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A comparative study of postoperative outcomes between minimally invasive living donor hepatectomy and open living donor hepatectomy: The Korean organ transplantation registry

Jae Do Yang, MD[a], Kwang Woong Lee, MD, PhD[b], Jong Man Kim, MD, PhD[c], Myoung Soo Kim, MD, PhD[d], Jae Geun Lee, MD, PhD[d], Koo Jeong Kang, MD, PhD[e], Dong Lak Choi, MD, PhD[f], Bong Wan Kim, MD, PhD[g], Je Ho Ryu, MD, PhD[h], Dong Sik Kim, MD, PhD[i], Shin Hwang, MD, PhD[j], In Seok Choi, MD, PhD[k], Jai Young Cho, MD, PhD[l], Yang Won Nah, MD, PhD[m], Young Kyoung You, MD, PhD[n], Geun Hong, MD, PhD[o], Hee Chul Yu, MD, PhD[a,*]

[a] Department of Surgery, Jeonbuk National University Medical School, Jeonju, Korea
[b] Department of Surgery, Seoul National University College of Medicine, Seoul, Korea
[c] Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea
[d] Department of Surgery, Yonsei University College of Medicine, Seoul, Korea
[e] Department of Surgery, Keimyung University School of Medicine, Daegu, Korea
[f] Department of Surgery, Catholic University of Daegu, Daegu, Korea
[g] Department of Surgery, Ajou University School of Medicine, Suwon, Korea
[h] Department of Surgery, Pusan National University Yangsan Hospital, Pusan, Korea
[i] Department of Surgery, Korea University College of Medicine, Seoul, Korea
[j] Department of Surgery, Asan Medical Center, Seoul, Korea
[k] Department of Surgery, Konyang University Hospital, Daegeon, Korea
[l] Department of Surgery, Seoul National University Bundang Hospital, Seongnam, Korea
[m] Department of Surgery, Ulsan University Hospital, Ulsan, Korea
[n] Department of Surgery, Catholic University of Korea School of Medicine, Seoul, Korea
[o] Department of Surgery, Ewha Women's University College of Medicine and Graduate School of Medicine, Seoul, Korea

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ABSTRACT

Background: This study evaluated the safety and effectiveness of minimally invasive living donor hepatectomy in comparison with the open procedure, using Korean Organ Transplantation Registry data.
Methods: We reviewed the prospectively collected data of all 1,694 living liver donors (1,071 men, 623 women) who underwent donor hepatectomy between April 2014 and December 2017. The donors were grouped on the basis of procedure type to the minimally invasive procedure group ($n = 304$) or to the open procedure group ($n = 1,390$) and analyzed the relationships between clinical data and complications.
Results: No donors died after the procedure. The overall complication rates after operation in the minimally invasive procedure group and the open procedure group were 6.2% and 3.5%, respectively. Biliary complications were the most frequent events in both groups (minimally invasive procedure group, 2.4%; open procedure group, 1.6%). The majority of complications occurred within 7 days after surgery in both groups. The duration of hospitalization was shorter in the minimally invasive procedure group than in the open procedure group (9.04 ± 3.78 days versus 10.29 ± 4.01 days; $P < .05$).
Conclusion: Based on its similar outcomes in our study, minimally invasive donor hepatectomy cannot be an alternative option compared with the open procedure method. To overcome this, we need to ensure better surgical safety, such as lower complication rate and shorter duration of hospitalization.

Introduction

Living donor liver transplantation (LDLT) has become an established treatment modality in patients with end-stage liver disease

* Reprint requests: Hee Chul Yu, MD, PhD, Department of Surgery, Jeonbuk National University Hospital, 20 Geonji-ro, Deokjin-gu, Jeonju 54907, Korea.
E-mail address: hcyu@jbnu.ac.kr (H.C. Yu);
Twitter: @hirojawa

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because of the shortage of deceased-donor organs. LDLT was first performed in pediatric recipients in 1989 and in adult recipients in 1993.[1,2] Its safety and feasibility has subsequently been well documented during the past several decades. The most important concern in LDLT is donor safety; however, the permanent large abdominal incision scar created during conventional open surgery may cause mental and physical stress in some living donors, especially young women, leading to hesitation regarding the decision to undergo donor hepatectomy.

Minimally invasive liver surgery, which has many advantages over conventional open surgery, has been developed during the past 2 decades for the treatment of benign or malignant liver diseases.[3–5] The application of graft procurement in LDLT can help minimize skin incision and related wound complications during donor hepatectomy, ensuring donor safety. Although a few studies have reported the technical feasibility and comparable outcomes of minimally invasive liver surgery versus conventional open surgery, careful validation using larger studies is needed to achieve standardization and widespread application.

Thus, this study aimed to accurately compare morbidity and complications between minimally invasive and conventional open procedures for living donor hepatectomy, using the Korean Organ Transplantation Registry (KOTRY), which is a prospectively collected database of a nationally representative cohort of Korean patients.

Materials and Methods

Patients and study design

KOTRY initiated a national organ transplantation registration system in April 2014. The registry is composed of 5 cohorts representing 5 types of solid organ transplantation: kidney, liver, heart, lung, and pancreas. The liver cohort consists of a central coordination unit, a medical research coordinating center, and 27 participating transplantation centers. The KOTRY liver cohort contains data from donors and recipients and performs at least 60% of all Korean liver transplantations. Each of the independent institutional review boards at the 27 transplantation centers approved the study protocol. All patients provided written informed consent before enrollment in the study.

All 1,694 living donors registered in KOTRY between April 2014 and June 2017 were enrolled in the study. We prospectively reviewed the medical records of all donors, including age, sex, medical history, body mass index, hospital stay, liver volume estimated using computed tomography or magnetic resonance imaging, graft-to-recipient weight ratio, and remnant liver volume. All donor complication types were recorded, including infections, vascular complications, biliary complications, wound-healing problems, and others. Laboratory data including total levels of bilirubin, aspartate transaminase, alanine aminotransferase, alkaline phosphatase, and gamma glutamyl transpeptidase were collected 6 months and 1 year after surgery.

The 1,694 donors were grouped into the minimally invasive procedure group ([MI] $n = 304$) and the open procedure group ([OP] $n = 1390$). The MI group consisted of donors who underwent laparoscopic surgery, including laparoscopic ($n = 277$) and robotic hepatectomy ($n = 27$). We compared the relationship between morbidity and prognosis in the 2 groups.

Statistical analysis

Data were expressed as mean ± standard deviation for continuous variables and n (%) for categorical variables. We performed the analysis using SPSS v 21 software (IBM Corp, Armonk, NY, USA). The Fisher exact test or the χ^2 test was used to determine the significance of intergroup differences for categorical variables. We used the independent-samples Student's t test or analysis of variance to determine the significance of differences of continuous variables between the groups. Statistical significance was accepted at $P < .05$.

Results

Demographics

During the study period, 1,071 men and 623 women donated their livers. The median follow-up period after surgery was 32 months (range, 11–38 months). The mean donor age was lower in the OP group than in the MI group (30.88 ± 10.51 years versus 33.12 ± 11.77 years; $P < .01$). The proportion of donors who were related to their recipients did not differ between the MI and the OP groups (83.2% vs 86.3%; $P = .76$). The mean donor body mass index was lower in the OP group than in the MI group (23.61 ± 5.37 kg/m^2 versus 24.32 ± 3.06 kg/m^2; $P < .01$). There were no significant intergroup differences in the proportions of donors with histories such as hypertension, diabetes, and smoking or alcohol consumption.

The proportion of right-side graft donation was higher in the MI group than in the OP group (91.7% vs 86.4%; $P < .01$). In addition, the mean graft volume was higher in the MI group (746.50 ± 177.57 mL versus 778.13 ± 180.94 mL; $P = .01$). There were no significant intergroup differences in the graft-to-recipient weight ratio, remnant liver volume, or rate of macrovesicular steatosis (Table I).

Overall complications

The overall complication rates were 6.2% ($n = 19$) in the MI group and 3.5% ($n = 50$) in the OP group ($P = .23$). The most common complication type was biliary complications, including bile leak and stricture, in both groups (MI, 2.4%; OP, 1.6%). In the MI group, the rates of bleeding, vascular complications, and wound-healing problems were 0.6, 0.6, and 1.2%, respectively, versus 0.1, 0.5, and 0.7%, respectively, in the OP group.

None of the donors died after the hepatectomy in either group (Table II). The major complication (Clavien–Dindo grade ≥3) rate was approximately 2% in both groups. Regarding class 3a complications, total and biliary complications were slightly more common in the OP group. Meanwhile, the rate of class 3b complications was higher in the MI group. However, none of these differences was significant (Fig 1). Most complications occurred within 7 days after surgery in both groups (68% and 66%, respectively, Fig 2). The most common operation of donor complication was right lobectomy in both groups (6.2% vs 3.4%, Table III).

In the 27 robotic hepatectomies there were 2 overall complications (7.4%). Complication types were bleeding (1, class 2) and wound problems (1, class 2). Aspartate transaminase levels at 1 year after donation were lower in the MI group than in the OP group (20.4 ± 5.5 mg/dL versus 22.4 ± 9.1 mg/dL, $P = .03$). Conversely, total bilirubin levels at 6 months after donation were higher in the MI group (0.84 ± 0.39 mg/dL versus 0.74 ± 0.36 mg/dL, $P < .01$). However, no differences in these indices between the groups were noted at 1 year. Others, such as alkaline phosphatase and gamma glutamyl transpeptidase demonstrated slightly higher in OP group but were not significant differences between the group. Meanwhile, the duration of hospitalization was shorter in the MI group than in the OP group (9.04 ± 3.78 days versus 10.29 ± 4.01 days, $P < .01$, Table IV).

Table I
Baseline characteristics

	MI (n = 304)	OP (n = 1,390)	P value
Sex of donor, male:female (male %)	168:136 (55.3)	903:487 (65.0)	.043*
Age of donor, y	33.12 ± 11.77	30.88 ± 10.51	**<.01**†
BMI of donor, kg/m^2	23.61 ± 5.37	24.32 ± 3.06	**<.01**†
Relationship			.76*
Living related donor	253 (83.2)	1,199 (86.3)	
Living unrelated donor	51 (16.8)	191 (13.7)	
Hypertension	10 (3.3)	38 (2.7)	.99*
Diabetes	1 (0.3)	15 (1.1)	.83*
Smoking			.95*
Never	212 (69.7)	926 (66.6)	
Former	19 (6.3)	80 (5.8)	
Current	71 (23.4)	373 (26.8)	
Alcohol consumption			.99*
None	154 (50.7)	728 (52.4)	
Social drinking	144 (47.4)	626 (45.0)	
Habitual drinking	5 (1.6)	31 (2.2)	
Unknown	1 (0.3)	5 (0.4)	
Previous laparotomy	28 (9.21)	98 (7.1)	.79*
Graft type			
Left lobectomy with MHV	2 (0.7)	20 (1.4)	
Right lobectomy with MHV	10 (3.3)	40 (2.9)	
Left lateral segmentectomy	5 (1.6)	6 (0.4)	
Left lobectomy without MHV	6 (2.0)	29 (2.1)	
Right lobectomy without MHV	279 (91.7)	1,201 (86.4)	
Right posterior sectionectomy	1 (0.3)	12 (0.9)	
Others	1 (0.3)	1 (0.07)	
Graft volume, mL	778.13 ± 180.94	746.50 ± 177.57	**.01**†
Graft-to-recipient weight ratio	1.20 ± 0.34	1.18 ± 0.42	.29†
Remnant liver volume, %	0.37 ± 0.06	0.375 ± 0.09	.12†
Macrovesicular steatosis, %	3.61 ± 3.99	4.33 ± 27.52	.35†

Statistically significant P values (*bold*).
MI, minimally invasive group; *OP*, open group; *BMI*, body mass index; *MHV*, Middle hepatic vein.
* The χ^2 test.
† The t test.

Table II
Postoperative donor complications according to Clavien-Dindo grade

	Bleeding		Vascular		Biliary*		Wound†		Others‡	
	MI	OP	MI	OP	MI	OP	MI	OP	MI	OP
Grade I	0	0	1	2	5	6	3	4	2	7
Grade II	1	0	0	0	0	0	0	6	0	0
Grade IIIa	0	0	1	3	1	12	0	1	0	1
Grade IIIb	1	0	0	2	2	4	1	2	1	1
Grade IVa	0	0	0	0	0	0	0	0	0	0
Grade IVb	0	2	0	0	0	0	0	0	0	0
Grade V	0	0	0	0	0	0	0	0	0	0
Total (%)	2(0.6)	2(0.1)	2(0.6)	7(0.5)	8(2.4)	22(1.6)	4(1.2)	10(0.7)	3(0.9)	9(0.6)

The total complication rates: 6.2% (19) in the MI group and 3.5% (50) in the OP group, (P = .23)
MI, minimally invasive group; *OP*, open group.
* Biliary stricture and bile leakage.
† Wound discharge, dehiscence.
‡ Cardiopulmonary problem and other problems.

Discussion

LDLT has become an alternative lifesaving method that reduces patient waiting time and mortality.[6] Although recipient outcomes after LDLT are similar or superior to those after deceased-donor liver transplant, concerns regarding donor safety appear to be increasing. The overall use of LDLT in the United States increased sharply during the late 1990s; however, the expansion of LDLT was restricted after reports of fatal donor complications in the literature and by the global media.[7–9]

Despite good outcomes for recipients, LDLT is an extremely complicated surgical procedure, and donor safety remains an issue of concern. Some systematic reviews reported that donor morbidity rates after hepatectomy varied from 10% to 67%, including a biliary complication rate of 6.2% after hepatectomy.[10,11] Patel et al[12] reported an overall complication rate of 29.1% in a US cohort study of 533 donors. The rate of major complications (defined by a Clavien–Dindo grade of ≥3) was 3.5%. Donor age >50 years was associated with a higher risk of major complications.[12]

Meanwhile, our major complication rate was slightly lower than those reported previously. The living donor complication rate is lower in Asia. In particular, studies by large centers in Korean reported overall complication rates of 1.6%–3.2%.[13–15] In 2017, Lee et al[16] reported results using multicenter data for 832 living donors. The overall, biliary, and major complication rates were 9.3%, 1.7%, and 1.9%, respectively. Of the 16 patients with major complications,

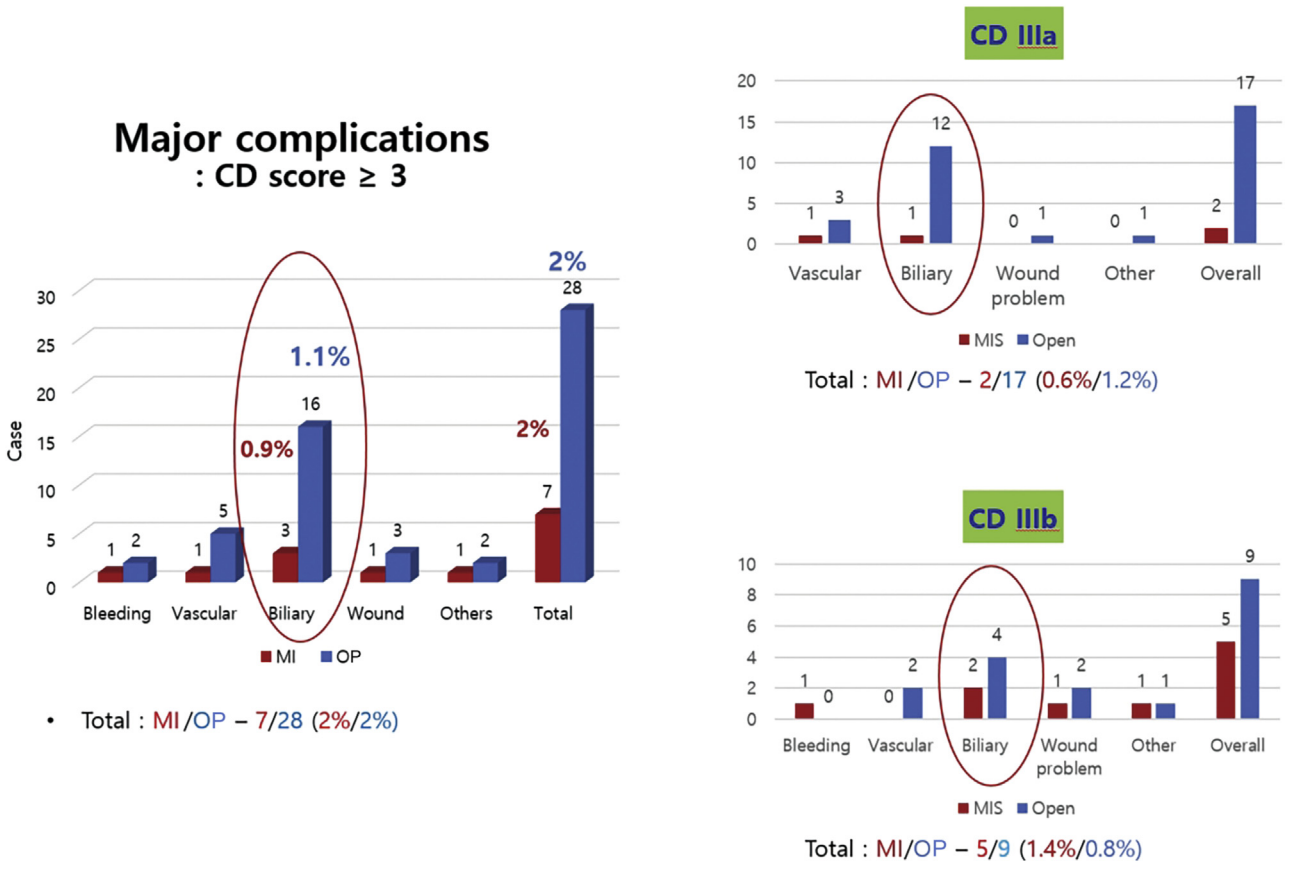


Fig 1. Major complications (Clavien–Dindo grade ≥3) rate in both groups. *CD*, Clavien-Dindo; *MI*, minimally invasive group; *OP*, open group; *MIS*, minimal invasive surgery.

9, 2, and 7 experienced biliary complications, biliary strictures, and bile leakage, respectively.[16]

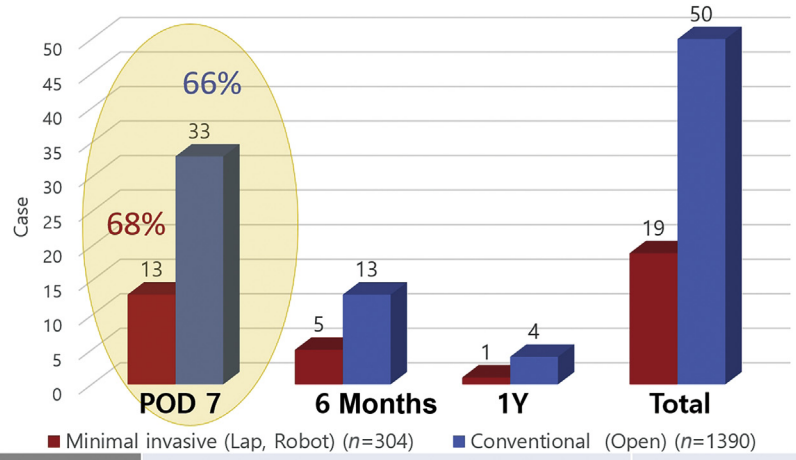
The study by Lee et al[16] was the first to report results using KOTRY data and was unable to compare MI hepatectomy with OP donor hepatectomy and had a short follow-up (19 months). Nonetheless, biliary complications were the most common type of major complication among living liver donors, which agree with our results. To reduce biliary complications, the selection of donors with a favorable biliary anatomy before surgery is extremely important. In addition, minimizing hilar dissection, which can injure the bile duct, and a short warm ischemia time are required. The use of intraoperative cholangiography, sonography, and real-time indocyanine green near-infrared fluorescence imaging can reduce the risk of bile duct injury.

Actually, many studies have reported the negative effects felt by donors, including mental and physical stress after OP donor surgery. Yuke et al[17] reported results using multicenter data for 374 living donors. Living donors with complications for scar and longer hospital stay had lower quality of life.[17] Humphreville et al[18] reported that LDLT donors' most common symptom after donation was incisional discomfort (34%). Depression symptoms were self-reported by 24 donors (22.4%) after donation.[18] In our donor group, females and young donors were a high proportion because LDLT is performed more often than deceased-donor liver transplant. Most donors are siblings and adult children in Korea. They worried about the wound scar and pain before surgery.

MI surgery has many advantages such as reduced surgical site infection, less pain, better cosmetic results, shorter hospital stay, and quicker return to normal life compared with OP surgery. In a systemic review of donor complications after laparoscopic hepatectomy, Park et al[19] reported complication rates of 4.4% to 23% for left hepatectomy and 3.8% to 20% for right hepatectomy. In addition, the duration of hospital day ranged from 6.3 to 12.1 days.[19] These figures are roughly in line with our findings. In our study, length of stay had minimal difference (9 vs 10 days) and indicated a slightly longer length of stay than those for OP donor procedures in the United States. This represents a different culture of hospital stay between the East and the West, but still does not seem to explain a higher complication rate.

Regarding our laboratory findings, aspartate transaminase, alanine aminotransferase, and bilirubin levels were higher in the MI group than in the OP group at 6 months after surgery, but the differences did not persist at 1 year. These findings might be attributable to the higher proportion of patients who underwent right lobectomy in the MI group. In our study, the relatively positive safety outcomes for LDLT donors appear to reflect improvements in surgical techniques and experiences compared with earlier reports.

Our study had some limitations. First, these data did not include information about specific operative factors such as intraoperative blood loss or operative times. These parameters were not included in the KOTRY data and they should be provided in the future. Second, fewer patients underwent laparoscopic surgery than OP surgery. The tendency for the MI group to appear to have a high incidence of complications, including biliary problems, is believed to be attributable to the relatively small number of registered patients compared with the OP group, especially data that included



Postop day	Postoperative complications		*P*-value
	MI (*n*=304,%)	OP (*n*=1390,%)	
7 days	13 (4.2)	33 (2.3)	0.2
6 months	5 (1.6)	13 (0.9)	1
1 year	1 (0.3)	4 (0.3)	1
Total	19 (6.2)	50 (3.5)	0.23

Fig 2. Occurrence period of postoperative complications in both groups. *POD*, postoperative day; *MI*, minimally invasive group; *OP*, open group.

Table III
Postoperative complications according to operative method in both group

Operation (MI/OP)	MI	OP	*P* value
Left lobectomy with MHV (2/20)	0	1(5)	
Right lobectomy with MHV (10/40)	0	0	
Left lateral segmentectomy (5/6)	0	0	
Left lobectomy without MHV (6/29)	0	1 (3.4)	
Right lobectomy without MHV (279/1,201)	19 (6.8)	47(3.9)	.43
Right posterior sectionectomy (1/12)	0	1(8.3)	
Other (1/1)	0	0	

MI, minimally invasive group; *OP*, open group; *MHV*, middle hepatic vein.

Table IV
Postoperative laboratory findings and hospital stays

	MI (n = 304)	OP (n = 1390)	*P* value
AST, 6 months (IU/L)*	22.8 ±15.8	24.6 ±10.4	
AST, 1 y (IU/L)†	20.4 ± 5.5	22.4 ± 9.1	
ALT, 6 months (IU/L)*	20.8 ± 14.0	21.2 ± 13.2	
ALT, 1 y (IU/L)†	18.7 ± 10.9	19.1 ± 10.6	
ALP, 6 months (IU/L)*	109 ± 21.4	112 ± 29.3	**<.01**
ALP, 1 y (IU/L)	84 ± 14.2	91 ± 16.8	
GGT, 6 months (IU/L)*	105 ± 31.2	109 ± 29.2	
GGT, 1 y (IU/L)	55 ± 15.4	61 ± 14.3	
Total bilirubin, 6 months (mg/dL)*	0.84 ±0.39	0.74 ±0.36	
Total bilirubin, 1 y (mg/dL)†	0.84 ± 0.36	0.84 ± 0.38	
Duration of hospitalization (days)	9.04 ± 3.78	10.29 ± 4.01	**<.01**

Statistically significant *P* values (*bold*).
MI, minimally invasive group; *OP*, open group; *AST*, aspartate transaminase; *ALT*; alanine aminotransferase; *ALP*; alkaline phosphatase; *GGT*, gamma glutamyl transpeptidase; *IU/L*, international unit per liter.
* After postoperative 6 months.
† After postoperative 1 y.

the initial MI experience, which may have affected the results. The MI group consisted of donors who underwent laparoscopic surgery, including laparoscopic (n = 277, 91.2%) and robotic hepatectomy (n = 27, 8.8%). Robotic surgery is performed in only one Korean center. Those who underwent robotic surgery were well-selected patients. All of these were right hepatectomy, and no major postoperative complications occurred. Therefore, we do not believe robotic donor hepatectomy is appropriate for general practice compared with the laparoscopic method. We need to do additional comparative research. Third, data on detailed short-term postoperative outcomes, including laboratory data, were relatively insufficient. Last, the selection criteria for MI and OP donor hepatectomy were not clear. Transplant surgeons in our large centers, which mostly contain KOTRY registration, would not have performed with strict indications because they have many experiences in hepatic resection. On the other hand, it is believed that the open method should be safely implemented in the case of a complex anatomic structure such as a branch arising from the opposite side and short length that is generally difficult to perform with laparoscopic methods.

Nevertheless, our study is one of the largest registry studies to compare the safety of laparoscopic and OP donor hepatectomy, using multicenter data in the Korean population.

In conclusion, MI donor hepatectomy demonstrated similar outcomes compared with OP surgery in our data. It cannot be a suitable replacement in regard to surgical safety. To overcome this, we need to ensure better outcomes, such as lower complication rates and shorter duration of hospitalization.

Conflict of interest/Disclosure

The authors have no conflict of interest to disclose.

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