J Anesth (2009) 23:67–74
DOI 10.1007/s00540-008-0708-1

Journal of
Anesthesia



# Before–after study of a restricted fluid infusion strategy for management of donor hepatectomy for living-donor liver transplantation

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**Abstract**

*Purpose.* Intraoperative fluid infusion strategy remains controversial. Many animal model studies have shown that restricted fluid infusion reduces blood loss, though reports on this topic in humans are rare. The purpose of this study was to determine the effects on volume of blood loss of a restricted fluid infusion strategy for hepatectomy in donors for living-donor liver transplantation.

*Methods.* A before–after study design was used with prospective consecutive data collection. A total of 22 patients who underwent living-donor hepatectomy were enrolled. Eleven patients who were managed before the implementation of restricted-volume fluid administration comprised the standard-volume group, and 11 who were evaluated after the implementation of the restricted-volume infusion strategy comprised the restricted-volume group. In the standard-volume group, the donors were given 10 $ml \cdot kg^{-1} \cdot h^{-1}$ of lactated Ringer's solution and additional plasma expander corresponding to blood loss. In the restricted-volume group, the donors received 5 $ml \cdot kg^{-1} \cdot h^{-1}$ of lactated Ringer's solution until the resection of the hepatic graft, followed by 15 $ml \cdot kg^{-1} \cdot h^{-1}$ of lactated Ringer's solution after the completion of resection until the end of the operation.

*Results.* Intraoperative blood loss was less in the restricted-volume group (445 ± 193 ml) than in the standard-volume group (1331 ± 602 ml; $P < 0.01$). Intraoperative fluid infusion was also less in the restricted-volume group (4130 ± 563 ml) than in the standard-volume group (5634 ± 1260 ml; $P < 0.01$). There were no differences in length of hospital stay or side effects between the two groups.

*Conclusion.* Our restricted-volume strategy reduced blood loss and had no adverse effects during living-donor hepatectomy.

**Key words** Restricted volume · Limited volume · Restricted fluid · Donor hepatectomy · Living-donor liver transplantation

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Received: December 19, 2007 / Accepted: October 11, 2008

## Introduction

Fluid infusion strategy remains a matter of debate. The standard approach to the patient with hypotension presumed due to hemorrhage has been to infuse large volumes of fluid as early and as rapidly as possible, in order to restore intravascular volume and hemodynamic stability and to maintain vital organ perfusion. In some laboratory studies [1,2], vigorous fluid infusion reduced the risk of death. However, some laboratory studies [3–5] have recently reported that aggressive fluid infusion may be harmful, resulting in increased blood loss and, subsequently, greater mortality, and that restricted-volume infusion may be preferable.

Few clinical studies have evaluated the effectiveness of restricted-volume infusion strategies in humans. A systematic review [6] investigating the timing and volume of fluid administration identified only six randomized controlled trials, and found no evidence to either support or not support the use of early or larger-volume fluid administration for patients with bleeding. More studies have been expected on this topic in humans.

We performed the present before–after study to determine whether a restricted fluid infusion strategy would reduce blood loss, and to assess its side effects in patients undergoing donor hepatectomy for living-donor liver transplantation (LDLT).

## Participants, materials, and methods

### *Participants*

The study protocol was approved by our institutional ethics committee. Written informed consent was obtained from each patient. Twenty-two consecutive patients undergoing living-donor hepatectomy for LDLT from January 1998 to September 2001 were

enrolled. All patients underwent preoperative evaluation, including blood chemistry, blood cell counts, and serological testing for possible contagious or transmissible diseases, as well as determination of respiratory and cardiovascular profiles. Donors were selected from among family members of recipients, based on tissue compatibility and physical and laboratory findings.

*Anesthetic and surgical techniques*

All 22 patients received general anesthesia and additional thoracic epidural analgesia. Anesthesia was maintained with 2:1 nitrous oxide: oxygen and 0.2%–1.0% isoflurane. Muscle relaxation was obtained with intermittent doses of 1–2 mg vecuronium bromide as required. Ventilation was adjusted to maintain arterial carbon dioxide partial pressure at 35–40 mmHg. An epidural catheter was inserted via T10–11 or T11–12, and, after a test dose, 10 ml 1% lidocaine was injected, immediately followed by continuous infusion of 1% lidocaine at a rate of 10 $ml \cdot h^{-1}$. To avoid allogeneic blood transfusion, autologous blood was prepared from the patients.

All surgeries were performed by a single surgical team of three surgeons, who had already experienced more than 50 hepatectomy operations for LDLT before undertaking this study and had had in total more than 20 years' experience as surgeons. They used the same surgical techniques and equipment throughout the study. All grafts were performed by left lateral segmentectomy or extended left lateral segmentectomy without the middle hepatic vein [7]. Procurement of the graft was performed using an ultrasonic aspirator and bipolar electrocautery without clamping and without graft manipulation.

*Study design*

A before–after intervention study was performed. From January 1998 to May 2000, donors were given fluid using a standard-volume strategy. Initially, 10 $ml \cdot kg^{-1}$ lactated Ringer's solution (LR) was administered within 30 min to replace fluids lost during overnight fasting. This was followed by 10 $ml \cdot kg^{-1} \cdot h^{-1}$ LR until the end of the operation as essential fluid infusion during surgery. With the addition of the essential fluid infusion, as for replacement of blood loss, we infused twice the volume of the blood loss with hydroxyethyl starch (HES) or plasma protein fraction (PPF).

From May 2000 until September 2001, a restricted-volume infusion strategy had been implemented. The donor received 5 $ml \cdot kg^{-1} \cdot h^{-1}$ of lactated Ringer's until resection of the hepatic graft. After completion of the resection, fluid infusion was followed by 15 $ml \cdot kg^{-1} \cdot h^{-1}$ LR until the end of the operation. No initial fluid therapy and no additional volume for blood loss were administered. In addition, if systolic blood pressure decreased below 80 mmHg in this group, vasopressor administration was planned in case of necessity. In both groups, if the patient had his/her own autologous blood, which had been collected 1 or 2 weeks before the surgery, it was retransfused when the hemoglobin concentration was less than 10 $g \cdot dl^{-1}$ during the operation.

*Principal measurements*

During the surgery, intraoperative blood loss, total fluid volume, urinary output, graft weight, and operative duration were measured.

Intraoperative blood loss was the amount of blood loss determined by weighing gauze pads which had absorbed blood and measuring the blood loss in the suction apparatus. Blood loss was measured every 15–20 min during surgery. We also compared amounts of blood loss before and after resection of the graft. As variables representative of the circulation throughout the operation, the vital signs were determined at four time points: at start of surgery, at 1 h after the start of surgery, at graft dissection, and at the end of surgery. After the surgery, the length of hospital stay, hematologic findings, and complications were evaluated. Length of hospital stay was determined as the number of days from the operation to discharge from the hospital. Hemoglobin, aspartate aminotransferase, alanine aminotransferase, total bilirubin, C-reactive protein, white blood cell count, and body temperature were measured every day.

Postoperative management was performed based on the usual general surgical care.

*Statistical analysis*

The Statistical Package for Social Sciences (SPSS 16.0 for Windows; SPSS, Chicago, IL, USA) was used for statistical analysis. For comparisons of the mean differences between the two groups, the *t*-test was used, with a significance level of $P < 0.01$, based on the results of homoscedasticity obtained by Levine's test for equality variance. All $P$ values were two-tailed. $P$ values less than 0.01 were considered significant.

In addition, the factors that might affect the amount of blood loss were analyzed by correlation analysis. After excluding the effect of fixing other factors, those factors that showed correlation in the correlation analysis were analyzed with a partial correlation coefficient, which shows the intensity of the relation to the focused two variables alone, in order to know if these factors might be affected by any other factors.

## Results

### *Baseline characteristics*

All patients were healthy and had normal liver function. Eleven patients were included in the standard-volume group and 11 in the restricted-volume group. Preoperative profiles of the patients in the two groups are summarized in Table 1. There were more men in the standard-volume (73%) than in the restricted-volume group (45%). However, there were no differences between the groups in age, height, weight, or hemoglobin level before the operation.

### *Intraoperative blood loss, fluid infusion, and vital signs*

Intraoperative blood loss was less in the restricted-volume group (445 ± 193 ml) than in the standard-volume group (1331 ± 602 ml; $P < 0.01$; Table 2). In particular, blood loss before resection of the graft was less in the restricted-volume group ($P < 0.01$; Table 2). Intraoperative fluid requirement was less in the restricted-volume group (4130 ± 563 ml) than in the standard-volume group (5634 ± 1260 ml; $P < 0.01$). Blood pressure and central venous pressure (CVP) in the restricted-volume group were lower than those in the standard-volume group, though not to statistically significant extents (Table 3). No vasopressors were administered during the surgery in the restricted-volume group.

### *Length of hospital stay and other findings*

The restricted-volume group had no adverse effects such as abnormal blood chemistry findings, hematologic findings, complications, or prolongation of hospital stay. Table 4 shows hospital stay, peak aspartate aminotransferase, peak alanine aminotransferase, and peak total bilirubin results as assessments of liver function, and

**Table 1.** Patient characteristics

| Characteristic | Standard group $n = 11$ | Restricted group $n = 11$ | $P$ value |
|---|---|---|---|
| Age (years) | 38.1 ± 5.7 | 35.7 ± 5.6 | 0.31 |
| Male sex (%) | 73 | 45 | |
| Height (cm) | 169.7 ± 5.7 | 164.5 ± 7.0 | 0.67 |
| Weight (kg) | 62.7 ± 9.3 | 61.4 ± 9.3 | 0.73 |
| Hemoglobin before the operation ($g \cdot dl^{-1}$) | 12.9 ± 1.8 | 12.1 ± 2.1 | 0.35 |

Values are means ± SD

**Table 2.** Intraoperative data

| Variable | Standard group $n = 11$ | Restricted group $n = 11$ | $P$ value |
|---|---|---|---|
| Blood loss (g) | 1331 ± 602 | 445 ± 193 | <0.01 |
| Before resection | 1025 ± 520 | 340 ± 171 | <0.01 |
| After resection | 306 ± 209 | 106 ± 34 | 0.07 |
| Total fluid volume (ml) | 5634 ± 1260 | 4130 ± 563 | <0.01 |
| Lactated Ringer's solution (ml) | | | |
| Before resection | 2745 ± 619 | 2026 ± 370 | <0.01 |
| After resection | 1045 ± 434 | 1888 ± 356 | <0.01 |
| Hydroxyethyl starch (ml) | | | |
| Before resection | 1090 ± 801 | 0 | <0.01 |
| After resection | 91 ± 202 | 136 ± 234 | 0.63 |
| Plasma protein fraction (ml) | | | |
| Before resection | 181 ± 355 | 0 | <0.01 |
| After resection | 181 ± 226 | 0 | 0.02 |
| Autologous blood (ml) | | | |
| Before resection | 144 ± 320 | 0 | 0.17 |
| After resection | 300 ± 312 | 48 ± 87 | 0.02 |
| Urinary output (ml) | 989 ± 629 | 920 ± 883 | 0.83 |
| Graft weight (g) | 331 ± 77 | 315 ± 92 | 0.64 |
| Operative duration (min) | 461 ± 136 | 452 ± 62 | 0.84 |
| Before resection (min) | 308 ± 51 | 289 ± 45 | 0.38 |

Values are means ± SD

**Table 3.** Hemodynamics during surgery

| | Start of surgery | One hour after start | Graft dissection | End of surgery |
|---|---|---|---|---|
| Standard group ($n = 11$) | | | | |
| Heart rate (beats·min$^{-1}$) | 78.6 ± 16.1 | 87.3 ± 17.7 | 81.4 ± 16.7 | 86.8 ± 14.1 |
| Systolic blood pressure (mmHg) | 95.9 ± 11.1 | 120.5 ± 16.7 | 114.1 ± 12.4 | 127.7 ± 21.5 |
| Diastolic blood pressure (mmHg) | 52.7 ± 11.7 | 69.5 ± 14.9 | 64.5 ± 10.1 | 70.5 ± 14.9 |
| Central venous pressure (mmHg) | 6.1 ± 2.3 | 7.7 ± 2.5 | 7.1 ± 2.6 | 8.3 ± 2.5 |
| Restricted group ($n = 11$) | | | | |
| Heart rate (beats·min$^{-1}$) | 66.4 ± 11.2 | 76.6 ± 12.0 | 75.2 ± 10.2 | 76.2 ± 10.2 |
| Systolic blood pressure (mmHg) | 101.8 ± 9.0 | 115.9 ± 13.0 | 109.9 ± 12.9 | 124.1 ± 13.0 |
| Diastolic blood pressure (mmHg) | 58.6 ± 6.7 | 66.8 ± 8.7 | 60.1 ± 7.4 | 64.5 ± 6.1 |
| Central venous pressure (mmHg) | 8.0 ± 2.1 | 8.3 ± 1.7 | 6.2 ± 1.7 | 7.1 ± 1.8 |

Values are means ± SD
There were no statistically significant differences between the groups

**Table 4.** Postoperative data

| Variable | Standard group $n = 11$ | Restricted group $n = 11$ | $P$ value |
|---|---|---|---|
| Hospital stay (days) | 18.5 ± 6.3 | 20.7 ± 3.5 | 0.30 |
| Lowest hemoglobin (g·dl$^{-1}$) | 9.9 ± 0.9 | 9.0 ± 1.3 | 0.09 |
| Peak aspartate aminotransferase (IU·l$^{-1}$)[a] | 271 ± 150 | 253 ± 109 | 0.74 |
| Peak alanine aminotransferase (IU·l$^{-1}$)[a] | 314 ± 202 | 267 ± 111 | 0.50 |
| Peak total bilirubin (mg·dl$^{-1}$)[a] | 1.8 ± 0.9 | 1.5 ± 0.4 | 0.20 |
| Peak body temperature (°C)[a] | 38.4 ± 0.4 | 38.3 ± 0.6 | 0.90 |
| Peak C-reactive protein (mg·dl$^{-1}$)[a] | 7.7 ± 3.8 | 8.4 ± 1.5 | 0.54 |
| Peak white blood cell count (μl$^{-1}$)[a] | 12600 ± 36 | 16300 ± 36 | 0.27 |

Values are means ± SD
There were no statistically significant differences between the groups
[a]The highest values during hospital stay

peak white blood cell count, and peak C-reactive protein as assessments of infection. There were no significant differences between the groups in any of these variables.

### *Correlation analysis of the factors that affected the amount of blood loss*

In correlation analysis of the factors that might affect the amount of blood loss, total infusion amount, LR infusion amount before hepatectomy, HES infusion amount before hepatectomy, PPF infusion amount before hepatectomy, and blood infusion amount after hepatectomy showed significant correlation, at $P < 0.01$, to amount of blood loss (Table 5). In addition, operative duration showed strong correlation, at $P = 0.02$. Then the partial correlation coefficients of total infusion and LR infusion, which were thought to be the cause of reducing the amount of blood loss in this study, were obtained, as the factors showing significant differences might be affected each other. In the partial correlation coefficient analysis, the zero-order correlation of total infusion to the amount of blood loss, for example, was 0.925 with $P < 0.01$ of significant probability, while in the first-order correlation, the partial correlation coefficient of total infusion to the amount of blood loss with the fixed HES before resection was 0.831 with $P < 0.01$ of significant probability, suggesting strong correlation (Table 6). The HES infusion amount did not affect the correlation between total infusion and the amount of blood loss; the correlation of total infusion to the amount of blood loss was still detected if the effect of HES before resection was removed. The factors other than total infusion amount and LR infusion amount before hepatectomy showed the same results. These results show that total infusion amount and LR infusion amount before hepatectomy truly affected the amount of blood loss, without HES infusion amount before hepatectomy, PPF infusion amount before hepatectomy, blood infusion amount after hepatectomy, and operative duration having any effect. It was suggested that the lower total infusion amount and lower LR infusion amount before hepatectomy in the present restricted-infusion group decreased their total amount of blood loss.

## Discussion

Our study demonstrated that a restricted-volume fluid infusion strategy was significantly more likely than a

**Table 5.** The Pearson's correlation coefficients of other factors to blood loss

| | Mean | SD | Correlation coefficient | *P* value |
|---|---|---|---|---|
| Blood loss | 888.00 | 629.37 | 1.000 | |
| Height | 167.09 | 6.80 | 0.135 | 0.55 |
| Weight | 62.05 | 9.07 | 0.161 | 0.47 |
| Operative duration | 456.82 | 103.53 | 0.497 | 0.02 |
| Total infusion | 4882.41 | 1224.60 | 0.925 | <0.01 |
| LR before resection | 2385.68 | 619.01 | 0.684 | <0.01 |
| HES before resection | 545.45 | 785.42 | 0.731 | <0.01 |
| PPF before resection | 90.91 | 262.15 | 0.609 | <0.01 |
| Blood before resection | 71.82 | 232.47 | 0.403 | 0.06 |
| LR after resection | 1466.59 | 579.50 | –0.440 | 0.04 |
| HES after resection | 113.64 | 214.47 | –0.268 | 0.23 |
| PPF after resection | 90.91 | 181.68 | –0.661 | <0.01 |
| Blood after resection | 173.86 | 258.23 | 0.658 | <0.01 |
| Graft weight | 322.95 | 83.53 | 0.347 | 0.11 |
| Urine | 954.77 | 749.29 | 0.331 | 0.13 |
| SBP at start of surgery | 98.86 | 10.34 | 0.156 | 0.49 |
| At 1 h after start | 118.18 | 14.76 | 0.299 | 0.18 |
| At graft dissection | 112.00 | 12.53 | 0.094 | 0.68 |
| At end of surgery | 125.91 | 17.43 | 0.292 | 0.19 |
| DBP at start of surgery | 55.68 | 9.79 | 0.172 | 0.44 |
| At 1 h after start | 68.18 | 12.01 | 0.022 | 0.92 |
| At graft dissection | 62.32 | 8.93 | –0.068 | 0.76 |
| At end of surgery | 67.50 | 11.52 | 0.407 | 0.06 |
| HR at start of surgery | 72.50 | 14.94 | 0.473 | 0.03 |
| At 1 h after start | 81.95 | 15.71 | 0.216 | 0.33 |
| At graft dissection | 78.27 | 13.88 | 0.347 | 0.11 |
| At end of surgery | 81.50 | 13.31 | 0.356 | 0.10 |
| CVP at start of surgery | 7.05 | 2.36 | –0.369 | 0.09 |
| At 1 h after start | 8.00 | 2.09 | –0.018 | 0.90 |
| At graft dissection | 6.64 | 2.19 | 0.154 | 0.50 |
| At end of surgery | 7.68 | 2.17 | 0.277 | 0.21 |

LR, lactated Ringer's solution; HES, hydroxyethyl starch; PPF, plasma protein fraction; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; CVP, central venous pressure

**Table 6.** Partial correlation to blood loss

| Variables | Zero-order correlation | *P* value | Control | First-order correlation | *P* value |
|---|---|---|---|---|---|
| Total infusion | 0.925 | <0.01 | HES before resection | 0.831 | <0.01 |
| | 0.925 | <0.01 | PPF before resection | 0.885 | <0.01 |
| | 0.925 | <0.01 | PPF after resection | 0.871 | <0.01 |
| | 0.925 | <0.01 | Blood after resection | 0.868 | <0.01 |
| | 0.925 | <0.01 | Operative duration | 0.900 | <0.01 |
| LR before resection | 0.684 | <0.01 | HES before resection | 0.735 | <0.01 |
| | 0.684 | <0.01 | PPF before resection | 0.476 | 0.01 |
| | 0.648 | <0.01 | PPF after resection | 0.720 | <0.01 |
| | 0.684 | <0.01 | Blood after resection | 0.513 | <0.01 |
| | 0.684 | <0.01 | Operative duration | 0.698 | <0.01 |

LR, lactated Ringer's solution; HES, hydroxyethyl starch; PPF, plasma protein fraction

standard-volume infusion strategy to reduce blood loss in living-donor hepatectomy. We also found that length of hospital stay and rate of adverse effects were the same in these two groups. Our results agree with the findings of previous investigations in animals [3–5,8], which demonstrated that aggressive fluid infusion may be harmful, resulting in increased blood loss and, subsequently, greater mortality, and that restricted-volume infusion may be preferable. The authors of these studies suggested that restricted-volume fluid administration

avoided increases in blood pressure, dilution of clotting factors, and decreases in blood viscosity, and thereby decreased bleeding. We think these factors are particularly important in patients undergoing donor hepatectomy for living-donor liver transplantation (LDLT), especially before the resection of the graft. Actually, in the present study, before resection, a statistically significant reduction of blood loss was demonstrated in the restricted-volume group. Our study revealed reduction of blood loss with a restricted-volume fluid strategy.

The best fluid management strategy has yet to be established [9]. One systematic review [8] of animal studies explored the reason for the different outcomes of fluid strategies and found that the effect of fluid therapy depended on the severity of hemorrhage. When the hemorrhage was severe enough, such as after an injury to the aorta or when more than 50% of a rat's tail was removed, fluid therapy reduced the risk of death. However, when hemorrhage was less severe, such as after injury to vessels other than the aorta, or when less than 50% of the rat's tail was removed, fluid therapy increased the risk of death. These results may be consistent with our findings, because in our study, the surgery most likely involved minor liver parenchyma damage without major vascular injury, and hemorrhage was probably not severe.

In humans, few clinical studies have evaluated the effectiveness of restricted-volume fluid strategies. As noted above, a systematic review [6] investigating the timing and volume of fluid administration identified only six randomized controlled trials and found no evidence to either support or not support the use of early or larger-volume fluid administration. For example, in the field of prehospital care, one prospective clinical study found that delay of aggressive fluid resuscitation until operative intervention improved the outcome for hypotensive patients with penetrating torso injuries [10], though it did not demonstrate reduction of blood loss; however, the method of randomization used in that study was inadequate [6]. One trial reported that hypotensive resuscitation during active hemorrhage did not affect outcome [11]; based on the systematic review [8] noted above, the reason for this may be that the authors did not stratify patients by severity of hemorrhage. The protocol of restricted-volume infusion in our study might be thought to be effective in patients who do not have severe hemorrhage; in consequence, it is possible that our protocol should not be applied in those with severe hemorrhage. Fluid volume therapy may need to be performed according to classification of the severity of hemorrhage, and more evidence regarding fluid infusion strategy may be needed.

Several studies have examined whether a low CVP is associated with less blood loss during hepatectomy. However, it is not easy to demonstrate that a lower CVP is related to a reduction of blood loss during liver surgery. Some prospective studies [12] have failed to demonstrate whether this is the case, while other studies which demonstrated the effectiveness of a low CVP were retrospective studies [13]. One prospective study [14], showed that patients with a low CVP (<5 $cmH_2O$) had significantly lower blood loss. However, the low CVP was obtained by chance and not by intention. Only a few randomized controlled studies of a lower CVP have been reported. In our study, there was no statistically significant difference in CVP between the two groups, suggesting that the usefulness of CVP measurement as an indicator of volume status may be limited.

Patients in our restricted-volume group had no adverse effects on hepatic or renal function, nor did they have an increased length of hospital stay. One study [15] of a low CVP strategy showed that, despite success in reducing blood transfusion in liver resection patients, rates of postoperative renal failure and 30-day mortality were increased. In addition, there is a report of a case of severe pulmonary embolism in an LDLT donor [16] in whom hypovolemic fluid therapy was considered one of the causes of the embolism. In our study, the beneficial outcome of the restricted-volume strategy may have been due to the increase in the volume of fluid administered after the completion of hepatic grafting.

Administration of hydroxyethyl starch (HES), more of which was infused in the standard-volume group in our study, may be criticized, because HES solutions cause several abnormalities in hemostasis [17]. In the present study, HES was infused for replacement of blood loss when blood loss increased. Thus, the more blood loss was increased, the more HES was infused, and the HES amount before resection showed a significant correlation, at $P < 0.01$, to the amount of blood loss (Table 5). However, our HES was a low-molecular-weight (70 kDa) starch and has less effect on hemostasis than other types of HES [18,19]. We administered only 1090 ± 801 ml of HES, which was not enough to influence hemostasis [20], and the infusion of HES was not completed before the completion of liver resection. We believe it is unlikely that a hemostatic abnormality would have led to clinically significant bleeding in this study; however, to completely rule out the effect of HES, we may have to carry out, for example, only an LR infusion study without HES.

In regard to sex distribution, there was a considerable difference between our two groups. In the standard-volume group there were more men ($n = 8$) than women ($n = 3$). All the women in both groups were premenopausal, and estrogen has an effect on hemostasis and thrombosis. However, estrogen increases coagulation [21] and increases fibrinolysis [22]. In addition, for cardiovascular disease, estrogen is a favorable factor in

regard to lipid profile and vasodilatation [23]. Because of these many effects, we could not demonstrate that there was a sex-specific difference in hemostasis [21–23]. As a result, we do not believe that this sex difference is the main reason for our beneficial outcome.

As an infusion method after the completion of the hepatectomy, we increased fluid infusion, followed by 15 $ml \cdot kg^{-1} \cdot h^{-1}$ lactated Ringer's solution (LR) until the end of the operation, in order to avoid the side effects of restricted-volume infusion. In regard to reducing blood loss, maintaining a restricted infusion volume may cause less blood loss. However, as noted above, in one study [15], a low CVP strategy showed that rates of postoperative renal failure and 30-day mortality were increased with a restricted infusion volume. In addition, one case report demonstrated severe pulmonary embolism in an LDLT donor [16]. We thought that our restricted-volume infusion might induce a hypovolemic condition; to avoid this side effect, we increased the fluid infusion. In our study, the increase in the volume of fluid administered after the completion of hepatic grafting may have been a factor in the beneficial outcome of the restricted-volume strategy.

Our study has several important limitations. First, the number of patients was small, and they were not randomized to the two treatment groups. However, our hospital performs this surgery at a rate of, at most, one case per month, making it difficult to perform a randomized study for this surgery.

Another important limitation of this study is that it is possible that a learning effect for surgeons affected the results of the study. However, we do not believe that this is the main reason for the observed decrease in blood loss, because our hospital began performing this surgery in 1991 and we have performed this surgery at a low rate, with fewer than ten cases per year. In addition, we do not believe that the same three experienced surgeons with the same surgical technique and equipment would have achieved marked improvement during the period of this study alone. Prior to the start of this study, they had already performed, in total, more than 50 cases of this surgery.

We conclude that our restricted-volume fluid management protocol reduced blood loss in living-donor hepatectomy, and that large randomized controlled trials of this protocol are warranted in patients with nonsevere intraoperative hemorrhage.

*Acknowledgments.* We thank Drs. Takashi Hashimoto, Tatsuya Suzuki, and Satoshi Kondo, the transplantation surgeons, for their support and cooperation. We also thank ex-professor and chair, David Bevan, the Department of Anesthesia, University of Toronto, and ex-professor, Hirotada Katsuya, Department of Anesthesiology and Medical Crisis Management, Nagoya City University, for critical reading of our manuscript and valuable suggestions.

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