原 著

Preoperative Examination Findings for Prediction of Use of Inotropic Agents at Weaning from Cardiopulmonary Bypass

Taketo Nakamura, MD, PhD*, Ryu Okutani, MD, PhD**

This study was performed at the Department of Anesthesiology, Osaka City General Hospital and Children's Hospital.

Abstract

Object: Postoperative left ventricular dysfunction often occurs after cardiopulmonary bypass (CPB), requiring inotropic drug administration to achieve adequate hemodynamic status. The purpose of our study was to determine whether preoperative examination findings can predict the use of inotropic agents at separation from CPB in patients undergoing mitral valve repair without preoperative heart failure.

Methods: Patients who underwent a mitral valve repair procedure between November 2009 and November 2010 were studied. Inotropic support was defined as use of milrinone at separation from CPB, and was implemented as clinically indicated. Echocardiography and laboratory data before surgery were retrospectively examined and compared between the patients who require inotropic support (Group M) and who did not (Group C).

Results: We analyzed 33 patients who underwent a mitral valve repair procedure, 14 of whom required inotropic support. There were no significant differences in CPB time and cross clamp time, and no differences in contraction or diastolic function shown by echocardiography. However, NT pro-BNP in Group M was higher than that in Group C.

Conclusion: Elevation of preoperative NT-pro BNP, irrespective of echocardiography findings, was found to be a predictor of inotropic support at separation of CPB in patients without preoperative heart failure.

Key words; mitral valve repair, preoperative examination, transthoracic echocardiography, NT-pro BNP

Introduction

Postoperative left ventricular dysfunction often occurs after cardiopulmonary bypass (CPB), requiring inotropic drug administration to achieve adequate hemodynamic status[1]. Such contractile dysfunction may occur in patients with normal preoperative ventricular dysfunction after CPB and usually resolves around 24 hours after surgery[2]. Although many clinicians may treat patients prophylactically with inotropic agents at separation from CPB, those drugs should be administered selectively, because of an increasing risk of tachycardia, dysrhythmia, and myocardial ischemia[3].

Previous studies have identified such factors as increased age, low ejection fraction (EF), female gender, cardiomegaly, history of congestive heart failure (CHF), repeat operation, emergency operation, recent myocardial infarction, and left main coronary artery disease as associated with a need for inotropic support[4]. However, pathologic changes associated

*Department of Anesthesia, Kobe Kaisei Hospital, Hyogo, Japan
**Department of Anesthesia, Osaka City General Hospital and Children's Hospital, Osaka, Japan

with moderate-severe valvular heart disease are longstanding and known as risk factors for inotropic support after CPB[1]. Unfortunately, it is difficult to predict the necessity of inotropic agents at separation from CPB in the light of preoperative data.

The purpose of this study was to examine whether we can predict the use of inotropic agents at separation from CPB with reference to preoperative examination findings in patients without preoperative heart failure undergoing mitral valve repair.

Methods

Following institutional review board approval, patients who had undergone mitral valve repair from November 2009 to November 2010 were enrolled.

Patients who had a mitral valve repair due to mitral regurgitation were included. Exclusion criteria were NYHA > 2, history of cardiac surgery, history of ischemic coronary disease, history poorly controlled diabetes mellitus, history of poorly controlled hypertension, and emergency operation.

All patients underwent a transthoracic echocardiography (TTE) examination within 1 month prior to the surgical procedure. Comprehensive TEE was performed for all patients before CPB. Patients who received inotropic support at separation from CPB were placed in Group M, while those who did not were placed in Group C.

The medical records of all included patients were reviewed. Age, sex, height, weight, and preoperative examination findings were collected. TTE results were reviewed to determine left ventricular ejection fraction (EF), left ventricular end-diastolic diameter (Dd), left ventricular end-systolic diameter (Ds), E/e' (mitral annular velocity), and e'.

In our institute, all surgical procedures were conducted under general anesthesia. Routine anesthetic care was used perioperatively and there were no changes in anesthetic management during the study period. No preanesthetic medication was administered. Anesthesia was induced with propofol, fentanyl and rocuronium, and maintained with sevoflurane (1.0-2.0%) in a mixture of O_2/air and fentanyl. Anesthesia was kept with propofol and fentanyl during CPB.

All the patients underwent midline sternotomy approach. Full heparinization was carried out, with a goal of an activated clotting time greater than 400sec. Each patient was placed in CPB and retrograde cardioplegia in addition to antegrade cardioplegia was delivered, then they were systemically drifted to 34°C throughout the cross-clamp time. Mitral valve repair was performed with a loop technique[5]. A water injection test with saline confirmed no regulation. After completion of the procedure, the aortic cross clamp was released. Temporary arterial and ventricular pacing wires were placed in a standard fashion, as necessary. And then it was checked that there were no air bubbles in cardiac cavity. After an appropriate rest period and gradual rewarming, the patient was weaned from CPB. Inotropic support during separation from CPB was bolus of milrinone (50μg/kg) and continuous infusion (0.25-0.75μg/kg/min). The right ventricle was usually directly inspected in the surgical wound, left ventricle was evaluated using TEE. Inotropic support was given for signs of low cardiac output (cardiac index < 2.2 l/min/m^2 usually accompanied by hypotension despite infusion of fluids. In addition, norepinephrine was administered to maintain blood pressure. Support was implemented by the certifying anesthesiologist as clinically indicated (inability to separate from CPB, hypotension).

Protamine was given to reverse the heparin effect and decannulation was performed. After surgery, all patients were transferred to the intensive care unit.

All statistical analyses were performed with Fischer's exact test or a chi-square test as appropriate, and continuous data were analyzed using a Mann-Whitney U test. The variability of the values of NT-pro BNP is wide, so logarithm of values were also compared.

Results

A total of 33 patients underwent mitral valve repair procedure from November 2009 to November 2010,

Table 1 Patient characteristics

	Group M	Group C	P value
Cases (M/F)	14 (6/8)	19 (9/10)	0.401
Age (years)	65±11	61±12	0.301
Height (cm)	156±8	159±12	0.502
Weight (kg)	50±10	56±15	0.184
Severity of MR			
mild	0	0	
moderate	1	2	
severe	13	17	
HT/DM (person)	0/1	0/0	

Data are shown as the number of patients or the mean±SD.
MR: mitral regurgitation.

Table 2 Characteristic of CPB and cross clamp time

	Group M	Group C	P value
CPB time (min)	134±21	120±22	0.07
cross clamp time (min)	101±24	108±21	0.08
AF (separation from CPB)	1	0	

Data are shown as the number of patients or the mean±SD or number of patients.
CPB: cardiopulmonary bypass, AF: atrial fibrillation at separation from CPB.

and their demographics are presented in **Table 1**. 14 patients (42%) required inotropic support at separation from CPB, 19 patients did not. There were no differences in regard to sex, age, height, weight, and past histories. Women showed a slightly higher need of inotropic support than men (44 vs. 40%). There were no significant differences in CPB time between Group M and Group C (134±21 vs. 120±22 minutes, p=0.07). There were no significant differences in cross clamp time between Group M and Group C (101±24 vs. 108±21 minutes, p=0.08) (**Table 2**).

An analysis of preoperative TTE data was shown in **Fig. 1**. EF between Group M and Group C did not differ, 61±9 vs. 60±9% (P=0.19). Dd between Group M and Group C also did not differ, 50±8 vs. 51±7 mm (P=0.51). Ds between Group M and Group C also did not differ, 33±9 vs. 34±5 mm (P=0.43). E/e' between Group M and Group C also did not differ, 15.8±4.3 vs. 14.3±3.2 (P=0.25). There were no differences about e' between Group M and Group C, 7.4±0.9 vs. 8.0±2.7 cm/s (P=0.51).

Analyses of laboratory data showed that preoperative NT-pro BNP in Group M (941±1,497 pg/ml) was significantly higher than that in Group C (294±400 pg/ml) and Log[NT-pro BNP] (6.1±1.2) was significantly higher than that in Group C (5.0±1.2) (**Fig. 2**).

Discussion

Of 33 patients who underwent mitral valve repair in a 1-year period, 42% received inotropic support. We examined preoperative risk factors for the need of inotropic support at separation from CPB, which revealed that increased NT-pro BNP prior to surgery was associated with use of such support, even in patients with normal LV contraction and dilatation shown by echocardiography.

NT-pro BNP in plasma is a biomarker secreted from myocardial cells and well correlated with left ventricular end diastolic pressure (LVEDP)[6]. In a previous study, elevated LVEDP was also found to be an independent predictor of inotropic support at separation from CPB[2]. A frequent cause of elevated LVEDP is left ventricular hypertrophy (LVH), which is a risk factor for diastolic dysfunction, while Royster et al. reported that higher LVEDP was associated with worse outcome[7]. In our study, there were no differences in echocardiography findings between the

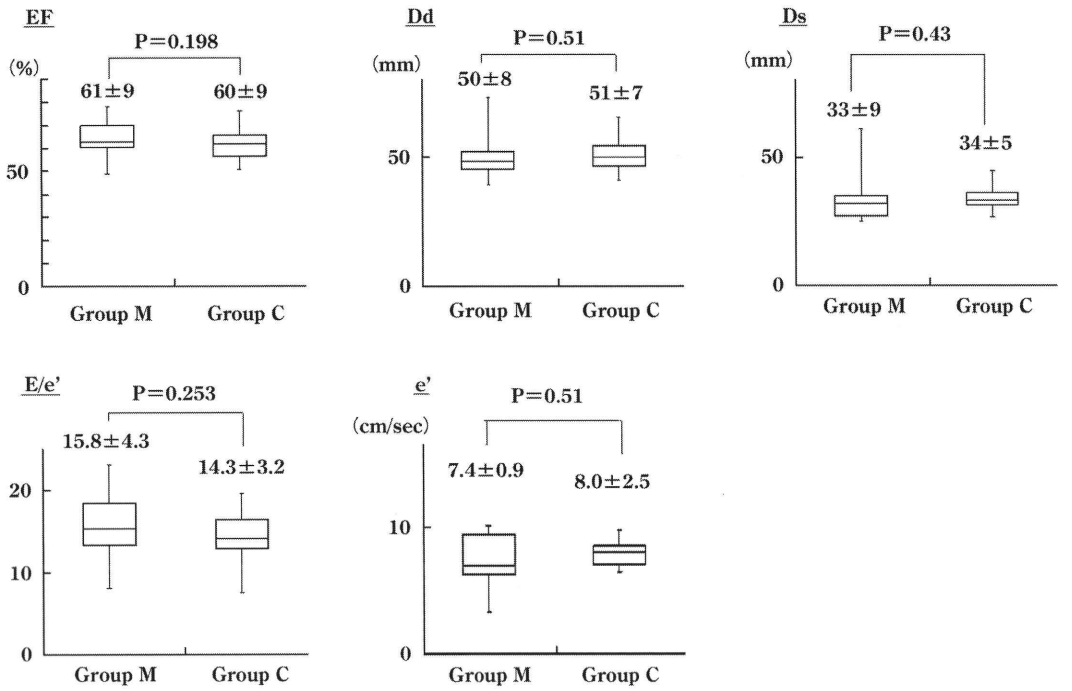

Figure 1 Preoperative transthoracic echocardiography findings

No significant differences were found in regard to the investigated parameters in preoperative TEE findings between the two groups. EF=ejection fraction, Dd=left ventricle diameter at end diastole, E/e'=peak early diastolic left ventricle filling velocity/spectral tissue Doppler of early diastolic phase, e'=spectral tissue Doppler of early diastolic phase.

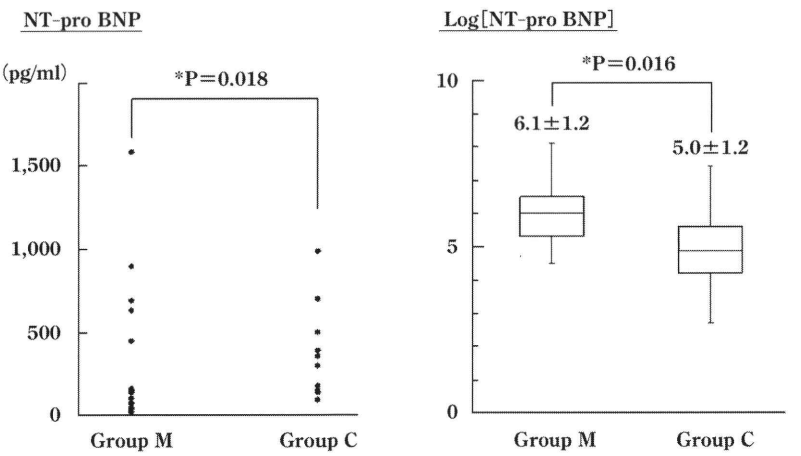

Figure 2 Preoperative NT-pro BNP and log[NT-pro BNP]

The value of NT-pro BNP was significantly higher in group M than that in group C. The value of log[NT-pro BNP] in Group M was significantly higher than that in Group C.

groups. Furthermore, E/e' showed an increasing trend and might have indicated diastolic dysfunction in both groups. Myocardial damage might have existed in the Group M patients, though heart failure was not recognized by clinical signs or results of echocardiography.

Imdad reported that left ventricular dysfunction, as shown by reduced ejection fraction and low cardiac index, was found to be an independent predictor of inotropic support[4]. Although ventricular dysfunc-

tion after CPB is largely a transient phenomenon related to ischemia, left ventricular dilation, and reduced compliance, poor LV function continues to be one of the most significant predictors of postoperative inotropic support[2].

Phosphodiesterase enzyme (PDE) is ubiquitous in the cardiovascular system and has characteristic substrate specificities, along with kinetic and responses to pharmacological agents[8]. Milrinone, which is a specific PDE III isozyme in myocardium and vascular smooth muscle, and a selective inhibitor of cAMP, causes an increase in cardiac output through combined positive inotropic and vasodilative effects without oxygen consumption[9]. Administration of milrinone was reported to provide safe perioperative management by achieving a stable hemodynamic condition, and also reduced the postoperative doses of dobutamine and epinephrine in cardiac surgery patients[10].

In conclusion, elevation of preoperative NT pro-BNP, irrespective of echocardiography findings, was a predictor of inotropic support at separation of CPB in patients without heart failure.

References

1) Butterworth JF 4th, Legault C, Royster RL, et al: Factors that predict the use of positive inotropic drug support after cardiac valve surgery. Anesth Analg 1998; 86: 461–7.
2) Royster RL: Myocardial dysfunction following cardiopulmonary bypass: recovery patterns, predictors of inotropic need, theoretical concepts of inotropic administration. J Cardiothorac Vasc Anesth 1993; 7 (4 Suppl 2): 19–25.
3) Lazar HL, Buckberg GD, Foglia RP, et al: Detrimental effects of premature use of inotropic drugs to discontinue cardiopulmonary bypass. J Thorac Cardiovasc Surg 1981; 82: 18–25.
4) Ahmed I, House CM, Nelson WB: Predictors of inotropic use in patients undergoing concomitant coronary artery bypass graft (CABG) and aortic valve replacement (AVR) surgeries at separation from cardiopulmonary bypass (CPB). J Cardiothorac Surg 2009; 4: 24–9.
5) Yozu R, Shin H, Maehara T, et al: Post-access cardiac surgery. Experience with 34 cases at Keio University Hospital. Jpn J Thoracic Cardiovasc Surg 2001; 49: 360–4.
6) Maeda K, Tsutamoto T, Wada A, et al: Plasma brain natriuretic peptide as a biochemical marker of high left ventricular end-diastolic pressure in patients with symptomatic left ventricular dysfunction. Am Heart J 1998; 135: 825–32.
7) Royster RL, Butterworth JF 4th, Prough DS, et al: Preoperative and intraoperative predictors of inotropic support and long-term outcome in patients having coronary artery bypass grafting. Anesth Analg 1991; 72: 729–36.
8) Silver PJ: Biochemical aspects of inhibition of cardiovascular low (Km) cyclic adenosine monophosphate phosphodiesterase. Am J Cardiol 1989; 63: 2–8A.
9) Levy JH, Ramsay J, Bailey JM Jr: Pharmacokinetics and pharmacodynamics of phosphodiesterase-III inhibitors. J Cardiothorac Anesth 1990; 4 (suppl 5): 7–11.
10) Yamaguchi A, Tanaka M, Naito K, et al: The efficacy of intravenous milrinone in left ventricular restoration. Ann Thorac Cardiovasc Surg 2009; 15: 233–8.