# Preoperative Brain Natriuretic Peptide and Atrial Arrhythmias After Coronary Artery Bypass Graft Surgery

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***Objective:*** **To assess the association of preoperative brain natriuretic peptide with atrial arrhythmias and length of stay after cardiac surgery.**

***Design:*** **A retrospective data analysis.**

***Setting:*** **All data were collected from patients who underwent cardiac surgery at a single institution, an academic hospital, between 2005 and 2010.**

***Participants:*** **Patient data were collected from the authors' institution's Perioperative Health Documentation System of cardiac surgeries.**

***Interventions:*** **None.**

***Measurements and Main Results:*** **The major findings were that individuals with a 10-pg/mL increase in brain natriuretic peptide were 1.005 (95% CI: 1.002, 1.009) times more likely to have an atrial arrhythmia than those with no increase in brain natriuretic peptide. A brain natriuretic peptide value ≥306 pg/mL was calculated to best predict an atrial arrhythmia. Those above the threshold were 1.455 (95% CI: 1.087, 1.947) times more likely to have an atrial arrhythmia than those below the threshold. Individuals above the threshold had a median of 3 days in the intensive care unit compared to 1 day for those below the threshold, as well as median hospital stays of 11 days for those below the threshold.**

***Conclusions:*** **The results indicated that elevated brain natriuretic peptide was associated with increased risk of atrial arrhythmias and prolonged length of hospital stay after cardiac surgery. Identifying at-risk patients is important to guide preventative strategies for postoperative atrial arrhythmias.**



***KEY WORDS: arrhythmias, cardiac, coronary artery bypass, natriuretic peptide, brain***

AFTER CORONARY ARTERY BYPASS GRAFT (CABG) surgery, patients are at risk for the development of atrial arrhythmias, including atrial fibrillation, atrial flutter, supraventricular tachycardia, and premature atrial contractions. Atrial fibrillation (AF) is the most common cardiac rhythm disturbance, occurring in 25% to 40% of patients undergoing cardiac surgery.[1,2] Postoperative atrial arrhythmias are associated with increased risk of morbidity, mortality, readmission to the intensive care unit (ICU), length of hospital and ICU stay, perioperative myocardial infarction, congestive heart failure, and stroke.[3–11] Because of the challenges of predicting and preventing AF, there has been substantial interest in the use of biomarkers to identify patients who are at risk for atrial arrhythmias. One of these potential biomarkers is brain natriuretic peptide (BNP).[12–16]

BNP commonly is used for detecting congestive heart failure, but recently has been examined as a possible biomarker for atrial arrhythmias.[11] BNP is released predominantly from the ventricular myocytes in response to left ventricular hypertrophy, which has been associated with AF.[17–21] Previous attempts to determine an association between elevated preoperative BNP levels and atrial arrhythmias following CABG surgery have provided conflicting results. In a prospective trial of 144 consecutive surgeries, Ata et al found an association between preoperative BNP and postoperative AF (226 pg/mL, in those with AF *v* 65.2 pg/mL, in those without AF; $p < 0.001$).[22,23] In contrast, Sezai et al[24] did not show a statistically significant association between preoperative BNP and AF in 234 consecutive patients (137.2 ± 215.7 pg/dL, in those with AF *v* 149.7 ± 262.0 pg/dL, in those without AF; $p = 0.751$). Thus, the relationship between BNP concentrations and AF is controversial. Furthermore, these studies had a limited sample size, and they were reported from very different surgical settings. Although conducted retrospectively, the authors' data were collected prospectively at the time of surgery and will be the largest study to assess the relationship between BNP and AF.

Identifying predictors of atrial arrhythmias in patients undergoing cardiac surgery can help clinicians identify candidates for preventive treatments, to reduce the morbidity and mortality associated with postoperative AF. The goals of this study were to evaluate whether preoperative BNP predicted atrial fibrillation post-CABG and to investigate if BNP was associated with prolonged ICU and hospital length of stay.

## METHODS

With approval from both institutions' Institutional Review Board and Research Subjects Review Board, a retrospective analysis of prospectively collected data from the Perioperative Health Documentation System that were acquired between 2005 and 2010 was performed. Data were collected from both

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the hospital and anesthesia records, which integrated preoperative, intraoperative, and postoperative outcomes.

### Statistical Methods

The authors assessed the relationship between preoperative BNP and atrial arrhythmias using unadjusted logistic regression, followed by a backwards selection multivariate logistic regression model, adjusting for unevenly distributed covariates. Covariates were selected based upon previously determined relationships between the covariate and postoperative AF. The selection included all potential covariates, the squares of the continuous covariates, and interactions between BNP and the covariates. The authors analyzed 29 predetermined potential covariates between patients who developed atrial arrhythmias and patients who did not, using a student's t-test (for continuous variables), chi-square test (for dichotomous variables), or Wilcoxon rank sum test (for non-normal distributions). Any variable with a p value $< 0.10$, between those who did and did not develop an atrial arrhythmia, were considered to be covariates and adjusted for in the analysis. Although originally included in the analysis, postoperative medications were removed because of their use, possibly resulting from arrhythmias, and not a predictor of arrhythmias. A sensitivity analysis including all patients with BNP concentrations and imputed data for those with missing covariate data was performed; imputed data were not used in the final analysis.

The authors determined a threshold BNP concentration to best predict atrial arrhythmias following CABG surgery, using a receiver operating characteristic (ROC) analysis and the Youden index (the sum of the sensitivity and specificity). Using the calculated threshold value, an unadjusted and adjusted multivariate logistic regression model, with the same covariates as the adjusted model for a one-unit increase in BNP, was performed to assess the risk of atrial arrhythmias in individuals above and below the BNP threshold.

Kaplan-Meier analyses, using the calculated threshold value, were conducted to assess the lengths of ICU and hospital stay. Wilcoxon and log-rank tests were used to compare the lengths of stay between those above and below the BNP threshold. Lengths of ICU and hospital stay were defined as the duration of stay from the date of surgery to the date of ICU and hospital discharge, respectively. SAS software version 9.2.2 (SAS Institute, Cary, NC) and PASS 11 software for Windows (NCSS, Kaysville, UT) were used for all statistical analyses.

## RESULTS

The authors evaluated 18,064 patients who underwent cardiac surgery between 2005 and 2010. Of these patients, 9,378 were excluded because they did not have preoperative BNP concentrations, and an additional 3,887 were removed because of missing covariate data or being statistical outliers. The remaining 4,765 patients were included in the analysis (Fig 1). The baseline characteristics (Table 1) for individuals who developed atrial arrhythmias and those who did not were found to be different for all but 3 covariates: Smoking, preoperative atrial flutter, and preoperative nonsteroidal anti-inflammatory drug use.

Those who did not develop an atrial arrhythmia were found to have an average BNP concentration of 315.9 pg/mL, and those who did develop an atrial arrhythmia had an average concentration of 557.5 pg/mL. For a 10-unit increase in BNP, the unadjusted odds ratio for an atrial arrhythmia was 1.0005 (95% CI: 1.00047, 1.00054; $p < 0.001$). For the adjusted model, the odds ratio was (95% CI, p value) when adjusting for baseline BNP, age, body mass index, ejection fraction, race, sex, American Society of Anesthesiologists physical status classification, creatinine, smoking, preoperative AF, chronic obstructive pulmonary disease/asthma, preoperative statin, preoperative beta-blocker, preoperative anti-arrhythmic medication, length of surgery, valve surgery, creatinine squared, BNP squared, interaction of BNP and length of surgery, and an interaction of BNP and valve surgery. The adjusted odds ratio for a 10-unit increase in BNP is 1.005 (95% CI: 1.002, 1.009; standard error: 0.000291; $p = 0.004$) for patients who did not have valve surgery and had the mean length of surgery.

The calculated threshold value was 306 pg/mL, with a sensitivity of 61.7% and specificity of 70.5%, for a Youden index of 1.322. The area under the curve for the ROC analysis was 0.718 (Fig 2). The positive predictive value of the

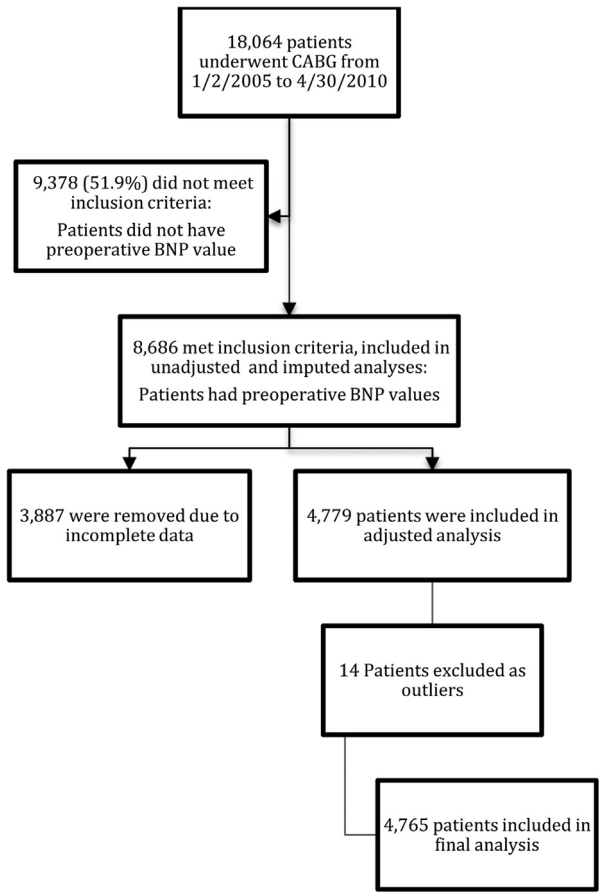


**Fig 1. Flow chart of included and excluded patients from the authors' institutions' Perioperative Documentation System of cardiac surgeries 2005-2010.**