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Global end-diastolic volume could be more appropiate to reduce intraoperative bleeding than central venous pressure during major liver transection

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Abstract

Background: Central venous pressure often fails to identify the true value of cardiac preload. Our purpose is to investigate whether Global End-Diastolic Volume (GEDV) values can control hemodynamic parameters for the measurement of fluid volume, cardiac preload and blood loss during liver transection.

Methods: This was a prospective clinical study that included patients undergoing liver resection. All patients were monitored by means of PiCCO technology and 222 hemodynamic measurements were performed in 74 patients. Fluid restriction was used. Transpulmonary thermodilutions were performed at different times of surgery, namely: 1. at the beginning of surgery; 2. before hepatectomy and after selective vascular exclusion (Time 1); 3. approximately half way through the liver transection (Time 2); and 4. after liver resection (Time 3).

Results: One hundred and twenty-nine of the 222 GEDV values were decreased (prevalence of hypovolemia of 58.1%). However, twenty two of the 222 CVP values were decreased (prevalence of 10.8%). Sensitivity of CVP with regard to volume depletion (GEDV > 650 mL m^{-2}) on the times (1, 2 and 3) were 16.28 (95% CI: 4.08–28.48), 18.18 (95% CI: 5.65–30.75) and 21.43 (95% CI: 7.83–35.03), respectively. There was no correlation between CVP and GEDV.

Conclusions: GEDV values may be more appropriate for monitoring cardiac preload during liver transection.

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Key words: global end-diastolic volume; central venous pressure; preload; liver resection; hemodynamic monitoring

The maintenance of low central venous pressure values (CVP < 5 mm Hg) during liver resection has been considered one of the main strategies to minimize intraoperative bleeding, by means of a reduction of pressure in the hepatic veins [1, 2]. Increased blood loss and transfusion requirements are related to increased perioperative morbidity and mortality [3–8]. However, CVP often does not identify the true value of blood volume, fluid changes, fluid responsiveness and cardiac preload; sometimes, there is no relation between low CVP values and blood loss during liver resection [9]. Modern hemodynamic parameters such as the global end-diastolic volume index and variation in stroke volume have been demonstrated to be superior to pressure-based preload parameters, such as CVP and pulmonary arterial occlusion pressure [10–12]. We hypothesized that monitoring other hemodynamic parameters such as GEDV (Global End-Diastolic Volume), during liver resection would provide more accurate cardiac preload information. We will use this advanced monitoring for therapeutic management and to reduce blood loss during liver resection.

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Our purpose is to investigate if GEDV values can successfully control the measurement of fluid volume and blood loss during liver transection, in a liver resection model of fluid restriction.

METHODS

This was a prospective clinical study that included patients undergoing liver resection with primary or metastatic liver tumours. It was approved by our local Ethics Committee and informed consent was obtained from the patients. Only patients with two or more liver segments resected were included. We excluded patients with cardiopulmonary parameters that would prevent appropriate management of the patient preload.

We analyzed the following demographic and clinical data: age; sex; histological diagnosis; bleeding during liver transaction; hepatic transection time; and hospital stay. Laboratory test results included in the analysis were as follows: preoperative transection haemoglobin (Hb) and haematocrit (Hct) levels; postoperative transection Hb and Hct levels; postoperative creatinine level (24 hours after surgery); postoperative urea (24 hours after surgery); bilirubin (Bb) on the 5th postoperative day; prothrombin time on the 5th postoperative day; postoperative liver failure; Bb over 3 mg dL^{-1}; and prothrombin time under 50% on the 5th postoperative day.

In all individuals 5F thermistor-tipped arterial line (Pulsiocath, Pulsion Medical System, Feldkirchen, Germany) was inserted in the femoral artery and connected to a hemodynamic monitor (PiCCO$_2$: Pulsion Medical System, Feldkirchen, Germany). Based on transpulmonary thermodilution following the injection of 15 mL cold 0.9% NaCl via a conventional central venous catheter, the following were determined: Cardiac Index (CI); Global End-Diastolic Volume (GEDV); Stroke Volume Variation (SVV); Extravascular Lung Water Index (ELWI); Systemic Vascular Resistance Index (SVRI); central venous pressure (CVP); heart rate (HR); as well as systolic blood pressure (SBP). Each PiCCO measurement represents an average of three consecutive thermodilution measurements within 5 minutes.

A fluid restriction model was used in the study (1 mL kg^{-1} h^{-1}). Transpulmonary thermodilutions were performed at different times of surgery, namely: 1. at the beginning; 2. before hepatectomy and after selective vascular exclusion (Time 1); 3. approximately half way through the liver transection (Time 2); 4. after liver resection (Time 3); 5. in the postoperative intensive care unit; and 6. if the patient needed it, due to perioperative haemodynamically significant changes. CVP, systolic and diastolic pressure and heart rate were also recorded at each of these time points. During surgery, we tried to maintain GEDV values of less than 650 mL m^{-2}. Volume restriction was applied (1 mL kg^{-1} h^{-1}), while furosemide (10–20 mg), nitroglycerine or dopamine (1–5 μg kg^{-1} min^{-1}) were used at low doses, if necessary. We tried to maintain a systolic blood pressure > 90 mm Hg by adjusting the volume or using low doses of noradrenaline.

Selective vascular control was performed in all patients before liver resection. We used an ultrasonic dissector, namely CUSA, for liver transection.

STATISTICAL ANALYSIS

Quantitative parameters were expressed as frequencies and continuous variables as mean, median and standard deviation. Correlations between different parameters were studied using the Pearson correlation test and the Spearman correlation test. We used sensitivity, specificity, positive predictive value, negative predictive value and Receiver Operating Characteristic (ROC) curves to predict central venous pressure with regard to volume depletion (GEDV< 650 mL m^{-2}). For statistical analysis we used SPSS15.0®. Statistical significance was defined as $P < 0.01$.

RESULTS

Patients

A total of 74 patients were included. The mean age was 58 ± 15 years and 43% were female. The median stay was 9 days. Liver metastases from colorectal cancer were diagnosed in 20 patients (27%). The mean blood loss during liver transection was 203 ± 189 cc with a mean postoperative haemoglobin and hematocrit level of 11.8 ± 4 and 36.5 ± 6 respectively. The median time of liver transection was 50 minutes (10–120). Moreover, 3 ± 1 liver segment resections were performed (Table 1).

HEMODYNAMIC PARAMETERS

The mean CVP (T1: 9.22 ± 3.13, Time 2: 8.3 ± 3.2, T3: 7.6 ± 3.88; normal 1–9 mm Hg) was higher than 5 mm Hg, whereas mean GEDV was below the normal low limit (Time 1: 618 ±

Table 1. Perioperative data collection

Male/Female	44/31
Age (yrs)	58 ± 15
Creatinin postoperative (mg dL^{-1})	1.2 ± 3.5
Preoperative haemoglobin (g dL^{-1})	12.3 ± 1.8
Postoperative haemoglobin (g dL^{-1})	11.8 ± 4
Preoperative hematocrit (%)	36.5 ± 6
Postoperative hematocrit (%)	3.,5 ± 5,5
Bilirubin 5th postoperative day (mg dL^{-1})	3.1 ± 13
Postoperative time of prothrombin 5th day (sec)	13.4 ± 2.8
Blood loss (mL)	203 ± 189
Transection time (min)	50´(10–120)
Resected segments number	3±1
Hospital stay (days)	9

Table 2. Perioperative hemodynamic data

Parameter	Time 1 (Pre-resection)	Time 2 (Resection)	Time 3 (Post-resection)	Normal Range
CVP (mm Hg)	9.22 ± 3.13	8.3 ± 3.2	7.6 ± 3.88	1–9
GEDV (mL m^{-2})	618 ± 153.3	596.1 ± 219.8	624.51 ± 294.31	650–800
CI (L min^{-1} m^{-2})	2.49 ± 0.5	2.34 ± 0.8	2.5 ± 0.91	3–5
SVRI (Dynes cm^{-5} m^{-2})	2647.8 ± 911.88	2969 ± 312.38	2601 ± 841.78	1700–2400
ELWI (mL kg^{-1})	8.56 ± 3.2	8.79 ± 4.05	9.3 ± 5.9	3–7

CVP — central venous pressure; GEDV — global end-diastolic volume; CI — cardiac index; SVRI — systemic vascular resistance index; ELWI — extravascular lung water index

Table 3. Comparison of global end-diastolic volume (GEDV) and central venous pressure (CVP)

		GEDV ≤ 650 mL m^{-2}	GEDV > 650 mL m^{-2}
Time 1 (Pre-resection)	CVP ≤ 5 mm Hg	7	2
	CVP > 5 mm Hg	36	29
Time 2 (Resection)	CVP ≤ 5 mm Hg	8	0
	CVP > 5 mm Hg	36	30
Time 3 (Post-resection)	CVP ≤ 5 mm Hg	9	5
	CVP > 5 mm Hg	33	27

Table 4. Statistical analysis of the predictive value of central venous pressure with regard to volume depletion (GEDV ≤ 650 mL m^{-2})

	Time 1 (Pre-resection)	Time 2 (Resection)	Time 3 (Post-resection)
Sensitivity (95% CI)	16.28 (4.08–28.48)	18.18 (5.65–30.75)	21.43 (7.83–35.03)
Specificity (95% CI)	93.55 (83.29–100)	100 (98.33–100)	84.38 (70.23–98.52)
Positive predictive value (95% CI)	77.78 (45.06–100)	100 (93.75–100)	64.29 (35.61–92.96)
Negative predictive value (95% CI)	44.62 (31.76–57.47)	45.45 (32.68–58.2)	45 (31.58–58.42)
Prediction of normal range (95% CI)	58.11 (46.19–70.03)	51.35 (39.29–63.41)	54.24 (42.22–68.28)

GEDV — global end-diastolic volume; CI — confidence interval

Table 5. Correlation of baseline and follow-up levels of CI (cardiac index) to GEDV (global end-diastolic volume) and CVP (central venous pressure), respectively

	Time 1 (Pre-resection)	Time 2 (Resection)	Time 3 (Post-resection)
Correlation GEDV/CVP	r = 0.164, *P* = 0.211	r = 0.015, *P* = 0.9	r = 0.018, *P* = 0.89
Correlation GEDV/CI	r = 0.267, *P* = 0.02	r = 0.381, *P* = 0.003	r = 0.296, *P* = 0.022
Correlation CVP/CI	r = 0.287, *P* = 0.021	r = 0.1, *P* = 0.446	r = 0.026, *P* = 0.845

153.3, Time 2: 596.1 ± 219.8, Time 3: 624.51 ± 294.31; normal: 650–800 mL m^{-2}) (Table 2). 129 of the 222 GEDV values were decreased (prevalence of hypovolemia of 58.1%). However, twenty two of the 222 CVP values were decreased (prevalence of 10.8%) (Table 3).

PREDICTIVE VALUE OF CVP WITH REGARD TO HYPOVOLEMIA

The sensitivity, specificity, as well as positive (PPV) and negative predictive values (NPV) of CVP with regard to volume depletion (GEDV < 650 mL m^{-2}) at different times were as follows: T1 (16.28 %, 93.55 %, 77.78 % and 44.62 %); T2 (18.18 %, 100 %, 100 % and 45.45 %); T3 (21.43 %, 84.38 %, 64.29 % and 45%) (Table 4). We found a poor predictive capacity to show hypovolemia with CVP for different times: area under the curve (Curves ROC) of 0.576, 0.573 and 0.556 respectively There was no correlation between CVP and GEDV at different times: T1 (r = 0.164; *P* = 0.211), T2 (r = 0.015; *P* = 0.9) and T3 (r = 0.018; *P* = 0.89). (Table 5, Fig. 1).

CORRELATION LEVELS OF CI TO GEDV AND CVP RESPECTIVELY

GEDV significantly correlated to CI at all three times: (Time 1: r = 0.267, *P* = 0.02; Time 2: r = 0.386, *P* = 0.003; Time 3: r = 0.296, *P* = 0.022). However, CVP did not correlate: T1 (r = 0.287, *P* = 0.02), T2 (r = 0.1, *P* = 0.446) and T3 (r = 0.026, *P* < 0.845). (Table 5, Figs 2, 3).

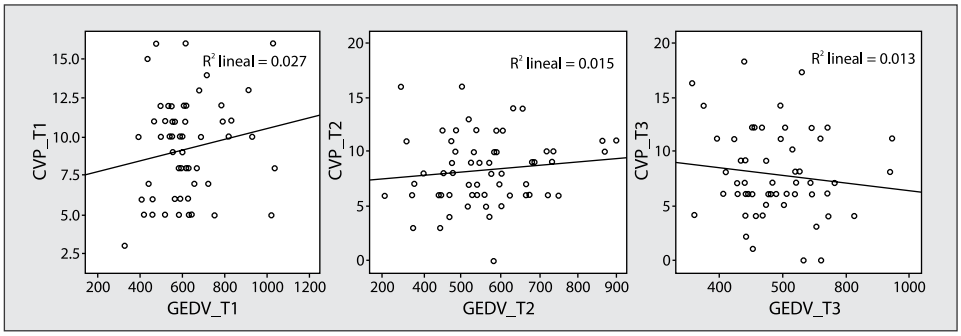

Figure 1. No correlation between GEDV (Global End-Diastolic Volume) and CVP (Central Venous Pressure) (T1, T2, T3)

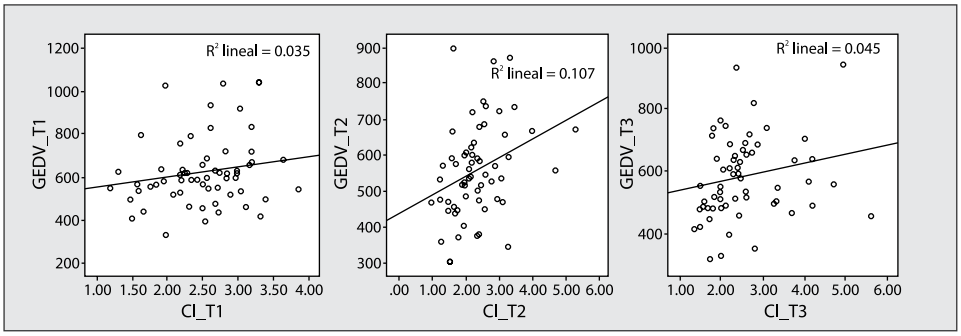

Figure 2. Significant correlations between GEVD (Global End-Diastolic Volume) and CI (Cardiac Index) (T1, T2, T3)

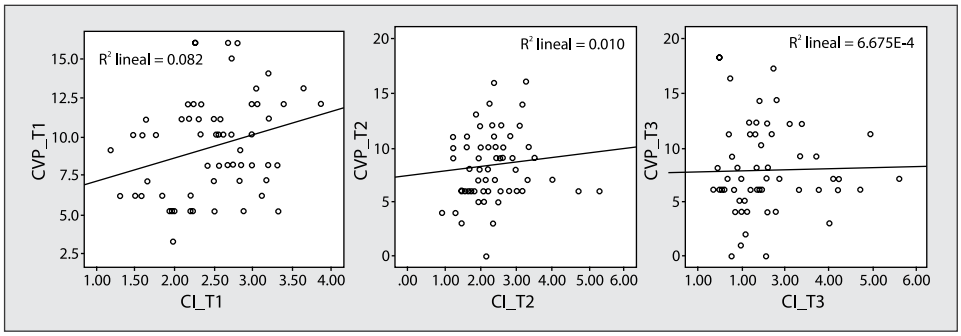

Figure 3. No correlation between CVP (Central Venous Pressure) and CI (Cardiac Index) (T1, T2, T3)

OUTCOME

All patients were volume-resuscitated according to PiCCO parameters. The mean postoperative creatinine level (mg dL^{-1}) was 1.28 ± 3.5 while the mean Bilirubin level (mg dL^{-1}) and prothrombin time (in sec) on the fifth postoperative day were 3.1 ± 1.3 and 13.4 ± 2.8 respectively. The median hospital stay was 9 days (Table 1).

DISCUSSION

Blood loss during liver transection has been related to increased morbidity and mortality. One of the strategies used to limit blood loss involves reducing the pressure of the hepatic veins [2]. Patients with blood loss over 2000 mL have shown an association with a significant increase in mortality of up 43%. Management of a low cardiac preload allows the pressure of the hepatic veins and blood loss during hepatic transection to be reduced. Maintenance of low central venous pressure values (below 5 mm Hg) can reduce the bleeding to a mean of 200 mL; in contrast, if CVP values are over 5 mm Hg, blood loss can reach values of about 1000 mL. Smyrniotis *et al.* [7], considered that CVP values over 5 mm Hg were associated with greater blood loss and longer hospital stays. Considering CVP values under 5 mm Hg, there were no differences in blood loss with respect to the methods used for vascular access. Historically, liver surgical groups have considered that CVP can identify cardiac preload and, therefore, limit blood loss during liver transection. It is very important to know the exact cardiac

preload value in order to identify the fluid volume of the patient and whether fluid changes are related to cardiac output. However, the question remains whether CVP is the best indicator of cardiac preload. In 2008, Mark *et al.* [9] performed an exhaustive review of the medical literature which included 24 studies involving a total of 803 patients. In five studies, CVP was compared with blood volume management, while 19 studies determined the relationship between CVP values and changes in cardiac performance when there were fluid challenges. They concluded that CVP values were not related to blood volume and were limited in predicting cardiac hemodynamic response to fluid changes; they also doubted the ability of CVP to allow one to make decisions with regard to fluid volume therapy. In our study, we tried to determine the value of new parameters, such as GEDV, in order to more accurately identify the value of intravascular fluid volume and the cardiac preload, for reducing bleeding during transection, as well as improving fluid management during hepatic transection. Identifying these values using PiCCO technology, dynamically, in real-time, will allow us to improve our therapeutic decisions. Haemodynamic monitoring employing PiCCO system parameters has been used in numerous studies with surgical or non-surgical patients who required intensive care [13–15]. However, there is a great difference between septic patients and surgical patients regarding the duration of ventilation or surgical hemodynamic changes. Although in liver surgery this monitoring has been used in patients during liver transplantation [16, 17], there are few references in the literature about liver transection controlled by stroke volume variation (SVV) and GEDV values [18]. Our aim was to investigate whether GEDV values can successfully control the measurement of fluid volume and, therefore, blood loss during liver transection and cardiac function. In our study we did not find good correlations between CVP and GEDV. Indeed, 129 of the 222 GEDV values were decreased (prevalence of hypovolemia of 58.1%). However, twenty two of the 222 CVP values were decreased (prevalence of 10.8%). Moreover, the sensitivity of CVP with regard to volume depletion (GEDV < 650 mL m^{-2}) at the three times (1, 2 and 3) was very low.

We obtained intravascular fluid status before starting liver resection, both during liver transection and after resection. This allowed us to gain optimal control of fluid therapy, without organ dysfunction, and with minimal blood loss at each step of the operation. Pre-resection and during liver resection, GEDV values showed better sensitivity for assessing volume status and correlation with cardiac index with respect to CVP values and, therefore, to the management of fluid therapy. Pre-, intra- and post-resection GEDV values were related to CI ($P = 0.000$). However, no significant relationship existed between the values of CVP and cardiac functionality. Cardiac preload values after vascular exclusion and using a restrictive fluid model and measured by pre-resection GEDV values, allowed for a low level of bleeding during resection. In our study, the mean blood loss was 200 ± 189 mL, maintaining postoperative haemoglobin of 11.8 ± 4 mg dL^{-1}. An optimal cardiac preload management using GEDV assessment, before and during parenchymal transection may minimize blood loss, due to blood loss in liver resection being proportional to the pressure gradient of the vascular walls. However, we also have to control the optimal fluid volume status in order to obtain adequate tissue perfusion and functionality in the target organs.

Our patients were treated with a fluid restricted model for avoiding blood loss, due to which we had to control perioperative renal function. Our patients tolerated this fluid restriction model and it did not compromise renal function. Thus, the successful control of fluid volume by means of GEDV values may help us to control postoperative renal function [19].

These results mean that maintaining good control of fluid volume and blood loss during liver transection, by means of GEDV values, is related with liver dysfunction. Therefore, we can use such parameters to prevent postoperative liver failure, due to our control of hepatic sinusoidal pressure [20].

Thus, during liver transection we have to assess volume status and balance fluid infusion in order to avoid blood loss and inadequate tissue perfusion. We consider that if there is a successful correlation and control, we may limit perioperative morbidity, as well as the dysfunction of various organs [2].

In conclusion, our results demonstrate that GEDV values are appropriate and safe parameters that may be used for monitoring cardiac preload, blood loss limitations, as well as predicting changes in cardiac output due to volume therapy during liver transection.

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