evaluate uterine activity. Maternal blood pressure and heart rate were recorded every 5 min for 15 min after establishing epidural analgesia, after the administration of an additional bolus dose, and once an hour on average.

Prior to epidural analgesia, parturients received an intravenous infusion of 500–1000 ml lactated Ringer's solution. When the Visual Analogue Scale (VAS) of pain (0–100 mm) was higher than 60 mm or the parturient requested analgesia, an epidural puncture was performed with a 17-gauge Tuohy needle by a loss of resistance method using saline at the left lateral position; a catheter was then placed 3–4 cm in the L2–3 or L3–4 epidural space. After confirming the absence of a return of blood or cerebrospinal fluid in the catheter, we injected 3 ml of 0.2% ropivacaine to rule out an intrathecal catheter location. Thereafter, we injected 4 ml of 0.2% ropivacaine twice in 10 min. Fifteen minutes after administering the initial dose, the dermatomal level of loss of coldness was examined using alcohol-soaked cotton.

All parturients were randomly divided into two groups by an envelope method. The PCEA group (n = 29) received anesthetics with a patient-controlled pump (CADD-Legacy PCA, model 6300; Smiths Medical Japan, Tokyo, Japan). The settings of the device were as follows: basal infusion rate at 6 ml·h^{-1}, bolus injection of 5 ml, maximum number of bolus injections at 5 times per hour, and lockout interval of 10 min. The CEI group (n = 29) received anesthetics with a syringe pump (1235N; ATOM, Tokyo, Japan) at a constant rate of 10 ml·h^{-1}. Epidural anesthetic solutions in the two groups were the same: 0.1% ropivacaine mixed with 0.0002% fentanyl. If parturients of the CEI group complained of pain and required pain relief, an additional 8 ml of 0.2% ropivacaine was administered through the epidural catheter.

We recorded the Visual Analogue Scale (VAS) of pain before epidural administration, after checking hypoesthesia levels to cold, and at the time of delivery. After delivery, the number of additional analgesic administrations was reviewed with a recorder in the PCA pump for the PCEA group. The additional analgesic doses and the total doses were then calculated for both groups. After the delivery and removal of the pump, midwives interviewed the parturients about their satisfaction of analgesia using the VAS.

Anesthetic complications such as nausea, hypotension, and itching were noted as a yes/no occurrence. Hypotension was defined as a more than 30% decrease in systolic blood pressure from the value before the analgesia. It was treated with intravenous fluid administration or ephedrine 5 mg i.v.

Demographic data, dose of anesthetic, outcome of labor, and side effects were analyzed with the Mann-Whitney test. Data were expressed as the mean ± SD or the median and range as appropriate. $P < 0.05$ was considered statistically significant.

Results

The demographic data were not significantly different between the two groups (Table 1). The VAS of pain before analgesia was 74 (range 55–94) in the PCEA group and 70 (50–100) in the CEI group. The dermatomal hypoesthesia level for cold on the right and left sides in the PCEA group were T11 (T6-L1) and T10 (T4-L1) respectively. Those in the CEI group were T10 (T4-L1) and T10 (T4-L1), respectively, at establish-

Table 1. Demographic data and delivery outcome

Parameter	PCEA group (n = 29)	CEI group (n = 29)
Age (years)	29 ± 5	30 ± 4
Height (cm)	160.1 ± 5.3	159.6 ± 5.1
Weight (kg)	62.7 ± 7.4	63.6 ± 8.7
Gestational week	39.7 ± 1.2	39.3 ± 1.3
Cervical dilation (cm)	4 (1–6)	3 (1–7)
Duration of labor		
First stage (h)	3.8 ± 2.5	3.3 ± 2.3
Second stage (h)	2.7 ± 2.0	1.9 ± 1.6
Mode of delivery		
Spontaneous	13 (45%)	16 (55%)
Instrumental (forceps/vacuum)	1/15 (3%/51%)	0/13 (0%/45%)
Apgar score		
1 min	8 (8–9)	8 (8–9)
5 min	9 (8–10)	9 (8–10)
Umbilical arterial pH	7.29 ± 0.05	7.30 ± 0.04

Results are the mean ± SD; median (range); or number (%)

Table 2. Hourly doses of local anesthetic and fentanyl

Parameter	PCEA group (n = 29)	CEI group (n = 29)
Local anesthetic		
Basal dose ($mg \cdot h^{-1}$)	6	10
Additional dose ($mg \cdot h^{-1}$)	3.3 ± 2.5	7.6 ± 7.6
Total dose ($mg \cdot h^{-1}$)*	9.3 ± 2.5	17.6 ± 7.6
Fentanyl		
Basal dose ($\mu g \cdot h^{-1}$)	12	20
Additional dose ($\mu g \cdot h^{-1}$)	6.6 ± 4.1	0
Total dose ($\mu g \cdot h^{-1}$)	18.6 ± 4.1	20.0 ± 0

Results are the mean ± SD
* $P < 0.05$

Table 3. Complications of anesthesia

Complication	PCEA group (n = 29)	CEI group (n = 29)
Nausea	1 (3.4%)	0
Hypotension	0	0
Pruritus	2 (6.9%)	2 (6.9%)

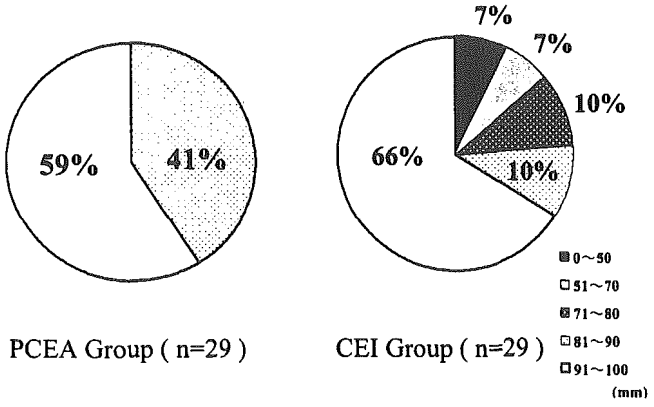

Fig. 1. Satisfaction of parturients using the Visual Analogue Scale (VAS). All parturients in the patient-controlled epidural anesthesia (PCEA) group showed satisfaction with the labor analgesia using a VAS above 81 mm, whereas 24% of parturients of the conventional continuous epidural infusion (CEI) group showed satisfaction below 70 mm

ment of analgesia. The duration of labor, incidence of instrumental delivery, Apgar score, and umbilical arterial pH were not significantly different between the two groups.

The basal dose of local anesthetic was higher in the CEI group by 4 mg for each hour than in the PCEA group. The total dose per hour in the CEI group was also significantly higher than in the PCEA group ($P < 0.05$) (Table 2). The additional local anesthetic dose for each hour was not significantly different between the two groups.

Satisfaction about labor analgesia using the VAS scale is shown in Fig. 1. In the PCEA group, the "satisfactory" VAS was above 81 mm in all patients. In the CEI group, 24% of parturients had a VAS of less than 80 mm, and 14% parturients had a VAS of less than 50 mm. The incidences of nausea, hypotension, and itching were not significantly different between two groups (Table 3).

Discussion

We found that PCEA provides better satisfaction with less local anesthetic than does CEI when we used ropivacaine with 0.0002% fentanyl. The ropivacaine dose in the PCEA group was less than that in the CEI group by 35%. This is consistent with the results of previous studies, which reported that use of PCEA can reduce the local anesthetic requirement by 42%–47% compared to CEI [7–10]. Some studies [11,12] with PCEA using ropivacaine also demonstrated that PCEA reduces drug consumption (17.6% and 24.9%, respectively) compared to CEI. However, PCEA was programmed with a demand-only regimen in those studies, so it is not appropriate to compare their results with ours.

One of the advantages of reducing the local anesthetic requirement during labor analgesia is that it decreases the degree of motor blockade [13] and the number of instrumental deliveries [14,15]. Not only the dose of the local anesthetic but the characteristics of the drug affect the degree of motor block. Both bupivacaine and ropivacaine have been used in obstetrical analgesia practice [1–10] because of the low placental transfer of the drugs and the high quality of the

analgesia. Toxicity to the cardiovascular and central nervous systems is greater with bupivacaine than with ropivacaine [16,17]. Furthermore, ropivacaine is associated with less motor blockade [18]. Therefore, we chose ropivacaine instead of bupivacaine to overcome these drawbacks.

Prior to the establishment of epidural analgesia, we did not use a test dose solution containing epinephrine. Recent studies [19,20] have shown that aspiration could detect almost all intravenous migration of a multiorifice catheter in laboring women. Norris et al. [20] recommended that practitioners consider abandoning the routine use of epinephrine in a test dose when providing epidural labor analgesia with a multiorifice catheter and using dilute local analgesic solutions.

In this study, the basal dose of the same study solution in the PCEA group was 6 ml·h^{-1}, whereas that in the CEI group was 10 ml·h^{-1}. Despite the higher basal dose in the CEI group, they tended to use a higher dose of additional ropivacaine than in the PCEA group. One of the reasons for this might be related to the possibility that addition of fentanyl to the rescue solution in the PCEA group may hasten the onset of analgesia [21].

As far as the dose of additional epidural anesthetic is concerned, Lee et al. [22] used 5–10 ml of 0.25% ropivacaine, and Collis et al. [23] used 10–15 ml of 0.2% ropivacaine with fentanyl 2 μg·ml^{-1} for breakthrough pain during labor. Therefore, we believe that 8 ml of 0.2% ropivacaine is appropriate and safe for labor. However, it is possible that the content and dose of additional local analgesic affects the results.

Several points should be considered as the reason for the superiority of PCEA to CEI. First, the time interval from pain sensation to drug administration was longer in the CEI group than in the PCEA group. When the parturients in the CEI group felt labor pain, they complained to the midwives, and they in turn informed a doctor. The doctor then injected the local anesthetics. This long process might cause parturient anxiety, resulting in augmentation of pain and additional local anesthetic requirement. Parturients in the PCEA group could obtain the drug injection upon their request. Curry et al. [10] reported that PCEA could reduce a dose of 0.125% bupivacaine by 43% compared to CEI. They also noted significantly higher satisfaction with PCEA than with CEI.

Second, PCEA by itself might bring high satisfaction of analgesia to the parturients [10]. This is because parturients in the PCEA group could inject the analgesic themselves and lessen their own pain. According to van der Vyver [24], it is difficult to evaluate a parturient's satisfaction because it includes many factors, such as the parturient's expectation for labor analgesia, the quality of communication with the medical team, and the outcome of labor. He investigated nine reports and found that VAS satisfaction was extremely high with both PCEA and CEI; there were no significant differences between two groups in all reports. Therefore, we must consider the quality of communication with parturients our their impression about the outcome of labor. In our study, VAS satisfaction of parturients after delivery tended to be higher in the PCEA group. Narrative comments on pain relief in both groups were as follows. In the PCEA group, some parturients mentioned that their labor pain was relieved before it became severe using a rescue agent by pushing the PCEA button. They experienced slight pain, and others said that they had had no labor pain at all after initiation of epidural analgesia. On the contrary, parturients who showed low VAS satisfaction in the CEI group mentioned that they had to wait to receive the effect of analgesics, and others said that they felt severe pain several times during labor because they hesitated to request a rescue bolus dose from the medical staff.

The outcome of labor, or the effect on the fetus, is another issue to be considered. In our study, the parameters analyzed were not significantly different between the two groups. These results were similar to those of previous investigations [7–12]. Finally, one may argue that the nonblinded setting in this study might influence the results of the consumption of analgesics and the satisfaction score.

Conclusion

PCEA is an effective means of providing optimal analgesia and better satisfaction during labor with less local anesthetic requirement compared with the conventional CEI.

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Noninvasive assessment of left ventricular pressure–area relationship using transesophageal echocardiography and tonometry during cardiac and abdominal aortic surgery

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Abstract
Purpose. The purpose of this study was to noninvasively evaluate intraoperative left ventricular (LV) performance by an online pressure–area relationship using transesophageal echocardiography (TEE) and tonometry.
Methods. In study 1, LV pressure with a micromanometer catheter, LV cross-sectional area with TEE, direct radial pressure, and tonometric arterial pressure were simultaneously recorded in 5 patients (10 measurements) undergoing cardiac surgery. End-systolic elastance (E′es) was determined from pressure–area loops during inferior vena caval (IVC) occlusion. In study 2, in 16 patients undergoing repair of abdominal aortic aneurysm, LV performance (E′es; effective arterial load, E′a, and LV end-diastolic area, LV-EDA) was examined by noninvasive assessment of pressure–area loops using TEE and tonometry at aortic cross-clamping and unclamping.
Results. E′es by tonometric arterial pressure closely correlated with E′es by LV pressure ($r = 0.92$) in study 1. E′es at aortic clamping were not significantly different from those at unclamping. The clamping increased LV-EDA and E′a by approximately 13% and 44%, and the unclamping significantly decreased by 9% and 22%, respectively.
Conclusion. Our results demonstrated that online tonometric arterial pressure and LV area measured by automated border detection (ABD) of TEE might be used to calculate E′es to estimate LV contractility and allow the estimation of LV performance during aortic clamping and unclamping.

Key words Left ventricular contractility · Noninvasive monitor · Preload · Afterload

Introduction

Analysis of the left ventricular (LV) pressure–volume relationship is useful for characterizing the determinants of ventricular performance, including preload, afterload, and contractility [1,2]. The clinical application of such relationship has been, however, limited due to technical difficulties in acquiring LV pressure and volume data throughout the cardiac cycle. Standard imaging techniques require frame-by-frame manual analysis, whereas the use of invasive conductance catheter and sonomicrometry techniques is not well suited for clinical settings [3–6]. Transesophageal echocardiography (TEE) has been widely used for intraoperative monitoring of LV function, and automated border detection (ABD) data have been demonstrated using this approach in humans [7–10]. Automated echocardiographic measures of the LV cavity area have been shown to closely correlate with changes in LV volume [7–14]. Based on the assumption that LV pressure is similar to that of the aorta and femoral artery during the ejection phase, Gorcsan et al. [9] constructed LV pressure–area loops using automated echocardiographic LV area and recording femoral arterial pressure, and demonstrated a good correlation between end-systolic pressure–area relationship using LV pressure and femoral arterial pressure.

Arterial pressure waveforms can be measured noninvasively and continuously by the use of arterial tonometry [15–17]. Arterial tonometry provides accurate and reliable real-time monitoring of blood pressure even during induced hypotension [16]. The purpose of this study was to evaluate LV performance intraoperatively by online pressure–area relationship using ABD of TEE and arterial tonometry in a manner similar to pressure–volume analysis. Using this method, we evaluated LV performance at aortic clamping and unclamping, which are known to cause rapid changes in hemodynamic variables.

Materials and methods

After obtaining institutional approval and informed consent, two studies were performed.

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Study 1: Correlation between LV pressure–area relationship and radial arterial or tonometric pressure–area relationship

Five patients (two men and three women), aged 70 ± 5 years (range, 63–76), undergoing valve replacement or coronary artery bypass were enrolled in the study. General anesthesia was induced with diazepam 0.2 mg·kg^{-1} and fentanyl 20 μg·kg^{-1}. Endotracheal intubation was facilitated by vecuronium. Anesthesia and muscle relaxation were maintained by fentanyl, diazepam, and vecuronium. Ventilation was controlled with a tidal volume of 10 ml·kg^{-1} at a rate that maintained a stable Pa_{CO_2} at 30–40 mmHg.

Echocardiography was performed using a 5.0-MHz transesophageal transducer (model 21364A; Hewlett-Packard, Andover, MA, USA) and ultrasound system (Sonos 2500, model 2406A; Hewlett-Packard) with ABD capabilities [11]. Transgastric midshort-axis view was used, with the midpapillary muscle level as the anatomic landmark, by positioning the transducer to uniform wall thickness. This plane was selected because of the difficulties encountered in obtaining true long-axis lengths from the transesophageal approach. Previous studies have identified the presence of a linear relationship between cross-sectional area and LV volume [7,9–14]. The threshold for discriminating blood from tissue backscatter characteristics was directly influenced by manual gain settings, and thus overall transmit, time gain compensation, and lateral gain controls were carefully adjusted by visual inspection as a compromise between cavity clutter and wall dropout. A region of interest was manually drawn immediately beyond the LV endocardial border to exclude the right ventricular cavity. The area of pixels within the selected region of interest identified as blood density was calculated from each frame and displayed as a waveform in real time.

Patients were instrumented with 20-G fluid-filled radial arterial catheters, connected to strain-gauge pressure transducers (Baxter, Irvine, CA, USA). A continuous noninvasive tonometric blood pressure monitoring instrument (Jentow; Colin Electronics, Komaki, Japan) was also attached to the extended wrist pressured against the contralateral radial artery. A cuff was wrapped around the brachial artery. The output of tonometric sensor was calibrated by the oscillometric blood pressure measured on the brachial artery every 2.5 min. This device records radial arterial pressure by compressing the radial artery between the radius bone and the pressure sensor. The compressing force was adjusted so as not to narrow the artery but establish a steady contact with the artery through the flat surface of the sensor, with the force level adjust to be equivalent to the intravascular pressure [16]. A median sternotomy was performed, and a micromanometer catheter (Micro-Tip pressure transducer, MPC-500; Miller, Houston, TX, USA) was advanced into the LV through the right upper pulmonary vein.

The analog data of the LV area from ABD and arterial pressure waveforms from the tonometry were captured at a sampling frequency of 200 Hz using an analog-to-digital converter (Mac Lab; Analog Digital Instrument, Castle Hill, Australia). LV pressure and area signals were plotted using customized software and graphics routines, and the pressure–area loops were displayed on a monitor. The pressure signal was plotted after a delay of approximately 30 ms with respect to the area signal to allow for the time required for the automated system to calculate the area from each frame. The duration of the delay was adjusted for each run by aligning the point immediately preceding isovolumic contraction on the pressure waveform with the first occurrence of maximal area.

To construct LV pressure–area loops, LV end-diastolic pressure waveforms, defined as the point just after isovolumic contraction, were advanced to manually align the LV end-diastolic pressure with LV end-diastolic area (EDA), defined as the first occurrence of the maximum area. To construct arterial pressure–area loops, arterial pressure waveforms were advanced to manually align the minimum arterial pressure with LV-EDA just before the beginning of decreased point from the maximum area for each run. End-diastole was selected as the point for alignment because the majority of arterial pressure tracings did not have a clearly defined dicrotic notch to indicate end-systole. Slight adjustments in timing were made by visual inspection of the pressure–area loops to most approximate LV ejection pressure with the systolic pressure–area trajectory bounded by the range of area values. These adjustments were made by adding or subtracting approximately 30-ms increments to the pressure signals. LV contractility was then estimated by the method of Sagawa [1,2] for calculating the end-systolic pressure–volume relationship, or end-systolic elastance, by applying these calculations to the pressure–area loops.

Accordingly, end-systole was defined as the occurrence of the maximal pressure–area point in each pressure–area loop, and the slope of these points from differently loaded beats determined E′es by an iterative linear regression method [13]. Pressure-area elastance values were designated E′es to differentiate the term from the Ees values of end-systolic elastance from the pressure-volume data. E′es was obtained during cardiac surgery, and before and after cardiopulmonary bypass (CPB), using inferior vena caval (IVC) occlusion maneuvers by ten recordings in five patients. Echographic LV area, LV pressure, and radial and tonometric pressure data were recorded at end-expiratory period.

Study 2: LV performance during aortic clamping and unclamping

Studies were performed in 20 consecutive patients (14 men and 6 women), aged 72 ± 6 years (range, 61–83) undergoing repair surgery for infrarenal abdominal aortic aneurysm. Four patients were excluded because of poor-quality transgastric echocardiographic images and poor-quality tonometric blood pressure waveforms. Therefore, the study group consisted of 16 patients: 11 men and 5 women. After securing an intravenous access, epidural block was established to the mid-thoracic level with 1% or 2% mepivacaine. General anesthesia was induced with thiamylal and fentanyl. Endotracheal intubation was facilitated by vecuronium. Anesthesia and muscle relaxation were maintained by nitrous oxide-oxygen, isoflurane, fentanyl and vecuronium. Ventilation was controlled with a tidal volume of $10\,ml \cdot kg^{-1}$ at a rate to maintain Pa_{CO_2} between 30 to 40 mmHg.

Echocardiographic and arterial pressure data were recorded and analyzed using the same methods described for study 1. End-diastolic area (EDA) and end-systolic areas (ESA) were also collected before and after aortic clamping and unclamping. The effective arterial load (E′a) was calculated as [end-systolic pressure·(EDA − ESA)$^{-1}$] [2], and the fractional area change (FAC) was calculated as [(EDA − ESA)·(EDA)$^{-1}$]. E′es was determined as the slope of end-systolic points in the pressure-area loops during aortic cross-clamping and unclamping.

Statistical analysis

Data were expressed as mean ± standard deviation (SD). To assess the degree to which tonometric arterial blood pressure could be used to estimate E′es with LV pressure, linear regression analysis by the method of least squares was performed because E′es derived from high-fidelity LV pressure was the gold standard to which E′es by the arterial pressure signal was compared. Bias of E′es from the three methods was evaluated using Bland-Altman method. Data obtained after aortic clamping and unclamping were analyzed in relation to the indices measured before clamping and unclamping by using a Wilcoxon signed-rank test. $P < 0.05$ was defined as significant.

Results

Study 1

Ten IVC occlusion maneuvers were performed in the five patients. Figure 1 shows an example of waveform data during IVC occlusion and corresponding simultaneous LV pressure–area loops and tonometric pressure–area loops.

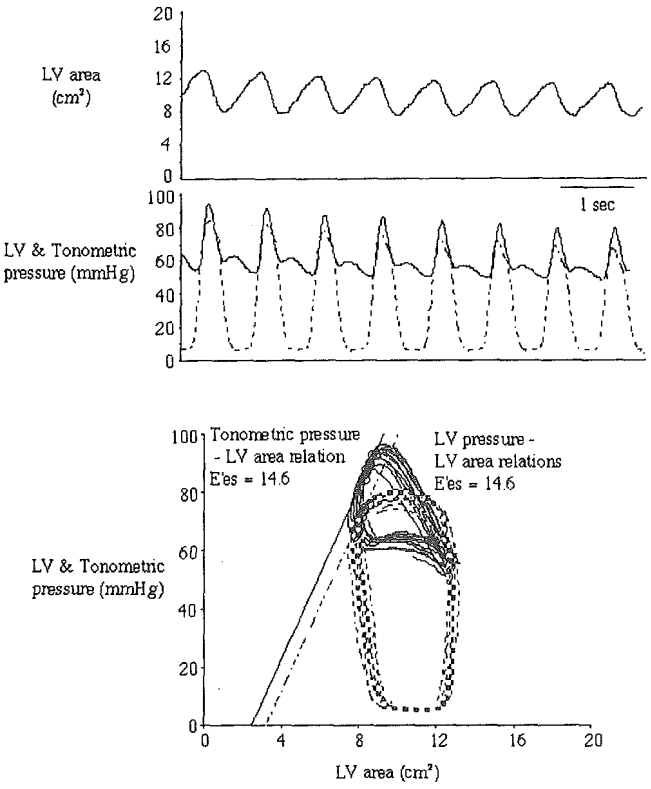

Fig. 1. An example of waveform data during inferior vena caval occlusion and corresponding simultaneous left ventricular (LV) pressure–area loops (*dotted lines*) and tonometric pressure–area loops (*solid lines*)

The mean fall in systolic blood pressure by IVC occlusion was 31 ± 11 mmHg for LV pressure, 35 ± 16 mmHg for radial pressure, and 36 ± 16 mmHg for tonometric pressure. The magnitude of the fall in systolic blood pressure was not significantly different among the three measurements. Estimates of E′es by tonometric pressure–area relationship closely correlated to the E′es estimates by LV pressure–area relationship (Fig. 2; $r = 0.92$, SE of the estimate = $4\,mmHg \cdot cm^{-2}$, $y = 0.86x + 1.26$). Estimates of E′es from radial arterial pressure also closely correlated with E′es from LV pressure ($r = 0.90$, SE of the estimate = $5\,mmHg \cdot cm^{-2}$, $y = 0.98x + 2.81$). Estimates of E′es from tonometric pressure also closely correlated with E′es from radial arterial pressure ($r = 0.84$, SE of the estimate = $6\,mmHg \cdot cm^{-2}$, $y = 0.73x + 3.43$). Analysis by the Bland–Altman method of the estimates of E′es from tonometoric pressure, E′es from LV pressure, and E′es from direct radial pressure are shown in Fig. 2. No systematic measurement errors were seen.

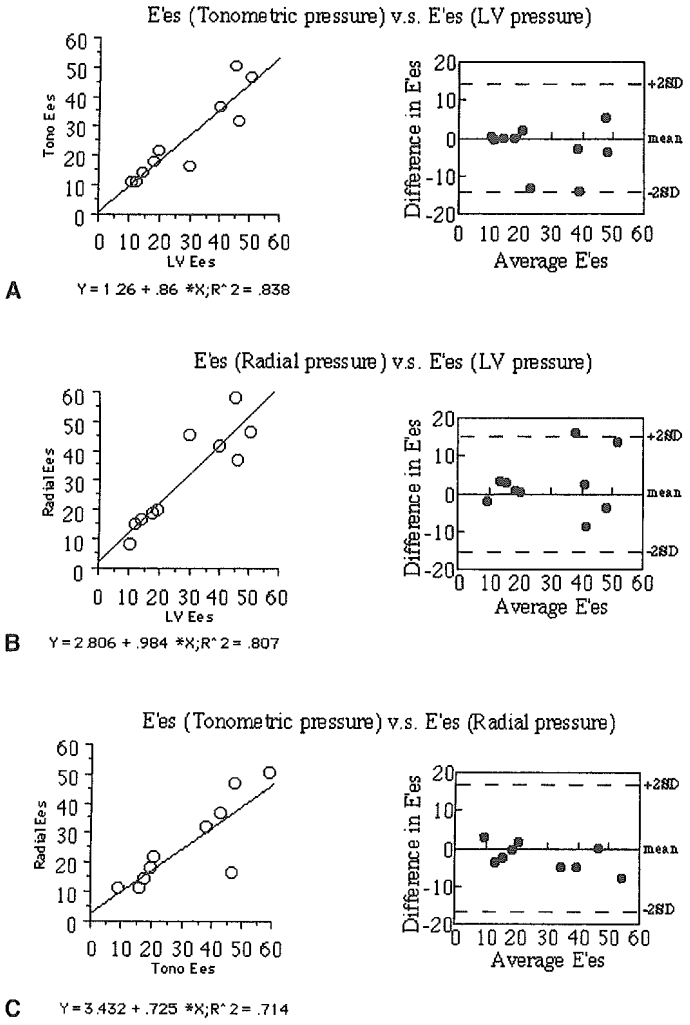

Fig. 2. Relationship between E'es (end-systolic elastance) values derived from LV pressure, radial pressure, tonometric pressures (*left*), and results of Bland–Altman bias analysis (*right*). **A** E'es from LV pressure versus E'es from tonometric pressure; **B** E'es from LV pressure versus E'es from radial pressure; **C** E'es from radial pressure versus E'es from tonometric pressure

Study 2

The surgical approach was transabdominal, and the average duration of aortic cross-clamping was 60 ± 15 min. Aortic cross-clamping significantly increased LV EDA by approximately 13%, and inversely, unclamping significantly decreased LV EDA by 9% (Table 1). E'a significantly increased by 44% by aortic clamping and significantly decreased 22% by unclamping. FAC was 56% before clamping. Aortic clamping significantly decreased FAC by 15%, whereas unclamping significantly increased FAC by 13% (Table 1).

Estimates of E'es from tonometric pressure closely correlated with E'es from radial arterial pressure (Fig. 3) during aortic clamping (r = 0.95, SE of the estimate = 2.4 mmHg·cm^{-2}, y = 0.98x + 1.03) and unclamping (r = 0.96, SE of the estimate = 2.4 mmHg·cm^{-2}, y = 0.87x + 1.73). There was no significant difference between E'es at clamping and at unclamping (Table 1).

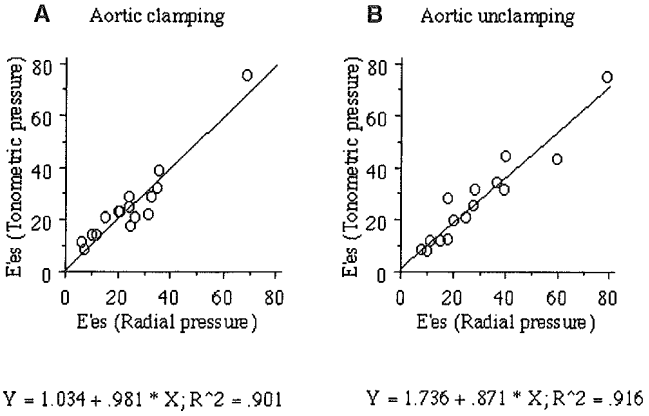

Fig. 3. Relationship between E'es values derived from radial pressure and tonometric pressures obtained at aortic cross-clamping (**A**) and unclamping (**B**)

Table 1. Changes in left ventricular end-diastolic area (EDA), fractional area change (FAC), effective arterial load (E'a), end-systolic elastance (E'es) from tonometric or direct radial pressure–area relations, and preload recruitable stroke force (PRSF) at aortic cross-clamping and unclamping

	Aortic clamping		Aortic unclamping	
	Before	After	Before	After
EDA (cm^2)	7.1 ± 2.6	8.0 ± 2.9*	7.7 ± 2.7	7.0 ± 2.6*
FAC (%)	55.7 ± 19.4	47.2 ± 17.6*	49.5 ± 19.0	56.0 ± 19.6*
E'a (mmHg·cm^{-2})	28.1 ± 13.1	40.5 ± 23.3*	36.8 ± 15.6	28.7 ± 13.1*
E'es (tonometric pressure) (mmHg·cm^{-2})	25.2 ± 15.6		25.9 ± 17.8	
E'es (direct radial pressure) (mmHg·cm^{-2})	24.6 ± 15.1		27.8 ± 19.6	

Data are mean ± SD
* $P < 0.05$ vs. before

Discussion

The LV end-systolic pressure-volume relationship or end-systolic elastance, Ees, is a measure for assessing cardiac contractility in animals and humans and is relatively independent of loading conditions [1,2,4,18]. Limitations in acquiring LV pressure as well as volume, however, have made it difficult to apply Ees as a routine intraoperative assessment of LV performance. Our study demonstrated that measures of LV cavity area by ABD of TEE and tonometric arterial pressure could be combined to construct online pressure–area loops, determining LV end-systolic pressure–area relations, E′es.

There are inevitable limitations in using two-dimensional data to represent three-dimensional volume and peripheral arterial pressure to represent LV pressure. LV area and volume cannot maintain a linear relationship over a wide range of values due to the determinants of each variable. However, previous investigators showed a linear relationship between changes in LV area and volume [7,9–14]. Gorcsan et al. [7,13] have shown the presence of a good relationship between LV area (using echocardiographic ABD) and LV volume (measured by electromagnetic flow probes). On the other hand, peripheral arterial pressure differ from LV pressure or aortic pressure due to a variety of factors, such as characteristics of arterial vascular system, viscous properties of blood, wave reflection, and quality of aortic valve. A small progressive rise in systolic pressure typically occurs from the ascending aorta to the peripheral arteries, and this pressure wave amplification is most pronounced in smaller, more distal arteries, such as the radial artery. Although differences in their absolute values existed also in our study, changes in radial arterial systolic pressure with IVC occlusions were similar to changes in LV pressure during an ejection phase. The E′es by tonometric pressure–area loops closely correlated with E′es by LV pressure–area loops (see Fig. 2). It has also been shown that LV end-systolic elastance can be estimated from pressure measurements in the femoral artery [9] and the radial artery [19]. Therefore, it is suggested that E′es using our noninvasive methods in clinical settings can substitute for LV end-systolic pressure–volume relationship.

Arterial pressure waveforms can be measured noninvasively and continuously by the use of arterial tonometry [15–17]. The latter method provides accurate and reliable real-time monitoring of blood pressure even during induced hypotension [16]. Sato et al. [17] performed a validation study of the tonometric blood pressure monitoring during Valsalva maneuver and the tilting test. They demonstrated that the beat-to-beat variability of tonometric pressure almost perfectly corresponded to that of intraarterial pressure in the physiologically significant frequency range. They concluded that the tonometric waveform was almost equal to the intraarterial waveform, except for the early systole, when a discrepancy between the two waveforms may exist. In this study, we were able to demonstrate that estimates of E′es from tonometric pressure closely correlated with E′es from LV pressure, and also with E′es by radial arterial pressure (see Fig. 2). Therefore, end-systolic pressure measured by tonometry can be used as a surrogate of LV pressure at end-systolic points during acute alterations in loading conditions to determine end-systolic pressure–area relations, E′es.

To estimate the LV end-systolic elastance, a rapid change in loading condition is necessary. In clinical settings, however, such interventions are not usually feasible. Accordingly, we utilized the aortic cross-clamping and unclamping technique, which is employed routinely during abdominal aortic surgery, to construct E′es. Several investigators have reported the hemodynamic changes in response to abdominal aortic clamping and unclamping [20–27]. To our knowledge, however, there are no studies that have used the aortic clamping and unclamping for intraoperative measurement of LV end-systolic elastance. Our results showed that aortic clamping and unclamping caused a rapid change in afterload thus allowing the determination of E′es. The data also showed that E′es did not differ between aortic clamping and unclamping. On the other hand, FAC, which is a two-dimensional substitute of ejection fraction (EF), was decreased by approximately 17% during clamping relative to that before clamping as well as after unclamping. The FAC can be influenced by loading conditions other than the contractile state. Thus, the decreases in FAC and EF during aortic clamping may be largely due to an increase in afterload rather than a decrease in LV contractility because of the lack of change in E′es.

In addition to LV contractility, changes in preload and afterload could be estimated during aortic clamping and unclamping by our methods. LV-EDA increased by about 20% at aortic clamping and recovered at aortic unclamping, indicating a significant increase in preload during aortic cross-clamping. This finding is consistent with other studies [20,28]. Previous studies have reported that aortic clamping is not associated with significant increases in pulmonary capillary wedge pressure [24] or central venous pressure [21], although this maneuver increased LV end-diastolic volume measured by radionuclide angiocardiograms by about 30% [20,28]. A decrease in LV diastolic compliance might render the pulmonary capillary wedge pressure a poor index of LV preload, and thus LV-EDA measured by TEE is a valuable adjunct in guiding preload evaluation in patients undergoing repair of abdominal aortic aneurysm [28]. Regarding changes in LV afterload, we obtained effec-

tive arterial load (E'a) as an alternative to afterload and found E'a to be increased by about 50% at aortic clamping and recovered after unclamping (see Table 1). These changes in afterload are in agreement with those shown in previous studies in which aortic cross-clamping increased systemic vascular resistance by about 25%–35% [21–25] or increased LV end-systolic wall stress measured echocardiographically by about 26% [20].

In conclusion, we demonstrated, in the present study, the feasibility of using tonometric pressure to simulate LV ejection pressure to determine LV end-systolic pressure–area relationship. These measurements were validated by the combined recording of ABD of TEE to simulate LV volume change. This noninvasive measurement of LV performance enables us to estimate LV performance during aortic cross-clamping and unclamping.

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Obstetrical and Pediatric Anesthesia

Labour analgesia guided by echocardiography in a parturient with primary dilated cardiomyopathy

[L'analgésie guidée par échocardiographie pendant le travail chez une parturiente atteinte d'insuffisance cardiaque primitive]

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Purpose: To evaluate the effects of intrathecal analgesics on cardiac function during labour analgesia using echocardiography in a parturient with idiopathic dilated cardiomyopathy (DCM).

Clinical features: Induction of labour was planned in a 35-yr-old primiparous woman suffering from DCM. In order to stabilize hemodynamics in this patient, we induced continuous spinal analgesia with an infusion of fentanyl and epinephrine. Although her analgesia was well maintained for three hours during the first stage of labour, the patient complained of pain towards the second stage of labour. At this point, we administered bupivacaine intrathecally to alleviate her pain. Transthoracic echocardiography showed that the left ventricular end-diastolic and systolic dimensions, as well as the ejection fraction were not impaired by use of these analgesic medications.

Conclusion: Measurement of left ventricular dimensions by echocardiography allowed us to monitor the patient's response to intrathecal analgesic medications. In this patient with DCM, analgesia with intrathecal fentanyl and bupivacaine was well tolerated.

Objectif : *Évaluer les effets d'analgésiques intrathécaux sur la fonction cardiaque pendant le travail en utilisant l'échocardiographie chez une patiente qui présente une insuffisance cardiaque primitive (ICP).*

Éléments cliniques : *L'induction du travail était planifiée chez une primipare de 35 ans souffrant d'ICP. Une rachianalgésie continue avec une perfusion de fentanyl et d'épinéphrine a été induite pour stabiliser l'hémodynamique. L'analgésie avait été bien maintenue pendant trois heures au cours de la première phase du travail, mais la patiente a eu des douleurs pendant la seconde phase. Nous avons donc donné de la bupivacaïne intrathécale. L'échocardiographie transthoracique a montré que les dimensions télédiastoliques et systoliques du ventricule gauche, de même que la fraction d'éjection, n'étaient pas atteintes par l'usage de ces analgésiques.*

Conclusion : *La mesure des dimensions du ventricule gauche par échocardiographie a permis de vérifier la réaction à l'analgésique intrathécal. L'administration intrathécale de fentanyl et de bupivacaïne a été bien tolérée chez cette patiente atteinte d'ICP.*

REGIONAL analgesia for labour is not contraindicated in a patient with idiopathic dilated cardiomyopathy (DCM) when the patient's coagulation is normalized. Although there may be a detrimental effect on the cardiac function following epidural or intrathecal administration of local anesthetics as a result of sympathetic blockade, previous reports have demonstrated successful management of parturients with DCM by the use of regional analgesia during their labour.[1,2] Discrepancies amongst these reports may be due to different cardiovascular responses to different analgesic medications. In order to elucidate the cause, it may be beneficial to evaluate the effects of neuraxial anesthetic agents on cardiac function during labour analgesia. We report on the successful management of a parturient with DCM, who received continuous spinal analgesia (CSA) with fentanyl during the first stage of labour, as well as a bolus injection of intrathecal bupivacaine as the cervix became fully dilated. Of greater importance, this report shows the usefulness of

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measuring left ventricular dimensions by echocardiography, which allowed us to monitor in a detailed manner the patient's response to analgesic medications in the setting of DCM.

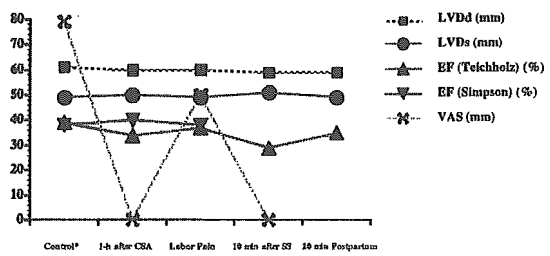
Case report

A 35-yr-old primiparous woman, who was 175 cm in height and weighed 73 kg was transferred to our institution at six weeks gestational age. She had a history of primary DCM diagnosed at 22 yr of age following episodes of syncope. Termination of her pregnancy was offered by an attending obstetrician, but was declined by the patient. Her mother was diagnosed with DCM, and her brother had died soon after his birth with a cardiac event. However, the patient remained asymptomatic as long as she limited her physical exercise prior to pregnancy with a regimen of metoprolol 120 mg *po* daily. Her functional physical status at the time of presentation was consistent with the New York Heart Association Class II. Her electrocardiogram (ECG) at eight weeks gestational age showed normal sinus rhythm with an abnormal Q wave in lead I and the first degree atrioventricular block. A Holter ECG showed 3% premature ventricular complexes. Echocardiographic evaluation demonstrated grade II mitral valve regurgitation with dilated left ventricle (LV). LV measurements demonstrated that the LV end-diastolic dimension was 60 mm (normal 40–55 mm) and the end-systolic dimension of the LV was 49 mm (normal 30–45 mm) without increased LV wall thickness. The ejection fraction was 32%.

The echocardiac evaluations of the patient at 20, 24, 28 and 32 weeks gestational age demonstrated no significant changes when compared to the initial findings at eight weeks gestational age. However, she felt slight dyspnea when she walked, beginning at 27 weeks gestational age.

At 38 weeks gestational age, the patient went into early labour with cervical dilation of 4 cm and uterine contractions every ten minutes, at which time the obstetrician decided to start an oxytocin augmentation. For maternal surveillance, ECG and pulse oximetry, as well as continuous arterial pressure with a radial arterial catheter and central venous pressure (CVP) were monitored from the right internal jugular vein. In addition, repeated transthoracic echocardiographic evaluations (SONOS 5500 ultrasonograph, Philips Co., Bothell, WA, USA) were performed during and after labour. Fetal monitoring included conventional cardiotocography. For *iv* fluids the patient received Ringer's Lactate at 200 mL·hr^{-1}.

A continuous spinal catheter (22 gauge Spinocath, B. Braun, Melsungen, Germany) was placed at the



BP (mmHg)	116/68	96/57	112/65	106/53	86/56
HR (bpm)	86	96	91	99	112
CVP (mmHg)	5	3	3	4	3

FIGURE Hemodynamic parameters and visual analogue scores (VAS) during and after labour
*One hour before initiation of labour analgesia. CSA = continuous spinal analgesia; SS = spinal shot; BP = blood pressure; HR = heart rate; CVP = central venous pressure; LVDd = left ventricular end-diastolic dimension; LVDs = left ventricular end-systolic dimension; EF = ejection fraction with Teichholz and/or Simpson method.

L3–4 intervertebral level into intrathecal space 3 cm beyond the spinal tap position, using an over-the-needle (27 gauge) technique. Since the patient complained of painful labour with a visual analogue score (VAS) of 79 mm at this time, labour analgesia was initiated with intrathecal fentanyl 25 μg plus epinephrine 40 μg (diluted with 5% dextrose, total 1.5 mL) through the intrathecal catheter, followed by an hourly infusion of fentanyl 25 μg plus epinephrine 40 μg (diluted with normal saline at an infusion rate of 5.0 mL·hr^{-1}). This resulted in adequate pain relief (VAS was 0 mm) without a hemodynamic change (Figure).

Three hours after the initiation of CSA, she requested additional pain relief and her VAS had increased to 50 mm. At this time, hemodynamic data including arterial blood pressure, heart rate, CVP, LV dimensions and ejection fraction were unchanged (Figure). The *iv* rate was increased to 400 mL·hr^{-1}, then 1 mg of hyperbaric bupivacaine diluted in normal saline was intrathecally administered every 30 min for three doses. However, this did not adequately relieve the patient's pain, so we suspected her catheter might have migrated or fallen out. When we checked the depth of the catheter, it was withdrawn 2 cm from the initial positioning, and cerebrospinal fluid was not aspirated through the catheter. Since her cervix was dilated to 7–8 cm, we decided to perform a combined spinal-epidural. Hyperbaric bupivacaine 2.5 mg and fentanyl 25 μg were administered by a 27-gauge

Whitacre needle through the 17-gauge epidural needle (Adjustable Durasafe CSE needle system, Becton-Dickinson, Franklin Lake, NJ, USA). The epidural catheter was then successfully placed. This resulted in satisfactory analgesia with VAS of 0 mm with a minimal hemodynamic change (Figure). The cephalad level of sensory blockade to cold was bilaterally T6 ten minutes after drug administration.

Eighty minutes later, she delivered a neonate with assistance of forceps, weighing 2316 g with Apgar scores of 8 and 9 at one and five minutes, respectively. We did not need to use the epidural catheter. The intrapartum and postpartum course of the mother was uneventful without side effects of respiratory depression or nausea/vomiting, and only mild pruritus. Her cardiac status remained stable throughout.

On postpartum day one, the patient noted a very mild headache when in the upright position, which did not require any treatment.

Discussion

DCM is characterized by cardiac enlargement and impaired contractility. The incidence of the disease which has a familial component is reported to be one case per 10,000 to 20,000 population. Women with DCM have traditionally been advised not to continue their pregnancy, because increases in intravascular volume and cardiac output as pregnancy progresses are often not well tolerated. However, a retrospective cohort study suggested that women with stable DCM might not experience such a decline in cardiac status during pregnancy.[3]

For labour and delivery, effective analgesia may blunt the hemodynamic effects of uterine contractions and the associated pain response, if a parturient tolerates hemodynamic changes during regional anesthesia. Use of local anesthetics for labour and delivery is not contraindicated in patients with DCM, because mild reduction of cardiac afterload due to the vasodilation could be beneficial for myocardial function. However, it is possible that a large dose of local anesthesia may cause impairment of myocardial function.

In order to minimize the change of hemodynamic status, CSA with infusion of fentanyl is one option for these patients. As expected, the LV end-diastolic and systolic dimensions as well as ejection fraction were not affected with continuous infusion of fentanyl and epinephrine in this patient. It has been reported that an intrathecal injection of fentanyl provides a rapid onset of analgesia without evidence of sympathetic blockade.[4,5] In this case, the patient's hemodynamics were stable during the bolus and continuous infusion of fentanyl. Epinephrine was added to augment the analgesic effect of intrathecal fentanyl, by stimulation of α_2 receptors.[6] This combination provided adequate analgesia in early labour, but as the patient's labour became more active, the spinal narcotic alone appeared to be insufficient towards the second stage of labour. Therefore, we changed the analgesic to intrathecal bupivacaine. It may be possible to define in advance, based upon serial echocardiography during pregnancy, whether a patient with DCM could tolerate regional labour analgesia including local anesthetic agents. Previous reports have demonstrated successful management of parturients with DCM using local anesthetic agents.[1,2] However, it is hard to evaluate the extent to which regional anesthesia with local anesthetic agents can influence cardiac function without a measure of LV dimension. Therefore, echocardiographic measurements can be helpful in these cases for the choice of anesthetic agents and optimizing fluid loading, as well as the prevention of developing pulmonary edema.

Some articles suggest usefulness of impedance cardiography or transesophageal echocardiography for monitoring of cardiac function during Cesarean section.[2,7] However, these monitors are relatively invasive or inconvenient during labour, compared with transcutaneous echocardiography. In this patient, the addition of spinal bupivacaine was well tolerated hemodynamically, proven by the use of an intrapartum echocardiography. Otherwise, dobutamine or other catecholamines may be required to augment cardiac contractility, in addition to fluid loading under the vigilance of CVP and echocardiographic monitoring.

In this report, the ejection fraction changed minimally after administration of bupivacaine. Some reports demonstrate that increased LV end-diastolic dimension (> 45 mm/body surface area) and decreased ejection fraction (< 30%) are related to a poor prognosis in DCM patients.[7,8] Furthermore, reduced thickness in the LV posterior wall is a sensitive marker of unfavourable clinical course.[9] It is likely that wall thickness is a compensatory mechanism for contractility failure. These parameters may be predictors of the tolerance for cardiovascular changes following regional anesthesia. Blood pressure and LV function measured by echocardiography in this patient were stable.

The major disadvantage of CSA is a risk of postdural puncture headache (PDPH). However, the over-the-needle-catheter used in this patient minimized the risk of PDPH due to less potential for leakage of CSF around the catheter because the outer diameter of the spinal needle is smaller than the diameter of the catheter. This newly designed catheter is

also superior to the microcatheter-through-needle technique of placing a spinal catheter in terms of ease of insertion, retraction of the needle, ease of threading of the catheter, spread of the anesthetic agent, and the incidence of obstruction or kinking of the catheter.[10]

In conclusion, continuous spinal infusion of fentanyl and epinephrine, using a catheter-over-needle system, provided satisfactory analgesia during the first stage of labour in the parturient with DCM. Furthermore, the addition of spinal bupivacaine was also well tolerated hemodynamically, as demonstrated by the use of intrapartum echocardiography in this patient.

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Notes

Determination of Oxycodone and Hydrocotarnine in Cancer Patient Serum by High-Performance Liquid Chromatography with Electrochemical Detection

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We developed an HPLC procedure using electrochemical detection for the quantitation of oxycodone and hydrocotarnine in cancer patients serum. An eluent of methanol:acetonitrile:5 mM pH 8 phosphate buffer (2:1:7) was used for the mobile phase. The calibration curve was linear in the range from 10 ng/mL to 100 ng/mL. The recovery of oxycodone and hydrocotarnine was 97.2% and 90.5%, respectively. The relative standard deviations within-runs and between-runs for the assay of oxycodone or hydrocotarnine were less than 4.8%. The method developed here was better than the method reported previously.

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Oxycodone is a thebaine derivative with ~0.5 - 0.7 times the analgesic potency of morphine in humans. Oxycodone has been in clinical use since 1917 in Europe and America. Twelve-hour controlled-release oxycodone has been in clinical use since 1997 in America, and since 1998 in Germany. Although the injection formulation of oxycodone and hydrocotarnine has been in clinical use since 1926 in Japan, it was rarely used for the treatment of cancer pain, because morphine was mostly used.

Hydrocotarnine is a non-drug opium alkaloid thought to enhance the analgesic effect of opioids. The detailed pharmacokinetics/pharmacodynamics is unclear; and how it should be used for patients with cancer has not been established.

Twelve-hour, controlled-release oxycodone has been in clinical use since 2003 in Japan, and the cases for which the injection formulation of oxycodone and hydrocotarnine are used are expected to increase.

We developed an HPLC procedure using electrochemical detection for the quantitation of oxycodone and hydrocotarnine in the serum of patients who used the injection formulation of oxycodone and hydrocotarnine appropriately.

Experimental

Reagents

Oxycodone (Lot. No. T2-00001) and hydrocotarnine (Lot. No. SBH002) were kindly supplied by Takeda Co. (Osaka, Japan). One percent Codeine (internal standard) was purchased from Takeda Co. (Osaka, Japan). The solvents to be used for the mobile phase were of chromatographic grade. All other chemicals were of special reagent grade.

Chromatography

Chromatograms were obtained using a PU-2080 pump (Nihon Bunko) equipped with an electrochemical detector, Coulochem II5200A and Model 5020 (MCMEDICAL). An XTerra® RP18 column (5 μm, 4.6 mm × 50 mm i.d., Waters, Japan) at an ambient temperature (40°C) was used to separate the oxycodone, hydrocotarnine, and codeine. The separation of the oxycodone, hydrocotarnine and codeine was achieved using an eluent of methanol:acetonitrile:5 mM pH 8 phosphate buffer (2:1:7). The voltage of the working electrode of the electrochemical detector was set at 800 mV.

Sample treatment

Blood samples (2.0 mL) were immediately centrifuged at 3000 rpm for 10 min. To 1.0-mL serum sample (standard or unknown) was added 100 μL codeine (internal standard, 25 ng/mL), 0.5 mL 4 M NaOH, and 4 mL butyl chloride. The samples were then mixed for 15 min, centrifuged for 10 min at 3000 rpm, and the butyl chloride (top layer) was transferred to a clean glass tube. The remaining aqueous layer was extracted by another 4 mL butyl chloride using the same procedure. The combined butyl chloride extract was then evaporated. The dried residue was reconstituted in 200 μL mobile phase, and 40 μL solution was injected into the HPLC.

Determination of oxycodone and hydrocotarnine in patient serum

A patient with cancer pain hospitalized at Kitasato University Hospital was tested after obtaining the informed written consent

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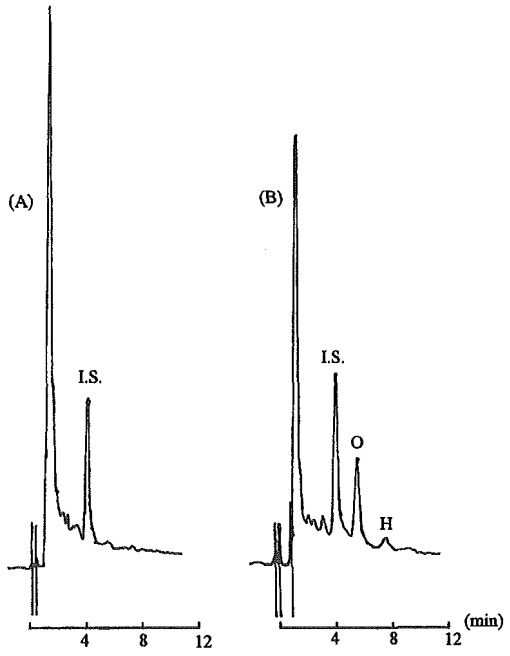

Fig. 1 Chromatograms of control serum (A) and patient serum (B). O, oxycodone; H, hydrocotarnine.

Table 1 Mobile phases examined

Mobile phase	NH_4HCO_3			CH_3OH	CH_3ON
	Mol	pH	Ratio	Ratio	Ratio
1	5 mM	8.0	80	0	20
2	10 mM	8.0	80	0	20
3	5 mM	10.0	80	0	20
4	5 mM	8.0	80	4	16
5	5 mM	8.0	80	20	0
6	5 mM	8.0	80	18	2
7	5 mM	10.0	80	20	0
8	5 mM	9.0	80	20	0

Table 2 Mobile phases examined

Mobile phase	Na_2HPO_4			CH_3OH	CH_3ON
	Mol	pH	Ratio	Ratio	Ratio
9	5 mM	8.0	70	20	10
10	5 mM	8.0	80	20	0
11	5 mM	8.0	76	20	4
12	5 mM	8.0	70	14	20
13	5 mM	8.0	70	30	0
14	5 mM	8.0	64	12	24
15	5 mM	8.0	67	11	22

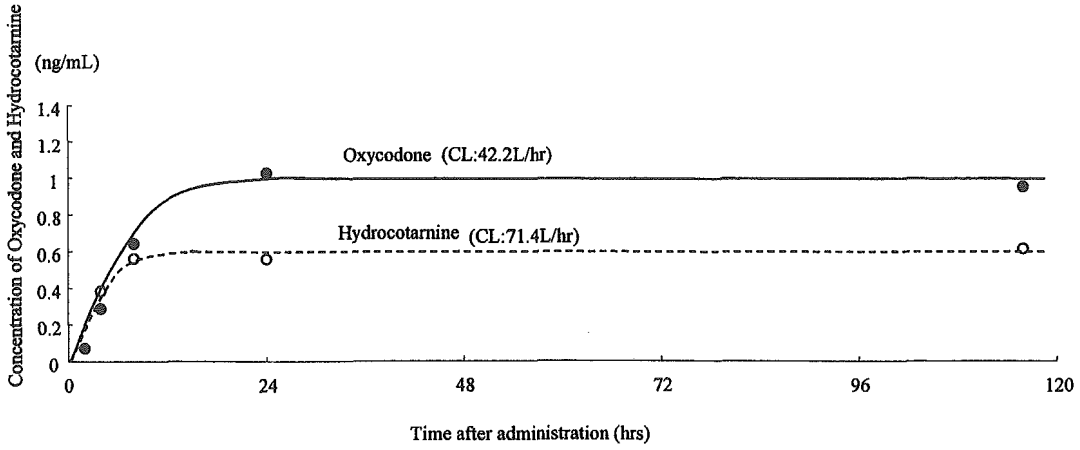

Fig. 2 Time course of the concentration in patient serum. Oxycodone (40 mg/day) and hydrocotarnine (10 mg/day) were continuously injected into the vein by a syringe pump.

of the patient regarding blood collection. Blood samples (2.0 mL) were taken from a peripheral vein at the following times: 2, 4, 8, 24 and 116 h after continuous infusion of oxycodone (40 mg/day) and hydrocotarnine (10 mg/day) into the vein with a syringe pump.

Results and Discussion

Chromatographic separation and quantitative response

The mobile phases shown in Tables 1 and 2 were examined for the separation of oxycodone, hydrocotarnine, codeine and interference in serum. As a result, optimal separation on the chromatogram was obtained using a mobile phase of methanol:acetonitrile:5 mM pH 8 phosphate buffer (2:1:7). Figure 1 shows typical chromatograms obtained from the control serum and the patient serum. A linear-regression analysis of the standard curve from 10 ng/mL to 100 ng/mL yielded the following equation: $y = 0.0479x - 0.0613$ ($r = 0.999$, oxycodone), $y = 0.0296x - 0.0014$ ($r = 0.998$, hydrocotarnine). A good correlation was obtained between the ratio of the peak of oxycodone or hydrocotarnine to codeine and the concentration of oxycodone or hydrocotarnine in the serum. The lower limit of quantification was 0.5 ng/mL for oxycodone, and 0.6 ng/mL for hydrocotarnine ($S/N = 2$). The relative standard deviations within-runs ($n = 10$) and between-runs ($n = 5$) for the assay of oxycodone or hydrocotarnine were less than 4.8% (Table 3). The recovery of oxycodone and hydrocotarnine was 97.2% and 90.5%, respectively. The method developed here was better than the method reported previously.[1,2]

Determination of oxycodone and hydrocotarnine in patient serum

The analytical method was applied to determine oxycodone

Table 3 Reproducibility for analyses

Concentration/ ng mL^{-1}	Within-run (C.V.%, $n = 10$)		Between-run (C.V.%, $n = 5$)	
	Oxycodone	Hydrocotarnine	Oxycodone	Hydrocotarnine
10	3.4	3.8	4.3	4.8
100	2.1	3.3	4.1	4.6

and hydrocotarnine in patient serum. Figure 2 shows the time course of the oxycodone and hydrocotarnine concentration in the serum. The clearance of oxycodone and hydrocotarnine calculated from the above concentration after 24-h continuous infusion was 42.2 L/h and 71.4 L/h, respectively. The oxycodone clearance obtained was approximately same as that reported by Royhia *et al.*,[3] and the clearance of hydrocotarnine is greater than that of oxycodone.

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Rapid injection of epidural mepivacaine speeds the onset of nerve blockade

[L'injection péridurale rapide de mépivacaïne accélère l'installation du bloc nerveux]

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Purpose: When used intraoperatively, mepivacaine can produce a satisfactory sensory block. However, insufficient information is available concerning the factors that affect the speed of nerve blockade with epidural analgesia. The optimal rate of injection of mepivacaine has not been determined. We examined whether the speed of epidural infusion of mepivacaine affects the speed of nerve blockade.

Methods: Forty patients, physical status ASA I–II, scheduled for gynecological abdominal surgery, were enrolled in this double blind randomized trial. A catheter was inserted 4 cm in the epidural space in the midline at L1–L2. Three minutes after a test dose of 2 mL plain 1% mepivacaine over four seconds, 8 mL were injected epidurally at a rate of 1 mL·sec^{-1} (fast group) or 0.05 mL·sec^{-1} (slow group). Sensory and motor blockade, blood pressure, and heart rate were assessed at five, ten, and 15 min after the epidural injection.

Results: There was a significant difference in the spread of sensory blockade at five minutes after the epidural injection between the two groups, but not at ten and 15 min. Blood pressure decreased at five and ten minutes, recovered at 15 min in the fast group, and remained stable in the slow group.

Conclusion: Rapid injection of mepivacaine in the epidural space produced a more rapid onset of epidural block than slow injection, but there was no difference in the final extent of the block.

Objectif : *Utilisée pendant l'opération, la mépivacaïne peut produire un bloc sensitif satisfaisant. Cependant, il y a peu d'information sur les facteurs qui modifient la vitesse d'installation du blocage nerveux avec l'analgésie péridurale. La vitesse optimale de l'injection de mépivacaïne n'est pas connue. Nous avons vérifié si la vitesse de perfusion péridurale de la mépivacaïne modifiait la vitesse du d'installation-blocage nerveux.*

Méthode : *Quarante patientes, d'état physique ASA I–II, devant subir une intervention gynécologique abdominale ont participé à l'étude randomisée et à double insu. Un cathéter a été inséré à 4 cm dans l'espace péridural interépineux de L1–L2. Trois minutes après l'injection d'une dose test de 2 mL de mépivacaïne simple à 1 % pendant quatre secondes, 8 mL ont été injectés dans l'espace péridural à 1 mL·sec^{-1} (groupe rapide) ou 0,05 mL·sec^{-1} (groupe lent). Le blocage sensitif et moteur, la tension artérielle et la fréquence cardiaque ont été évalués à cinq, dix et 15 min après l'injection péridurale.*

Résultats : *La diffusion du blocage sensitif était significativement différente entre les groupes cinq minutes après l'injection, mais non 10 et 15 min après. La tension artérielle a baissé à cinq et dix minutes, s'est rétablie à 15 min dans le groupe rapide et est demeurée stable dans le groupe lent.*

Conclusion : *L'injection rapide de mépivacaïne dans l'espace péridural a produit une installation plus rapide du bloc péridural que l'injection lente, mais il n'y a pas eu de différence dans l'étendue finale du bloc.*

SEVERAL reports describe the factors that affect the speed of sensory blockade in epidural anesthesia.[1–5] However, the influence of the speed of epidural infusion remains unclear and the optimal rate of injection of mepivacaine has not been determined.

A time sequence is apparent during blockade of peripheral nerve action potentials by local anesthetics.[6] Sympathetic precedes sensory blockade, and leads to hypotension, tachycardia, and cutaneous warmth through extensive vasodilatation. The decrease in blood pressure can be used as an indicator of the spread of sympathetic nerve blockade. Sensory and motor nerve blockade can be evaluated by cutaneous coolness and skeletal muscle weakness, respectively.

We designed the current study to compare two rates of injection of mepivacaine into the epidural space to determine whether rate of injection affects the speed of nerve blockade.

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Methods

After giving informed consent, 40 female patients, ASA physical status I and II, scheduled for gynecological abdominal surgery were enrolled in this double blind randomized trial. They represented all consecutive in-patients scheduled for gynecological surgery during the latter six months of 2003. Patients were excluded if there was any contraindication to epidural anesthesia or communication difficulties that would influence postoperative assessment. Also excluded were pregnant women or women with childbearing potential, individuals with ongoing alcohol or drug abuse, or who had been administered drugs known to interfere with drug metabolism. Each patient was randomly allocated to one of two groups; those in group F received a fast injection of mepivacaine and those in group S a slow injection.

All patients received lactated Ringer's solution at a rate of 1 $mL \cdot kg^{-1}$ for one hour before arrival in the operating room and at 10 $mL \cdot kg^{-1} \cdot hr^{-1}$ during the subsequent observation period. Operating room temperature was kept at 25° centigrade. The epidural puncture was performed at the L1–L2 interspace with a 17-gauge Tuohy needle using the midline approach, with patients remaining in the lateral decubitus position. The epidural space was identified using a loss of resistance to saline technique. Less than 1 mL of saline was injected after the needle had entered the epidural space. A 19-gauge epidural catheter was passed through the needle with the bevel directed cephalad. Following withdrawal of the needle, 4 cm of catheter were left in the epidural space. An injection of mepivacaine 1% at room temperature was given through the epidural catheter. Three minutes after the test dose of 2 mL over four seconds, 8 mL were injected at either rate of 1 $mL \cdot sec^{-1}$ (group F) or 0.05 $mL \cdot sec^{-1}$ (group S) with the patient in the supine position.

Sensory and motor blockade, blood pressure, and heart rate were assessed at five, ten, and 15 min after the end of injection of the main dose of mepivacaine. The sensory assessment was started in the block zone and moved towards the no block zone. Sensory block was considered to have occurred when the sensation of cold was markedly reduced or abolished. A dermatome was considered blocked only if the block could be demonstrated bilaterally. Motor blockade was assessed by recording motor function of the lower limbs (modified Bromage scale) immediately after each evaluation of sensory block: 0 = no paralysis (full flexion of knees and feet); 1 = inability to raise extended legs (able to move knees); 2 = inability to flex knees (able to flex ankle joints); 3 = inability to flex ankle joints (unable to flex ankle joints and knees). The assessments were performed by an anesthesiologist who was unaware of group assignment.

Within group comparisons were made by analysis of variance with repeated measures, and between group comparisons were made by analysis of variance with non-repeated measures. If significant differences were detected by analysis of variance, individual means were compared by using the Student-Newman-Keuls test. Differences were considered statistically significant if $P < 0.05$. Expecting that a clinically significant difference in the number of bilaterally blocked dermatomes is four segments and that the standard deviation of the data is 4, sample size calculation indicated that 16 patients in each group would be required to detect a difference with an $\alpha = 0.05$ and $ß = 0.20$.

Results

A total of 40 patients were included in this double-blind study. The epidural technique was well accepted by all patients. Demographic characteristics were similar in the two groups (Table I).

Mean blood pressures are shown in Table II. Although time was measured from the point at which the epidural injection was finished, no differences were found at each assessment time between the two groups. However, mean blood pressure decreased slightly at five and ten minutes, recovered at 15 min in the fast group, whereas it remained stable in the slow group. Heart rate did not change during the observation period in the two groups.

The number of dermatomes blocked at each assessment time is shown in Table III. The spread of sensory blockade in the fast group was rapid, showing no difference between the ten and 15 min time points. In the slow group, the spread increased gradually, resulting in a significant difference between any two assessment times. At five minutes, significantly more dermatomes were blocked in the fast injection group compared with the slow group ($P < 0.01$), but at ten and 15 min there were no significant differences between the groups. Table IV shows the number of patients in whom perineal blockade was present at five, ten and 15 min. At the five-minute assessment time, perineal blockade with bilateral block of the second to fourth sacral dermatomes occurred in 13 patients in group F and three patients in group S ($P < 0.05$, Chi squared test).

No difference was found in motor blockade between both groups. All patients had either bilateral grade 0 or 1 block throughout the investigation. Nine patients in group F and ten patients in group S had a bilateral Bromge grade 1 blockade by 15 min after epidural injection of the main dose of mepivacaine.

TABLE I Demographic characteristics of the patients

	Group F (fast injection)	*Group S (slow injection)*	
Age (yr)	51.6 ± 12.3	51.4 ± 10.3	NS
Height (cm)	156.1 ± 4.5	156.4 ± 5.7	NS
Weight (kg)	55.0 ± 7.3	55.1 ± 7.9	NS
Depth to epidural space (cm)	3.9 ± 0.6	3.8 ± 0.7	NS

Data expressed as mean ± SD. NS = no significant difference between groups.

TABLE II Mean blood pressure

	Mean blood pressure (mmHg)		
Time after injection (min)	*Group F (fast injection)*	*Group S (slow injection)*	
0	82.1 ± 9.7	80.8 ± 12.1	NS
5	77.5 ± 11.2*	80.0 ± 12.2	NS
10	76.0 ± 10.5*	79.4 ± 10.0	NS
15	79.1 ± 14.1	78.9 ± 8.6	NS

Data are expressed as mean ± SD. NS = no significant difference between groups. *$P < 0.05$ *vs* baseline.

TABLE III Number of dermatomes blocked

	Number of bilaterally blocked dermatomes		
Time after injection (min)	*Group F (fast injection)*	*Group S (slow injection)*	
5	13.6 ± 3.2	7.6 ± 3.1	$P < 0.01$
10	15.2 ± 3.7*	14.2 ± 3.4*	NS
15	16.4 ± 3.1*	16.7 ± 3.3*†	NS

Data are expressed as mean ± SD. NS = no significant difference between groups. *$P < 0.01$ *vs* five minutes. †$P < 0.01$ *vs* ten minutes.

TABLE IV Number of patients with perineal blockade

	Number of patients with perineal blockade		
Time after injection (min)	*Group F (fast injection)*	*Group S (slow injection)*	
5	13	3	$P < 0.05$
10	16	14	NS
15	17	18	NS

NS = no significant difference between groups.

Discussion

The influence of epidural infusion speed on the speed of onset of epidural anesthesia remains controversial. The disagreement among authors describing its influence may be, partially, explained by differences in study design such as comparing spread of sensory blockade at different moments after local anesthetic injection, using different local anesthetic solutions, adapting different rates of epidural injection, and performing epidural puncture at a different interspace. Cardoso *et al.* described that there were no differences between epidural infusion rate and the speed of sensory blockade, when infusing 15 mL of 2% lidocaine over 30 sec or three minutes.[7] They compared spread of sensory blockade ten and 15 min after the injection of the solution. The intrinsic potency of lidocaine is similar to that of mepivacaine.[8] Also, the speed of onset of sensory blockade is enhanced by an increase in dose achieved by either an increase in concentration or in the volume of local anesthetic solution.[1,9] Therefore, the 15 mL of 2% lidocaine used by Cardoso *et al.* may have produced more rapid blockade than the 8 mL of 1% mepivacaine used in our study. Also, there may have been an undetected but significant difference in the spread of sensory blockade at five minutes after the injection. Rosenberg *et al.* reported that the decrease of blood pressure during the first 30 min did not differ between two injection rates with bupivacaine.[10] In the present study, a significant difference was shown in the decrease of mean blood pressure between the two injection rates, possibly due to the injection of a low volume of lactated Ringer's solution before epidural injection and a more rapid onset of block with mepivacaine compared with bupivacaine. In general, vasodilatation leads to tachycardia following hypotension. However, heart rate did not change until the end of the observation period. The number of patients with dermatomes blocked above T4 was four in the fast group and five in the slow group and the suppression of cardiac sympathetic innervation may, partly, explain the decrease in heart rate. In the caudal epidural space Blanco *et al.* found no correlation between the speed of injection and the speed of onset of sensory blockade.[11] Stabilization and onset are slower and drug requirements larger for caudal than for lumbar epidural anesthesia.[2]

Injecting a constant volume of anesthetic solution epidurally produces an instantaneous increase in epidural pressure with a subsequent return toward preinjection values. Characteristically, the curve of epidural pressure *vs* time exhibits three successive components: the peak, the descent, and the residual values.[12] The first part of the epidural pressure curve has been known as the forced response curve, derived from expansion of the epidural space induced by the administration of a given volume of anesthetic. The second part of the curve constitutes the free response curve, based on intrinsic properties of the epidural space such as compliance and resistance. Finally, the