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Research Article

Pressure versus volume indices to guide fluid infusion early after living donor liver transplantation: A prospective randomized controlled trial

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Central venous pressure;
Stroke volume;
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Serum lactate

Abstract *Background:* Fluid resuscitation in early post-operative (PO) period after liver transplantation (LT) can be very detrimental for both graft and patient's outcome. Central venous pressure (CVP) was commonly used to guide fluid resuscitation after LT; yet, volumetric indices like stroke volume (SV) or right ventricular end diastolic volume (RVEDV) have gained more support recently. We tested the hypothesis that use of any of the three parameters to guide fluid therapy in the early PO period after living donor liver transplantation (LDLT) will not elaborate any changes in fluid volumes infused or graft and patient outcome.

Patients and methods: Sixty patients undergoing LDLT allocated based on the parameter guiding the fluid therapy in the first 72 h in ICU into one of three groups, G-CVP (control), G-SV and G-RV groups 20 patients each using CVP, SVI and RVEDVI respectively to guide fluid therapy. Based on the guiding parameter assessed every 4 h, fluid therapy was administered as 500 ml boluses followed by reassessment of the guiding parameter for further fluid infusion. Fluids infused over three days in the ICU were used as a primary outcome. Hemodynamics, graft and renal functions, and graft and patient outcome were recorded as secondary objectives.

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Results: CVP and PCWP were significantly higher in G-SV and G-RV compared to the CVP group while other hemodynamic parameters did not show significant differences between the groups. Fluid volume infused and urine output were significantly higher in G-SV and G-RV compared to G-CVP group. Laboratory and survival data did not differ among the studied groups.
Conclusion: The use of the CVP to guide fluid infusion after LT is a safe and effective alternative to more logistically demanding techniques as SV and RVEDVI without any negative impact on patient hemodynamic or metabolic homeostasis.

1. Introduction

Liver transplantation (LT) is associated with inevitable hemodynamic and volume changes during the operative period that may extend into the early post-operative (PO) period. Proper volume replacement protocol in early PO period may be remedial, protecting patients against volume-overload induced complications especially pulmonary complications [1,2]. Low central venous pressure (CVP) concept, (CVP < 5 mm Hg) was adopted to prevent liver congestion by facilitating hepatic venous drainage and reducing the possibility of bleeding [3–5]. Yet, pressure measurements are always subjected to the influence of cardiac compliance and vascular resistance jeopardizing their accuracy and questioning their credibility [6–8]. Recently, several volumetric parameters were tested for superiority over CVP for guiding fluid resuscitation in the intensive care as stroke volume (SV) and right ventricular end diastolic volume yet, this is highly demanding since they require the routine insertion of regular fiber-optic pulmonary artery catheter to measure SV or a special high frequency pulmonary artery catheter to measure the RVEDV [9]. Previous investigators tested the association between volume indices and pressure indices for guiding fluid replacement during early PO period after several surgical settings [10,11]. Most of these trials enrolled patients for cadaveric grafts in whom, the full liver can better tolerate volume loads without increased risks on graft functions. None addressed the efficacy of parameters used to guide fluid therapy exclusively in recipients receiving partial, living donor grafts We designed this prospective, randomized, controlled, double-blind study to test the hypothesis that fluid resuscitation guided by CVP, SV or RVEDV will not lead to significant difference in the amount of fluid infused in the early ICU stay (3 days) in living-donor transplant recipients as a primary outcome measure. Serum lactate as a surrogate of both graft functionality and the impact of use of each of these parameters on the hemodynamics and transplantation outcome constituted secondary objectives in this trial.

2. Patients and methods

After approval of the local ethical and legal committee, 81 living-donor liver transplant (LDLT) recipients admitted for LT in Mansoura University Liver LT between October 2007 and January 2011 were assessed for eligibility for this study. Preoperative informed consent for enrollment in this randomized controlled double-blind trial were secured from participating recipients. The study involved patients of either sex aging between 30 and 60 years old. Patients with known porto-pulmonary hypertension (diagnosed either preoperatively or intra operatively), patients with abnormal dimension of right atrium, right ventricle or left ventricle in preoperative echocardiography, patients with any grade II single or multiple valvular heart diseases or patients who sustained massive bleeding and blood product transfusion during the intraoperative phase (more than 10 units of RBCs and fresh frozen plasma) were excluded from the study. We also excluded patients who came to the ICU on vasopressors or inotropes. A series of 60 closed envelopes were prepared including one of the three groups and for each patient, anesthesia resident picked up a closed envelops before admitting the patient to the intensive care unit ICU). Patients were not aware by the applied protocol and data recording was done by ICU resident who was not aware of the study protocol. On admission to the ICU, patients already have an arterial catheter in the left radial artery for invasive blood pressure monitoring and a 7.5-French modified continuous thermal fiber optic pulmonary artery catheter (CCO/SvO2/CEDV Edwards Life Science, Irvine, CA, USA) in the right internal jugular vein. The attending physician confirmed the correct position of the pulmonary artery catheter tip by fluoroscopy and catheter position is corrected as appropriate. Patient is attached to the ICU monitor (Angstrom AS5 Monitor (Datex – Ohmeda AS5, Microvitec display Ltd., Bolling Road, Bradford, UK)) for monitoring of ECG, invasive arterial blood pressure, pulse oximetry, central venous pressure (CVP) and pulmonary capillary wedge pressure (PCWP). For continuous monitoring of mixed venous oxygen saturation (SvO2), stroke volume index (SVI), cardiac index (CI), right ventricular end diastolic volume index (RVEDVI), and right ventricular ejection fraction (RVEF), the pulmonary artery catheter transducers were attached to a specific monitor (Vigilance, Edwards Life Science, Irvine, CA, USA). Systemic vascular resistance index (SVRI), pulmonary vascular resistance index (PVRI), the right ventricular stroke work index (RVSWI), and the left ventricular stroke work index were calculated from the recorded data. Urine output was recorded every hour. The study took place during the first 72 h in the ICU. Patients received continuous background infusion of 1000 ml of glucose 10% and 500 ml of RA solutions over 15 h (100 ml h^{-1}) as well as mandatory volume for daily drug administration then, further fluid administration during the study period took the form of boluses of 500 ml of RA over 60 min. Patients fallen into one of three groups, 20 patients each, based on the parameter guiding the fluid administration recorded every 4 h. A trigger value was predetermined for each of the three parameters based on pilot work in our institute. In CVP group (G-CVP), patient received fluid boluses if CVP was $\leqslant$4 mm Hg to keep the CVP between 4–5 mm Hg. In stroke volume group (G-SV), fluid boluses were administered if SVI recorded was $\leqslant$55 ml m^2 beat and in RVEDVI group (G-

RVV), fluid boluses were administered if RVEDVI recorded was $\leqslant$110 ml m^2. Thirty minutes after bolus administration, the controlling parameter is measured and if necessary, another bolus is administered till the desired limit is accomplished. Random blood sugar was kept below 150 mg dl with insulin infusion. Any blood loss was replaced by matching volume of homologues RBCs and fresh frozen plasma in a ration of 3–1 to keep hemoglobin above 8 gm dl. Albumin was infused if serum albumin was less than 3.0 g dl^{-1}. When CVP exceeded 6 mm Hg and urine output was less than 1 ml kg in the last two successive hours, 10 mg of Frisimide were injected intravenously for graft protection. The primary outcome parameter in this trial was the amount of fluid infused over the first three ICU days. Secondary objective was to assess the outcome including serum lactate as a surrogate of perfusion status and early graft function, renal functions, graft functions, ICU stay as well as patient and graft survivals. Hemodynamic data were recorded as an average of 6 daily readings (every 4 h). Laboratory investigations were performed through sampling from the arterial line every 12 h as a part of the routine post-transplant care program. Routine chest X-ray (PA view) was taken every morning and catheter position is readjusted under fluoroscopy if needed. Data were collected by ICU resident who was not aware by the study protocol.

2.1. Statistical analysis

From the results of pilot work in our center, we assumed to a mean difference between the studied groups of 40% regarding the volume of fluid infused in the three postoperative days (collective) to be of clinical significance using β-error of 0.1 and two-tailed α = error of 0.05. A priori sample size estimation proposed 54 patients in the three groups to be sufficient. Normality of recorded data was tested using Kolmogorov–Smirnov test. Continuous data exhibited normal distribution and were analyzed for statistical differences using two tailed independent sample Student's t test with equal variance assumed and presented as mean (SD). Analysis was performed by Statistical package for social sciences (SPSS) Ver. 17, New Orchard Road Armonk, New York 10504-1722, USA. A p value of 0.05 or less was considered significant.

3. Results

We assessed 81 patients for eligibility in this trial, 21 were excluded either for non-meeting the inclusion criteria (17 patients), denying enrollment in the study (2 patients) and massive blood transfusion (n = 2). Sixty patients were randomized into one of the three study groups 20 patients each. Three patients were excluded from the study in the G-CVP group, 2 cases in the G-SV group and 2 patients in the G-RV group due to protocol violation, so, 53 patients were finally statistically analyzed (Fig. 1). Patient's characteristics, operative data and patient outcome were homogenous among the studied groups with no baseline differences (Table 1). Averaged daily hemodynamic data did not show any statistically significant differences apart from the PCWP that were statistically higher in both G-SV and G-RV groups compared to G-CVP group during the three PO days (Table 2). Table 3 presents the data of the fluid guiding parameters in the three groups over the study period. When the volumetric parameters (SVI and RVEDVI) were used as fluid guiding parameters, CVP, SVI and RVEDVI were all significantly higher in both G-SV and G-RV groups compared to the G-CVP (Table 3). No significant differences existed between the laboratory profiles of patients in the studied groups neither did the serum lactate (Table 4, Fig. 2 and 3). Fig. 4 illustrates the total volume of fluids infused daily and the daily urine output in the studied groups. In G-RV and G-SV groups, the volume of fluid infused and the urine output daily were significantly higher compared to the G-CVP group and by day three, the fluid infused in G-RV group was also significantly larger compared to the G-SV group (p = 0.01) (Fig. 4).

4. Discussion

Our null hypothesis was rejected. The use of volumetric parameters (SVI and RVSWI) to guide the fluid infusion in the early PO period after LT invited more fluid volume compared to the traditional use of CVP without affecting neither graft nor patient outcomes in this trial.

During the operative phase of LT, fluids are sequestered into the third space, this effect also persists in the stressful early PO period and may even be augmented by the immunosuppression protocol that favors salt and water retention necessitating the adoption of a fluid infusion protocol that maintains stable hemodynamics while achieving a negative fluid balance to recruit the excess fluid from the third space into the central circulation [1,12]. Previous investigators compared several parameters to assess preload and test fluid responsiveness during liver transplantation who may be overload intolerant [13,14]. Yet, no specific research was conducted in the early PO period after LDLT. This is particularly important as during LDLT, the venous drainage of the graft constitutes a major challenge due to venous reconstruction using the donor's native right hepatic vein and segmental veins instead of the wider diameter common hepatic nein. Yet, the reduced sized graft still receives the entire portal flow from the recipient splanchnic circulation. Adoption of a low CVP is a graft-saving technique in which, keeping the CVP around 4–5 mm Hg helps facilitating the venous drainage of the graft at this early phase until the portal pressure starts to fad during the next PO days [15].

In our trial, fluid administration guided by either SVI or RVEDVI led to significantly higher CVP and PCWP in G-SV and G-RV groups compared to G-CVP group. This increase in the filling pressures could be attributed to the significantly larger fluid volume infused in both G-SV and G-RV groups compared to that infused in G-CVP group. Other hemodynamic data, in our trial, support this assumption. Filling pressures depends not only of preload, but also on myocardial compliance and afterload status. The absence of any significant differences between the study groups in systemic and pulmonary vascular resistance strongly nullify the possibility of contribution of vascular resistance in generating this increase in the pressure parameters (CVP and PCWP). Meanwhile, Siniscalchi and his co-investigators stated that the right ventricular contractility is not altered in uncomplicated liver transplantation which also excludes the involvement of early cardiac contractile abnormalities as a precursor for such increase in the cardiac filling pressures [16]. RVEF and SV,

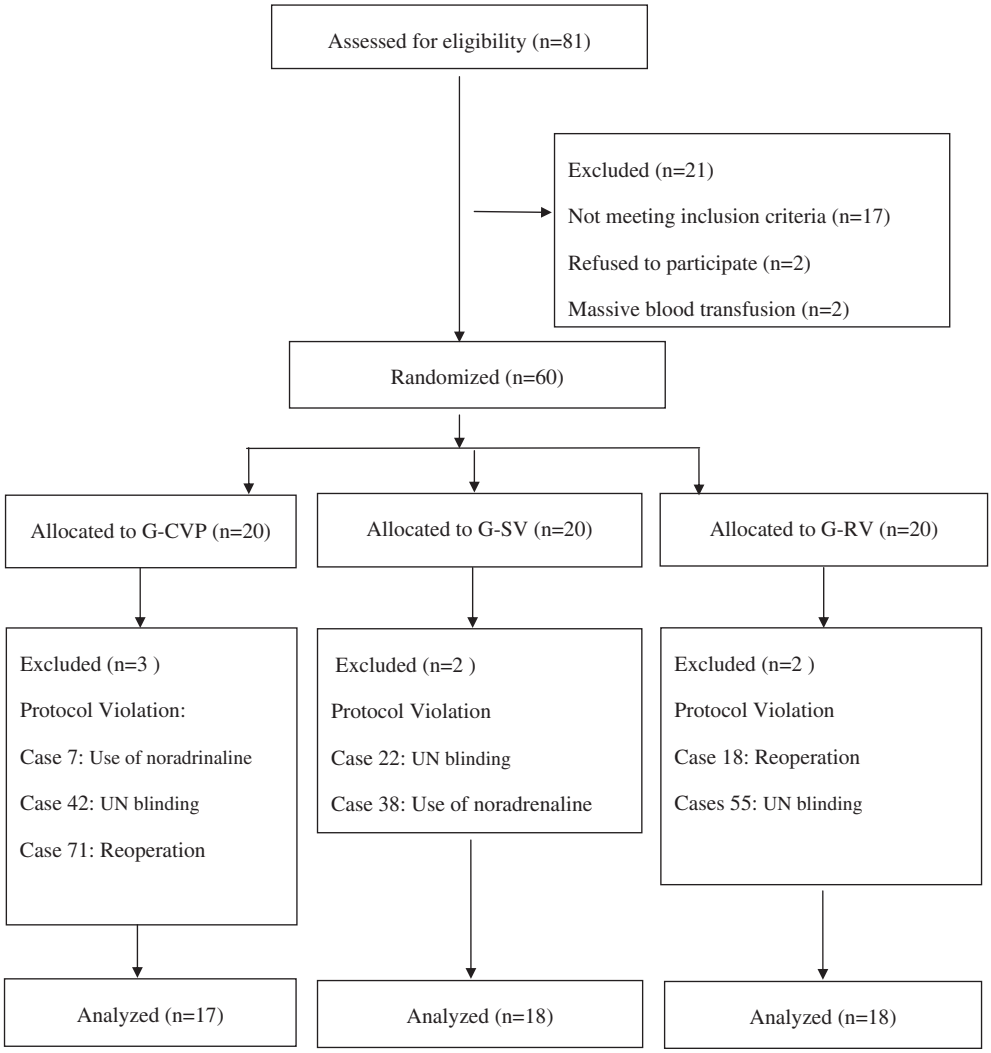

Figure 1 CONSORT patient's flow diagram.

Table 1 Patient characteristics, operative data and outcome parameters of G-CVP, (n = 17), G-SV (n = 18 and G-RV (n = 18) groups.

	G-CVP, n = 17	G-SV, n = 18	G-RV, n = 18
Age (years)	49.8 ± 10.5	50.9 ± 7.9	48.1 ± 5.3
Male gender (%)	92.3	89.3	92.8
Preoperative MELD score	16.6 ± 5.6	15.2 ± 2.1	15.4 ± 3.2
Worm ischemia time	64.8 ± 11.8	68.5 ± 10.0	62.4 ± 19.9
Gwbw ratio	1.3 ± 0.2	1.2 ± 0.3	1.3 ± 0.2
ICU admission hemoglobin (g dl)	9.8 ± 2.1	9.6 ± 1.7	10.0 ± 2.4
ICU admission hematocrite (%)	26.3 ± 4.3	25.9 ± 3.8	26.3 ± 4.8
Extubation time	3.7 ± 3.6	3.3 ± 1.7	3.2 ± 2.9
Patients receiving RBCs in ICU (%)	23.1	39.3	17.9
Patients receiving plasma in ICU (%)	33.3	35.7	32.1
Pleural effusion	85.2%	85.7%	89.3%
Infections during ICU stay (%)	0.07	0.11	0.14
ICU stay (days)	6.1 ± 2.2	5.1 ± 2.5	5.3 ± 2.9
Three months patient's survival (%)	85.2	89.3	85.7
Three months graft's survival (%)	96.4	100	92.9

Data are expressed as mean ± standard deviation.

Table 2 Hemodynamic data of the G-CVP (n = 17), G-SV (n = 18) and G-RV (n = 18) groups.

	G-CVP, n = 17	G-SV, n = 18	G-RV, n = 18	Difference (95% CI) G-CVP and G-SV	Difference (95% CI) G-CVP and G-RV	Difference (95% CI) G-SV and G-RV
HR Day 1	86.9 ± 6.5	86.1 ± 6.3	87.3 ± 7.9	0.80(−5.25 to 6.85)	−0.40(−7.26 to 6.46)	−1.20(−7.97 to 5.57)
HR Day 2	84.1 ± 4.2	83.9 ± 5.1	83.6 ± 6.2	0.20(−4.19 to 4.59)	−0.50(−4.44 to 5.44)	0.30(−5.02 to 5.62)
HR Day 3	83.9 ± 3.2	82.8 ± 6.1	82.7 ± 4.4	1.10(−3.44 to 5.64)	1.20(−2.42 to 4.82)	0.10(−4.88 to 5.08)
MAP Day 1	86.9 ± 8.2	91.8 ± 9.6	90.5 ± 13.1	−4.89(−13.28 to 3.49)	−3.56(−13.79 to 6.68)	1.33(−9.45 to 12.11)
MAP Day 2	84.2 ± 11.8	91.4 ± 9.3	92.5 ± 10.6	−7.14(−17.13 to 2.85)	−8.23(−18.75 to 2.29)	−1.09(−10.48 to 8.30)
MAP Day 3	85.9 ± 8.6	91.8 ± 9.6	90.4 ± 12.9	−5.96(−14.54 to 2.62)	−4.53(−14.89 to 5.83)	1.43(−9.30 to 12.17)
PCWP Day 1	8.2 ± 1.9	10.9 ± 1.9*	11.4 ± 2.2*	−2.70(−4.53 to −0.87)	−3.20(−5.16 to −1.24)	−0.90(−2.42 to 1.42)
PCWP Day 2	8.9 ± 1.5	11.7 ± 1.6*	12.4 ± 2.4*	−2.80(−4.29 to −1.31)	−3.50(−5.37 to −1.63)	−0.70(−2.61 to 1.21)
PCWP Day 3	8.6 ± 1.8	12.3 ± 1.6*	12.8 ± 1.6*	−3.70(−5.33 to −2.07)	−4.20(−5.83 to −2.57)	−0.50(−2.02 to 1.03)
RVEF Day 1	43.8 ± 4.4	46.1 ± 4.2	47.3 ± 6.9	−2.30(−6.34 to 1.74)	−3.50(−8.98 to 1.98)	−1.20(−6.61 to 4.21)
RVEF Day 2	45.1 ± 4.1	48.1 ± 3.3	48.4 ± 5.1	−3.00(−6.50 to 0.50)	−3.30 (−7.65 to 1.05)	−0.30(−4.31 to 3.72)
RVEF Day 3	47.3 ± 3.1	50.5 ± 4.2	47.3 ± 3.7	−3.20(−6.70 to 0.31)	−1.90(−5.12 to 1.32)	1.30(−2.45 to 5.05)
SVRI Day 1	1343.2 ± 112.7	1349.3 ± 129.7	1437.8 ± 426.9	−6.10(120.28 to 108.08)	−94.60(−387.99 to 198.79)	−88.50(−384.98 to 207.98)
SVRI Day 2	1331.5 ± 89.5	1416.5 ± 185.7	1299.8 ± 199.1	−85.00(−221.9 to 54.95)	31.70(−113.32 to 176.72)	116.70(−64.17 to 297.57)
SVRI Day 3	1421.8 ± 238.6	1323.1 ± 198.4	1373.7 ± 221.9	−98.70(−107.45 to 304.85)	48.10(−168.36 to 264.56)	−50.60(−248.35 to 47.15)
PVRI Day 1	79.3 ± 7.5	84.8 ± 8.8	85.9 ± 10.6	−3.50(−11.2 to 4.18)	−4.60(−13.22 to 4.02)	−1.10(−10.28 to 8.08)
PVRI Day 2	83.2 ± 8.0	86.3 ± 8.7	88.1 ± 12.2	−3.10(−10.9 to 4.77)	−4.90(−4.63 to 4.83)	−1.80(−11.78 to 8.18)
PVRI Day 3	86.4 ± 6.7	87.9 ± 10.4	89.9 ± 8.6	−1.50(−9.71 to 6.71)	−3.50(−10.72 to 3.71)	−2.00(−10.97 to 6.97)
RVSWI Day 1	7.6 ± 0.9	8.1 ± 1.6	8.2 ± 1.9	−0.56(−1.71 to 0.68)	−0.62(−2.01 to 0.77)	0.06(−1.72 to 1.59)
RVSWI Day 2	7.8 ± 0.9	8.2 ± 1.4	8.5 ± 1.4	−0.35(−1.49 to 0.79)	−0.63(−1.79 to 0.53)	−0.28(−1.62 to 1.06)
RVSWI Day 3	8.4 ± 0.7	8.9 ± 1.1	9.2 ± 1.4	−0.52(−1.38 to 0.34)	−0.85(−1.87 to 0.17)	−0.33(−1.49 to 0.84)
LVSWI Day 1	52.9 ± 4.7	48.7 ± 5.0	50.9 ± 4.4	4.20(−0.39 to 8.79)	2.00(−2.28 to 6.28)	−2020(−6.64 to 2.23)
LVSWI Day 2	52.9 ± 3.9	54.4 ± 5.2	54.6 ± 4.5	−1.50(−5.86 to 2.86)	−1.70(−5.69 to 2.290	−0.20(−4.79 to 4.39)
LVSWI Day 3	54.1 ± 3.9	56.3 ± 4.0	58.0 ± 3.1	−2.20(−5.93 to 1.53)	−4.60(−7.92 to 1.28)	−3.90(−7.87 to 0.07)

HR = heart rate, MAP = mean arterial pressure, PCWP = pulmonary capillary wedge pressure, RVEF = right ventricular ejection fraction, SVRI = systemic vascular resistance index, PVRI = pulmonary vascular resistance index, RVSWI = right ventricular stroke work index, LVSWI = left ventricular stroke work index. Data are expressed as mean ± standard deviation.
* $P < 0.05$ compared to the G-CVP group.

Table 3 Guiding parameters data of the G-CVP ($n = 17$), G-SV ($n = 18$) and G-RV ($n = 18$) groups.

	G-CVP, $n = 17$	G-SV, $n = 18$	G-RV, $n = 18$	Difference (95% CI) G-CVP and G-SV	Difference (95% CI) G-CVP and G-RV	Difference (95% CI) G-SV and G-RV
CVP Day 1	4.3 ± 0.9	6.2 ± 1.2*	6.6 ± 1.4*	−1.90(−2.93 to −0.87)	−2.30(−3.39 to −1.20)	−0.40(−1.61 to 0.81)
CVP Day 2	4.4 ± 0.7	6.6 ± 0.9*	6.8 ± 1.5*	−2.20(−2.99 to −1.41)	−2.40(−3.53 to −1.27)	−0.20(−1.41 to 1.01)
CVP Day 3	4.8 ± 1.5	6.3 ± 2.3*	6.7 ± 1.6*	−1.70(−3.03 to −0.37)	−1.90(−3.36 to −0.44)	−0.20(−1.54 to 1.14)
SVI Day 1	53.9 ± 5.2	68.9 ± 6.3*	72.3 ± 9.9*	−7.85(−13.26 to −2.44)	−18.39(−25.86 to −10.92)	−10.54(−18.36 to 2.72)
SVI Day 2	55.9 ± 5.5	67.3 ± 5.9*	68.5 ± 5.9*	−5.45(−10.78 to −0.12)	−12.67(−18.02 to −7.32)	−7.22(−12.77 to 1.67)
SVI Day 3	52.5 ± 4.7	62.0 ± 4.5*	64.5 ± 7.1*	−4.55(−8.88 to −0.22)	−12.06(−17.72 to −6.40)	−7.51(−13.07 to 1.95)
RVEDVI Day 1	105.1 ± 11.9	131.8 ± 20.9*	121.8 ± 19.3*	−21.86(−29.36 to −14.36)	−16.76(−23.65 to −9.87)	50.10(−0.68 to 10.88)
RVEDVI Day 2	106.5 ± 13.1	121.3 ± 10.4*	118.2 ± 11.4*	−17.79(−24.65 to −10.63)	−13.68(−20.53 to −6.83)	4.11(−1.87 to 10.09)
RVEDVI Day 3	109.8 ± 12.6	117.9 ± 13.9*	130.3 ± 22.1*	−12.14(−19.05 to −5.230	−9.53(−16.49 to −2.56)	2.61(−3.00 to 8.23)

CVP = central venous pressure, SVI = stroke volume index and RVEDVI = right ventricular end diastolic volume index.
Data are expressed as mean ± standard deviation.
* $P < 0.05$ compared to the G-CVP group.

although not statistically significant, increased proportionally with increased RVEDV in our trial indicating sound contractile functions. The preserved contractile functions will always reduce the RVEDVI and hence, in this trial, the use of RVEDVI as a guiding parameter led to increased volume of fluid infused compared to the use of CVP which is a pressure parameter affected crucially by any change in myocardial compliance that is always reduced in the early PO period after LTX leading to rapid increase of CVP with infusion of lower volumes of fluid and delayed descent of the CVP value after the bolus infusion.

Weather this reduction in the fluid volume in the G-CVP group compared to the other groups had a negative impact on patient outcome or not is a crucial question. To answer this question, two points had to be investigated. First is the hemodynamic stability of the patients in the early PO days and secondly, is the impact of the fluid protocol on graft and patient outcome parameters. A comparable stable hemodynamic profile in the three groups was achieved with the use of CVP to guide fluid therapy in our trial with the infusion of significantly lower fluid volume compared to both G-SV and G-RV groups. Increased volume infused in G-SV and G-RV compared to G-CVP was not associated with significant increase in the RVEF in our trial. This lack of correlation between the volume infused and the output represented by RVEF means that this extra fluid volume is located on the plateau phase of the Frank–Starling curve. Previous investigators demonstrated that after a critical level of RVEDVI, any additional increase in the preload will not generate a similar increase in the cardiac output and hence, will not be of any benefit to the patient [17].

In contradiction to our results, Paul and his co-workers, in their systematic review, stated that the use of CVP to guide fluid replacement will increase the likelihood for development of volume overload and pulmonary edema (ref icu fluid 3). However, on analyzing the studies enrolled in this systematic review, it was found that 39.8% of the patients enrolled in these studies underwent post coronary artery bypass surgery, that is almost always associated with grave changes in the pulmonary capillary permeability due to pro-inflammatory response of the cardiopulmonary bypass machine [18] as well as early post-operative changes in myocardial perfusion and subsequently myocardial compliance and functions [19–21]. These changes negate the extrapolation of the results of the systematic review done by Paul and his co-workers to post-transplantation period investigated in our work.

There were no significant differences between G-SV and G-RV groups in any parameter in this trial. Other investigators demonstrated a good correlation between SV and RVEDV in several surgical settings in agreement with our findings [22,23].

Mixed venous oxygen saturation and serum lactate are dynamic end points for hemodynamic and metabolic status after LT. In this trial, neither of them demonstrated any significant differences between groups. A similar profile was observed in laboratory data reflecting graft and renal functions as well as other outcome parameters like graft and patient survival rates, infection rate or ICU stay. Although urine output was significantly higher in G-SV and G-RV groups compared to the G-CVP group, yet, urine volume was within the accepted clinical range in the three groups (> 1 ml kg h^{-1}). These data indicate a matching safety profile of the three parameters used to guide fluid therapy. It could be concluded from our work that

Table 4 Laboratory data of the G-CVP (n = 17), G-SV (n = 18) and G-RV (n = 18) groups.

	G-CVP, n = 17	G-SV, n = 18	G-RV, n = 18	Difference (95% CI) G-CVP and G-SV	Difference (95% CI) G-CVP and G-RV	Difference (95% CI) G-SV and G-RV
Createnine Day 1	1.0 ± 0.2	1.1 ± 0.2	1.0 ± 0.2	−0.06(−0.27 to 0.15)	−0.02(−0.24 to 0.19)	0.04(0.17 to 0.25)
Createnine Day 2	1.2 ± 0.2	1.1 ± 0.3	1.0 ± 0.3	0.11(−0.13 to 0.35)	0.19(−0.04 to 0.42)	0.08(−0.17 to 0.33)
Createnine Day 3	0.9 ± 0.2	1.1 ± 0.2	0.9 ± 0.3	−0.09(−0.27 to 0.09)	−0.03(−0.23 to 0.17)	0.06(−0.14 to 0.26)
Serum urea Day 1	49.6 ± 13.9	50.5 ± 10.9	50.4 ± 11.9	−0.90(−12.6 to 10.80)	−0.80(−12.92 to 11.32)	0.10(−10.59 to 10.79)
Serum urea Day 2	47.6 ± 7.9	49.8 ± 8.8	48.1 ± 8.6	−2.20(−10.07 to 5.67)	−0.50(−8.26 to 7.27)	1.70(−6.47 to 9.87)
Serum urea Day 3	46.9 ± 7.0	46.7 ± 7.8	47.0 ± 7.1	0.20(−6.78 to 7.18)	−0.10(−6.75 to 6.55)	−0.30(−7.33 to 6.73)
*P*h Day 1	7.4 ± 0.0	7.4 ± 0.1	7.4 ± 0.0	−0.07(−0.13 to −0.003)	−0.06(−0.12 to 0.0004)	0.02(−0.02 to 0.07)
*P*h Day 2	7.3 ± 0.0	7.3 ± 0.0	7.3 ± 0.0	−0.005(−0.02 to 0.01)	−0.004(−0.01 to 0.01)	0.00(−0.01 to 0.01)
*P*h Day 3	7.3 ± 0.0	7.3 ± 0.0	7.3 ± 0.0	0.006(−0.00 to 0.02)	0.005(−0.01 to 0.02)	−0.00(−0.01 to 0.01)
Paco2 Day 1	35.1 ± 3.8	34.1 ± 3.0	35.9 ± 2.8	1.00(−2.21 to 4.21)	−0.89(−4.00 to 2.22)	−1.89(−4.59 to0.82)
Paco2 Day 2	35.7 ± 1.6	34.1 ± 1.9	34.7 ± 1.6	1.59(−0.07 to 3.25)	0.95(−0.56 to 2.46)	−0.64(−2.32 to1.04)
Paco2 Day 3	35.2 ± 1.6	34.5 ± 2.7	34.0 ± 3.4	−0.23(−2.34 to 1.88)	1.19(−1.30 to 3.68)	1.42(−1.47 to 4.310
Svo2 Day 1	84.9 ± 7.7	35.1 ± 8.2	84.8 ± 5.6	−0.20(−7.64 to 7.24)	0.10(−6.19 to 6.39)	0.30(−6.28 to 6.88)
Svo2 Day 2	80.0 ± 7.3	81.4 ± 7.6	80.5 ± 8.9	−1.40(−8.43 to 5.62)	−0.50(−8.18 to 7.18)	0.90(−6.91 to 8.71)
Svo2 Day 3	75.8 ± 8.6	78.1 ± 10.5	81.9 ± 6.9	−2.30(−11.34 to 6.74)	−6.10(−13.42 to 1.22)	−3.80(−12.16 to4.56)

PaCo2 = plasma partial carbon dioxide tension and SvO2 = mixed venous oxygen saturation.
Data are expressed as mean ± standard deviation.

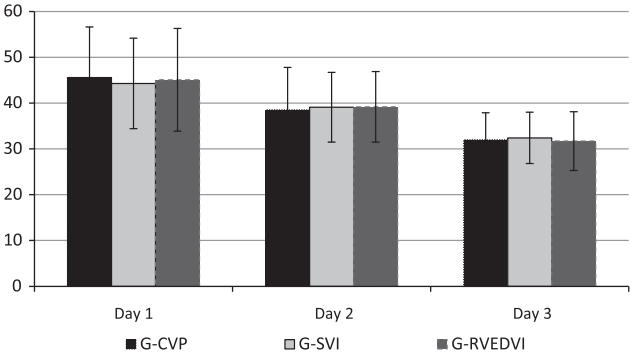

Figure 2 Daily serum lactate of G-CVP (n = 17), G-SV (n = 18) and G-RV (n = 18) groups. Data are expressed as mean ± standard deviation.

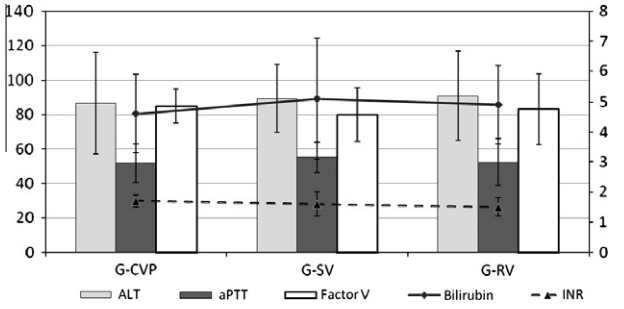

Figure 3 Liver functions and coagulation profile of G-CVP (n = 17), G-SV (n = 18) and G-RV (n = 18) groups. Data are expressed as mean ± standard deviation. INR and Bilirubin are plotted at the secondary X axis (right).

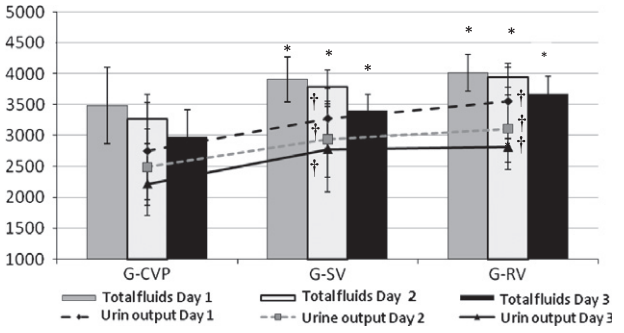

Figure 4 Fluid input and urine output in G-CVP (n = 17), G-SV (n = 18) and G-RV (n = 18) groups. Data are expressed as mean ± standard deviation. $^{*}P < 0.05$ compared to the G-CVP group regarding fluid volume. $^{\#}P < 0.05$ compared to the G-SV group regarding fluid volume. $^{\dagger}P < 0.05$ compared to the G-CVP group regarding urine output.

CVP could be safely used as a guide for fluid therapy in the intensive care after liver transplantation with efficacy and safety similar to more logistically demanding parameters like stroke volume and RVEDVI. Moreover, less fluid was infused with the use of CVP, a trend that proved to be more

adventitious in the ICU practice recently especially in this overload-sensitive cohort.

The use of dynamic indices for assessment of preload and to guide fluid infusion could have added to the value of this trial if used as a benchmark to compare the tested parameters, yet, for logistic limitations, it was not applied in our study. Another limitation in this trial was the lack of possibility of assessment of myocardial contractility in the early PO period, depraving the investigator from the possibility of having a direct measurement of one of the main contributing factor in generating the results of this trial. A trans- oesophygeal echocardiography supported study is required to nullify the limitations in our trial.

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