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Influence of Body Mass Index ≥ 30 on Pure Laparoscopic Donor Right Hepatectomy

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Background: Pure laparoscopic donor right hepatectomy (PLDRH) for donors with obesity has not been previously investigated. This study aimed to investigate the influence of donor obesity (BMI ≥ 30 kg/m²) on and clinical outcomes after PLDRH.

Material/Methods: Records of all living donors who underwent PLDRH between November 2015 and May 2018 and open conventional donor right hepatectomy (CDRH) between January 2011 and October 2015 at Seoul National University Hospital were retrospectively reviewed. The donors were divided into 3 groups: PLDRH BMI ≥ 30 , PLDRH BMI < 30 , and CDRH BMI ≥ 30 .

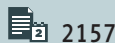
Results: Donors in the PLDRH BMI ≥ 30 group (n=7) were compared with those in the PLDRH BMI < 30 (n=65; control 1) and CDRH BMI ≥ 30 (n=8; control 2) groups. Graft weight was significantly heavier in PLDRH BMI ≥ 30 than in control 1 ($P=0.012$). The lowest hemoglobin (Hb) value was higher ($P=0.014$) and Δ Hb% was lower ($P=0.005$) in PLDRH BMI ≥ 30 than in control 1. Similarly, the lowest Hb value was higher ($P=0.021$) and Δ Hb% was lower ($P<0.001$) in PLDRH BMI ≥ 30 than in control 2. The peak alanine aminotransferase (ALT) ($P=0.029$) and Δ ALT% were higher in PLDRH BMI ≥ 30 than in control 2. No significant differences in hospital stay and postoperative complications were found between PLDRH BMI ≥ 30 and control 1, as well as between PLDRH BMI ≥ 30 and control 2.

Conclusions: This study revealed that PLDRH is feasible in donors with obesity.

MeSH Keywords: Hepatectomy • Laparoscopy • Liver Transplantation • Living Donors • Obesity

Abbreviations: ALT – alanine aminotransferase; BMI – body mass index; CDRH – conventional donor right hepatectomy; GRWR – graft-to-recipient ratio; Hb – hemoglobin; MRS – magnetic resonance spectroscopy; PLDH – pure laparoscopic donor hepatectomy; PLDRH – pure laparoscopic donor right hepatectomy

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Background

Since Cherqui et al. first reported on pure laparoscopic donor hepatectomy (PLDH) in 2002 [1]. PLDH has been increasingly performed and the type of graft has also been expanded from left lateral section to left hemiliver and, recently, right hemiliver [1–13]. Laparoscopic hepatectomy is associated with fewer overall complications, less blood loss, and shorter hospital stay compared with open liver resection [12]. Thus, experienced centers opt to perform PLDH even for right hepatectomy. Reports showing the safety and feasibility of PLDH, including pure laparoscopic donor right hepatectomy (PLDRH), are increasing [11–15].

Although PLDRH has been demonstrated to both a practical and safe method as compared to open conventional donor right hepatectomy (CDRH), the selection criteria still vary from one center to another [13–17]. PLDRH in obese donors also remains controversial. In gastric cancer surgery, obesity itself is a preoperative risk factor, and a laparoscopic procedure in patients with obesity is considered difficult [18]. Nevertheless, laparoscopic colorectal resection is reported to be safe and technically and oncologically feasible in patients with obesity [19–21]. Although obese donors with body mass index (BMI) ≥ 30 is not an absolute contraindication for living donor liver transplantation (LDLT) [22,23], the impact of obesity on outcome of PLDRH may be different from other surgeries. However, to our knowledge, no study reporting the influence of obesity on the outcome of PLDH, especially PLDRH, has been conducted. Thus, this study aimed to evaluate the role of obesity on the surgical outcomes of PLDRH.

Material and Methods

Study design

This retrospective study was performed in accordance with the 1975 Helsinki Declaration and approved by the institutional review board of Seoul National University Hospital (IRB no. 1907-102-1048). Figure 1 summarizes the study design. The definition of obesity is BMI ≥ 30 kg/m². Medical records of donors who underwent PLDRH at Seoul National University Hospital between November 2015 and May 2018 were retrospectively reviewed. Two different comparative analyses were performed. In analysis 1, donors with a BMI ≥ 30 kg/m² were compared with donors with a BMI < 30 kg/m² (control 1). To overcome possible selection bias, outcomes of a single donor surgeon, and those who underwent extended right hepatectomy sacrificing the middle hepatic vein were excluded and sex was matched. In analysis 2, donors with a BMI ≥ 30 kg/m² who underwent PLDRH were compared with donors with a BMI ≥ 30 kg/m² who underwent CDRH, which was performed

between January 2011 and October 2015 (control 2). The period was limited to the most recent 5 years before PLDRH initiation at our center to minimize time bias. To overcome possible selection bias, donors with a BMI < 30 kg/m², outcomes of a single donor surgeon and those who underwent left hepatectomy were excluded. Because of the small number of donors, sex was not initially matched in analysis 2.

Donor evaluation

Live donor evaluation at our center is described in detail elsewhere [11,24,25]. While liver biopsy was not routinely performed, magnetic resonance spectroscopy (MRS) to determine fat fraction and magnetic resonance cholangiopancreatography in lieu of intraoperative cholangiography were routinely performed since 2009 [24]. Liver biopsy was selectively performed in potential donors having a fat fraction of > 8 –10% based on MRS considering together with old age, liver function abnormality, or high BMI. Macrovesicular steatosis $< 10\%$ was accepted. A multi-disciplinary weight-loss program was initiated for donors who's MRS fat fraction is > 8 –10%, also taking into account the condition of the recipient [25]. MRS was performed after the weight reduction program.

Our center started the PLDH program in November 2015 [26]. After accumulating experience, we performed approximately 90% of donor hepatectomies under pure laparoscopic technique without any selection criteria. A high BMI was not a contraindication for PLDH. Open conventional donor hepatectomy was performed only when the pure laparoscopic system was not available, when a well-trained scopist was not available, when the donor or the family opted for the open technique, or when the graft was right anterior section [27].

Statistical analysis

Data were analyzed with the SPSS software (version 22; SPSS, Inc., Chicago, IL). Data were presented as mean \pm standard deviation or as number and percentage. Continuous variables were compared using the nonparametric Mann-Whitney U test, whereas categorical variables were compared using Fisher's exact test. A *P* value < 0.05 was considered statistically significant.

Results

From November 2015 to May 2018, 196 live donors underwent PLDRH at Seoul National University Hospital, of which 7 males had a BMI ≥ 30 kg/m². The characteristics and outcomes of the 7 donors with a BMI ≥ 30 kg/m² who underwent PLDRH are summarized in Table 1. Mean BMI was 31.1 kg/m² and mean estimated remnant liver volume was 33.0%. Mean operative time was 317.1 min, and mean macrovesicular steatosis,

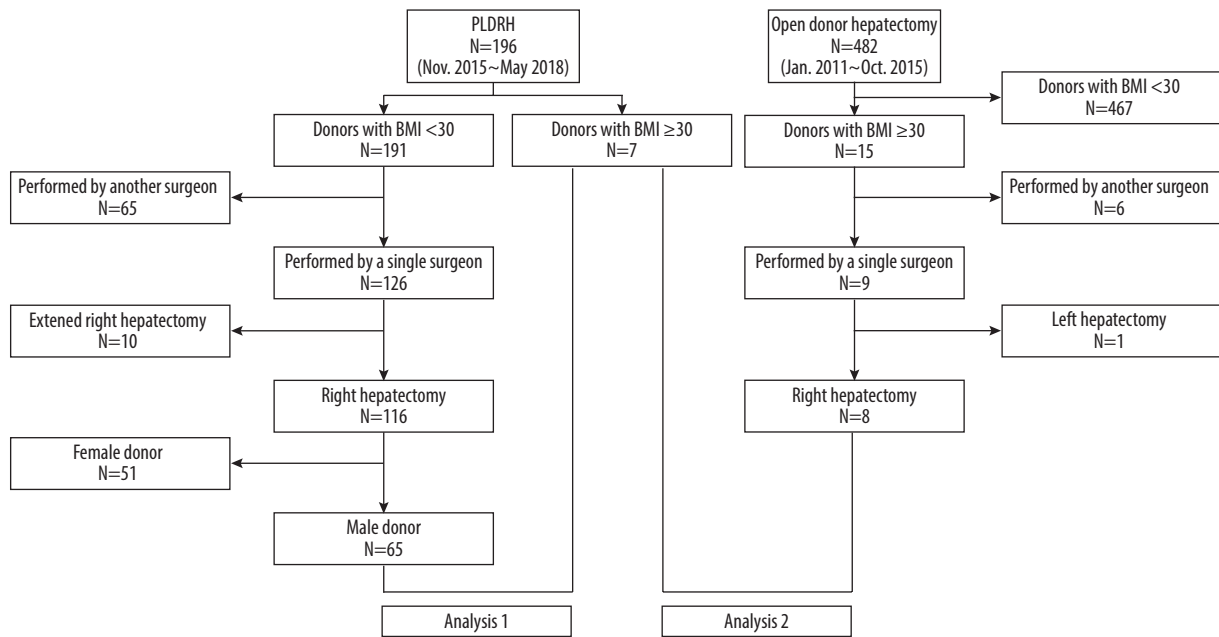


Figure 1. Study design.

which was assessed by liver biopsy during donor hepatectomy, was 3.1%. Mean graft weight was 935.7 g, and mean graft-to-recipient ratio (GRWR) was 1.4. No donors experienced postoperative complications or rehospitalization.

The characteristics and outcomes of the recipients are presented in Table 2. Of the 7 recipients, 5 were male and 2 were female. Mean body weight was 69.9 kg, and mean model for end-stage liver disease (MELD) score was 16.3. Four patients (57.1%) had an early major complication, which was defined as postoperative complication greater than grade III on the Clavien-Dindo classification occurring within 30 days. All the recipients survived until the last follow-up (i.e., >1 year after transplantation), except one recipient who died 1 month after liver transplantation because of intracerebral hemorrhage.

Analysis 1 (PLDRH BMI ≥ 30 vs. PLDRH BMI < 30)

In analysis 1, there were 65 donors whose BMI were < 30 kg/m² who underwent PLDRH (control 1). Graft weight was significantly heavier in the 7 donors whose BMI were ≥ 30 kg/m² than in control 1 (935.7 vs. 775.2 g; $P=0.012$). The lowest hemoglobin (Hb) value was higher (13.4 vs. 12.4 g/dL; $P=0.014$) and Δ Hb%, which was calculated as Δ Hb%=[(preoperative Hb–postoperative Hb)/preoperative Hb]×100, was lower (11.1% vs. 17.6%; $P=0.005$) in donors whose BMI were ≥ 30 kg/m² than in control 1. No significant differences in age, estimated remnant volume, preoperative blood tests, operative time, fatty change, real GRWR, hospital stay, and postoperative complications between

the 2 groups were found (Table 1). Similarly, there were no significant differences in characteristics and postoperative outcomes of the 2 groups of recipients (Table 2).

Analysis 2 (PLDRH BMI ≥ 30 vs. CDRH BMI ≥ 30)

In analysis 2, 8 donors whose BMI were ≥ 30 kg/m² underwent CDRH (control 2). There were more female donors in control 2 (7: 0 vs. 3: 5; $P=0.026$). The lowest hemoglobin (Hb) value was higher (13.4 vs. 10.7 g/dL; $P=0.021$) and Δ Hb% was lower (11.1% vs. 24.1%; $P<0.001$) in PLDRH donors whose BMI were ≥ 30 kg/m² than in control 2. The peak alanine aminotransferase (ALT) (242.9 vs. 140.0 IU/L; $P=0.029$) and Δ ALT% (1045.7% vs. 597.7%; $P=0.029$), which was calculated as Δ ALT%=[(peak ALT–preoperative ALT)/preoperative ALT]×100, were higher in PLDRH donors whose BMI were ≥ 30 kg/m² than in control 2. There were no significant differences in the other characteristics and surgical outcomes between the 2 groups (Table 1). Similarly, there were no significant differences in characteristics and surgical outcomes between the 2 groups of recipients (Table 2).

Discussion

The prevalence of obesity is increasing worldwide [28]. Obesity is known to be associated with serious health risks [29]; can increase the risk of postoperative complications in general surgery, including pulmonary infection, wound problem, and

Table 1. Demographic characteristics and postoperative outcomes of PLDRH donors with BMI ≥ 30 kg/m², control 1, and control 2.

| Variables | PLDRH, BMI ≥ 30 (N=7) | Control 1 | | Control 2 | |
|--|-------------------------------|-----------------------------|-----------|------------------------------|-----------|
| | | PLDRH, BMI < 30 (N=65) | P-value | Open, BMI ≥ 30 (N=8) | P-value |
| Age, mean \pm SD, years | 29.4 \pm 7.0 | 29.4 \pm 10.3 | 0.562 | 33.4 \pm 11.0 | 0.613 |
| Sex | 7: 0 | 65: 0 | NS | 3: 5 | 0.026 |
| BMI, mean \pm SD, kg/m ² | 31.1 \pm 1.6 | 24.1 \pm 2.9 | < 0.001 | 32.0 \pm 1.5 | 0.189 |
| Estimated remnant volume, mean \pm SD, % | 33.0 \pm 3.0 | 34.5 \pm 3.7 | 0.242 | 35.9 \pm 3.7 | 0.152 |
| Estimated GRWR, mean \pm SD | 1.5 \pm 0.2 | 1.4 \pm 0.3 | 0.148 | 1.4 \pm 0.2 | 0.232 |
| Preoperative blood tests, mean \pm SD | | | | | |
| Hb, g/dl | 15.1 \pm 1.1 | 15.1 \pm 0.9 | 0.775 | 14.1 \pm 2.5 | 0.336 |
| Total bilirubin, mg/dl | 0.7 \pm 0.4 | 0.7 \pm 0.3 | 0.766 | 0.9 \pm 0.7 | 0.867 |
| AST, IU/L | 21.6 \pm 12.8 | 18.3 \pm 4.7 | 0.932 | 20.0 \pm 8.8 | 0.779 |
| ALT, IU/L | 23.1 \pm 10.9 | 21.4 \pm 10.0 | 0.614 | 21.1 \pm 10.9 | 0.779 |
| Operative time, mean \pm SD, minutes | 317.1 \pm 15.8 | 319.3 \pm 51.1 | 0.621 | 302.6 \pm 28.3 | 0.281 |
| Fatty change, mean \pm SD, % | | | | | |
| Macrovesicular | 3.1 \pm 2.2 | 1.9 \pm 1.9 | 0.089 | 2.8 \pm 2.1 | 0.779 |
| Microvesicular | 1.9 \pm 1.7 | 1.6 \pm 2.1 | 0.343 | 3.4 \pm 3.2 | 0.397 |
| Graft weight, mean \pm SD, g | 935.7 \pm 153.5 | 775.2 \pm 150.5 | 0.012 | 936.0 \pm 80.3 | 0.867 |
| GRWR, mean \pm SD | 1.4 \pm 0.3 | 1.2 \pm 0.3 | 0.315 | 1.4 \pm 0.4 | 1.000 |
| Estimated blood loss, mean \pm SD, ml | 456.0 \pm 112.6 | 344.6 \pm 267.1 | 0.235 | 487.5 \pm 184.2 | 0.769 |
| Intraoperative transfusion, n (%) | 0 | 0 | NS | 0 | NS |
| Postoperative blood tests, mean \pm SD | | | | | |
| Hb, g/dl | | | | | |
| Lowest | 13.4 \pm 0.8 | 12.4 \pm 1.2 | 0.014 | 10.7 \pm 2.3 | 0.021 |
| Δ Hb% ¹ | 11.1 \pm 4.0 | 17.6 \pm 7.1 | 0.005 | 24.1 \pm 6.0 | < 0.001 |
| Total bilirubin, mg/dl | | | | | |
| Peak | 3.6 \pm 1.1 | 4.7 \pm 1.7 | 0.061 | 3.0 \pm 0.8 | 0.463 |
| Δ Bilirubin% ² | 497.0 \pm 373.1 | 686.1 \pm 395.8 | 0.119 | 345.9 \pm 279.1 | 0.463 |
| AST, IU/L | | | | | |
| Peak | 196.7 \pm 65.4 | 208.6 \pm 63.4 | 0.669 | 143.1 \pm 56.3 | 0.121 |
| Δ AST% ³ | 971.1 \pm 485.6 | 1080.2 \pm 361.5 | 0.588 | 665.1 \pm 293.8 | 0.232 |
| ALT, IU/L | | | | | |
| Peak | 242.9 \pm 105.9 | 239.4 \pm 74.0 | 0.962 | 140.0 \pm 64.9 | 0.029 |
| Δ ALT% ⁴ | 1045.7 \pm 426.2 | 1189.9 \pm 548.0 | 0.683 | 597.7 \pm 184.6 | 0.029 |
| Hospital stay, mean \pm SD, days | 7.4 \pm 0.5 | 8.0 \pm 1.6 | 0.571 | 8.6 \pm 1.2 | 0.054 |

Table 1 continued. Demographic characteristics and postoperative outcomes of PLDRH donors with BMI ≥ 30 kg/m², control 1, and control 2.

| Variables | PLDRH, BMI ≥ 30 (N=7) | Control 1 | | Control 2 | |
|--|-------------------------------|-----------------------------|---------|------------------------------|---------|
| | | PLDRH, BMI < 30 (N=65) | P-value | Open, BMI ≥ 30 (N=8) | P-value |
| Postoperative complications, n (%) | | | | | |
| Grade I | 0 | 1 (1.5) | 1.000 | 0 | NS |
| Wound problem | 0 | 1 (1.5) | | 0 | NS |
| Pleural effusion | 0 | 1 (1.5) | | 0 | NS |
| Grade II | 0 | 3 (4.6) | 1.000 | 0 | NS |
| Intra-abdominal fluid collection requiring antibiotics | 0 | 2 (3.1) | | 0 | NS |
| Portal vein partial thrombus | 0 | 1 (1.5) | | 0 | NS |
| Grade IIIa | 0 | 1 (1.5) | 1.000 | 0 | NS |
| Biliary leakage requiring endoscopic stenting | 0 | 1 (1.5) | | 0 | NS |
| Rehospitalization, n (%) | 0 | 3 (4.6) | 1.000 | 0 | NS |

PLDRH – pure laparoscopic donor right hepatectomy; SD – standard deviation; BMI – body mass index; GRWR – graft-to-recipient ratio; Hb – hemoglobin; AST – aspartate aminotransferase; ALT – alanine aminotransferase; GGT – gamma-glutamyl transferase; POD – postoperative day. Complications were graded according to the Clavien-Dindo classification.

¹ $\Delta\text{Hb}\% = [(\text{Preoperative Hb} - \text{postoperative Hb}) / \text{Preoperative Hb}] \times 100$.

² $\Delta\text{Bilirubin}\% = [(\text{Peak bilirubin} - \text{preoperative bilirubin}) / \text{Preoperative bilirubin}] \times 100$.

³ $\Delta\text{AST}\% = [(\text{Peak AST} - \text{preoperative AST}) / \text{Preoperative AST}] \times 100$.

⁴ $\Delta\text{ALT}\% = [(\text{Peak ALT} - \text{preoperative ALT}) / \text{Preoperative ALT}] \times 100$.

thrombotic events; and can prolong the length of hospital stay [30–33]. Currently, we are in the minimally invasive surgery era, and laparoscopic procedures in gastric and colorectal surgeries are sufficiently feasible in obese patients, albeit considered to be difficult [18,19]. However, little is known about laparoscopic hepatectomy, especially in obese donors. Nevertheless, there are 2 factors to be considered in obese live donors: one is the safety of using a liver graft from an obese donor in LDLT and the other is the feasibility of pure laparoscopic hepatectomy. To address these 2 factors, analyses 1 and 2 were performed in this study.

Previous studies reported that grafts from obese donors, in the absence of graft steatosis, could be safely transplanted [22,23]. Consistent with the finding of the previous studies, our results in analysis 2 showed that all 15 donors whose BMI were ≥ 30 kg/m² (7 PLDRH and 8 CDRH) safely underwent right hepatectomy. All the grafts from the 15 donors were successfully transplanted, and all recipients survived until the last follow-up, except one who died 1 month after liver transplantation because of intracerebral hemorrhage. Macrovesicular and microvesicular steatoses were evaluated microscopically by liver biopsy, which was performed during donor hepatectomy. Mean macrovesicular steatosis was 2.9%, with a maximum value of 7.0%.

Analysis 1 showed that the graft was heavier and larger, the lowest Hb level was higher, and $\Delta\text{Hb}\%$ was lower in PLDRH donors whose BMI were ≥ 30 kg/m² than PLDRH donors whose BMI were < 30 kg/m². However, no significant difference in operative time between PLDRH BMI ≥ 30 and PLDRH BMI < 30 groups was found. A large liver did not always provide a large cut surface. Moreover, there are other factors that affect operative time other than the liver size. Anatomical variation in portal vein, hepatic vein, or bile duct may also prolong operative time [34,35] Abdominal muscularity or abdominal shape can also affect operative time [36]. Abdominal muscularity in donors with a low BMI could make abdominal inflation difficult, thereby providing a small working space. Thus, a high BMI itself is not significantly associated with a longer operative time. In this study, the lowest Hb level and $\Delta\text{Hb}\%$ were assessed to determine the actual blood loss instead of estimated blood loss. The total amount of fluid in the suction bottles were measured, which was used to estimate the total intra-operative blood loss. However, this may include the irrigation fluid, thereby introducing bias. The higher lowest Hb level and lower $\Delta\text{Hb}\%$ could be explained by the lower actual blood loss in PLDRH donors whose BMI were ≥ 30 kg/m² than in PLDRH donors whose BMI were < 30 kg/m² or could be because the effect of bleeding on

Table 2. Demographic characteristics and postoperative outcomes of PLDRH recipients of donors with BMI ≥ 30 kg/m², control 1, and control 2.

| Variables | Control 1 | | | Control 2 | |
|------------------------------------|-------------------------------|-----------------------------|---------|------------------------------|---------|
| | PLDRH, BMI ≥ 30 (N=7) | PLDRH, BMI < 30 (N=65) | P-value | Open, BMI ≥ 30 (N=8) | P-value |
| Sex, Male: Female | 5: 2 | 44: 21 | 1.000 | 6: 2 | 1.000 |
| Age, mean \pm SD, years | 61.1 \pm 7.1 | 53.6 \pm 11.3 | 0.062 | 51.1 \pm 12.1 | 0.152 |
| Body weight, mean \pm SD, kg | 69.9 \pm 8.3 | 64.6 \pm 12.1 | 0.190 | 69.8 \pm 13.9 | 0.694 |
| Underlying etiology, n (%) | | | | | |
| Hepatitis B virus | 3 (42.9) | 41 (63.1) | 0.419 | 4 (50.0) | 1.000 |
| Hepatitis C virus | 2 (28.6) | 3 (4.6) | 0.071 | 1 (12.5) | 0.569 |
| Alcoholic | 1 (14.3) | 9 (13.8) | 1.000 | 0 | 0.467 |
| Others | 1 (14.3) | 12 (18.5) | 1.000 | 3 (37.5) | 0.569 |
| Hepatocellular carcinoma, n (%) | 6 (85.7) | 41 (63.1) | 0.409 | 6 (75.0) | 1.000 |
| MELD score, mean \pm SD | 16.3 \pm 7.5 | 14.9 \pm 5.4 | 0.956 | 15.4 \pm 4.8 | 0.867 |
| Hospital stay, mean \pm SD, days | 19.9 \pm 9.0 | 18.3 \pm 10.5 | 0.584 | 17.0 \pm 9.3 | 0.515 |
| Early major complications, n (%) | 4 (57.1) | 15 (23.1) | 0.074 | 1 (12.5) | 0.119 |
| Late major complications, n (%) | 1 (14.3) | 19 (29.2) | 0.665 | 1 (12.5) | 1.000 |

PLDRH – pure laparoscopic donor right hepatectomy; SD – standard deviation; MELD – Model for End-Stage Liver Disease. Complications were graded according to the Clavien-Dindo classification.

total Hb, which is related to volume, was less in the former because of a higher BMI.

Moreover, analysis 2 showed that the lowest Hb level was higher, Δ Hb% was lower, and peak ALT level and Δ ALT% were higher in PLDRH donors whose BMI were ≥ 30 kg/m² than in CDRH donors whose BMI were ≥ 30 kg/m². The higher lowest Hb level and lower Δ Hb% reflect less actual blood loss; the higher peak ALT level and Δ ALT%, hepatocyte injury. ALT is one of the markers of liver injury [37]. Limited feedback in pure laparoscopic procedure during liver mobilization and transection may cause hepatocyte injury. The force of the surgeon's hand is transmitted through the long surgical laparoscopic instrument. The distribution area to which force is transmitted through this laparoscopic instrument is focal and narrow. Thus, laparoscopic procedure may exert excessive force on a particular area. Similar findings were shown in our previous reports comparing PLDRH with CDRH without limiting to high BMI donors [11,13]. The length of hospital stay tended to be shorter in PLDRH donors whose BMI were ≥ 30 kg/m² than in CDRH donors whose BMI were ≥ 30 kg/m²; however, the difference is not statistically significant. We previously reported that the operative time and hospital stay in PLDRH are shorter recently than when it was first performed [13]. Thus, considering the initial learning curve of PLDRH, the length of stay

may be significantly shorter in PLDRH donors whose BMI were ≥ 30 kg/m² than in CDRH whose BMI were ≥ 30 kg/m² after the accumulation of experience.

No donors whose BMI were ≥ 30 kg/m² experienced postoperative complications, and no significant differences in postoperative complications between the 2 groups of recipients were found based on analyses 1 and 2. The results from analyses 1 and 2 indicate the safety of using a liver graft from an obese donor in LDLT and performing pure laparoscopic hepatectomy in obese donors.

Our study has some limitations. The retrospective study design, small sample size, and possible selection bias possibly result in confounding factors that favor the outcomes in obese donors. Furthermore, this study was performed in a single center and was based on a single surgeon's experience; thus, generalizing the findings to other centers is difficult. In addition, difference in the prevalence of obesity by race or ethnicity was not considered. In 2016, the prevalence of obesity among adults was 4.7% in Korea, 36.2% in the United States, and >20.0% in most European countries [38]. Further evaluation by multicenter studies is needed. Nevertheless, to the best of our knowledge, this is the first report showing the influence of a high BMI on PLDRH outcomes.

Conclusions

Right grafts from obese donors whose BMI were ≥ 30 kg/m², in the absence of marked graft steatosis, can be safely transplanted under a pure laparoscopic method. Nonetheless, careful donor selection and evaluation are required before transplantation.

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Conflicts of interest

None.