

## Fluid Optimization in Liver Surgery

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### Abstract

**Study's purposes:** To reduce bleeding, hepatectomies are usually performed maintaining low central pressure (CVP) combined with extrahepatic control flow and this management can lead hemodynamic instability and reduction in oxygen delivery. This study analyzes hemodynamic changes and so the derived fluid management, in patients undergoing liver resection, through the Vigileo/FloTrac system.

**Basic procedures:** Seventeen patients were included. Low CVP, below 4 mmHg, was reached by loop diuretics. Hemodynamic parameters were recorded and blood gas analysis was also performed. At the end of resection, fluid replacement was carried out with 500 ml of crystalloid solution in 20 minutes evaluating changes in CVP, Cardiac Index (CI) and Stroke Volume Variation (SVV).

**Main findings:** During Pringle maneuver, Cardiac Index resulted stable through a modification in heart rate and vascular resistances ( $p < 0.01$ ). Only SVV significantly changed during Pringle maneuver ( $p = 0.03$ ) and not CVP ( $p = 0.8$ ). In all patients the oxygen delivery was maintained upper 600 ml/min/m<sup>2</sup>. Fluid optimization was performed with 1917 ml  $\pm$  1161 ml of crystalloid solution with a significant reduction in SVV ( $p < 0.01$ ) about 7% despite a CVP of 5 mmHg.

**Conclusions:** We suppose that SVV can replace CVP in major hepatectomy management. Regarded results we can conclude that a good peripheral perfusion can be reached also with a fluid restrictive regimen avoiding overload and postoperative edema.

**Keywords:** Cardiovascular system-responses; Fluid therapy; Heart-cardiac output

### Introduction

Blood loss is the major complication during liver resection and morbidity and mortality are directly related with bleeding and transfusions [1,2]. To avoid this, hepatic surgery is performed with the maintenance of a low central pressure combined with extrahepatic control flow. The intermittent Pringle maneuver (IPM), which consists in clamping the hepatoduodenal ligament and blocks the hepatic inflow [3], is frequently applied. However the combination between low CVP and vascular exclusion can determine hemodynamic instability and systemic hypoperfusion that can persist at the end of resection and increase mortality according to the new concept of goal directed therapy.

Goal directed therapy (GDT) is a perioperative management that improve tissue perfusion and outcome, through cardiac output or oxygen delivery optimization [4]. Actually, dynamic hemodynamic parameters such as SVV (stroke volume variation), have been shown to be superior to CVP in predicting fluid responsiveness. According to this idea, in this surgery, a monitoring more advanced than CVP, avoiding pulmonary artery catheterization, results essential. In fact, Swan-Ganz remains a gold standard but with limitations in the use for invasiveness and complications such as arrhythmias, valvular lesions and rupture of the pulmonary artery [5].

Consequently the technique of arterial waveform analysis, considered minimally invasive, was developed. FloTrac/Vigileo is one of available devices for the assessment of hemodynamic parameters through the minimal invasive methods of analysis of arterial pressure waveform. FloTrac/Vigileo provides continuous cardiac output (CO), stroke volume (SV) and stroke volume variation (SVV) through an existing arterial line. Potential advantages of this system are the absence of manual calibration, the need of a peripheral artery and also an automatic recalibration every 60 sec to assess changes in arterial compliance.

The purpose of this study is the analysis of hemodynamic status in patients undergoing major hepatic surgery, optimizing fluid replacement at the end of resection using Vigileo/FloTrac system hemodynamic monitoring.

### Methods

Permission was obtained from the local Ethical Committee (ID 656/11). After written informed consent was obtained from all subjects, patients, aged 30-70 years, with American society of anesthesiologist physical status I-III, scheduled for elective major hepatic surgery, from September 2011 to February 2012 were enrolled in this study.

Exclusion criteria were refusal of enrolment, cirrhosis, systolic ventricular contractility or diastolic relaxation alterations, ischemic or

valvular diseases, absence of sinus rhythm and impaired renal function.

General anesthesia was induced with propofol 2 mg/kg IV, and sufentanil 0.5 mcg /kg IV, and tracheal intubation was facilitated with cisatracurium 0.15 mg/kg IV, then maintained with a continuous infusion of 0.3 mcg/Kg/h IV.

Anaesthesia maintenance was performed with sevoflurane (in an oxygen/air mixture) and sufentanil in continuous infusion (3-5 mcg/Kg/min). The minimum alveolar concentration of sevoflurane was set to achieve a Bispectral Index (BIS) value between 40 and 60 [6].

Mechanical ventilation was set with a tidal volume of 8 ml/kg, PEEP 0 cmH<sub>2</sub>O and with an inspiration/expiration rate of 1:2. These parameters remained stable during the procedure. The respiration rate was adjusted to obtain an etCO<sub>2</sub> between 38-45 mmHg. The monitoring was performed with ECG, pulse oximetry and non-invasive blood pressure before induction and after a 20 G catheter was placed in left radial artery and connected to Vigileo/FloTrac system, and after zeroing CO was displayed with SVV.

A double-lumen venous catheter was placed in right internal jugular vein to monitor CVP, venous oxygen saturation (Svo<sub>2</sub>) and for rapid infusion. Initially, to achieve a low CVP (between 2 and 4 mmHg), loop diuretics were administered; norepinephrine was infused if mean arterial pressure was less than 60 mmHg or oxygen deliveries below 600 ml/m<sup>2</sup>.

The intermittent Pringle maneuver (IPM), which consists in clamping the hepatoduodenal ligament and blocks the hepatic inflow [3] is applied during surgery [7].

Hemodynamic parameters and BIS were recorded every 15 min during 3 periods: before (Time 1), during (Time 2) and after pedicle

clamping (Time 3). Arterial and venous blood gas analysis was performed during surgical intervention. At the end of resection, a fluid replacement was carried out with 500 ml of crystalloid solution in 20 minutes evaluating changes in CVP, CI and SVV.

The algorithm used in this study, was based on a cutoff for SVV of 13% to distinguish between fluid responders and not [8]. Specifically, if SVV is greater than 13%, patients should respond to fluid replacement with an increase in Stroke Volume.

### Statistical analysis

A general linear model for repeated measurements was applied in order to evaluate the relationship between time and the following parameters: MAP, heart rate (HR), systemic vascular resistance index (SVRI), CI, SV, SVV, CVP. A post-hoc analysis with Bonferroni correction was carried out too.

Mean and Standard Deviations (SD) were used to report data. The statistical significance level was set at p=0.05 and SPSS software 12.0 was used to perform the analysis.

### Results

17 patients (9 men and 8 women) undergoing liver surgery (13 for liver metastases and 4 for primitive liver cancer), were enrolled. They were 58 ± 10 years old; the median body surface area was 1.89 ± 0.3 m<sup>2</sup> with body weight 75 ± 14 kg and height 167 ± 7 cm.

The maintenance of anaesthesia with sevoflurane with a median MAC of 1.6% resulted adequate with a median BIS value of 41. During anaesthesia a mean diuresis of 2 ml/kg/h was maintained. No patients need norepinephrine infusion. In Table 1 data of parameters under study are shown with respect to Time.

	PAM	FC	RSVI	CI	SV	SVV	PCV
Time 1	83.65 (8.99)	71.20 (8.08)	1290.18 (224.37)	2.60 (0.34)	64.03 (7.05)	12.15 (3.80)	2.08 (1.29)
Time 2	87.06 (12.96)	79.20 (10.48)	1480.00 (323.17)	2.51 (0.36)	62.49 (7.36)	14.65 (4.24)	1.85 (1.31)
Time 3	80.24 (9.93)	70.60 (12.87)	1125.06 (223.10)	2.89 (0.44)	72.53 (9.19)	7.47 (1.51)	5.23 (1.80)

**Table 1:** Mean (SD) of parameters at the three points in time.

As far as changes in time are concerned, no significant associations with time were found with respect to MAP. So despite low CVP, MAP resulted stable within normal range of values also during clamping without relevant changes with a median of 87 ± 12.96 mmHg. Moreover CI resulted stable during extrahepatic control flow (p=0.71). The results of the post hoc analysis are shown in Table 2. During Pringle maneuver we noted a significant increase in HR and in systemic resistances (respectively p<0.01 and 0.02).

	FCT	RSVI	CI	SV	SVV	PCV
Time 1 vs. Time 2	<0.01	<0.02	0.71	0.35	0.03	0.80
Time 1 vs. Time 3	1	<0.01	<0.01	<0.01	<0.01	<0.01
Time 2 vs. Time 3	0.03	<0.01	<0.01	<0.01	<0.01	<0.01

**Table 2:** Post hoc analysis (p-values).

Furthermore between Time 1 and 2 we did not observe a statistical significance in CVP variation but in SVV (p=0.8 and 0.03).

At the end of liver resection, fluid replacement was carried out with 500 ml of crystalloid solution in 20 minutes with a median of 1917 ml ± 1161 ml of crystalloid solution and during this stage, SVV significantly changed (p<0.01) and resulted in a reduction about 7% in all patients demonstrating an adequate fluid replacement despite a median CVP of 5 mmHg. Median estimated blood loss is 335 ml ± 319 ml so no patient needed blood transfusion.

### Discussion

Blood loss is the major complication during liver resection and morbidity and mortality are directly related with bleeding and transfusions [2,9]. Hepatectomies can be complicated also by an important hemodynamic instability resulting from low CVP and Pringle maneuver.

In fact a CVP of 5 mmHg or less is considered optimal and has been showed to be associated with less bleeding during parenchymal transection and reduced need of transfusion [10,11] but it should increase the risk of air embolism and systemic tissue hypoperfusion.

Ya Guo et al. evaluated the influence of different values of low CVP on hemodynamic parameters, oxygen transport and the rate of blood loss during partial hepatectomy in pig models [12]. They founded that blood loss in the CVP  $\geq 5$  cmH<sub>2</sub>O group was more significant and also that there was a significant reduction in MAP, CO and CI with CVP < 2 cmH<sub>2</sub>O.

DO<sub>2</sub> decreased when CVP < 2 cmH<sub>2</sub>O, VO<sub>2</sub> when CVP < 1 cmH<sub>2</sub>O, and ERO<sub>2</sub> when CVP < 1 cmH<sub>2</sub>O. So they concluded that a CVP at 2 to 3 cmH<sub>2</sub>O seems to be optimal for hepatic resection to avoid bleeding, hemodynamic instability and also failure in oxygen delivery.

So this management minimize mortality, facilitates operative control of hemorrhage, but also preserves renal function [13].

In this study we describe hemodynamic changes that occur during major liver resections, performed in non-cirrhotic patients, associating to traditional monitoring the Vigileo/FloTrac system. Actually dynamic parameters such as SVV (stroke volume variation), have been shown to be superior to CVP and static data in predicting fluid responsiveness so Swan-Ganz is rarely used for limitations in invasiveness and complications such as arrhythmias, valvular lesions and rupture of the pulmonary artery [14]. Consequently the technique of arterial waveform analysis, considered minimally invasive, was developed. FloTrac/Vigileo provides continuous cardiac output (CO), stroke volume (SV) and stroke volume variation (SVV) through an existing arterial line. Potential advantages of this system are the absence of manual calibration, the need of a peripheral artery and also an automatic recalibration every 60 sec to assess changes in arterial compliance. This system is validated by various studies, for example Hofer et al. compared FloTrac/Vigileo system and PiCCO for prediction of fluid responsiveness using SVV and founded the same accuracy [15]. A meta-analysis published in 2009 on *Journal of Cardiothoracic and Vascular Anesthesia* conclude that, with the introduction of software version 1.07, there was an improvement of FloTrac/Vigileo that results comparable to thermodilution measurements [16]. Vigileo/FloTrac system seems adequate also in patients with circulatory failure after liver transplantation [17].

So SVV is a dynamic parameter helpful in determining fluid responsiveness with a cutoff of 13%. Previously, during liver resection with hepatic vascular exclusion, important hemodynamic changes were demonstrate with cardiac output reduction and increase in systemic vascular resistance with a compensatory role for arginine vasopressin and sympathetic systems [18] that explains the hemodynamic tolerance, despite the marked decrease in venous return, after caval clamping. We performed only portal triad clamping but also we observed a sympathetic compensatory phenomenon characterized by stability in Cardiac Index and in MAP balanced by a statistically significant modification in HR and SVRI despite a reduction in venous return.

Thanks to the use of the Vigileo/FloTrac we observed changes between CVP and SVV. Stroke volume variation seemed not to be in relationship, in any moment of liver resection, with central venous pressure. It is moreover important that this one, unlike SVV, did not result in statistical changes before and after Pringle maneuver.

A previous systematic review demonstrated a very poor relationship between CVP and blood volume and so CVP should not be used to make clinical decisions regarding fluid management [19]. In addition, in other studies SVV results usefulness in predict hypovolemia in septic shock, in reduced cardiac function and in cardiac surgical patients [20-22].

The same should be considered regard liver resection with next application of arterial waveform-derived dynamic variables for anesthesiology management [23], mentioning that SVV seems a predictor of blood loss as previously evaluated in donors undergoing right hepatectomy [24]. The use of SVV in major abdominal surgery improves outcome [25] and stability [26] related to the concept of goal directed therapy (GDT), in surgical patients. Goal directed therapy (GDT) is a perioperative management that improve tissue perfusion and outcome, through cardiac output or oxygen delivery optimization [26].

Shoemaker et al. introduced in 1980 the GDT into the perioperative care of high risk surgical patients [27] with a reduction in mortality from 38 to 21%.

We can identify high risk surgical patients such as patients with individual mortality risk greater than 5% (ASA IV mortality 18.3% and V mortality 93.3%) [28] or with a surgical risk greater than 5% [28,29]. In intra and postoperative period, the increase in oxygen consumption causes organ dysfunction and also morbidity and mortality especially in this kind of patients unable in provide for rising oxygen delivery. However, Hamilton et al. demonstrated an advantage with the application of GDT also in patients with moderate risk [30].

GDT is based on supranormal values of Cardiac Index and of Oxygen Delivery and consumption that we simply reached thought the use of Vigileo.

In this study, stability during Pringle maneuver allows maintaining a DO<sub>2</sub> greater than 600 ml/min/m<sup>2</sup> with a median VO<sub>2</sub> of 108 ml/min/m<sup>2</sup> and then an ERO<sub>2</sub> of 11%.

Blood gas analysis performed during Pringle maneuver demonstrated SvO<sub>2</sub> greater than 75% and pH within normal range showing a good peripheral perfusion. Blood lactate concentration achieved a maximum of 7 mmoli/L that, we suppose, resulted from a reduction in hepatic metabolism rather than from reduced perfusion.

So despite low CVP, in all patients oxygen delivery was maintained upper 600 ml/min/m<sup>2</sup>; so we can conclude that a good peripheral perfusion can be reached also with a fluid restrictive regimen avoiding overload and postoperative edema.

For hemodynamic optimization, seems reasonable that indirect perfusion indexes should be used in low risk patients and/or surgery, while for high risk should be used a more advanced monitoring. This is true especially in liver resection where we reach initially an extreme hypovolemia until a fluid replacement at the end of surgery.

## Funding

Only departmental funds were used for this study. No external funds were obtained

## Implication Statement

Blood loss is the major complication during liver resection so hepatic surgery is performed with a low central pressure combined with extrahepatic control flow.

The purpose of this study is the analysis of hemodynamic status in patients undergoing major hepatic surgery using Vigileo/FloTrac monitoring.

## Contributions

- De Cosmo Germano: Study design and writing up of the first draft of the paper.
- Levantesi Laura: Study design, patient recruitment, data collection and writing up of the first draft of the paper.
- Chiara de Waure: Data analysis with a results section review.
- Oggiano Marco: Patient recruitment, data collection and writing up of the first draft of the paper.
- Elisabetta Congedo: Patient recruitment, data collection and writing up of the first draft of the paper.
- Federico Fiorini: Patient recruitment, data collection and writing up of the first draft of the paper.
- Flaminio Sessa: Patient recruitment, data collection and writing up of the first draft of the paper.

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