Fluid management guided by stroke volume variation failed to decrease the incidence of acute kidney injury, 30-day mortality, and 1-year survival in living donor liver transplant recipients

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Received March 28, 2012; accepted May 30, 2012

Abstract

Background: Low central venous pressure (CVP) produced by fluid restriction has been applied to liver transplant recipients in order to decrease blood loss. However, CVP is not reliable for monitoring intravascular volume and ventricular filling. In addition, doubts remain over the association between fluid restriction and acute kidney injury (AKI). We tested the utility of stroke volume variation (SVV), derived from the FloTrac/Vigileo system, as a decision-making tool in fluid management. We examined the differences in fluid administration, urine output, postoperative AKI, and 30-day and 1-year survival rates between liver transplant recipients with fluid management guided by SVV and CVP.

Methods: We retrospectively collected data on our liver transplant recipients with a Model for End-stage Liver Disease score less than 30 and serum creatinine lower than 1.5 mg/dL from 2007 to 2010. Recipients in 2007 and 2008 who received CVP-guided fluid management served as the control group. Recipients in 2009 and 2010 who received fluid administration triggered by SVV were recruited as the study group. The estimated blood loss, urine output, and fluid administered during the operation were recorded. Renal function was assessed using the RIFLE criteria on postoperative days 1 and 5. We also recorded the 30-day and 1-year survival.

Results: Significantly more diuretic use and urine output were noted in the control group in spite of similar fluid administration. However, there was no significant difference in blood loss, AKI, or 30-day and 1-year survival rates.

Conclusion: The outcomes of living donor liver transplant patients who had fluid therapy guided by an SVV less than 10% were similar to those of patients who were given fluids to reach a CVP of 10 mmHg. Our findings suggest that the two measures of vascular filling are similar in liver transplant recipients with demographic characteristics similar to those of our patients.

Keywords: acute kidney injury; central venous pressure; liver transplantation; stroke volume variation

1. Introduction

Intraoperative fluid management of the transplant recipient influences perioperative complications,1 and studies have suggested that maintaining a low central venous pressure (CVP) in the liver recipient by fluid restriction reduces blood loss and improves patient survival.2–5 However, there is
evidence suggesting that fluid restriction increases the risk of acute kidney injury (AKI) in some recipients. Affected patients suffer more episodes of acute rejection and experience an increase in mortality rate.

Studies to determine optimal fluid management have used CVP to estimate intravascular filling. The severity of illness of the patients in these studies differed significantly, but CVP was uniformly used as a measure of intravascular volume. The variable results of these studies suggest, however, that CVP may not be a reliable tool to guide fluid management.

Arterial-derived pulse pressure monitors are a relatively new development in the field of hemodynamic monitoring. The FloTrac/Vigileo (FTV) system version 1.07 (Edwards Lifesciences, Irvine, CA, USA) is a non-calibrated sensor that relays information about the characteristics of the arterial impulse. The monitor contains software that calculates the cardiac output from demographic data and the geometry of the arterial curve. The derived values are reliable, as they have a small dispersion of measured cardiac outputs.

Stroke volume variation (SVV) is used as a surrogate to measure shifts in position of the Frank–Starling curve. Investigators have reported that a fluid bolus given to patients with an SVV > 10% increases blood pressure and cardiac output. An SVV of greater than 10% discriminated fluid responsiveness with a sensitivity of 94% and a specificity of 94%. However, to date, very little information has been reported on the association between fluid administration directed by SVV and the outcomes of AKI, 30-day and 1-year survival rates.

A comprehensive approach to fluid management should minimize the risk of AKI, so kidney function should be an important end-point to measure when designing goal-directed fluid therapy. We therefore tested the utility of SVV as a decision-making tool in fluid-guided therapy. We examined the association between fluid administration guided by an SVV value greater than 10% and standard measures of patient outcome in a group of liver transplant recipients. The findings were compared with outcomes for patients managed using CVP.

2. Methods

After Institutional Board approval (VGH-201011029IC), we retrospectively collected data for recipients with a Model for End-stage Liver Disease (MELD) score of less than 30 and a serum creatinine level lower than 1.5 mg/dL. We excluded patients with MELD scores greater than 30 because they constituted a minority of our patient population and experienced higher morbidity and mortality. Recipients in 2007 and 2008 who received CVP-guided fluid management served as the control group. Recipients in 2009 and 2010 who received fluid administration guided by SVV were recruited as the study group. A total of 50 recipients were recruited, with 25 in each group. All surgical procedures were performed by the same group of surgeons.

2.1. Anesthesia protocol

We attached a five-lead electrocardiogram, pulse oximeter, noninvasive blood pressure cuff, and auditory evoked potential sensor (version 1.4; Alaris Medical Systems, Basingstoke, UK) to patients prior to induction of general anesthesia. Propofol (1–2 mg/kg) and fentanyl (5 μg/kg) were used to induce general anesthesia. Cisatracurium (0.2 mg/kg) was used for muscle relaxation and to facilitate intubation.

Continuous infusions of propofol and fentanyl were used for maintenance of anesthesia. The dose of propofol was adjusted to keep the Auditory Evoked Potential Index between 15 and 25. The fentanyl infusion protocol was 3 μg/kg/h for the first hour, 2 μg/kg/h for the following 2 hours, and then 1 μg/kg/h until the end of surgery. After induction, a 20-G radial arterial and a double-lumen right internal jugular venous line were inserted (Arrow International, Reading, PA, USA) to measure the CVP and administer fluids. The radial arterial line was connected to the FTV system with software version 1.07 to monitor the SVV.

2.2. Fluid management

Patients in the control and study groups received a constant infusion of 5% albumin solution (10 mL/h) and Ringer’s lactate solution (100 mL/h). Coagulation products were given based on the results of kaolin-activated thromboelastography (TEG 5000 series; Haemoscope, Skokie, IL, USA). Packed red blood cells were transfused to maintain a hemoglobin concentration > 10 g/dL.

We administered a 250 mL bolus of crystalloid to the study patients if their SVV was greater than 10%. If the mean arterial blood pressure fell below 20% of the preoperative value and the SVV was less than 10%, a 10-μg bolus dose of norepinephrine was given. None of our patients required a continuous infusion of vasopressor during surgery. If urinary output was less than 0.5 mL/kg/h, an additional 250 mL crystalloid was given for the first hour. If there was persistent oliguria (<30 mL/h for 2 hours or more), a single 20-mg dose of furosemide was given.

CVP was used to guide fluid management in the control group. Fluids were administered in order to keep the CVP between 8 mmHg and 10 mmHg. A bolus dose of norepinephrine was administered if the mean arterial blood pressure was less than 20% of the preoperative value and the CVP was greater than 10 mmHg. Furosemide 20 mg was given if the CVP was higher than 10 mmHg after laparotomy.

2.3. Postoperative care

Following surgery, all liver transplant recipients were sent to the transplant intensive care unit, intubated and ventilated. All patients received the same immunosuppressant regimen: intraoperative induction with methylprednisolone (1 g) tapered to oral prednisolone 20 mg on the seventh postoperative day, and a calcineurin inhibitor (tacrolimus or cyclosporine) with mycophenolate mofetil. The steroid was withdrawn within 6 months after transplantation. Because the frequency of early postoperative renal insufficiency was reported to be similar in patients treated with cyclosporine or tacrolimus, we did not analyze these two groups separately. No nonsteroidal anti-
inflammatory drugs (NSAID) or aminoglycoside antibiotics were used in transplant recipients.

2.4. Outcome variables

The estimated blood loss, urine output, and fluid administered were totaled for the operative time, and renal function was assessed using the serum creatinine level. We calculated the ratio of the preoperative creatinine to the creatinine values on postoperative days 1 and day 5. Patients were assessed using the RIFLE classification for AKI (Risk, Injury, Failure, Loss, and End-stage Kidney). Patients who experienced a 50% increase in serum creatinine level were defined as having an additional risk, while a 100% increase was categorized as injury, and 200% as failure. We also recorded 30-day and 1-year survival rates.

2.5. Statistical analysis

The parametric and categorical demographic data were compared using the independent t test and Chi-square test, respectively. The perioperative fluid intake, blood loss, and urine output were analyzed using the Mann—Whitney U test. The incidence of postoperative acute kidney injury (AKI) and the, 30-day and 1-year survival rates were also analyzed by Chi-square test. A p value < 0.05 was considered statistically significant. Statistical treatment of all data was carried out using SPSS 17.0 (SPSS Inc., Chicago, IL, USA).

3. Results

The patients’ demographic profiles are shown in Table 1. There was no significant difference between the CVP and SVV groups in terms age, MELD score, or preoperative creatinine level. The stage/category of chronic kidney disease stage in the two groups of patients is shown in Table 1. Only two patients in the study group and three in the control group were in stage III renal failure. There was no significant difference in the rest of the demographic features including body mass index, baseline mean blood pressure, preoperative hemoglobin level, International Normalized Ratio, and total bilirubin.

Indications for liver transplant are shown in Table 2. Seven patients in each group had hepatitis C virus infection. There were few patients with acute liver failure in our study because we excluded all patients with a MELD score >30.

The amount of fluids administered, norepinephrine dosage, pH value 10 minutes after reperfusion, and blood products given are shown in Table 3. Blood loss was similar between the two groups (study subjects 4720.44 ± 2998.49 mL vs. controls 5251.20 ± 5672.36 mL), and there was no significant difference in the volume of blood products administered (Table 3). The total amount of fluid administered to the study group (9068.70 ± 3239.34 mL) did not differ from that given to the controls (8396.23 ± 2424.43 mL). The only significant difference was a higher urine output (3.43 ± 2.24 mL/kg/h) and greater diuretic use (25/25) in our control group compared with the study group (2.26 ± 1.49 mL/kg/h and 14/25, respectively).

The number of cases with AKI assessed by RIFLE is shown in Table 4. The cause of death and 30-day and 1 year survivals are shown in Table 5. There was no significant difference noted between the two groups. Mortality was primarily due to graft failure with postoperative AKI.

4. Discussion

Fluid management guided by SVV did not change the incidence of AKI or 30-day and 1-year survival rates in our

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Table 1

<table>
<thead>
<tr>
<th>Study group</th>
<th>Control group</th>
<th>p</th>
</tr>
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<tbody>
<tr>
<td>Number of patients (M/F)</td>
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<td>25(14/11)</td>
</tr>
<tr>
<td>Age (y)</td>
<td>52.74 ± 9.81</td>
<td>54.96 ± 9.14</td>
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<td>Body mass index (kg/m²)</td>
<td>25.52 ± 3.19</td>
<td>23.73 ± 2.56</td>
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Table 2

<table>
<thead>
<tr>
<th>Indications for liver transplantation</th>
<th>Study group (n = 25)</th>
<th>Control group (n = 25)</th>
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<tr>
<td>Acute hepatitis with liver failure</td>
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<tr>
<td>HBV</td>
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<td>3</td>
<td></td>
</tr>
<tr>
<td>HCV</td>
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<td>0</td>
<td></td>
</tr>
<tr>
<td>Liver cirrhosis without hepatocellular carcinoma</td>
<td></td>
<td></td>
<td>1.000</td>
</tr>
<tr>
<td>Alcoholism</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>HBV</td>
<td>5</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>HCV</td>
<td>4</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Non-B, non-C</td>
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<td>0</td>
<td>0.490</td>
</tr>
<tr>
<td>Liver cirrhosis with hepatocellular carcinoma</td>
<td></td>
<td></td>
<td>1.000</td>
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<tr>
<td>Alcoholism</td>
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</tr>
<tr>
<td>HBV</td>
<td>6</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>HCV</td>
<td>2</td>
<td>3</td>
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<tr>
<td>Non-B, non-C</td>
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<tr>
<td>HBV + HCV</td>
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</table>

HBV = hepatitis B virus; HCV = hepatitis C virus.
Postoperative day 5

Data are presented as mean ± standard deviation.

*p < 0.05.

study. To our knowledge, no study has examined the association between fluid administration guided by SVV and standardized measures of renal and patient outcome in liver transplant recipients.

Our study was limited by the use of a historical control and small patient numbers. However, perioperative AKI is a serious complication. There is evidence to suggest that flow-based monitoring is superior to pressure-based data in order to optimize fluid management. Therefore, we did not conduct a randomized controlled study. Rather, we changed our intraoperative management to incorporate flow-based monitoring and conducted a retrospective review to assess the effectiveness of this change in management.

Our study population was matched for demographic features. Potential confounding variables that affect fluid administration were controlled in our study by using a single protocol for blood product transfusion and well-defined target points for SVV and CVP. Uniform protocols were also used to administer adequate hydration in order to preserve renal function.19,20 Therefore, both groups of patients received the same immunosuppressant regimen, and no NSAID-type drugs or aminoglycoside antibiotics were used. There is evidence to suggest that dynamic measurements of SVV are superior to CVP in assessing fluid responsiveness in mechanically ventilated patients.21 However, some investigators have criticized the reliability of the FTV system due to a lack of calibration.21

The amount of fluid administered to our study and control groups was not significantly different whether we used an SVV of 10% or a CVP of 8–10 mmHg as our target point for fluid administration. Combined with the similarity in patient outcomes, our study suggests that fluid management guided by SVV derived from the FTV system is of equal value to that based on CVP measurements.

Previous studies have shown a significant influence of CVP upon the amount of blood loss during the dissection phase of surgery.5–7,22,23 Our impression that a SVV of 10% and a CVP of 8–10 mmHg are physiologically similar is further strengthened by the insignificant differences in blood loss,
acute renal failure, and 30-day and 1-year survival rates between our study and control groups.

Furosemide was administered to all patients in our control group. As a result, in spite of similar fluid administration, a significantly higher urine output was noted in our control group. In liver failure patients, fluid is retained but shifted to the interstitial space. This may compensate for the higher urine output in the control group. Therefore, no difference in AKI and inotrope use was noted between our control and study patients.

Investigators have presented conflicting evidence about whether intentional hypovolemia increases the risk of renal failure or adverse patient outcomes. We noted that there was a considerable difference in patients’ severity of illness between studies, more perioperative complications being observed where there was a greater severity of illness. The interaction between variables requires further investigation.

Additional studies are required to focus on patients with stage III CKD to identify confounding variables that could influence the use of CVP compared with SVV in liver transplant recipients. A comparison of outcomes using multiple end-points for each technique is needed to determine the degree of concordance between the two measures of intravascular filling. Further, testing the same end-points in patients with different severities of illness is needed to segregate the effects of intravascular filling, severity of liver disease, and patient outcome.

In conclusion, the outcomes of living donor liver transplant patients who had fluid therapy guided by an SVV of 10% were similar to those of patients who were given fluids to reach a CVP of 810 mmHg. Our findings suggest that the two measures of vascular filling are feasible for patients with our demographic characteristics.

References


Table 5

Causes of death, and 30-day and 1-year survival rates.

<table>
<thead>
<tr>
<th>Cause of death</th>
<th>Study group (n = 25)</th>
<th>Control group (n = 25)</th>
<th>p</th>
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</thead>
<tbody>
<tr>
<td>Graft failure with postoperative day 5 acute kidney injury, n (%)</td>
<td>1 (4.00)</td>
<td>1 (4.00)</td>
<td>1.000</td>
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<tr>
<td>Graft failure without postoperative day 5 acute kidney injury, n (%)</td>
<td>0 (0)</td>
<td>0 (0)</td>
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<tr>
<td>Sepsis</td>
<td>0</td>
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<tr>
<td>30-day survival, n (%)</td>
<td>24 (96.00)</td>
<td>23 (92.00)</td>
<td>1.000</td>
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<tr>
<td>1-year survival, n (%)</td>
<td>23 (92.00)</td>
<td>22 (88.00)</td>
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</table>


