Information as of November 2014

NT-proBNP

somewhat different

NT-proBNP may be used to help detect, diagnose and evaluate the severity of heart failure.

An Update & Suggestions on How to Use It

ExamOne's NT-proBNP Experience

ExamOne recently reviewed their experience with N-terminal Pro B-type Natriuretic Peptide (NT-proBNP) in the screening of insurance applicants aged 45 up from the years 2008 to 2010 (i.e. the test was not performed due to any specific clinical or laboratory indication). A total of 98,671 applicants were included (54.4% male and 46.5% female). For each sex the population was divided into 3 age bands, 45-54, 55-64 and 65 up. The mean and median values were higher in each successively older age band and were consistently greater in females than males. The relative difference between males and females in the mean and median values decreased with increasing age.

	Males		Females	
Ages	Mean	Median	Mean	Median
45-54	40.07	24	64.45	46
55-64	64.14	35	85.69	55
65+	166.27	66	175.57	97

In general, there was little correlation between the NT-proBNP levels and other tests included in a typical insurance lab profile. The exception was the serum creatinine. Mortality results were adjusted in a multivariate way for any interaction with other laboratory values.

Using the Social Security death master file the relative risk for mortality was calculated for each gender and age band. When risk was calculated relative to the median values for each sex and age band, the risk clearly varied with age, sex and NT-proBNP level. For any given level the relative risk decreased as the age increased. In addition, for any given NT-proBNP level and age the relative risk of mortality was substantially higher in males than in females. This pattern of mortality mirrored that seen in the clinical literature and other studies of insurance applicants.

Mean Hazard Ratio by Sex, Age, and NT-ProBNP Range

Females

NT-proBNP		45-54		55-64		65+	
Min	**Max**	**% Applicants**	**Hazard Ratio**	**% Applicants**	**Hazard Ratio**	**% Applicants**	**Hazard Ratio**
0	**249**	98.3 %	1.00	95.7 %	1.00	84.3 %	1.00
250	**499**	1.3 %	4.12	3.4 %	3.53	10.8 %	1.84
500	**749**	0.2 %	4.95	0.5 %	3.04	2.2 %	3.97
750	**999**	0.1 %	12.02	0.2 %	13.79	0.9 %	0.00
1000	∞	0.1 %	26.55	0.2%	40.37	1.8 %	12.57

Males

NT-proBNP		45-54		55-64		65+	
Min	**Max**	**% Applicants**	**Hazard Ratio**	**% Applicants**	**Hazard Ratio**	**% Applicants**	**Hazard Ratio**
0	**249**	99 %	1.00	97.1 %	1.00	88.4 %	1.00
250	**499**	0.6 %	5.75	2.0 %	4.67	6.1 %	4.27
500	**749**	0.2 %	8.71	0.5 %	3.04	1.7 %	6.37
750	**999**	0.1 %	5.85	0.2 %	0.00	1.3 %	5.16
1000	∞	0.1 %	32.75	0.3 %	11.44	2.5 %	9.43

Confidence interval includes 1.0 (p< .05)

In addition, the above noted pattern of mortality was similar if the 2008 Valuation Basic Table (VBT) was used as the referent population rather than the median values for the NT-proBNP. This would suggest that the risk associated with an elevation of NT-proBNP would translate to the insurance underwriting environment.

Mean Mortality by Sex, Age, and NT-proBNP Range (as percentage of 2008 VBT)

Females

NT-proBNP		45-54		55-64		65+	
Min	**Max**	**% Applicants**	**VBT Ratio**	**% Applicants**	**VBT Ratio**	**% Applicants**	**VBT Ratio**
0	**249**	98.3 %	0.75	95.7 %	0.86	84.3 %	0.97
250	**499**	1.3 %	3.10	3.4 %	3.03	10.8 %	1.78
500	**749**	0.2 %	3.73	0.5 %	2.61	2.2 %	3.84
750	**999**	0.1 %	9.04	0.2 %	11.82	0.9 %	0.00
1000	∞	0.1 %	19.97	0.2%	34.60	1.8 %	12.18

Males

NT-proBNP		45-54		55-64		65+	
Min	**Max**	**% Applicants**	**VBT Ratio**	**% Applicants**	**VBT Ratio**	**% Applicants**	**VBT Ratio**
0	**249**	99.0 %	0.89	97.1 %	0.83	88.4 %	0.73
250	**499**	0.6 %	5.14	2.0 %	3.87	6.1 %	3.11
500	**749**	0.2 %	7.78	0.5 %	2.52	1.7 %	4.65
750	**999**	0.1 %	5.22	0.2 %	0.00	1.3 %	3.76
1000	∞	0.1 %	29.24	0.3 %	9.48	2.5 %	6.87

Confidence interval includes 1.0 (p< .05)

Considerations

Unfortunately, only a small number of applicants had NT-proBNP values in the highest ranges. For example, only 0.68% had values greater than or equal to 500 pg/ml and only 0.22% had values greater than or equal to 1000 pg/ml. Thus, the confidence intervals are wide and the certainty associated with the relative risk for mortality at these extreme values is limited.

Clinical articles have shown that the NT-proBNP levels can be reliably increased by certain medical conditions including; coronary artery disease, congestive heart failure, valvular heart disease, atrial fibrillation, left ventricular hypertrophy, pulmonary hypertension and chronic obstructive lung disease.

Furthermore, data from the clinical literature would also suggest that if the above noted conditions associated with an increase in the NT-proBNP level can be excluded by a combination of clinical history, physical examination and laboratory and other testing such as echocardiography, stress testing cardiac catheterization etc., there is little predictive ability for mortality associated with the test itself.

NT-proBNP and Resting ECG

Several clinical papers have indicated a similar sensitivity and specificity for electrocardiography (ECG) and NT-proBNP for detection of significant heart disease, with a probable small advantage for the latter, especially for the detection of valvular heart disease. However, these studies indicated that in many cases there was little overlap between the two tests i.e. either one or the other was positive, not both.

A recent study on insured lives by Hannover Re also showed a comparable degree of protective value for mortality for the NT-proBNP and resting ECG. As was noted in the clinical papers, this study also showed only a limited degree of overlap between the two tests in insurance applicants.

While the ECG and NT-proBNP uncovered an overall similar total amount of mortality risk in a block of business, they did not necessarily do so in the same individuals. Thus, the tests seem, in practice, to be more complements to one another in overall risk assessment rather than direct, interchangeable substitutes.

A recent Hannover Re study

The lack of overlap between the ECG and NT-proBNP opens up the possibility for antiselection in situations where only one test or the other is being performed by an insurer and the applicant is aware of the result of the other test. Since, at present, the resting ECG is more commonly performed in the clinical and insurance environments, it is more likely that this potential antiselection would come from that direction. The extent of this risk is uncertain at present. Only time will tell if it is of practical concern in the underwriting environment but caution would seem to suggest a graduated replacement if a substitution of one test for another is being considered.

One should also be aware of the possible effects of an elevated serum creatinine on the NT-proBNP results and take this information into account in making risk appraisal decisions on insurance applicants.

Should the applicant have one of the medical conditions known to increase the NT-proBNP it would also be important to not “double dip” by rating the blood test and the underlying condition that is causing its elevation, unless the NT-proBNP level exceeds that which would normally be seen with the known cardiovascular impairment.

One frequently asked question is whether the NT-proBNP alone is an adequate direct substitute for an exercise stress test. Since the NT-proBNP is similar to but perhaps modestly better than a resting ECG, it is likely not a one for one replacement for the exercise test, any more than a resting tracing would be a replacement for a treadmill.

NT-proBNP testing in underwriting

A few suggestions on how to use NT-proBNP in the underwriting process are summarized below.

1. Testing with NT-proBNP could be instituted where no cardiac testing is currently being performed. This would clearly have a benefit in terms or reducing mortality. The biggest problem would be the additional cost of the testing, which would be an addition to the current budget. This could be mitigated to an extent by targeting the implementation to areas with the largest potential bang for the buck i.e. older individuals with a higher prevalence of heart disease or demographic areas where cardiovascular claims have been high in a particular company.
2. It could be added to an existing testing protocol that includes a resting ECG. It clearly is complementary to the latter test and both together have greater protective value than either test alone in detecting mortality. The downside to this approach is the increased cost. This could be offset to a degree by implementing this change at higher application amounts where the potential mortality savings could outweigh the additional cost.
3. It could be used to replace a resting ECG in the current age and amount testing grid. The NT-proBNP is cheaper and easier to obtain than the resting ECG and appears to have at least an equal and probably greater overall protective value. However, there is incomplete overlap between the two tests. Thus, not all applicants with an abnormal ECG will have an abnormal NT-proBNP and vice versa. This opens up the possibility of antiselection from those with a known abnormal ECG. With this in mind the recommendation would be to introduce the change in an incremental pattern beginning at lower policy amounts so that experience could be tracked and problem areas identified.
4. The NT-proBNP could be part of a comprehensive program to replace the exercise test in some parts of the age an amount grid. As noted above, the test is not a one for one substitute for the exercise test in terms of mortality protective value. However, if one thinks holistically and looks at the overall mortality savings on a block of business the use of the NT-proBNP could in theory replace at least some stress testing if it were (a) expanded alone to ages and amounts below where testing is currently being performed

and/or (b) combined with the resting ECG in selected cells of the grid (more than the ones just being evaluated with the exercise test at present). The expectation is that the cheaper cost and improved convenience and timeliness of NT-proBNP could permit the expanded testing without a substantial net cost impact. The idea would be that the composite protective value of the expanded testing would roughly equal that found with the stress testing alone. Whether this protective value equation works for the block of business as a whole depends highly on the specifics regarding the implementation. The devil is truly in the details.

However the NT-proBNP test might be employed, the underwriting guidelines for using it should encompass the key facts noted above and should include the following:

1. Ratings should vary with the age and sex of the applicant
2. Ratings should vary with the degree of elevation of the NT-proBNP
3. Caution is probably in order for guidance on the higher test values as there is little credible experience in this range
4. Some accommodation should be made for the effect an elevated creatinine may have on the test values
5. Credit should be available if, after evaluation, key cardiovascular causes for an elevated test are eliminated. The more thorough the evaluation and the greater the number of potential causes excluded , the greater the credit
6. Care should be taken to account for comorbid conditions (CAD, valvular disease etc.) that can increase the NT-proBNP levels so as to avoid “double dipping” and debiting the same condition twice.

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