Pediatr Gastroenterol Hepatol Nutr. 2021 Nov;24(6):528-534
https://doi.org/10.5223/pghn.2021.24.6.528
pISSN 2234-8646·eISSN 2234-8840

Pediatric Gastroenterology, Hepatology & Nutrition
pghn

Original Article

Check for updates

Donor Surgical Morbidity in Pediatric Living-Donor Liver Transplant: A Portuguese Experience

José Pedro Fernandes dos Santos [1], **Ricardo Martins** [1,2] and **Maria Francelina Lopes** [1,3]

[1]University of Coimbra, Faculty of Medicine, Coimbra, Portugal
[2]Surgery Department, Centro Hospitalar e Universitario de Coimbra EPE (CHUC), Coimbra, Portugal
[3]Pediatric Surgery Departement, Centro Hospitalar e Universitario de Coimbra EPE (CHUC), Coimbra, Portugal

OPEN ACCESS

Received: Jun 10, 2021
Revised: Sep 1, 2021
Accepted: Sep 5, 2021

Correspondence to
José Pedro Fernandes dos Santos
Faculty of Medicine, University of Coimbra, Azinhaga de Santa Comba, Coimbra 300-214, Portugal.
E-mail: jose.pfdossantos@gmail.com

ORCID iDs
José Pedro Fernandes dos Santos
https://orcid.org/0000-0001-5184-1318
Ricardo Martins
https://orcid.org/0000-0001-5340-7582
Maria Francelina Lopes
https://orcid.org/0000-0002-7001-7217

Conflict of Interest
The authors have no financial conflicts of interest.

ABSTRACT

Purpose: Living-donor liver transplant emerged as an alternative treatment for end stage liver disease due to the lack of cadaveric organs availability that met the demand. In Portugal, pediatric living-donor liver transplant (P-LDLT) was initiated in 2001 in Portugal in order to compensate for the scarcity of cadaveric organs for such cases. The aim of this study was to retrospectively analyze the morbi-mortality of the 28 donors included in P-LDLT program performed at Coimbra's Pediatric Hospital (CHUC), a Portuguese reference center.
Methods: We retrospectively collected pertinent donor data and stratified complications according to Clavien's scoring system.
Results: In total, 28.6% (n=8) of the donors had surgical complications. According to Clavien-Dindo's classification, two donors had major complications (Clavien grade ≥3), four donors had grade 2 complications, and two donors had grade 1 complications. There were no P-LDLT-related mortalities in the present case series. The most common verified complications were biliary tract injuries and superficial incisional infections, which are consistent with the complications reported in worldwide series.
Conclusion: These patients from CHUC shows that donor hepatectomy in P-LDLT is a safe procedure, with low morbidity and without mortality.

Keywords: Liver transplantation; Living donors; Morbidity

INTRODUCTION

Pediatric liver transplantation is the state-of-the-art treatment for children with established or with a high risk of end-stage liver disease (P-ESLD). Pediatric living-donor liver transplant (P-LDLT) has become a viable and feasible strategy that aims to ameliorate the cadaveric organ shortage experienced by health centers around the world. New surgical innovations and the increasing incidence rate of P-ESLD have caused an upsurge in the use of LDLT. The number of required surgeries has increased by 11-fold since 1991, though the number of donors did not follow this tendency [1]. Due to a shortage of cadaveric organs, there is a significant delay in surgical timing, which can be fatal for children. Currently, the donor death rate and surgical morbidity related to pediatric liver transplant are 0.13% and 10-40% [2,3], respectively. Morbi-

mortality in donors is the main obstacle to the use and evolution of LDLT. Assuring donors' safety is the main priority of this major procedure on a healthy individual.

The first attempts of pediatric liver transplantation using a living adult donor were reported in 1988 by Raia et al. [4] who described two complete procedures in which both recipients died. In 1989, Strong et al. [5] described the first successful P-LDLT using a graft obtained from an adult. This technique was first described in the Western world; however, it is especially prevalent in Asian countries where organ donation rates from the deceased are very low.

Coimbra's Pediatric Hospital (CHUC) is a tertiary academic center that has served as the national reference center for pediatric liver transplant since 1994. P-LDLT has been performed since 2001 [6]. Additionally, CHUC is among the 18 European centers which are integrated in European Reference Network TransplantChild [7].

This paper presents the experiences of clinicians at CHUC regarding donors' surgical morbidity in P-LDLT. A retrospective analysis of surgical outcomes was made and categorized according to the Classification of Surgical Complications by Dindo et al. [8].

MATERIALS AND METHODS

This study was approved by the Ethics Committee of the Faculty of Medicine, University of Coimbra and followed the Institutional and European Commission rules and Helsinki's ethical standards with the use of deidentified and anonymized data for human medical research.

A retrospective revision of clinical records from a single institution was performed, analyzing the medical charts of all donors (n=28) who underwent hepatectomy in P-LDLT (recipients under 18 years of age) in CHUC from April 27, 2001 to September 30, 2018. In addition, we collected the pertinent data of recipient-donor pairs included in the pediatric liver transplant database. No donors were excluded from the study.

The collected data included characteristics of both the recipient and the donor, such as sex, age, body mass index (BMI), ABO compatibility, date of the procedure, and primary indication for P-LDLT. The surgical and imagiological data collected included the type and volume of graft collected, total liver volume, remnant liver volume (RLV), and postoperative surgical complications, including morbidity and mortality within the first 90 days after donor hepatectomy.

Only healthy volunteers aged between 18 and 50 years, who were ABO-compatible with the recipient, had a BMI between 18 and 28 kg/m^2 and had no medical or psychiatric illness were considered for donor evaluation.

The donors' preoperative study at CHUC followed an established and strict protocol, which included a psychosocial evaluation, health status evaluation, exclusion of metabolic or infectious diseases, study of the hepatic vascular and biliary anatomy, and evaluation of the total liver and graft volumes in order to determine the percentage of RLV.

Analytic pre-donation studies include a full blood count and biochemical study, a complete coagulation study, and viral serology. Depending on the receptor's disease, α-1-antitrypsin dosing and plasmatic ceruloplasmin and copper dosing were performed.

https://doi.org/10.5223/pghn.2021.24.6.528

An imaging study done prior to donor hepatectomy was performed using computed tomography (CT), magnetic resonance imaging (MRI), and angiography with hepatic three-dimensional (3D) anatomical reconstruction. CT angiography with 3D reconstruction was used to minutely analyze the vascular anatomy of the liver. These imagiological studies were also valuable in calculating the total liver and graft volume, which were essential aspects of a complete preoperative study. MRI allowed a detailed evaluation of the biliary tract, and it was useful for the assessment of hepatic steatosis (sensitivity: 81% and specificity: 100%) [9]. Percutaneous hepatic biopsy was done in selected cases (four donors in our series) due to altered hepatic enzymology (n=2), cryptogenic cirrhosis (n=1) and non-described justification (n=1).

The decision to include an individual as a donor in the P-LDLT program ultimately depended on the feasibility of the procedure (decided by the surgical team) and the endorsement of the Admissibility Verification Entity (composed by Ethics Committee members).

Postoperative surgical complications were graded according to the Clavien-Dindo. Classification of Surgical Complications, which is presented in **Table 1** [8]. A major complication is defined as any kind of surgical morbidity with a grade ≥3 based on the Clavien-Dindo classification system.

RESULTS

A total of 28 hepatectomies for P-LDLT were performed. There were no aborted donor operations. Each donor experienced complete recovery after the donation. There were no deaths or need for postoperative donor liver transplant. The number of procedures performed throughout the years can be seen in **Fig. 1**.

The donor's medical charts and the prospective P-LDLT database (containing the pertinent information of recipient-donor pairs) were analyzed, and several aspects regarding the demographic characteristics of our study population are presented in **Table 2**.

As **Table 2** presents, the female-to-male ratio preponderance was 1.8 and slightly elevated BMI average was observed. The only child who did not have a parental relationship with

Table 1. Clavien-Dindo classification of surgical complications

Grade 1	Any deviation from normal postoperative care without the need for pharmacological treatment or surgical, endoscopic, and/or radiological interventions. The permitted therapeutic regimens are: drugs such as antiemetics, antipyretics, analgesics, and diuretics; electrolytes; and physiotherapy. This grade also includes wound infections that opened at the bedside.
Grade 2	Requiring pharmacological treatment with drugs other than the drugs permitted for grade I complications. Blood transfusions and total parenteral nutrition are also included.
Grade 3	Requiring surgical, endoscopic, and/or radiological intervention: 3a: Intervention not under general anesthesia; 3b: Intervention under general anesthesia.
Grade 4	Life-threatening complication (including CNS complications)* requiring IC/ICU management: 4a: Single organ dysfunction (including dialysis); 4b: Multiorgan dysfunction.
Grade 5	Death of a patient.
Suffix "d"	If the patient suffers from a complication at the time of discharge, the suffix "d" (for "disability") is added to the respective grade of complication. This label indicates the need for a follow-up to fully evaluate the complication.

CNS: central nervous system, IC: intermediate care, ICU: intensive care unit.
*Brain hemorrhage, ischemic stroke, subarachnoid bleeding, but excluding transient ischemic attacks.
Adapted from Dindo et al. (Ann Surg 2004;240:205-13) [8].

https://doi.org/10.5223/pghn.2021.24.6.528

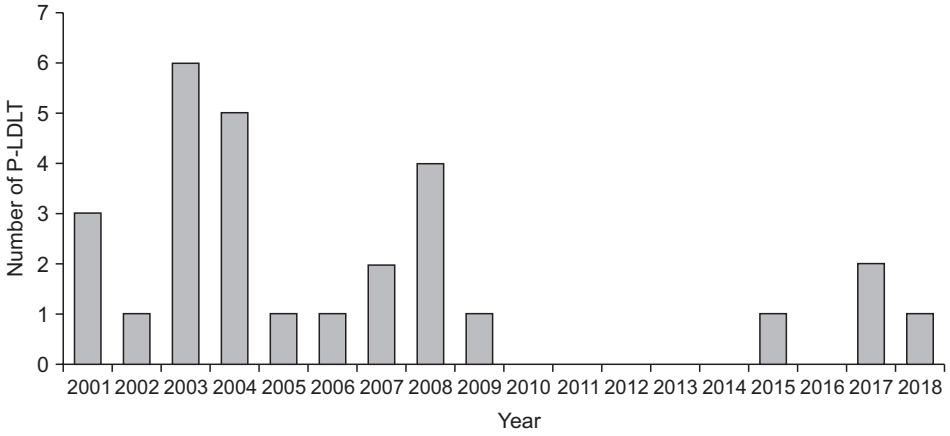

Fig. 1. Pediatric living-donor liver transplant (P-LDLT) procedures from April 2001 to September 2018.

Table 2. Donor demographics

Characteristic	Value (n=28)
Age (yr)	33.6 (18–47)
Sex	
Female	18 (64.3)
Male	10 (35.7)
Body mass index (kg/m^2)	23.14 (18–31)
Indications for P-LDLT	
Biliary atresia	11 (39.3)
α-1-antitrypsin deficiency	8 (28.6)
Cryptogenic cirrhosis	3 (10.7)
Multifocal hepatocarcinoma	1 (3.6)
Fetal hepatoblastoma	1 (3.6)
Type 1a glycogenosis	1 (3.6)
Acute hepatic failure	1 (3.6)
Wilson's disease	1 (3.6)
Choledochal type I cyst	1 (3.6)
Relationship with recipient	
Mother	18 (64.3)
Father	9 (32.1)
Uncle	1 (3.6)
ABO incompatibility	0
Type of graft	
Left lateral sectionectomy	20 (71.4)
Left hepatectomy	6 (21.4)
Right hepatectomy	2 (7.1)
Mean graft volume (cm^3)*/Mean remnant liver volume (%)†	
Left lateral sectionectomy	242.7/82.8
Left hepatectomy	382.5/67.5
Right hepatectomy	841/39.5
Days of hospital stay	7.15 (6–12)
Overall postoperative morbidity rate within 90 days	8 (28.6)
Postoperative liver insufficiency	0
Death	0

Values are presented as mean (range), number (%), or number only.
P-LDLT: pediatric living-donor liver transplant.
*Graft volume was obtained pre-operatively in 26 patients with an average of 322 cm^3, ranging from 179 cm^3 to 1,051 cm^3.
†The average remnant liver volume, determined in 24 donors, was 76% (minimum of 35% to a maximum of 89%).

the donor received the graft from an uncle. The most common indication for P-LDLT was biliary atresia.

https://doi.org/10.5223/pghn.2021.24.6.528

Table 3. Donors' complications according to the Clavien-Dindo classification

Clavien grade		Complication	n	Relative %	Absolute %
1		Partial respiratory insufficiency	1	3.6	12.6
		Paralytic ileum	1	3.6	12.6
2		Bile leakage	2	7.1	24.8
		Superficial incisional infection	2	7.1	24.8
3	3a	N/A	0	0	0
	3b	Incisional hernia	1	3.6	12.6
4	4a	Hemoperitoneum	1	3.6	12.6
	4b	N/A	0	0	0
5		N/A	0	0	0
Total			8	28.6	100

N/A: not applicable.
Adapted from Dindo et al. (Ann Surg 2004;240:205-13) [8].

A total of 28 procedures were done, with left lateral sectionectomy having been the most common one (n=20; 71.4%), followed by left hepatectomy (n=6; 21.4%) and right hepatectomy (n=2; 7.1%).

The overall postoperative morbidity rate within 90 days after the donor's hepatectomy was 28.6% (n=8 patients). However, these complications were mainly minor, except for 7.1% of the cases (n=2 with Grade ≥3 complications) (**Table 3**).

Two patients developed grade 1 complications. One of them developed partial respiratory insufficiency, which was treated with kinesiotherapy and oxygen supplementation. The other patient experienced paralytic ileum that was resolved with conservative treatment.

Grade 2 complications occurred in another four donors. Of these, two donors developed post-surgical bile leakage and both were successfully managed with drainage maintenance and antibiotic therapy. The other two donors presented with a superficial incisional infection, which required antibiotics and resuturing with local anesthesia.

Major complications were found in two patients. One of the donors developed a postoperative abdominal hernia, which required surgical repair under general anesthesia (Grade 3b). The incisional hernia was detected within the first 90 days after the donation, though the laparorrhaphy was performed after that period. The other donor experienced a hemoperitoneum followed by hypovolemic shock and was immediately taken to the operating room for urgent hemostasis (Grade 4a).

DISCUSSION

Donor safety is a matter of paramount importance in LDLT. Complications arise in up to 40% of the patients within the first year after transplant. However, 95% of procedure-related morbidities is solved within the first postoperative 90 days [3]. Large retrospective series have reported that 21% of donors experience only one complication after the procedure, and 17% develop two or more surgical complications. The most common surgical morbidities after donor hepatectomy are reported in the literature: biliary leak, 36.9%; bacterial infection, 12%; and incisional hernia, 6%. Pulmonary effusion, neuropraxia, and intrabdominal abscess account for 11% of the surgical morbidities has been reported [10]. Our series reports the existence of the same most common complications as the ones reported in the literature, except for neuropraxia or intrabdominal abscess.

https://doi.org/10.5223/pghn.2021.24.6.528

Although there was a relatively small number of surgeries in CHUC thus far, the donor morbidity rate is comparable with results obtained worldwide. Within the first three months after donation, the verified overall complication rate was 28.6%. However, Abecassis et al. [3] found that surgical morbidities, such as incisional hernia, bowel obstruction, and psychological complications, may develop as late as 5 to 10 years post-transplant. Apart from the small number of surgeries (due to both a low demand for this kind of procedure and the prioritization of cadaveric grafts for pediatric liver transplant), the retrospective analysis of donors' data was also a limitation in this study. The medical charts did not have a complete informative description of some procedure details.

Even though donor mortality is a rare event (0.5% for right hepatectomy and 0.1-0.3% for left hepatectomy [2,3], it should be addressed as a catastrophe as it affects the recipient, the families of both the donor and recipient, and all of the clinicians involved in the LDLT process. From 1999 to 2017, 23 deaths worldwide have been reported [11]. All efforts should be made to minimize the possibility of donor mortality. Accumulated center know-how, full pre-donation study, strict donor selection criteria, new surgical techniques and intra-operative management, and qualified postoperative patient care are crucial to the improvement of donor outcomes [12]. Knowing the overall rate and types of complications and comparing the results from the CHUC case series with the ones reported worldwide is important for a continuous institutional self-evaluation and improvement.

In conclusion, LDLT performed in our center is a safe and feasible treatment option for select pediatric cases. It was verified that CHUC's complication rate is lower than the complication rates verified in large series. Therefore, P-LDLT presents as a viable treatment option for selected cases of P-ESLD.

REFERENCES

1. Holcomb GW 3rd, Murphy JP, Ostlie DJ, St. Peter SD. Ashcraft's pediatric surgery. 6th ed. London: Elsevier, 2014:607-31.
2. Renz JF, Roberts JP. Long-term complications of living donor liver transplantation. Liver Transpl 2000;6(6 Suppl 2):S73-6.
PUBMED | CROSSREF
3. Abecassis MM, Fisher RA, Olthoff KM, Freise CE, Rodrigo DR, Samstein B, et al. Complications of living donor hepatic lobectomy--a comprehensive report. Am J Transplant 2012;12:1208-17.
PUBMED | CROSSREF
4. Raia S, Nery JR, Mies S. Liver transplantation from live donors. Lancet 1989;2:497.
PUBMED | CROSSREF
5. Strong RW, Lynch SV, Ong TH, Matsunami H, Koido Y, Balderson GA. Successful liver transplantation from a living donor to her son. N Engl J Med 1990;322:1505-7.
PUBMED | CROSSREF
6. Maciel JRC, Lopes MF, Furtado E. [Pediatric living donor liver transplant - the Portuguese reference center experience]. [master's thesis]. Coimbra: University of Coimbra; 2013. Portugal.
7. Laezza N, Pessanha I, Lopes JP, Cunha C, Lopes MF. Experience report from a Center integrated in an European Reference Network. Paper presented at: I Encontro do Internato Médico da Zona Centro; 2018 Nov 16; Aveiro, Portugal.
CROSSREF
8. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004;240:205-13.
PUBMED | CROSSREF

9. Rinella ME, McCarthy R, Thakrar K, Finn JP, Rao SM, Koffron AJ, et al. Dual-echo, chemical shift gradient-echo magnetic resonance imaging to quantify hepatic steatosis: implications for living liver donation. Liver Transpl 2003;9:851-6.
PUBMED | CROSSREF
10. Ghobrial RM, Freise CE, Trotter JF, Tong L, Ojo AO, Fair JH, et al. Donor morbidity after living donation for liver transplantation. Gastroenterology 2008;135:468-76.
PUBMED | CROSSREF
11. Brige P, Hery G, Chopinet S, Palen A, Azoulay D, Gregoire E. Morbidity and mortality of hepatic right lobe living donors: systematic review and perspectives. J Gastrointestin Liver Dis 2018;27:169-78.
PUBMED | CROSSREF
12. Lauterio A, Poli C, Cusumano C, Di Sandro S, Tripepi M, Mangoni I, et al. Living-donor liver transplantation: donor selection criteria and postoperative outcomes. A single-center experience with a 10-year follow-up. Transplant Proc 2013;45:2680-3.
PUBMED | CROSSREF