Pediatric living donor liver transplantation: results of laparoscopic vs. open graft removal

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ABSTRACT

Introduction. Laparoscopic graft removal for pediatric living donor liver transplantation (PLDLT) reduces morbidity and surgical aggressiveness for the donor. It is important to assess whether the approach used for removal purposes compromises implantation. The objective of this study was to analyze PLDLT progression in children according to whether the graft had been removed laparoscopically or through open surgery.

Materials and methods. A retrospective, analytical cohort study of PLDLTs carried out in our institution from 2009 to 2020 was carried out.

Results. Transplantation was performed in 14 patients, with a median age of 34.5 (R: 6-187) months. In 6 donors (42%), graft removal was conducted laparoscopically. In 1 donor (7%), removal was initiated laparoscopically, but conversion was required. This patient was included within the open surgery group, which consisted of 8 (58%) donors.

No differences were found in terms of operating times, ICU stay, hospital stay, complications during admission, or complications post-admission in the recipient.

The surgical approach did not compromise the length of the vessels to be anastomosed in any graft, and it added no extra difficulty to implantation.

No differences were found in terms of removal times or hospital stay for the donor. Only 1 donor from the laparoscopy group required re-intervention due to bleeding following port insertion.

Conclusion. PLDLT patients had similar results regardless of the removal approach used, which did not compromise the structures of the graft to be anastomosed, or add any extra difficulty to implantation.

KEY WORDS: Pediatric liver transplantation; Living donor; Laparoscopy; Liver graft removal.

TRASPLANTE HEPÁTICO PEDIÁTRICO DE DONANTE VIVO, RESULTADOS EN FUNCIÓN DE EXTRACCIÓN DEL INJERTO POR LAPAROTOMÍA *VS.* LAPAROSCOPIA

RESUMEN

Introducción. La extracción laparoscópica del injerto para el trasplante hepático pediátrico de donante vivo (THPDV) es una herramienta que reduce la morbilidad y agresividad quirúrgica en el donante. Es importante estudiar si la vía de extracción compromete el implante. El objetivo del estudio es analizar la evolución del THPDV en el niño en función de si el injerto fue extraído por vía abierta o laparoscopia.

Material y métodos. Estudio de cohortes retrospectivo y analítico de los THPDV realizados entre 2009 y 2020 en nuestro centro.

Resultados. Se trasplantaron 14 pacientes, con edad mediana de 34,5 (R: 6-187) meses.

En 6 donantes (42%) se realizó la extracción del injerto vía laparoscópica. En un donante se inició la extracción por laparoscopia, pero fue necesaria la conversión (7%), esté se clasificó en el grupo de laparotomía, compuesta por 8 (58%) donantes.

No se encontraron diferencias en el tiempo quirúrgico, en los días en la unidad de cuidados intensivos, en la estancia hospitalaria, en las complicaciones durante el ingreso ni en las complicaciones postingreso en el receptor.

El abordaje quirúrgico no comprometió en ningún injerto la longitud de los vasos a anastomosar, sin suponer una dificultad en el implante.

No se evidenciaron diferencias en el tiempo de extracción ni en los días de hospitalización del donante. Solo un donante del grupo de laparoscopia precisó reintervención por sangrado de la incisión de un trocar.

Conclusión. Los pacientes con THPDV presentan resultados similares, independientemente de la vía de extracción del injerto. La vía de abordaje no comprometió las estructuras del injerto a anastomosar, ni dificultó el momento del implante.

PALABRAS CLAVE: Trasplante hepático pediátrico; Donante vivo; Laparoscopia; Extracción injerto hepático.

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INTRODUCTION

Pediatric liver transplantation (PLT) is the only definitive solution for patients with terminal liver cirrhosis, irrespective of its etiology. Biliary atresia is the most frequent cause of PLT[1], which stands as a healing solution for metabolic conditions. This is why the number of transplantations in the context of these pathologies has not ceased to increase in the last years[2]. In patients with neoplastic liver pathologies, such as advanced hepatoblastoma, PLT is required for healing purposes.

Owing to the great number of pathologies eligible for PLT, more children require transplantation than there are brain-dead donor organs available. This deficit, along with the fact early PLT prior to patient deterioration has been clearly demonstrated to increase survival rates[2–5], has caused pediatric living donor liver transplantation (PLDLT) to increase. This technique allows the number of grafts available to grow, and PLT to be scheduled at the right time for the patient. The donor is typically a parent or another healthy close relative. Therefore, it is essential to offer them a procedure as successful as possible and with limited complications.

In order to reduce morbidity and facilitate the donor's recovery, Cherqui published the first laparoscopic liver graft removal with subsequent successful implantation in a pediatric patient in 2002[6]. Multiple studies support the benefits of minimally invasive graft removal for the donor[4,6-14]. However, there are fewer articles describing graft progression in pediatric patients. For instance, Soubrane[13] described the progression of 124 LDLTs, but did not compare this series with open surgery. Broering[14] compared graft and pediatric patient progression in 72 open surgery grafts vs. 72 laparoscopic grafts, with no significant differences between groups.

The objective of this study was to compare progression and short- and long-term results of the PLDLTs carried out in our institution according to whether graft removal had been performed laparoscopically or through open surgery.

MATERIALS AND METHODS

A retrospective, analytical cohort study of PLDLT patients from our institution, which is a third-level reference hospital in terms of liver pathologies, was carried out. Progression results from the laparoscopic PLDLT group were compared with those from the open surgery group. All patients had undergone surgery in our institution from 2009 to 2020.

The variables analyzed included sex, age at PLT, baseline condition, previous transjugular intrahepatic portosystemic shunt (TIPS), previous surgery, segment implanted, operating time, ICU and hospital stay, complications during admission (or early complications), re-intervention, complications post-admission (or late complications), re-admission, and follow-up time. Donor age, sex, BMI, operating time, complications, and hospital stay were analyzed in both groups.

Donors were selected by the General Surgery Department from our institution using the same standardized criteria (lack of pathology, lack of vascular and biliary malformations, etc.) in both groups. Patients were not randomized according to the surgical approach used. At first, graft removals were all conducted through open surgery, but in December 2018, the first laparoscopic removal was carried out, and since then, the laparoscopic approach has routinely been attempted. If the patient is eligible to be a donor, there are no contraindications associated with the laparoscopic approach.

Qualitative variables were expressed as an absolute number and a percentage, whereas quantitative variables were expressed as a mean with standard deviation, or as a median with range. Statistical analysis was performed using the *SPSS STATISTICS V.21* software (Armonk, NY, USA). The statistical tests used were Chi-squared test for qualitative variables, and Mann-Whitney U test for quantitative variables. Statistical significance was established at $p < 0.05$.

DESCRIPTION OF LAPAROSCOPIC GRAFT REMOVAL

All surgeries carried out in the donors were left hepatectomies. Therefore, both open and laparoscopic procedures were performed by the same surgeon from the Hepatobiliary and Pancreatic Surgery Unit of the adult General Surgery Department from our institution. The last 4 procedures were conducted using 3D vision, which facilitates surgery as it allows structures to be better visualized.

The donor received subcutaneous enoxaparin every 24 hours for 10 days. A prophylactic dose of amoxicillin-clavulanic acid was administered.

The technique used was classic left hepatectomy[9,10], while respecting the artery of segment IV if the outflow tract was the left hepatic artery (Fig. 1). For laparoscopic hepatectomy, 4 ports and a small Pfannenstiel incision for specimen removal purposes were used. This technique consists of the following:

The round ligament and the left triangular ligament are freed. The liver hilum is dissected, and a Pringle maneuver is prepared by passing a ribbon with a vascular tourniquet through the omental foramen (A). The left hepatic artery (B) and the left portal branch (C) are identified, and hepatic transection is initiated to the right of the round ligament using an ultrasonic coagulation and bipolar sealing device. The large portal and arterial branches are ligated by means

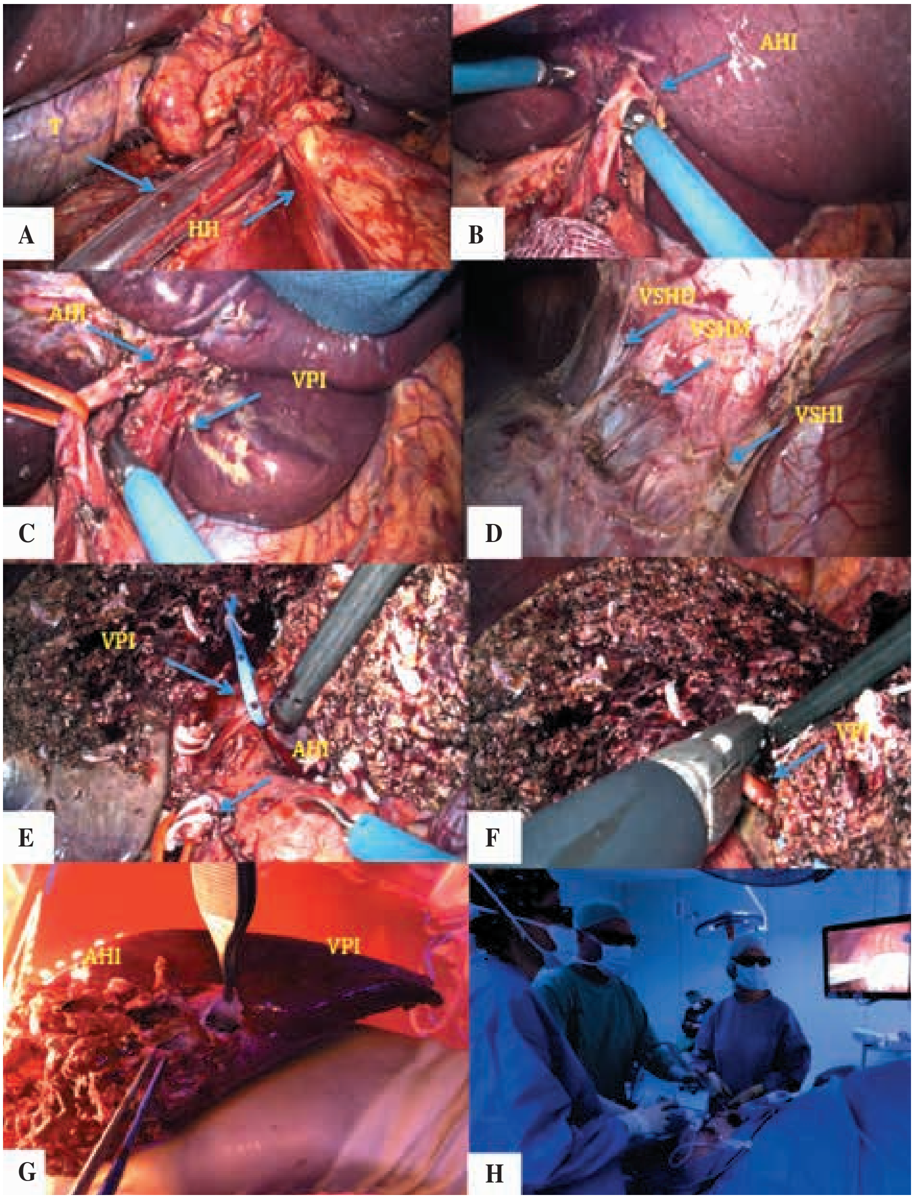

Figure 1. Laparoscopic left hepatectomy. A) Pringle maneuver: identification of the liver hilum with prophylactic vascular tourniquet. B) Dissection of the left hepatic artery (AHI). C) Dissection of the left portal vein (VPI). AHI identified with a red ribbon. D) Identification of the suprahepatic veins (VSH). E) Division of the AHI, which had been previously clipped using a polymer clip. Previous division of the liver parenchyma can be observed. F) Division of the VPI using an automatic endo-stapler. G) Bench surgery. The vascular structures to be anastomosed can be noted. H) Laparoscopic left hepatectomy with 3D vision. T: tourniquet; HH: liver hilum; AHI: left hepatic artery; VPI: left portal vein; VSHD: right suprahepatic vein; VSHM: middle suprahepatic vein; VSHI: left suprahepatic vein.

of polymer clips. The left suprahepatic vein is identified with a ribbon (D).

Once the structures have been identified, communication between both operating rooms is crucial. The pediatric surgeon, who will be conducting the recipient's hepatectomy, will indicate when precisely to clamp and divide the vascular structures of the donor in the left hepatic artery using polymer clips (D), and in the vein using the endo-stapler (E), in order to reduce graft ischemic time as much as possible. Once the graft has been freed, it is removed using a laparoscopic bag through a small Pfannenstiel incision (G). Following graft removal, an ex-situ lavage with Celsior solution is performed, and the graft is taken to the pediatric operating room.

RESULTS

14 patients underwent transplantation. Median age was 34.5 (R: 6-187) months. Patient clinical characteristics are featured in table I.

In 6 recipients (42%) (3 boys and 3 girls), grafts were removed laparoscopically. In 1 donor (7%), removal was initiated laparoscopically, but conversion was required. This patient was included within the open surgery group, which consisted of 8 (58%) recipients (3 boys and 5 girls) (Table II).

Median age was 34.5 (R: 8-85) months in the laparoscopy group, and 43 (R: 6-187) months in the open surgery group, with no differences between groups (p = 0.082).

Table I. **Patient clinical characteristics.**

Variable	*Results*
Sex	6 M 8 F
Age (months)	34.5 (6-187)
Baseline condition	Biliary atresia: 5 (35.7%) Familial cholestasis: 1 (7.1%) Congenital liver fibrosis: 2 (14.2%) Hepatoblastoma: 3 (21.3%) Idiopathic cirrhosis: 2 (14.2%) Alagille syndrome: 1 (7.1%)
Graft weight (g)	300 (190-360)
Graft weight (g)/ recipient weight (kg)	27.55 ± 12.8
TIPS	Yes: 3 (21.3%) No: 11 (78.7%)
Previous surgery	None: 3 (21.3%) Laparoscopic Kasai procedure: 3 (21.3%) Open Kasai procedure: 1 (7.1%) Liver biopsy: 6 (42.6%) Extended right hepatectomy: 1 (7.1%)
Follow-up time (months)	39.99 (10-136)

Hepatectomy and implantation time was 679.17 ± 57.83 minutes in the laparoscopy group, and 608.57 ± 41.4 minutes in the open surgery group (p = 0.170). All patients received segments II-III of the donor's left liver.

Mean graft weight was 300 g (190-360), and graft/recipient weight ratio was 27.55 ± 12.8 graft g recipient kg.

Hospital stay was 43.60 ± 27.68 days in the laparoscopy group, and 40.14 ± 17.22 days in the open surgery group (p = 0.322). ICU stay was 7.17 ± 5.34 days vs. 10.88 ± 8.27 days (p = 0.272).

The surgical approach did not compromise the length of the vessels to be anastomosed in any graft, and it added no extra difficulty to implantation. In 2 patients from the laparoscopy group (33%) and in 1 patient from the open surgery group (14%), a cadaveric vascular graft was required – in one case as a result of portal cavernoma, and in the other two cases because recipient and graft veins were considerably far away from each other (the cadaveric graft was the only one available).

No differences in postoperative complications were found between groups (p = 0.872). In the laparoscopy group, 1 patient had postoperative bleeding requiring surgical review three times – once due to bleeding of a hepatic artery branch, and twice as a result of diffuse bleeding, which was attributed to a coagulation disorder postoperatively –, and subsequently, hepatic artery stenosis – detected at ultrasonography and requiring re-anastomosis. 1 patient had self-limited rectal bleeding, which was attributed to anticoagulation treatment. 1 patient had self-limited left diaphragmatic paralysis. And finally, 1 patient had biliary leak with biloma abscess at the bilioenteric anastomosis, which required surgical review. In the open surgery group, 1 patient had biloma, which was successfully managed with conservative treatment. 1 patient had biliary leak associated with pleural effusion, which required re-intervention. 1 patient had hepatic artery stenosis and collection, which required re-intervention in the same surgical maneuver. And finally, 1 patient died as a result of graft failure due to portal vein thrombosis – this patient required multiple re-interventions and underwent transplantation three times, with a poor clinical progression after each transplantation. Following discharge, only 1 patient from the laparoscopy group required re-admission and re-intervention due to persistent biliary leak and cholangitis, which required bilioenteric re-anastomosis – this girl developed lymphoproliferative syndrome one year following PLT. In the open surgery group, 5 patients required re-admission. The difference was not significant (p = 0.086), but more re-admissions were required in this group. Causes of re-admission included 2 cases of cholangitis, 1 case of intrahepatic collection associated with biliary leak, 1 case of biliary obstruction, and 1 case of viral pneumonia as a result of immunosuppressive treatment – this patient subsequently died.

When stratifying complications during admission and post-admission according to Clavien-Dindo classification[17], more major complications were recorded in the open surgery group than in the laparoscopy group, but the total comparison between complications was not significant.

No differences in demographic variables – donor sex, age, and body mass index (BMI) – according to the removal approach used were found, with donor characteristics being analogous in both groups. No intraoperative complications were recorded in any graft removal procedure. In 1 donor, removal was initiated laparoscopically, but conversion to open surgery was required as a result of poor visualization of the liver hilum structures to be dissected, thus resulting in a 1/7 (14%) conversion rate. This case was included within the open surgery group, with operating time incorporating both laparoscopy and open surgery, which means total operating times in the open surgery group may have been slightly distorted. No blood transfusion or hepatectomy were required. No differences were found in terms of removal times (p = 0.588) or hospital stay for the donor (p = 0.226). Only 1 donor from the laparoscopy group required re-intervention and transfusion due to bleeding following port insertion (Table III).

DISCUSSION

Pediatric living donor liver transplantation (PLDLT) is a type of PLT that increases the amount of organs available

Table II. Progression analysis according to graft removal approach.

Variable	*Laparoscopy (n = 6)*	*Open surgery (n= 8)*	*p value*
Sex	3 M 3 F	3 M 5 F	0.219
Age (months)	34.5 (R: 8-85)	43 (R: 6-187)	0.084
Operating time (min)	679.17 ± 57.829	608.57 ± 41.404	0.170
ICU stay (days)	7.17 ± 5.345	10.88 ± 8.271	0.272
Hospital stay (days)	43.60 ± 27.682	40.14 ± 17.218	0.322
Complications during admission	Yes: 4 No: 2	Yes: 5 No: 3	0.872
Type of complications during admission	• Bleeding (x3) + hepatic artery stenosis • Low digestive bleeding • Diaphragmatic paralysis • Biliary leak + cholangitis	• Portal thrombosis: 1 • Pleural effusion+ biliary leak • Spontaneously healed biloma • Hepatic arterial stenosis + collection	
Complications during admission according to Clavien-Dindo	Grade I: 1 Grade II: 1 Grade III: 1 Grade IV: 1 Grade V: 0	Grade I: 0 Grade II: 0 Grade III: 2 Grade IV: 3 Grade V: 1	
Complications post-admission	Yes: 1 No: 5	Yes: 5 No: 3	0.16
Type of complications post-admission	• Biliary leak + cholangitis + lymphoproliferative syndrome	• Intrahepatic collection • Biliary obstruction • Cholangitis: 2 • Cholangitis • Death	
Complications post-admission according to Clavien-Dindo	Grade I: 0 Grade II: 0 Grade III: 1 Grade IV: 0 Grade V: 0	Grade I: 0 Grade II: 1 Grade III: 3 Grade IV: 0 Grade V: 1	
Re-admission	Yes: 1 No: 5	Yes: 5 No: 3	0.16
Re-intervention	Yes: 2 No: 4	Yes: 6 No: 2	0.119
Cause of re-intervention (early + late re-intervention)	• Bleeding (x3) + hepatic artery stenosis • Biliary leak: 1	• Bleeding: 1 • Biliary stenosis: 2 • Biliary leak: 1 • Portal vein thrombosis: 1 • Hepatic artery stenosis: 1	
Deaths	0	2 (viral pneumonia + intracerebral hemorrhage)	

Table III. Analysis of donor progression according to graft removal approach.

Variable	*Laparoscopy (n = 6)*	*Open surgery (n = 8)*	*p value*
Age (years)	39.67 ± 5.680	38 ± 3.464	0.231
Sex	Father: 2 Mother: 4	Father: 4 Mother: 2	0.21
BMI	23.96	24.57	0.31
Operating time	351.67 ± 69.474	380.83 ± 56.605	0.588
Time to discharge	6.00 ± 0.632	5.67 ± 0.816	0.226
Complications	1 re-intervention: bleeding following port insertion	1 hypertrophic scar	

for transplantation, and therefore, the number of pediatric patients healed[3-5]. Early PLT before deterioration has demonstrated increased survival rates in pediatric patients with liver pathologies[2-5]. Early PLT allows surgery to be scheduled at the right time for each patient, thus avoiding deterioration as a result of liver cirrhosis progression and complications due to the lack of an optimal cadaveric donor.

In tumor patients, especially in the presence of hepatoblastoma, it allows transplantation to be carried out in the ideal window between chemotherapy cycles. It also favors tumor hepatectomy, which becomes easier thanks to tumor reduction following chemotherapy, and it prevents chemotherapy effects in terms of healing. In our series, PLDLT allowed us to choose the right time for transplantation in 3 patients with hepatoblastoma.

Another advantage is the reduction of graft ischemic times as compared to cadaveric donors[2-4] (total absence of cold ischemia). In this respect, coordination between both surgical teams proves particularly important. In our institution, previously identified donor structures are clamped and divided once the recipient's hepatectomy has been completed in order to reduce ischemic times.

The main drawback of PLDLT as compared to pediatric cadaveric donor liver transplantation (PCDLT) is the reduced length of the vessels and the bile duct to be anastomosed, which makes implantation more difficult and increases complications. In adults, various studies have demonstrated a larger amount of vascular and biliary complications in LDLT than in CDLT[15,16]. However, a more recent study[7] showed no significant differences in terms of vascular and biliary complications between both transplantation types, suggesting that healthcare institutions' experience with LT translates into fewer LDLT complications as compared to CDLT.

PLDLT allows transplantation to be carried out in pediatric patients at the right time, thus avoiding deterioration, which would be inevitable if they had to wait for PCDLT. It also offers a glimmer of hope to those patients that will most likely not survive until PCDLT is available. Therefore, according to patient's condition and expected deterioration, and in the absence of an ideal cadaveric donor, the donor is assessed in order to schedule LDLT.

Given that the donor is a healthy individual who decides to altruistically donate part of their liver to a sick child, it is crucial to reduce morbidity and risks. To this end, and thanks to the advance of surgery, laparoscopy has emerged as an important tool for donor hepatectomy in the last decades. In the hands of an expert surgeon, recovery benefits and improved esthetic results have been clearly demonstrated in various studies[4,6-12]. In our sample, no severe complications were recorded in any of the donors using either of the surgical approaches, with no differences in operating times and hospital stay.

There is a misbelief that laparoscopic grafts may compromise implantation because vessels might be shorter. The main objective of our study was to compare whether the surgical approach used compromised implantation and subsequent progression in the patient. In our series, the surgical approach did not compromise the vascular structures of the graft to be anastomosed in any case. In 2 patients from the laparoscopy group (33%) and in 1 patient from the open surgery group (14%), a vascular graft was required, not as a result of lack of vein in the graft, but due to the absence of a suitable portal vein in the recipient.

In our small series, no progression differences in terms of complications, ICU stay, hospital stay, re-intervention, or re-admission were found between groups. These results are consistent with those from the largest series published up until now[14], which compared progression in 72 pediatric recipients of open surgery grafts vs. 72 pediatric recipients of laparoscopic grafts. The authors concluded there are no differences regarding graft and patient progression according to the removal approach used. In our study, a tendency towards more severe complications according to the Clavien-Dindo classification was observed in the open surgery group, both in complications during the first admission and during re-admission. However, given the limited number of patients in our series, we do not believe this demonstrates that open surgery removal increases complications for the recipient. It should be mentioned that these were the first PLDLTs with open surgery removal carried out in our institution, and therefore, the learning curve may have caused complications to increase in this group.

Regarding the most frequent complications, such as biliary leak/stenosis or hepatic vessel thrombosis/stenosis, the results from our series are similar to those described in the articles reviewed[13,14], with no differences according to the removal approach used. Nevertheless, given the small sample size, a percentage or statistic comparison of this type of complications and deaths could not be conducted between groups, or with other series published[13,14].

Given the benefits of laparoscopic graft removal for the donor, and considering there were no differences in terms of recipient progression, it seems reasonable to suggest that minimally invasive graft removal in PLDLT stands as a safe and effective tool in the hands of experienced surgeons. However, a much larger patient cohort would be required to categorically assert this.

The main limitation of our study lies in the fact it has a small sample size, with much larger series of LDLT available in the literature[2,4,16]. However, our study features a small sample size comparison which has been described in one study only[14], potentially giving rise to larger studies in the future. Another limitation lies in the lack of a standardized tool or variable allowing graft anastomosis difficulty to be measured, since this is usually subjectively assessed according to the surgeon's experience.

Even after analyzing and comparing complications and complication severity, the small size of both groups makes it difficult to draw statistically supported assumptions and claim that complications are similar in both. Instead, we should describe complications and verify that they are not significantly more frequent in one group than in the other.

This is a retrospective study comparing the first PLDLTs carried out in our institution, which means the learning curve may have had a negative impact on open surgery group results. Even though a randomized, prospective study would provide with better scientific evidence, it seems unethical to do so given the clear advantages laparoscopy has demonstrated, which means retrospective studies are the only option.

CONCLUSION

PLDLT patients had similar results, regardless of whether graft removal had been carried out laparoscopically or through open surgery.

The surgical approach did not compromise the structures of the graft to be anastomosed, or add any extra difficulty to implantation.

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