J Anesth (2008) 22:347–353
DOI 10.1007/s00540-008-0647-x

Journal of Anesthesia

Preoperative plasma brain natriuretic peptide level is an independent predictor of postoperative atrial fibrillation following off-pump coronary artery bypass surgery

Toshimasa Akazawa, Hiroko Nishihara, Hitomi Iwata, Kengo Warabi, Masayuki Ohshima, and Eiichi Inada

Department of Anesthesiology and Pain Medicine, Juntendo University, 2-1-1 Hongo, Bunkyo-ku, Tokyo 113-8421, Japan

Abstract

Purpose. Atrial fibrillation (AF) is a frequent complication after coronary artery bypass surgery. Postoperative AF can lead to thromboembolic events, prolonged hospital stay, and increased costs. Recent reports have shown that an elevated plasma brain natriuretic peptide (BNP) level is associated with AF. The purpose of this prospective study was to test the hypothesis that preoperative BNP level is a predictor of postoperative AF following off-pump coronary artery bypass surgery (OPCAB).

Methods. One hundred and fifty patients without a history of AF undergoing elective isolated OPCAB were enrolled. Plasma BNP level was measured preoperatively. Heart rate and rhythm were continuously monitored during the first 72 h after surgery.

Results. Twenty-six patients (17.3%) exhibited postoperative AF. This proportion is similar to those reported in earlier studies. Univariate analysis demonstrated that age (odds ratio [OR], 1.060; 95% confidence interval [CI], 1.008 to 1.114; $P = 0.023$), previous myocardial infarction (MI; OR, 2.628; 95% CI, 1.031 to 6.697; $P = 0.043$), and BNP level (OR, 7.336; 95% CI, 2.401 to 22.409 / log BNP level; $P < 0.001$) were accurate predictors of postoperative AF. Stepwise multivariate regression analysis indicated age (OR, 1.059; 95% CI, 1.002 to 1.120; $P = 0.043$) and BNP level (OR, 6.272; 95% CI, 1.980 to 19.861/ log BNP level; $P = 0.002$) as the only independent predictors of postoperative AF.

Conclusion. Preoperative BNP level is an independent predictor of postoperative AF following OPCAB. Our findings permit us to stratify the risk of AF and to plan prophylactic strategies in high-risk patients.

Key words Plasma brain natriuretic peptide level · Postoperative atrial fibrillation · Off-pump coronary artery bypass surgery

Address correspondence to: T. Akazawa
Received: November 26, 2007 / Accepted: May 20, 2008

Introduction

Atrial fibrillation (AF) is a common complication after coronary artery bypass graft (CABG) surgery, with a reported incidence of 20% to 40% [1]. Postoperative AF can lead to thromboembolic events, hemodynamic deterioration, and increased hospital costs [1]. Off-pump coronary artery bypass (OPCAB) surgery has been widely used over the past decade. However, controversy still remains as to whether OPCAB can reduce the incidence of postoperative AF [2–5]. Although a recent metaanalysis showed OPCAB significantly reduced the incidence of postoperative AF compared with conventional CABG [6], the incidence of postoperative AF following OPCAB has been reported to remain high, at 21%–32% [2,3,7–9]. Several factors, including low ejection fraction, and cardiac arrest have been reported as predictors of postoperative AF following conventional CABG [5,10–12]. On the other hand, some perioperative factors have also been reported to be predictors of postoperative AF following OPCAB [7,8,13]. Biomarkers indicating the inflammatory status of the patient, such as baseline C-reactive protein level, postoperative interleukin-6 level, and white blood cell count have been reported as independent predictors following conventional CABG and OPCAB [14,15]. However, only advancing age has consistently been shown to be associated with the development of postoperative AF following both conventional CABG and OPCAB [3,5,8,9]. Recent reports have shown that left ventricular (LV) diastolic dysfunction is a predictor of the development of AF [16,17]. The mechanism is speculated to be that LV relaxation abnormalities lead to high left atrial pressure and distension, causing vulnerability to AF [18,19].

The causes of diastolic dysfunction include myocyte hypertrophy, aging, post-infarct scarring, and epicardial ischemia [20]. Patients undergoing OPCAB frequently exhibit some of these factors and have impaired LV diastolic function, because most of such patients have severe triple-vessel disease, with hypertension, advanced age, and previous myocardial infarction (MI).

LV filling pressure is known to be elevated in patients with LV diastolic dysfunction. It is also known that elevated LV filling pressure leads to increased plasma brain natriuretic peptide (BNP) levels [21]. BNP has been established as a valuable biomarker to diagnose heart failure caused by both systolic and diastolic dysfunction [22,23]. BNP has also been shown to be useful for the guiding of therapy and monitoring of heart failure during treatment [24].

As a consequence, in the present study, we hypothesized that elevated preoperative plasma BNP level would be a predictor of postoperative AF following OPCAB.

Methods

Our study involved 150 consecutive patients without preoperative AF undergoing elective OPCAB at our institution between June 1, 2005, and August 31, 2006. Our study met with Institutional Review Board (IRB) approval and informed consent was obtained from all patients. Patients with significant valvular heart disease, acute myocardial infarction less than 1 week old, or chronic renal failure on hemodialysis were excluded from our study. Patients undergoing minimally invasive direct coronary artery bypass (MIDCAB) through left anterior thoracotomy during the period were also excluded.

Preoperatively, plasma BNP levels were measured using an immunoezymometric assay kit (E-test TOSOH II; Tosoh, Tokyo, Japan). According to the manufacturer's instructions, normal values were less than 18.4 $pg{\cdot}ml^{-1}$. The sensitivity of the assay (minimal detectable quantity) is 4 $pg{\cdot}ml^{-1}$. Correlation with a conventional radioimmunoassay was close (r = 0.995) [25,26]. Both the measurement of BNP level and 12-lead ECG recordings were performed 2 days before the surgery. Preoperative left ventricular ejection fraction (LVEF) was measured by transthoracic echocardiography 2 to 4 weeks before surgery.

All patients received 20 mEq magnesium supplementation, given intravenously the day before surgery for prophylaxis against perioperative arrhythmia. Cardiac medications, including beta-blockers, angiotensin converting-enzyme inhibitors, diuretics, and nitrates were continued until the morning of surgery. Angiotensin-receptor blockers were omitted on the day of surgery to prevent persistent perioperative hypotension.

Anesthesia was induced by the administration of midazolam 0.1 $mg{\cdot}kg^{-1}$ and fentanyl 5–8 $\mu g{\cdot}kg^{-1}$, and intubation was facilitated by the administration of vecuronium 0.15 $mg{\cdot}kg^{-1}$. Anesthesia was maintained with sevoflurane, oxygen, and air. Fentanyl was added as required to a total dose of about 15 $\mu g{\cdot}kg^{-1}$.

Median sternotomy was performed in all patients, and the bilateral internal thoracic arteries were harvested. The right gastroepiploic artery, radial arteries, or saphenous veins were harvested if necessary. After heparinization to achieve an activated clotting time greater than 300 s, three pericardial stitches were placed to facilitate exposure of the posterior or lateral site of the anastomoses. In all patients, surgery was performed using either the Acrobat stabilizer system (Guidant, Santa Clara, CA, USA) or the Octopus 2 myocardial stabilization device (Medtronic, Minneapolis, MN, USA). The anastomoses were performed in sequence, starting with the left circumflex artery (LCX) territory (obtuse marginal [OM] branches and posterolateral [PL] branches of the LCX), then the left anterior descending artery (LAD) territory (LAD and diagonal [DG] branches), and lastly the right coronary artery (RCA) territory (posterior descending artery [PDA] and atrioventricular (AV)-node branches [AV]). During the anastomosis, an intraluminal shunt was inserted. In all patients, the LAD was bypassed with the left internal thoracic artery. A cell-saving device was used for all of the patients.

All patients were transferred to the intensive care unit (ICU) intubated and ventilated. The patients were extubated as soon as they met the standard criteria. All of our patients received intravenous nitroglycerin (0.1 to 8 $\mu g{\cdot}kg^{-1}{\cdot}min^{-1}$) infusions for the first 24 h unless they were hypotensive (systolic pressure <90 mmHg). Potassium deficiency was promptly treated as necessary to maintain electrolyte balance within the normal range.

Heart rate and rhythm were continuously monitored during the first 72 h after surgery, using a bedside monitor in the ICU and telemetry in the hospital unit. Twelve-lead ECG recordings were performed before surgery, 1 h after surgery, daily for first 3 days after surgery, and whenever AF was suspected by continuous monitoring.

Values for normally distributed continuous variables are expressed as means ± SD and were compared between groups with the unpaired t-test; non-normally distributed continuous variables are expressed as medians (interquartile ranges) and were compared with the Mann-Whitney U-test. Dichotomous variables are presented as numbers and percentages and were analyzed with the χ^2 test. Multiple logistic regression analysis was used to identify variables that were independently correlated with postoperative AF, among those significantly associated on univariate analysis, with backward stepwise selection. Variables with a probability value of less than 0.05 were entered in the analysis and variables with a probability value of more than 0.10 were removed.

Receiver operating characteristic (ROC) curves were generated to determine the accuracy and optimal threshold of BNP for predicting postoperative AF. The optimal cutoff value for each index was defined by the highest sum of sensitivity and specificity. The area under the ROC curve (AUC) was used as an index of global performance, with an AUC of 0.5 indicating no discrimination ability.

As the distribution of BNP levels was positively skewed, a natural log transformation was used. We confirmed that both the results obtained by the raw data and the natural log-transformed data to compare BNP levels in both groups by the Mann-Whitney *U*-test were identical. Therefore, the result was expressed by the raw data for the Mann-Whitney *U*-test. Statistical significance was defined as a *P* value of less than 0.05. Statistical analysis was performed using SPSS for Windows version 14 (SPSS, Chicago, IL, USA).

Results

Table 1 shows the baseline characteristics of our patients. Twenty-six patients (17.3%) exhibited postoperative AF. The patients belonging to the AF group were significantly older ($P = 0.011$). A significantly greater number of patients from the AF group had suffered previous MI ($P = 0.038$). There were also significant differences in LVEF ($P = 0.043$) and preoperative BNP level ($P < 0.001$) between the two groups. No significant difference was detected in the use of drugs between the two groups. No association was noted between postoperative AF and the site of revascularization. Univariate analysis showed that age ($P = 0.023$), previous MI ($P = 0.043$), and BNP level ($P < 0.001$) were accurate predictors of postoperative AF (Table 2). However, stepwise multivariate regression analysis indicated that age and BNP level were the only independent predictors of postoperative AF (Table 2). To determine the accuracy of plasma BNP level for predicting the postoperative AF, an ROC curve was generated. The AOC was 0.74 ($P < 0.001$). A cutoff plasma BNP level of 78.9 pg·ml^{-1} was found to be the optimal threshold. The sensitivity and specificity of this value were 0.77 and 0.72, respectively. Table 3 shows the postoperative data. AF occurred 24 to 72 h following surgery in all patients in the AF group, who were housed in a general-care ward, and pharmacological cardioversion, performed in general-care wards, successfully converted AF to a sinus rhythm. None of the patients exhibiting postoperative AF required intensive care to treat severe hemodynamic deterioration. No significant difference was detected in the length of hospital stay or in the length of ICU stay when these factors compared between the two groups.

Table 1. Baseline characteristics

Variable	AF ($n = 26$ patients)	Non-AF ($n = 124$ patients)	*P*
Preoperative			
Age (years)	71 ± 8	66 ± 10	0.011
Female	3 (12%)	26 (21%)	0.237
Hypertension	20 (77%)	96 (77%)	0.956
Diabetes	11 (42%)	68 (55%)	0.245
Previous MI	19 (73%)	63 (51%)	0.038
No. of diseased vessels	2.9 ± 0.3	2.7 ± 0.6	0.11
Ca antagonist	11 (42%)	53 (43%)	0.968
Beta antagonist	9 (35%)	41 (33%)	0.879
ACEI	4 (15%)	15 (12%)	0.647
Diuretics	6 (23%)	22 (18%)	0.526
Nitrates	19 (73%)	84 (68%)	0.594
LVEF	0.49 ± 0.14	0.57 ± 0.12	0.043
Plasma BNP level (pg·ml^{-1})	106 (73–191)	46 (20–91)	<0.001
Perioperative			
Duration of surgery (min)	326 ± 81	304 ± 70	0.284
Fluid balance in operating room (ml)	3011 ± 1480	3490 ± 1114	0.657
RBC transfusion in operating room (units)	1.1	0.9	0.385
Number of distal anastomoses	3.8 ± 1.3	3.8 ± 1.3	0.898
Revascularization of PDA	19 (73%)	76 (61%)	0.257
Revascularization of OM	10 (38%)	47 (38%)	0.957

Normally distributed continuous variables are expressed as means ± SD and were compared between groups with the unpaired *t*-test; non-normally distributed continuous variables are expressed as medians (interquartile ranges) and were compared with the Mann-Whitney *U*-test. Dichotomous variables are presented as numbers and percentages and were analyzed with the χ^2 test

AF, atrial fibrillation; MI, myocardial infarction; ACEI, angiotensin-converting enzyme inhibitor; LVEF, left ventricular ejection fraction; BNP, brain natriuretic peptide; RBC, red blood cell; PDA, posterior descending branch; OM, obtuse marginal branch

Discussion

In the present study the incidence of postoperative AF was 17.3%. This is compatible with results described in previous reports [8,9,13]. The preoperative BNP level was found to be the strongest predictor of AF following OPCAB.

In all of the patients with postoperative AF, pharmacological cardioversion, performed in general-care wards, successfully converted the AF to a sinus rhythm. Consequently, the time required by patients with post-

Table 2. Logistic analysis to assess predictors of postoperative atrial fibrillation

Variable	Univariate analysis		Multivariate analysis	
	OR (95% CI)	*P*	OR (95% CI)	*P*
Preoperative				
Age (years)	1.060 (1.008–1.114)	0.023	1.059 (1.002–1.120)	0.043
Female	0.492 (0.137–1.766)	0.276		
Hypertension	0.956 (0.356–2.655)	0.972		
Diabetes	0.604 (0.257–1.420)	0.247		
Previous MI	2.628 (1.031–6.697)	0.043	2.082 (0.756–5.739)	0.156
No. diseased vessels	2.971 (0.719–12.273)	0.132		
Ca antagonist	0.982 (0.418–2.311)	0.982		
Beta antagonist	1.072 (0.440–2.611)	0.879		
ACEI	1.321 (0.400–4.362)	0.648		
Diuretics	1.293 (0.502–3.325)	0.527		
Nitrates	1.006 (0.723–1.398)	0.595		
LVEF	0.016 (0.000–1.262)	0.064		
Plasma BNP level	7.336 (2.401–22.409) / log BNP level	<0.001	6.272 (1.980–19.861) / log BNP level	0.002
Perioperative				
Duration of surgery (min)	0.996 (0.990–1.002)	0.199		
Fluid balance in operating room (ml)	1.000 (0.999–1.001)	0.586		
RBC transfusion in operating room (units)	1.053 (0.845–1.313)	0.645		
Number of distal anastomoses	1.006 (0.723–1.398)	0.973		
Revascularization of PDA	1.714 (0.670–4.384)	0.261		
Revascularization of OM	1.024 (0.429–2.443)	0.957		

OR, odds ratio; CI, confidence interval; MI, myocardial infarction; ACEI, angiotensin-converting enzyme inhibitor; LVEF, left ventricular ejection fraction; BNP, brain natriuretic peptide; RBC, red blood cell; PDA, posterior descending branch; OM, obtuse marginal branch

Table 3. Postoperative data

	AF group	Non-AF group	
ICU length of stay (days)	1.2 ± 0.4	1.1 ± 0.3	NS
Hospital length of stay (days)	14.6 ± 9.3	12.3 ± 6.9	NS
Number of patients with neurological complications	0	0	

NS, not significant

operative AF to stay in the ICU and in the hospital was not significantly prolonged.

Various studies have been performed to examine independent predictors of the incidence of postoperative AF following CABG surgery. In patients undergoing conventional coronary artery bypass, several factors have been reported to be associated with the incidence of postoperative AF. These include low ejection fraction and the influence of cardioplegic arrest [5,10–12]. On the other hand, not much information is available on the independent predictors of postoperative AF following OPCAB [7–9,13,14]. Anastomoses of the ramus medianus, and some other perioperative factors, including BNP level in pericardial fluid, intraoperative fluid balance, intraoperative core temperature, and postoperative cardiac index have been reported as predictors of AF following OPCAB [7–9]. Biomarkers indicating inflammatory status, such as baseline C-reactive protein level, postoperative elevation of interleukin-6, and white blood cell count have been reported as independent predictors of AF following both conventional CABG and OPCAB [13–15]. However, only advancing age has consistently been shown to be associated with the development of postoperative AF following both conventional CABG and OPCAB [3,5,8,9]. Consequently, we examined independent predictors of postoperative AF following OPCAB from the viewpoint of left ventricular (LV) function.

Our results show that preoperative plasma BNP level is an independent predictor of postoperative AF following OPCAB. Wazni et al. [27] reported that preoperative BNP levels predicted postoperative AF following cardiac surgery. As they suggested, an elevated BNP level has been shown to be associated with AF in some reports [28,29]. BNP is secreted in response to the mechanical stretch of LV myocytes. Some clinical investigations have shown that BNP is a valuable biomarker to diagnose heart failure. In patients with both LV systolic and diastolic dysfunction, plasma BNP level was shown to be elevated by the elevation of LV filling pressure [21]. The usefulness of BNP for monitoring heart failure has also been shown by several studies demonstrating changes in BNP levels during recompensation therapy in heart failure, related to hemodynamic parameters [24]. Consequently, the patients with elevated BNP level in our study were considered to have had preoperative heart failure caused by systolic or diastolic dysfunction, leading to increased left atrial pressure and subsequent vulnerability to AF.

Some studies have reported the association of diastolic dysfunction and lone AF [16,17]. It is conceivable that the mechanism involved is that LV relaxation abnormalities cause elevation of LV end-diastolic pressure, leading to a high left atrial pressure. The left atrium and pulmonary vein are thus distended and stretched, and therefore potentiate electrical remodeling, leading to a reduction in the atrial effective refractory period, resulting in vulnerability to AF [18,19]. Left atrial pressure can increase during bypass surgery and the distension and stretch of the left atrium and pulmonary vein can be caused by the dislocation of the heart for anastomosis, which may play an inciting role. Causes of diastolic dysfunction include myocyte hypertrophy, aging, post-infarct scarring, and epicardial ischemia [20]. The frequent association of impaired LV diastolic function has been suggested in patients undergoing OPCAB, because, in most of these patients, there is significant stenoses of multiple coronary arteries, hypertension, and previous myocardial infarction (MI).

Some previous studies have shown that low LV ejection fraction (LVEF) is a predictor of postoperative AF following CABG [11,12]. Our results show that the LVEF in patients from the AF group was significantly lower compared to that in the non-AF group. However, the LVEF was not shown to be an independent predictor of postoperative AF following OPCAB. In patients with impaired LV function, the end-diastolic pressure is elevated, mainly due to diastolic dysfunction [30]. Therefore, from the viewpoint of the association between elevated end-diastolic pressure and atrial pressure, diastolic function is suggested to be more important in the prediction of postoperative AF following OPCAB. This leads us to the conclusion that the predictivity of BNP is better than that of LVEF, because both systolic and diastolic dysfunction can be detected by BNP. Further investigation is required to validate the association between diastolic function and the incidence of postoperative AF, by studies that evaluate LV function using Doppler echocardiographic measurement.

Our results showed that age was an independent predictor of postoperative AF following OPCAB, and we also found significant differences between our two groups in the LVEF and in the proportion of patients with previous myocardial infarction (MI). Some reports have shown that elevation of BNP is caused by advanced age, infarction size, and LVEF [31–33]. Left atrial enlargement was also reported to be an independent predictor of postoperative AF [34]. An association between left atrial volume and BNP was reported in several studies [35]. Therefore, it appears that the strong predictability of BNP for postoperative AF is attributable to the association between BNP and other predictive factors.

Hakala et al. [36] and Nakamura et al. [7] reported that the preoperative BNP level was not an independent predictor of postoperative AF following CABG. This difference from our findings may be partly explained by the fact that the preoperative BNP level in our patients was more elevated than the levels in their patients, indicating that the LV function in their patients was not as impaired as that in our patients.

Zangrillo et al. [9] reported that grafting of the ramus medianus could be an independent predictor of postoperative AF following OPCAB. They suggested that the lifting of the heart to access the lateral side may stretch the left atrium and increase the risk of AF. We did not specify the use of the ramus medianus in our patients; consequently, the association of anastomoses of the ramus medianus and the incidence of AF was not evaluated by our study. In our patients, the heart was dislocated most prominently during the anastomoses of the obtuse marginal branches. Our data showed no significant association between the incidence of AF and the anastomoses of the obtuse marginal branches. This result was compatible with that of Zangrillo et al. [9].

Our data revealed no significant differences between the pharmacological agents given to the patients in the AF and non-AF groups. This can be accounted for by the study design. The prophylaxis of postoperative AF by the pharmacological improvement of diastolic function prior to surgery is speculated to be effective, including the use of beta-blockers, angiotensin-converting-enzyme inhibitors, and angiotensin-receptor blockers.

Study limitations

First, this study was conducted at a single institute, with a relatively small sample size. Multicenter studies with larger populations are warranted. Second, short-duration self-limiting AF could have been missed, and ECG was not monitored after the first 72 h until discharge from the hospital. Therefore, the incidence of AF in our study could have been underestimated. Third, LVEF was measured 2 to 4 weeks before surgery, and the BNP level was measured 2 days before surgery. The LV function could have improved or deteriorated during this period. These differences in measurement times could have contributed to the better predictivity of postoperative AF shown by BNP compared with LVEF.

In conclusion, the preoperative plasma BNP level was shown to be an independent predictor of postoperative

AF following OPCAB. Our findings permit us to stratify the risk of AF and to plan prophylactic strategies in high-risk patients.

References

1. Aranki SF, Shaw DP, Adams DH, Rizzo RJ, Couper GS, VanderVliet M, Collins JJ Jr, Cohn LH, Burstin HR. Predictors of atrial fibrillation after coronary artery surgery. Current trends and impact on hospital resources. Circulation. 1996;94:390–7.
2. Athanasiou T, Aziz O, Mangoush O, Weerasinghe A, Al-Ruzzeh S, Purkayastha S, Pepper J, Amrani M, Glenville B, Casula R. Do off-pump techniques reduce the incidence of postoperative atrial fibrillation in elderly patients undergoing coronary artery bypass grafting? Ann Thorac Surg. 2004;77:1567–74.
3. Hakala T, Pitkanen O, Hartikainen J. Cardioplegic arrest does not increase the risk of atrial fibrillation after coronary artery bypass surgery. Eur J Cardiothorac Surg. 2004;25:415–8.
4. Salamon T, Michler RE, Knott KM, Brown DA. Off-pump coronary artery bypass grafting does not decrease the incidence of atrial fibrillation. Ann Thorac Surg. 2003;75:505–7.
5. Enc Y, Ketenci B, Ozsoy D, Camur G, Kayacioglu I, Terzi S, Cicek S. Atrial fibrillation after surgical revascularization: is there any difference between on-pump and off-pump? Eur J Cardiothorac Surg. 2004;26:1129–33.
6. Cheng DC, Bainbridge D, Martin JE, Novick RJ. Does off-pump coronary artery bypass reduce mortality, morbidity, and resource utilization when compared with conventional coronary artery bypass? A meta-analysis of randomized trials. Anesthesiology. 2005;102:188–203.
7. Nakamura T, Azuma A, Sawada T, Sakamoto K, Yamano T, Yaku H, Matsubara H. Brain natriuretic peptide concentration in pericardial fluid is independently associated with atrial fibrillation after off-pump coronary artery bypass surgery. Coron Artery Dis. 2007;18:253–8.
8. Hosokawa K, Nakajima Y, Umenai T, Ueno H, Taniguchi S, Matsukawa T, Mizobe T. Predictors of atrial fibrillation after off-pump coronary artery bypass graft surgery. Br J Anaesth. 2007; 98:575–80.
9. Zangrillo A, Landoni G, Sparicio D, Benussi S, Aletti G, Pappalardo F, Fracasso G, Fano G, Crescenzi G. Predictors of atrial fibrillation after off-pump coronary artery bypass graft surgery. J Cardiothorac Vasc Anesth. 2004;18:704–8.
10. Ascione R, Caputo M, Calori G, Lloyd CT, Underwood MJ, Angelini GD. Predictors of atrial fibrillation after conventional and beating heart coronary surgery: a prospective, randomized study. Circulation. 2000;102:1530–5.
11. Evrard P, Gonzalez M, Jamart J, Malhomme B, Blommaert D, Eucher P, Installe E. Prophylaxis of supraventricular and ventricular arrhythmias after coronary artery bypass grafting with low-dose sotalol. Ann Thorac Surg. 2000;70:151–6.
12. Guler N, Ozkara C, Dulger H, Kutay V, Sahin M, Erbilen E, Gumrukcuoglu HA. Do cardiac neuropeptides play a role in the occurrence of atrial fibrillation after coronary bypass surgery? Ann Thorac Surg. 2007;83:532–7.
13. Lo B, Fijnheer R, Nierich AP, Bruins P, Kalkman CJ. C-reactive protein is a risk indicator for atrial fibrillation after myocardial revascularization. Ann Thorac Surg. 2005;79:1530–5.
14. Ishida K, Kimura F, Imamaki M, Ishida A, Shimura H, Kohno H, Sakurai M, Miyazaki M. Relation of inflammatory cytokines to atrial fibrillation after off-pump coronary artery bypass grafting. Eur J Cardiothorac Surg. 2006;29:501–5.
15. Abdelhadi RH, Gurm HS, Van Wagoner DR, Chung MK. Relation of an exaggerated rise in white blood cells after coronary bypass or cardiac valve surgery to development of atrial fibrillation postoperatively. Am J Cardiol. 2004;93:1176–8.
16. Thamilarasan M, Grimm RA, Rodriguez LL, Sun JP, Odabashian JA, Agler DA, Morehead A, Chung MK, Klein AL, Thomas JD. Left ventricular diastolic dysfunction in lone atrial fibrillation determined by Doppler tissue imaging of mitral annular motion. Am J Cardiol. 2000;86:1026–9, A10.
17. Tsang TS, Gersh BJ, Appleton CP, Tajik AJ, Barnes ME, Bailey KR, Oh JK, Leibson C, Montgomery SC, Seward JB. Left ventricular diastolic dysfunction as a predictor of the first diagnosed nonvalvular atrial fibrillation in 840 elderly men and women. J Am Coll Cardiol. 2002;40:1636–44.
18. Satoh T, Zipes DP. Unequal atrial stretch in dogs increases dispersion of refractoriness conducive to developing atrial fibrillation. J Cardiovasc Electrophysiol. 1996;7:833–42.
19. Ravelli F, Allessie M. Effects of atrial dilatation on refractory period and vulnerability to atrial fibrillation in the isolated Langendorff-perfused rabbit heart. Circulation. 1997;96:1686–95.
20. Angeja BG, Grossman W. Evaluation and management of diastolic heart failure. Circulation. 2003;107:659–63.
21. Iwanaga Y, Nishi I, Furuichi S, Noguchi T, Sase K, Kihara Y, Goto Y, Nonogi H. B-type natriuretic peptide strongly reflects diastolic wall stress in patients with chronic heart failure: comparison between systolic and diastolic heart failure. J Am Coll Cardiol. 2006;47:742–8.
22. Maisel AS, Krishnaswamy P, Nowak RM, McCord J, Hollander JE, Duc P, Omland T, Storrow AB, Abraham WT, Wu AH, Clopton P, Steg PG, Westheim A, Knudsen CW, Perez A, Kazanegra R, Herrmann HC, McCullough PA. Rapid measurement of B-type natriuretic peptide in the emergency diagnosis of heart failure. N Engl J Med. 2002;347:161–7.
23. Maisel AS, Koon J, Krishnaswamy P, Kazenegra R, Clopton P, Gardetto N, Morrisey R, Garcia A, Chiu A, De Maria A. Utility of B-natriuretic peptide as a rapid, point-of-care test for screening patients undergoing echocardiography to determine left ventricular dysfunction. Am Heart J. 2001;141:367–74.
24. Johnson W, Omland T, Hall C, Lucas C, Myking OL, Collins C, Pfeffer M, Rouleau JL, Stevenson LW. Neurohormonal activation rapidly decreases after intravenous therapy with diuretics and vasodilators for class IV heart failure. J Am Coll Cardiol. 2002;39:1623–9.
25. Kono M, Yamauchi A, Tsuji T, Misaki A, Igano K, Ueki K, Fujishima M, Ueda A, Inouye K, Nakao K, Imura H. An immunoradiometric assay for brain natriuretic peptide in human plasma (in Japanese). Kaku Igaku. 1993;13:2–7.
26. Yabuuchi H, Tatsumi M, Tateshima S, Masutani T, Okamono Y. Correlation beween plasma BNP levels measured by enzyme immunoassay and radioimmunoassay (in Japanese). Igaku Kensa. 2005;54:908–11.
27. Wazni OM, Martin DO, Marrouche NF, Latif AA, Ziada K, Shaaraoui M, Almahameed S, Schweikert RA, Saliba WI, Gillinov AM, Tang WH, Mills RM, Francis GS, Young JB, Natale A. Plasma B-type natriuretic peptide levels predict postoperative atrial fibrillation in patients undergoing cardiac surgery. Circulation. 2004;110:124–7.
28. Lee SH, Jung JH, Choi SH, Lee N, Park WJ, Oh DJ, Rhim CY, Lee KH. Determinants of brain natriuretic peptide levels in patients with lone atrial fibrillation. Circ J. 2006;70:100–4.
29. Inoue S, Murakami Y, Sano K, Katoh H, Shimada T. Atrium as a source of brain natriuretic polypeptide in patients with atrial fibrillation. J Card Fail. 2000;6:92–6.
30. Zile MR, Brutsaert DL. New concepts in diastolic dysfunction and diastolic heart failure: part I: diagnosis, prognosis, and measurements of diastolic function. Circulation. 2002;105:1387–93.
31. Redfield MM, Rodeheffer RJ, Jacobsen SJ, Mahoney DW, Bailey KR, Burnett JC Jr. Plasma brain natriuretic peptide concentration: impact of age and gender. J Am Coll Cardiol. 2002;40: 976–82.
32. Nakagawa K, Umetani K, Fujioka D, Sano K, Nakamura T, Kodama Y, Kitta Y, Ichigi Y, Kawabata K, Obata JE, Takano H, Inobe Y, Kugiyama K. Correlation of plasma concentrations of

B-type natriuretic peptide with infarct size quantified by tomographic thallium-201 myocardial scintigraphy in asymptomatic patients with previous myocardial infarction. Circ J. 2004;68: 923–7.

33. Yasue H, Yoshimura M, Sumida H, Kikuta K, Kugiyama K, Jougasaki M, Ogawa H, Okumura K, Mukoyama M, Nakao K. Localization and mechanism of secretion of B-type natriuretic peptide in comparison with those of A-type natriuretic peptide in normal subjects and patients with heart failure. Circulation. 1994;90:195–203.
34. Nakai T, Lee RJ, Schiller NB, Bellows WH, Dzankic S, Reeves J 3rd, Romson J, Ferguson S, Leung JM. The relative importance of left atrial function versus dimension in predicting atrial fibrillation after coronary artery bypass graft surgery. Am Heart J. 2002;143:181–6.
35. Barclay JL, Kruszewski K, Croal BL, Cuthbertson BH, Oh JK, Hillis GS. Relation of left atrial volume to B-type natriuretic peptide levels in patients with stable chronic heart failure. Am J Cardiol. 2006;98:98–101.
36. Hakala T, Hedman A, Turpeinen A, Kettunen R, Vuolteenaho O, Hippelainen M. Prediction of atrial fibrillation after coronary artery bypass grafting by measuring atrial peptide levels and preoperative atrial dimensions. Eur J Cardiothorac Surg. 2002;22: 939–43.