



New trials of antiplatelet therapy continue to redefine optimal management strategies for patients with atherothrombotic disease and patients with atrial fibrillation.

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## HEART FAILURE

## Natriuretic-peptide-guided HF meds cut mortality in meta-analysis

MARCH 22, 2010 | Steve Stiles

Melbourne, Australia - Outpatients with chronic, primarily systolic heart failure lived longer if their medical management was guided by natriuretic-peptide-assay results, compared with med adjustments based on "usual clinical care," in a meta-analysis that had to rely on a limited number of randomized, controlled trials [1].

Also, important heart-failure-specific outcomes could not be analyzed across studies due to differences in how they were defined.

"We were not able to meta-analyze some key clinical end points on which this approach may have a beneficial impact," write Dr Pramote Porapakkham and associates (Monash University and Alfred Hospital, Melbourne, Australia) in the March 22, 2010 issue of the *Archives of Internal Medicine*. Such end points include heart-failure hospitalization, in particular, as natriuretic-guided therapy "and accompanying intensification of use of standard HF pharmacological therapies should theoretically have a favorable impact on this outcome."

The group identified eight trials randomizing 41 to 499 outpatients with NYHA class 2-4 chronic heart failure and an LVEF <50% to therapy directed by B-type natriuretic peptide (BNP) or N-terminal proBNP (NT-pro-BNP) levels or usual care. They included the STARS-BNP, TIME-CHF, BATTLESCARRED, PRI MA, and SIGNAL-HF studies and encompassed 1726 patients followed for a mean of 16 months (range three to 24 months).

The guiding biomarker was BNP in three of the studies and NT-proBNP in five. In all, the idea under exploration was whether, in patients managed conventionally, adjustments to evidence-based heart-failure meds aimed at pushing natriuretic peptide levels down to prespecified targets would further improve outcomes.

The meta-analysis showed an all-cause mortality relative risk (RR) of 0.76 (95% CI 0.63-0.91; p=0.003) for biomarker-guided therapy compared with the usual-care control group; the TIME-CHF trial accounted for fully one-half of the benefit.

In a subgroup analysis based solely on TIME-CHF and BATTLESCARRED, the only studies to report the necessary data, patients younger than 75 years had an all-cause mortality RR for guided therapy of 0.52 (95% CI 0.33-0.82; p=0.005). No such significant reduction was observed in older patients. "The reason for this is uncertain," the group writes. "Older patients may have more comorbid diseases, including hypertension, chronic kidney disease, diabetes mellitus, and dysrhythmia, that make them less able to tolerate target doses of medication than those in younger age groups. They may also be less responsive to these therapies."

There was no significant overall RR change for all-cause hospitalization across the three studies that reported the end point; STARS-BNP accounted for 80% of the effect. Nor was there a significant difference favoring either strategy for "survival free of any hospitalization" in the two studies providing that end point; TIME-CHF accounted for 82% of that finding.

In general, patients on guided management achieved target ACE-inhibitor and beta-blocker dosages about twice as often as those managed conventionally.

The authors say they've identified three relevant ongoing randomized trials (North Star, EXIMPROVE, and PROTECT) not included in their analysis.

As reported by [heartwire](#) in December 2009, PROTECT was halted at an enrollment of 151 patients out of a planned 300 when management guided by NT-proBNP showed a significant advantage for the primary end point at one year. The difference—in a composite that included worsening heart failure, HF hospitalization, and CV death—was significant at p=0.008, reported the trial's sponsor, Hoffmann-La Roche (Berne, Switzerland).

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## Source

1. Porapakkham P, Porapakkham P, Zimmet H, et al. B-type natriuretic peptide-guided heart failure therapy. A meta-analysis. *Arch Intern Med* 2010; 170:507-514.

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