Research Article

Correlation between brain natriuretic peptide and right ventricular systolic pressure in patients with decompensated heart failure

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Abstract

Background: Brain natriuretic peptide (BNP) is a cardiac hormone with diuretic, natriuretic, and vasodilatory properties produced by the heart ventricles in response to volume expansion and pressure load. The concentration of BNP is highest in the artery of healthy individuals but in heart failure patients it is shifted to the ventricles. Plasma BNP levels are influenced by many factors including age, renal function, medications, and arrhythmias. BNP is released in response to improved myocardial relaxation and it also plays an important role in the regulatory response to acute elevation in ventricular volume by opposing the effects of the activated renin, angiotensin, and aldosterone system.

Objective: To evaluate the correlation between Brain natriuretic peptide (BNP) and right ventricular systolic pressure (RVSP) in patients with decompensated heart failure.

Materials and Methods: In this retrospective-chart review, electronic data and medical records between 1 January 2013 and 31 December 2013 were reviewed to screen patients for inclusion into the study. Inclusion criteria included patients admitted to King Abdulaziz Medical City - Cardiac Center (KAMC-CC) with diagnosis of decompensated heart failure and Right Ventricular Systolic Pressure (RVSP) more than 35 mmhg on admission, aged 50 years or older with ejection fraction ≤ 35%, Brain Natriuretic Peptide (BNP) value and Echocardiography (2D) were assessed at least once, the time difference between BNP measurement and Echocardiography less than 72 hours, and New York Heart Association (NYHA) Class III – IV. On the other hand, patients with impaired renal function (serum creatinine > 133 µmol/l), atrial arrhythmia, congenital heart disease and cardiogenic shock were excluded. Demographic and clinical data including BNP and RVSP were recorded for eligible patients. Patients were divided into four groups according to their RVSP readings (30-40, 40-50, 50-60, and > 60 mmhg). ANOVA was utilized to assess for group differences.

Result: 388 patients with decompensated heart failure were screened during the period from January to December 2013. Only 27 patients met inclusion criteria. The increase in RVSP was associated with an increase in BNP until RVSP reaches a value of > 60 mmhg where BNP starts to decline. The differences between the four groups were statistically significant ($F = 5.3$, $p = 0.007$). Post hoc analysis was performed to test the difference between the individual groups and indicated a significant difference between Group one vs. Group two (mean difference: –215.5 ± 71.7, CI: 17.1 to 413.8, $p = 0.03$) and Group one vs. Group three (mean difference: 234.3 ± 63.8, CI: –414.02 to –60.69, $p = 0.006$).

Conclusion: The study results indicate an association between RVSP and BNP. The increase in RVSP is associated with an increase in BNP until RVSP reaches a value of > 60 mmhg where BNP starts to decline. This correlation can be clinically useful in assessing prognosis and in helping physicians to predict BNP values with known RVSP values and vice versa. Further studies with larger sample size are required to confirm these interesting results.

Key Words: Brain natriuretic peptide (BNP), right ventricular systolic pressure (RVSP), King Abdulaziz Medical City, Saudi Arabia

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Introduction

Heart failure (HF) affects approximately 10% of individuals over the age of 65.[1] Several classifications for heart failure exist based on the side of the heart that is affected, risk for developing severe disability, and functional limitations.[2] Acute decompensated heart failure (ADHF) is defined as new or worsening of signs and symptoms of heart failure that has

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developed rapidly.[3] Common causes for developing ADHF are usually cardiac, including: uncontrolled hypertension (the most common cause), ischemia and arrhythmia. Non-cardiac causes include: infection, pulmonary embolus and pulmonary heart disease.[3]

There are several methods for diagnosing HF, one of which is the use of biochemical markers such as natriuretic peptides. The history of the natriuretic peptides discovery was in 1956 when early researches showed similarities between granules in endocrine glands with the cells found in atria by using electron microscope.[4] Different types of natriuretic peptides can be used as biomarkers. These include: Atrial Natriuretic peptide (ANP), C-type Natriuretic peptide (CNP), Dendroaspis Natriuretic peptide (DNP), urodilatin, and Brain Natriuretic Peptide (BNP).[5] The ideal Biomarker should be highly specific, sensitive and has the ability to be reproduced and standardized across different laboratories. None of the Natriuretic Peptides meet the definition of an ideal biomarker. BNP or Nt-ProBNP Biomarkers can be used in the diagnosis of heart failure and should be performed when there are signs and symptoms of heart failure that are ambiguous or confounding with the disease states.[9]

BNP is a cardiac hormone with diuretic, natriuretic, and vaso-dilatory properties produced by the heart ventricles in response to volume expansion and pressure load. The concentration of BNP is highest in the artery of healthy individuals, but in heart failure patients it is shifted to the ventricles.[6] Plasma BNP levels are influenced by many factors including age, renal function, medications and arrhythmias.[8] BNP is released in response to improved myocardial relaxation and also plays an important role in the regulatory response to acute elevation in ventricular volume by opposing the effects of the activated renin, angiotensin and aldosterone system.[7]

Right ventricular systolic pressure (RVSP) in normal patients is stable in both genders until they reach the age of 50. Afterwards, RVSP increases progressively in a linear manner and is significantly higher in patients older than 75 years of age.[10] The normal ranges of RVSP for those younger than 50 years old ranges from 16mmHg to 39 mmHg and for those older than 75 years old the RVSP is between 17 mmHg to 52 mmHg. RVSP can be measured by echocardiography (ECHO) based on the estimated flow of the tricuspid regurgitant jet velocity.[11] The equation of Bernoulli estimates RVSP (RVSP = 4V2 + RAP) assessed (RAP) is the right atrial pressure assumed to be constant at 10 mmHg in patients with normal hearts.[10] Few studies were conducted to assess the relationship between RVSP and BNP in patients with decompensated heart failure. Therefore, this study was conducted to further examine their correlation.

Materials and Methods

Study Design

In this retrospective chart-review study, electronic data and medical records (QUADRAMED as well as Outpatient pharmacy medication recording system) at king Abdulaziz Medical city were reviewed to screen patients for inclusion into the study [Figure 2]. Demographic and clinical data including age, gender, weight, body mass index, RVSP, BNP, troponin I, ejection fraction (EF), serum creatinine, mean blood pressure, heart rate, glycated hemoglobin, NYHA class and associated co-morbidities (Hypertension, diabetes. dyslipidemia, coronary syndrome, stent and cardiomyopathy) were recorded for eligible patients.

Patients were divided into four groups based on their RVSP values; (Group one: 30–40 mmhg, Group two: 40–50 mmhg, Group three: 50–60 mmhg, and Group four: >60 mmhg). Serum creatinine was measured within 24 hours of BNP collection, while EF was measured within 24 hours of RVSP measurement. The study was approved by the Institutional Review Board of King Abdulaziz Medical city.

Study Setting

This study was conducted at KAMC-CC which is located within King Abdulaziz medical City in Riyadh, Saudi Arabia and has more than 1025 beds. King Abdulaziz Medical City-Cardiac Center has also one of the most comprehensive programs for the management of heart problems in Saudi Arabia and the Gulf Region.

Study Subjects

Inclusion criteria were: patients with RVSP more than 35 mmHg on admission, age of 50 years and above, ejection fraction ≤ 35%, RVSP values assessed using Transthoracic Doppler echocardiography, and the time difference between BNP collection and RVSP measurement not exceeding 72 hours. On the other hand, younger patients (< 50 years old), patients with chronic renal impairment (serum creatinine more than 133 μmol/l), atrial arrhythmia, congenital heart disease and cardiogenic shock were excluded [Figure 2].

Data Analysis

All data were coded and entered into SPSS (IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.). ANOVA was utilized to assess for group differences. *P* value less than 0.05 was considered significant.

Result

388 patients with decompensated heart failure at King Abdulaziz Medical City - Cardiac Center were screened for inclusion into the study during the period from January to December 2013. Out of the 388 patients screened in this study, 27 patients met our inclusion criteria. The demographics characteristics are shown in Table 1. Results from this study indicate that the increase in RVSP was associated with an increase in BNP until an RVSP of >60 mmhg where BNP starts to decline [Tables 2 and 3, Figure 1]. The differences between the four groups were statistically significant (F = 5.3, $p = 0.007$) [Table 2]. Post Hoc analysis was conducted to test the differences between the individual groups and indicated a significant difference between Group one vs. Group two and Group one vs. Group three [Table 3].

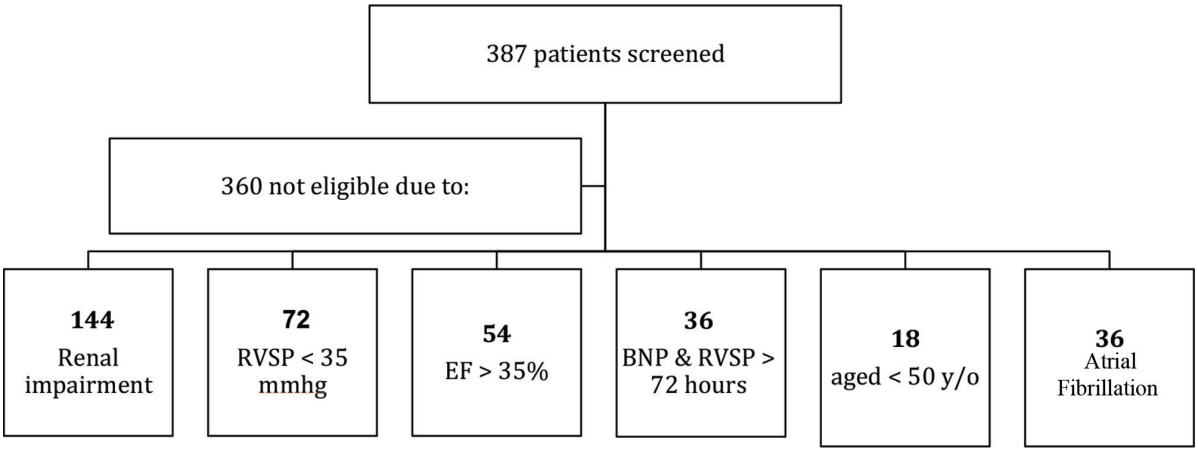

Figure 2: Reasons for exclusion

Table 1: Patient's characteristics

Parameter	Group one	Group two	Group three	Group four
Number of patients	5	6	11	5
Mean age	60.4 (σ:7.8)	58.5 (σ:12.8)	65 (σ:6.8)	67.3 (σ:15)
Gender (Male)	60% (3)	87.5% (5)	46.1% (5)	100% (5)
Mean serum creatinine (μmol/L):	70.06 (σ:25.2)	92.62 (σ:22.2)	98.09 (σ:29.6)	80.5 (σ:12.6)
Mean A1C	8.7 (σ:2.1)	8.05 (σ:2.06)	8.5 (σ:2.76)	9.51 (σ:1.5)
Mean body mass index (BMI)	30.6 (σ:7.5)	27.2 (σ:3.1)	28.6 (σ:6.8)	29.3 (σ:7.4)
Comorbidities				
Hypertension (HTN)	60%	66.6%	81.8%	100%
Dyslipidemia (DLP)	40%	66.6%	72.7%	80%
Diabetes mellitus (DM)	60%	83.3%	81.8%	100%
Ischemic cardiomyopathy (ICM)	40%	50%	36.3%	60%
Old Acute coronary syndrome (ACS)	40%	16.6%	18.1%	20%
Drug eluting stent	40%	16.6%	9.09%	0%
Bare metal stent	0%	0%	0%	20%
Asthma	50%	0%	9.09%	0%

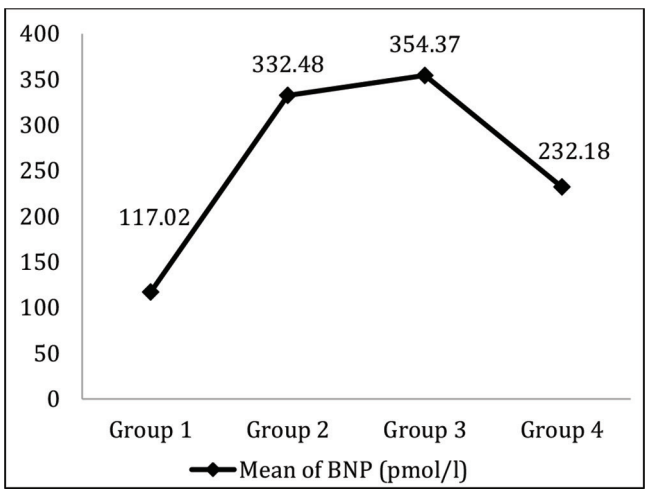

Figure 1: Means plots of BNP for each RVSP group

Discussion

In this study, RVSP was positively associated with BNP which is in line of previously published studies.[15] A novel finding in our study was the increase of in BNP until a RVSP of > 60 mmhg, after which, BNP started to decline. The result of this study could be explained by understanding the physiological actions of BNP which include decrease in vascular resistance as well as an increase in natriuresis.[12] Thus, the net effect of BNP is lowering systemic blood pressure and afterload, yielding an increase in cardiac output. Therefore, BNP is increased in heart failure patients with increased level of RVSP in an attempt to reduce blood pressure and increase cardiac output. The loss of this association at the high RVSP values needs further investigation.

In support of our findings, BNP and Nt-ProBNP levels are reduced with the long term treatment with angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers,

Table 2: Mean BNP result per RVSP groups**

RVSP groups*	Number of patients	Mean BNP (pmol/L)	95% Confidence interval for mean
1.00	5	117.02 (σ: 82.312)	14.81–219.22
2.00	6	332.48 (σ: 134.190)	191.66–473.31
3.00	11	354.37 (σ: 128.006)	268.38–440.37
4.00	5	232.18 (σ: 101.541)	106.10–358.26
Total	27	282.93 (σ: 144.598)	225.72–340.13

*Group one: 30–40 mmHg, Group two: 40–50 mmHg, Group three: 50–60 mmHg, Group four: >60 mmHg.
**ANOVA test was significant ($F = 5.3$, $p = 0.007$)

Table 3: Post Hoc analysis for differences in BNP between RVSB groups

(I) RVSP group	(J) RVSP group	Mean difference (I-J)	Standard error	Significance	95% Confidence interval	
					Lower bound	Upper bound
1.00	2.00	–215.465*	71.673	.030	–413.81	–17.12
	3.00	–237.354*	63.841	.006	–414.02	–60.69
	4.00	–115.162	74.860	.432	–322.32	92.00
2.00	1.00	215.465*	71.673	.030	17.12	413.81
	3.00	–21.888	60.072	.983	–188.13	144.35
	4.00	100.303	71.673	.512	–98.04	298.65
3.00	1.00	237.354*	63.841	.006	60.69	414.02
	2.00	21.888	60.072	.983	–144.35	188.13
	4.00	122.192	63.841	.250	–54.48	298.86
4.00	1.00	115.162	74.860	.432	–92.00	322.32
	2.00	–100.303	71.673	.512	–298.65	98.04
	3.00	–122.192	63.841	.250	–298.86	54.48

*The mean difference is significant at the 0.05 level.
**Tukey HSD was used.

B-Blockers and spironolactone because they can reverse the remodeling process.[9] The Australian-New Zealand Carvedilol Heart Failure Trial observed that Carvedilol decreased mortality rates and heart failure admissions in patients with higher BNP levels.[13]

Studies have also shown that if the values of the BNP at discharge are lower than admission values, the patients are less likely to have adverse events like readmission for HF or even death.[14] In VALHEFT study, BNP values of HF patients were measured at baseline and after four months and it was found that patients with decreasing BNP values had a significantly better prognosis.[14] In the RESOLVD pilot study, initiating metoprolol therapy was associated with an initial rise in BNP levels compared with placebo.[13] Our study had some limitations as it was a retrospective chart review and only a small sample size was included making comparisons difficult without the adequate statistical power. The small sample size resulted from the strict inclusion criteria that we applied to exclude confounding factors that have an effect on the BNP levels correlation. We suggest further studying the topic utilizing a prospective design and larger sample size.

Conclusion

Our results indicate an association between RVSP and BNP. This correlation can be clinically useful in assessing prognosis and in helping the physicians to predict BNP values with known RVSP values and vice versa. Further studies with larger sample size are required to confirm this result.

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