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Thoracic epidural blockade preserves left ventricular early diastolic filling assessed by transesophageal echocardiography

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Abstract

Purpose. The objective of this study was to examine the effect of thoracic epidural anesthesia (TEA) on left ventricular systolic and diastolic function assessed by transesophageal echocardiography under general anesthesia.

Methods. Sixteen patients were allocated to control (n = 8) and TEA (n = 8) groups. We administered 1% mepivacaine (8.9 ± 1.2 ml) into the thoracic epidural space in the TEA group.

Results. The concomitant decline of the left vertricular systolic functional parameters, such as end-systolic diameter and fractional shortening, was observed, whereas preload, as measured by end-diastolic diameter, and afterload, as measured by end-systolic wall stress, were unchanged. No significant alteration was observed in early peak velocity or deceleration rate. The deceleration time was independent of heart rate and was unchanged.

Conclusion. High TEA reduces fractional shortening without any changes in preload and afterload, indicating impairment of systolic function, but early peak velocity, deceleration rate, and deceleration time, which are the indices of diastolic function, are not changed during high TEA combined with general anesthesia.

Key words: Thoracic epidural anesthesia, Left ventricular diastolic function, Transesophageal echocardiography, Transmitral flow

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Introduction

The heart has both systolic and diastolic functions, and impairment of either function produces heart failure. The decline of diastolic function is the earliest sign of myocardial ischemia, preceding development of pump failure [1]. The effects of anesthetics on left ventricular (LV) diastolic function have been little studied, as contrasted with the effects of anesthetics on LV systolic function [2–4]. Furthermore, few investigators have reported changes in LV diastolic function in patients who undergo thoracic epidural anesthesia (TEA).

Transmitral flow velocity measured by pulsed-wave Doppler techniques is an established index of LV diastolic function, which is easily and exactly measured by transesophageal echocardiography (TEE). The values obtained by this noninvasive technique show a close relationship to measures obtained by angiographic and radionuclide techniques [5].

To our knowledge, there are few reports describing the simultaneous evaluation of the effects of TEA on both LV systolic and diastolic functions. The objective of this study was to examine the effect of TEA on LV systolic and diastolic function assessed by TEE under general anesthesia.

Materials and methods

The research plan was approved by the ethics committee of our institution, and all patients gave their informed consent before participation in the study. Twenty patients scheduled for elective mastectomy or thoracotomy were selected for the study. Their ASA physical status was class I or II, and no patient had ischemic heart disease, valvular disease, congenital heart disease, or any other cardiac disease. The clinical characteristics of the patients are summarized in Table 1.

The patients were allocated randomly into a control group (CONT group; $n = 8$) and an epidural group (EPI group; $n = 8$). All patients were premedicated with hydroxyzine hydrochloride (25 mg) 40 min before induction of anesthesia. In the operating theater, electrodes for electrocardiographic (standard II and V_5 leads) monitoring were placed. A 20 G Teflon catheter was inserted into the radial artery under local anesthesia for continuous monitoring of arterial blood pressure. The arterial pulse wave was recorded on a polygraph (Life Scope 11, Nihon Kohden, Tokyo, Japan) throughout the study. The systolic and diastolic arterial blood pressures (SAP, DAP), mean arterial blood pressure (MAP), and heart rate (HR) were extracted from the record. An epidural catheter was inserted 2–3 cm cephalad at the T4 level into the epidural space. Two milliliters of 1% mepivacaine solution was given as a test dose.

Anesthesia was induced with fentanyl (2–4 $\mu g \cdot kg^{-1}$) and midazolam (0.15 $mg \cdot kg^{-1}$). Vecronium bromide (0.15 $mg \cdot kg^{-1}$) was given to facilitate endotracheal intubation. Anesthesia was maintained with 66% nitrous oxide, and additional fentanyl was given in bolus doses of 1–2 $\mu g \cdot kg^{-1}$. Respiration was controlled mechanically with a capnometer (Capnomac Ultima ULT-Svi-31-04, Datex, Helsinki, Finland) to maintain the end-tidal CO_2 at 35–40 mmHg. After induction of anesthesia, we placed a biplane transducer (Aloka 5 Mhz, Aloka, Tokyo, Japan) into the esophagus for TEE. The images were recorded on a videotape for later analysis. Echocardiographic measurements were performed by trained anesthesiologists. Baseline measurements (T_0) were made 15 min after induction of anesthesia. After baseline measurements, we injected 7–10 ml of 1% mepivacaine (EPI group) or saline (CONT group) into the epidural space through epidural catheters. The dose of mepivacaine for the EPI group, estimated from age and height, was considered sufficient to extend the minimal sensory block from T1 to T5 [6]. The second and third observations were made 10 min (T_1) and 20 min (T_2), respectively, after injection of local anesthetic or saline. The level of sensory blockade was identified after recovery from anesthesia. At the end of the operation, we injected the same dose of mepivacaine or saline that was used after induction, and the level of sensory blockade was tested by the pinprick method after emergence from anesthesia in the recovery room. Patients who showed sensory blockade of at least T1–5 were included in this study (Table 2). Other hemodynamic parameters were also recorded at these three observation times. All measurements were performed on the day of the operation and prior to surgery.

The TEE probe was adjusted to obtain a short axis at midpapillary muscle level. The LV end-systolic diameter (ESD, in centimeters) and end-diastolic diameter (EDD, in centimeters) were observed by M-mode.

Fractional shortening (FS) was calculated from the formula:

Table 1. Clinical characteristics of patients

Group	Sex	ASA	Age (yr)	Weight (kg)	Height (cm)	Epidural dose (ml)
Control	2M, 6F	6I, 2II	44 ± 16	57.9 ± 14.1	155.9 ± 13.9	9.3 ± 1.3
Epidural blockade	2M, 6F	5I, 3II	51 ± 8	54.2 ± 10.6	153.0 ± 7.4	8.9 ± 1.2

Age, weight, height and epidural dose are expressed as mean ± SD.

Table 2. Level of sensory blockade characteristics of patients receiving epidural blockade

Patient no.	Age (yr)	Sex	Weight (kg)	Height (cm)	Epidural dose (ml)
1	39	F	52.5	155	10
2	54	F	38.0	150	10
3	48	F	57.0	147	8
4	45	F	57.0	149	7
5	54	F	56.0	150	8
6	52	F	43.0	145	8
7	63	M	57.0	162	10
8	58	M	73.5	166	10

The level of sensory blockade was tested by the pinprick method.
All patients showed analgesia at least from T1 to T5.

$$FS\,(\%) = \frac{EDD - ESD}{EDD} \times 100$$

Wall stress is the force applied on the ventricular wall and was expressed using the Laplace equation [7]. To obtain the end-systolic wall stress (ESWS, $10^3 dyn \cdot cm^{-2}$), we used the following formula, in which the end-systolic wall thickness equivalent to the width of the LV anterior wall is abbreviated ESWT (millimeters):

$$ESWS\left(10^3 dyn \cdot cm^{-2}\right) = 0.334 \times \frac{SAP \times ESD}{ESWT \times \left(1 + \frac{ESWT}{ESD}\right)}$$

After the first procedure, the transducer was withdrawn 3–5 cm so that the mitral valve might be visualized on the long axis view of the LV. The sample volume of the pulsed-wave Doppler system was placed at the tip of the leaflets in the center of mitral inflow and adjusted to be as parallel as possible.

Figure 1 shows transmitral flow schematically. The following variables were derived from the mitral valve Doppler tracings as indices of LV diastolic function: the E wave, representing the initial flow of blood into the LV produced by the transmitral pressure gradient after aortic valve closure; and the A wave, the subsequent flow reflecting active contraction of the left atrium. Early peak velocity was defined as the height of the E wave, and atrial peak velocity was derived from the height of the A wave. The ratio of early to atrial peak velocity (E/A) was calculated. The decreasing rate of peak velocity in the E wave and the time from peak to zero level are termed the deceleration rate (DR) and deceleration time (DT), respectively. DT was calculated as the time from the peak of the E wave to the time when the descending E wave intercepts the zero line. These systolic and diastolic variables were determined at the end-expiratory phase by detachment of the ventilator circuit from the patients.

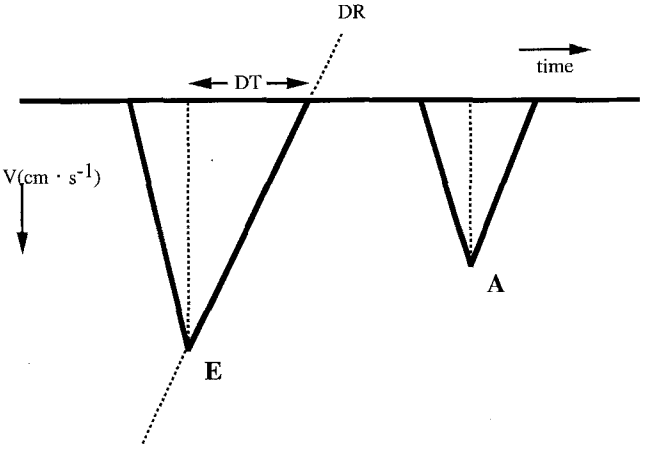

Fig. 1. Schematic pattern of normal transmitral flow velocity (V). E, Early peak velocity ($cm \cdot s^{-1}$); A, atrial peak velocity ($cm \cdot s^{-1}$); DT, deceleration time (ms); DR, deceleration rate ($cm \cdot s^{-2}$)

All hemodynamic and echocardiographic variables are presented as the mean ± SD. The unpaired t-test was used to test the differences between groups for quantitative data, and the chi-square test was used to test the differences for qualitative data. Analysis of variance (ANOVA) was used to examine the significance of the differences of repeated measurements within a group. When a significant difference was identified by ANOVA, Dunnet's procedure was used to examine the differences from baseline. The statistical analysis was performed on a computer using a program package (Super ANOVA version 1.11, Abacus Concept, Berkeley, CA, USA). A probability value less than 0.05 was considered to be statistically significant.

Results

In 1 of the 12 patients in the EPI group, an adequate echocardiographic image could not be obtained. As another 3 patients in the EPI group showed an excessive fall of systolic blood pressure below 80 mmHg, we were obliged to administer a bolus of ephedrine immediately after the T_2 measurement. Therefore we excluded the data from these 4 patients in the EPI group from our statistical analysis. Systolic parameters by TEE in 6 patients and ESWS in 7 patients could be obtained in the EPI group. As for the CONT group, systolic parameters could be obtained by TEE in 7 of 8 patients and by DT, DR, and ESWS in 5 of 8 patients.

The clinical characteristics of each patient group are presented in Table 1. No significant differences were found between the groups in sex, age, weight, height, or ASA status. The average doses of saline and mepivacaine were 9.3 ± 1.3 ml and 8.9 ± 1.2 ml, respectively.

Table 2 shows the age, sex, weight, height, epidural dose, and level of sensory blockade in each patient of the EPI group. All of the EPI group patients demonstrated analgesia at least from T1 to T5. The hemodynamic parameters and variables reflecting the LV systolic and diastolic functions at times T_0, T_1, and T_2 in each group are summarized in Table 3. There were no significant differences between the two groups in hemodynamic and echocardiographic data at baseline. No significant changes in any parameters were noted in the CONT group at any sample time. In contrast, significant decreases in SAP, DAP, MAP, and HR were observed in the EPI group at T_1 and T_2.

Of the LV systolic functional parameters, FS was de-

Table 3. Hemodynamic and echocardiographic variables

Variable	Group	*n*	Baseline, T_0	T_1	T_2
SAP(mmHg)	EPI	8	117.9 ± 19.3	94.4 ± 8.0**	91.4 ± 8.3**
	CONT	8	108.2 ± 13.0	103.5 ± 9.0	101.3 ± 8.5
MAP (mmHg)	EPI	8	83.4 ± 15.4	67.9 ± 8.9**	64.5 ± 7.4**
	CONT	8	82.4 ± 10.3	76.5 ± 12.1	75.2 ± 11.6
DAP (mmHg)	EPI	8	66.2 ± 15.2	54.6 ± 11.3**	51.1 ± 10.8**
	CONT	8	69.4 ± 11.0	63.0 ± 17.1	62.2 ± 16.4
HR (bpm)	EPI	8	66.6 ± 8.9	58.3 ± 7.1**	56.0 ± 6.3**
	CONT	8	59.0 ± 6.7	57.2 ± 7.7	56.0 ± 6.3
ESD (cm)	EPI	6	2.5 ± 0.4	3.1 ± 0.6**	3.1 ± 0.6**
	CONT	7	2.8 ± 0.9	2.8 ± 0.9	2.8 ± 0.9
EDD (cm)	EPI	6	4.3 ± 0.5	4.5 ± 0.9	4.4 ± 1.0
	CONT	7	4.5 ± 0.9	4.4 ± 1.2	4.4 ± 1.1
FS (%)	EPI	6	41.5 ± 5.9	31.6 ± 5.8**	29.7 ± 4.6**
	CONT	7	38.1 ± 9.8	39.7 ± 10.6	36.3 ± 10.3
Early peak velocity ($cm \cdot s^{-1}$)	EPI	8	55.1 ± 6.7	54.1 ± 7.0	54.4 ± 7.6
	CONT	8	56.6 ± 5.6	55.0 ± 6.3	55.6 ± 4.6
Atrial peak velocity ($cm \cdot s^{-1}$)	EPI	8	33.7 ± 6.9	29.0 ± 5.4**	26.7 ± 3.6**
	CONT	8	31.9 ± 2.5	31.3 ± 4.8	32.1 ± 4.8
E/A ratio	EPI	8	1.72 ± 0.51	1.93 ± 0.45**	2.09 ± 0.48**
	CONT	8	1.76 ± 0.28	1.80 ± 0.52	1.84 ± 0.32
DR ($cm \cdot s^{-2}$)	EPI	8	451.0 ± 75.2	423.7 ± 41.9	430.3 ± 50.5
	CONT	5	460.6 ± 103.7	463.0 ± 111.9	471.8 ± 100.9
DT (ms)	EPI	8	119.9 ± 26.7	130.4 ± 19.9	127.1 ± 17.0
	CONT	5	122.0 ± 23.9	118.0 ± 21.7	122.0 ± 21.7
ESWS ($10^3 dyn \cdot cm^{-2}$)	EPI	7	46.3 ± 12.2	42.4 ± 6.6	43.2 ± 7.3
	CONT	5	39.6 ± 18.5	36.4 ± 14.8	36.0 ± 11.2

SAP, Systolic arterial blood pressure; EPI, epidural blockade; CONT, control; MAP, mean arterial blood pressure; DAP, diastolic arterial blood pressure; HR, heart rate; ESD, end-systolic diameter; EDD, end-diastolic diameter; FS, fractional shortening; E/A, early to atrial peak; DR, deceleration rate; DT, deceleration time; ESWS, end-systolic wall stress.
Values are mean ± SD. ** $P < 0.01$ versus baseline (T_0).

creased significantly at T_1 and T_2 in the EPI group, whereas ESD increased significantly.

The diastolic functional parameters showed complex patterns of change. There was no significant alteration in early peak velocity, DR, or DT. The atrial peak velocity decreased, and the E/A ratio increased significantly at T_1 and T_2 in the EPI group.

None of the patients in either group showed electrocardiographic or regional wall motion abnormalities suggesting myocardial ischemia at any time.

Discussion

High TEA has been reported to impair LV systolic function with a blockade of cardiac sympathetic segments [8–12]. However, this observation remains controversial. In other investigations, TEA has been found to improve LV contractility [13] or to have no effect on it [14].

In our study of systolic function, the most prominent finding after administration of TEA was that ESD increased while EDD was unchanged, resulting in a decrease in FS. These findings are almost entirely in accordance with those reported by Wattwil et al. [8]. They used transthoracic echocardiography to examine the influence of TEA on sympathetic block and the systemic effect of local anesthetics in subjects who received 5ml of bupivacaine. In their investigation the LVEDD was not altered by TEA, whereas the LVESD increased significantly, as was also seen in the present study. However, we need to use caution in comparing the studies, because the sympathetic tone with and without general anesthesia may differ in our study and theirs, although in our study, the influence of high sympathetic tone under awareness may have been eliminated.

Goertz et al. [9] administered about 20ml of mepivacaine (0.25% and 0.5%) in the thoracic epidural space and found that TEA produced no significant

change in any of the systolic, diastolic, MAP, HR, LV endsystolic and end-diastolic areas, and ESWS, although the LV maximal elastance (E_{max}) was reduced significantly by TEA. E_{max} is known to be a most powerful indicator of LV contractility independently of loading conditions, derived from the pressure–volume relationship [15]. These two investigations and others [10–12] provide evidence that TEA impairs systolic function.

On the other hand, it is important to consider the systemic effects of absorbed local anesthetics used for TEA on systolic function. Bupivacaine is a well-known cardiac depressant. Moreover, Wattwil et al. [8] concluded that reduced contractility from high TEA did not seem to be caused entirely by sympathetic blockade, but partly by the systemic effect of bupivacaine. Although we did not determine the plasma concentration of mepivacaine in the study, it is likely that it might increase to some extent. This might partly contribute to the impaired systolic function.

In contrast to these studies, Kock et al. [13] investigated patients with coronary artery disease under high TEA using radionuclide angiography. They found that high TEA improved global and regional LV ejection fraction and presumed that this might be mainly caused by the reduction of myocardial oxygen demand. Blomberg et al. [14] found that TEA reduced pulmonary capillary wedge pressure (PCWP) without a significant change in stroke volume in patients with severe coronary artery disease. The discrepancies between our results and theirs were probably due to differences between patient groups with and without coronary artery disease.

Our study showed that TEA did not alter EDD or ESWS, finding no changes in preload or afterload due to TEA. These findings are in agreement with those of Wattwil et al. and others [8–11]. Many investigators have pointed out that TEA does not change preload. However, this seems to be inconsistent with our common understanding of epidural anesthesia: that it reduces the venous return by dilating peripheral vessels. One explanation for this inconsistency is that compensatory vasoconstriction occurring within the unblocked area preserves the venous return, as was indicated by Bonica [16]. Another explanation is that, as Ottesen et al. [11] described in their study, the unchanged left atrial pressure after TEA might imply that a combination of decreased venous return and impairment of myocardial contractility occurs if the preload is equivalent to the left atrial pressure.

Concerning afterload, to our knowledge only our study and that of Goertz et al. [9] determined the ESWS during high TEA. Goertz et al. found that contrary to their expectation, ESWS was not significantly affected by TEA, as noted in the present study. Accordingly, we speculate that the fall of systolic blood pressure in our study is due not to the reduced afterload but to decreased contractility. The experimental protocol of Goertz et al. differed from ours in that they injected local anesthetics in the epidural space before intubation, which enabled them to obtain more accurate levels of sensory blockade than we did. However, our experimental protocol may be superior to theirs, in that we could serially examine hemodynamic changes after TEA.

LV diastole is conventionally divided into four phases: isovolumic relaxation, rapid ventricular filling, diastasis, and atrial systole. As evaluated by pulsed-wave Doppler techniques, the former two phases correspond to E-velocity, DR, and DT, and the last phase to atrial peak velocity [17,18]. The most important findings of this study are the unchanged E-velocity, DR, and DT, the last of which is a measure of how rapidly the early diastolic filling stops and is much less affected by HR than the others [19,20], indicating no decline in isovolumic relaxation and rapid ventricular filling with a blockade of cardiac sympathetic segments.

As described in previous reports [19–21], the E/A ratio is influenced by a number of factors, including HR, age, preload, and afterload. In contrast, E-velocity, DT, and DR are independent of HR but dependent on loading conditions. In the present study the loading conditions remained stable. The atrial peak velocity has been reported to be parallel to HR. Harrison et al. [20] found that for each increase of 10 beats per minute in HR, the atrial peak velocity can be expected to increase by $8\,cm \cdot s^{-1}$. Our study showed a reduction in atrial peak velocity. It is difficult, however, to interpret whether this is due simply to the decrease in HR or to left atrial dysfunction caused directly by TEA. Further examination of patients with a similar protocol, with HR kept constant by pacing, might make it possible to elucidate the mechanism of the effect of TEA on left atrial function.

There are some limitations to our method. First, it might have been better to keep the HR constant by pacing. However, as stated above, the main parameter affected by HR is atrial peak velocity, not early peak velocity. Thus, it is possible to evaluate the effects of TEA on at least early diastolic filling with the method we used. Second, all our measurements were performed under general anesthesia. Nitrous oxide and midazolam are believed to have adverse myocardial effects [3,22], which might have influenced the results of our study. However, the hemodynamics did not change over time in the CON_T group, as contrasted with the EPI group. Finally, diastolic function is complex and still not completely understood. Although we used some indices of diastolic function, they are limited and do not adequately define the overall diastolic function.

We conclude that high TEA, combined with general anesthesia, reduces HR and LVFS without any alterations in preload and afterload, indicating impairment of systolic function, but that early peak velocity, DR, and DT, which are indices of diastolic function, are not changed during high TEA.

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