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Research Article

D-dimer Level Is Non-Specifically Elevated Post-Living-Related Liver Transplantation in Children

Hadil Samir Darwish*, Nermin Mohamed Adawy, Magdy Anwar Saber, Noha Mohamed Radwan

Department of Pediatric Hepatology, Gastroenterology, and Nutrition, National Liver Institute, Menoufia University, Shebin El-Koom, Egypt

Abstract

Background/Objective: D-dimer, a soluble fibrin degradation product, is used to be a marker of vascular thrombosis. However, it has been reported to be elevated in different pathological conditions other than thrombosis. Moreover, its pattern post-liver transplantation (LT) in children is not known. So, we aimed to report its pattern within the first-month post-LT in children and its level in different early post-LT complications. Methods: It is a retrospective observational cohort study in which 52 children who underwent living-related liver transplantation (LRLT) were included. All the available clinical, imaging, and laboratory data including D-dimer level were collected from the patients' files. Those who developed complications within the first post-LT month were assigned to the complication group (n=41), and others were assigned to the non-complication group (n=11). Results: D-dimer level pre-LT ranged from 0.12-16.41 mg/l, with no significant difference between the complication and non-complication groups. Postoperatively, the D-dimer levels were elevated and did not normalize till the postoperative day (POD) 30. The minimum reported level was 1.2 mg/l on POD0 while the maximum one was 33.12 mg/l on POD12. There were no significant differences between the complication and non-complication groups about the D-dimer level from the pre-LT day till the POD30 ($p>0.05$). The D-dimer level at the onset of the different complications showed no significant difference among the thrombotic, ACR, and the other complication subgroups ($p=0.748$). Moreover, the vascular thrombosis subgroup didn't show a significant difference between the D-dimer level before- and at the onset of thrombosis ($p=0.480$). Conclusion: D-dimer is non-specifically elevated within the 1st-month post-LRLT in children with no clear trend. Moreover, it doesn't normalize till the end of the 1st post-LT month. Being high early postoperatively doesn't necessarily indicate vascular thrombosis or other complications but rather the nature of the transplantation circumstances.

Keywords

Acute Cellular Rejection, Children, D-Dimer, Living-Related Liver Transplantation, Post-Liver Transplantation Complications, Vascular Thrombosis

1. Introduction

D-dimer is a soluble fibrin degradation product that results from the degradation of vascular thrombi through the fibrinolytic mechanism. Since its introduction in laboratory assessments, it has been used to rule out thromboembolism

*Corresponding author: hadilsamirdarwish@liver.menofia.edu.eg (Hadil Samir Darwish)

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when it is negative. However, while its positivity could suggest thromboembolism, other disease possibilities are still there [1, 2]. Thus measuring D-dimer level has been used widely in many thromboembolic situations, e.g., deep vein thrombosis, pulmonary embolism, and disseminated intravascular coagulation. Nevertheless, D-dimer increases in many situations other than thrombotic disorders, e.g., trauma including surgeries, thrombolytic therapy, sepsis, renal diseases, and liver diseases [3].

Some studies reported the relation of D-dimer to the occurrence of vascular thrombosis post-liver transplantation (LT) [4]. However, it is known that there are many changes in the hemostatic system in hepatic patients [5]. These changes require a long time to normalize post-LT. All this raises the concern about using D-dimer to diagnose the occurrence of thrombosis post-LT; among other complications.

The level of D-dimer post-LT in children was not described before. Knowing D-dimer kinetics in pediatric recipients post-LT may help predict early thrombosis, either recurrent or de novo [4, 6]. In the present study, we aimed to report the post-LT D-dimer level in pediatric recipients to understand its early post-operative behavior. Secondly, we aimed to evaluate its diagnostic specificity for early post-LT complications.

2. Methods

2.1. Study Population

It is a retrospective observational cohort study in which all children who underwent living-related liver transplantation (LRLT) from April 2003 to December 2022 at the National Liver Institute (NLI), Menoufia University were recruited. This study was approved by the NLI Research Ethics Committee (NLI IRB 00014014) with an IRB number of 00558/2024 and conformed to the 1975 Declaration of Helsinki and its later amendments. Informed consent was waived due to the retrospective design.

Of the 91 cases transplanted during the study duration, 39 cases were excluded and the remaining 52 cases were included according to the inclusion and exclusion criteria as shown in Figure 1.

2.2. Patients' Data Collection

For all included cases in the study, the available following data were retrieved from the patient files in the liver transplant unit archive:

1. Age at LT
2. Sex
3. Etiological diagnosis
4. Reported complications within the first postoperative month: Defining the complication type was according to the medical reports in the patient file and it was supported by the reported clinical, laboratory, imaging, and pathological data (when done).
5. Laboratory parameters: pre-LT
   1) Liver function tests
   2) Complete blood count
   3) C reactive protein and Procalcitonin
   4) Prothrombin time and international normalized ratio
   5) Partial thromboplastin time
   6) Fibrinogen and fibrin degradation products
6. D-dimer level pre-LT and within the first-month post-LT:
   1) D-dimer levels for each day were registered.
   2) When an am and pm measure of D-dimer of the same day was present, the mean value was calculated for this day.
   3) For comparison of the D-dimer level of different complications, the D-dimer levels were reported at the time of onset of each complication. When the D-dimer level is not available at the time of the complication onset, the case was removed from this comparison.

2.3. Complications and Group Classifications

The studied cases were divided into two groups; the complication group and the non- complication group. The complication group comprised 41 cases while the non-complication group comprised 11 cases.

2.3.1. Complication Group

Any recipient who had any graft-related or extra-graft complication within the 1st post-operative month was allocated to the complication group. The complication group was later on subdivided into either thrombotic- or non-thrombotic-complication subgroup.

2.3.2. Non-Complication Group

Any case that didn't develop any significant graft-related or extra-graft complication within the first post-LT month was allocated to the non-complication group.

2.4. Statistical Analysis

Quantitative variables were expressed as mean ± standard deviation or a median (minimum-maximum) depending on the nature of the data, while qualitative variables were expressed as the number (percentage) of individuals with a condition. For quantitative data, statistical significance was tested by independent samples *t*-test or by the non-parametric Mann-Whitney U test as indicated. The significance of qualitative data was tested with the Chi-square test or Fisher's exact test. Results were considered significant if the *P*-value was < 0.05. Statistical analysis was performed using SPSS, version 22 (SPSS Inc., Chicago, IL, USA).

3. Results

3.1. Demographic Data and Etiological Diagnosis of the Studied Cases

The age of the LRLT recipients of the present study ranged from 1 year to 18 years, with a median of 5.95 years, with no significant difference between the complication and non-complication groups (p=0.494). There was slight male predominance (60%) with no significant sex difference between the studied groups (p=0.760) (Table 1).

The included 52 cases comprised 13 diagnoses. The commonest diagnosis was for post-Kasai etiology (23%), followed by Crigler Najjar syndrome type 1 (17%), and progressive familial intrahepatic cholestasis (15%). Other reported etiologies are shown in Figure 1. There was no statistical significance between the complication and non-complication groups concerning the distribution of the etiological diagnosis (P=0.420, data not shown).

3.2. Laboratory Parameters of the Studied Recipients

The pre-LT laboratory parameters showed significantly higher levels of ALT, AST, GGT, and CRP in the complication group (P<0.05, for all). On the other hand, there was no significant difference between both groups with regard to the other pre-LT laboratory parameters (Table 1).

3.3. Complication Types Within the First Month Post-LT

3.3.1. Reported Complications in the Individual Recipient

Of the included 52 cases, 41 recipients developed complications within the 1st-month post-LT. Twenty-eight recipients developed a single complication while 13 recipients developed more than one complication. The commonest single graft-related complication was acute cellular rejection (ACR) (12; 29.3%) followed by vascular thrombosis (6; 14.6%), while the commonest single extra-graft complication was sepsis and gut leak (2; 4.9%, for each). The other reported single and multiple complications are presented in Table 2.

3.3.2. Frequency of Individual Complications

The frequency of each type of the reported complications revealed that ACR was the most prevalent (16 cases, 27.6%), followed by vascular thrombosis (14 cases, 24.11%), pneumonia (8 cases, 13.8%), then sepsis (3 cases, 5.2%). The frequency of the other reported complications within the first postoperative month is presented in Table 3.

3.4. D-dimer Levels Within the First Month Post-LT

D-dimer level pre-LT ranged from 0.12-16.41 mg/l, with no significant difference between the complication and non-complication groups (p=0.087). Postoperatively within the 1st postoperative month, the D-dimer levels were always elevated and didn't reach the normal level. The levels ranged from a minimum of 1.2 mg/l on POD0 to a maximum of 33.12 mg/l reached on POD12. There were no significant differences between the complication and non-complication groups with regard to the D-dimer level from the pre-LT day till the POD30 (p>0.05, for all) (Table 4).

The median D-dimer level of the complication group through the 1st month post-LT showed a higher trend than those in the non-complication group, despite insignificant statistically (P>0.05) (Table 4 and Figure 2A). On the other hand, the thrombotic complication group didn't show a higher trend of median D-dimer level than the non-thrombotic subgroup through the 30 days post-LT (Figure 2B).

The D-dimer level at the onset of the different complications showed no significant difference among the thrombotic (median 9 mg/l), ACR (median 6.18 mg/l), and the other complication subgroups (median=5.2 mg/l) with a p-value of 0.748 (Figure 2C). Moreover, the vascular thrombosis subgroup didn't show a significant difference (p=0.480) between the D-dimer level before the onset of thrombosis and at the onset of thrombosis (Figure 2D).

4. Discussion

LT is the end solution for many liver diseases in children. The improved outcome of LT in children is dependent on many factors as innovative immunosuppression, skillful surgical techniques, and good pre-and post-operative management [7]. Timely diagnosis and treatment of postoperative complications have a significant impact on the successful outcome [8]. However, many of the post-operative investigations could be misleading if not appropriately understood.

D-dimer level is increased in thrombosis and theoretically is an acceptable marker for post-LT vascular thrombosis. However, the D-dimer levels and behavior post-LT in children are not known, limiting its diagnostic value for post-LT complications, specifically vascular thrombosis. So, in this study, we aimed to describe the post-LT D-dimer levels to understand their kinetics and behavior. To the best of our knowledge, it is the first study that describes the D-dimer level post-LRLT in children.

In the present study, the D-dimer level was elevated post-LT in all studied recipients with a wide range, from a minimum of 1.2 mg/l on POD0 to a maximum of 33.12 mg/l reached on POD12. The D-dimer level didn't normalize till the POD 30 (Table 4 and Figure 2A).

Understanding the kinetics of D-dimer post-LT in children is of utmost importance to avoid any misinterpreted results. In

agreement with our study, Dindo et al [9] found that D-dimer is non-specifically elevated after surgery hampering its usage in predicting postoperative thromboembolism. They found that after retroperitoneal and liver surgery, the D-dimer can peak on day 7 postoperatively to high levels reaching 4000 ng/ml (500-14,400) and normalizing within 38 days (+/-11).

On the other hand, it was found that in superficial surgery not opening the abdominal cavity such as open hernia repairs, the D-dimer peak did not exceed the normal range (300 ng/ml, 100–500) [9].

This elevated D-dimer could be due to an activation of the coagulation/ fibrinolysis systems due to the tissue injuries occurring during this major surgery. Previously, Nguyen et al [10] found that both laparoscopic and open gastric bypass surgeries induce a hypercoagulable state with activation of the coagulation/ fibrinolysis system with increased D-dimer level. Also, recently Sakamoto et al [11] reported increased D-dimer levels following hepatobiliary-pancreatic surgery.

In the present study, the trend of the D-dimer level in those who developed complications was higher than in those who passed the first month post-LT without complications (Figure 2A). Interestingly, there was a high frequency of reported complications within the first post-operative month. The most frequent complications were for ACR (27.6%) followed by vascular thrombosis (24.11%), pneumonia (13.8%), gut leak (5.2%), and 3.45% for each of bile leak, acute kidney injury (AKI), sepsis, bleeding, and convulsions.

Unfortunately, there is a lack of previous studies investigating the D-dimer level post-LT in children and their correlation with post-LT complications. Park et al [12] studied the predictive role of the D-dimer level in AKI in LDLT in adults. The main finding of this study was that a high D-dimer level (>0.5 mg/L) was an independent predictor of postoperative development of AKI. The prevalence of AKI was significantly higher in the high D-dimer group than in the normal D-dimer group. The D-dimer level and the proportion of patients with a high D-dimer level significantly increased with more severe AKI. In addition, patients with a high D-dimer level or AKI had more severe morbidities and higher mortality rates.

Although the mechanism underlying the relationship between D-dimer and AKI is unclear, a high D-dimer level may reflect inflammatory coagulation and fibrinolysis thus contributing to the development of AKI in these critically ill patients. In our study, there was a report of 2 cases with AKI. The D-dimer level of one of them at the time of the development of AKI was 22.35 mg/L.

In the present study, the D-dimer level was reported to be high in different complications post-LT without differentiating levels. Despite the theoretically expected higher levels in those with vascular thrombosis, the trend of the D-dimer level for those who developed thrombosis was not significantly different from those who developed non-thrombotic complications from POD0-POD30 (Figure 2B). At the onset of thrombosis, the median of D-dimer was higher but not significant than the median of both the ACR and other complications at the time of their onset (Figure 2C). Moreover, the D-dimer level at the onset of vascular thrombosis was not significantly higher than the levels before its occurrence (P=0.480) (Figure 2D).

In an adult study, Zhang et al [4] reported that D-dimer level on the first day after liver transplant is related to thrombosis recurrence and is an independent risk factor for postoperative thrombosis recurrence.

The absence of diagnostic specificity of D-dimer level for vascular thrombosis in the present study could be explained by the high D-dimer level in all children post-LT due to the effect of surgery on the activation of the coagulation/ fibrinolytic system. Also, many of the reported complications other than vascular thrombosis in our study could affect increasing the D-dimer level due to the inflammatory process and inflammatory mediators. For example, during infection, the injurious effect of the pathogen on vascular endothelium integrity can activate the coagulation system [13]. Moreover, the immunosuppressives may affect the level of D-dimer through their thrombogenic effects. Tacrolimus–associated thrombotic microangiopathy is an uncommon side effect. This can be attributed to the cytotoxic effect on vascular endothelium [14].

5. Limitation of the study

Several limitations of the present study are to be highlighted. First, the retrospective nature of the study with the possibility of the presence of hidden biases. Second, the absence of operative data to correlate with the post-LT D-dimer level; examples: the duration of the operation with its different phases as cold and worm ischemia time. Third, the relatively small number of the studied cases. Fourth, the one-month duration of the study is another limitation. Studying for a longer time till normalization of the D-dimer will uncover the actual kinetics of the D-dimer post-LT. However, there was an absence of sufficient data to extend the study duration till D-dimer normalization. Fifth, we are not sure that only one assay method was used to measure the D-dimer level through this long duration. Variations could be present between different analytical methods. A prospective well-designed study on a larger sample size with longitudinal follow-up of D-dimer level till normalization will avoid these reported limitations. It also could uncover if, after normalization of the D-dimer, a further elevation could have a diagnostic specificity for different post-LT complications.

6. Conclusion

Within the first month post-LT, the D-dimer level is non-specifically elevated in all the studied LT recipients and doesn't reach the normal level till the POD30. Despite being statistically insignificant, it has a higher trend in those who develop postoperative complications. Moreover, it lacks diagnostic specificity for vascular thrombosis. Further studies of a larger number of recipients till normalization of D-dimer to clarify its dynamics post-LT in children are recommended.

Abbreviations

AIH: Autoimmune Hepatitis
ALF: Acute Liver Failure
CHF: Congenital Hepatic Fibrosis
HCC: Hepatocellular Carcinoma
HCV: Hepatitis C Virus
LT: Liver Transplantation
n: Number
PFIC: Progressive Familial Intrahepatic Cholestasis
ACR: Acute Cellular Rejection
NA: Not Applicable
POD: Post-Operative Day
AKI: Acute Kidney Injury
HAT: Hepatic Artery Thrombosis
HV: Hepatic Vein
PV: Portal Vein
PVT: Portal Vein Thrombosis
ALP: Alkaline Phosphatase
ALT: Alanine Transaminase
AST: Aspartate Transaminase
CRP: C Reactive Protein
dl: Deciliter
FDPs: Fibrin Degradation Products
g: Gram
GGT: γ-Glutamyltransferase
INR: International Normalized Ratio
mg: Milligram
µl: Microliter
PT: Prothrombin Time
PTT: Partial Thromboplastin Time
TLC: Total Leucocyte Count

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Author Contributions

Darwish HS, Adawy NM, Saber MA, Radwan NM involved in the study concept and design; Darwish HS and Radwan NM involved in the recruitment of patients and contributed to data acquisition; Darwish HS performed the statistical analysis and designed the tables and figures; Darwish HS, Adawy NM, Radwan NM performed data interpretation; Darwish HS and Radwan NM wrote the manuscript; all the authors reviewed the manuscript and finally approved it for submission.

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Conflicts of Interest

The authors declare no conflicts of interest.

Appendix

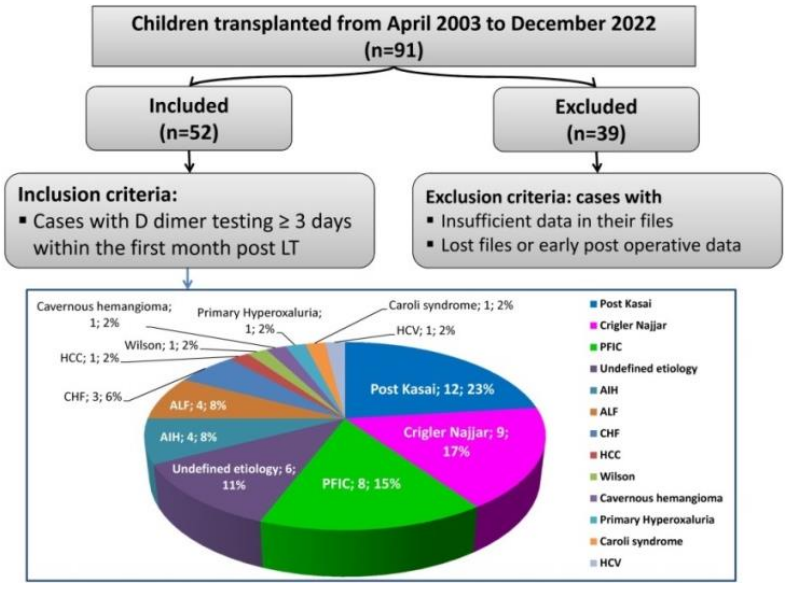

Figure 1. *Flow chart of the included and excluded cases within the study with different etiologies of the included LT recipients.*

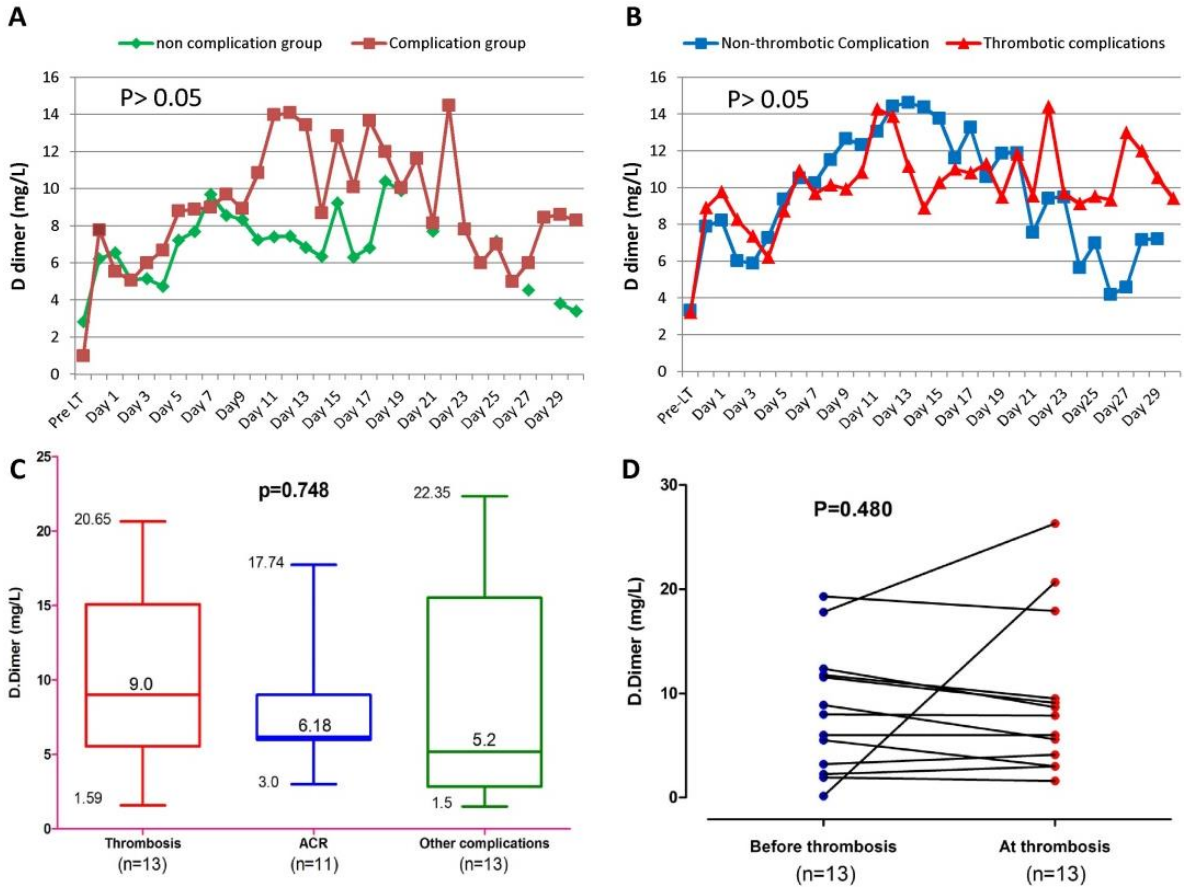

Figure 2. *D-dimer level post-LT.*

A: Line graph of the D-dimer level of both the complication and non-complication groups from the pre-LT to the POD30. B: line graph of the D-dimer level of both the thrombotic and non-thrombotic complication subgroups from the pre-LT to the POD30. C: Box and whiskers graph of the D-dimer level at the onset of the different complications; thrombotic, acute cellular rejection, and other complications. D: line graphs of the D-dimer level pre- and at the onset of the vascular thrombosis of individual cases.

Table 1. *Demographic and laboratory parameters of the studied groups*

Item	Total (n=52)	Complication group (n=41)	Non-complication group (n=11)	*P* value
Age at LT (years)	5.95 (1.0-18)	5.95 (2.0-18)	6.5 (2-16)	0.494
Sex (female)	21 (40%)	17 (41.5%)	4 (36.4%)	0.760
Pre-LT laboratory parameters				
Total bilirubin (mg/dl)	11.4 (0.2-70)	10.9 (0.7-70)	21.6 (0.2-29.8)	0.476
Direct bilirubin (mg/dl)	5.0 (0.04-43.1)	5.8 (0.1-43.1)	1.7 (0.04-21)	0.308
Total proteins (g/dl)	6.37±1.0	6.36±1.1	6.42±0.61	0.874
Albumin (g/dl)	3.37±0.82	3.25±0.8	3.74±0.82	0.085
ALT (U/L)	69 (8.0-659)	78 (8.0-659)	31 (14.0-483)	0.012
AST (U/L)	98 (28-335)	123 (36-301)	43 (28-335)	0.036
ALP (U/L)	374 (21-1452)	393 (21-1452)	254 (78 -837)	0.124
GGT (U/L)	77 (2.0-692)	121 (11-692)	22 (2.0-184)	0.010
INR	1.3 (0.93-9.0)	1.3 (1.0-9.0)	1.27 (0.93-2.7)	0.580
PT (seconds)	14.8 (10.8-60)	14.3 (10.8-60)	17.1 (11-30.8)	0.851

Item	Total (n=52)	Complication group (n=41)	Non-complication group (n=11)	*P* value
PTT (seconds)	40.2 (21.9-166)	40 (22-166)	40.4 (21.9-67)	0.566
Fibrinogen (mg/dl)	262 (30-520)	244 (30-520)	262 (156-342)	0.971
FDPs (mg/L)	17.5 (10-40)	10 (10-40)	40 (10-40)	0.456
Hemoglobin (g/dl)	10.0±1.58	9.88±1.51	10.61±1.84	0.219
TLC ($\times10^3/\mu l$)	5.2 (1.4-20.8)	4.7 (1.4-20.8)	5.2 (4.5-10.9)	0.314
Platelets ($\times10^3/\mu l$)	116 (34-643)	115 (34-643)	182 (55-426)	0.649
CRP (mg/dl)	5.9 (0.1-64)	7.0 (0.2-64)	2.0 (0.1-26.2)	0.045
Procalcitonin (µg/L)	0.19 (0.03-9.3)	0.21 (0.03-9.3)	0.07 (0.05-0.4)	0.356

Table 2. *Reported complications in the individual recipients within the first postoperative month.*

Complication type		Frequency	%
Recipients with single complication (n=28)			
Graft-related	ACR	12	29.3
	Vascular thrombosis	6	14.6
	Bile leak	2	4.9
	HV stenosis	1	2.43
	Sepsis	2	4.9
	Gut leak	2	4.9
Extra-graft	Pneumonia	1	2.43
	Pulmonary embolism	1	2.43
	Pleural effusion with underlying lung collapse	1	2.43
Recipients with multiple complications (n=13)			
Small for size + PVT		1	2.43
Splenic infarcts + pneumonia		1	2.43
Pneumonia + ACR		1	2.43
Pneumonia + convulsions		1	2.43
Vascular thrombosis + AKI		1	2.43
Gut leak + ACR		1	2.43
PV stenosis + chylous ascites		1	2.43
Heart failure + pneumonia		1	2.43
Bleeding* + pneumonia		1	2.43
Bleeding + HAT + radial artery thrombosis		1	2.43
Pneumonia + PVT + ACR		1	2.43
HAT + PVT + AKI		1	2.43
Pneumonia + ACR + HAT + convulsions		1	2.43
Total		41	100 %

Bleeding*: is intraperitoneal hemorrhage

Table 3. *Frequency of the individual complication within the first postoperative month.*

Complication	Frequency	%
Graft- related complications		
Acute cellular rejection	16	27.6
Vascular thrombosis	14	24.11
Bile leak	2	3.45
Hepatic vein stenosis	1	1.72
Small for size	1	1.72
Portal vein stenosis	1	1.72
Extra-graft complications		
Pneumonia	8	13.8
Gut leak	3	5.2
Acute kidney injury	2	3.45
Sepsis	2	3.45
Bleeding	2	3.45
Convulsions	2	3.45
Heart failure	1	1.72
Chylous ascites	1	1.72
Pleural effusion with underlying lung collapse	1	1.72
Pulmonary embolism	1	1.72
Total frequency of individual complications	58	100%

Table 4. *D-dimer levels of the studied LT-recipients from pre-LT day to postoperative day 30.*

D-dimer level (mg/L)	Total (N= 52)	Complication group (N=41)	Non- complication group (N=11)	P value
Pre LT	1.0 (0.12-16.41)	1.0 (0.12-16.41)	2.85 (0.45-6.0)	0.087
POD 0	7.7 (1.2 -32.0)	7.80 (1.20 -32.0)	6.24 (3.0 -19.69)	0.987
POD 1	5.62 (1.5 -32.0)	5.56 (1.50 -32.0)	6.55 (2.0 -8.82)	0.573
POD 2	5.07 (1.5-22.35)	5.07 (1.50 -22.35)	5.10 (2.0-14.25)	0.793
POD 3	5.9 (1.38 -25.37)	6.0 (1.38 -25.37)	5.15 (2.06 -9.2)	0.704
POD 4	6.0 (1.5 -17.40)	6.69 (1.5 – 15.0)	4.75 (2.0 -17.40)	0.298
POD 5	8.8 (1.5 – 24.0)	8.8 (1.5 -24.0)	7.24 (3.0 – 21.2)	0.747
POD 6	8.38 (2.25-21.25)	8.9 (2.25-21.25)	7.7 (4.8-16.25)	0.881
POD 7	9.0 (2.0-24.0)	9.0 (2.0-24.0)	9.7 (5.83-15.93)	0.762
POD 8	9.07 (2.4-24.75)	9.7 (2.4-24.75)	8.57 (6.85-15.59)	0.655
POD 9	8.9 (2.4-24.25)	8.93 (2.4-24.25)	8.36 (7.02-14.37)	0.727
POD 10	9.7 (3.0-23.7)	10.86 (3.0-23.70)	7.25 (6.27-13.0)	0.378
POD 11	12.4 (3.0-22.83)	13.99 (3.0-22.83)	7.41 (6.0-12.31)	0.065
POD 12	12.15 (3.0-33.12)	14.1 (3.0-33.12)	7.45 (4.86-14.55)	0.211

D-dimer level (mg/L)	Total (N= 52)	Complication group (N=41)	Non- complication group (N=11)	P value
POD 13	12.11 (3.0-22.54)	13.44 (3.0-22.54)	6.85 (5.40-14.60)	0.070
POD 14	8.44 (3.0-32.0)	8.69 (3.0-32.0)	6.35 (4.47-14.80)	0.233
POD 15	12.85 (3.0-21.5)	12.85 (3.0-21.5)	9.24 (3.83-14.64)	0.618
POD 16	8.08 (3.0-22.46)	10.1 (3.0-22.46)	6.32 (3.8-8.0)	0.170
POD 17	12.60 (1.5-21.06)	13.68 (1.5-21.06)	6.83	0.769
POD 18	12.0 (1.5-18.30)	12.0 (1.5-18.30)	10.4 (7.12-13.67)	1.000
POD 19	9.91 (1.5-21.0)	10.05 (1.5-21.0)	9.91 (7.42-12.40)	1.000
POD 20	11.69 (1.5-22.5)	11.63 (1.5-22.5)	-------	NA
POD 21	8.1 (3.0-21.0)	8.16 (3.0-21.0)	7.72	0.833
POD 22	14.5 (3.0-19.5)	14.5 (3.0-19.5)	-------	NA
POD 23	7.82 (5.0-16.32)	7.82 (5.0-16.32)	-------	NA
POD 24	6.0 (3.82-13.90)	6.0 (3.82-13.9)	-------	NA
POD 25	7.18 (5.0-14.07)	7.01 (5.00-14.07)	7.18	1.000
POD 26	5.0 (3.68-13.69)	5.0 (3.68-13.69)	-------	NA
POD 27	5.9 (2.7-20.0)	6.0 (2.7-20.0)	4.55 (3.20-5.9)	0.571
POD 28	8.47 (5.88-12.0)	8.47 (5.88-12.0)	-------	NA
POD 29	8.61 (3.82-12.11)	8.61 (5.84-12.11)	3.82	0.400
POD 30	8.15 (3.4-12.0)	8.30 (8.0-12.0)	3.4	0.500

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