Challenges for the Basis of Practice

Natriuretic Peptide Measurements in Managing Heart Failure
In Theory and in Practice

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Many studies have described the role of B-type natriuretic peptide or its amino-terminal byproduct (NT-pro-B-type natriuretic peptide) in clinical practice, including several published or ongoing randomized clinical trials. However, the debate over natriuretic peptide testing continues, mostly related to the appropriateness of testing as decision support for the management of heart failure. The most accepted use is to improve recognition of heart failure when the diagnosis has been overlooked or questioned after consideration of clinical signs and symptoms.1,2 This is the basis of the class IIa recommendation for natriuretic peptide measurement in the urgent care setting when diagnosis is uncertain.3 It has been further suggested that serial natriuretic peptide measurement in the setting of known heart failure can help guide therapy, whereas critics have argued that evidence-based drug therapy for heart failure should be implemented and titrated similarly regardless of natriuretic peptide levels. Knowing the precise natriuretic peptide level on a routine basis has yet to be consistently proven to improve the delivery of care or to change outcomes for the better. This has led to a class IIb recommendation for serial B-type natriuretic peptide measurement in the latest guideline updates.3 Within the setting of this ambiguity, I will describe my own opinions (and biases) for measuring natriuretic peptide levels (Table 1).

First, the absence of information about a specific natriuretic peptide level on a patient does not necessarily interfere with my ability to diagnose heart failure clinically or to assess its severity. The knowledge of a particular natriuretic peptide level does not provide specific indications or contraindications to treatment recommended by the evidence-based clinical guidelines. Therefore, I personally do not routinely measure natriuretic peptide levels on all patients at all clinic visits, nor do I measure natriuretic peptide levels routinely at the time of admission for heart failure. However, I do believe that natriuretic peptide levels can provide an additional objective measure of cardiac insufficiency in the form of a reproducible, widely available, and relatively inexpensive blood test. Assessment of natriuretic peptide levels can be helpful in selected patients at the bedside regarding disposition and treatment plans (especially when patients have been admitted for decompensated heart failure), such as the determination of how closely I need to monitor an individual’s clinical status, when to conduct additional testing, or when to schedule a follow-up appointment after a hospital discharge. In particular, when encountering an unexplained rise in natriuretic peptide levels in a patient without new complaints, I often put more effort toward further investigations into potential contributing factors. In contrast, for a clinically euvoletic patient with persistently high but stable natriuretic peptide levels, I will confirm that all evidence-based drug therapies are being given (potentially attempt to be more aggressive in my neurohormonal and vasodilator therapy prescription) but will be judicious in up-titrating loop diuretics unless there is other evidence suggesting that my volume assessment may be inaccurate. In other words, I use natriuretic peptide levels in the clinical context to refocus the components of evidence for my decisions rather than to drive them.

The clinical utility of natriuretic peptide testing may depend on both the patient’s clinical context and the clinician’s comfort level and experience with interpreting the natriuretic peptide levels. In a busy emergency department where multitasking and triage decisions are common, the availability of natriuretic peptide levels may facilitate more prompt decisions to treatment or disposition plans. However, routine testing has yet to confirm incremental benefit even in the urgent care setting.4 In contrast, a seasoned clinician encountering a familiar and well-treated patient with stable clinical status during a routine outpatient clinic visit may find a natriuretic peptide value not particularly additive to the overall assessment and treatment plan. That being said, we also lack data to establish the optimal testing interval and clinical utility for common monitoring tests, such as echocardiography.

I do not routinely order follow-up natriuretic levels during heart failure hospitalizations, particularly when patients are responsive to their treatment plans. However, I nonetheless admit that seeing improvements in natriuretic peptide levels can be reassuring, and therefore some clinicians find such information “helpful.” In such cases, the decision to order a follow-up natriuretic peptide level may be based on the level of clinical suspicion or reassurance needed by the clinician. In cases where self-reported symptoms may not be as reliable, following natriuretic peptide levels can be informative. On the other hand, a patient who describes worsening heart failure symptoms with ambiguous clinical signs and exhibits a low natriuretic peptide level may prompt the search for potential underlying noncardiac causes. In my opinion, further routine testing may not be as helpful unless there are changes in the clinical context.
There are strong evidence to support the use of natriuretic peptide levels in the acute setting for diagnostic and prognostic indications, especially in patients with ambiguous but suspected signs and symptoms of heart failure. Routine measurements of natriuretic peptide levels may not be necessary and have not been validated or justified by randomized controlled trials. Natriuretic peptide levels can be helpful in making the determination as to how closely patients should be monitored or evaluated. Elevated natriuretic peptide levels generally provide reliable and objective indications of disease severity but should be interpreted in the clinical context. For low natriuretic peptide levels, reassurance of relatively low-risk profiles and/or investigations into other potentially non-cardiac causes of symptoms are warranted. Natriuretic peptide levels do not specify the underlying causes or indicate specific interventions, and variability in serial measurements can be challenging to interpret.

Some investigators have proposed a framework of how to use specific ranges of natriuretic peptide levels as treatment targets. This is based on the observation that ambulatory patients with >30% reduction in their natriuretic peptide levels have a better long-term prognosis. However, reliance on assay levels to guide therapy is inhibited by increasing recognition that both biologically active and inactive forms are detected by current assays. Even when directional change correlates with changing cardiac signs and symptoms, the degree of change varies widely among individuals, between different assays used, and can be affected by several confounders. To override clinical judgment with a treatment algorithm based on natriuretic peptide levels requires more precise assays and more reliable therapies than we currently have available.

We also lack specific drugs or treatment strategies that consistently lower natriuretic peptide levels, which may explain why there is a lack of specific guideline recommendations despite its promise. One major concern regarding routine serial natriuretic peptide testing is the potential harm of overzealous drug titration (particularly with loop diuretics) in response to elevated natriuretic peptide levels. After almost a decade of clinical use and experience from several randomized studies, what is not commonly emphasized in the findings is the relative safety of such a biomarker-influenced approach when applied with sound clinical judgment in educated hands. At present, I see no noticeable trend of “harm” in the presence of biomarker data. However, although promising and even tempting, I do not titrate drugs based on changes in natriuretic peptide levels or set a target level but take it as only one of many factors to be weighed in the decision-making process. This is particularly true in elderly patients, in whom polypharmacy may be less well tolerated, where there may be less benefit with a natriuretic peptide-guided approach.

Clinicians caring for patients with heart failure are no strangers to ambiguity of clinical presentation and imprecision of diagnostic and monitoring tools. Despite the lack of consensus regarding the clinical utility and monitoring ranges of natriuretic peptide testing, few would deny that natriuretic peptide testing has provided a new dimension in the care of patients with heart failure. In fact, one can even argue that the academic community may have put too high a barrier for adoption on natriuretic peptide testing, while we continue to rely on other assessment tools that can be far more expensive or less scrutinized. Ongoing investigations will likely help to clarify what are the optimal treatment strategies and targets based on natriuretic peptide levels. In the meantime, anyone who demands the ultimate proof or “evidence” for the clinical utility of natriuretic peptide testing should reflect on what evidence should be demanded for a diagnostic test and whether such standards have been imposed on other clinical tests.

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**References**


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