overweight and obese patients compared with lean patients.[8)] There are several potential mechanisms responsible for the inverse association between NPs and BMI.[1)4)] Although the reason for the relationship is unknown, the increased concentration of the NP clearance receptor on adipocyte cells may suggest that increased clearance is the reason for lower NP levels in obese patients. Another possibility is that impaired synthesis and release of NPs from myocytes in obese subjects must have a role in the mechanisms underlying their reduced circulating levels. Also, a molecule produced in the lean mass and possibly mediated by sex steroid hormones (possibly androgens) may suppress either synthesis or release of NPs from cardiomyocytes. This study showed that obese patients tend to have lower plasma NP concentrations compared to non-obese patients. However, additional analysis is required to confirm these results. First, in order to analyze diagnostic and prognostic capabilities for NP-proBNP, age-specific consideration was necessary as NT-proBNP levels vary for diagnosing HF in patients with acute breathlessness. Second, to determine if NT-proBNP was equally useful across all BMI categories, affecting variables such as age, sex and renal function would have to be adjusted in Cox analysis. Third, optimal cut points of NPs for major adverse cardiac event by receiver operating characteristic analysis for prognosis would be necessary.

B-Type Natriuretic Peptide in Acute Myocardial Infarction

An elevated serum BNP level after the onset of an AMI can be used not only as an independent risk factor but also as a predictive marker of left ventricular (LV) remodeling.[9)] However,

NP variation depending on measurement time after myocardial infarction needs to be considered. Maisel et al.[10] showed that NP levels might seem discordantly low in patients presenting early with HF symptoms that developed rapidly, in under approximately 1-2 hour. In these conditions, BNP gene expression has insufficient time between the initial trigger of increased ventricular wall stress and the measurement of NP levels to up-regulate peptide production. In addition, the ideal time for serum NP sampling has been subject to debate as the changing pattern of BNP levels in patients with AMI is highly dynamic. The first peak level of BNP develops 20 hours after AMI onset, and the second peak level presents on approximately the fifth day. This second peak level of NPs might reflect the degree of LV remodeling after index MI. Our study addressed the changing patterns of BNP, demonstrating the biphasic elevation during early and long-term phase. The early phase serum BNP level measured from 2 to 6 days after the onset of an AMI, and not at admission, is an independent predictor for LV remodeling as shown by this long-term follow-up study.[11]

In this study, NT-proBNP was measured on arrival. As mentioned above, in case of early arrival after onset of AMI, it is possible not to increase NT- proBNP levels. In addition, it is important to consider infarction size or location because the trigger for increased ventricular wall stress was much higher for a large myocardial infarction or anterior wall infarction than for a small infarction or non-anterior wall. However, this study[6] did not show the extent of infarction or location distribution in study groups. Therefore, a selection bias when enrolling patients into study groups was likely.

In conclusion, in case of analyzing NPs as a prognostic marker in AMI, it is important to consider BMI as well as age, sex and renal function. Also, several associated factors such as sample time or infarction size and location confound the effects of NPs as prognostic factors since their levels are highly dynamic depending on the associated factors.

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