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TRANSOESOPHAGEAL DOPPLER MONITORING FOR FLUID AND HEMODYNAMIC TREATMENT DURING LUNG SURGERY

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ABSTRACT. Introduction. Patients undergoing lung resection are vulnerable to fluid overhydration. Recently, goal-directed fluid therapy using transoesophageal Doppler monitoring (TDM) has been shown to improve postoperative clinical outcome. The aim of this study was to assess the feasibility of TDM during open-chest procedures for guiding fluid and hemodynamic treatment. **Methods.** We performed an observational prospective study including 127 high-risk patients undergoing lung cancer resection. A restrictive fluid strategy was targeted to achieve a stroke volume index (SVI) ≥ 30 ml/min/m^2. Besides standard hemodynamic measurements, stroke volume index (SVI), corrected flow time (FTc), maximal acceleration (MA) and velocity (PV) were recorded during two-lung ventilation (TLV) and one-lung ventilation (OLV). **Results.** Doppler flow tracings could not be obtained in 4 patients during TLV (3.1%) and in 6 patients during OLV (4.9%). Preoperatively, 96 pts had SVI ≥ 30 ml/min/m^2 (N-SVI group) whereas 21 patients had SVI < 30 ml/min/m^2 (L-SVI group) associated with lower FTc values. After OLV, SVI transiently decreased ($-17 \pm 9\%$; $P < 0.05$) in the N-SVI group whereas in the L-SVI group, SVI increased steadily until the end of surgery ($+40 \pm 12\%$). Other flow-related parameters as well as heart rate and mean arterial pressure remained unchanged. Surgical and medical characteristics did not differ between the two groups, except that larger volumes of colloids were administered intraoperatively in the L-SVI group ($+2.2 \pm 0.6$ ml/min/h compared with N-SVI group, $P < 0.05$). **Conclusion.** In thoracic surgical patients, TDM can be used to detect and correct low flow conditions and to guide hemodynamic support during the intraoperative period.

KEY WORDS. transoesophageal Doppler, hemodynamic, lung surgery, one-lung ventilation.

INTRODUCTION

Given concerns regarding the clinical utility and the safety profile of flow-directed balloon tipped pulmonary artery catheter, alternative minimally invasive techniques for cardiac output estimation have emerged over the last two decades [1–4]. Transoesophageal Doppler monitoring (TDM) allows non-invasive beat-to-beat measurement of blood flow in the descending aorta, based on direct measurements of red cell velocity and aortic diameter [5, 6]. This simple and reproducible technique has been validated for cardiac output measurement against the reference techniques, namely thermodilution, the Fick method and electromagnetic flow meters [3, 4].

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Using TDM, optimization of fluid therapy has been shown to improve clinical outcome and to shorten the hospital length of stay after various types of cardiac and non-cardiac procedures, except thoracic surgery [7–9]. Actually, accurate Doppler flow profile and aortic diameter measurements might be difficult to obtain during intra-thoracic surgical manipulations and one-lung ventilation (OLV). In these thoracic surgical patients, excessive fluid infusion (e.g., >3.5 l/24 h) and conventional ventilation with high tidal volume and inspiratory pressure have been identified as major risk factors of mortality and acute lung injury (ALI) [10]. Accordingly, the current perioperative risk-reducing strategies entail the application of low tidal volume and a restrictive fluid regimen over the first 24 h. An individualized hemodynamic approach guided by TDM's parameters would likely improve tissue oxygen transport by correcting "silent" hypovolemia while preventing fluid overload.

This pilot study was designed to assess the feasibility of continuous flow measurements using TDM during open-chest procedure and to describe the hemodynamic response in patients managed by a standardized protocol regarding the administration of fluid and vasopressor drugs.

MATERIAL AND METHODS

Patient selection

Between September 2005 and December 2007, 579 consecutive patients scheduled for elective lung cancer resection were screened for the presence of known risk factors for cardiopulmonary complications: planned pneumonectomy or bi-lobectomy, age >65 years, history of chronic alcohol consumption (>60 g/day), diabetes mellitus, cardiac insufficiency (left ventricular ejection fraction <40%, or a history of past acute heart failure), coronary artery disease (history of myocardial infarct, Q wave on the ECG, positive stress test or coronary angiogram), cerebrovascular disease and predicted postoperative lung perfusion of <55% of total lung perfusion. Patients with at least three risk factors were considered eligible for the study. Patients with preoperative arrhythmia and contraindications to TDM (i.e., oropharyngeal or oesophageal abnormalities, coagulation disorders, coarctation or aneurysm of the aorta) were all excluded. This observational study was approved by the local university hospital ethics committee and written informed consent was obtained from all selected patients.

Patient management

After patient arrival in the operating room, an intravenous (i.v.) infusion of normal saline was started and standard anesthetic monitoring was applied, including continuous three-lead ECG, pulse oximetry (SpO_2), invasive arterial monitoring and bispectral analysis of the EEG (BIS). An epidural catheter was inserted at the T4/T5 or T5/T6 interspace and thoracic epidural anesthesia (TEA) was conducted with a mixture of bupivacaine 0.25% and fentanyl 0.0002% administered intraoperatively (initial bolus of 7–10 ml followed by 0.1 ml/kg/h) and continued at a lower dosage (bupivacaine 0.1% and fentanyl 0.0002%) for the first 48–72 postoperative hours. All patients underwent lung resection through an antero-lateral thoracotomy and received antibiotics for 24 h (cefuroxime 1.5 g/8 h).

Anesthesia was induced with sufentanil (5–10 mcg) and propofol (1.5–2.5 mg/kg). After loss of consciousness, neuromuscular block was achieved with rocuronium (0.6 mg/kg), a left-sided double-lumen tube was inserted and its correct position was confirmed by fiberoptic bronchoscopy. Using a pressure controlled mode, the lungs were ventilated with low tidal volume (4–6 ml/kg ideal body weight) and positive end expiratory pressure (PEEP) that was set at the lower inflection point of the pressure-volume curve. The respiratory rate and the inspiratory oxygen fraction were adjusted to target $SpO_2 > 94\%$ and end-tidal CO_2 concentrations between 4 and 5.5%. Anesthesia was maintained stable by adjusting the rate of propofol infusion to achieve BIS values between 40 and 50. Body temperature was kept above 36°C using fluid and air warming devices.

Following tracheal intubation, a TDM device covered with a gel-instillable latex sheath was inserted orally in the mid-oesophagus and connected to the data-processing/recording console (Hemosonics 100 Arrow International, Reading PA). The tip of this flexible oesophageal probe contains two ultrasonic transducers: a 5 MHz pulsed Doppler transducer (mounted at 60°, with a divergent planar beam angle of 40°) that interrogates blood flow over the entire aortic cross-section, and a 10 MHz M-mode echo (mounted at 90°, with a thin divergent beam of 4°) that allows high resolution identification of the aortic borders. Demographic data (age, height and weight) were introduced into the recording console. The position of the TDM was periodically adjusted to detect the largest aortic diameter and to obtain sharply defined flow velocity waveforms with minimal spectral dispersion and high-pitched acoustic signals.

Measurements

A complete set of Doppler flow-related variables was recorded at the following consecutive time periods: (1) during two-lung ventilation (TLV), 5 min after tracheal intubation in the supine position baseline and in the lateral decubitus before surgical incision, (2) 2 min, 10 min, 20 min, and 30 min after the start of OLV, (3) after chest closure. The same investigator, trained to this technique, performed all the measurements that were averaged over 5 min after achieving a stable hemodynamic state. The ultrasonic hemodynamic flow profile was updated every 8 s and included stroke volume (SV), corrected flow time (FTc), peak velocity (PV), maximal acceleration (MA). SVI was calculated as the ratio of SV to body surface area.

Standard hemodynamic and respiratory variables were also averaged over each three study periods and included the heart rate (HR), mean arterial pressure (MAP), tidal volume (V_T) as well as plateau inspiratory pressure ($P_{plateau}$) and positive end expiratory pressure (PEEP).

Demographic, clinical, surgical and anesthetic data as well as perioperative complications were abstracted from a prospective registry including all patients who underwent thoracic surgery. These data were collected by a study nurse, entered in the database and crossed checked for accuracy. Intra – and postoperatively, the use of vasopressor drugs was recorded as well as the urine output, chest drainage and the amount of fluid intake (colloids, crystalloids and blood products). On the first day after surgery, arterial oxygen pressure (PaO_2 in kPa) was measured using a blood gas analyzer (ABL-5 10 analyzer, Radiometer, Copenhagen, Denmark) and the oxygenation index was calculated as the PaO_2/FIO_2 ratio.

Design of the study

In this prospective cohort study, fluid intake and vasoactive drugs were prescribed according to a standardized protocol. Intraoperatively, fluid management guidelines included: (1) crystalloids to compensate for preoperative fasting (2–3 ml/kg over 30 min) as well as urinary and evaporative fluid losses (2 ml/kg/h), (2) colloids to replace surgical blood losses (1:1 volume ratio), (3) additional colloids (repeated biol of 200 ml) in patients with low stroke volume index (SVI < 30 ml/min/m^2), (4) i.v. vasoconstrictors (ephedrine 5 mg and/or phenylephrine 50 mcg) to correct vasoplegia (arterial pressure <90 mmHg and SVI ≥ 30 ml/min/m^2), 5) red blood cell concentrates if hemoglobin level below 80 g/l). For the first 48 h after surgery, i.v. crystalloids and oral drinks were limited within a range of 20–25 ml/kg/day, the transfusion threshold was set at 80 g/l and diuretics were given if body weight gain exceeded 1.5 kg.

Based on the first hemodynamic assessment obtained after TDM insertion, patients were separated into two groups: those with low SVI (<30 ml/min/m^2; L-SVI group) and those with normal SVI (>30 ml/min/m^2; N-SVI group).

Statistical analysis

Data are expressed as means ± SD or numbers (%). Kolmogorov–Smimov test was used to test for normality. Unpaired Student *t*-test, Mann–Whitney *U* tests and Chi-squared tests were used as appropriate for comparison between groups. Two-way analysis of variance was used to evaluate the effects of time, group allocation and their interaction on the continuous variables. When statistical significance was reached, the Bonferroni post hoc test was used to compare the L-SVI and N-SVI groups at each time points. One-way analysis of variance with Dunnett's multiple comparisons test was used to compare variable at each time point with baseline preoperative values. The statistical software SPSS version 13.0 was used and $P < 0.05$ was considered significant.

RESULTS

Over a 3-year period, 579 patients underwent elective lung resection and 127 of them presented with three or more risk factors for cardiopulmonary complications. Insertion of the Echo-Doppler probe did not require direct laryngoscopy in any patient. Before surgical incision, appropriate Doppler flow signals with aortic wall tracings were obtained in 117 patients within less than 2 min in 98 cases (77.2%) and 3 to 4 min in the remaining cases (18.1%). Doppler-related flow parameters could not be obtained in 4 patients during two-lung ventilation (3.1%) and in 6 patients during OLV (4.9%). Failure to achieve correct Doppler flow tracings were always associated with irregular or poorly defined inner borders of the descending aorta. There was no complication related to the use of TDM.

At the start of surgery, 21 patients had low SVI (L-SVI group) and 96 pts had SVI higher than 30 ml/min/m^2 (N-SVI group). The two groups did not differ regarding demographic and preoperative clinical and functional data (Table 1).

The time course of transoesophageal Doppler parameters is illustrated in Figure 1. Preoperatively, patients in the L-SVI group presented significantly lower FTc compared with those in the N-SVI group. After the start of OLV, SVI transiently decreased ($-17 \pm 9\%$; $P < 0.05$) in the N-SVI group whereas in the L-SVI group, it increased steadily until the end of surgery (+ 40 ± 12% and 13 ± 6% compared with baseline values, respectively). In both groups, the aortic diameter remained constant (4.5 ± 1.8% variation) and there

Table 1. Demographic and clinical patient's characteristics; mean (SD) or number (%)

	N-SVI group $n = 96$	L-SVI group $n = 21$
Age (year)	63 (12)	61 (11)
BSA (m^2)	1.82 (0.18)	1.86 (0.21)
Gender (M/F)	15/6	59/37
ASA classes 3 and 4 (n [%])	41 (35)	10 (48)
Medical history (n [%])		
Hypertension	50 (52)	14 (67)
Coronary artery disease	26 (27)	5 (24)
Heart Failure	22 (23)	5 (24)
Diabetes mellitus	17 (18)	3 (14)
Alcohol	27 (28)	8 (38)
Current smoker	68 (71)	16 (76)
Ex-smoker (>6 months)	9 (9)	3 (14)
Lung functional volume		
FVC, % predicted value	73 (13)	70 (12)
FEV_1, % predicted value	69 (11)	67 (12)
Laboratory data		
Hb (g/l)	136 (16)	139 (18)
Creatinine (mg/l)	77 (16)	81 (16)

Data are expressed as means (standard deviation) or number of patients (or percentage, %).
BSA, body surface area; FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 s; Hb, hemoglobin.
No statistical difference between the two groups.

was no significant change in MA and PV throughout the study period. At the end of surgery, all Doppler flow parameters were comparable between the two groups.

In both groups, HR and MAP remained stable throughout the whole procedure and similar increases in $P_{plateau}$ occurred following the start of OLV (Table 2).

As shown in Table 3, perioperative surgical and medical characteristics did not differ between the two groups, except that larger volumes of colloids were administered intraoperatively in the L-SVI group compared with the N-SVI group (+2.2 ± 0.6 ml/min/h, $P < 0.05$). None of the patients required the administration of blood products.

Mortality and morbidity data were comparable in the two groups. Overall, 30-day mortality rate was 1.7% and 19% of patients presented at least one major non-fatal complication. Noteworthy, postoperative creatinine serum levels did not differ from preoperative values and were similar in the two groups.

DISCUSSION

This is the first study that demonstrates the feasibility and safety of TDM during open-chest procedures under combined general and thoracic epidural anesthesia. Besides detecting hypovolemia in 18% of high-risk patients for cardiopulmonary complications, TDM was useful to individualized intraoperative fluid infusion and vasopressor therapy by integrating Doppler flow measurements with standard hemodynamic parameters.

In all anesthetized patients, probe was easily inserted without causing any damage in the upper airways and the oesophageal tract. The echo M-mode was particularly helpful to optimize probe positioning and Doppler flow recordings. Aortic diameter and flow velocity profile could be traced in the large majority of patients (92%), except in those with undefined aortic walls due to abnormalities of the descending aorta. Opening the chest, switching from two- to one-lung ventilation and intrathoracic surgical manipulations did not interfere with Doppler flow readings as far the oesophageal probe was repeatedly repositioned by an experienced investigator. The accuracy of TDM is partly operator-dependent and a training period for handling the transoesophageal probe and optimizing the Doppler flow signals has been shown to improve the reliability of the hemodynamic measurements [11].

Although transoesophageal echocardiography offers greater accuracy regarding diagnostic purposes, this sophisticated technique is too expansive for routine clinical use in surgical patients and requires highly trained personal. Other non-invasive flow-related techniques (i.e., partial carbon dioxide rebreathing, thoracic impedance and arterial pressure wave form analysis) are less operator-dependent, do not require deep sedation and can be applied over longer periods [12]. Nevertheless, TDM is currently regarded as the best validated technique for cardiac output measurements and for goal-directed fluid therapy in non-thoracic surgery [7]. The validity of Doppler-based flow measurements has been demonstrated against the standard thermodilution technique and the Fick method, showing excellent correlation ($r = 0.96$ and $r = 0.97$, respectively) with minimal mean bias (ranging from 0.03 to 0.21 and $l/min/m^2$) and clinically acceptable limits of agreement [13]. In addition to HR and MAP, TDM-related flow parameters provide the opportunity to get a thorough knowledge on the mechanisms of hemodynamic disturbances. Changes in SVI and FTc changes have been shown to correlate with volume and cardiac preload although they might also be affected by increased vascular resistance and compromised ventricular function [5, 6, 14]. On the other hand, MA and PV values have been used as valuable indirect markers of myocardial contractility [15, 16].

In this cohort study, the intraoperative goal-oriented fluid protocol was aimed to achieve SVI of at least 30 $ml/min/m^2$ while maintaining systolic arterial pressure above 90 mmHg (without testing fluid responsiveness). A ''low flow'' profile characterized by low SVI and low FTc

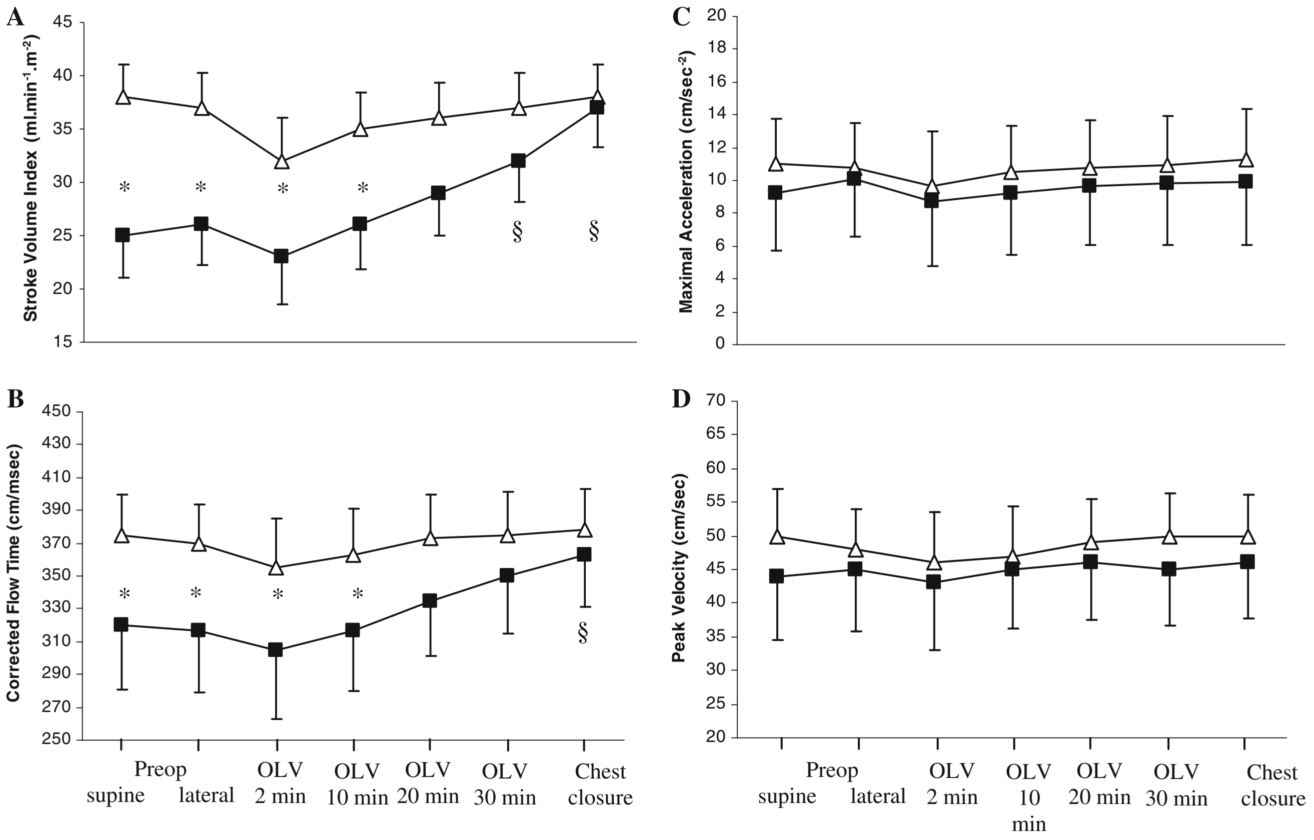

Fig. 1. Perioperative time course of Doppler flow-related variables: (a) Stroke volume Index, (b) Corrected Flow Time, (c) Maximal Acceleration and (d) Peak Velocity. $\star P < 0.05$ versus N-SVI group at the corresponding time point. $^{\S}P < 0.05$ versus preoperative baseline value (supine) in L-SVI group.

values (less than 30 ml/min/m^2 and less than 350 ms, respectively) was detected preoperatively in 18% of patients whereas normal MA and PV values ruled out significant impairment in ventricular function. Since conventional hemodynamic parameters, – blood pressure and heart rate – did not differ from those in patients with "normal flow" pattern, TDM was useful to detect intravascular volume depletion based on arbitrary cut-off values that have been applied in previous investigations [17–19].

If left untreated, perioperative hypovolemia has been incriminated in organ dysfunction and impaired tissue healing as a result of activation of the renine–angiotensin–aldosterone system, splanchnic ischemia, gut bacterial translocation and amplification of the inflammatory response [20–23]. Conversely, early restoration of circulating blood volume with colloids has been shown to attenuate these pathological events while improving tissue oxygen transport [18, 20, 24]. In the current study, similar clinical outcomes and functional parameters (e.g., oxygenation index, serum creatinine) in the two groups might be attributed to the correction of the "low flow" profile with additional colloids.

McKendry et al. used a slightly higher cut-off value (35 ml min^{-1}m^2) to discriminate between low and normal SVI in sedated patients recovering from cardiac surgery [25]. In the postoperative period, targeting higher oxygen transport index and SVI values seems logical in order to match the increased oxygen consumption concomitant with anesthesia emergence, weaning from the ventilator and increasing body temperature. Other clinical studies have used FTc (>350 ms), systolic pressure/flow variation and/or the response to a fluid challenge (increase in SV $> 10\%$) to guide fluid therapy according to the Franck–Starling relationship [7, 14, 17–19].

Although the use of TDM coupled with fluid maximization algorithms has been shown to improve clinical outcomes in patients undergoing cardiac, abdominal and orthopedic surgical procedure, a similar approach might reach different outcomes in thoracic surgical patients, owing to the "vulnerability" of thoracic surgical patients to fluid overload and the risk of ALI associated with even slight increases in hydrostatic capillary pressure [26]. Besides surgical trauma, the sequence of one-lung/two-lung ventilation promotes neutrophil recruitment and triggers the release of reactive oxygen/nitrogen species as

Table 2. Perioperative surgical and medical characteristics, mean (SD) or number (%)

	N-SVI group $n = 96$	L-SVI group $n = 21$
Intraoperative period		
Pneumonectomy or bi-lobectomy, n pts (%)	29 (30)	5 (24)
Duration of anaesthesia, min	170 (50)	176 (58)
Duration of surgery, min	139 (44)	165 (54)
Duration of OLV, min	68 (18)	73 (21)
Intravenous crystalloids, $ml/kg^{-1}/h^{-1}$	4.1 (2.1)	4.2 (2.2)
Intravenous colloids, $ml/kg^{-1}/h^{-1}$	3.6 (0.8)	5.7 (1.8)⋆
Phenylephrine, mg	728 (443)	788 (487)
Ephedrine, mg	7.9 (6.6)	8.4 (6.1)
Postoperative period (first 24 h)		
Total fluid intake, ml/24 h	1295 (486)	1196 (655)
Diuresis, ml/24 h	498 (334)	481 (234)
Chest drainage, ml/24 h	318 (172)	202 (125)
PaO_2/FIO_2, kPa	48.1 (6.2)	50.2 (5.9)
Blood hemoglobin at POD1, g/l	119 (13)	121 (20)
Serum creatinine at POD1, mg/l	78 (16)	76 (12)

PaO_2/FIO_2, ratio of arterial oxygen pressure to inspiratory fraction of oxygen; POD1, first postoperative day.
⋆$P < 0.05$ between the two groups.

Table 3. Perioperative hemodynamic and respiratory parameters, mean (SD) or number (%)

	Preoperative	OLV	Chest closure
Heart rate, beat/min			
N-SVI group	69 (12)	68 (11)	70 (14)
L-SVI group	72 (13)	70 (14)	74 (16)
Mean arterial pressure, mmHg			
N-SVI group	79 (9)	76 (10)	80 (12)
L-SVI group	77 (10)	75 (13)	78 (15)
Tidal volume, ml/kg			
N-SVI group	5.7 (1.1)	5.3 (1.2)	5.9 (1.9)
L-SVI group	5.5 (1.3)	5.1 (1.0)	5.8 (1.7)
Inspiratory plateau pressure, cm H_2O			
N-SVI group	17 (4)	22 (6)[a]	19 (5)
L-SVI group	15 (6)	21 (8)[a]	17 (7)
PEEP, cm H_2O			
N-SVI group	4.1 (0.9)	4.6 (1.3)	4.8 (1.5)
L-SVI group	3.9 (1.1)	4.3 (1.4)	4.6 (1.6)

OLV, one-lung ventilation; PEEP, positive end expiratory pressure.
[a] $P < 0.05$, between OLV and Preoperative periods.

well as pro-inflammatory cytokines [27]. A "leaky" alveolar-capillary barrier, impairment in alveolar fluid clearance mechanisms (e.g., disruption of lymphatic vessels, down-regulation of β_2-receptor in alveolar type II cells) and elevated hydrostatic pulmonary capillary pressure due to fluid administration and/or heart failure may all contribute to facilitate fluid extravasation and the onset of ALI. In line with these experimental data, several observational studies have confirmed that perioperative overhydration (>3–4 l i.v. fluids over the first 24 h, or positive fluid balance of > 13 ml/kg) is an independent risk factor for acute lung injury [28]. Accordingly, restriction of fluid intake over the first 24–48 h in addition to ventilating the lung with low tidal volume has been largely advocated, particularly in patients undergoing pneumonectomy. Conversely, maximizing cardiac output guided by flow/pulse pressure variations or SV response to fluid challenges may potentially result in deleterious increases in circulating plasma volume leading to lung oedema [29, 30].

There are several limitations to our results. First, although TDM appears to be feasible during open-chest procedure, SVI values were likely overestimated since TEA-induced sympathetic blockade increases blood flow in the descending aorta by redistributing blood volume from the upper areas towards the splanchnic and lower body compartments [31]. Further validation studies in patients receiving combined general/epidural anesthesia should be performed along with adjustments of the TDM internal software. Second, in contrast with other flow monitors (e.g., FlowTrac, PiCCO), the accuracy of Doppler flow measurements is highly operator-dependent, the failure rate approximates 10% and the utilization of TDM devices has been mainly restricted to the intraoperative period [32]. Despite improvements in probe's design and manufacturing, many clinicians are reluctant to extend TDM applications in the early postoperative period because of patient discomfort and the frequent loss of Doppler signals associated with electrical interferences, changes in body position and swallowing. Third, in this observational study, we did not address the question whether the restrictive fluid approach coupled with repeated vasopressor injection afforded better outcomes than maximizing the circulatory volume using dynamic cardiac preload markers. Assessment of blood/plasma volume and extravascular lung water content would be helpful not only for adjusting the rate of fluid administration but also for selecting the appropriate type of fluid (colloids vs. crystalloids) [33].

In conclusion, we found that TDM associated with conventional hemodynamic parameters provided the opportunity to detect low flow conditions while optimizing fluid infusion and vasopressor therapy in patients undergoing lung resection. Further studies are needed to define physiological surrogate endpoints for guiding intra- and postoperative fluid therapy and hemodynamic support in these patients ''at high-risk'' of lung edema. Other semi-invasive hemodynamic devices based on analysis of the arterial pressure wave and transpulmonary thermodilution offer the possibility to monitor circulatory parameters in all surgical patients during both the intraoperative and postoperative periods.

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