J Anesth (2005) 19:21–25
DOI 10.1007/s00540-004-0282-0

Journal of
Anesthesia

Does central venous pressure or pulmonary capillary wedge pressure reflect the status of circulating blood volume in patients after extended transthoracic esophagectomy?

Satomi Oohashi and Hiroshi Endoh

Department of Emergency and Critical Care Medicine, Niigata University Faculty of Medicine, 1-757 Asahimachi, Niigata 951-8150, Japan

Abstract
Purpose. We investigated whether central venous pressure (CVP) or pulmonary capillary wedge pressure (PCWP) can accurately reflect the status of circulating blood volume (CBV) during the perioperative period in adult patients after extended transthoracic esophagectomy.
Methods. In 16 adult patients undergoing esophagectomy, simultaneous measurements of CVP, PCWP, and CBV were made at the following seven points: baseline (before surgery) and at 0, 12, 24, 36, 48, and 60 h after admission to the intensive care unit (ICU). CBV was estimated at the bedside with a pulse-dye densitometry method using indocyanine green. The relationship between CBV and these filling pressures was analyzed by linear regression.
Results. A total of 122 paired observations were made. The mean value of CBV decreased by approximately −20% at admission to the ICU and increased by approximately 24% of baseline at 48 h after surgery. The time course of CVP and PCWP was similar to that of CBV: both decreased at admission to the ICU, then gradually increased, and peaked at 48 h after surgery. However, both pressures remained within normal ranges, and the actual changes from baseline were small. There was no significant relationship between CBV and CVP ($r = 0.17$, $P = 0.07$), and between CBV and PCWP ($r = 0.03$, $P = 0.78$).
Conclusion. Neither CVP nor PCWP accurately reflected the status of CBV in adult patients after extended transthoracic esophagectomy.

Key words Circulating blood volume · Central venous pressure · Pulmonary capillary wedge pressure · Extended transthoracic esophagectomy

Address correspondence to: H. Endoh
Received: July 15, 2004 / Accepted: October 7, 2004

Introduction

Accurate knowledge of changes in circulating blood volume (CBV) caused by blood loss or fluid sequestration during surgery would be of great value to guide postoperative fluid therapy. Traditionally, routine monitoring of central venous pressure (CVP), pulmonary capillary wedge pressure (PCWP), cardiac output, hematocrit, and urine volume has been used to guide fluid therapy [1,2]. Extended transthoracic esophagectomy with three-field lymphadenectomy includes transthoracic en bloc resection of the esophagus and combined bilateral neck, mediastinal, and abdominal lymph node dissections [3,4]. The procedure is usually associated with a large CBV change due to extensive fluid sequestration and blood loss, resulting in perioperative hemodynamic instability [5,6]. Recently, it has become possible to estimate CBV less invasively at the bedside by a pulse dye densitogram (PDD) method using indocyanine green (ICG) as an indicator [7]; the clinical validity of this method has been demonstrated in several studies [8,9].

The aim of this study was to clarify whether CVP or PCWP can reflect the status of CBV measured by the newly developed PDD method in adult patients undergoing extended transthoracic esophagectomy.

Materials and methods

Subjects

After institutional ethics committee approval had been obtained and the patients had given informed consent, 16 patients scheduled for extended transthoracic esophagectomy for carcinoma were enrolled between December 2001 and December 2002. Patients with impaired hearts (New York Heart Association class III or IV), hepatic function (serum total bilirubin

$>2.0\,mg\cdot dl^{-1}$), or renal function (serum creatinine $>2.0\,mg\cdot dl^{-1}$) were excluded.

Anesthesia and postoperative management

General anesthesia was induced with propofol ($1.5\,mg\cdot kg^{-1}$) and fentanyl ($2\,\mu g\cdot kg^{-1}$) and maintained with isoflurane (0.5%–2.0%) with 50%–60% nitrous oxide in oxygen and intermittent bolus injections of fentanyl ($1–2\,\mu g\cdot kg^{-1}$) as needed. After the surgery, all patients were admitted to the surgical intensive care unit (ICU) at our institute and mechanically ventilated in the synchronized intermittent mandatory ventilation (IMV) mode with positive end-expiratory pressure (PEEP) of 5 cm H_2O. All patients were sedated with continuous intravenous infusion of propofol ($0.3–3\,mg\cdot kg^{-1}\cdot h^{-1}$) and continuous epidural infusion of morphine hydrochloride ($3–5\,mg\cdot day^{-1}$) targeting a Ramsey sedation score of 3 or 4 during the study.

Measurements of hemodynamic variables and circulating blood volume

CVP was measured through a central venous catheter (CS-17702-E, Arrow International, Reading, PA, USA), which had been inserted through the left subclavian vein preoperatively. In the operating room, a radial artery was cannulated to measure arterial blood pressure and blood gas tensions. A thoracic epidural catheter was placed for postoperative analgesia in all patients. After induction of anesthesia, a pulmonary artery catheter (744HF75 Swan-Ganz CCO mbo CCO/SVO2, Edwards Lifesciences, Irvine, CA, USA) was inserted through the right subclavian vein. Arterial blood pressure, CVP, and PCWP were measured with a pressure transducer kit (UK901, Edwards Lifesciences) and a bedside monitor (CMS200, Phillip Medical systems, Best, Netherlands). After calibration and zeroing to atmospheric pressure, all pressures were measured at zero PEEP and end-expiration, using the mid-chest level as reference in supine position. Cardiac output was continuously measured by a thermodilution method using a computer system (Vigilance TM, Edwards Lifesciences).

CBV was estimated by the pulse dye densitogram (PDD) method using indocyaninegreen (ICG) as an indicator. Before injection of ICG, 0.5 ml of arterial blood was drawn to measure the hemoglobin concentration with a blood gas analyzer (Corning 280, Medifield, MA, USA), which is required to estimate ICG blood concentration, and then hemodynamic variables [heart rate, arterial pressure, CVP, PCWP, and cardiac index (CI)] were recorded. A probe of the dye densitogram (DDG) analyzer (DDG-2001, Nihon Kohden, Tokyo, Japan) was attached to the patient's nostril, and 20 mg of ICG in 5 ml of distilled water was injected in a bolus into the central venous catheter. The DDG analyzer measures the arterial ICG concentration using the PDD method and estimates the initial ICG concentration from the ICG elimination curve. Finally, the analyzer calculates CBV as the total dose divided by the initial concentration. This process usually needs approximately 10 min, and motion distortion or insufficient detection of pulse during this period sometimes results in failure to measure. In such a situation, the second measurement was made after at least a 30-min interval.

The time points for data collection were as follows: before operation (baseline), at admission to the ICU (T0), and at 12 (T12), 24 (T24), 36 (T36), 48 (T48), and 60 h (T60) after admission to the ICU.

Fluid balance (in milliliters) was calculated as infused volume − estimated blood loss − urine volume − chest and abdominal drainage − aspiration of gastric contents, and was calculated every 12 h in the ICU.

Statistical analysis

Analyses were performed with a statistical package (SPSS 11.0 for Windows, SPSS Inc., Chicago, IL, USA). Results are expressed as means ± standard deviation (SD). Comparison between different time points were made by one-way analysis of variance. When significance was found, Fisher's protected least significant difference test was used as a post hoc multiple comparison procedure.

The relationship between CBV and filling pressure (CVP and PCWP) was analyzed by linear regression analysis. Furthermore, the variables were changed to differences from their baseline values (ΔCBV, ΔCVP, and ΔPCWP), or to the percentage changes of their baseline values (relative CBV, relative CVP, and relative PCWP). Linear regression analysis was performed on these modified variables. $P < 0.05$ was considered statistically significant.

Results

All 16 patients were male and were successfully weaned from mechanical ventilatory support and discharged to the normal surgical ward within a week after surgery. The mean duration of ventilatory support was 3.5 ± 0.6 days (mean ± SD). The mean age was 66 ± 9 years and the mean weight was 52 ± 7 kg. The mean durations of anesthesia and surgery were 623 ± 118 min and 487 ± 128 min, respectively. During anesthesia and in the ICU, dopamine was continuously administered at a rate of $3–5\,\mu g\cdot kg^{-1}\cdot min^{-1}$ to maintain urine volume in 14 of the 16

Table 1. Changes in hemodynamic variables and circulating blood volume[a]

Measurement	Baseline	T0	T12	T24	T36	T48	T60
Heart rate (bpm)	73 ± 15	97 ± 9*	96 ± 18*	98 ± 18*	105 ± 17*	100 ± 15*	94 ± 17*
Systolic ABP (mmHg)	109 ± 14	133 ± 27*	114 ± 12†	120 ± 19	117 ± 26†	127 ± 24*	126 ± 25*
Diastolic ABP (mmHg)	60 ± 7	74 ± 15	66 ± 11†	67 ± 12	64 ± 16	71 ± 18	68 ± 18
Mean ABP (mmHg)	76 ± 8	93 ± 18*	82 ± 10	84 ± 14*†	81 ± 18†	90 ± 19*†	87 ± 18*
Hemoglobin (gram/dl)	11.3 ± 1.9	10.9 ± 0.9	10.0 ± 0.7*†	10.1 ± 1.2*	9.8 ± 1.4*†	9.7 ± 1.2*†	9.7 ± 1.3*†
CVP (mmHg)	9 ± 3	7 ± 3*	8 ± 2	8 ± 3	9 ± 3†	10 ± 3†	7 ± 2
PCWP (mmHg)	12 ± 3	10 ± 3*	10 ± 3*	9 ± 2*	10 ± 4	12 ± 2	8 ± 3*
CI ($l \cdot min \cdot m^{-2}$)	2.8 ± 0.7	3.3 ± 0.8	3.3 ± 0.9	3.2 ± 0.6	3.6 ± 0.8*	3.7 ± 0.9*	3.6 ± 0.7*
CBV ($ml \cdot kg^{-1}$)	80 ± 18	61 ± 12*	69 ± 21*	77 ± 17†	84 ± 15†	91 ± 15†	77 ± 12†
Fluid balance (ml)		2779 ± 976	660 ± 697†	790 ± 621†	283 ± 760†	295 ± 522†	−24 ± 429†

[a]Values are means ± SD. ABP, arterial blood pressure; CVP, central venous pressure; PCWP, pulmonary capillary wedge pressure; CI, cardiac index measured by the thermodilution method; CBV, circulating blood volume
T0, at admission to intensive care unit (ICU); T12, T24, T36, T48, and T60, every 12 h up to 60 h after admission to ICU, respectively
*$P < 0.05$ vs baseline; †$P < 0.05$ vs T0

patients. Prostaglandin E_1 was continuously administered at a rate of 0.05–0.10 $\mu g \cdot kg^{-1} \cdot min^{-1}$ against hypertension or to maintain urine volume in 9 of the 16 patients during the operation and the first day in the ICU. The daily amounts of fluid infusion and blood transfusion were determined based on blood pressure, heart rate, CVP, PCWP, cardiac output, urine output, and hematocrit.

A total of 112 paired observations of CBV and hemodynamic variables were obtained. The mean values of the individual variables and CBV are given in Table 1. CVP, PCWP, and CBV ranged between 1 and 17 mmHg, 3 and 24 mmHg, and 40 and 127 $ml \cdot kg^{-1}$, respectively.

Despite positive fluid balance during surgery (2779 ± 976 ml), CBV decreased at admission to the ICU (T0), then gradually increased, and peaked at 48 h after admission to the ICU (T48), probably corresponding to refilling phase. In response to increasing CBV, the cardiac index was also increased at T36, T48, and T60 as compared with baseline. The decrease and increase in CBV were equivalent to approximately −20.4% and 23.8% of baseline, respectively (upper panel in Fig. 1).

The time courses of CVP and PCWP were similar to that of CBV: both decreased at admission to the ICU, then gradually increased, and peaked at P48. However, both pressures remained within normal ranges, and the actual changes from baseline were small (lower panel in Fig. 1). Figure 2 (upper panels) shows scattered plots of CVP and CBV (left), ΔCVP and ΔCBV (middle), relative CVP (%), and relative CBV (%) (right). Figure 2 (lower panels) also shows scattered plots of PCWP and CBV (left), ΔPCWP and ΔCBV (middle), and relative PCWP (%) and relative CBV (%) (right). There were no significant relationships between these variables.

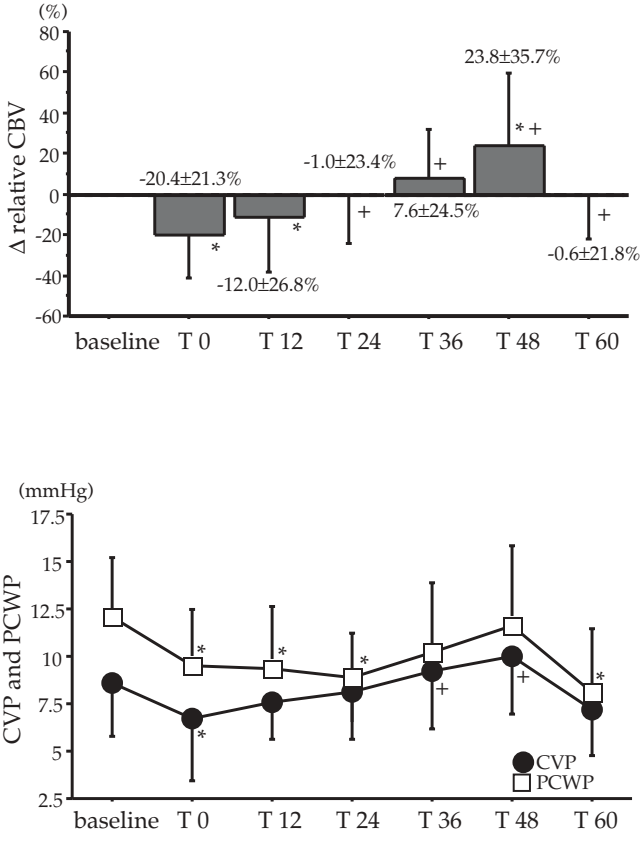

Fig. 1. Upper panel Percentage change in circulating blood volume (*CBV*) from baseline(Δ relative CBV). CBV decreased by approximately −20% at admission to ICU and increased by approximately 24% of baseline at 48 h after admission. *Baseline*, before surgery; *T0–T60*, at intervals of 12 to 60 h in ICU. *$P < 0.05$ vs baseline; †$P < 0.05$ vs T0. *Error bars* denote SD. **Lower panel** Changes in central venous pressure (*CVP*) and pulmonary capillary wedge pressure (*PCWP*). The time courses of both pressures were similar to that of CBV, and both remained within their normal ranges. Actual changes from baseline in both pressures were small (<5 mmHg)

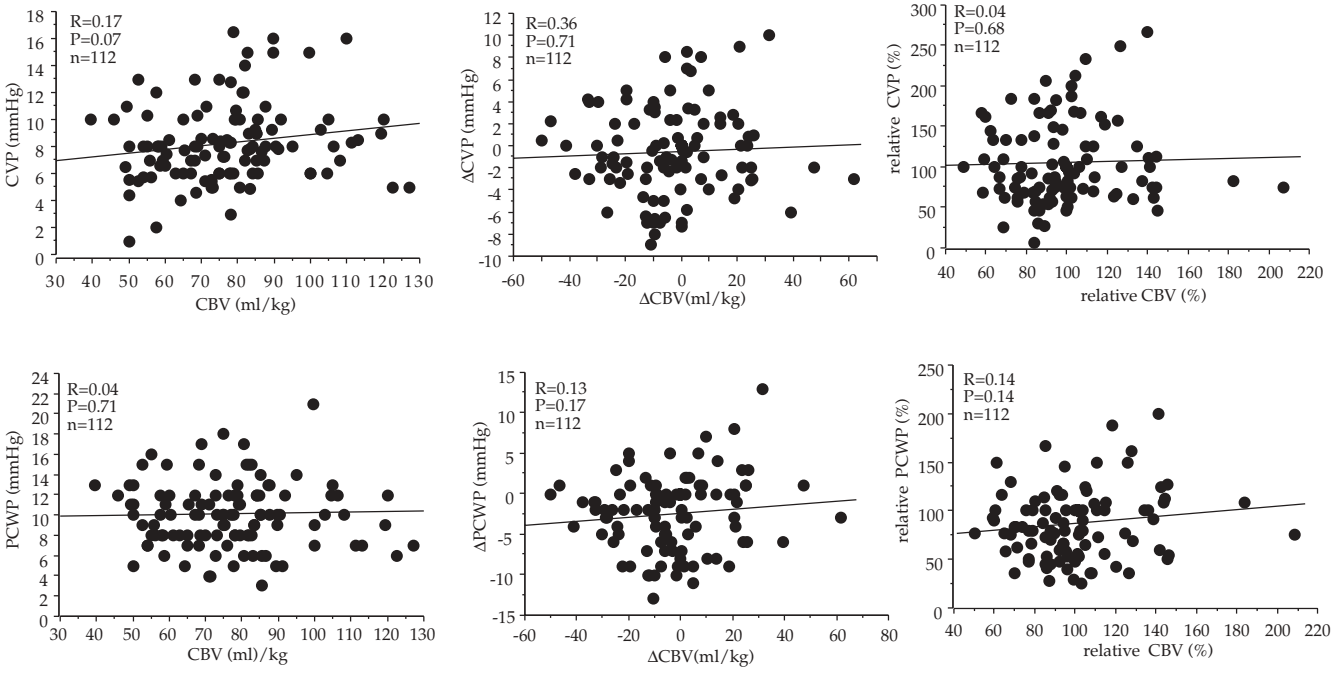

Fig. 2. Upper panel Scatter plot between circulating blood volume (*CBV*) (*x*-axis) and central venous pressure (*CVP*) (*y*-axis) (**left**), *ΔCBV* and *ΔCVP* (difference from baseline) (**middle**), and relative *CBV(%)* and relative *CVP(%)* (percentage change from baseline) (**right**). Regression coefficients and *P* values are shown in each plot. There were no statistically significant relationships between the variables. **Lower panel** Scatter plot between *CBV* (*x*-axis) and pulmonary capillary wedge pressure (*PCWP*) (*y*-axis) (**left**), *ΔCBV* and *ΔPCWP* (difference from baseline) (**middle**), and relative *CBV(%)* and relative *PCWP(%)* (percentage change know baseline) (**right**). Regression coefficients and *P* values are shown in each plot. There were no statistically significant relationships between the variables

Discussion

Extended transthoracic esophagectomy with three-field lymphadenectomy, consisting of en bloc transthoracic resection of the esophagus and combined bilateral neck, mediastinal, and abdominal lymph node dissections, is one of the most invasive surgical procedures and requires a long duration of surgery and anesthesia [3,4].

The surgical procedure usually induces a large change in CBV due to extensive fluid sequestration and blood loss, resulting in hemodynamic instability during anesthesia or in the ICU [5,6]. Thus, accurate assessments of the status of CBV are of great importance during perioperative management. However, in a clinical setting, the amount of infusion or blood transfusion has been determined simply based on CVP, PCWP, and clinical impressions without direct measurement of CBV [6].

The standard method for estimating CBV has been an indicator dilution method using Evans blue, radioiodinated human serum albumin (IHSA), or red blood cells. However, these techniques are time-consuming and are not repeatable at frequent intervals because of their retention in blood for several days. In contrast, ICG is firmly bound to plasma protein, is not subject to extravascular distribution, and does not accumulate in the body because of its rapid elimination by the liver [7]. The DDG method enables bedside measurements of arterial ICG concentration using two-wavelength light absorption without repeated blood samplings. The DDG analyzer estimates the initial ICG concentration by extrapolating the ICG elimination curve (2.5–6.0 min) to the first-pass time, and calculates CBV as the total dose divided by the initial ICG concentration [7–10]. In early validation testing studies comparing the IHSA dilution method in healthy volunteers, the DDG analyzer calculated CBV with an estimated error of approximately ±10% [8,9].

One of the main findings of this study is that in patients following extended transthoracic esophagectomy, CBV was changed significantly more than ±20%, and the time course of CVP and PCWP was similar to that of CBV; nevertheless, neither pressure had a significant relationship with CBV. Several researchers showed that CVP or PCWP does not reflect accurately the status of CBV. Shippy et al. [11] measured CBV by the ^{125}I-labeled HSA method and compared it with heart rate, arterial pressure, cardiac output, CVP, and PCWP on

1500 occasions on critically ill patients; they found a poor correlation between CBV and CVP ($r = 0.27$) and between CBV and PCWP ($r = 0.25$) during fluid resuscitation. They explained that CVP and PCWP are influenced by numerous complex compensatory responses and determined by both cardiac function and venous compliance, and concluded that neither may be equivalent to normal circulating blood volume. Similarly, Hoeft et al. [12] compared PCWP and CVP with CBV measured by the fiberoptic thermistor method with injection of cold ICG in 11 patients undergoing aortocoronary bypass surgery, and reported that there was no significant correlation between CBV and these conventional indicators of preload. They also explained that CVP and PCWP not only are determined by intravascular blood volume but also are affected by the compliance of the intra- and extrathoracic low pressure system, and concluded that CBV, but not CVP and PCWP, is a reliable index of blood volume and left ventricular preload in that population of patients. In addition, Motoyama et al. [13] showed that, especially after esophagectomy, an extensive fluid sequestration to the lung, mediastinum, and chest wall decreases the compliance of the superior vena cava and the bilateral cardiac ventricle, so that neither CVP or PCWP accurately reflects circulating blood volume. These results are in accordance with the present findings.

A criticism of this study is that CVP and PCWP data were clustered near the same value, resulting in their low correlation with CBV. Indeed, the mean value of both pressures remained within the normal range, and the variation of both pressures from baseline was small (<5 mmHg) (lower panels in Fig. 1). However, there was a large change in CBV during the study, which did not actually affect the filling pressures. These discrepancies between CBV and filling pressures may be attributable to the above-described reason or partly to the continuous infusion of low doses of dopamine during the study. Dopamine certainly increased cardiac output, as shown in Table 1, presumably reducing the filling pressures, which contributes to the low correlation with CBV.

In conclusion, consecutive bedside assessments of CBV by the PDD method using ICG demonstrated that extended transthoracic esophagectomy was associated with a large variation in CBV (±20% of baseline) during the perioperative period. However, CVP and PCWP did not show such variation. Thus, caution should be taken when extrapolating from filling pressures to CBV status during perioperative management of patients following extended esophagectomy.

Acknowledgments. We thank Professor and Chair Katuyoshi Hatakeyama and his colleagues at the Niigata University Hospital for their help in making this study possible.

References

1. Shoemaker W, Montogomery E, Kaplan E (1973) Physiologic patterns in surviving and nonsurviving shock patients. Use of sequential cardio-respiratory variables in defining criteria for therapeutic goals and warning of death. Arch Surg 106:630–636
2. Magder S (1998) More respect for the CVP. Intensive Care Med 24:651–653
3. Imamura M, Shimada Y, Kanda T, Miyahara T, Hashimoto M, Tobe T, Arai T, Hatano Y (1992) Hemodynamic changes after resection of the thoracic duct for en bloc resection of esophageal cancer. Surgery Today 22:226–232
4. Shinozawa Y, Ando N, Osaku M (1991) Fluid replacement therapy in esophagectomy—dry side or wet side? JJPEN 13:3–8
5. Mizote H, Katsuki N, Hikita S (1989) Nutritional and metabolic care for esophagectomy. JJPEN 11:157–162
6. Abo S, Kitamura M, Hshimoto M, Izumi K, Minamiya Y, Shikama T, Suzuki H, Temma K, Kamata S, Saito R (1996) Analysis of results of surgery performed over a 20-year period on 500 patients with cancer of the thoracic esophagus. Surgery Today 26:77–82
7. Iijima T, Aoyagi T, Iwao Y, Masuda J, Fuse M, Kobayashi N, Sankawa H (1997) Cardiac output and circulating blood volume analysis by pulse dye-densitometry. J Clin Monit 13:81–89
8. Iijima T, Iwao Y, Sankawa H (1998) Circulating blood volume measured by pulse dye densitometry. Anesthesiology 89:1329–1335
9. Haruna M, Kumon K, Yahagi N, Watanabe Y, Ishida Y, Kobayashi N, Aoyagi T (1998) Blood volume measurement at the bedside using ICG pulse spectrophotometry. Anesthesiology 89: 1322–1328
10. He YL, Tanigami H, Ueyama H, Mashimo T, Yoshiya I (1998) Measurement of blood volume using indocyanine green measured with pulse-spectrophotometry: its reproducibility and reliability. Crit Care Med 26:1446–1451
11. Shippy CR, Appel PL, Shoemaker WC (1984) Reliability of clinical monitoring to assess blood volume in critically ill patients. Criti Care Med 12:107–112
12. Hoeft A, Schorn B, Weyland A, Scholz M, Buhre W, Stepanek E, Allen S, Sonntag H (1994) Bedside assessment of intravascular volume status in patients undergoing coronary bypass surgery. Anesthesiology 81:76–86
13. Motoyama S, Kitamura M, Kibira S, Suzuki H, Kamata S, Saito R, Kimura K, Sasaki S, Taguchi K, Okuyama M, Miura M, Ogawa J (2000) Does central venous pressure reflect the circulating blood volume for the decrement of compliance just after esophagectomy? Surgery Today 30:11–15