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Letter to Editor

Using NT-proBNP as a criterion for heart failure hospitalization

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The matched case-control, single-centred, prospective study by Ozturk et al. was designed to compare the NT-proBNP levels between hospitalized congestive heart failure (CHF) patients and outpatients.[1] The main purpose of their study was to define a certain cut-off NT-proBNP value for hospitalization of CHF patients. We will address five points to challenge their study design and presentation (As summarized in Figure 1):

1- The small sample size and wide range of NT-proBNP (with wide standard error) in the patient group (range: 245-35,000) may present low analysis power.
2- In order to define a cut point level of NT-proBNP, the area under curve (AUC) should be used.
3- According to Table 3 in their article, confounding variables should be defined and analyzed separately.
4- Since mean of NT-proBNP may vary by age, dividing the patients based on age (<50, 50-75, >75 years) would have been more appropriate.
5- In Table 1, that showed baseline characteristics of patients in their paper, data about outpatients (n = 32) should have been separated according to normal and stabilized heart failure (HF) groups.

We also should mention additional comments about using BNP or NT-proBNP in diagnosis of CHF:

- Adding brain natriuretic peptide (BNP) or NT-proBNP tests to standard clinical assessment has been shown to be valuable for an accurate and efficient diagnosis and prognostication of HF. Thus, the use of BNP or NT-proBNP may be associated with improved clinical outcomes.[2]
- NT-proBNP may be elevated in a number of other diseases such as heart muscle disease, valvular heart disease, arrhythmia, pulmonary heart disease, stroke and sepsis. Meanwhile, patient-related factors like sex, age, renal and liver failure, hypertension, glucocorticoids use, obesity (negative effect), and also cardioactive drugs may influence the results.[2,3]
- One of the most useful aspects of this test is its negative predictive value. This can be very helpful in patients who need to be reassured about not actively being in CHF.[4]
- Since the gold standard for HF diagnosis in obese patients is hard to precisely define in any situation, using BNP in those patients may not be appropriate.

Technical problems about BNP or NT-proBNP measurement should also be considered:

- NT-proBNP measurement in the central laboratory offers tight quality control and may be the preferred way to go if very precise measurements are desired.[3]
- It was a consensus that the 1-hour time limit should direct which type of test to use.[4]

Potential overall accuracy of NT-proBNP in the diagnosis of HF in primary care measured by the AUC has been uniformly high across studies.[5]

However, false negative results may be obtained in some situations including:

- HF patients with low BNPs are mainly patients with borderline left ventricular systolic dimension (LVSD) or are on cardioactive drugs known to lower NT-proBNP concentrations.
- NT-proBNP concentrations should be mentioned according to age. The rule-out value of NT-proBNP in this setting is well documented.[5] Patients with NT-proBNP concentrations < 300 pg/ml are very unlikely to have HF (negative predictive value of 99%).

Patients with NT-proBNP concentrations > 450 pg/ml (< 50 years of age), > 900 pg/ml (50–75 years), and > 1800 pg/ml (> 75 years) have a very high probability of having HF as the cause of their acute dyspnea (although the clinical judgment must also consider other diagnoses, namely acute coronary syndrome and pulmonary embolism).

- According to age, patients with NT-proBNP concentrations between 300 pg/ml and 450, 900, or 1800 pg/ml have several other diagnostic possibilities that should be considered.

Finally, cut-points are not yet clearly defined and more work is required to optimize them. In consultation with the local biochemical laboratory, local centers should be audited before deciding on cut-points in their own populations. Characteristics analysis must also be considered.[3]

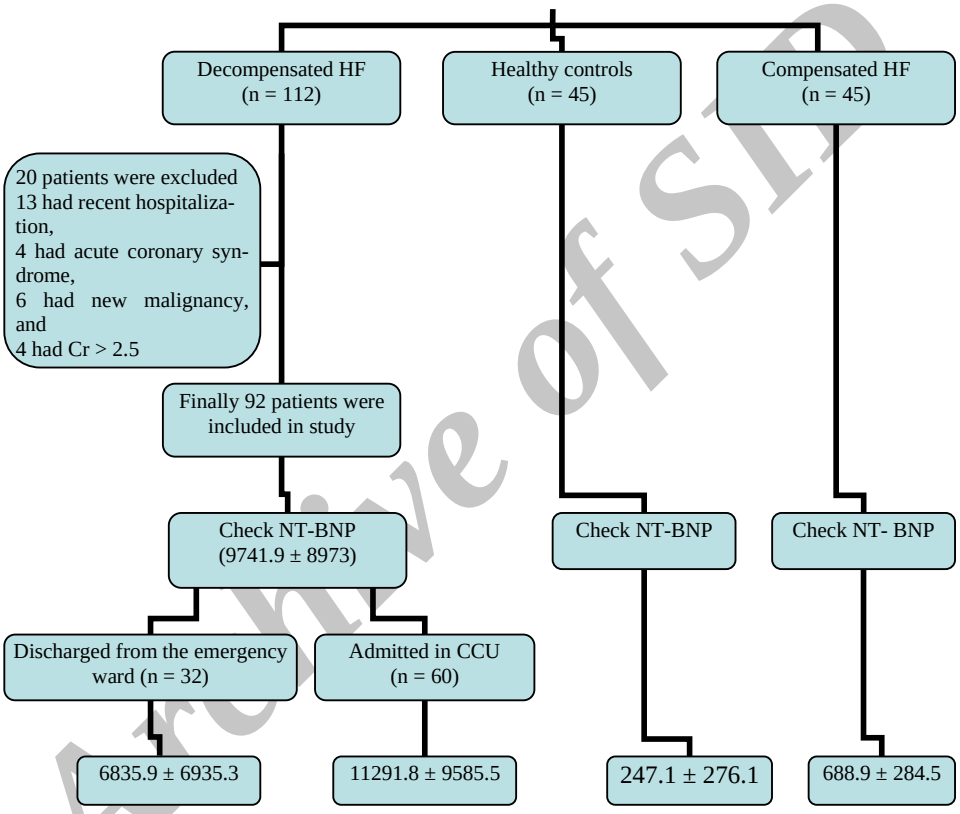

Figure 1. Summary of the study design by Ozturk et al.
(Values of NT-BNP are expressed as mean ± SE)

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Conflict of Interests

Authors have no conflict of interests.

References

1. Ozturk TC, Unluer E, Denizbasi A, Guneysel O, Onur O. Can NT-proBNP be used as a criterion for heart failure hospitalization in emergency room? J Res Med Sci 2011; 16(12): 1564-71.
2. Kim HN, Januzzi JL, Jr. Natriuretic peptide testing in heart failure. Circulation 2011; 123(18): 2015-9.
3. Januzzi JL, Jr., Chen-Tournoux AA, Moe G. Amino-terminal pro-B-type natriuretic peptide testing for the diagnosis or exclusion of heart failure in patients with acute symptoms. Am J Cardiol 2008; 101(3A): 29-38.
4. Young JB, Correia NG, Francis GS, Maisel A, Michota F. Testing for B-type natriuretic peptide in the diagnosis and assessment of heart failure: what are the nuances? Cleve Clin J Med 2004; 71 Suppl 5: S1-17.
5. Bettencourt PM. Clinical usefulness of B-type natriuretic peptide measurement: present and future perspectives. Heart 2005; 91(11): 1489-94.