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ORIGINAL ARTICLE

Retrospective Study

Living donor liver transplantation with body-weight more or less than 10 kilograms

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Data sharing: Informed consent was not obtained but the presented data are anonymized and risk of identification is low.

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Abstract

AIM: To compare the outcomes of pediatric patients weighing less than or more than 10 kg who underwent liver transplantation.

METHODS: Data for 196 pediatric patients who underwent living donor liver transplantation between June 1994 and February 2011 were reviewed retrospectively. The information for each patient was anonymized and de-identified before analysis. The data included information regarding the pre-transplant conditions, intraoperative fluid replacement and outcomes for each patient. The 196 patients were divided into two groups: those with body weights of less than 10 kg were included in group 1 (G1; n = 101), while those with body weights of more than 10 kg were included in group 2 (G2; n = 95). For each group, the patients' ages, body weights, heights, pediatric end stage liver disease scores, anesthesia times, and warm and cold ischemic times were analyzed. In addition, between-group comparisons were also made. Mann-Whitney U tests were used to compare all the variables except for complications and survival rates, which were analyzed using χ^2 tests and Kaplan-Meier tests, respectively.

RESULTS: The general medical conditions of the G1

patients were worse than those of the G2 patients, as shown by the higher pediatric end stage liver disease scores and poorer *Z*-scores. In addition, the pre-operative Hb and serum albumin levels were all lower for the G1 patients than for the G2 patients. The G1 patients also had significantly more intraoperative blood loss than the G2 patients. In addition, the intraoperative fluid requirements for the G1 patients, including leukocyte poor red blood cell transfusions, 5% albumin infusions and crystalloid infusions, were significantly higher than those for the G2 patients. The risk of intraoperative portal vein thrombosis was higher for the patients in G1 than for those in G2. However, the one-year survival rates (95.9% and 96.8% for G1 and G2, respectively) and three-year survival rates (94.9% and 94.6% for G1 and G2, respectively) for both groups were similar.

CONCLUSION: Patients weighing less than 10 kg typically have poorer conditions, but their survival rates are comparable to those of children weighing more than 10 kg.

Key words: Pediatric; Body weight; Pre-transplant condition; Fluid; Living donor liver transplantation; Outcome

Core tip: Although pediatric patients weighing less than 10 kg who underwent living donor liver transplantation usually had worse pre-transplant conditions, more intraoperative bleeding and more portal vein complications, their three-year survival rate was 94%, a rate comparable to that achieved by children weighing more than 10 kg. A prerequisite for achieving these excellent results is good and effective teamwork. Cooperation between surgeons, plastic surgeons, and anesthesiologists in the operating theater is fundamental, but the contributions of radiologists are also critical. Radiologists should be available in the operating room to perform Doppler ultrasounds or place vascular stents, as required.

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INTRODUCTION

Performing living donor liver transplantation (LDLT) for pediatric patients, especially those with body weights of less than 10 kg, poses a challenge for all the participants in the liver transplant team, including anesthesiologists[1,2]. The outcomes of such transplants for pediatric patients weighing less than 10 kg differ from those for pediatric patients weighing more than 10 kg[1-4]. We have previously reported that the average change in core temperature during an LDLT for pediatric patients weighing less than 10 kg is significantly different from that in heavier children[5]. Furthermore, a lower survival rate for lower weight children was reported by Arnon *et al*[3], and according to other studies, this poorer survival results from higher risks of perioperative vascular complications, bile duct complications and infections[4,6,7]. In pediatric kidney transplantation, the ideal body weight for a recipient has also been found to be greater than 10 kg[8]. Most of the previous reports regarding pediatric organ transplantation have primarily evaluated the outcomes in terms of the morbidity and mortality of the procedure in question[1-4]. However, little information can be found in the literature concerning the anesthetic fluid requirements for pediatric patients with different body weights undergoing LDLT. Thus, the aim of the current study was to evaluate, analyze, and compare data retrospectively regarding the anesthetic fluid requirements for pediatric patients weighing less and more than 10 kg who underwent LDLT, while at the same time also comparing and analyzing the complications and survival rates for such patients.

MATERIALS AND METHODS

Ethics approval

This retrospective study was approved by the Institutional Review Board for Human Studies of Chang Gung Memorial Hospital (101-1945B).

Patient selection and data collection

We collected and analyzed the data from the anesthesia records of pediatric patients who underwent LDLT between June 1994 and February 2011. The information for each patient was anonymized and de-identified before analysis. The general anesthesia, intraoperative monitoring and blood transfusion protocols used[9], as well as their documentation[10], were similar to those described in previously published reports[5,9,11-13]. Estimated blood losses were made through visual estimations of a small (250 mL) suction bottle (Receptal® Accurate Measurement Device, Hospira, Inc. Lake Forest, Il 60045, United States) and the weight of laparotomy sponges. The pediatric patients were divided into two groups: those with body weights of less than 10 kg were included in group 1 (G1), while those with weights of more than 10 kg were included in group 2 (G2). For each group, the patients' ages, body weights, heights, pediatric end stage liver disease scores (PELDS), anesthesia times, and warm and cold ischemic times were analyzed. In addition, between-group comparisons were made.

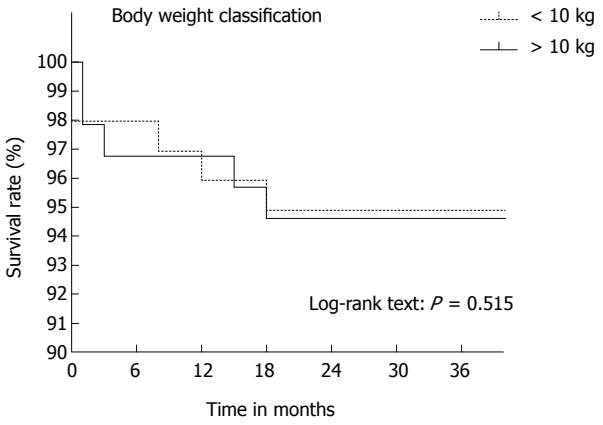

Figure 1 Three-year survival rate (%) between groups.

Table 1 The gender and age specific *Z*-scores of the measurements in height and weight in both groups

	< 10 kg (group 1) *Z*-score	> 10 kg (group 2) *Z*-score
Male height	-3.364 (n = 51)	-2.43 (n = 53)
Male weight	-2.977 (n = 51)	-1.07 (n = 53)
Female height	-3.266 (n = 50)	-1.504 (n = 42)
Female weight	-3.277 (n = 50)	-0.046 (n = 42)

The calculation of Z-score follows that used by the National Health and Nutrition Examination Survey (NHANES) 2000[14].

Table 2 Patients' characteristics between groups

	G1 (n = 101)	G2 (n = 95)	*P* value
Age (mo)	16.1± 25.1	67.6 ± 49.1	< 0.001
Weight (kg)	7.8 ± 1.2	18.6 ± 11.2	< 0.001
Height (cm)	69.6 ± 6.0	103.1 ± 23.9	0.006
PELD score	15.9 ± 10.9	6.8 ± 8.9	< 0.001
Hemoglobin (g/dL)	9.2 ± 1.7	10.0 ± 1.7	0.003
Serum albumin (g/L)	3.1 ± 0.6	3.5 ± 0.7	< 0.001
Serum creatinine (mg/dL)	0.8 ± 0.3	0.7 ± 0.14	0.113
Total bilirubin	18.4 ±11.0	8.4 ± 9.3	< 0.001
INR	1.45 ± 0.8	1.07 ± 0.2	< 0.001
APTT (S)	44.4 ± 18.9	37.3 ± 13.2	0.001
Platelet (1000/μL)	191.0 ± 110	163.1 ± 117	0.015

PELD: Pediatric end stage liver disease; INR: International normal ratios; APTT: Activated partial thromboplastine times; G1: Those with body weights of less than 10 kg were included in group 1; G2: Those with weights of more than 10 kg were included in group 2.

The gender and age specific *Z*-scores of the height and weight measurements were also calculated[14]. Likewise, intraoperative blood loss, ascitic loss and fluid replacement amounts were recorded and compared. Laboratory data, including hemoglobin (Hb) levels, serum albumin levels, platelet counts, activated partial thromboplastine times (APTT), international normal ratios (INRs), serum creatinine levels, total bilirubin levels and pH levels were also collected, analyzed, and compared between groups. All data related to body weight were converted to a per-kg basis for comparison. The frequency of perioperative morbidity and one- and three-year survival rates were also compared between the groups.

Statistical analysis

Mann Whitney *U* tests were used to compare data for all the variables, except for the morbidity and one- and three-year survival rates. The incidences of morbidity were compared by χ^2, while the one- and three-year survival rates were compared by Kaplan-Meier tests. A *P* value < 0.05 was regarded as statistically significant. Data are presented as mean ± SD.

The statistical methods used in this study were reviewed by Dr. Shao-Chun Wu of Chang Gung University, Taiwan.

RESULTS

The patient etiologies (for G1 and G2, respectively) were as follows: biliary atresia (92 patients and 70 patients), neonatal hepatitis (7 and 4), glycogen storage disease (0 and 12), Alagille syndrome (1 and 5), urea cycle disease (1 and 0), fulminant hepatitis (0 and 1), cryptogenic (0 and 1), Wilson's disease (0 and 1) and hepatitis C virus (0 and 1). Table 1 shows the gender- and age-specific *Z*-scores for the height and weight measurements in both groups. The *Z*-score in G1 was < -3, which indicated that the patients had suffered from moderate to severe malnutrition[14]. Table 2 shows the characteristics of the patients in G1 and G2. The PELD scores were significantly higher for the G1 patients, while the pre-operative Hb and serum albumin levels were all lower for the G1 patients. The coagulation test results indicated that APTT and INR were both significantly prolonged in G1 patients and that the G1 patients had higher total bilirubin levels and platelet counts before the operation. Table 3 shows that the average anesthesia time for G1 was longer than the average time for G2, but also that the warm and cold ischemic times were similar between the groups. The extubation times were significantly longer among the G1 patients compared with the times for the G2 patients (Table 4). The absolute amount of blood loss for the two groups was similar. When body weight was taken into consideration and the data were converted to a per-kg basis, it was revealed that the G1 patients had significantly more ascites and greater blood loss per kilogram. Therefore, the G1 patients received significantly more crystalloids, 5% albumin and red blood cells to replace their losses (Table 3). Table 4 shows that the G1 patients also required more sodium bicarbonate to maintain acceptable pH levels and also received more supplemental calcium. Table 5 shows the outcomes of the patients: the perioperative morbidities, except for portal vein complications, were similar between the groups; the one- and three-year survival rates were also similar between the groups (Figure 1). G1 had significantly more perioperative

Table 3 Anesthesia time, intraoperative blood loss and fluids replacement

	G1 (n = 101)	G2 (n = 95)	P value
Anesthesia time (h)	13.5 ± 9.3	13.3 ± 2.2	0.035
Blood loss (mL)	215.3 ± 238.8	284.8 ± 447.8	0.573
Blood loss (mL/kg)	28.6 ± 36.7	15.0 ± 21.2	< 0.001
Ascites (mL/kg)	234 ± 379	161.3 ± 383	< 0.001
Crystalloid (mL/kg/h)	16.8 ± 5.5	12.1 ± 5.5	< 0.001
Red blood cells (mL/kg)	29.0 ± 29.0	10.0 ± 17.3	< 0.001
Fresh frozen plasma (mL/kg)	1.5 ± 7.6	5.1 ± 11.0	0.571
5% Albumin (mL/kg)	8.8 ± 6.8	2.3 ± 2.0	< 0.001
Sodium bicarbonate (mEq/kg)	3.4 ± 1.9	2.3 ± 1.9	< 0.001
Calcium chloride (mg/kg)	0.7 ± 0.5	0.34 ± 0.3	< 0.001
Lasix administration (mg/kg)	0.5 ± 1.9	1.0 ± 2.9	0.884
Cold ischemic time (min)	58.6 ± 20.5	65.5 ± 29.1	0.243
Warm ischemic time (min)	49.5 ± 13.9	47.6 ± 14.9	0.226

P < 0.05 was regarded as significant. G1: those with body weights of less than 10 kg were included in group 1; G2: those with weights of more than 10 kg were included in group 2.

Table 4 Intra- and postoperative laboratory data between groups

	G1 (n = 101)	G2 (n = 95)	P value
pH - after anesthesia	7.34 ± 0.07	7.36 ± 0.07	0.060
pH - dissection	7.27 ± 0.06	7.30 ± 0.07	0.003
pH - anhepatic	7.26 ± 0.06	7.29 ± 0.10	0.013
pH - reperfusion	7.23 ± 0.06	7.27 ±.09	0.006
pH - end of surgery	7.28 ± 0.07	7.29 ± 0.08	0.215
INR post-operation	2.1 ± 1.0	1.9 ± 0.6	0.900
APTT post-operation (second)	77.2 ± 25.5	55.2 ± 20.9	< 0.001
Platelet post-operation (1000/μL)	109.5 ± 62.9	128.3 ± 74.6	0.070
Postoperative hemoglobin (g/dL)	7.6 ± 1.3	8.5 ± 1.5	0.001
Hemoglobin at extubation (g/dL)	8.2 ± 1.5	8.8 ± 1.5	0.072
Extubation time (h)	61.1 ± 243.5	23.6 ± 36.0	0.047

INR: International normal ratios; APTT: Activated partial thromboplastine times; G1: Those with body weights of less than 10 kg were included in group 1; G2: Those with weights of more than 10 kg were included in group 2.

portal vein thrombosis compared with G2, with an odds ratio of 14.143 and a 1.783-112.174 95% confidence interval. Although G1 had more incidences of perioperative portal vein thrombosis, those cases were detected quickly and treated immediately[4], and thus did not seem to affect the survival rates. Overall, the survival rates for both groups were similar, with 95.9% and 96.8% one-year survival rates and 94.9% and 94.6% three-year survival rates for G1 and G2, respectively (Figure 1 and Table 5).

DISCUSSION

Our results showed that the G1 patients had significantly different preoperative conditions compared with the G2 patients (Tables 1 and 2). Although the current study included only living donor liver transplantation, organ allocation has nothing to do with PELDS[15]. However, when PELDS were applied to the patients in this study, the G1 patients were indeed found to have higher average PELDS values, with mean values of 15.9 ± 10.9 and 6.8 ± 8.9 for G1 and G2, respectively. PELDS provide a useful model consisting of five objective parameters: total serum bilirubin, INR, albumin, growth failure and age. PELDS can predict death or deterioration in the condition of the patient that may require transfer to the intensive care unit while the patient awaits liver transplantation[16]. The PELDS and the Z-score, an anthropometric parameter for malnutrition[17], indicated that the medical conditions of the G1 patients were indeed worse and that their indications for liver transplantation were relatively urgent compared with those for the G2 patients. Furthermore, more challenging complications and difficulties are to be expected in LT for pediatric patients weighing less than 10 kg[1-4]. Table 3 further revealed that the total anesthesia time for G1 patients was significantly longer than that for G2 patients, most likely because of more difficult placement of arterial lines and the central venous catheter. In addition, more surgical time was needed for G1 patients to solve the intraoperative vascular complications, such as portal vein thrombosis[4,18]. Significant differences in ascites and blood loss were also noted when body weight was taken into consideration. High blood loss index is a risk factor that contributes to poor outcomes of the graft in pediatric LT[19]. The mean blood loss values for G1 and G2 were 28.6 ± 36.7 and 15.0 ± 21.2 mL/kg, respectively. Higher blood loss in infants weighing less than 10 kg has also been reported in open heart surgery[20]. Indeed, blood loss and transfusion requirements were correlated inversely with age and body weight[20]. More blood loss may cause more labile hemodynamic changes, the development of metabolic acidosis and higher incidences of ionized hypocalcemia[12]. Table 3 shows that the G1 patients received significantly more crystalloids (16.8 ± 5.5 *vs* 12.1 ± 5.5), more RBC (29.0 ± 29.0 *vs* 10.0 ± 17.3) and more 5% albumin (8.8 ± 6.8 *vs* 2.3 ±

Table 5 Comparison of the morbidity and mortality between groups

	G1 (n = 101)	G2 (n = 95)	P value
Bile duct complication	5	7	0.528
Hepatic artery complication	9	3	0.092
Hepatic vein complication	2	6	0.274
Portal vein complication	12	1	0.001
Reopen	19	13	0.324
One-year survival rate (%)	95.9	96.8	0.515
Three-year survival rate (%)	94.9	94.6	0.515

G1: those with body weights of less than 10 kg were included in group 1; G2: those with weights of more than 10 kg were included in group 2.

2.0) to meet their losses and that they also received more sodium bicarbonate and supplemental calcium chloride to correct for metabolic acidosis and ionized hypocalcemia[21,22].

Fluid homeostasis differs between infants and children, with the body's water content decreasing gradually from neonate to infant and from child to adult[23]. G1 patients received more crystalloids, based not only on more blood and ascitic fluid loss, but also on the recommended fluid requirements reported by Holiday and Segar[24] and the massive intraoperative fluid shift in liver transplantation setting (Table 3).

Table 5 shows that the postoperative complications, except for portal vein thrombosis, and the one- and three-year survival rates, were similar between the groups. Portal vein thrombosis is a serious complication of LT, which is associated with high morbidity and mortality in pediatric liver transplantation[19,25,26]. In this study, we experienced 13 cases (12 in G1 and 1 in G2) of perioperative portal vein thrombosis, detected by routine perioperative Doppler ultrasound[4]. Early detection and surgical intervention are crucial in treating portal vein complications. Seven patients with portal vein complications were detected intraoperatively by Doppler ultrasound[4,18]; immediate surgical interventions, such as graft reposition, collateral shunt ligation, thrombectomy and reconstruction of the portal vein, local infusion of heparin through inferior mesenteric vein catheter and endovascular stenting rescued 5/7 patients' grafts, as well as ensuring the patient's survival[18]. Multivariate analysis showed that body weight less than 10 kg and age less than one year old were important risk factors of portal vein thrombosis[4]. Although the exact mechanism of portal vein thrombosis is not clear, it is probable that both mechanical factors and hypercoagulopathy contribute to these thrombotic events[26], despite the patients having profound coagulation defects[27]. The hemostasis system of chronic or end-stage liver disease is complex: the pro- and anti-hemostatic pathways can change concomitantly in liver disease, but the change of the anti-hemostatic pathways is usually not well reflected in the routine coagulation tests, because in the latter measures, only the quantity of the procoagulant factors of the complex hemostatic system[27,28]. End-stage liver disease patients may be in hemostatic balance or a rebalanced condition, providing good hemostatic function, but on the other hand, both bleeding and thrombotic complications in the same patient can be encountered[27,28], as seen in our G1 patients (Table 5). The concern for the high incidence of intraoperative portal vein thrombosis in patients weighing less than 10 kg[4] resulted in the administration of significantly less FFP in G1 compared with G2, despite having more bleeding (Table 3).

We have reported that 8.4% of our pediatric LDLT had acquired hyponatremia at the end of the operation. The cause is not related to the body weight, but the only risk factor was administration of more than 3.5 ml/kg per hour of hypotonic solution[29].

In conclusion, the G1 patients had worse preoperative conditions, as shown by their lower *Z*-scores and higher PELDS compared with the G2 patients. The G1 patients also had more ascites and more blood loss intraoperatively, and required more intensive fluid resuscitation. G1 patients also had more incidences of perioperative portal vein thrombosis, indicating that infants with body weights of less than 10 kg have more surgical and anesthesia risks compared with infants weighing more than 10 kg. When a life-saving procedure can achieve a three-year survival rate of over 94%, it is worthwhile to perform it, no matter how difficult and complicated the procedure may be, even with known high potential lethal complications, such as portal vein thrombosis. A prerequisite for achieving these excellent results is good and effective teamwork. Cooperation between surgeons, plastic surgeons, and anesthesiologists in the operating theater is fundamental; however, the contributions of radiologists are also critical. Radiologists should be available in the OR to perform Doppler ultrasounds before closing the abdomen at the end of the LT procedure to assure sufficient flow in the portal and hepatic arteries[30], and they should also be able to insert a portal vein stent at the operating table if necessary. When a patient has indications requiring an LT, a low body weight of less 10 kg should not be viewed as a reason to delay performing the procedure.

COMMENTS

Background

In the pediatric surgical setting, patients with body weight less than 10 kg are reported to have higher surgical risk in cardiac surgery, and in kidney and liver transplantation in terms of morbidity and mortality.

Research frontiers

This study showed that pediatric weight less than 10 kg had a worse pre-transplant condition, intraoperative bleeding and had higher portal vein complications; however, their 3 year survival was 94%, which was almost as good as that achieved in children of more than 10 kg.

Innovations and breakthroughs

Good cooperation between surgeons, plastic surgeons and anesthesiologists are fundamental in the operating theater; however, the contribution of radiologists is also mandatory. They should be available in the OR to perform Doppler ultrasound before closing the abdomen at the end of a liver transplantation (LT) procedure to assure sufficient flow in the portal, hepatic and hepatic artery, and they should also be able to insert portal vein stent at the operating table if needed.

Applications

This study showed that when there is an indication for liver transplantation, small body weight (less than 10 kg) should not be a reason to delay or hesitate in performing the liver transplantation.

Terminology

Small pediatric patient less than 10 kg is not a contraindication for living donor liver transplantation.

Peer-review

A good and informative paper.

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