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Left ventricular diastolic filling during coronary artery bypass surgery in patients with diabetes mellitus and/or hypertension

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Abstract: To evaluate left ventricular diastolic filling (DF) using transesophageal Doppler echocardiography in 40 patients with or without diabetes mellitus and/or hypertension, we measured DF after induction of anesthesia, before and after cardiopulmonary bypass (CPB), and at the end of coronary artery bypass surgery (CABS). In 13 patients with complete measurements, there was no significant change in DF but diastolic filling time became shorter and peak velocity during atrial contraction increased significantly following CPB. In the other patients, the assessment of DF could be performed accurately in CABS patients without diabetes and/or hypertension, but not in CABS patients with these disorders because of a high incidence of fusion of the E-A waves, which is an indicator of impaired DF. When heart rate (HR) was more than 75 beats·min^{-1} (RR interval of less than 800 ms), the incidence of fusion points was significantly higher in patients with diabetes and/or hypertension than without (13 of 29 *s* 1 of 9, $P < 0.05$). It is suggested that a slower HR (less than 75 beats·min^{-1}) is desirable in CABS patients with these disorders to avoid impairment of DF due to either prolonged systolic time or isovolumic relaxation time.

Key words: Coronary artery bypass surgery, Left ventricular diastolic filling, Transesophageal echocardiography, Hypertension, Diabetes mellitus

Introduction

Abnormal left ventricular (LV) diastolic function without LV systolic dysfunction has been observed in patients with coronary artery disease [1–3]. Although coronary artery bypass surgery (CABS) seems to improve LV systolic function immediately after revascularization [4], whether or not it has a similar effect on LV diastolic function could be expected after the surgery is still controversial [5–6]. Patients with diabetes or hypertension also have an abnormal LV diastolic function [7–10], but the effect of these diseases on surgical outcomes has not been clarified yet.

Since pulsed Doppler echocardiography has recently been validated for the assessment of LV diastolic filling [11–14], the present study was designed to evaluate the feasibility of measuring LV diastolic filling in CABS patients with or without diabetes and/or hypertension using transesophageal pulsed Doppler echocardiography.

Materials and methods

Study subjects

The protocol of this study was approved by the institutional research committee, and informed consent was obtained from each patient. We studied 40 patients scheduled for elective CABS in the Weiler Hospital of Albert Einstein College of Medicine: 24 men and 16 women with a mean age of 61.9 years (range from 41 to 84). Patients who had valvular disease or dysrhythmia were excluded from the study. Nineteen patients had a previous history of myocardial infarction, 14 had diabetes mellitus, and 29 patients had hypertension (12 patients had both diabetes mellitus and hypertension). Nineteen patients had ejection fractions over 50%, 10 had ejection fractions less than 50%, and the ejection fraction was not measured in the remaining 11. Of the 40 patients, 1 was classified as New York Heart Association (NYHA) class I, 11 as class II, 19 as class III, and 9 as class IV.

Anesthetic management

All patients were premedicated with morphine sulfate 0.1 mg·kg^{-1} and scopolamine 0.005 mg·kg^{-1} intramuscu-

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larly 90 min prior to arrival in the operating room. The radial artery was cannulated under local anesthesia for continuous monitoring of arterial blood pressure. A pulmonary artery catheter was inserted via the right internal jugular vein into the pulmonary artery before induction of anesthesia and cardiac output (CO) was measured by thermodilution method. Intraoperative monitoring included the following: electrocardiography (leads II and V_5), capnography, and pulse oximetry. Anesthesia was induced with a combination of either midazolam (2–3 mg) or diazepam (5–10 mg) and sufentanil (1–2 $\mu g \cdot kg^{-1}$). Muscle relaxation was obtained with vecuronium (0.1–0.15 $mg \cdot kg^{-1}$) or pancuronium (0.1–0.5 $mg \cdot kg^{-1}$). Anesthesia was then maintained with sufentanil (total 5–8 $\mu g \cdot kg^{-1}$) and, if necessary, supplemented with isoflurane at an end-tidal concentration of less than 1.0% in 100% oxygen.

Doppler echocardiography

After induction of anesthesia and tracheal intubation, an endoscopic phased array probe (3.75 MHz, ESB-37LR, Toshiba, Tokyo, Japan) was inserted into the esophagus and attached to a color Doppler imaging system (SSH-65A, Toshiba). The probe tip was positioned at 30–35 cm from the incisors to obtain the long-axis view of the heart and adjusted to direct the ultrasonic beam as parallel to the transmitral flow as possible under the guidance of color flow mapping. The sample volume (width 2 mm) was placed midway between the tip of the mitral leaflets and the mitral annulus. An appropriate sampling position was confirmed with the auditory and spectral outputs. The pulse repetition frequency was 4 or 6 KHz.

Pulsed Doppler measurements of transmitral flow were performed at the following four stages: stage 1—after induction of anesthesia; stage 2—pre-cardiopulmonary bypass (CPB) and before cannulation; stage 3—post-CPB and after decannulation; and stage 4—postoperatively following closure of the chest wall. Doppler data were recorded on a VHS video tape recorder (AG-6300, Panasonic, Osaka, Japan) with a simultaneous electrocardiographic recording.

The following five Doppler-derived indices were measured: (1) peak velocity during early ventricular filling (peak E velocity), (2) peak velocity during atrial contraction (peak A velocity), (3) the ratio of peak A velocity to peak E velocity (peak A/E ratio), (4) the ratio of area above the Doppler velocity envelope during atrial filling to the area during early filling (area A/E ratio), and (5) diastolic filling time (DFT). Doppler curves were traced along the modal velocity (the brightest portion of the velocity spectrum in the gray scales). The RR interval was measured on the electrocardiographic tracing of the Doppler records. All measurements were performed during the expiratory phase and all calculations were done on an off-line computer. Three measurements were performed in each parameter and the values were averaged. When the flow with atrial contraction began before the completion of the early rapid filling phase, the deceleration line of the velocity profile was extrapolated to the baseline between areas A and E. Figure 1 is a schematic illustration of the measurement.

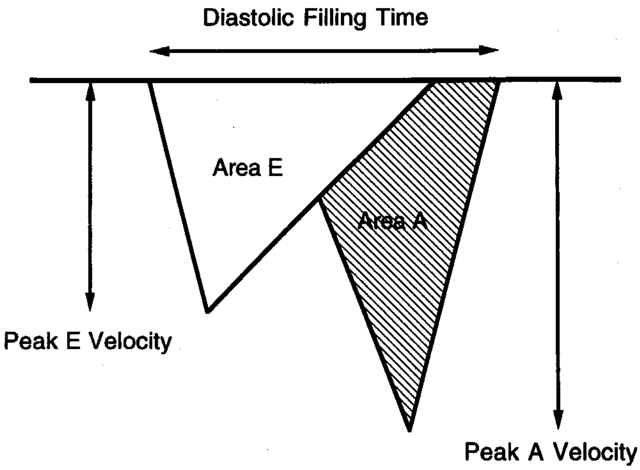

Fig. 1. Schematic illustration of Doppler flow velocity recording. Measurements were made of peak velocity during early filling (*peak E elocity*), peak velocity during atrial contraction (*peak A elocity*), diastolic filling time (*DFT*), and areas above the velocity envelope during early filling (*area E*) and during atrial filling (*area A*)

Hemodynamics

Hemodynamic variables pertinent to diastolic filling, heart rate (HR), and pulmonary capillary wedge pressure (PCWP) were measured. Stroke volume (SV) was calculated by dividing CO by HR. Those data were obtained at the four stages simultaneously with the Doppler measurements.

Statistical analysis

The repeated-measures analysis of variance (ANOVA) was used for the comparison of values between four stages and the Bonferroni *t*-test was used to isolate difference following ANOVA. The chi-square test was used to analyze the difference in incidence between groups and Fisher's exact test was used when the expected frequency was less than 5. Linear regression was used to examine the correlation of two variables. Unpaired *t*-test was used for intergroup comparison. All values are shown as means with standard deviation, and a probability value less than 0.05 was considered to be significant.

Results

There was a technical problem in 2 patients, who were excluded from the analysis, and a complete measurement of diastolic filling pattern in all four stages was possible in only 13 of the remaining 38 patients (34%). The measurement was not possible in 23 of 29 patients (79%) with a history of diabetes and/or hypertension and in 2 of 9 patients (22%) without those disorders, because of fusion of E-A waves or the presence of dysrhythmia. Those incidents occurred in the pre-CPB in 5 patients (20%), and in the post-CPB in 24 patients (96%) (in both pre- and post-CPB in 4 patients). The incidence of a fusion of E-A waves was significantly higher in patients with diabetes and/or hypertension than without ($P < 0.005$).

Doppler-derived diastolic indices and hemodynamic variables in 13 patients with a complete study

Comparison between four stages. There were no significant differences in peak E velocity, peak A/E ratio, and area A/E ratio between stages (Table 1). DFT was significantly shorter in stages 3 and 4 compared with both stages 1 and 2 ($P < 0.01$, $P < 0.01$). Peak A velocity was significantly higher at stage 3 compared with stage 1 ($P < 0.01$). However, it returned to the stage 1 level at stage 4.

HR increased significantly at stages 3 and 4 compared with both stages 1 and 2 ($P < 0.01$, $P < 0.01$). The RR interval was significantly shorter at stages 3 and 4 compared with both stages 1 and 2 ($P < 0.01$, $P < 0.01$). Because of an increase in HR, SV decreased significantly at stages 3 and 4 ($P < 0.01$, $P < 0.01$). There was no significant change in PCWP.

Influence of hemodynamics on Doppler-derived indices. DFT was significantly related to RR interval ($r = 0.8914$, $P < 0.001$). Peak A velocity was also significantly related to RR interval ($r = 0.5603$, $P < 0.001$). However, peak E velocity did not correlate with RR interval.

Correlation between DFT and RR interval in patients with and without diabetes and/or hypertension

As shown in Fig. 2, there was no significant difference in linear regression lines between patients with and without diabetes and/or hypertension.

Table 1. Comparison of Doppler-derived diastolic indices and pertinent hemodynamic variables between stages in 13 patients with a complete study

	Stage 1	Stage 2	Stage 3	Stage 4
Peak E velocity ($cm \cdot s^{-1}$)	59.6 ± 14.9	54.5 ± 16.4	59.4 ± 14.3	55.7 ± 14.4
Peak A velocity ($cm \cdot s^{-1}$)	54.2 ± 14.5	57.2 ± 13.2	64.5 ± 14.3**	59.3 ± 15.2
Peak A/E ratio	1.019 ± 0.521	1.153 ± 0.492	1.132 ± 0.343	1.107 ± 0.275
Area A/E ratio	0.434 ± 0.155	0.436 ± 0.158	0.460 ± 0.134	0.482 ± 0.120
Diastolic filling time (ms)	552.2 ± 148.8	461.1 ± 132.5*	329.8 ± 82.4**#	315.5 ± 79.3**#
RR interval (ms)	1030.8 ± 169.0	938.4 ± 153.7	739.3 ± 70.1**#	753.9 ± 111.5**#
Heart rate ($beats \cdot min^{-1}$)	59.7 ± 9.9	65.5 ± 10.2	81.8 ± 8.0**#	81.3 ± 12.8**#
Stroke volume (ml)	70.8 ± 14.7	61.9 ± 10.5	56.1 ± 6.4**	54.6 ± 12.2**
PCWP ($n = 12$) (mmHg)	12.9 ± 3.8	12.1 ± 4.1	12.6 ± 4.2	15.4 ± 4.4

Values are mean ± standard deviation.

Peak E velocity, peak velocity during early ventricular filling; Peak A velocity, peak velocity during atrial contraction; Peak A/E ratio, the ratio of peak A velocity to peak E velocity; Area A/E ratio, the ratio of area above Doppler velocity envelope during atrial filling to area during early filling; PCWP, pulmonary capillary wedge pressure.

* $P < 0.05$ *vs* stage 1, ** $P < 0.01$ *vs* stage 1, # $P < 0.01$ *vs* stage 2.

Table 2. Correlation between diastolic indices and hemodynamic variables in 13 patients with a complete study

	RR interval	Pulmonary capillary wedge pressure	Stroke volume
Peak E velocity	NS	NS	0.2764*
Peak A velocity	0.5603***	NS	NS
Peak A/E ratio	0.4778***	NS	0.3813**
Area A/E ratio	0.3932**	NS	NS
Diastolic filling time	0.8914***	NS	0.5613***

Values are correlation coefficients.

Peak E velocity, peak velocity during early ventricular filling; Peak A velocity, peak velocity during atrial contraction; Peak A/E ratio, the ratio of peak A velocity to peak E velocity; Area A/E ratio, the ratio of area above Doppler velocity envelope during atrial filling to area during early filling.

* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

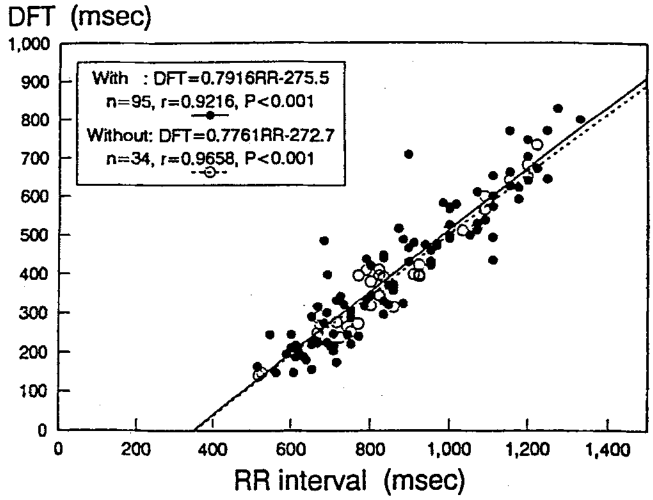

Fig. 2. Relationship between DFT and the RR interval in 29 patients with and 9 patients without diabetes and/or hypertension

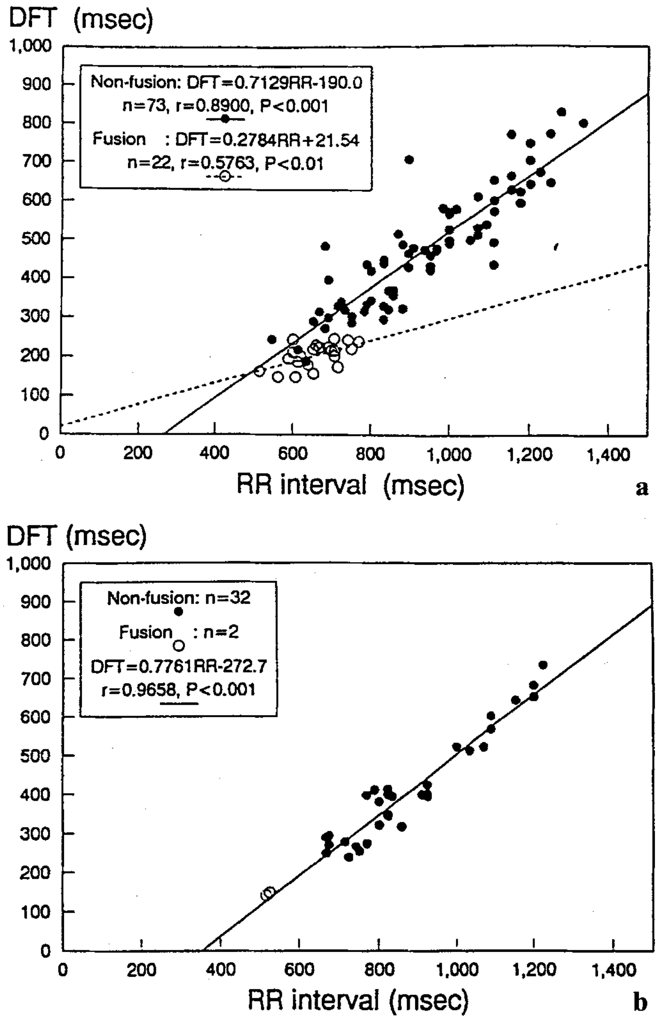

Fig. 3. Relationship between DFT and the RR interval **a** in 29 patients with diabetes and/or hypertension and **b** in 9 patients without diabetes and/or hypertension

Thirteen of 29 patients (45%) with diabetes and/or hypertension had a fusion of E-A waves at RR interval between 500 and 800 ms (Fig. 3a). However, only 1 of 9 patients without these disorders (11%) had a fusion at RR interval of 520 ms (Fig. 3b). At HR more than 75 beats·min^{-1} (RR interval of less than 800 ms), incidence of fusion points was significantly ($P < 0.05$) higher in patients with diabetes and/or hypertension than without.

Comparison of patients' profiles and hemodynamic variables between patients with and without diabetes and/or hypertension

There were no significant differences in age, sex, left ventricular end-diastolic pressure, history of myocardial infarction, and presence of regional wall motion abnormalities in the preoperative examination.

In patients with these disorders, HR significantly increased at stages 3 and 4 compared with both stages 1 and 2 ($P < 0.01$, $P < 0.01$), and SV decreased at stages 2, 3, and 4 compared with stage 1 ($P < 0.01$). PCWP also increased at stage 4 compared with stages 1 and 2 ($P < 0.05$, $P < 0.01$). In patients without these disorders, HR

Table 3. Comparison of hemodynamic variables between stages in patients with and without diabetes and/or hypertension

	Stage 1	Stage 2	Stage 3	Stage 4
With disease[a] (n = 28[b])				
Heart rate (beats·min^{-1})	59.8 ± 8.7	67.5 ± 18.0	87.9 ± 11.4**##	85.8 ± 11.6**##
Stroke volume (ml)	80.5 ± 24.4	62.4 ± 13.7**	56.7 ± 13.6**	54.0 ± 13.9**
PCWP (mmHg)	12.5 ± 4.1	11.7 ± 4.0	13.6 ± 3.5	14.9 ± 3.7*##
Without disease[a] (n = 9)				
Heart rate (beats·min^{-1})	58.8 ± 10.1	66.3 ± 8.3	84.8 ± 12.6**##	83.2 ± 14.6**##
Stroke volume (ml)	75.4 ± 15.5	65.0 ± 12.4	56.4 ± 7.2*	48.8 ± 11.9**#
PCWP (mmHg)	12.3 ± 3.3	12.0 ± 2.1	12.6 ± 5.1	14.2 ± 4.1

Values are mean ± standard deviation.
PCWP, pulmonary capillary wedge pressure.
* $P < 0.05$ *vs* stage 1, ** $P < 0.01$ *vs* stage 1, # $P < 0.05$ *vs* stage 2, ## $P < 0.01$ *vs* stage 2.
[a] Disease indicates the presence of diabetes and/or hypertension. [b] No data at stage 2 for one patient.

was significantly higher at stages 3 and 4 than at stages 1 and 2 ($P < 0.01$, $P < 0.01$), and SV was lower at stages 3 and 4 than at stages 1 and 2. Nevertheless, there were no significant differences in any variables in any stage between patients with and without diabetes and/or hypertension (Table 3).

Discussion

In terms of cardiac performance, diastolic function is equally as important as systolic function [15]. Abnormalities of diastolic function may precede impaired systolic function [16]. Recent studies of Doppler echocardiography have shown that abnormal LV relaxation occurs in patients with coronary artery disease and results in a decrease in peak velocity during early rapid filling and an increase in peak velocity during late filling associated with atrial contraction [17–21]. The results of the present study demonstrate that the assessment of LV diastolic filling can be performed accurately in CABS patients without diabetes and/or hypertension. However, it was difficult to assess CABS patients with these disorders because of the high incidence of fusion of E-A waves and other causes.

Successful CABS appears to result in normalization of early filling and decreased reliance on atrial contraction 1 week after surgery [19]. However, the immediate effects of CABS are still controversial. A study using the time constant for isovolumetric relaxation demonstrated immediate enhancement of LV relaxation after CABS [5]. In contrast, a deteriorated LV filling pattern after CABS was observed in an intraoperative Doppler study [6]. In addition to relaxation, hemodynamic conditions such as preload, afterload, contractility and HR can influence LV diastolic filling [22–26]. A combined hemodynamic and Doppler echocardiographic study suggested that the different mitral flow patterns are more related to hemodynamic status than to the type of disease such as coronary artery disease and to idiopathic congestive cardiomyopathy [27]. However, Diver et al. [28] showed that impaired diastolic function in patients with aortic stenosis persisted even when LV pressure was reduced to normal. Thus, an intrinsic abnormality of relaxation may be the primary factor which restores LV diastolic filling.

In the 13 patients in whom a complete series of measurements was performed, there were no significant changes observed in the diastolic filling pattern and Doppler-derived indices except for peak A velocity and DFT. In those patients, hemodynamics were maintained with either vasodilators and/or inotropic agents and no significant change was observed in any of the three variables measured before CPB. However, HR significantly increased and consequently SV significantly decreased following CPB. Both HR and the RR interval significantly influenced DFT. Thus, the assessment of LV diastolic filling can be performed accurately throughout surgery in CABS patients without diabetes mellitus and/or hypertension using pulsed Doppler echocardiography.

However, a fusion of E-A waves was frequently found in patients with these disorders following CPB. Since fused E-A waves could be an indicator of the impaired diastolic filling due to either prolonged systolic time or isovolumic relaxation time [29], it indicates that patients with diabetes and/or hypertension may have an abnormal DF [7–10]. Only one patient without these disorders had fusion of E-A waves at HR over 110 beats$\cdot$min^{-1} (RR interval of 520 msec). HR over 75 beats$\cdot$min^{-1} was significantly correlated with the fusion of E-A waves. In addition, this fusion mostly occurred after CPB, therefore, the degree of myocardial protection appears to be another important factor.

Hemodynamics were maintained by vasodilators and/or inotropic agents throughout surgery. There was no significant difference in any of the variables between patients with and without diabetes and/or hypertension. This indicated that routine monitoring of hemodynamic variables failed to detect impaired diastolic filling in patients with these disorders.

In conclusion, it is suggested that HR less than 75 beats$\cdot$min^{-1} is desirable during anesthesia and CABS for ischemic heart disease patients with these disorders.

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