Assessing the Benefits of B-type Natriuretic Peptide (BNP) for Heart Failure

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Abstract

B-type natriuretic peptide, abbreviated BNP, increases in the circulation when the left ventricle is being stretched and expanded. For this reason, high levels of BNP in a person's body may be a way to diagnose heart failure early in it's course or indicate a person's risk of clinically overt heart failure, allow for delay in progression of disease, measure it's severity, and predict serious and mortality associated complications with higher levels of BNP indicating a higher risk factor.

We investigate what other factors affect or do not affect BNP levels as well as what factors are effected by BNP levels. The factors selected were: troponin I levels, age, sex, number of heart related diagnoses, length of stay, and medications, troponin I, and ejection fraction. We considered that patients on medication would show a greater decrease in BNP levels than patients not on medication, patients with many heart related diagnoses would have higher BNP levels than patients with fewer diagnoses, and older patients would have higher BNP levels. Further, BNP levels would be associated with a longer hospital stay. What the relationship is between the BNP level and the troponin I level in CHF is not clear. How the BNP increases as the ejection fraction decreases also needs clarification. We extracted the data identified from over 700 patient records.

BNP levels and troponinI levels are not independent, increasing or decresing together. Since BNP and troponin I are dependent, high levels of both are associated with an increased hospital stay. As age and the number of heart related admissions to the hospital increases, so does the average BNP level of the patient. The study is not sufficiently powered to show the effect of medication. There is a relationship between increased BNP level and ejection fraction under 40%.

Background Information

Congestive heart failure is a health problem affecting 1.5 million new people a year in North America and Europe, it is also the main cause of hospitalization in people over 65 years of age. There are currently 15 million patients suffering from congestive heart failure in North America and Europe alone, a number that has increased 159 percent over the past 10 years. Since heart failure is such a prominent disease in our society, a lot of health care expenditure goes into its diagnosis and treatment; in the year 2001 the associated costs were approximately $24 billion (American Heart Association.)

Monitoring BNP levels is a new and highly efficient way of diagnosing heart failure as well as excluding non-cardiac causes of shortness of breath. This test circumvents the human error and inaccuracies involved with the present method of diagnosing congestive heart failure (CHF). The standard diagnostic practice is to have a physician listen to the patient's breath sounds for a specific sound associated with CHF. Listening to breath sounds is only accurate when the disease is advanced to the stage in which the pumping function of the heart is impaired. The pumping of the heart is impaired when the circulation pressure increases above the osmotic pressure of the blood proteins that keep fluid in the circulation, causing fluid to pass into the lung's airspaces. Since BNP levels rise before the disease reaches this advanced stage it would be beneficial to the patient to use BNP screening to catch the disease earlier. This project explored which factors, other than heart problems, do and do not effect the BNP levels of an individual. This is an important area to both research and pursue because it is cheaper for the hospital, potentially more accurate, and it is faster than the current diagnostic methods. Consequently, the patient can be treated earlier if he or she suffers from a cardiac problem.

When a person is suffering from congestive heart failure his or her heart is not able to supply the body with enough blood for one of two reasons; both explained by the Frank-Starling law of the heart. The Frank-Starling law of the heart states that the heart's muscle fibers are similar to springs, they must be stretched in order to contract. Therefore, if the heart does not fill up with enough blood, then the heart muscles are not stretched far enough to contract in a vigorous enough manner to pump blood throughout the body. However, if the muscle fibers are stretched too far, for too long, they will lose resiliency and will not be able to contract fully again. When the body is deprived of an adequate blood supply for too long the person will die or go into a coma.

Previous studies have been done proving that increased levels of BNP indicate an increased risk of heart failure. One study showed that after other cardiovascular risk factors were accounted for, increased BNP levels were associated with an increase in death, a first cardiovascular event, heart failure, atrial fibrillation, and a stroke or transient ischemic attack. (Wang,. Larson, et al.2004.) This study stated that the relation to BNP levels was strongest for atrial fibrillation and heart failure and was more effective than atrial natriuretic peptide for most outcomes. It has also been shown that higher levels of BNP indicate a higher risk of a poorer prognosis. (Fonarow, Horwich) Another more specific study showed that BNP levels along with other clinical data could be used to rule out or to diagnose heart failure in patients with acute dyspnea, shortness of breath. (Christian Mueller, M.D., Andre Scholer, Ph.D., et al. New England Journal of Medicine February 12, 2004.) This study used minimum BNP level of 500pg per milliliter as an indication of heart failure. It found that BNP testing was effective in ruling out heart failure as a diagnosis. Of the patients who did not receive BNP testing, 10 percent more were placed in intensive care than the patients who did receive BNP testing. And 6% more were diagnosed with heart failure. Patients tested for BNP levels also reduced the cost of treatment by 26 percent due to the fact that it was caught earlier. Another recent study, done in Japan, discovered that BNP levels when used with troponinI levels, can be a valuable tool for diagnosing and treating patients with congestive heart failure (Ishii, Cui, Kitagawa, et al., 2003.)

Hypothesis

The following factors will increase or decrease significantly depending on the BNP level of the individual; number of medications the patient is on, how many heart related diagnoses the patient has had in the past, age, length of stay, troponin I levels, and ejection fraction.

Methods and data

Statistical Analyses Defined. A number of statistical methods were used to interpret the data gathered from patient's medical records. The statistics that proved to be most helpful to this study were ANOVA, chi-square testing, and in some cases simple statistics such as the t-test and finding averages. The abbreviation ANOVA stands for Analysis Of Variance, this test is used when the means of many groups are being compared with one another, as opposed to the t-test which compares only two groups. The ANOVA test gives one significance value for all of the data being compared, rather than a value for every two sets of data. This is important because if you were to compare 20 sets of data and one pair was "significant" it does not mean that all the data is significant, but the ANOVA test gives you one significance value for all the sets of data combined. The chi-square test is another way to test for statistical significance and it does this by comparing observed frequencies to expected frequencies (counts) of membership in a N-by-N cross table. For a chi-square significance value to be considered significant, there must be a difference between the observed and expected distribution of the data. Chi-square charts show exactly how data points are distributed within groups.

Charts and Grap

How the variables were scored in order to be run through the statistical analyses

TroponinI value	score
<1	0
= >1	1

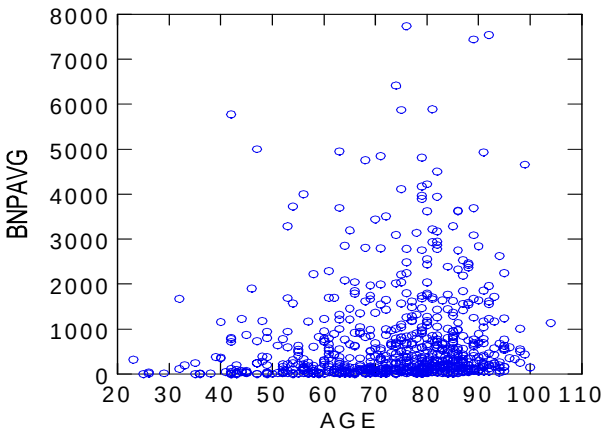
BNP value	score
<175	0
175-400	1
401-600	2
601-1000	3
>1000	4

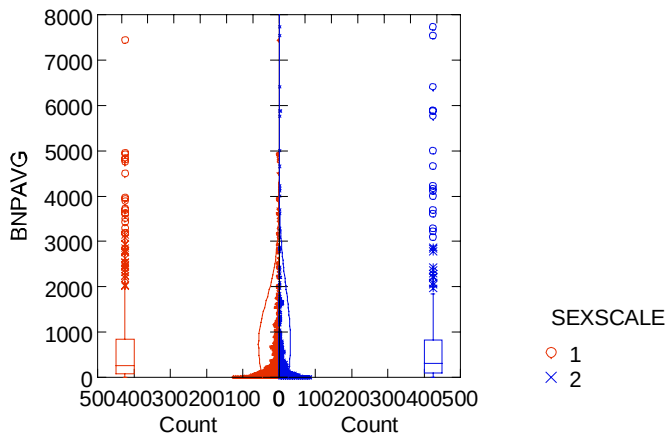
Medication value	score
on medication	0
not on med.	1

BNP value	score
<50%	0
= >50%	1

Age value	score
< 41	1
41-65	2
66-75	3
76-85	4
>85	5

Ejection Fraction value	score
= >70	0
40-69	1
20-39	2
= <19	4





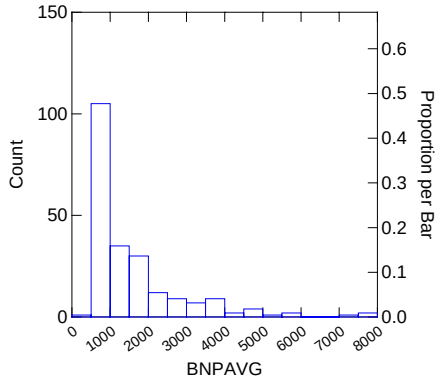
BNP, TroponinI, and Length of Stay To start comparing three variables at a time a new variable called TNIBNP was created. This variable combined data from BNP score and the troponinI score. Any patient with BNP over 1000 and troponinI over 0.65 was assigned a 1 and all the other patients were assigned a zero. The average length of stay and the average number of BNP related admissions to the hospital for each group are shown in the chart. The table shows that as troponinI and BNP levels increase, so does the average length of stay and number of hospital admissions. **BNP and Ejection Fraction**Ejection fraction measures the amount of blood pumped out of heart with each heart contraction. Since BNP levels increase as the heart muscles lose their ability to function, it would make sense that as BNP levels increase, ejection fraction values would decrease. This correlation is illustrated in the ANOVA test below, which is an example of a near perfect outcome. In this test BNP groups 0 and 1, as well as 2 and 3 were combined. **BNP and QRS Duration** The span of an EKG tracing is called the QRS duration. If the QRS duration is too long this means there is a problem with repolarization in the heart. The study tested proved that excessively high BNP levels result in higher QRS duration. This means that high BNP levels point towards a repolarization problem. The following graphs show an ANOVA test and a t-test, both with a p-value of .001, proving this discovery.

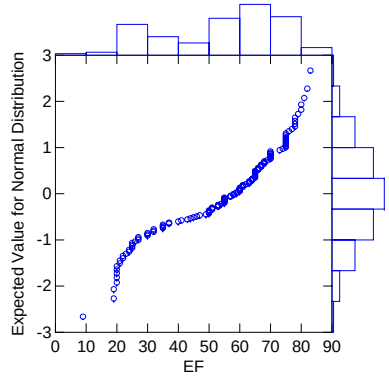
BNP and TroponinI Levels The p-value of the chi-square test comparing BNP score to TroponinI score was 0.00. This is considered significant. To further to prove the correlation the TroponinI score was broken up more so that levels less than .65 were scored zero, all levels between .65 and 1 were scored one, between 1 and 3 were scored two, between 3 and 6 were scored three, between 6 and 10 were scored four, and greater than 10 were scored five. The ANOVA test with the new TroponinI scores made a p-value of 0.00, further proving that the two variables are not independent. The ANOVA test uses one variable as a factor and the other as a continuous variable. If both variables were continuous, then a regression analysis would be done. The interest here was the strength of an association more than the amount of correlation between the variables. **BNP and Length of Stay** This graph shows that length of stay increases as BNP levels increase. The p-value of this test was .001 **BNP and Age** The scatter plot shows visually how BNP levels increase with age. Since there were so many groups it was not easy to represent the chi-square test in the form of a graph, so I combined age scale groups 1 and 2 into one group and I combined groups 3,4,and 5 into another group. I then used these two age groups and compared them to BNP score, not BNP average, the resulting graph is shown and has a p-value of .001 **BNP and Sex** The p-value of the t-test comparing BNP average to sex was .412 for the separate variance and was .394 for the pooled variance. Both of these values are insignificant, proving that sex does not effect BNP levels. **BNP and Medication** The medications involved in the study were furosemide, nesiritide, and the beta-blockers atenolol, metoprolol, esmolol, and propranolol. Beta-blockers are used to treat CHF patients because they slow nerve impulses to the heart by blocking beta receptor sites, making the patient's weakened heart work less hard. Nesiritide and furosemide are both used in CHF patients to reduce blood pressure. Nesiritide is an artificial form of BNP, and when given to a patient it lowers their natural BNP levels. This sounds counter-intuitive, but by giving the patient artificial BNP the body's feedback mechanism will work in favor of the patient. The feedback mechanism detects high levels of BNP and therefore tells the body to stop making more, reducing the level of natural BNP in their blood system. Since patients on Nesiritide would have artificially high BNP levels, they could alter the outcome of the experiment if they were included in the study. To be sure the data used was not contaminated with artificially high BNP levels, all patients who had their BNP levels measured after being given nesiritide were excluded from the study.Since these medicines are used to lower BNP levels only in people with CHF, the tests run only used patients who had been diagnosed with CHF. The p-value of this test is 0.00

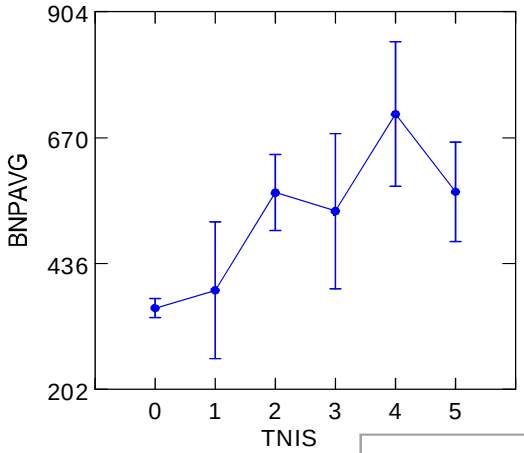
Results

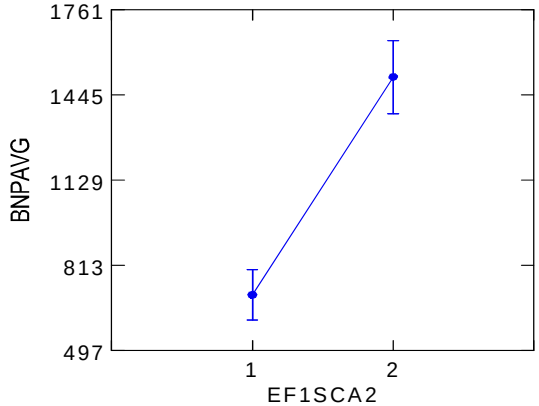
After conducting this project it was found that BNP levels and troponinI levels are not independent, they go up and down together. Since BNP and troponinI are co-dependent, high levels of both are associated with an increased hospital stay and high ejection fraction. As age and the number of heart related admissions to the hospital increases, so does the average BNP level of the patient. BNP levels are not affected by the sex of a patient, and medication decreases the BNP level only if the patient suffers from congestive heart failure (CHF).

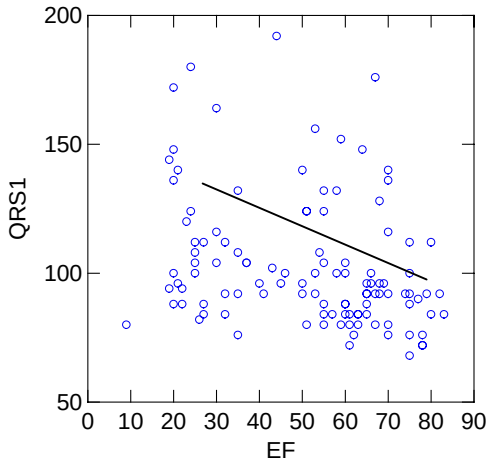
This information can be used to facilitate a quicker and more accurate diagnosis of patients. With an earlier diagnosis, patients with a cardiac disease can be treated sooner, and the patients not diagnosed with a cardiac disease can be released from the hospital or tested for other problems. Along with the health benefits of using BNP to diagnose CHF, hospitals will save money performing fewer unneeded tests, and many patients will be in the hospital for shorter stays.



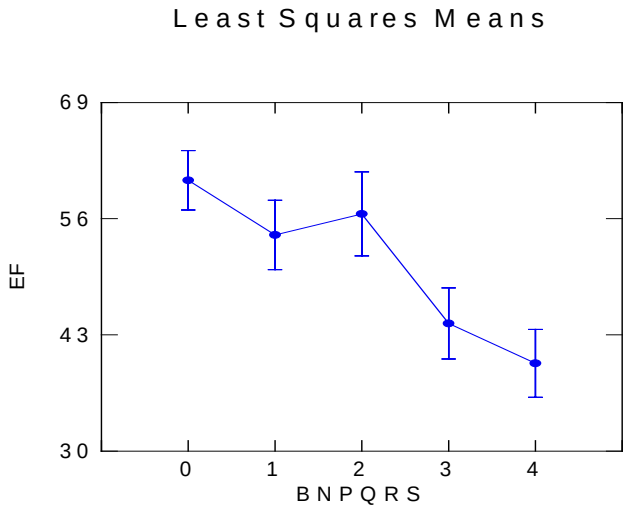


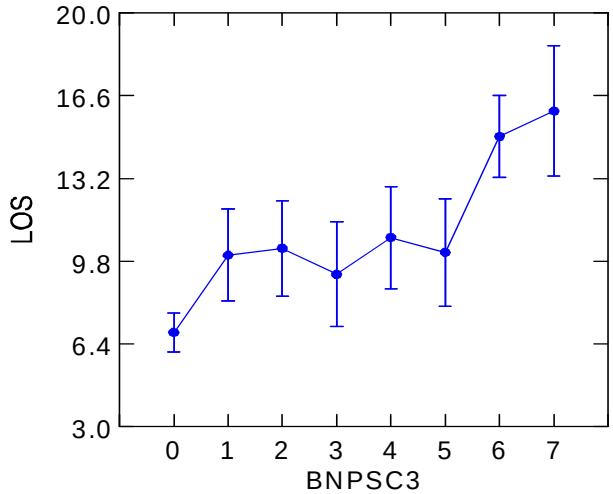






BNPSC	QRS < 100	QRS > 100	Total	N
0	48.4	28.6	39.6	44
1	12.9	6.1	9.9	11
2	19.4	18.4	18.9	21
3	19.4	46.9	31.5	35
Total	100	100	100	
N	62	49	P< 0.014	111





Delta BNP score (rows) by medication score (columns)

	0	1	total
0	94	494	588
1	4	130	134
total	98	624	722

Discussion

This study found that sex does not effect the BNP levels of an individual, and thus does not need to be accounted for when using BNP levels to help diagnose a patient. It also discovered and proved that BNP increases with age, a factor that must be taken into account when using BNP to diagnose a patient. While CHF also increases with age, the BNP level increase is disproportionate to the increase in CHF occurrences. Patients with higher BNP levels have more heart related diagnoses than patients with lower BNP levels. This means that if a patient has a history of heart problems and is presenting with symptoms of CHF, then a BNP test with high results could be an indication that the patient does have CHF. Currently BNP is not used on its own to diagnose CHF, it is either not used at all or is used in conjunction with listening to breath sounds. Since patients with high BNP levels have a longer average length of stay, if BNP was used as a diagnostic tool, many of these patients could be diagnosed earlier. Decreased ejection associated with increased BNP levels is further proof that BNP levels indicate heart problems. Now that it is known what other factors affect BNP levels, BNP can effectively be used in managing congestive heart failure