DONOR SAFETY IN LIVING DONOR LIVER TRANSPLANTATION: EXPERIENCE OF TWO MEDICAL CENTRES FROM ROMANIA AND REPUBLIC OF MOLDOVA

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ABSTRACT

Introduction. Living donor liver transplantation (LDLT) has become a feasible treatment modality for end-stage liver disease.
The objective of the study was to assess donor safety in LDLT.
Material and methods. The present study assessed donor safety in LDLT in 157 living donation procedures performed in two transplant centres: Bucharest (Romania) and Chisinau (Republic of Moldova). We reviewed data of living liver donors who underwent procedures between 2000 and 2020. The outcomes were evaluated over two time periods (2000-2009 and 2010-2020) using the validated Clavien 5-tier grading system.
Results. Different grafts were obtained from the 157 donor procedures (112 right lobe, 14 left lobe, and 31 left lateral segments). The mean age of living donors (LDs) was 33±8.62 years, proportion of men 47.1%.

RéSUMÉ

Introduction. La transplantation hépatique à partir d’un donneur vivant (THDV) est devenue une modalité de traitement réalisable pour les maladies hépatiques en phase terminale.
L'objectif de l'étude a été d'évaluer la sécurité des donneurs dans le cadre de la THDV.
Matériel et méthodes. La présente étude a analysé la sécurité des donneurs dans le cadre de la THDV à partir de 157 procédures réalisées par deux centres de transplantation: Bucarest (Roumanie) et Chisinau (République de Moldova). Nous avons examiné les données des donneurs vivants de foie (DV) qui ont subi des procédures entre 2000 et 2020. Les résultats ont...
The mean duration of surgery was shorter in the latest period than in initial period (347.4 vs. 257.57 min, p<0.001, respectively). One or more complications were experienced by 49.7% of donors and the rate of major complications was 5.1%. The two most common major complications were bile leakage (6.4%) and subphrenic access (5.7%). The rate of complications for LDs in the initial period of study was 1.33 and for the latest period 1.23.

Conclusions. Donor hepatectomy can be performed successfully with minimal and easily controlled complications. Biliary complications were the most common type of major donor complication among living LDs.

Keywords: living liver donor, hepatectomy, safety of living donor, complications, outcomes.

List of abbreviations
ALAT: alanine aminotransferase
ASAT: aspartate aminotransferase
BMI: body mass index
CT: computed tomography
GRWR: graft-to-recipient weight ratio
HS: hepatic steatosis
ICU: Intensive Care Unit
INR: International Normalized Ratio
ISGLS: International Study Group of Liver Surgery
LDLT: living donor liver transplantation
LFT: liver function test
LLD: living liver donor
LT: liver transplantation
MHV: middle hepatic vein
MRCP: magnetic resonance cholangiopancreatography
PCNB: percutaneous needle biopsy
PHLF: post-hepatectomy liver failure
POD: post operative day
PT: prothrombin time values
RL: right lobe
RLV: residual liver volume
SD: standard deviation
TB: total bilirubin
TLV: total liver volume
US: ultrasonography

Introduction
Liver transplantation (LT) is the treatment of choice for end-stage liver disease, but the continued shortage of deceased donors remains problematic. With the steady increase in LT over the last decades and the donor pool remaining largely stagnant, the shortage of organs for transplantation has become even more pressing because of the coronavirus disease 2019 (COVID-19) pandemic. Living donor liver transplantation (LDLT) has been widely used worldwide and has become an effective, lifesaving alternative to deceased donor liver transplantation. LDLT offers recipients the advantage of a high-quality graft...
and the possibility of avoiding delisting or death because of a change in clinical status. Despite good outcomes for recipients, LDLT is a very complicated surgical procedure, and donor safety remains an issue of concern. However, since the turn of the millennium, the operation has dramatically improved, rendering results like those of deceased donor liver transplantation. Assuring donors’ safety is the main priority of this major procedure on a healthy individual. A wide range of complication rates have been reported in donors after LDLT, reaching up to 78.3% in right lobe (RL) LD procedures. One of the recent studies confirms that outcomes of the living liver donors (LLD) group were worse than those of the matched healthy control group, despite the small number of deaths and medical morbidities in this group. A large-scale prospective cohort study was needed to better understand the risk factors and accurately determine the complication rates of LDLT. The safety of LLDs has been investigated in terms of surgical complications and in-hospital morbidity as short-term outcomes.

This paper presents the experiences of clinicians regarding donors’ surgical morbidity in two medical centers: Fundeni Clinical Institute, Bucharest (Romania) and Republican Clinical Hospital, Chisinau (Republic of Moldova). The analysis of surgical outcomes was made and categorized according to the Classification of Surgical Complications by Dindo et al.

THE OBJECTIVE OF THE STUDY was to evaluate the postoperative evolutions after LD hepatectomy.

MATERIALS AND METHODS

Study population

In this longitudinal study there were included 157 LLDs who underwent donor hepatectomy during the period March 2000 to December 2020, in two medical centers: Fundeni Clinical Institute, Bucharest (Romania) and Republican Clinical Hospital, Chisinau (Republic of Moldova), and have had no less than one year of follow up after surgery (2000-2009 retrospective evaluation, 2015-2020 prospective evaluation). The approval was granted by the Committee of Ethics in Research of the State University of Medicine and Pharmacy “Nicolae Testemitanu” Chisinau (approval 33, No 44, 12.05.2016). An informed consent was signed by the patients.

Donation was voluntary in all cases. Only potential donors who met the universally accepted primary selection criteria for LDLT were evaluated according to each local protocol, with minor differences between centres. The details of the surgical technique applied in donor operations were described in a previous report. To evaluate the changes in perioperative donor characteristics and outcomes over time, the patient cohort was further investigated over two time periods: [A] the initial period of LDLT activity (2000-2009); [B] the latest period (2010-2020) (Figure 1).

Data were evaluated and inclusion criteria were applied: age between 18 and 56 years, nondiabetes, compatibility of blood group ABO, absence of major abdominal surgery (except cholecystectomy), abstinence from smoking and discontinuation of contraceptive pills for 6 weeks, the graft-to-recipient weight ratio (GRWR) >0.8% and residual liver volume (RLV) ≥ 30% of total liver volume (TLV). The endpoint was the comparison of LLDs safety including postoperative laboratory findings (peak aspartate aminotransferase [ASAT], alanine aminotransferase [ALAT], total bilirubin [TB], prothrombin time [PT] values) and operative morbidity.

Design of the study

The study sample was composed of LDs classified based on the period of study: initial period 2000-2009 and latest period 2010-2020 (Figure 1). All LLDs were measured preoperatively with the normal liver function survey. Liver biopsy to exclude liver steatosis was not routinely performed, and this invasive procedure was applied only when steatosis was suspected from the donor’s medical history, physical examination, and preoperative studies (BMI ≥ 30 kg/m², elevated ASAT, ALAT, or TB levels, dyslipidemia, presence of metabolic risk factors, abnormal findings on computed tomography (CT) or abdominal ultrasonography (US) suggesting hepatic steatosis. For all 157 LLDs, wedge biopsy samples of both hepatic lobes were performed just after laparotomy and sent for frozen section examination. The remaining tissue was formalin-fixed and paraffin-embedded for hematoxylin and eosin staining.
Preoperative evaluation and selection guidelines for liver donation

A detailed multi-stage counselling during the donor work-up with regards to the operation, complications, and outcomes, which included LLDS to have a realistic view of the procedure, was performed. Healthy voluntary donors underwent a staged evaluation of suitability for donation.

Stage I contained a face-to-face interview with the prospective donor with a detailed discussion of the evaluation process, perioperative period, short- and long-term donor outcomes, including complications. It was followed by a clinical examination of the donor, review of medical history, basic laboratory tests (complete blood count, liver function tests, viral serology, renal function tests, lipid profile), including viral serology. Initially, unsuitable donors were advised to lose weight and offered an exercise and diet plan. They were reviewed following the weight loss and went on to stage II of evaluation if found suitable on review.

Stage II consisted of US and triphasic liver CT, needed to assess the hepatic volume, vascular anatomy, and steatosis. Liver volumes were estimated on CT scans using 3D reconstruction software (OsiriX MD). An algorithmic approach to graft selection was used, based on the donor functional RLV, expected GRWR, recipient and donor work-up with regards to the operation, complications, and outcomes, which included LLDS to have a realistic view of the procedure, was performed. Healthy voluntary donors underwent a staged evaluation of suitability for donation.

Stage II consisted of US and triphasic liver CT, needed to assess the hepatic volume, vascular anatomy, and steatosis. Liver volumes were estimated on CT scans using 3D reconstruction software (OsiriX MD). An algorithmic approach to graft selection was used, based on the donor functional RLV, expected GRWR, recipient and donor vascular anatomy. Volumetric measurements of the donor liver were obtained using preoperative imaging. The ratio of the donor remnant liver volume (RLV) was expressed as a percentage of the estimated total liver volume, while the actual procured graft weight in grams was recorded on the back table after flushing with cold perfusion solution.

Suitable donors went onto stage III, which included evaluation of the biliary anatomy with magnetic resonance cholangiopancreatography (MRCP) and a multidisciplinary review by the chief surgeon, surgical team, hepatologists, psychiatrist, gynecologists (in female donors), cardiologists and anesthesiologists. Following this, the transplant papers were put up for approval by a state health authority's legal authorization committee (Committee of Ethics of Fundeni Clinical Institute, Bucharest, Romania, and Independent Committee of Approvals of Transplantation from Republic of Moldova).

Preoperative data

Donor data including age, gender, BMI, preoperative LFT, platelets, TB level, degree of steatosis on biopsy, TLV, RLV based on the volumetry CT were collected retrospectively (2000-2014) and prospectively (2015-2018).

Surgical technique and postoperative management

The incision was usually a reverse L with midline, being used for donors with a suitable body habitus. Both teams have used various surgical techniques to ensure LDs safety and graft reconstruction. Right lobe without middle hepatic vein (MHV) is the current standard and to prevent outflow obstruction at the anterior section, sizable (>5 mm diameter) tributaries of the middle hepatic vein were reconstructed with various kinds of interposition grafts in back-table surgeries. The standard techniques for procurement and implantation were employed. The detailed surgical techniques of donor hepatectomy is described elsewhere.

The donor was usually extubated in the operation room and monitored in the intensive care unit (ICU). All LDs were closely monitored during the first 1 or 2 days after donation, especially for the timely detection of bleeding. Oxygenation, nutritional support with early feeding, and early ambulation were emphasized. Intravenous patient-controlled analgesia was routinely used for 2 to 3 days after surgery. Discharge from the hospital was aimed for the 6th post-operative day after a satisfactory abdominal ultrasound, chest X-ray and liver function tests. The outpatient follow-up was once weekly for one month, following hospital discharge. The donors were followed up on a long-term basis in the outpatient department or by local physicians with standard blood investigations at 3, 6, 12 months and then annually.

Intraoperative and postoperative data

Details of the GRWR, duration of operation, volume of hemorrhage were analyzed for all groups. Postoperative variables including serum bilirubin, AST, ALAT, international normalized ratio (INR), on post operative day (POD) 1, POD 3 and POD7 were analyzed, to assess post operative recovery of liver function in the donor. The cut-off value of AST was established as 28 U/L, ALT 31 U/L, total bilirubin 1 mg/dL.

Complications

The Dindo-Clavien score was used to determine the severity of complications, and major complications were defined as Dindo-Clavien grade >3b. In case of more than one complication, the most serious was used for gradation. Bile leak was defined according to the International Study Group of Liver Surgery (ISGLS) as bilirubin concentration in the drain fluid at least three times the serum bilirubin on or after POD 3 or as the need for radiological or operative intervention resulting from biliary collections or bile peritonitis. Post-hepatectomy liver failure (PHLF)
was defined using the ‘50–50’ criteria for defining PHLF (serum bilirubin >2.9 mg/dL and prothrombin time <50% of normal (INR >1.9) on POD 5)³. Readmission to the hospital within the first 3 months was defined as early readmission.

**Outcome measurement**

The donor surgical primary outcomes were evaluated by length of hospital stay, morbidity of LDs (postoperative complications within the first 30 days) and mortality during the first 90 days after surgery. Secondary outcomes were duration of surgery, intraoperative hemorrhage, and volume of transfusion.

**Statistical analysis**

Continuous variables are presented as mean ± standard deviation (SD) in case of normal distributed data; if distribution of data was non-normal - as median and range. Nonparametric data are presented as relative frequency (percentage). The Pearson chi-square test and one-way ANOVA test were used to examine differences in demographic and clinical characteristics within the three groups, if distribution of data was normal. Kruskal-Wallis and Mann-Whitney U test were used for analysis of continuous variables with non-normal distribution and chi-square test for categorical variables. The outcomes between the groups were compared using least-squares means, the linear mixed model after log transformation, and cumulative logistic regression with generalized estimating equations. P-values lower than 0.05 were considered to indicate statistically significant differences. All statistical analyses were performed using IBM SPSS Statistics, version 26.0.

**RESULTS**

A total number of 157 LDs underwent donations, of whom 112 (71.34%) were right lobe donations. The mean age of LDs was 33±8.62 years (19-56 years), proportions of men 47.1% (74/157), mean BMI 24.33±3.28 kg/m² (17.5-34.0 kg/m²). The mean TLV was 1354±291.68 m³ (949-3030 m³).

**Donor baseline characteristics**

Table 1 shows the differences in the demographic and clinical features between the groups with different period of evaluation. Donors younger than 50 years

<table>
<thead>
<tr>
<th>Preoperative variables</th>
<th>Total n=157</th>
<th>Initial period n=48</th>
<th>Latest period n=109</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>General data</td>
<td></td>
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</tr>
<tr>
<td>Age (years), median ± SD (range)</td>
<td>33.00±8.62</td>
<td>33.00±8.28</td>
<td>34.00±8.80</td>
<td>0.78</td>
</tr>
<tr>
<td>Age &gt; 50 years, n (%)</td>
<td>6 (3.82)</td>
<td>2 (4.2)</td>
<td>4 (3.7)</td>
<td>0.88</td>
</tr>
<tr>
<td>Age &lt; 35 years, n (%)</td>
<td>92 (58.6)</td>
<td>32 (66.7)</td>
<td>60 (55.0)</td>
<td>0.173</td>
</tr>
<tr>
<td>Gender, male, n (%)</td>
<td>74 (47.1)</td>
<td>16 (33.3)</td>
<td>58 (53.2)</td>
<td>0.022</td>
</tr>
<tr>
<td>Relation with recipient</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Biological relation with recipient, n (%)</td>
<td>124 (79)</td>
<td>41 (85.4)</td>
<td>83 (76.2)</td>
<td>0.404</td>
</tr>
<tr>
<td>Nonbiological relation with recipient, n (%)</td>
<td>16 (10.2)</td>
<td>3 (6.3)</td>
<td>13 (11.9)</td>
<td>0.404</td>
</tr>
<tr>
<td>Without relations with recipient, n (%)</td>
<td>17 (10.8)</td>
<td>4 (8.3)</td>
<td>13 (11.9)</td>
<td>0.404</td>
</tr>
<tr>
<td>Type of relationship</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parents (mother, father), n (%)</td>
<td>49 (31.2)</td>
<td>25 (52.1)</td>
<td>24 (22)</td>
<td>0.01</td>
</tr>
<tr>
<td>Children (daughter, son), n (%)</td>
<td>41 (26.5)</td>
<td>6 (12.5)</td>
<td>35 (32.1)</td>
<td>0.01</td>
</tr>
<tr>
<td>Siblings (brother, sister), n (%)</td>
<td>15 (9.6)</td>
<td>12 (2.1)</td>
<td>14 (12.8)</td>
<td>0.14</td>
</tr>
<tr>
<td>Cousin/nephew, n (%)</td>
<td>17 (10.8)</td>
<td>6 (12.5)</td>
<td>11 (10.1)</td>
<td>0.14</td>
</tr>
<tr>
<td>Ance/aunt, n (%)</td>
<td>2 (1.3)</td>
<td>2 (4.2)</td>
<td>0 (0)</td>
<td>0.01</td>
</tr>
<tr>
<td>Husband / wife</td>
<td>15 (9.6)</td>
<td>4 (8.3)</td>
<td>11 (10.1)</td>
<td>0.14</td>
</tr>
<tr>
<td>Friend, n (%)</td>
<td>15 (9.7)</td>
<td>4 (8.3)</td>
<td>14 (12.8)</td>
<td>0.14</td>
</tr>
<tr>
<td>Anthropometry</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Height (m), median ± SD</td>
<td>1.70±0.09</td>
<td>1.68±0.09</td>
<td>1.72±0.09</td>
<td>0.009</td>
</tr>
<tr>
<td>Weight (kg), median ± SD</td>
<td>70.89±11.48</td>
<td>66.33±11.06</td>
<td>72.93±11.12</td>
<td>0.001</td>
</tr>
<tr>
<td>BMI (kg/m², median ± SD)</td>
<td>24.03±3.28</td>
<td>23.55±3.26</td>
<td>24.66±3.24</td>
<td>0.047</td>
</tr>
<tr>
<td>Body surface (m², median ± SD)</td>
<td>1.83±0.18</td>
<td>1.75±0.18</td>
<td>1.86±0.17</td>
<td>0.001</td>
</tr>
<tr>
<td>TLV, (m³, median ± SD)</td>
<td>1354.00±291.68</td>
<td>1320.54±205.46</td>
<td>1454.98±314.54</td>
<td>0.007</td>
</tr>
</tbody>
</table>

Abbreviations: SD, standard deviation; BMI, body mass index; TLV, total liver volume.
represented 149/157 (94.9%) cases and only 6 (3.82%) donors were older than 50 years. The mean age in the first and second period groups was 33.00±8.28 years (19-54 years) vs 34.40±8.80 years (20-56 years), respectively (p = 0.78). The males: female ratio was 1:1.14. In the first group of donors, the males: female ratio was 1:2, and in the second group 1:0.87. Statistically significant differences were observed by sex distribution: males 16 (33%) in the I group, and 58 (53.2%) in the II group, p = 0.002. This difference can be explained by the increase in the number of right hepatectomies, in which more men were involved. Most LDs were from urban area, 88/157 (56.1%). No differences were observed between groups in dependence of provenience (urban/rural). The most common relationship to the recipient were parent (30.3%) and child (26.5%). Statistically significant differences were observed between the groups: in the initial period there were more frequent relationships – parent as living donors and child as a recipient – 52.1% (25/48) vs 22% (22/109), p = 0.01, for initial and latest period, respectively. In the latest period, 32.1% (35/109) of LDs have been children of recipients. Seventeen (11.6%) of the donors have not had a biological relation with recipients, revealing the absence of statistically significant differences between the groups. In the latest period
of study, anthropometric data (height, weight, BMI, body surface and TLV) had statistically significant differences with the initial period, because of the highest number of males.

**Comparison of intraoperative characteristics**

The highest prevalence of right hepatectomy was characteristic for the latest period of study in comparison with initial period, 80.7% vs 43.8%, p<0.001, respectively (Figure 2, Table 2). Lateral left hepatectomy was more common in the initial period of study than for the latest period (41.7% vs 10.1%, p<0.001, respectively). No difference was observed between the study group for right hepatectomy with IV segment, left hepatectomy with IV segment and caudal lobe. The mean duration of surgery was shorter in the latest period than in the initial period (347.4±92.08 min vs 257.57±66.55 min, p<0.001, respectively) and graft weights were higher (510.02±274.46g vs 698.37±231.96g, p<0.001, respectively).

**Comparison of postoperative laboratory findings of donors**

<table>
<thead>
<tr>
<th>Postoperative variables</th>
<th>Total n=157</th>
<th>Initial period n=48</th>
<th>Latest period n=109</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALAT, POD1 (IU/L, median ± SD)</td>
<td>228.85±142.77</td>
<td>337.98±117.84</td>
<td>224.85±152.80</td>
<td>0.596</td>
</tr>
<tr>
<td>POD3 (IU/L, median ± SD)</td>
<td>187.73±169.59</td>
<td>170.90±93.53</td>
<td>191.62±94.13</td>
<td>0.666</td>
</tr>
<tr>
<td>POD7 (IU/L, median ± SD)</td>
<td>107.48±191.98</td>
<td>115.69±67.17</td>
<td>103.86±60.00</td>
<td>0.276</td>
</tr>
<tr>
<td>Peak value ALAT, (IU/L, median ± SD)</td>
<td>256.28±198.44</td>
<td>243.46±129.52</td>
<td>261.92±222.41</td>
<td>0.593</td>
</tr>
<tr>
<td>Peak value ASAT, (IU/L, median ± SD)</td>
<td>192.03±158.93</td>
<td>162.33±92.44</td>
<td>205.11±179.44</td>
<td>0.121</td>
</tr>
<tr>
<td>Duration of normalization of ALAT, (days), mean ±SD</td>
<td>19.47±9.15</td>
<td>19.54±9.70</td>
<td>19.43±8.95</td>
<td>0.945</td>
</tr>
<tr>
<td>TB, POD1 (mg/dL, median ± SD)</td>
<td>1.78±1.03</td>
<td>1.40±0.71</td>
<td>1.94±1.11</td>
<td>0.002</td>
</tr>
<tr>
<td>POD3 (mg/dL, median ± SD)</td>
<td>1.52±0.96</td>
<td>1.28±0.97</td>
<td>1.63±0.95</td>
<td>0.034</td>
</tr>
<tr>
<td>POD7 (mg/dL, median ± SD)</td>
<td>0.99±0.96</td>
<td>0.99±1.36</td>
<td>0.99±0.73</td>
<td>0.971</td>
</tr>
<tr>
<td>Peak value TB, (IU/L, median ± SD)</td>
<td>1.91±1.17</td>
<td>1.41±0.71</td>
<td>2.14±1.27</td>
<td>0.001</td>
</tr>
<tr>
<td>Duration of normalization of TB, (days), mean ±SD</td>
<td>5.37±4.33</td>
<td>4.54±2.93</td>
<td>5.74±4.78</td>
<td>0.111</td>
</tr>
<tr>
<td>INR, POD1 (median ± SD)</td>
<td>1.46±0.28</td>
<td>1.37±0.25</td>
<td>1.50±0.29</td>
<td>0.007</td>
</tr>
<tr>
<td>POD3 (median ± SD)</td>
<td>1.39±0.32</td>
<td>1.23±0.19</td>
<td>1.46±0.34</td>
<td>0.342</td>
</tr>
<tr>
<td>POD7 (median ± SD)</td>
<td>1.13±0.19</td>
<td>1.07±0.12</td>
<td>1.16±0.21</td>
<td>0.018</td>
</tr>
<tr>
<td>Peak value INR, (median ± SD)</td>
<td>1.60±0.54</td>
<td>1.52±0.85</td>
<td>1.63±0.34</td>
<td>0.250</td>
</tr>
<tr>
<td>Length of postoperative hospital stay, (days), mean ±SD</td>
<td>14.57±8.11</td>
<td>16.73±9.50</td>
<td>13.61±7.26</td>
<td>0.026</td>
</tr>
<tr>
<td>Length of ICU stay, (days), mean ±SD</td>
<td>3.66±2.05</td>
<td>3.60±1.95</td>
<td>3.69±2.10</td>
<td>0.990</td>
</tr>
</tbody>
</table>

Abbreviations: ALAT, alanin aminotransferase; ASAT, aspartate aminotransferase; TB, total bilirubin; INR, international normalization ratio; SD, standard deviation, POD 1,3,7, postoperative day 1,3,7; ICU, intensive care unit.

There were no donor deaths among the 157 donors in the study cohort. The rate of no-go hepatectomies was low, with only one donor (1/157, 0.6%) procedure aborted. One or more complications were experienced by 78 donors (49.7%), while an aggregate 199 complications were recorded; twelve donors (7.6%) experienced more than 5 complications. Regardless of graft type, the rate of major complications (grade ≥III) was 5.1% (8/157). The overall donor morbidity and major complication rates did not significantly differ over time, as reported in Table 4. The two most common major complications were bile leakage (n = 10 (6.4%)) and subphrenic access (n = 9 (5.7%)). The comparison of complications after donor hepatectomy between donors from initial and latest period group revealed no significant differences. A longer postoperative length of hospital stay was observed in the group from the initial period of study (16.73±9.50 days vs 13.61±7.26 days, p=0.026). No significant differences in the postoperative length of ICU stay were observed in LDs (p = 0.99).
(Table 3). The rate of complications was 1.33 for LDs in the initial period of study, and 1.23 for the latest period. Post-hepatectomy liver failure was not diagnosed in the LDs included in this study. None of the 112 LDs was readmitted in the hospital within the first three months.

**DISCUSSION**

LDLT has become an alternative lifesaving method that reduces patient waiting time and mortality. Donor safety must be mandatory in LDLT, and all clinicians involved have made every effort to minimize the risk of donor complications. However, in daily clinical practice, donor complications cannot be completely prevented. Lautiero et al. reported a morbidity rate of 33.3% and a major complication rate of 12.6% in an Italian cohort including 220 right lobe donors, 10 left lobe donors, and 15 left lateral segment donors. Adcock et al. reported an overall complication rate of 41% among right lobe donors in a Canadian cohort. The donor complication rate is lower in Asia, however, where LDLT is more widely performed because of a shortage of deceased donors. In a study of five Asian centers, Lo reported an overall complication rate of 15.8% and a reoperation rate among donors of 1.1%. Suh et al. reported major complication rates of 4.6% in South Korea. A right lobe graft was previously suggested as a risk factor for donor complications, but a large-scale study reported comparable outcomes for right lobe and left lobe donations.

In our experience, living RL donation is the preferred choice and probably reflects the confidence and surgical experience gained in hepatobiliary surgery and split-liver transplantation by the institutions actively involved in LDLT. Our study found that one or more complications were experienced by 49.7% donors. The data from our analysis fail to demonstrate a trend toward decreasing overall morbidity or the risk of major complications over time, although there was some decrease in the rate of complications in initial and latest period of study, 1.33 vs 1.23, respectively. Our data showed a midway incidence of major donor complications of 5.1%, in the range of 2-32% reported by another series. In line with another studies, the most common major complications were biliary complications (6.4%). Our study found a lower rate of no-go hepatectomies with only one donor (1/157, 0.6%) procedure aborted. In our experience, three donors had intraoperative complications, but all of
them had a complete recovery. Intraoperative donor complications may be under-reported in the literature, and despite not being graded by the Clavien classification they remain an important issue in LDs, because they may have a negative impact on the immediate and long-term outcomes.

The center experience, including strict donor selection, advances in surgical technique that reduces operative time and prevents blood loss, and post-donation patient care seem to play a crucial role in the improvement of donor outcomes. We performed a comprehensive study on donor safety in LDLT in Romania and Republic of Moldova thanks to a cooperative research agreement initiated by two transplant centers. 157 LD procedures performed in these two centers between 2000-2020 were analyzed, providing data on donor outcomes and donor postoperative complications. A better understanding of the mechanisms affecting donor outcome, and advances in the management of donor postoperative complications should revive the initial enthusiasm surrounding LD, especially in those centers where the use of this option has declined. Transparency in reporting results after LDLT is mandatory and we should continue to strive for zero donor mortality. Our study shows that cohort data provide an important means of investigating the safety in live liver donation.

Our study has several limitations that warrant consideration. First, the prospective cohort data contain information only for period 2015-2020, the period 2000-2015 was analyzed retrospectively. Second, because of the data shortage, we were unable to assess longitudinal changes.

**In conclusion**, donor hepatectomy can be successfully performed with minimal and easily controlled complications. Biliary complications were the most common type of major donor complications among LLDs. Comprehensive donor evaluation, surgical experience and technique, and close postoperative follow-up should allow for better outcomes.

**Author Contributions:**

Conceptualization, A.I.P., V.S.B.; methodology, A.I.P., V.S.B.; software, A.I.P.; investigation, A.I.P., V.S.B.; writing original draft preparation, A.I.P.; writing review and editing, A.V.H., I.P., V.S.B.; visualization, A.I.P.; supervision, V.S.B.; project administration, A.I.P. All the authors have read and agreed with the final version of the article.

**Compliance with Ethics Requirements:**

“The authors declare no conflict of interest regarding this article”.

“The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law.”

This study was approved by the Ethics of Resource Committee of the State University of Medicine and Pharmacy “Nicolae Testemițanu” (approval 33, No 44 from 12.05.2016) and all participants signed an informed consent.

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