

# The Prognostic Value of B-Type Natriuretic Peptide After Cardiac Surgery: A Comparative Study Between Coronary Artery Bypass Graft Surgery and Aortic Valve Replacement

Jean-Luc Fellahi, MD, PhD,\* Georges Daccache, MD,† Youssef Makroum, MD,\* Massimo Massetti, MD,\* Jean-Louis Gérard, MD,\* and Jean-Luc Hanouz, MD, PhD\*

**Objectives:** The influence of the cardiac surgical procedure on B-type natriuretic peptide (BNP) for the identification of high-risk patients has not been evaluated. This study aimed to compare the prognostic utility of pre- and postoperative BNP in predicting adverse long-term outcome after coronary artery bypass graft (CABG) surgery and aortic valve replacement (AVR).

**Design:** A retrospective study.

**Setting:** A university teaching hospital.

**Participants:** One hundred eighty-nine patients.

**Measurements and Main Results:** Preoperative, early postoperative (24 hours), and late postoperative (day 5) BNP levels were measured. Major adverse cardiac events (MACEs) within 12 months after surgery were chosen as study endpoints. The predictive abilities of BNP measurements were compared using receiver operating characteristic (ROC) curves. Patients were stratified by CABG surgery ( $n = 100$ ) and AVR ( $n = 89$ ). Thirty-four (18%) patients experienced 44 MACEs over the study period. Preoperative

BNP values were significantly different between groups. Postoperative BNP gradually increased by 431% on day 5 after CABG surgery and by 100% after AVR (both  $p < 0.001$  v preoperative values). Pre- and early postoperative BNP values were accurate in predicting MACEs after AVR (areas under the ROC curves: 0.78 [95% confidence interval, 0.66-0.90] and 0.76 [95% confidence interval, 0.62-0.89], respectively) and inaccurate after CABG surgery (0.54 [95% confidence interval, 0.38-0.70] and 0.54 [95% confidence interval, 0.36-0.73], respectively). The late postoperative BNP value was of limited value.

**Conclusions:** BNP measurements should take into account the type of cardiac surgery. Whatever the time of measurement, BNP accurately predicts long-term adverse outcome in valve surgery patients. A late postoperative BNP measurement is useless after cardiac surgery.

© 2012 Elsevier Inc. All rights reserved.

**KEY WORDS:** aortic valve replacement, biochemistry, coronary artery bypass graft surgery, surgery, outcomes, BNP

THE PROGNOSTIC VALUES of the pre- and postoperative B-type natriuretic peptide (BNP) and N-terminal pro-BNP measurements are valuable in the cardiac surgical setting on composite endpoints associating short- and long-term postoperative mortality and/or cardiac morbidity.<sup>1-9</sup> Higher preoperative values of BNP have been reported in patients with aortic stenosis,<sup>1</sup> and small increases in postoperative BNP levels have been suggested after aortic valve replacement (AVR) when compared with coronary artery bypass graft (CABG) surgery.<sup>10</sup> None of these studies examined the influence of the type of cardiac surgery on the clinical usefulness of natriuretic peptides for the identification of high-risk patients. The present authors previously showed that the magnitude of postoperative cardiac troponin I (cTnI) release after cardiac surgery was strongly related to the type of surgical procedure, and the accuracy of cTnI to predict adverse outcome was less in valve surgery than in coronary artery surgery.<sup>11</sup>

There is no consensus on the use of preoperative rather than postoperative BNP measurement to predict adverse outcome after cardiac surgery. A recent study suggested that preoperative BNP could be better than peak postoperative BNP for predicting hospital length of stay and longer-term mortality after primary CABG surgery.<sup>5</sup> Concerning long-term outcome, discrepancies exist in reports that only use early postoperative measurements of serum BNP,<sup>1,2,9</sup> and a late value of BNP

before discharge from the hospital has been found to be more relevant for long-term outcome prediction in the medical setting of acute heart failure.<sup>12</sup>

The objectives of the current study conducted in adult patients undergoing cardiac surgery were 2-fold: (1) to compare the prognostic utility of pre- and postoperative measurements of BNP in predicting long-term adverse cardiac outcome between 2 main types of elective cardiac surgery (ie, CABG and AVR surgery) and (2) to assess the value of a late postoperative BNP measurement in comparison with preoperative and early postoperative BNP values.

## METHODS

The authors used a comprehensive, prospectively recorded database describing the clinical and surgical characteristics of 238 consecutive adult patients undergoing conventional cardiac surgery with cardiopulmonary bypass at the Saint-Martin Hospital (Caen, France) from October 2005 to April 2006. This cohort of patients has been described in detail in a previous study from the authors' group, which aimed to address the prognostic implication of a multiple-marker approach associating postoperative serum BNP, cTnI, and C-reactive protein measurements.<sup>13</sup> Institutional approval was obtained from the Ethical Committee (Comité pour la Protection des Personnes Pitié-Salpêtrière, Paris, France). Waived written informed consent was authorized because the study was solely observational, and perioperative BNP measurements were performed systematically from a blood sample withdrawn for other routine blood tests during the routine care of patients, which conformed to standard procedures currently used in this institution. Inclusion criteria were elective cardiac surgical procedures with cardiopulmonary bypass (ie, primary CABG or AVR surgery). Emergency surgery (<24 hours), redo surgery, mitral valve repair or replacement, combined cardiac surgery, and unusual complex cardiac surgical procedures were excluded from the study.

The perioperative management of all included patients conformed to standard procedures currently used in this institution and is well described elsewhere.<sup>13</sup> Briefly, standardized total intravenous anesthesia

From \*CHU de Caen and †CHP Saint-Martin, Caen, France.

Address reprint requests to Jean-Luc Fellahi, MD, PhD, Pôle Anesthésie-Réanimation-SAMU-Coordination Hospitalière-Hémovigilance, CHU de Caen, Avenue de la Côte de Nacre, 14000 Caen, France. E-mail: fellahi-jl@chu-caen.fr

© 2012 Elsevier Inc. All rights reserved.

1053-0770/2604-0015\$36.00/0

<http://dx.doi.org/10.1053/j.jvca.2011.07.029>

(target-controlled propofol infusion, remifentanyl, and pancuronium bromide) and monitoring techniques (5-lead electrocardiogram, invasive arterial blood pressure, and central venous pressure) were used in all patients. Antifibrinolytic therapy (tranexamic acid, 15 mg/kg twice) was administered routinely. Cardiopulmonary bypass was performed under normothermia in all types of surgery, and myocardial protection was achieved by intermittent warm blood cardioplegia. The heart was defibrillated after aortic unclamping if sinus rhythm did not resume spontaneously. After the termination of cardiopulmonary bypass, all patients were admitted postoperatively into the cardiac intensive care unit for at least 48 hours and were assessed for tracheal extubation within 1 to 8 hours of arrival in the intensive care unit. Standard postoperative care included blood glucose control, intravenous heparin (200 U/kg) in patients with valve disease, and aspirin (300 mg, oral or intravenous) associated with low-molecular-weight heparin ([Nadroparin, 2,850 U anti-Xa, subcutaneous] Fraxiparine; Sanofi-Synthelabo, Paris, France) in patients with coronary artery disease, beginning 6 hours after surgery in the absence of significant mediastinal bleeding. Beta-blocking agents and statins were given as soon as possible postoperatively in chronically treated patients. Postoperative care was delivered by anesthesiologists in the intensive care unit and by cardiac surgeons in the ward. All of them were blinded for BNP levels. Preoperative, intraoperative, and postoperative variables were collected for all patients.

Serial blood samples were drawn into dry tubes the day before surgery (preoperative), at 24 hours after surgery (early postoperative), and at day 5 after surgery (late postoperative). BNP measurements were performed systematically from blood samples withdrawn for other routine blood tests. A technician who was unaware of the clinical and electrocardiogram data performed assays. BNP was analyzed with a sensitive and highly specific immunoassay (AxSYM BNP Meia Assay; Abbott Laboratories, Rungis, France). The assay allowed the detection of BNP within the range of 0 to 20,000 pg/mL with appropriate dilutions. The within-run coefficient of variation was 6%, and the between-run coefficient of variation was 9%.

Patients were stratified by the type of cardiac surgery as follows: elective CABG (group CABG) and elective AVR (group AVR). Nonfatal major cardiac events and all causes of death were recorded postoperatively and within 12 months after surgery after hospital discharge. The survivors after hospital discharge or their relatives, as well as their general practitioner and/or cardiologist, subsequently were contacted by telephone for a 1-year follow-up interview to obtain information. Nonfatal major cardiac events included (1) malignant ventricular arrhythmia defined as any sustained ventricular arrhythmia requiring treatment that occurred at any time within 12 months after surgery, (2) myocardial infarction defined as the appearance on 12-lead electrocardiogram recordings of new Q waves of more than 0.04 seconds and 1-mm deep or a reduction in R waves of more than 25% in at least 2 continuous leads of the same vascular territory at any time within 12 months after surgery, (3) cardiac dysfunction defined as clinical signs of congestive heart failure (eg, fluid retention, oliguria, basilar rales, and persistent chest infiltration requiring diuretic agents) and/or hemodynamic instability requiring inotropic support for at least 24 hours and/or a  $\geq 20\%$  decrease in preoperative to postoperative left ventricular ejection fraction during the postoperative period and as clinical signs of congestive heart failure requiring rehospitalization within 12 months after surgery, and (4) the need for new revascularization defined as percutaneous coronary angioplasty and/or CABG surgery within 12 months after surgery. In case of death, all information available (ie, hospital chart and death certificate) was used to classify death from a cardiac cause (eg, heart failure, myocardial infarction, or ventricular arrhythmia) or not (other causes). Sudden death was considered as death from a cardiac cause.

Major adverse cardiac events (MACEs) within 12 months after surgery were chosen as study endpoints and defined as 1 of the following: malignant ventricular arrhythmia, myocardial infarction, cardiac dysfunction, the need for myocardial revascularization, and death from cardiac cause as defined in the previous paragraph. The presence or absence of MACEs was judged by 2 independent experts who were blinded to concentrations of BNP. In case of disagreement, a 3rd blinded expert participated in a discussion with the first 2, and a consensus was reached.

Data were expressed as the mean  $\pm$  standard deviation or median (extremes) for nonnormally distributed variables (Kolmogorov-Smirnov test) or number and percentage as appropriate. Continuous variables were analyzed with the unpaired Student *t* and Mann-Whitney *U* tests according to their distribution. Categorical variables were compared by the Fisher exact method. Time course changes in BNP values were compared by the paired Wilcoxon test. Rank correlations among preoperative, early postoperative, and late postoperative BNP values were measured with the Spearman coefficient. To assess the discrimination of preoperative, early postoperative, and late postoperative BNP in predicting MACEs, the authors determined the empiric receiver operating characteristic (ROC) curves and calculated the areas under the ROC curves and their 95% confidence interval. A comparison of areas under the ROC curve was performed using a nonparametric paired technique as described previously.<sup>14</sup> A multiple forward stepwise logistic regression was performed to assess variables associated with 12-month MACEs. A parsimonious approach was used and included only the significant preoperative variables in the univariate analysis (*p* value of entry = 0.10). Preoperative and postoperative BNP concentrations were entered as continuous variables. The odds ratios and their 95% confidence interval of variables selected by the logistic model were calculated. Discrimination of the model was assessed by using *c*-statistics. A *p* value of less than 0.05 was considered significant, and all *p* values were 2-tailed. Statistical analyses were performed using Analyze-it Method Evaluation edition version 2.23 for Microsoft Excel Software (Leeds, England).

## RESULTS

Two hundred thirty-eight consecutive adult patients underwent surgery during the study period. Forty-nine (20%) patients were excluded because of emergency surgery (*n* = 7), mitral repair or replacement (*n* = 2), combined surgery (*n* = 35), and other complex or unusual cardiac surgical procedures (*n* = 5). The remaining 189 patients fulfilled inclusion criteria and were stratified by the type of surgical procedure as follows: CABG surgery (*n* = 100) and AVR (*n* = 89). The flow chart of the study is depicted in Figure 1. Baseline characteristics and intraoperative data for both groups of patients are shown in Table 1. As a consequence of an older age, an increased percentage of females, and the surgical procedure itself, the EuroSCORE was significantly higher in the AVR group (Table 1).

Five (3%) patients died in the hospital: 2 from cardiac causes (1 acute heart failure and 1 sudden death), 2 from pancreatitis, and 1 from multiple organ failure. Complete follow-up over the 12-month period after surgery was available in all surviving patients. One-year survival in the global population was 95%. Thirty-four (18%) patients experienced 44 MACEs over the study period. MACEs were malignant ventricular arrhythmia in 9 cases, myocardial infarction in 9 cases, cardiac dysfunction in 15 cases, coronary artery revascularization in 6 cases, and cardiac death in 5 cases. Postoperative data and 1-year outcome for both groups of patients are shown in Table 2. New onset of

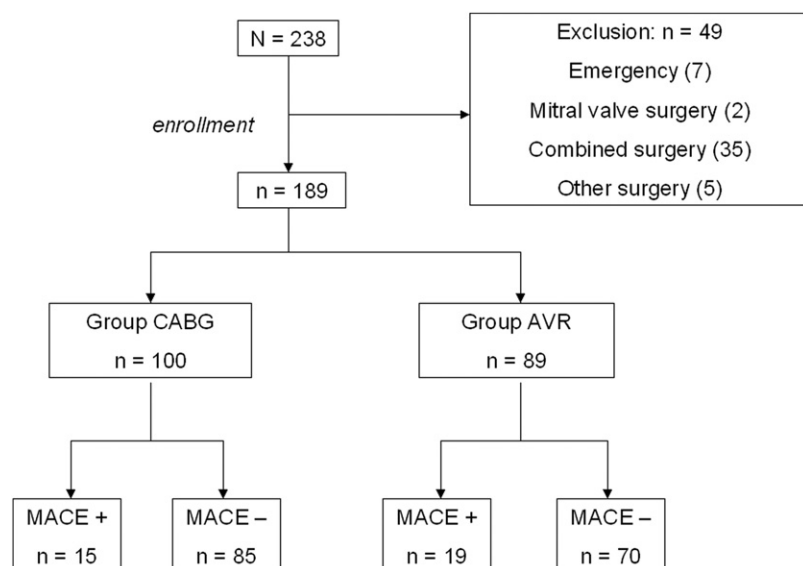


Fig 1. The study flow chart.

atrial fibrillation, postoperative inotropic support, and cardiac dysfunction were more frequent in the AVR group (Table 2).

The BNP blood samples were collected in all patients. Only preoperative BNP values were significantly different between groups (Table 3). The median serum BNP gradually increased during the postoperative period, by 431% at day 5 in the CABG group ( $p < 0.001$  v the preoperative value) and by 100% at day 5 in the AVR group ( $p < 0.001$  v the preoperative value) (Table

3). There were only moderate correlations among preoperative BNP and early and late postoperative BNP values (rank correlation  $r = 0.66$  [95% confidence interval, 0.57-0.74],  $p < 0.001$  and  $r = 0.56$  [95% confidence interval, 0.45-0.65],  $p < 0.001$ , respectively). There was also a moderate correlation between early and late postoperative BNP values (rank correlation  $r = 0.59$  [95% confidence interval, 0.49-0.68],  $p < 0.001$ ). Preoperative and early postoperative values of BNP were both

Table 1. Baseline Characteristics and Intraoperative Data in Patients Undergoing CABG Surgery and AVR

	Group CABG (n = 100)	Group AVR (n = 89)	p Value
Age (y)	68 ± 10	71 ± 10	0.022
Men	81 (81)	53 (60)	0.002
Women	19 (19)	36 (40)	
Body mass index (kg/m <sup>2</sup> )	27 ± 5	26 ± 5	0.268
EuroSCORE	4 (0-11)	6 (2-12)	<0.001
Left ventricular ejection fraction (%)	63 ± 12	63 ± 11	0.943
Hypertension	72 (72)	53 (60)	0.098
Chronic obstructive pulmonary disease	7 (7)	7 (8)	1.000
Diabetes mellitus	23 (23)	10 (11)	0.051
Stroke	3 (3)	6 (7)	0.388
Preoperative cardiac troponin I (ng/mL)	0.0 (0.0-3.7)	0.0 (0.0-0.5)	0.485
Serum creatinine (μmol/L)	101 ± 51	99 ± 25	0.734
Chronic treatment administered			
Nitrates	30 (30)	13 (15)	0.017
Calcium blockers	25 (25)	11 (12)	0.041
Beta-blockers	75 (75)	29 (33)	<0.001
Renin-angiotensin system inhibitors	51 (51)	38 (43)	0.319
Diuretics	17 (17)	36 (40)	<0.001
Statins	68 (68)	27 (30)	<0.001
Cardiopulmonary bypass time (min)	97 ± 26	115 ± 31	<0.001
Aortic cross-clamping time (min)	53 ± 18	79 ± 25	<0.001
Type of cardioplegia			
Anterograde	100 (100)	79 (89)	<0.001
Anterograde + retrograde	0 (0)	10 (11)	

Abbreviations: AVR, aortic valve replacement; CABG, coronary artery bypass grafting.

NOTE. Values are mean ± standard deviation or median (extremes) or number (%).

**Table 2. Postoperative Data and 1-Year Outcome in Patients Undergoing CABG Surgery and AVR**

	Group CABG (n = 100)	Group AVR (n = 89)	p Value
Postoperative outcome			
Peak serum cardiac troponin I (ng/mL)	2.8 (0.4-46.6)	4.8 (1.3-70.9)	<0.001
Inotropic support	4 (4)	16 (18)	0.003
New onset of atrial fibrillation	28 (28)	42 (47)	0.009
Acute renal failure*	12 (12)	15 (17)	0.487
Mediastinal bleeding (mL)	506 ± 199	584 ± 316	0.095
Length of stay in intensive care unit (d)	3 (2-9)	3 (2-51)	0.219
Hospital discharge (d)	7 (2-28)	7 (2-51)	0.357
1-year outcome			
Malignant ventricular arrhythmia	5 (5)	4 (5)	1.000
Myocardial infarction	7 (7)	2 (2)	0.232
Cardiac dysfunction	2 (2)	13 (15)	0.002
Myocardial revascularization	5 (5)	1 (1)	0.270
Cardiac death	1 (1)	4 (5)	0.299
MACE	15 (15)	19 (21)	0.344
Overall mortality	2 (2)	7 (8)	0.119

Abbreviations: AVR, aortic valve replacement; CABG, coronary artery bypass grafting; MACE, major adverse cardiac events defined as malignant ventricular arrhythmia and/or myocardial.

NOTE. Values are mean ± standard deviation or median (extremes) or number (%).

\*Acute renal failure was defined as a (peak postoperative creatinine – preoperative creatinine)/preoperative creatinine ratio >30%.<sup>15</sup>

very accurate in predicting MACEs after AVR, whereas late postoperative BNP was of a more limited value (Table 4). No significant discrimination was found for BNP values in predicting long-term adverse cardiac outcome after CABG surgery whatever the time of measurement, as shown by areas under the ROC curves (Table 4). A comparison of the discriminations of preoperative, early postoperative, and late postoperative BNP values in predicting MACEs for both types of surgery is depicted in Figure 2A and B. Using a logistic model that included age, preoperative left ventricular ejection fraction, standard EuroSCORE, and pre- and postoperative BNP, only the EuroSCORE and preoperative BNP were independent predictors of long-term adverse outcome (adjusted odds ratios = 1.225 [95% confidence interval, 1.046-1.434] and 1.001 [95% confidence interval, 1.000-1.002], respectively). The logistic model provided moderate discrimination (c-statistics = 0.67 [95% confidence interval, 0.59-0.74]), with 82% of cases correctly classified.

## DISCUSSION

The main findings of the present study were that (1) preoperative measurement of BNP differs between coronary and

valve surgery patients, whereas postoperative BNP values markedly increase whatever the type of cardiac surgery; (2) whatever the time of measurement, BNP is very accurate in predicting long-term adverse cardiac outcome after AVR and inaccurate after CABG surgery; and (3) a late postoperative BNP measurement probably is useless for routine practice in the cardiac surgical setting. In other words, the use of BNP in stratifying patients' cardiac risk on a long-term basis after primary elective cardiac surgery depends on both the type of surgery and the time of measurement.

Pre-and/or postoperative BNP measurements have been found to be good predictors of adverse outcome after cardiac surgery.<sup>1-6,9,13</sup> Preoperative BNP could be more accurate than the EuroSCORE, whereas peak postoperative BNP could add little to preoperative BNP alone for predicting hospital stay and mortality after elective CABG surgery.<sup>5,6</sup> In the present study, only preoperative BNP used as a continuous variable was an independent predictor of long-term adverse cardiac outcome. However, the discrimination of the logistic model was moderate.

None of the previously published studies assessed the influence of the type of cardiac surgery on the clinical usefulness of BNP measurement. Higher preoperative values of BNP have

**Table 3. Preoperative and Early Postoperative and Late Postoperative BNP Values in Patients Undergoing CABG Surgery and AVR**

BNP (pg/mL)	Group CABG (n = 100)	Group AVR (n = 89)	p Value
Preoperative	104 (8-5,017)	235 (8-2,018)	<0.001
Early postoperative	382 (76-2,268)*	410 (95-1,670)*	0.520
Late postoperative	551 (95-3,553)*†	470 (99-2,079)*‡	0.378

Abbreviations: AVR, aortic valve replacement; BNP, serum B-type natriuretic peptide; CABG, coronary artery bypass grafting.

NOTE. Values are median (extremes); p value refers to between-group comparisons.

\*p < 0.001 versus preoperative.

†p < 0.001 versus early postoperative.

‡p < 0.01 versus early postoperative.



**Table 4. Analysis of the ROC Curves and Discrimination of Preoperative and Early and Late Postoperative BNP Measurements in Predicting the Occurrence of Long-term Major Adverse Cardiac Events in Patients Undergoing CABG Surgery and AVR**

Surgery	BNP Measurement	Area Under the ROC Curve (95% Confidence Interval)	p Value
Global (n = 189)	Preoperative	0.67 (0.56-0.78)	0.002
	Early postoperative	0.66 (0.54-0.77)	0.004
	Late postoperative	0.61 (0.51-0.70)	0.015
CABG (n = 100)	Preoperative	0.54 (0.38-0.70)	0.320
	Early postoperative	0.54 (0.36-0.73)	0.324
	Late postoperative	0.54 (0.40-0.69)	0.288
AVR (n = 89)	Preoperative	0.78 (0.66-0.90)	<0.001
	Early postoperative	0.76 (0.62-0.89)	<0.001
	Late postoperative	0.66 (0.53-0.79)	0.006

Abbreviations: AVR, aortic valve replacement; BNP, B-type natriuretic peptide; CABG, coronary artery bypass grafting; ROC, receiver operating characteristic.

been reported in patients with aortic stenosis,<sup>1</sup> and small increases in postoperative BNP levels have been suggested after AVR when compared with CABG surgery,<sup>10</sup> thereby suggesting that BNP release could differ according to the cardiac surgical procedure itself. In the current study, a higher preoperative level and a proportionally less postoperative increase of BNP in AVR patients when compared with CABG patients was found, confirming previous results.<sup>1,10</sup> It also was found that preoperative values only differed according to the type of cardiac surgery, whereas no more significant difference was observed during the postoperative period. It suggests that preoperative BNP could depend mainly on the underlying cardiac disease and the profile of patients, whereas other causes are responsible for prolonged postoperative BNP release.<sup>15,16</sup> Numerous factors may contribute to the postoperative release of BNP after cardiac surgery such as cardioplegia, myocardial

damage, infarction, abrupt changes in heart loading conditions, or the occurrence of a systemic inflammatory response syndrome, so the increase in BNP is equivocal during the postoperative period. Impairment in renal function frequently is observed after cardiac surgery and also may act as a confounder, which has been shown to affect BNP prognostic ability in various clinical conditions.<sup>17,18</sup> Previous works suggested that the increase of BNP in coronary patients could reflect the extent of myocardial ischemia<sup>19</sup> and that ischemia would be the main secretion stimulus for BNP during cardiac surgery.<sup>1</sup> Thus, an elevated postoperative BNP may indicate inappropriate cardiac protection and/or inappropriate grafting procedure. An elevated postoperative BNP also may indicate a more severe underlying cardiac disease that could evolve unfavorably on a long-term basis. These 2 hypotheses are not exclusive, and the reliability of BNP in predicting long-term adverse outcome in AVR

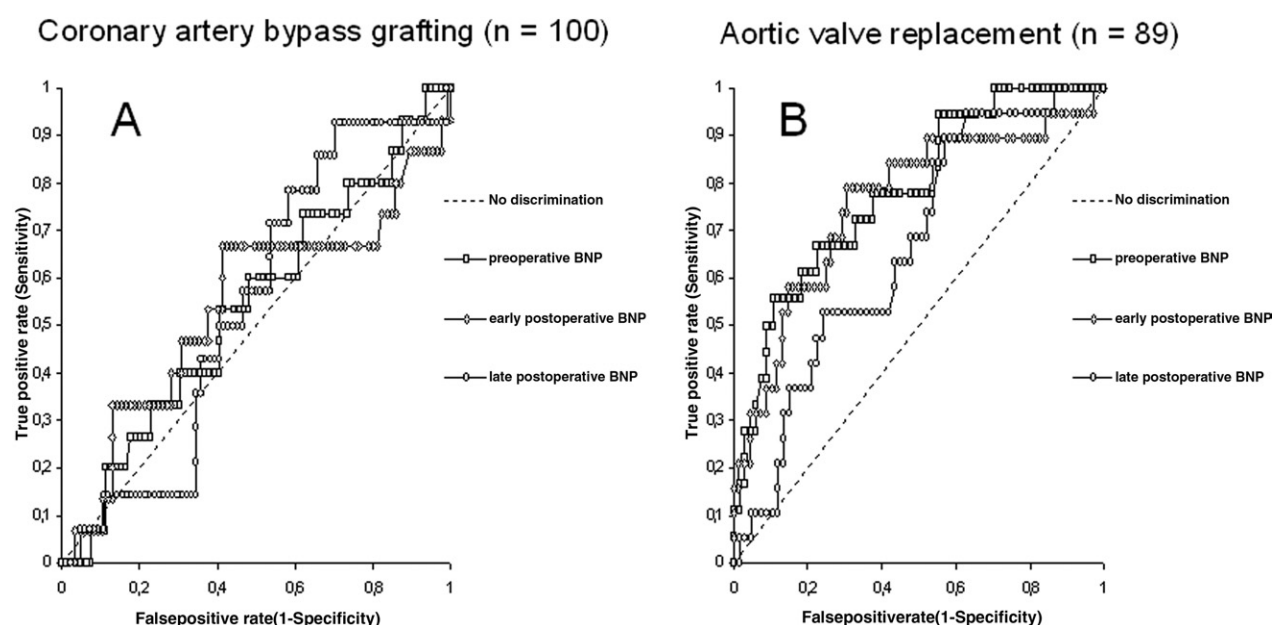


Fig 2. ROC curves showing the relation between sensitivity and 1-specificity in determining the predictive value of preoperative, early postoperative, and late postoperative BNP for the diagnosis of long-term major adverse cardiac events in patients undergoing (A) CABG surgery and (B) AVR. The dotted diagonal line is the no-discrimination curve. No significant difference was observed among curves.

patients suggests that BNP could be a good marker of the severity of chronic mechanisms, such as long-term left ventricular volume overload and increased wall tension after left ventricular hypertrophy or valve disease.<sup>20</sup> Although markedly increased during the postoperative period, BNP was inaccurate in predicting long-term adverse cardiac outcome after coronary artery surgery. Interestingly, Mahla et al<sup>21</sup> suggested the most important fact with BNP measurement after noncardiac surgery could be the actual postoperative level reached rather than the percentage change. These findings are potentially in accordance with this comment because the authors observed similar peak values of BNP and rates of MACEs after both AVR and CABG surgery. However, the lack of discrimination of BNP in predicting long-term adverse outcome after CABG surgery, contrasting with the very good discrimination after AVR, suggests the most important point after cardiac surgery could be the reason why BNP levels increase rather than the percentage change or the postoperative level reached. Why does BNP increase after cardiac surgery? The reasons could differ markedly according to the type of cardiac surgery and from one patient to another. Furthermore, all proposed reasons probably do not have similar consequences on short- and long-term prognosis. A myocardial ischemia-related increase in postoperative BNP could have a major prognostic value on a long-term basis, whereas a similar increase because of abrupt changes in heart-loading conditions during the postoperative period could be negligible. Unfortunately, at the bedside, the authors were unable to determine the main causes and mechanisms of BNP release for a given patient. Thus, despite equivalent BNP release after CABG and AVR surgery, it is not surprising that the discrimination of BNP (and its subsequent clinical utility) markedly differs between both types of cardiac surgery.

Finally, the authors found that a late postoperative BNP measurement was unable to track the actual peak postoperative value and of more limited diagnostic value than preoperative or early postoperative BNP measurement after valve surgery. This last result is somewhat different from those observed in the setting of decompensated heart failure in which a late value of BNP, close to discharge from the hospital, has been found to be more relevant for long-term outcome prediction.<sup>12</sup> Thus, unless very late postoperative BNP levels provide interesting prognostic abilities in future studies, preoperative or early postoperative BNP measurements should be preferred in the cardiac surgical setting.

Some important remarks must be included to indicate the limitations of the current study. First, the study was a sub-analysis of previously published data and subsequently was not designed specifically to address the primary hypothesis alone. Nevertheless, the authors believe that the data provide some new information about the potential limitations of serum BNP concentration as a predictor of adverse cardiac outcome after routine cardiac surgical procedures. The study also was conducted in a single center with a relatively small sample size, leading to wide confidence intervals around the ROC curves for both CABG and AVR surgery. This analysis was retrospective with relative inhomogeneity in subgroups. Because larger prospective studies previously provided threshold values for BNP measurements to predict adverse outcome, it was estimated that the present study actually was not designed to do it. Second, even though numerous causes can explain postoperative BNP release after cardiac surgery, the larger proportion of postoperative cardiac dysfunction after AVR could have influenced the discrimination of postoperative BNP in a favorable manner. Third, the authors used a traditional biologic approach by using BNP alone. The present authors recently showed that an integrating approach measuring postoperative multiple cardiac biomarkers improved the risk assessment of adverse cardiac outcome within 12 months after conventional cardiac surgery.<sup>13</sup> Further studies should compare a combination of preoperative BNP and postoperative cTnI with clinical risk scores to better identify high-risk patients on a long-term basis and definitely clarify what cardiac biomarkers may add to existing methods of risk stratification in the cardiac surgical setting. Finally, the present study did not test appropriate strategies to improve outcomes in identified high-risk patients. Future studies also should prospectively address this important issue.

In conclusion, the use of perioperative BNP measurement for clinical practice in cardiac surgery should take into account the type of cardiac surgical procedure, as previously shown with cTnI. When compared with coronary artery bypass surgery, AVR is associated with higher preoperative BNP values and a proportionally smaller increase during the postoperative period. Whatever the time of measurement, BNP can predict the long-term adverse cardiac outcome in valve surgery patients but seems of poor value in coronary artery bypass surgery. Lastly, a late postoperative BNP measurement probably is useless for routine practice in the cardiac surgical setting.

## REFERENCES

1. Berendes E, Schmidt C, Van Aken H, et al: A-type and B-type natriuretic peptides in cardiac surgical procedures. *Anesth Analg* 98: 11-19, 2004
2. Hutfless R, Kasanegra R, Madani M, et al: Utility of B-type natriuretic peptide in predicting postoperative complications and outcomes in patients undergoing heart surgery. *J Am Coll Cardiol* 43: 1873-1879, 2004
3. Cuthbertson BH, McKeown A, Croal BL, et al: Utility of B-type natriuretic peptide in predicting the level of peri- and postoperative cardiovascular support required after coronary artery bypass grafting. *Crit Care Med* 33:437-442, 2005
4. Fox AA, Shernan SK, Collard CD, et al: Preoperative B-type natriuretic peptide is an independent predictor of ventricular dysfunction and mortality after primary coronary artery bypass grafting. *J Thorac Cardiovasc Surg* 136:452-461, 2008
5. Fox AA, Muehlschlegel JD, Body SC, et al: Comparison of the utility of preoperative versus postoperative B-type natriuretic peptide for predicting hospital length of stay and mortality after primary coronary artery bypass grafting. *Anesthesiology* 112:842-851, 2010
6. Fellahi JL, Daccache G, Rubes D, et al: Does preoperative B-type natriuretic peptide better predict adverse outcome and prolonged length of stay than the standard EuroSCORE after cardiac surgery? *J Cardiothorac Vasc Anesth* 25:256-262, 2011
7. Cuthbertson BH, Croal BL, Rae D, et al: N-terminal pro-B-type natriuretic peptide levels and early outcome after cardiac surgery: A prospective cohort study. *Br J Anaesth* 103:647-653, 2009

8. Kerbaul F, Collart F, Giorgi R, et al: Increased plasma levels of pro-brain natriuretic peptide in patients with cardiovascular complications following off-pump coronary artery surgery. *Intensive Care Med* 30:1799-1806, 2004
9. Provenchère S, Berroëta C, Reynaud C, et al: Plasma brain natriuretic peptide and cardiac troponin I concentrations after adult cardiac surgery: Association with postoperative cardiac dysfunction and one-year mortality. *Crit Care Med* 34:995-1000, 2006
10. Georges A, Forestier F, Valli N, et al: Changes in type B natriuretic peptide (BNP) concentrations during cardiac valve replacement. *Eur J Cardiothorac Surg* 25:941-945, 2004
11. Fellahi JL, Hédoire F, Le Manach Y, et al: Determination of the threshold of cardiac troponin I associated with an adverse postoperative outcome after cardiac surgery: A comparative study between coronary artery bypass graft, valve surgery, and combined cardiac surgery. *Crit Care* 11:R106, 2007
12. Logeart D, Thabut G, Jourdain P, et al: PredischARGE B-type natriuretic peptide assay for identifying patients at high risk of readmission after decompensated heart failure. *J Am Coll Cardiol* 43:635-641, 2004
13. Fellahi JL, Hanouz JL, Le Manach Y, et al: Simultaneous measurement of cardiac troponin I, B-type natriuretic peptide, and C-reactive protein for the prediction of long-term cardiac outcome after cardiac surgery. *Anesthesiology* 111:250-257, 2009
14. DeLong ER, DeLong DM, Clarke-Pearson DL: Comparing the areas under two or more correlated receiver operating characteristic curves: A nonparametric approach. *Biometrics* 44:837-845, 1988
15. Provenchère S, Plantefève G, Hufnagel G, et al: Renal dysfunction after cardiac surgery with normothermic cardiopulmonary bypass: Incidence, risk factors and effect on clinical outcome. *Anesth Analg* 96:1258-1264, 2003
16. Morimoto K, Mori T, Ishiguro S, et al: Perioperative changes in plasma brain natriuretic peptide concentrations in patients undergoing cardiac surgery. *Surg Today* 28:23-29, 1998
17. Austin WJ, Bhalla V, Hernandez-Arce I, et al: Correlation and prognostic utility of B-type natriuretic peptide and its amino-terminal fragment in patients with chronic kidney disease. *Am J Clin Pathol* 126:506-512, 2006
18. Goei D, Schouten O, Boersma E, et al: Influence of renal function on the usefulness of N-terminal pro-B-type natriuretic peptide as a prognostic cardiac risk marker in patients undergoing noncardiac vascular surgery. *Am J Cardiol* 101:122-126, 2008
19. Richards AM, Nicholls MG, Yandle TG, et al: Plasma N-terminal pro-brain natriuretic peptide and adrenomedullin: New neurohormonal predictors of left ventricular function and prognosis after myocardial infarction. *Circulation* 97:1921-1929, 1998
20. Struthers AD: Introducing a new role for BNP: As a general indicator of cardiac structural disease rather than a specific indicator of systolic dysfunction only. *Heart* 87:97-98, 2002
21. Mahla E, Baumann A, Rehak P, et al: N-terminal pro-brain natriuretic peptide identifies patients at high risk for adverse cardiac outcome after vascular surgery. *Anesthesiology* 106:1088-1095, 2007