

## Prognostic value of NT-proBNP in stable coronary artery disease – better than cardiac risk assessment

The prognostic value of NT-proBNP in stable coronary artery disease (CAD) has been confirmed in a large mortality study of more than 1 000 patients over a period of nine years.<sup>1</sup> The study, conducted in Denmark, showed that the measurement of NT-proBNP performed immediately before coronary angiography provided important prognostic information on mortality that is independent of invasive measurements of left ventricular function and the severity of coronary artery disease.

This finding extends the value of NT-proBNP as a marker of risk among patients with acute coronary syndromes to a new population of patients with stable coronary artery disease who are at 'intermediate' risk.

NT-proBNP was measured using the commercially available immunoassay (Elecys proBNP, Roche Diagnostics). This assay measures the N-terminal fragment (NT-proBNP), which is derived from brain (b-type) natriuretic peptide (BNP), a peptide hormone released primarily from the cardiac ventricles in response to myocyte stretch.

The study, designed as a prospective observational study, assessed the NT-proBNP levels from serum samples taken between 1991 and 1993 from 1 034 patients who underwent elective coronary angiography at the Rigshospitalet in Copenhagen. No patients were lost to follow-up in this cohort. Two experienced cardiologists, blinded to the patients' NT-proBNP results, evaluated the first angiogram taken. The LVEF was calculated from a single view (right anterior oblique, 30 degrees) by the area-length method.

After a median follow-up of 9.2 years, 288 of the 1 034 patients (28%) had died. The median NT-proBNP level for all subjects was elevated (169 pg/ml; interquartile range 63–456) and was significantly lower among patients who survived than among those who died [120 pg/ml (interquartile range 50–318) vs 386 pg/ml (range 146–897),  $p < 0.001$ ].

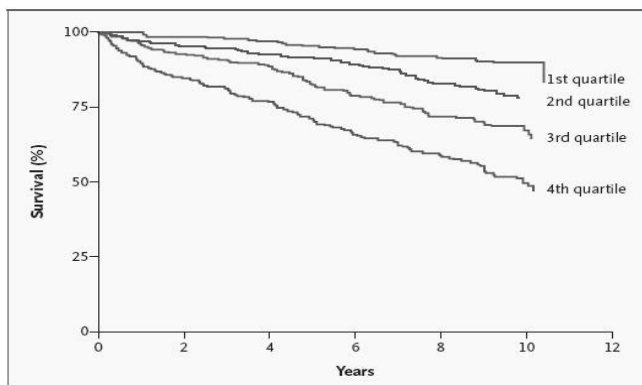
The patients were divided into subgroups according to quartiles of NT-proBNP. Patients with NT-proBNP in the upper quartile were older, had

a higher left ventricular end-diastolic pressure, and were more likely to have a history of myocardial infarction, clinically significant coronary artery disease and diabetes. The LVEF, body mass index (weight in kg divided by the square of the height in m), and creatinine clearance rate were lower than among patients with NT-proBNP levels in the lowest quartile.

The NT-proBNP level increased with the severity of angiographic disease and of left ventricular systolic dysfunction. In the subgroup of the population with normal LVEF (i.e.  $\geq 60\%$ ; 506 patients), the level of NT-proBNP was significantly higher in patients with, than in those without coronary artery disease.

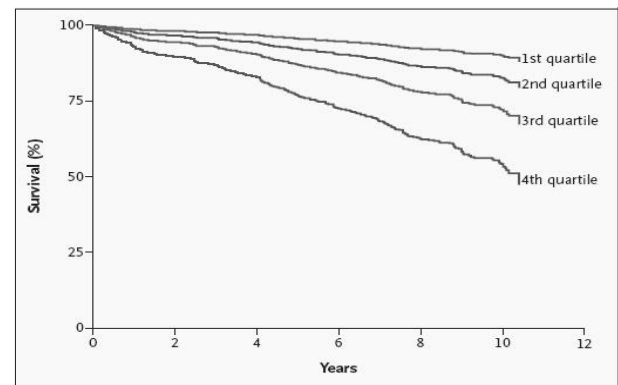
The overall survival among patients with stable CAD according to quartiles of NT-proBNP is shown in Fig. 1, while Fig. 2 shows the adjusted estimates of overall survival among patients (adjusted for age, presence or absence of diabetes, smoking status, LVEF, presence or absence of suspected heart failure and severity of angiographic CAD).

Of interest is the fact that in this study,



**Fig. 1.** Overall survival among patients with stable coronary artery disease, according to quartiles of NT-pro-BNP. The NT-pro-BNP levels were as follows: first quartile,  $< 64$  pg/ml; second quartile, 64–169 pg/ml; third quartile, 170–455 pg/ml; and fourth quartile,  $> 455$  pg/ml;  $p < 0.001$  by the log-rank test for the overall comparison among the groups.

From: Kragelund C, et al. *N Engl J Med* 2005; 352(7): 666-675.



**Fig. 2.** Adjusted estimates of overall survival among patients with stable coronary disease, according to quartiles of NT-pro-BNP. The survival estimates have been adjusted for age, presence or absence of diabetes, smoking status, left ventricular ejection fraction, presence or absence of suspected heart failure, and severity of angiographic coronary disease. The NT-pro-BNP levels were as follows: first quartile,  $< 64$  pg/ml; second quartile, 64–169 pg/ml; third quartile, 170–455 pg/ml; and fourth quartile,  $> 455$  pg/ml;  $p < 0.001$  by the log-rank test for the overall comparison among the groups. From: Kragelund C, et al. *N Engl J Med* 2005; 352(7): 666-675.

NT-proBNP was elevated in patients with stable angina, a condition characterised by transient ischaemic episodes. It was also elevated in patients with angiographically verified coronary atherosclerosis, regardless of left ventricular systolic function. Recent studies have suggested that ischaemia promotes the release of BNP but the responsible mechanisms still remain to be fully elucidated.<sup>2</sup>

The authors noted that NT-proBNP added value to risk stratification and could potentially identify patients who would benefit the most from specific treatment strategies, and make it possible to avoid over-treating patients at low risk – of great value in environments with limited resources.

Further studies of treatment strategies guided by NT-proBNP levels are needed to strengthen this finding and

place NT-proBNP firmly in routine use for clinical risk stratification in patients with stable CAD.

1. Kragelund C, Bjorn G, Lars K, Hildebrandt P, Steffensen R. N terminal pro-B-type natriuretic peptide and long-term mortality in stable coronary artery disease. *N Engl J Med* 2005 **352**(7): 666–675.
  2. D'Souza SP, Baxter GF. B type natriuretic peptide: a good omen in myocardial ischaemia. *Heart* 2003; **89**: 707–709.
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