Assessment of cardiac preload by indicator dilution and transoesophageal echocardiography

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Summary

Background and objective Assessment of cardiac preload is of major importance in the management of critically ill patients. Echocardiographic determined left ventricular end-diastolic area and indicator dilution derived intrathoracic blood volume are used as surrogates for cardiac preload. However, no controlled comparison studies on the relationship between induced changes in end-diastolic area and intrathoracic blood volume and concomitant changes in stroke volume index are available.

Methods The effects of a change in body position on these variables were investigated in 10 anaesthetized patients.

Results Intrathoracic blood volume and end-diastolic area decreased by 18 ± 11% and 27 ± 13% respectively. Stroke volume index concomitantly decreased by 19 ± 11%. Correlation analysis revealed a close relation between stroke volume index and intrathoracic blood volume (r = 0.75) and end-diastolic area (r = 0.76).

Conclusions Within the observed range of data, intrathoracic blood volume and end-diastolic area are equivalent indices of cardiac preload.

Keywords: ECHOCARDIOGRAPHY, Doppler; HAEMODYNAMICS, cardiac output, cardiac volume, stroke volume; INDICATOR DILUTION TECHNIQUES.

Introduction

Knowledge on actual cardiac preload is one of the essentials to optimize systemic haemodynamics during anaesthesia and intensive care. However, direct, volumetric measurement of cardiac preload is difficult to perform in clinical routine [1,2]. Conventional evaluation of cardiac preload is mainly based on measurements of cardiac filling pressures such as central venous and pulmonary capillary wedge pressures (CVP, PCWP) [1–3]. However, CVP and PCWP often fail to provide valid information on cardiac preload [1–4] and more direct measures are needed [1,3,4]. Currently, two methods have gained acceptance during anaesthesia and in the intensive care unit. First, transoesophageal echocardiography (TOE) has been increasingly used for the assessment of left ventricular (LV) filling [4–6]. In particular, the LV end-diastolic area (EDA) in the transgastric mid-papillary short-axis view has been used as an index of cardiac preload [4–7]. Second, the transpulmonary thermal-dye indicator dilution technique enables bedside measurement of intrathoracic blood volume (ITBV) [1,3,7,8]. ITBV has been shown to be more indicative for cardiac preload than PCWP and CVP [1,3,9,10]. However, controlled comparison studies on the validity of EDA vs. ITBV as indicators of cardiac preload are lacking. Thus, in the present prospective, controlled clinical study we investigated the effects of a deliberate change in intravascular volume distribution on EDA and ITBV and on the relationship between these two preload indices with stroke volume index.

Accepted February 2001
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The present investigation was not supported by any external grants.
Methods

After approval by the institutional review board committee and patients’ written informed consent, the study was performed in 10 anaesthetized patients (of whom six were female), ASA classification II before elective surgical procedures. None of the patients had a history of cardiovascular disease or were taking cardiovascular medication.

Premedication consisted of flunitrazepam (0.02 mg kg\(^{-1}\) p.o.) on the evening before surgery as well as 1 h before induction of anaesthesia. Upon arrival in the operating suite, ECG leads II and V5 were attached and continuously monitored (Sirecust 961, Siemens, Germany). All patients received 7 mL kg\(^{-1}\) of crystalloid (Eufusol\(^{\text{TM}}\), Braun Melsungen, Germany) and 7 mL kg\(^{-1}\) of a colloid infusion (Gelafundin\(^{\text{TM}}\), Braun Melsungen, Germany) before the first set of measurements were made. No additional fluids were given throughout the study period. A central venous catheter (12 F, Arrow Int., Reading, PA, USA) was placed in the right atrium via the right or left subclavian vein. The correct position of the right atrial catheter was verified by TOE once anaesthesia had been instituted.

General anaesthesia was induced with sufentanil 2 \(\mu\)g kg\(^{-1}\) and midazolam 0.05 mg kg\(^{-1}\). Pancuronium bromide 0.1 mg kg\(^{-1}\) was administered to facilitate endotracheal intubation. Anaesthesia was maintained with sufentanil 2–3 \(\mu\)g kg\(^{-1}\) h\(^{-1}\) and midazolam 150 \(\mu\)g kg\(^{-1}\) h\(^{-1}\). Neither vasoactive drugs nor inhalational anaesthetics were administered throughout the study period. Patients lungs were mechanically ventilated in a volume-controlled mode with positive end-expiratory pressure of 5 cmH\(_2\)O. Respiratory minute volume was adjusted to maintain normocarbia with an inspired oxygen fraction of 0.5.

Haemodynamic variables including heart rate (HR), mean arterial and right atrial pressures (MAP, RAP) were continuously recorded; indicator dilution measurements and echocardiographic studies were performed after induction of anaesthesia (I) and after raising the patient into the sitting position (II). Pressure transducers were positioned in the mid-axillary level when patients were supine and at the level of the fifth intercostal space anteriorly in the sitting position.

TOE studies were performed using an echocardiography system equipped with a multiplane TOE probe (Vingmed CFM 800, Vingmed, GE Medical Systems, USA). In the transgastric mid-papillary short axis view, the end-diastolic (EDA) and end-systolic areas (ESA) were measured by manually tracing the endocardial border. An average of three consecutive heart beats throughout the respiratory cycle was used for measurements. The fractional area change (FAC) was calculated using standard formula and expressed as a percentage. All measurements were performed off-line from tape recordings by two independent observers, which were blinded to haemodynamic data and the results of indicator dilution measurements.

Transpulmonary double indicator dilution measurements of CO and ITBV were performed using a combined 4 F fibreoptic-thermistor catheter (Pulsiocath PV 2024\(^{\text{TM}}\), Pulsion Medical Systems, Germany) inserted 40 cm upwards into the descending aorta via a 5 F introducer (Arrow Int., Reading, USA) in the left femoral artery. The fibreoptic-thermistor catheter was connected to an opto-electronic device (COLDSystem\(^{\text{TM}}\), Pulsion Medical Systems, Germany) which enables simultaneous detection of thermo- and dye-dilution curves. Thermo- and dye-dilution measurements were made by triple bolus injection of 20 mL ice-cooled saline and two additional bolus injections of 20 mL ice-cooled indocyanine green dye (ICG) (1.25 mg mL\(^{-1}\)) into the right atrium. Injections were randomly spread over the respiratory cycle. Thermo- and dye-dilution curves obtained in the aorta were digitized and stored on a microcomputer. Cardiac output was assessed by the thermodilution technique. Intrathoracic blood volume (ITBV) was calculated from cardiac output and the mean transit time of the dye tracer between the site of injection and the site of detection (mtt\(_{\text{dye}}\)) [7, 9–11].

\[
\text{ITBV} = \frac{\text{CO} \times \text{mtt}_{\text{dye}}}{(\text{mL})}
\]  \hspace{1cm} (1)

All volume- and flow-related variables were normalized to body surface area or body weight.

Statistics

Results in the table and figures are expressed as mean ± standard deviation (SD). Paired Student’s t-tests were used to compare data obtained before...
and after transfer from the supine to the 45° sitting position. A value of $P \leq 0.05$ was considered significant. Correlation analyses between SVI and ITBV as well as between SVI and EDA were performed before and after the deliberate change in body position. All statistical procedures were performed on a microcomputer using the SPSS/PC+™ statistical software package.

**Results**

The mean age of the patients was $43 \pm 11$ years (range: 22–57 years). The mean body weight and height were $68 \pm 12$ kg and $170 \pm 6$ cm respectively. Haemodynamic data are presented in Table 1. The effects of the sitting position on EDA, end-systolic area (ESA), ITBV and fractional area change (FAC) are also demonstrated in Table 1. The linear regression analysis between the volumetric indices (EDA and ITBV) vs. SVI is depicted in Figs 1 and 2, whereas Fig. 3 demonstrates the relationship between RAP and SVI.

In our patients mean arterial pressure and RAP significantly decreased after changing the patients’ position from supine to sitting (Table 1). In contrast, systemic vascular resistance increased (Table 1). In response to the change in body position, intrathoracic blood volume and stroke volume index decreased by $18 \pm 11\%$ ($P < 0.05$) and $19 \pm 11\%$ ($P < 0.05$) respectively. In addition, EDA significantly decreased by $27 \pm 13\%$ ($P < 0.05$) after transfer from the supine to the sitting position. As ESA also significantly decreased, FAC remained unchanged (Table 1).

**Table 1.** Haemodynamic variables during the supine and sitting position

<table>
<thead>
<tr>
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<th>I</th>
<th>II</th>
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<tr>
<td>HR (min$^{-1}$)</td>
<td>73 ± 12</td>
<td>67 ± 11</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>97 ± 15</td>
<td>84 ± 16*</td>
</tr>
<tr>
<td>RAP (mmHg)</td>
<td>6 ± 3</td>
<td>2 ± 2*</td>
</tr>
<tr>
<td>CI (L min$^{-1}$)</td>
<td>2.5 ± 0.3</td>
<td>1.8 ± 0.3*</td>
</tr>
<tr>
<td>SVI (mL m$^{-2}$)</td>
<td>35 ± 7</td>
<td>28 ± 7*</td>
</tr>
<tr>
<td>SVRI (dyn s cm$^{-6}$ m$^{-2}$)</td>
<td>2970 ± 474</td>
<td>3638 ± 516*</td>
</tr>
<tr>
<td>ITBV (mL m$^{-2}$)</td>
<td>646 ± 89</td>
<td>516 ± 106*</td>
</tr>
<tr>
<td>EDA (m$^{-2}$)</td>
<td>16.3 ± 1.7</td>
<td>11.9 ± 2.8*</td>
</tr>
<tr>
<td>ESA (m$^{-2}$)</td>
<td>7.2 ± 2.4</td>
<td>5.5 ± 2.2*</td>
</tr>
<tr>
<td>FAC (%)</td>
<td>56 ± 11</td>
<td>55 ± 9</td>
</tr>
<tr>
<td>$\text{SvO}_2$ (%)</td>
<td>87 ± 4</td>
<td>79 ± 4*</td>
</tr>
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Values are mean ± SD. HR, heart rate; MAP, mean arterial pressure; RAP, right atrial pressure; CI, cardiac index; SVI, stroke volume index; SVRI, systemic vascular resistance index; ITBV, intrathoracic blood volume; EDA, enddiastolic area; ESA, endsystolic area; FAC, fractional area change; $\text{SvO}_2$, central venous oxygen saturation.

*Significant influence of sitting position (II) vs. supine position (I) ($P < 0.05$).

Fig. 1. Linear regression analysis between SVI and ITBV. SVI is depicted on the y-axis and ITBV on the x-axis. SVI and ITBV are closely correlated with each other.

Fig. 2. Linear regression analysis between SVI and EDA. A close correlation between SVI and EDA was observed, suggesting that the decrease in EDA is accompanied by a concomitant decrease in SVI.

Central venous oxygen saturation significantly decreased from 89 ± 4 to 79 ± 4%.

Regression analysis revealed a linear correlation between ITBV and SVI (r = 0.75) (Fig. 1). Similarly, EDA and SVI were closely correlated (r = 0.76) (Fig. 2). In contrast, only a weak relation could be observed for RAP vs. SVI (r = 0.40) (Fig. 3).

**Discussion**

The results of the present study demonstrate that a controlled change from the supine to the sitting body position causes a significant decrease in both ITBV and EDA in anesthetized patients. The concomitant reduction in stroke volume index strongly correlates with the decrease in ITBV as well as with the decrease in EDA. These findings suggest that ITBV and EDA are equivalent measures of cardiac preload in this clinical setting.

Assessment of cardiac preload is of primary importance in guiding volume therapy of the critically ill patient during anaesthesia and intensive care [1–3,5]. Commonly, cardiac filling pressure such as CVP and PCWP are used to guide fluid therapy in clinical routine [1–3]. However, recent studies have demonstrated that CVP and PCWP are sometimes misleading, in particular when changes in intrathoracic pressure and/or changes in myocardial compliance occur [1–3,8–10].

During past years, transoesophageal echocardiography has been used increasingly for assessment of cardiac preload [4,5,12–14]. Determination of the EDA is a measure of left ventricular filling [5,12] and has been shown to correlate well with changes in stroke volume during volume therapy or graded blood withdrawal in different studies [5,13]. Second, indicator dilution derived ITBV has been suggested as a sensitive indicator of cardiac preload as volume changes preferentially alters the volume in the intrathoracic compartment which serves as the primary reservoir for the left ventricle [1,3,7,15,16]. Accordingly, ITBV has been shown to correlate well with respective changes in SVI [1,9,17]. However, until now there has been a lack of controlled studies which focus on the relationship between EDA and SVI vs. ITBV and SVI, i.e. the validity of both volume-related indices as a measure of cardiac preload. Thus, in the present study we investigated the effects of a controlled change in body position from supine to 45° head up on EDA, ITBV, SVI, and the relationship between these variables. We have recently demonstrated that this change in body position is very effective in producing an alteration in cardiac preload reflected by a decrease in ITBV [17].

As expected, we observed a significant and consistent decrease in EDA in our patients after changing to the sitting position. Our results are in line with findings of Greim and his colleagues who also observed a significant correlation between EDA and stroke volume, the coefficient of correlation being 0.89 [6]. However, in their study the correlation deteriorated when the CI was lower than 3 L min⁻¹ m⁻² [6]. In our patients, the initial CI after induction of anaesthesia averaged below this threshold (2.5 L min⁻¹ m⁻²) and decreased significantly after the controlled change in body position. Our patients are thus to be compared with the subgroup of patients in the study of Greim and his colleagues with low CI, which may in part explain the lower coefficient of correlation between EDA and SVI. In our patients, the cardiac index in the sitting position was remarkably low indicating that the amount of volume loading prior to induction of anaesthesia could not completely compensate for the change in blood

© 2001 European Academy of Anaesthesiology, European Journal of Anaesthesiology, 18, 662–667
volume distribution. However, despite a significant decrease after changing to the sitting position, central venous oxygen saturation was within normal margins and no other signs of inadequate systemic perfusion were observed.

Recently, Tousignant and his colleagues studied the effects of volume loading with 500 mL of pentastarch on EDA, PCWP and SVI in a group of ICU patients and a second group of postoperative cardiac surgical patients [4]. They additionally stratified their patients according to the haemodynamic response after volume loading in patients with an adequate response to fluid administration resulting in an increase in stroke volume of 20% or more vs. patients with an increase of less than 20% [4]. EDA increased only in responders, whereas PCWP significantly increased in both responders and non-responders [4]. PCWP and EDA were significantly lower in responders and volume recruitable increases in SV could only be demonstrated in a small number of patients. Tousignant and his colleagues found only a modest correlation between SVI and EDA ($r = 0.60$). However, the patients included in their study represented a heterogeneous population, which cannot directly be compared with our patients, who did not suffer from haemodynamic instability. As the effects of a change in cardiac preload on stroke volume depends on the ascending part of the Frank–Starling curve, the results of the present study should thus be limited to patients with normal or only moderately depressed cardiac function. In patients with severely impaired left ventricular function, cardiac preload cannot be used as a major determinant of stroke volume.

The study of Tousignant and his colleagues demonstrate that changes in PCWP are not positively correlated with changes in stroke volume, indicating that the PCWP was not indicative for cardiac preload in their patients [4]. In the present study, RAP showed also only a weak correlation with SVI (Fig. 3). This finding is of particular relevance, as factors, which are known to alter the relationship between intravascular pressure and volume [15] (such as changes in intrathoracic pressure or catecholamine infusion) did not play a role in the present study.

In our patients, we found a significant decrease in ITBV after the change into the sitting position, which was correlated to a decrease in SVI (Fig. 2). In a study in patients undergoing aorto-coronary bypass grafting, Hoeft and his colleagues observed that changes in central blood volume (which represents ITBV minus right heart volume) correlate well with changes in stroke volume index [1]. In their study, CBV was indicative for hypovolaemia despite increased CVP and PCWP immediately after surgery [1]. More recently, in an observational investigation, Hinder and his colleagues studied the effects of cardiopulmonary bypass on cardiovascular volume status assessed by echocardiography, dye dilution and conventional pressure monitoring [7]. Hinder and colleagues found that both CVP and PCWP did not correlate with perioperative changes in EDA and ITBV. Moreover, absolute changes in ITBV and EDA were correlated with each other, Spearman’s correlation coefficient being 0.87 [7]. In contrast to our study, Hinder and his colleagues investigated neither the relation between ITBV and SV nor that between EDA and SVI, and volume replacement followed the clinical course instead of controlled variation resulting in a wide range of data.

As the calculation of ITBV by indicator dilution is partially based on cardiac output concerns have been raised with respect to a potential mathematical coupling of ITBV and SV data, which might also have influenced the observed correlation between these parameters in the current study. However, Lichtwarck-Aschoff and his colleagues recently demonstrated that a mathematical coupling between ITBV and SVI is unlikely [9]. They studied the effects of $\alpha$-adrenergic stimulation with dobutamine in an experimental model of blood withdrawal and re-transfusion. Although substantial changes in ITBV occurred after blood withdrawal, variation of cardiac output by dobutamine infusion did not result in concomitant changes in ITBV during normo- and hypovolemia respectively [9]. These experimental findings have recently been verified by McLuckie and her colleagues in a clinical setting [18]. Thus, we have no reason to question the validity of the observed relationship between ITBV and SVI, which compared favourably with the relationship between EDA and SVI.

**Conclusion**

In summary, we observed a significant decrease in ITBV and EDA after a standardized change from the supine to sitting body position, which was correlated...
with changes in SVI. We conclude that within the observed range of data both indicator dilution derived intrathoracic blood volume and echocardiographically derived end-diastolic area are equivalent indices of cardiac preload.

References