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The Relationships Between BNP and Neurocardiac Injury Severity, Noninvasive Cardiac Output, and Outcomes After Aneurysmal Subarachnoid Hemorrhage

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Abstract

Introduction: Neurocardiac injury, a type of myocardial dysfunction associated with neurological insult to the brain, occurs in 31–48% of aneurysmal subarachnoid hemorrhage (aSAH) patients. Cardiac troponin I (cTnI) is commonly used to diagnose neurocardiac injury. Brain natriuretic peptide (BNP), another cardiac marker, is more often used to evaluate degree of heart failure. The purpose of this study was to examine the relationships between BNP and (a) neurocardiac injury severity according to cTnI, (b) noninvasive continuous cardiac output (NCCO), and (c) outcomes in aSAH patients. **Method:** This descriptive longitudinal study enrolled 30 adult aSAH patients. Data collected included BNP and cTnI levels and NCCO parameters for 14 days and outcomes (modified Rankin Scale [mRS] and mortality) at discharge and 3 months. Generalized estimating equations were used to evaluate associations between BNP and cTnI, NCCO, and outcomes. **Results:** BNP was significantly associated with cTnI. For every 1 unit increase in *log* BNP, cTnI increased by 0.05 ng/ml ($p = .001$). Among NCCO parameters, BNP was significantly associated with thoracic fluid content ($p = .0003$). On multivariable analyses, significant associations were found between BNP and poor mRS. For every 1 unit increase in *log* BNP, patients were 3.16 times more likely to have a poor mRS at discharge ($p = .021$) and 5.40 times more likely at 3 months ($p < .0001$). **Conclusion:** There were significant relationships between BNP and cTnI and poor outcomes after aSAH. BNP may have utility as a marker of neurocardiac injury and outcomes after aSAH.

Keywords

brain natriuretic peptide, cardiac troponin I, aneurysmal subarachnoid hemorrhage, neurocardiac injury, noninvasive cardiac output

Neurocardiac injury, a type of myocardial dysfunction associated with neurological insult to the brain, occurs in 31–48% of patients after aneurysmal subarachnoid hemorrhage (aSAH; Cremers et al., 2016; Frangiskakis et al., 2009; Hravnak et al., 2009). It is widely accepted that neurocardiac injury is caused by an acute release of catecholamines that results from elevated intracranial pressure post hemorrhage (Banki et al., 2005; Macmillan, Grant, & Andrews, 2002; Salem et al., 2014). Manifestations of neurocardiac injury often include cardiac arrhythmias, widened QT intervals, depressed cardiac output (CO) and ejection fraction on echocardiogram, and elevated serum cardiac troponin I (cTnI; Hravnak et al., 2009). Neurocardiac injury is typically diagnosed using elevated cTnI level ($\geq$0.3 ng/ml) and myocardial-wall motion abnormalities on echocardiogram within the first 5 days following aneurysm rupture (Frangiskakis et al., 2009; Hravnak et al., 2009). Elevated cTnI levels are seen in 20–68% of aSAH patients who have no prior history of cardiac disease or myocardial infarction. In addition, elevated cTnI level has been associated with poorer Hunt and Hess (HH) grade, Fisher grade, and neurological status on hospital admission as well as with increased risk for developing cardiopulmonary complications and delayed cerebral ischemia

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(Miketic, Hravnak, Sereika, & Crago, 2010; Naidech et al., 2005; Tung et al., 2004). These findings suggest that the development of neurocardiac injury implies a greater degree of neurological insult.

Demographic and prior comorbidity risk factors for neurocardiac injury include advanced age, coronary artery disease, hypertension, and other cardiovascular disorders (Wybraniec, Mizia-Stec, & Krzych, 2014). Although neurocardiac injury after aSAH is often transient (Salem et al., 2014), evidence suggests that it is associated with increased mortality (Kilbourn, Ching, Silverman, McCullough, & Brown, 2015). In addition, neurocardiac injury is independently associated with poorer functional outcomes in aSAH patients (Crago et al., 2004; Hravnak et al., 2009). The reason for this association may be related to the impact of hypotension, arrhythmias, and depressed ejection fraction and stroke volume (SV) on cerebral blood flow (Hravnak et al., 2009; Schillinger, 2005).

Brain natriuretic peptide (BNP) is a 32-amino-acid peptide that is released in response to cardiac myocyte stretch due to elevated filling pressures (Meaudre et al., 2009) and helps to regulate blood pressure and fluid balance (Vanderheyden et al., 2004). BNP is produced by cardiac ventricular cardiomyocytes as well as in the hypothalamus (Kawamura, Inoue, Sakai, & Nakashima, 2012; Takahashi et al., 1992; Vanderheyden et al., 2004). Health-care providers often use BNP diagnostically during the evaluation of patients presenting with symptoms of acute dyspnea to determine whether their etiology is of a cardiac or pulmonary origin (Davis, Espiner, & Richards, 1994). Meaudre et al. (2009) reported that 25 (80%) patients diagnosed with aSAH had a BNP level greater than 100 ng/L during the first 3 days after aneurysm rupture, whereas by the 7th day, levels remained elevated above 100 ng/L in only 4 patients (13%). Researchers have also reported significant associations between BNP level and cTnI level, cardiac dysfunction measured by transthoracic echocardiogram (regional-wall motion abnormalities, reduced left ventricular function, and diastolic dysfunction), and the development of pulmonary edema after aSAH (Tung et al., 2005). Finally, Tung et al. (2005) found increased BNP levels to be significantly associated with increased inpatient mortality in aSAH patients who had no prior history of myocardial infarction or congestive heart failure.

The degree to which BNP level correlates with the severity of neurocardiac injury, CO, and functional outcomes after aSAH is not well established in the literature. It also remains unclear whether BNP level can be used as an independent predictor of neurocardiac injury in this population. Although BNP level is associated with cardiac dysfunction according to echocardiogram, it would also be helpful to determine whether there is a relationship between BNP level and noninvasive continuous cardiac output (NCCO) parameters. Determining the relationships between BNP and NCCO and functional outcomes could help to determine whether BNP could be used as a biomarker for neurocardiac injury and poor outcomes after aSAH.

The overarching purpose of this study, therefore, was to examine the relationships between BNP and (1) neurocardiac injury severity, (2) NCCO, and (3) outcomes in aSAH patients. The specific aims of this study were to (1) determine the relationship between BNP level and the degree of neurocardiac injury as defined by cTnI level, (2) examine the relationship between BNP level and NCCO monitoring parameters, and (3) assess the relationship between BNP level and outcomes (mortality and modified Rankin Scale [mRS]) at hospital discharge and 3 months after aSAH.

Method

Sample and Setting

Patients between the ages of 21 and 75 years who were admitted to the neurological intensive care unit (NICU) of a single academic medical center after being diagnosed with aSAH by computed tomography and/or cerebral angiogram and assigned a Fisher grade >1 by the attending neurosurgeon were eligible to participate. We enrolled patients between October 2014 and October 2015. We excluded those who had preexisting chronic neurological disease, traumatic subarachnoid hemorrhage, mycotic aneurysms, or myocardial infarction within the past year. We obtained written informed consent from all participating patients or their legal representatives based on an institutional review board–approved protocol. All aSAH inpatients received standard nursing and medical care in the NICU.

Measures

We collected and assessed data from the time of enrollment in the study until 14 days after the time of aneurysm rupture or until discharge if patients were discharged before Day 14.

Demographic and clinical characteristics. We obtained basic demographic information including severity of injury, aneurysm information, age, race, gender, and past medical history from the patient, family, or medical record. Specifically, we obtained severity of injury (HH grade and Fisher grade) from the neurosurgical notes in the patient's clinical record. The HH Scale is used to grade the severity of nontraumatic SAH based on symptoms at presentation to the emergency department (Hunt & Hess, 1968).

Neurocardiac injury and BNP. Members of the research team collected blood samples once daily for the purpose of the study. We also used peak daily BNP and cTnI values from samples that were collected as a part of regular patient care in the analyses. Samples were obtained from an arterial or central line and then immediately transported to the in-hospital lab for processing. The analysis was performed in the hospital lab by the in-house staff.

BNP was measured by chemiluminescence on a Beckman Coulter Access analyzer (Beckman Instruments, Inc., Chaska, MN) using the Lumi-Phos 530 ready-to-use chemiluminescent reagent formulation containing alkaline phosphatase substrate, Lumigen PPD, at the hospital laboratory. The lower limit of analytical range for BNP was 1 pg/ml, and the upper limit was 5,000 pg/ml.

We used cTnI levels to represent severity of neurocardiac injury. cTnI was quantified by a Beckman Coulter Access AccuTnI assay (Beckman Instruments, Inc.), a two-site immunoenzymatic assay that uses the chemiluminescent substrate Lumi-Phos 530, at the hospital laboratory. The lower analytical limit for cTnI was 0.001 ng/ml, and the upper limit was 75 ng/ml. We used cTnI as a continuous variable.

NCCO monitoring. We used an Food and Drug Administration (FDA)-approved NCCO device (NICOM®, Cheetah Medical, Wilmington, DE) to continuously record CO measurements. This device's function is based on transthoracic Bioreactance® monitoring that analyzes relative phase shifts of an oscillating current traversing the thorax surface. Continuously obtained data were downloaded on each patient at a minimum frequency of one data point every 30 s. The NCCO parameters were continuously collected on each patient over 14 days after the onset of bleeding. The research team applied four noninvasive sensor pads on the right upper corner, left upper corner, right lower corner, and left lower corner of the anterior chest wall. In the analyses, we averaged NCCO data over 5-min intervals. Variables we collected through NCCO included CO, cardiac index (CI), SV, SV index (SVI), SV variation (SVV), thoracic fluid content (TFC), ventricular ejection time (VET), cardiac contractility (dx/dt), and heart rate (HR).

Outcomes. We assessed patient outcomes at discharge and at 3 months post aSAH using the mRS. The mRS is a self-appraisal of functional disability that covers both mental and physical adaptations (Bonita & Beaglehole, 1988). It is widely used in stroke populations and contains seven levels; 0 = *no symptoms at all*, 1 = *no significant disability despite symptoms*, 2 = *slight disability* (*unable to perform all activities*), 3 = *moderate disability* (*able to walk without assistance*), 4 = *moderately severe disability* (*unable to walk without assistance*), 5 = *severe disability* (*bedridden, incontinent, in nursing home*), and 6 = *death* (Bonita & Beaglehole, 1988). We completed the mRS at discharge using information from the medical record. For the 3-month mRS, we conducted patient interviews either in person or over the phone when patients and the research team could not meet. If patients were unable to complete the interview, a family member or caregiver answered the questions. For our analyses, we dichomotized mRS scores as good (mRS 0–2) or poor (mRS 3–6). Inpatient records or family members provided information regarding the outcome of patient mortality.

Statistical Analyses

To describe the sample, we used frequency distributions for categorical variables and means and standard deviations for normally distributed continuous variables or medians and interquartile ranges for nonnormally distributed continuous variables. We used IBM SPSS 22 and SAS 9.3 for the analyses, with a p value of less than .05 indicating significance. Due to nonnormal distribution of the data, we used logarithmic transformation for BNP levels in each analysis and for certain NCCO variables.

Table 1. Characteristics of Patients in the Sample.

Characteristic	Statistics
Age in years (mean ± *SD*)	54.5 ± 11.1
Admission GCS (mean ± *SD*)	12.3 ± 4.1
Gender: female, *n* (%)	28 (93.3)
Race, *n* (%)	
White	28 (93.3)
Black	2 (6.7)
Admission Hunt and Hess, *n* (%)	
Grade 1	1 (3.3)
Grade 2	13 (43.3)
Grade 3	10 (33.3)
Grade 4	4 (13.3)
Grade 5	2 (6.7)
mRS at discharge, *n* (%)	
Poor (mRS 3–6)	16 (53.3)
Good (mRS 0–2)	14 (46.7)
mRS at 3 months, *n* (%)	
Poor (mRS 3–6)	14 (48.3)
Good (mRS 0–2)	15 (51.7)
Mortality at discharge, *n* (%)	4 (13.3)
Mortality at 3 months, *n* (%)	5 (17.24)

Note. $N = 30$. GCS = Glasgow Coma Scale; mRS = modified Rankin Scale; *SD* = standard deviation.

We included BNP and cTnI levels collected over the entire study period and used the daily peak values of each in the analysis as time-varying variables. To evaluate the longitudinal association between BNP and cTnI, we used generalized estimating equation (GEE) with BNP levels as the independent variable and cTnI level as the dependent variable without covariate adjustment. As mentioned above, for BNP level, we used logarithmic transformation.

We also used GEE to analyze the relationship between BNP level and NCCO, with BNP level as the independent variable and NCCO values averaged over 5-min intervals as the dependent variable. For each BNP level (all data points used), we used the NCCO data for the 30 min before and after the blood draw for BNP-level determination (1 hr total). We used logarithmic transformation for BNP level as well as for CO, CI, SV, SVI, TFC, dx/dt, and VET. The only two NCCO variables that we did not log transform were HR and SVV.

In order to assess the relationship between BNP level and outcomes, we again conducted GEE. We included all BNP levels collected over the study period as the independent variable and treated mRS as a categorical variable dichotomized as good and poor, as described above. We included mortality in the analysis as a dichotomous variable. Once again, we used the logarithmic transformation of BNP level for these analyses.

Results

We recruited 30 patients in this study. As shown in Table 1, patients were predominantly female, middle aged, and Caucasian.

Table 2. Daily Mean (*M*) and Standard Deviation (*SD*) of Brain Natriuretic Peptide (BNP), Cardiac Troponin I (cTnI), and Noninvasive Continuous Cardiac Output (NCCO) Monitoring Parameters in the 14 Days After Subarachnoid Hemorrhage.

	Days After Subarachnoid Hemorrhage																											
	1		2		3		4		5		6		7		8		9		10		11		12		13		14	
Study parameter	*n*	*M* (*SD*)	*n*	*M* (*SD*)	*n*	*M* (*SD*)	*n*	*M* (*SD*)	*n*	*M* (*SD*)	*n*	*M* (*SD*)	*n*	*M* (*SD*)	*n*	*M* (*SD*)	*n*	*M* (*SD*)	*n*	*M* (*SD*)	*n*	*M* (*SD*)	*n*	*M* (*SD*)	*n*	*M* (*SD*)	*n*	*M* (*SD*)
BNP	1	469.00 (—)	10	520.3 (634.5)	12	381.38 (342.78)	18	317.75 (399.27)	18	378.89 (607.27)	19	310.42 (662.85)	19	187.79 (378.10)	17	316.76 (639.50)	16	274.50 (468.07)	15	318.04 (442.62)	15	414.40 (589.93)	12	502.17 (887.86)	11	540.55 (933.12)	10	221.80 (380.53)
cTnI	23	0.61 (2.06)	16	0.44 (0.92)	17	0.20 (0.28)	22	0.16 (0.15)	22	0.10 (0.03)	23	0.11 (0.04)	20	0.11 (0.03)	20	0.11 (0.06)	19	0.10 (0.01)	17	0.10 (0.01)	17	0.20 (0.40)	16	0.16 (0.20)	13	0.15 (0.12)	12	0.11 (0.04)
CO	2	4.50 (1.16)	10	6.00 (1.62)	18	5.97 (1.41)	24	5.57 (1.54)	27	5.30 (1.60)	25	5.28 (1.68)	26	5.76 (2.53)	24	5.52 (1.72)	22	6.15 (2.07)	23	5.72 (2.33)	21	5.46 (2.14)	18	5.23 (1.97)	16	5.57 (1.68)	12	5.85 (1.65)
CI	2	2.44 (0.17)	16	3.19 (0.90)	18	3.25 (0.74)	24	3.03 (0.94)	27	2.90 (0.99)	25	2.92 (1.01)	26	3.09 (1.23)	24	2.92 (0.86)	22	3.30 (1.18)	23	3.05 (1.13)	21	2.93 (1.07)	18	2.80 (1.06)	16	2.95 (0.88)	12	3.05 (1.07)
HR	2	16.61 (1.35)	11	12.56 (2.28)	18	13.09 (2.87)	25	12.04 (1.37)	28	11.83 (1.23)	27	11.92 (1.22)	26	11.56 (0.54)	25	11.46 (1.00)	23	11.91 (1.34)	23	11.61 (0.26)	22	11.33 (1.80)	19	11.51 (0.08)	19	11.58 (1.68)	13	10.84 (3.22)
SV	2	55.01 (15.54)	11	79.69 (33.35)	18	71.04 (22.15)	24	71.39 (25.21)	27	65.74 (22.78)	25	65.49 (19.83)	26	69.99 (24.01)	24	66.41 (19.42)	22	69.10 (22.65)	23	65.92 (22.58)	21	63.65 (23.90)	18	60.59 (19.90)	16	65.95 (18.23)	12	69.35 (20.89)
SVI	2	29.83 (2.77)	11	42.30 (16.99)	18	38.79 (11.40)	24	39.11 (15.63)	27	35.96 (13.27)	25	36.36 (11.96)	26	38.00 (13.34)	24	35.34 (10.49)	22	37.14 (13.23)	23	35.32 (11.52)	21	34.18 (12.54)	18	32.51 (11.24)	16	34.95 (9.82)	12	36.30 (14.09)
SVV	2	17.27 (0.91)	11	14.16 (3.85)	18	14.06 (3.30)	24	14.75 (3.96)	27	15.09 (3.25)	25	14.88 (3.02)	26	15.47 (3.67)	24	16.06 (2.94)	22	15.17 (2.99)	23	15.76 (2.49)	21	16.02 (3.20)	18	16.44 (3.07)	16	16.68 (3.57)	12	16.00 (3.84)
TFC	2	36.86 (13.31)	11	46.04 (12.81)	18	45.75 (12.19)	25	43.88 (16.31)	27	48.85 (21.35)	25	51.91 (23.68)	26	49.81 (24.44)	24	48.52 (23.83)	22	50.74 (25.52)	23	50.83 (26.88)	21	55.63 (30.60)	18	56.27 (31.95)	16	54.82 (34.68)	12	49.00 (23.70)
dx/dt	2	127.51 (50.28)	11	159.31 (134.55)	18	157.81 (103.02)	24	161.58 (115.23)	27	155.17 (114.46)	25	151.70 (105.90)	26	147.23 (114.05)	24	139.96 (93.50)	22	147.70 (93.38)	23	139.19 (83.72)	21	140.21 (104.08)	18	131.85 (120.02)	16	131.47 (84.75)	12	126.42 (87.20)
VET	2	183.39 (15.83)	11	245.60 (58.46)	18	248.61 (56.98)	24	239.50 (55.29)	27	229.65 (54.19)	25	229.00 (50.05)	26	233.43 (64.44)	24	220.13 (46.30)	22	229.38 (49.67)	24	224.61 (38.39)	21	216.64 (51.67)	18	201.84 (34.97)	16	212.61 (45.44)	12	210.13 (43.57)

Note. CI = cardiac index; CO = cardiac output; dx/dt = maximum aortic flow (indirect measure of contractility); HR = heart rate; *SD* = standard deviation; SV = stroke volume; SVV = stroke volume variation; SVI = stroke volume index; TFC = thoracic fluid content; VET = ventricular ejection time.

Table 3. Relationship Between Patients' ($N = 30$) Brain Natriuretic Peptide (BNP) Levels and Noninvasive Continuous Cardiac Output Monitoring (NCCO) Parameters for 30 Min Before and After Blood Was Drawn for Each BNP Measurement.

NCCO Parameter	Estimate	Standard Error	*p* Value
log cardiac output	0.02	0.04	.578
log cardiac index	0.03	0.04	.572
Heart rate	−0.16	0.16	.317
log stroke volume	0.05	0.03	.106
log stroke volume index	0.05	0.03	.098
Stroke volume variation	−0.24	0.37	.515
log thoracic fluid content	0.09	0.02	.0003*
log dx/dt	0.05	0.04	.192
log ventricular ejection time	0.00	0.03	.871

Note. dx/dt = maximum aortic flow (indirect measure of contractility).
* = statistically significant at $p < .05$.

The majority of patients had an admission HH grade of 2 (43%) or 3 (33%). At discharge, 16 patients (53.3%) had poor mRS scores, while at 3 months post hemorrhage, 14 (48.3%) had poor scores. A total of five patients died during the course of the study, four before hospital discharge and one before the follow-up at 3 months. An additional patient was lost to the 3-month follow-up. The daily mean cTnI was 0.20 ng/ml, with a minimum value of 0.04 ng/ml and maximum of 10.36 ng/ml. The daily mean BNP level was 322.99 pg/ml, and the minimum and maximum values were 5.00 pg/ml and 2,676.00 pg/ml, respectively. The mean time of NCCO monitoring was 8.89 days, ranging from 1.05 to 13.70 days. The daily means and standard deviations for BNP, cTnI, and the NCCO parameters are shown in Table 2.

GEE modeling on daily peak cTnI and BNP levels showed a statistically significant association between these measures. For every 1 unit increase in *log* BNP, cTnI increased by 0.05 ng/ml ($p = .001$).

Table 3 shows the relationship between BNP levels and NCCO parameters without covariate adjustment. The results indicate that *log* BNP level increases by 0.09 pg/ml for every 1 unit increase in *log* TFC ($p = .0003$). There was no statically significant relationship between BNP level and any other NCCO-derived variable.

On univariable analyses, there were significant associations between *log* BNP and poor mRS score at 3 months, mortality at 3 months, and mortality at discharge. There was a trend toward significance for the association between *log* BNP and poor mRS score at discharge. For every 1 unit increase in *log* BNP, patients were 1.26 and 4.90 times more likely to have poor mRS scores at discharge ($p = .069$) and at 3 months ($p < .0001$), respectively. Furthermore, for every 1 unit increase in *log* BNP, patients were 1.42 and 1.43 more likely to die at discharge ($p = .032$) and at 3 months ($p = .031$), respectively. Results were similar for multivariable analyses (Table 4). BNP remained a significant predictor for poor outcome even after controlling for age and HH grade. For every 1 unit increase in *log* BNP, patients were 3.16 times more likely to have a poor mRS score at discharge ($p = .021$) and 5.40 times more likely to have a poor mRS score at 3 months ($p < .0001$).

Discussion

Our main finding in the present study, that BNP level post aSAH increases as cTnI level increases, supports the use of BNP as a marker of neurocardiac injury in aSAH patients. The relationship between these two biomarkers may be mediated by the catecholamine surge that occurs after aneurysm rupture and that often results in myocardial dysfunction and subsequent neurocardiac injury (Hravnak et al., 2009). BNP is secreted in response to the injury, inflammation, and cardiac myocyte stretch and its levels gradually increase (Meaudre et al., 2009).

We also sought to assess the relationship between BNP level and cardiac function based on a novel approach using NCCO. We were able to demonstrate that BNP level increases as TFC, a marker of pulmonary edema, increases. This finding is not surprising, given the relationship between BNP level and increased myocardial stretch and wall tension (Bhatia, Nayyar, & Dhindsa, 2003). TFC, as measured by NCCO, is a qualitative measure of directional changes in total TFC (Kang et al., 2012). Therefore, as thoracic fluid volume increases, theoretically both myocardial stretch and wall tension will increase. Subsequently, BNP will be secreted, and BNP levels will continue to rise.

As we previously mentioned, BNP is secreted from the hypothalamus and cardiac myocytes. The reason for elevated BNP level could be the stretching of cardiac myocytes or it could be secondary to the effect of bleeding and elevated intracranial pressure on the hypothalamus. The significant relationship we observed between BNP level and TFC supports the hypothesis that BNP is secreted in response to atrial stretching rather than due to the direct effect of bleeding on the hypothalamus. Our findings could also indicate that the myocardial damage occurring after aSAH mimics congestive heart failure, which signifies the importance of avoiding hypervolemia in those patients. However, we did not assess intravascular volume in this analysis.

Tung et al. (2004) found that elevated BNP levels are associated with myocardial necrosis, pulmonary edema, and left ventricular systolic and diastolic dysfunction early after SAH. However, we were unable to demonstrate that elevated BNP was significantly associated with depressed myocardial function by any variable measured with NCCO with the exception of elevated TFC. Possibly our sample size was too small to detect such a change, and this is a study limitation. It is also possible that the use of vasopressors for blood pressure support in this population may have affected the NCCO parameters, which is also a significant limitation of the study.

Yarlagadda et al. (2006) found BNP levels greater than 600 pg/ml to be a significant indicator of mortality after aSAH, while Duello, Nagel, Thomas, Blackshear, and Freeman (2015) did not find any significant relationship between BNP elevation and increased mortality. We also did not observe a relationship between BNP and mortality in the present study. We did find, however, that elevated BNP was associated with poorer mRS score at discharge and 3 months after aSAH and that this association was independent of age and HH grade. No

Table 4. Multivariable Analysis of the Relationships Between Brain Natriuretic Peptide (BNP) and Outcomes at Hospital Discharge and 3 Months Post Hemorrhage.

	mRS at Discharge, $n = 30$			mRS at 3 Months, $n = 29$			Mortality at Discharge, $n = 30$			Mortality at 3 Months, $n = 29$		
Variable	*OR*	95% CI	*p* Value	*OR*	95% CI	*p* Value	*OR*	95% CI	*p* Value	*OR*	95% CI	*p* Value
log BNP	3.16	[1.19, 8.39]	.021*	5.40	[3.24, 8.99]	<.0001*	1.30	[0.92, 1.84]	.130	1.28	[0.90, 1.82]	.175
Age	3.18	[1.84, 5.51]	<.0001*	.96	[0.84, 1.10]	.573	–		–	–		–
HH grade	86.29	[2.11, 3526.99]	.019*	6.53	[0.98, 43.27]	.052	1.69	[0.35, 8.24]	.518	2.05	[0.45, 9.28]	.352

Note. CI = confidence interval; HH = Hunt and Hess; mRS = modified Rankin Scale; *OR* = odds ratio.
* = statistically significant at $p < .05$.

other study, to our knowledge, has investigated the relationship between BNP level and poor mRS score in the aSAH population. Taub et al. (2011) found that elevated BNP levels are independently associated with cerebral infarction following aSAH. Sviri, Shik, Raz, and Soustiel (2003) reported that elevated BNP levels are related to severity of bleeding and vasospasm following aSAH. McGirt et al. (2004) found that elevated BNP level was independently associated with hyponatremia and predicted the 2-week Glasgow Coma Scale score. However, the pathophysiological mechanism linking elevated BNP level and poorer functional outcomes remains unclear. Whether poor outcomes are an indirect result of elevated BNP levels or a direct result of alternative mechanisms still requires further investigation. Future studies should involve larger sample sizes and analysis of other potential variables. Once this further investigation is conducted, BNP may prove to be a valuable independent marker of neurocardiac injury.

Conclusion

The clinical implications of this study relate to the significant relationship between BNP and cTnI levels and to the association between elevated BNP level and poor mRS score in aSAH patients, even after age and injury severity are taken into account. We conclude that elevated BNP level can be indicative of myocardial damage after aSAH and can be used for prognosticating poor functional outcomes in this patient population. With the expanding neuro-monitoring role of the bedside nurse at the NICU, we recommend that nurses monitor BNP values once they are available.

Author Contribution

A. McAteer contributed to conception, design, data acquisition, and interpretation; drafted the manuscript; critically revised the manuscript; gave final approval; and agrees to be held accountable for all aspects of work, ensuring integrity and accuracy. M. Hravnak contributed to conception, design, data acquisition, and interpretation; drafted the manuscript; critically revised the manuscript; gave final approval; and agrees to be held accountable for all aspects of work, ensuring integrity and accuracy. Y. Chang contributed to data, analysis, and interpretation; critically revised the manuscript; gave final approval; and agrees to be held accountable for all aspects of work, ensuring integrity and accuracy. E. A. Crago contributed to conception, design, data acquisition, and interpretation; drafted the manuscript; critically revised the manuscript; gave final approval; and agrees to be held accountable for all aspects of work, ensuring integrity and accuracy. M. J. Gallek contributed to interpretation, critically revised the manuscript, gave final approval, and agrees to be held accountable for all aspects of work, ensuring integrity and accuracy. K. M. Yousef contributed to conception, design, data acquisition, and interpretation; drafted the manuscript; critically revised the manuscript; gave final approval; and agrees to be held accountable for all aspects of work, ensuring integrity and accuracy.

Declaration of Conflicting Interests

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