

NT-pro BNP in risk assessment of those having stable coronary atherosclerotic heart disease (CAD)

N Terminal-pro Brain Natriuretic Peptide (NT-pro BNP) is produced by cardiac muscle cells (myocytes) in response to cardiac wall stress and myocardial ischemia. NT-pro BNP has been shown to predict all-cause mortality in insurance applicants without a history of heart disease,¹ as well as in the general population.² It has been found to improve future cardiovascular risk estimation when considered along with classic cardiovascular risk assessors.³ It has also been identified as an indicator of future mortality risk in those having stable coronary atherosclerotic heart disease (CAD).^{4,5}

Kragelund found that 84 percent of individuals referred for coronary arteriography due to symptoms (classic angina pectoris) or signs (ischemia on exercise stress testing or nuclear stress myocardial imaging) had significant CAD. In addition, NT-pro BNP levels, obtained before the coronary arteriography, correlated well with the severity of identified CAD. They were also good indicators of future mortality risk over nine years of follow-up. Bibbins-Domingo also found NT-pro BNP levels to correlate with the severity of CAD and with future all-cause mortality risk in a group of California patients with stable CAD. Kragelund's study shows that overall survival appreciably diminishes in the fourth quartile of NT-pro BNP in those having stable CAD.

Using accepted methodology^{6,7} to determine the mortality ratios for the various quartiles of NT-pro BNP identified by both Kragelund and Bibbins-Domingo produces the results shown in the table below.

What underwriters should know

In those having confirmed stable coronary atherosclerotic heart disease:

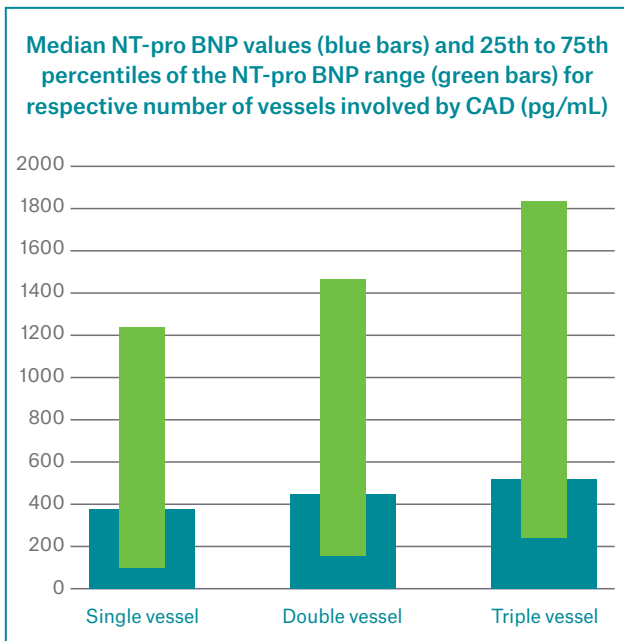
- NT-pro BNP levels below 150 pg/mL are associated with relatively good prognosis. NT-pro BNP levels below 75 pg/mL support consideration for awarding a credit in underwriting an applicant with stable CAD.
- NT-pro BNP levels greater than 450 pg/mL may be associated with an increased mortality risk of at least four tables of extra mortality above standard.
- Since NT-pro BNP levels vary with age and gender, it should be noted that these cut points are representative of a population that is 70–85 percent male between ages of 55 and the late 60s.

Since NT-pro BNP values normally rise with age, and are somewhat higher in women, the mean ages and percent female composition for each of the quartile groups is presented in the second column from the right. Mortality ratios for the respective quartiles are found in the far right hand column. It is apparent that future mortality risk is relatively good in the first two quartiles. This roughly represents NT-pro BNP values below 150 pg/mL for those aged from about 55 into the late 60s. Those in the first quartile (NT-pro BNP values roughly below 75 pg/mL) might even be considered for the awarding of a credit, at least from the data provided by the above two studies.

| Study lead author | NT-pro BNP quartile | NT-pro BNP range | Mean age (% female) | Mortality ratio % |
|------------------------------|---------------------|------------------|---------------------|-------------------|
| Kragelund ⁴ | 1st | 5-63 pg/mL | 54 (28) | 76 |
| | 2nd | 64-169 pg/mL | 58 (30) | 117 |
| | 3rd | 170-455 pg/mL | 59 (26) | 167 |
| | 4th | 456 pg/mL and up | 64 (25) | 198 |
| Bibbins-Domingo ⁵ | 1st | 8.06-73.95 pg/mL | 61 (20) | 82 |
| | 2nd | 74-174.5 pg/mL | 67 (15) | 85 |
| | 3rd | 175.1-459 pg/mL | 68 (24) | 137 |
| | 4th | 460 pg/mL and up | 72 (15) | 263 |

Future mortality represented in the fourth quartile finds mortality ratios similar to those that may be determined using traditional algorithms of risk assessment for various presentations of CAD. This roughly represents NT-pro BNP values above 450 pg/mL for the same age band noted above. It would seem, at least from survival data supplied from Kragelund and Bibbins-Domingo, that NT-pro BNP values below 150 pg/mL would suggest a very favorable future mortality risk for those having stable CAD, whereas those having NT-pro BNP values above 450 pg/mL would likely demonstrate mortality risk representative of their CAD presentation as evaluated by traditional underwriting algorithms.

Since myocardial ischemia results in elevation of NT-pro BNP, it would be logical that the greater the ischemic burden, the higher the NT-pro BNP level, and that various levels of NT-pro BNP elevation might indicate the extent of coronary artery involvement (e.g., single vessel versus multi-vessel disease). A study by Ndrepepa⁸ provides some insight into NT-pro BNP levels relative to various degrees of coronary artery involvement. The study population was unique in that subjects included not only those with stable CAD (number = 385), but also those with unstable angina and myocardial infarction (number = 299). The mean age was 65.8 years and 26.6 percent were female. All received coronary arteriography after having their NT-pro BNP levels determined. The graph below shows NT-pro BNP levels relative to the number of coronary arteries involved:



The NT-pro BNP values progressively rise as the number of coronary arteries involved increases.

| | Coronary artery involvement | | |
|---|-----------------------------|--------------|--------------|
| | 1 vessel | 2 vessel | 3 vessel |
| Median NT-pro BNP (pg/mL) | 385.5 | 463.0 | 533.8 |
| 25 th -75 th percentile | 117.2-1266.0 | 135.0-1480.5 | 221.8-1809.4 |

However, the 25th to 75th percentile ranges demonstrate such a large degree of overlap between the respective numbers of involved vessels that, at least in this study, it would seem that NT-pro BNP levels would not be helpful in differentiating between single and multi-vessel disease in cases where coronary arteriography data was not present.

Key points

- Survival in those with stable CAD is relatively good when their NT-pro BNP results are in the first two quartiles.
- Survival in those with stable CAD is decidedly worse in those having NT-pro BNP values in the fourth quartile.
- NT-pro BNP levels are not helpful in determining the anatomic extent of CAD.

References

¹Clark M, et al, NT-pro BNP as a Predictor of All-Cause Mortality in a Population of Insurance Applicants, *Journal of Insurance Medicine* 2014;44:7-16.

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