A
cute decompensated heart failure (ADHF) is a major
public health problem throughout the world. In the
United States alone, this condition accounts for >1
million hospitalizations annually, and it is likely that this
number will increase in the future just as it has done over the
past several decades.1 Although some progress has been made
in reducing in-hospital death rates and length of hospital stay
for ADHF, mortality and readmission rates over the 6-month
period after discharge remain alarmingly high. In addition,
costs of managing patients with ADHF are substantial, with
≈60% of all funds spent on heart failure being consumed
during hospitalizations. Despite recognition of the importance
of ADHF, however, there has been little progress in either
defining universally accepted management strategies or gen-
erating new treatment approaches that alter these outcomes.

The use of biomarkers to detect risk, assess prognosis, and
guide management of disease has been a major advance in the
practice of medicine. Measurement of B-type natriuretic
peptide (BNP) or the amino terminal fragment of the precu-
sor protein (NT-proBNP) have been shown to be useful in
detecting the presence of heart failure in dyspneic patients
and in determining prognosis.2–4 Although measurement of
these peptides is widely used, questions about whether the
test results can effectively help guide management strategies
and whether they lead to better outcomes at lower cost to the
healthcare system have not been fully addressed.5,6 In this
issue of Circulation, Moe and colleagues7 present results of
the IMPROVE-CHF study in which they assess the incre-
mental value of measuring NT-proBNP in confirming the diag-
nosis of heart failure in patients who presented to the
emergency department (ED) with dyspnea believed to be of
cardiac origin and whether access to NT-proBNP levels leads
to cost savings without compromising clinical outcomes. Of
particular note is that they sought to answer these questions in
Canada, a country with publicly funded universal health care
that mandates the judicious allocation of healthcare resources.
The issues addressed in the IMPROVE-CHF study are highly
relevant clinically, and the setting in which they were
addressed offers several advantages. Not only is ADHF an
important clinical problem in Canada,8 but the healthcare
system affords the opportunity to assess the value of NT-
proBNP in a setting in which expenditures are not influenced
by access to care and resource use is more carefully regulated
than in the United States.9 Both of these factors would tend to
provide a more structured framework in which to assess the
added value of measuring NT-proBNP.

The results of IMPROVE-CHF are consistent with those of
previous studies using natriuretic peptides in that they con-
firm the added predictive value of measuring NT-proBNP in
dyspneic patients who present to the emergency room. In the
present study, knowledge of NT-proBNP levels also was
associated with an ED stay that was on the average 42
minutes shorter than when patients were managed by con-
ventional means alone without access to peptide levels. The
likelihood of being admitted to hospital, the length of stay of
those patients who were admitted, and rate of in-hospital
mortality, however, were not significantly altered by knowl-
edge of NT-proBNP levels. Of great importance was the
finding that rehospitalization over a 60-day period after
discharge was significantly reduced from 20% to 13% and
that direct medical costs for all services for the entire period
were lower when providers had knowledge of NT-proBNP
levels. Not surprisingly, these benefits appeared to be greater
in patients for whom the initial evaluation was less certain
that the dyspnea was due to heart failure. Unlike previous
studies, the results of this Canadian trial failed to
demonstrate that NT-proBNP was better than clinical assessment
in determining whether dyspnea was due to heart failure,3,10 a
founding perhaps related to the skills of the providers or the
patient admixture seen at the centers at which this study was
performed. The results did show, however, that the addition
of information about NT-proBNP levels to the conventional
assessment in the ED significantly increased the receiver-
operating characteristics curve above that for clinical assess-
ment alone, confirming the incremental value of the test in
improving diagnostic accuracy.

What then does IMPROVE-CHF tell us about the value of
natriuretic peptide measurement in managing patients who
present to the ED with dyspnea? It confirms not only that
knowledge of NT-proBNP reduces uncertainty about the
diagnosis of heart failure but also that it may help improve
decision making that ultimately lead to reduced costs and
better outcomes. Although the study was powered to detect a
reduction in the time spent in the ED, the most compelling
information is the overall reduction in cost to the healthcare
system and the reduction in rehospitalizations when NT-
proBNP levels were made available. The cost analysis that

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was prospectively derived from this randomized trial appears to have been rigorously performed, and the conduct of the study in a locale in which health care is universal but more regulated than in the United States reduces the vagaries that can occur when access to health care is variable and management regimens are more “free-wheeling.” Given the spiraling costs of health care in the United States and throughout the industrialized world, these results should provide a strong rationale for measuring natriuretic peptides in patients who present with dyspnea. In addition, the results indicate that these cost savings can be accomplished without compromising patient care. In fact, the results suggest the intriguing possibility with this knowledge, overall practice patterns resulted in a significant reduction in rehospitalizations. Because rehospitalization rates for heart failure patients in the United States, Canada, and elsewhere around the world have been noted to be quite high (eg, 20% of the control population of IMPROVE-CHF was rehospitalized within 60 days), the results of IMPROVE-CHF are a welcome addition to the literature.

How convincing are these results, and how well can they be generalized to broader populations that are not cared for under a universal healthcare system? Although the overall pattern and consistency of results make it difficult to find fault with the concept that knowledge of natriuretic peptide levels helps improve management strategies that ultimately reduce costs and improve outcomes, exactly how these benefits came about remains uncertain. Were the better outcomes and cost savings related to the fact that more appropriate triage and early treatment decisions were made in the ED? Did knowledge of test results improve diagnostic accuracy, resulting in a higher percentage of appropriate hospitalizations and a reduction in inappropriate ones? Was there a greater likelihood of appropriate therapies being used, and were they used more vigorously in both in the inpatient and outpatient setting? Were diagnostic tests used more thoughtfully when NT-proBNP results were available? Unfortunately, results of IMPROVE-CHF included in this report are silent on all but the last of these issues. They do indicate, however, that knowledge of natriuretic peptide levels is associated with a trend toward less use of more advanced and expensive tests and, at least over a 60-day period, that this does not appear to compromise outcomes. Although a second NT-proBNP level was obtained after 72 hours in hospitalized patients, these values are not reported, making it impossible to determine whether the favorable effects of natriuretic peptide measurements were related to the initial or subsequent test or whether both contributed. Furthermore, we gain no insight into how often levels should be measured. It is possible that more frequent sampling either in hospital or after discharge might have been even more effective. In addition, the overall number of rehospitalizations was relatively small; the reduction seen with knowledge of NT-proBNP levels was only 18 patients; and the comparison between study groups just managed to achieve a level considered to be significant (eg, $P=0.0463$). Thus, it would be most helpful to have confirmatory studies performed in larger populations in different areas of the world to provide more confidence that measuring natriuretic peptides really does improve postdischarge outcomes.

Although the power calculation for determining sample size was based on reduction of time spent by the patients in the ED, this aspect of the study seems to be the least compelling. The observed duration of stay in the ED in both study groups was far less than that anticipated when the trial was initiated. To put the issue into perspective, the difference in ED stay in the control group whose NT-proBNP levels were not revealed between what was anticipated and what was seen in the trial was in the range of 2.7 hours, a value nearly 4-fold greater than the impact of knowledge of the NT-proBNP levels in IMPROVE-CHF. This reduction in ED time from what was anticipated may have been due to the influence of recently published Canadian guidelines for management of ADHF or to the impact of the providers’ knowing that these patients were being evaluated as part of a trial that was looking at utilization strategies. Similarly, recognition that certain patients were in the “active” study arm in which NT-pro-BNP levels were available may have increased the acularity with which tests, results, and triage decisions were processed. Although the conduct of the study in the Canadian system may have imposed a certain order on the process, it does raise questions about whether the same results would be possible in a less structured environment such as the United States or in a setting where providers are less familiar with or constrained by guidelines. Although the answers to these questions are not known, one is left with the strong suspicion that the benefits might be diluted in other settings or alternatively that they might be more substantial in an even more rigorously controlled environment.

These questions indicate that more work needs to be done in this area. The magnitude of the problem imposed by patients with ADHF is great in terms of both cost and human suffering. The need to improve management strategies is pressing. Although the present study does not provide all the answers, it does offer a compelling and persuasive argument that knowledge of natriuretic peptide levels in dyspneic patients who are evaluated in the ED offers sufficient incremental benefit and value and that it should be part of the routine armamentarium for the evaluation of these patients. The results of this study also provide a cogent argument for not relying on the results of this test alone because a correct diagnosis was best arrived at only when the test results were integrated into a framework that incorporated conventional clinical analysis of the patient’s condition. The message here also seems to be clear. We should not yet give up our stethoscopes or stop talking to our patients, particularly the ones who are short of breath.

Disclosures

None.

References


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