

# Association between Preoperative Cardiac Left Ventricular Dysfunction and Perioperative Intraaortic Balloon Pump in Patients Undergoing Off-Pump Coronary Artery Bypass Surgery

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## ABSTRACT

**Background:** Prophylactic use of intraaortic balloon pump (IABP) reduces hospital mortality in patients with left ventricular (LV) systolic dysfunction undergoing coronary artery bypass surgery (CABG); however, its association in patients with LV diastolic dysfunction is unclear. This retrospective study investigated the association between preoperative LV function and perioperative use of IABP in patients undergoing off-pump CABG (OPCAB) at a university hospital.

**Methods:** 100 consecutive patients who underwent OPCAB between January 1, 2011 and August 31, 2014 were studied. Preoperative LV function was categorized into four groups based on LV systolic and diastolic function determined with preoperative transthoracic echocardiography. The use of IABP was reviewed from medical records. The Mann-Whitney test, Pearson chi-square test, or Fisher exact test were used.

**Results:** Patients were categorized into the following groups: normal LV function (n = 43), isolated LV systolic dysfunction (n = 13), isolated LV diastolic dysfunction (n = 21), and combined LV systolic and diastolic dysfunction (n = 14). Intraoperative IABP use was significantly more frequent in patients with isolated LV systolic dysfunction, isolated LV diastolic dysfunction, and combined LV systolic and diastolic dysfunction than in those with normal LV function ( $P < .05$ ). Furthermore, IABP was used more frequently in patients who developed combined LV systolic and diastolic dysfunction postoperatively ( $P < .05$ ).

**Conclusion:** Not only the presence of preoperative systolic dysfunction but also LV diastolic dysfunction in the presence of normal LV systolic function were associated with increased use of IABP during and after OPCAB.

## INTRODUCTION

The prophylactic use of intraaortic balloon pump (IABP) has been shown to reduce in-hospital mortality in patients

with left ventricular (LV) systolic dysfunction undergoing coronary artery bypass surgery (CABG) by meta-analysis of randomized controlled trials [Miceli 2009; Pompeu 2012].

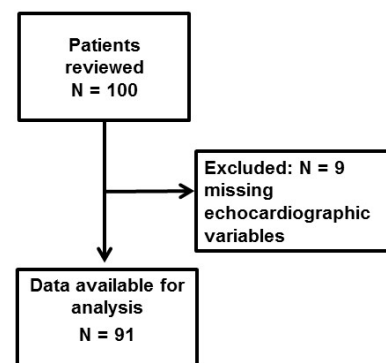
LV diastolic dysfunction was recently reported as an independent predictor of intensive care unit (ICU) stays as well as 30-day and 1-year major adverse cardiac events in patients with preserved LV systolic function undergoing elective off-pump coronary artery bypass (OPCAB), emphasizing the importance of evaluation of both systolic and diastolic LV function in these patients [Groban 2010; Lee 2012].

The purpose of this study was to investigate the association of preoperative cardiac function including LV diastolic function with perioperative IABP use in patients undergoing OPCAB.

## MATERIALS AND METHODS

This retrospective study included 100 consecutive patients who underwent primary OPCAB performed by a single surgeon at University Hospital between January 1, 2011 and August 31, 2014. This study was approved by the institutional ethics committee/review board (IRB No.14-7-11).

Clinical data for all patients including demographic and laboratory data, medical history, medication use, perioperative management, and postoperative outcomes were collected



Study inclusion/exclusion flow diagram. A total of 100 patients underwent off-pump coronary artery bypass surgery during the study period. After excluding patients without echocardiographic parameters (n = 9), data from the remaining 91 patients were included in the final analysis.

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Table 1. Preoperative Transthoracic Echocardiographic Variables

Echocardiographic variables	Left Ventricular Function			
	Normal function (n = 43)	Isolated systolic dysfunction (n = 13)	Isolated diastolic dysfunction (n = 21)	Combined systolic and diastolic dysfunction (n = 14)
LVEF, %	66.3 ± 6.7	39.6 ± 9.2*	67.6 ± 9.1†	34.6 ± 5.7*‡
LAD, mm	38.2 ± 5.1	39.3 ± 6.3	39.2 ± 5.6	42.6 ± 7.2*
IVST, mm	9.9 ± 1.5	9.0 ± 2.2	10.2 ± 1.7	9.8 ± 1.6
PWT, mm	10.4 ± 1.6	9.4 ± 1.0*	10.0 ± 1.5	10.1 ± 1.5
LVDs, mm	29.1 ± 4.9	42.9 ± 7.6*	28.7 ± 4.7†	44.7 ± 6.2*‡
LVDd, mm	45.9 ± 5.3	53.8 ± 7.4*	46.0 ± 4.2†	53.7 ± 5.6*‡
E/A ratio	0.75 ± 0.16	0.77 ± 0.19	0.75 ± 0.23	0.82 ± 0.31
DcT, ms	207.0 ± 65.1	225.2 ± 76.3	249.5 ± 61.1*	192.9 ± 65.4‡
E/e' ratio	8.7 ± 2.6	9.4 ± 2.7	16.7 ± 7.3*†	16.6 ± 5.1*†

Data are expressed as number of patients or mean ± standard deviation.

LVEF indicates left ventricular ejection fraction; LAD, left atrial diameter; IVST, interventricular septum thickness; PWT, posterior wall thickness; LVDs, left ventricular end systolic diameter; LVDd, left ventricular end diastolic diameter; E/A, ratio of peak early and late flow of mitral inflow; DcT, deceleration time; E/e', ratio of LV early diastolic filling velocity to the peak diastolic velocity of mitral septal annulus.

\*P < .05 compared with normal function; †P < .05 compared with isolated systolic dysfunction; ‡P < .05 compared with isolated diastolic dysfunction.

retrospectively from the anesthetic and medical records. Information collected included preoperative heart failure (HF), prior myocardial infarction (MI), renal dysfunction (serum creatinine > 2 mg/dL), hemodialysis (HD), and atrial fibrillation (AF).

Transthoracic echocardiography was performed by an experienced sonographer in all patients. Standard parasternal and apical two and four-chamber views were obtained. LV ejection fraction (LVEF) was calculated using the biplane Simpson's technique. Early transmitral inflow velocity (E), deceleration time, and late transmitral inflow velocity (A) were determined using pulsed-wave Doppler echocardiography in the apical four chamber view, and E/A ratio was acquired. Early diastolic mitral annular velocity (e') was determined by pulsed-wave tissue Doppler imaging at the septal side of mitral annulus, and E/e' ratio was acquired.

In this study, patients were categorized into four groups: normal LV function, isolated LV systolic dysfunction, isolated LV diastolic dysfunction, and combined LV systolic and diastolic dysfunction. LV systolic dysfunction was defined as LVEF < 50% [Dickstein 2008]. LV diastolic dysfunction was defined as E/e' > 15 or E/e' between 8 and 15 with brain natriuretic peptide (BNP) > 200 pg/mL and/or AF [Paulus 2007]. LVEF > 50% without accompanying diastolic dysfunction was defined as normal LV function. Isolated LV systolic dysfunction was defined as LV systolic dysfunction (LVEF < 50%) in the presence of normal LV diastolic function. Isolated LV diastolic dysfunction was defined as LV diastolic dysfunction in the presence of normal LV systolic function. Combined LV systolic and diastolic dysfunction was defined as systolic dysfunction with concomitant LV diastolic dysfunction.

General anesthesia was induced with propofol, fentanyl and/or continuous infusion of remifentanyl, and rocuronium or

vecuronium. Anesthesia was maintained with propofol or sevoflurane, fentanyl or continuous infusion of remifentanyl with an additional bolus infusion of fentanyl, and rocuronium or vecuronium. In addition to standard monitoring, additional monitoring included direct arterial pressure via a radial artery catheter, central venous pressure, pulmonary artery pressure, and mixed venous oxygen saturation. After anesthesia induction, all patients received continuous intravenous infusion of nitroglycerine, diltiazem, and a phosphodiesterase III inhibitor. Ephedrine, phenylephrine, dopamine, dobutamine, and/or norepinephrine were used if necessary. Packed red cells were transfused based on the discretion of the anesthesiologist. A cell salvage device was used in all patients. Heparin was administered at a dose of 100 IU/kg to achieve a target activated clotting time of 200-300 s after the dissection of internal mammary artery, radial artery, and/or saphenous vein grafts. Activated clotting time assessments were repeated every 60 min, and heparin was added as required. After completion of all anastomoses, protamine was administered at 1 mg/100 IU heparin and was supplemented as required to restore the activated clotting time to preoperative levels.

The adaptation of IABP use was not defined in detail in the medical and anesthetic records; however, in general, IABP was used intraoperatively in patients with refractory hemodynamic instability during anastomosis and postoperatively in patients with low cardiac output syndrome, at the discretion of the surgeon.

Patient characteristics, preoperative LV function, use of IABP, surgical and anesthetic data, length of ICU stay, intubation time, short-term adverse events, and mortality after OPCAB were extracted from the medical records.

Data were expressed as means ± SD. The Mann-Whitney test, Pearson chi-square test, or Fisher exact test were used

Table 2. Baseline Characteristics of Patients

	Left Ventricular Function			
	Normal function (n = 43)	Isolated systolic dysfunction (n = 13)	Isolated diastolic dysfunction (n = 21)	Combined systolic and diastolic dysfunction (n = 14)
Age, y	67.3 ± 9.2	66.2 ± 8.2	71.5 ± 7.3	68.2 ± 12.2
Female, %	14.0	7.7	52.4*†	7.1‡
BMI, kg/m <sup>2</sup>	24.7 ± 4.6	22.7 ± 2.5	23.4 ± 3.9	23.2 ± 4.1
EuroSCORE	2.0 ± 1.3	2.7 ± 1.6	2.7 ± 1.7	4.0 ± 1.8*†
NYHA (I/II/III/IV)	34/9/0/0	10/3/0/0	15/3/2/1	9/2/3/0
BNP, pg/mL	35.6 ± 37.9	93.4 ± 55.5*	96.2 ± 107.6*	636.2 ± 539.1*†‡
Heart failure	0	0	3*	2
Prior MI	9	11*	4†	5†
Hypertension	39	13	20	14
Diabetes mellitus	30	5	12	10
Hypercholesterolemia	37	9	20	7*‡
Atrial fibrillation	1	0	7*†	0‡
COPD	2	2	1	2
Renal dysfunction	4	1	3	6*
Hemodialysis	2	1	1	6*‡

Data are expressed as number of patients or mean ± standard deviation.

BMI indicates body mass index; EuroSCORE, European system for cardiac operative risk evaluation; NYHA, New York Heart Association functional classification; BNP, brain natriuretic peptide; new MI, myocardial infarction; COPD, chronic obstructive pulmonary disease.

\* $P < .05$  compared with normal function; † $P < .05$  compared with isolated systolic dysfunction; ‡ $P < .05$  compared with isolated diastolic dysfunction.

for statistical analyses. Two-sided  $P$  values of less than .05 were considered as statistically significant.

## RESULTS

A total of 100 patients underwent OPCAB during the study period. After excluding patients with incomplete echocardiographic variables ( $n = 9$ ), data from 91 patients were included in the final analysis (Figure).

There were 43, 13, 21, and 14 patients in the normal LV function, isolated LV systolic dysfunction, isolated LV diastolic dysfunction, and combined LV systolic and diastolic dysfunction groups, respectively (Table 1). LV end-systolic and end-diastolic diameters were greater in patients with isolated LV systolic dysfunction and in those with combined LV systolic and diastolic dysfunction than in patients with normal LV function and in those with isolated LV systolic dysfunction ( $P < .05$ ) (Table 1).

Patient baseline characteristics according to LV function are shown in Table 2. Patients with combined LV systolic and diastolic dysfunction had higher European system for cardiac operative risk evaluation values (EuroSCORE) than those with normal LV function and isolated LV diastolic dysfunction ( $P < .05$ ). The frequency of females was higher among patients with isolated LV diastolic dysfunction than those with normal LV function, isolated LV systolic dysfunction,

and combined LV systolic and diastolic dysfunction ( $P < .05$ ). Additionally, BNP levels were higher in patients with isolated LV systolic dysfunction, isolated LV diastolic dysfunction, and combined LV systolic and diastolic dysfunction than in those with normal LV function ( $P < .05$ ). Patients with isolated LV systolic dysfunction had higher incidence of prior MI compared with patients with normal LV function ( $P < 0.05$ ). Patients with isolated LV diastolic dysfunction had higher incidence of AF compared with patients with normal LV function and isolated LV systolic dysfunction ( $P < .05$ ). Patients with combined LV systolic and diastolic dysfunction had higher incidence of hemodialysis compared with patients with normal LV function, and isolated LV diastolic dysfunction ( $P < .05$ ).

Intraoperative use of IABP was more frequent in patients with isolated LV systolic dysfunction, isolated LV diastolic dysfunction, and combined LV systolic and diastolic dysfunction than patients with normal LV function ( $P < .05$ ) (Table 3).

Postoperative summary was shown in Table 4. Postoperative use of IABP was more frequent in patients with combined LV systolic and diastolic dysfunction than in those with normal LV function ( $P < .05$ ). The length of ICU stay was longer and higher in patients with combined LV systolic and diastolic dysfunction than in those with isolated LV systolic dysfunction ( $P < .05$ ). Moreover, newly developed bilateral plural effusion was more frequent in patients with combined

Table 3. Intraoperative Summary

	Left ventricular function			
	Normal function (n = 43)	Isolated systolic dysfunction (n = 13)	Isolated diastolic dysfunction (n = 21)	Combined systolic and diastolic dysfunction (n = 14)
Anesthesia time (min)	468.7 ± 59.5	481.9 ± 59.9	449.5 ± 67.5	466.1 ± 100.9
Operation time (min)	344.0 ± 53.6	362.1 ± 53.6	343.2 ± 64.4	348.2 ± 93.0
Grafts anastomosis (n)	4.4 ± 1.0	3.8 ± 0.7*	4.0 ± 1.1	4.2 ± 1.2
IABP (n)	1	3*	6*	6*

IABP indicates intraaortic balloon pump.

\* $P < .05$  compared with normal function.

LV systolic and diastolic dysfunction than in those with normal function and isolated LV diastolic dysfunction ( $P < .05$ ).

## DISCUSSION

Our results indicated that not only LV systolic dysfunction but LV diastolic dysfunction in the presence of normal LV systolic function was associated with perioperative use of IABP.

Intraoperative IABP is recommended for acute HF in OPCAB [Chassot 2004], especially during posterior vessel anastomoses in high risk patients with left main coronary artery stenosis, recent acute MI, unstable angina, or LVEF  $< 35\%$  [Kim 2001]. LV systolic dysfunction evaluated by EF is predicted to be a major risk factor for cardiac mortality in patients with heart disease. Long-term outcomes of OPCAB are closely related with cardiac function, and LV systolic function is suggested to be a major prognostic marker for adverse events associated with OPCAB [Arom 2001]. The relationship of IABP use with LV systolic dysfunction is also reported [Arom 2001; Yang 2016], but diastolic dysfunction is not well discussed and unclear because there are no established parameters of diastolic dysfunction.

The gold standard for diagnosis of LV diastolic dysfunction is measurement of elevated LV filling pressure by pressure monitoring; however, this approach cannot be routinely used. Therefore, several indices assessed by echocardiography, such as peak early-to-late trans-mitral flow velocity ratio (E/A), deceleration time (DcT), and systolic-to-diastolic pulmonary venous flow velocity ratio (S/D) with conventional Doppler are traditionally used. However, these parameters are greatly influenced by loading conditions, heart rate, and rhythm disturbances and provide limited information in several clinical situations [Leite-Moreina 2006; Matyal 2011; Nishimura 1997]. Recently introduced E/e' assessed by tissue Doppler was shown to be a good approximation of LV filling pressure even in patients with preserved or reduced LVEF, mitral regurgitation, or LV hypertrophy [Chang 2010; Iwabuchi 2012]. E/e' over 15 or between 8 and 15 and BNP  $> 200$  pg/mL are considered to be consistent with the presence of increased LV filling pressure [Paulus 2007]. In this way, indices of diastolic dysfunction have become stable and independent. Consequently, assessment of LV diastolic function

and the perioperative cardiac events have also become a focus of attention again. LV diastolic dysfunction has been shown to be associated with higher rates of morbidity and mortality during cardiac and non-cardiac surgeries [Canet 2011; Chang 2010; Fayad 2016; Flu 2010; Higashi 2013; Kaw 2016; Lee 2012; Matyal 2009; Salem 2006].

Our results indicated that not only isolated LV systolic dysfunction but isolated LV diastolic dysfunction with preserved LV systolic function were associated with perioperative use of IABP. The present study showed that even if the contractility is preserved, caution is necessary when the diastolic function is impaired. The reason why IABP usage increases in the case of diastolic dysfunction with preserved systolic function is not clear. However, in the case of diastolic dysfunction, the range of acceptance of LV diastolic volume is known as a narrow, and it is known that easily becomes hemodynamic instability, hypotension, pulmonary edema or HF. HF with preserved EF and concomitant diastolic dysfunction (HFpEF) accounts for approximately more than 50% of all patients with HF, and survival ratio associated with HFpEF is slightly higher than that with HF with reduced EF [Owan 2006]. In non-cardiac surgical patients, the presence of perioperative diastolic dysfunction is an independent predictor of postoperative congestive HF, including pulmonary edema and prolonged length of hospital stay [Canet 2011; Fayad 2016; Higashi 2013; Matyal 2009]. In the present study, all patients with preoperative heart failure had diastolic dysfunction and patients with isolated systolic dysfunction did not have heart failure.

Our results suggest that preoperative evaluation of not only the LV systolic but also the LV diastolic function is important in surgical patients. Our results also showed that combined LV systolic and diastolic dysfunction is higher risk than isolated LV systolic dysfunction. These results also showed that the combined use of systolic function by LVEF and diastolic function by E/e' was shown to be useful in predicting prognosis in patients with heart disease [Hirata 2009].

In the present study, our results contradict recent reports showing a relationship between diastolic dysfunction and CABG prognosis. Preoperative control of our study population, which was based on the New York Heart Association (NYHA) functional classification, was relatively good, although EuroSCORE in patients with combined LV systolic

Table 4. Postoperative Summary

	Left ventricular function			
	Normal function (n = 43)	Isolated systolic dysfunction (n = 13)	Isolated diastolic dysfunction (n = 21)	Combined systolic and diastolic dysfunction (n = 14)
Intubation time, h	16.1 ± 15.9	12.3 ± 17.9*	19.3 ± 24.4	61.6 ± 173.5
ICU stay, h	109.7 ± 85.2	88.5 ± 71.3	107.0 ± 73.2	157.9 ± 161.4†
Death, n	0	0	0	0
IABP, n	2	1	3	4*
Duration of inotropic support, h	67.1 ± 48.0	59.3 ± 40.1	73.0 ± 48.3	101.6 ± 90.0
New MI	0	0	1	0
Pleural effusion, n	3	1	0	5*‡
New AF, n	9	2	2	4
cerebral infarction, n	0	0	1	0
New AKI, n	13	2	2	4
RRT, n	0	0	0	1

Data are expressed as means ± standard deviation or number of patients.

ICU indicates intensive care unit; IABP; intraaortic balloon pump; New MI, newly developed myocardial infarction; plural effusion, newly developed bilateral plural effusion; new AF, newly developed atrial fibrillation; new AKI, acute kidney injury; RRT, newly developed renal replacement therapy.

\**P* < .05 compared with normal function; †*P* < .05 compared with isolated systolic dysfunction; ‡*P* < .05 compared with isolated diastolic dysfunction.

and diastolic dysfunction was higher than that in patients with normal LV function and isolated LV diastolic dysfunction. In the present study, intraoperative use of IABP was significantly more frequent among patients with LV diastolic dysfunction, which could contribute to improved midterm postoperative outcomes [Rubino 2009].

The present study has several limitations. First, this was a retrospective study and perioperative treatment strategies were not controlled. Second, CABG was performed by one surgeon, whereas preoperative echocardiographic examinations and anesthetic management were performed by several sonographers and anesthesiologists. Thus, inter-observer and inter-anesthesiologist variabilities in data cannot be excluded. Third, the exact criteria for timing and use of IABP could not be identified, as they were determined for each patient by one surgeon.

In conclusion, not only isolated systolic dysfunction but also the presence of preoperative LV diastolic dysfunction, isolated LV diastolic dysfunction, and combined LV systolic and diastolic dysfunction were associated with increased use of IABP during and after OPCAB.

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