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The impact of donor liver graft quality on postoperative outcome in liver transplant recipients. A single centre experience

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Abstract

Introduction. The Donor Risk Index (DRI) has become a universal score for organ allocation in liver transplantation (LT) worldwide. The aim of this study was to evaluate the impact of liver graft quality measured by DRI, CIT, WIT and donor age on intraoperative hemodynamics (reperfusion syndrome) and early postoperative outcome, defined as initial graft poor function (within 3 days of LT), of deceased donor liver transplant (DDLT) recipients. Secondary end-points were the assessment of the impact of graft quality on the intraoperative and postoperative day 1 hemostasis (evaluated using ROTEM assay). **Methods.** We retrospectively analyzed 135 patients who underwent deceased-donor LT between January 2013 and December 2014. Patient demographic data (age, sex, cause of End-Stage Liver Disease), preoperative paraclinical data (total bilirubin, creatinine, serum sodium), severity of liver disease scores (Model for End-Stage Liver Disease – MELD and MELD-sodium), intraoperative blood loss and blood products transfusion, incidence of post reperfusion syndrome, postoperative biochemical data (including total bilirubin, hepatic transaminases, lactate levels) and outcome (initial graft poor function diagnosis) were noted. Donor characteristics including DRI, CIT, WIT and donor age were noted. Coagulation was assessed by rotational thromboelastometry (ROTEM) after reperfusion of the graft and on postoperative day 1 in order to determine the effects of liver graft quality on hemostasis. **Results.** Donor age has significantly correlated with decreased derived ROTEM parameters time to the maximum velocity of clot formation – MaxVt ($p = 0.000$), area under the curve (AUC) ($p = 0.008$) and maximum clot elasticity (MCE) ($p = 0.018$) although no difference in transfusion requirements has been observed. A longer CIT was associated with an increase in AST and ALT observed during the early postoperative period: day 1 ALT ($p = 0.032$) and AST ($p = 0.008$), day 2 ALT ($p = 0.001$) and AST ($p = 0.001$) and day 3 AST ($p = 0.010$) and ALT ($p = 0.001$). Higher DRI correlated with higher bilirubin levels measured on postoperative day 1 ($p = 0.027$) and 2 ($p = 0.001$). Patients who developed initial graft poor function received liver grafts from older donors ($p = 0.05$) with a higher DRI ($p = 0.002$). **Conclusion.** Our results suggest a significant impact of donor age and DRI on perioperative coagulation kinetics that may be a result of initial graft poor function. Although CIT and DRI correlated with a more severe cholestasis and hepatocitolysis during the early postoperative period these seems to be short-lived.

Keywords: liver transplantation, liver graft, cirrhotic coagulopathy, outcome

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Introduction

Orthotopic liver transplantation (OLT) has become the treatment of choice for patients with End-Stage Liver Disease (ESLD) and Acute Liver Failure, since its first success in 1967 [1].

The relative low number of organ donors and the gap between organ demand and supply has new strategies to increase the donor pool. Marginal grafts have been used in order to increase number of transplanted organs and consequently reduce mortality on waiting list [2]. This made clinicians aware of the impact of donor organ quality on survival of the recipient as well as on graft survival after liver transplantation (LT) [3].

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Considering all these, numerous scores have been introduced to identify and predict recipient outcome based on donor criteria. The Donor Risk Index (DRI) was introduced by Feng et al. to predict the 3 year graft-survival after LT [4]. The most important donor characteristics that can influence the recipient's prognosis are: age, prolonged ischemia time, hypotension, inotropic support, gender mismatch, non heart-beating donors and liver steatosis [5, 6]. Due to the differences in national or institutional definition of marginal donors and different criteria for allocation of marginal grafts these studies have found conflicting results on risk factors for a poor outcome after liver transplantation.

The aim of this study was to evaluate the impact of liver graft quality measured by DRI, CIT, WIT and donor age on intraoperative hemodynamics (reperfusion syndrome) and early postoperative outcome, defined as initial graft poor function (within 3 days of LT), of deceased donor liver transplant (DDLT) recipients. Secondary end-points were the assessment of the impact of graft quality on the intraoperative and postoperative day 1 hemostasis (evaluated using ROTEM assay).

Patients and method

After obtaining approval of the Ethical Committee of the Fundeni Clinical Institute (46/2013 chairman Prof Dr M. Voiculescu), we retrospectively analyzed 135 DDLT recipients who underwent LT at Fundeni Clinical Institute between January 2013 and December 2014.

Data collection and definition

Preoperative data collected from patients' medical files included: age, sex, etiology of liver disease, MELD and MELD-sodium scores, platelet count, serum bilirubin, serum creatinine, International Normalized Ratio (INR) and fibrinogen levels. MELD and MELD-sodium scores were calculated based on these data.

Intraoperative recorded data were: duration of surgery, blood loss and blood products replacement, tranexamic acid and fibrinogen concentrate administration, duration of anhepatic phase, post reperfusion syndrome (PRS), mean blood pressure and vasopressor requirements, intraoperative lactate levels – 15 minutes into the neohepatic phase and at the end of surgery. PRS was defined as a decrease in mean arterial blood pressure of at least 30% than the previous value during the first 5 minutes after the unclamping of the inferior vena cava that lasted for at least 1 minute.

Postoperative laboratory results (hepatic transaminases: ALT – alanine aminotransferase and AST – aspartate aminotransferase, serum bilirubin and lactate levels, INR, platelet count and fibrinogen levels) were recorded daily for the first 5 postoperative days.

ROTEM assay

Rotational thromboelastometry (ROTEM) was performed 15 minutes into the neohepatic phase and 24 hours after liver transplantation. Four standard ROTEM tests were performed for each of the two time points: ExTEM (Extrinsec activated thromboelastometry), InTEM (intrinsec activated thromboelastometry), FibTEM (fibrinogen thromboelastometry) and ApTEM (Aprotinine tromboelastometry). Both standard ROTEM parameters (clotting time – CT, clot formation time – CFT, maximum clot firmness – MCF, maximum lysis – ML) and derived ROTEM parameters (thrombin potential index – TPI, maximum velocity of clot formation – MaxV, time to MaxV – MaxVt, area under the curve – AUC and maximum clot elasticity – MCE) were recorded. Hyperfibrinolysis was defined as ExTEM ML above 15% and ApTEM ML below 15%. Correction of hyperfibrinolysis with tranexamic acid was performed based on ROTEM assay and evidence of diffuse bleeding in the surgical field. Fibrinogen concentrate was administered in order to maintain a FibTEM MCF above 9 mm.

Outcome analysis

The presence or absence of initial graft poor function (IGPF) for each patient and PostAnaesthesia Care Unit length of stay (PACU LoS) were also noted. IGPF was defined in accordance to Nanashima et al. [7]: serum aminotransferase > 1500 U/l on two consecutive measurements within 72 h after LT.

Donor data

Donor data collected consisted of: age, sex, cause of brain stem death, height, weight, race, organ allocation, CIT and WIT. Due to the variance of donor age the 75 percentile was calculated and the donors divided into 2 groups: those that had the age equal and above 60 years (the 75th percentile) and those that had the age below 60 years (the 75th percentile).

DRI was electronically calculated by the organ donation team based on the formula provided by Feng S et al. [7]. Because the Fundeni Clinical Institute is a single nation center in liver transplantation, all graft allocations were considered national. Due to the fact that race, cause of cerebral death and organ allocation showed no or minimal variance we also analyzed the effect of age, CIT and WIT on postoperative outcome and hemostasis.

Anaesthetic management

All patients underwent LT under general anaesthesia. Induction was obtained with propofol (1-2 mg/kg), fentanyl (1-2 μg/kg) and succinylcholine (1-1.5 mg/kg). Neuromuscular blockade was obtained using atracurium with a loading dose (0.5 mg/kg) followed by boluses (0.1-0.2 mg/kg) at 20-45 minutes intervals or according to the attending anaesthesiologist

decision. Maintenance of anaesthesia was achieved using sevoflurane (titred to a MAC of 0.9-1.2) and fentanyl administered in intermittent boluses according to the attending anaesthesiologist decision. Intermittent positive pressure ventilation was applied. Standard intraoperative monitoring consisted of: continuous electrocardiogram, peripheral oxygen saturation, end-tidal carbon dioxide, invasive radial arterial blood pressure measurement, diuresis, central venous pressure and core temperature. Invasive hemodynamic parameters were monitored with pulse contour analysis using PICCO Plus®monitor (Pulsion Medical Systems, Munich, Germany) and a femoral line in all patients. Vasopressor support (noradrenaline) was titred in order to maintain a mean arterial pressure of $\geq$ 60 mmHg.

Blood management. Packed red blood cells were administered in order to maintain a hemoglobin level above 8 g/dL, fresh frozen plasma was administered in order to correct global factor deficiency as demonstrated by ROTEM assay, fibrinogen concentrate was administered in order to maintain a fibrinogen level above 100-120 mg/dL or a FibTEM MCF above 8 mm, platelets were transfused in order to maintain a platelet level above 25000/μL, tranexamic acid was administered in order to correct early hyperfibrinolysis as demonstrated by ROTEM assay (ExTEM ML above 15%) and signs of diffuse bleeding. No protamine was administered intraoperatively.

At the end of surgery patients were admitted to the PACU. Fast track and discharge to the surgical ward was applied in accordance to our local protocol [8].

Statistical analysis

Data are presented as mean ± standard deviation of the mean, median (min, max) otherwise percentage. Data distribution was examined in order to insure the proper statistical examination. Categorical variables (sex, co-morbidities, presence or absence of postreperfusion syndrome and presence or absence of IGPF) were analyzed with Chi-square test and quantitative data were analyzed with independent samples t-test. Mann-Whitney test was used when the analyzed data did not follow a normal distribution (DRI, CIT, WIT, donor age, recipients bilirubin, INR, sodium, creatinine, ExTEM CT, ExTEM CFT, EXTEM MCF, ExTEM ML, InTEM CT, InTEM CFT, InTEM MCF, FibTEM MCF, ApTEM CT, ApTEM ML, ExTEM TPI, InTEM TPI, MaxV, MaxVt, AUC, MCE, vasopressor requirements, blood loss, fresh frozen plasma and packed red blood cells transfusion, intraoperative and postoperative lactate levels, postoperative bilirubin, ALT, AST, INR, PACU LoS). For multivariate analysis of data considered significant in univariate analysis a binary logistic regression was used. All p-values are two-tailed. Statistical significance was considered at a p-value < 0.05. Statistical analysis was performed using SPSS (v19.0, IBM, Armonk, NY).

Results

Recipients' data

A total of 135 patients who underwent liver transplantation were included in this retrospective study. LT recipient characteristics are presented in Table 1 and intraoperative data are presented in Table 2.

Table 1. LT recipient characteristics

Recipient characteristic	Value
Age (years)	50.0 ± 13.1
Sex (male)	61.5% (n = 83)
Etiology	
HVB	34.8% (n = 47)
HVC	28.2% (n = 38)
Alcoholic	14.8% (n = 20)
Other	22.2% (n = 30)
Co-morbidities	
IHD	7.5% (n = 10)
DM	12.6% (n = 17)
AHT	12.6% (n = 17)
Platelet count (elements/μL)	74000 (12 000-1 038 000)
INR	1.5 (0.87-3.97)
Fibrinogen (mg/dL)	165 (122-592)
Total bilirubin (mg/dL)	2.6 (0.2-39.9)
Creatinine (mg/dL)	0.87 (0.2-4.07)
Sodium (mmol/L)	133 ± 12.1
MELD score	15 (7-35)
MELD-sodium score	19.5 (7-35)

Data are expressed as mean ± standard deviation, median (minimum, maximum) or percentage (number of patients)
HBV – hepatitis B virus, HCV – hepatitis C virus, IHD – ischemic heart disease, DM – diabetes mellitus, AHT – arterial hypertension, INR – international normalized ratio, MELD – Model for End-Stage Liver Disease

Table 2. Intraoperative variables during liver transplantation

Variable	Value
Blood loss (mL)	3250 (100-23 000)
PRBc (units)	4 (0-30)
FFP (units)	9 (0-45)
Duration of anhepatic phase (min)	46.8 ± 18.7
Lactate neohepatic (mmol/L)	4.29 ± 1.65
Lactate end of surgery (mmol/L)	2.8 (0.6-9.0)
Mean arterial pressure (mmHg)	73.3 ± 12.4
Maximum vasopressor support (μg/kg/min)	0.61 (0-6)

Data are expressed as mean± standard deviation, median (minimum, maximum)
PRBc – packed red blood cells, FFP – fresh frozen plasma

During surgery fresh frozen plasma (FFP) was transfused in 85.2% of patients (n = 115) and packed red blood cells (PRBc) in 83.0% of patients (n = 112). The incidence of PRS was 58.5% (n = 79) and the

incidence of hyperfibrinolysis diagnosed with ROTEM was 17.2% (n = 23) after reperfusion of the graft and tranexamic acid was administered in 17 patients (12.6%). Fibrinogen concentrate was administered in 45 patients (33.3%) with a median dose of 2 g (1-6). Vassopressor support was applied in 133 patients (98.5%) with a median dose of 0.61 μg/kg/min (0.1-6). ROTEM parameters recorded 15 minutes after reperfusion of the graft are presented in Table 3. The median length of PACU LoS was 6 days (range 3-30). IGPF was diagnosed in 26.6% (n = 35) patients. Post-operative laboratory results are presented in Table 4 and ROTEM parameters evaluated in the first post-operative day are presented in Table 3. Hyperfibrinolysis was detected on ROTEM assay in 4 patients (2.96%).

Donor data

The mean donor's age was 44.2 ± 14.94 (Fig. 1). Donor age > 60 was registered in 17 % of donors (n = 23). All donor characteristics are presented in Table 5.

Donor age:

Donor age above 60 significantly correlated with decreased intraoperative coagulation kinetics as

Table 3. ROTEM parameters 15 minutes after reperfusion of the graft and on 1st postoperative day

ROTEM parameter	15 minutes after graft reperfusion	1st postoperative day
ExTEM CT (s)	64.5 (29-227)	66 (33-1075)
ExTEM CFT (s)	241.5 (91-3000)	294 (105-4000)
ExTEM MCF (mm)	42 (7-62)	40 (7-59)
ExTEM ML (%)	4.5 (0-100)	6 (0-100)
InTEM CT (s)	224 (141-3000)	184 (87-3515)
InTEM CFT (s)	210.5 (67-3000)	229 (79-2000)
InTEM MCF (mm)	41.5 (2-63)	41 (13-60)
FibTEM MCF (mm)	9 (3-27)	10 (3-60)
ApTEM CT (s)	60 (41-156)	61 (41-908)
ApTEM ML (%)	4 (0-14)	4 (0-20)
ExTEM TPI	9.5 (2-54)	8 (1-42)
InTEM TPI	10 (2-75)	8.5 (1-46)
MaxV	9 (3-38)	11 (2-31)
MaxVt	68 (44-365)	70.5 (21-1690)
AUC	4272 (293-6182)	3861 (273-5922)
MCE	74 (8-161)	66 (16-146)

Data are expressed as median (minimum, maximum)
ExTEM (extrinsec activated thromboelastometry), InTEM (intrinsec activated thromboelastometry), FibTEM (fibrinogen thromboelastometry), ApTEM (aprotinine tromboelastometry), clotting time – CT, clot formation time – CFT, maximum clot firmness – MCF, maximum lysis – ML, thrombin potential index – TPI, maximum velocity of clot formation – MaxV, time to MaxV – MaxVt, area under the curve – AUC, maximum clot elasticity – MCE

Table 4. Daily postoperative paraclinical results registered in the LT recipients

	POD 1	POD 2	POD 3	POD 4	POD 5
ALT (U/L)	355 (27-2321)	248 (22-9678)	205 (19-3797)	178 (21-1342)	160 (21-648)
AST (U/L)	380 (60-7215)	174 (36-16119)	108 (16-3301)	85 (16-506)	61 (13-257)
Bil (mg/dL)	2.9 (0.3-26.0)	1.9 (0.3-16.4)	2.0 (0.2-22.3)	2.3 (0.3-28.8)	3 (0.2-18.0)
Lactate (mmol/L)	1.3 (0.4-5.5)	1.1 (0.4-12.4)	0.93 (0.3-3.1)	0.9 (0.3-4.4)	0.95 (0.4-3.3)
Platelet (/μL)	48000 (15000-581000)	40000 (8000-417000)	37000 (10000-424000)	41000 (13000-416000)	42000 (13000-259000)
Fibrinogen (mg/dL)	224 ± 80	257 ± 96	249 ± 104	241 ± 111	236 ± 107
INR	1.41 (0.98-3.52)	1.19 (0.94-3.02)	1.2 (0.83-3.38)	1.2 (0.97-2.59)	1.2 (0.99-2.34)

Data are expressed as mean ± standard deviation, median (minimum, maximum)
POD – postoperative day, ALT – alanine aminotransferase, AST – aspartate aminotransferase, Bil – total serum bilirubin, INR – international normalized ratio

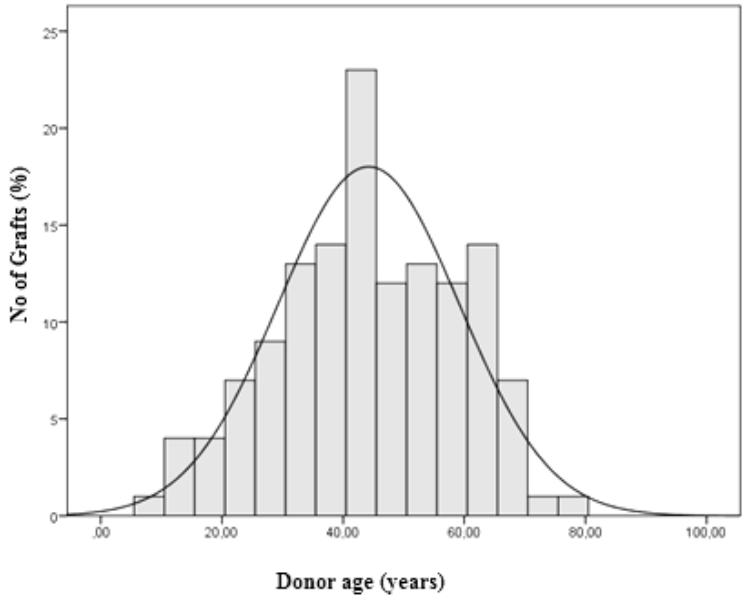

Fig. 1. Age distribution of liver graft donors

Table 5. Donor characteristics

Age (years)	44.2 ± 14.94
Cause of death	
Trauma	34.8% (n = 47)
Anoxia	2.3% (n = 3)
CVA	62.9% (n = 85)
Race	
White	100% (n = 135)
Donation after cardiac death	
No	100% (n = 135)
Partial/Split Liver	
No	100% (n = 135)
Height (cm)	168 (145-189)
Weight (kg)	82 (38-132)
Organ location	
National	100% (n = 135)
CIT (s)	290 ± 99.4
WIT (s)	30 (16-168)
DRI	1.55 ± 0.38

Data are expressed as mean ± standard deviation, median (minimum, maximum) or percentage (number of patients)
CVA – cerebrovascular accident, CIT – cold ischemic time, WIT – warm ischemic time, DRI – donor risk index

demonstrated by derived ROTEM parameters recorded 15 minutes after reperfusion of the graft: a significantly decreased MaxVt (p = 0.000), AUC (p = 0.008) and MCE (p = 0.018). No correlations were found between donor age and standard ROTEM parameters or standard coagulation tests (INR, platelets, fibrinogen). No differences in blood loss or transfusion were observed between patients receiving liver grafts from donors under 60 years and those receiving liver grafts from donors above 60 years. Data are presented in Table 6.

Cold Ischemic Time and Worm Ischemic Time:

The duration of CIT strongly correlated with the values of hepatic transaminases AST and ALT observed during the early postoperative period: day 1 ALT (p = 0.032) and AST (p = 0.008), day 2 ALT (p = 0.001) and AST (p = 0.001) and day 3 AST (p = 0.010) and ALT (p = 0.001).

We did not find any statistically significant correlations between WIT and intra- or postoperative variables.

Table 6. Differences in clot properties blood loss and transfusion observed between recipients of liver grafts from donors aged ≤ 60 years and > 60 years

Parameter	Donor age ≤ 60 years	Donor age> 60 years	P value
MaxVt (sec)	56.9 ± 8.3	122.6 ± 84.8	0.000
AUC	4732 ± 819	3740 ± 1268	0.008
MCE	95.2 ± 29.4	67.0 ± 28.2	0.018
Blood loss (L)	3 (0.1-23)	4 (0.5-18)	0.425
PRBc (U)	4 (0-30)	4 (0-16)	0.911
FFP (U)	9 (0-45)	12 (0-29)	0.070

Data are expressed as mean± standard deviation or median (minimum, maximum)
MaxVt – time to maximum velocity of clot formation, AUC – area under the curve, MCE – maximum clot elasticity, PRBc – Packed Red Blood cells, FFP – Fresh Frozen Plasma

Donor Risk Index:

Graft quality assessed by DRI strongly correlated with decreased coagulation kinetics after reperfusion of the liver graft: MaxV (p = 0.008), MaxVt (p = 0.001), InTEM TPI (p = 0.003), ExTEM TPI (p = 0.001) and MCE (p = 0.013) and increased serum bilirubin on postoperative day 1 (p = 0.027) and post-operative day 2 (p = 0.001).

Outcome and Initial Graft Poor Function:

The diagnosis of IGPF correlated with DRI and donor age (Table 7).

Table 7. Liver graft characteristics and intraoperative lactate levels associated with IGPF in liver transplantation

Donor characteristics	IGPF	No IGPF	P value
Donor age (years)	45.5 ± 14.6	39.8 ± 14.6	0.050
CIT (min)	251 ± 109	272 ± 88	0.323
WIT (min)	36 ± 18	35 ± 23	0.873
DRI	1.6 ± 0.3	1.4 ± 0.2	0.002
Lactate after reperfusion (μmol/L)	3.9 ± 1.39	5.07 ± 2.03	0.002
Lactate end of surgery (μmol/L)	2.64 ± 1.48	3.96 ± 1.76	0.001

Data are expressed as mean ± standard deviation
CIT – cold ischemia time, WIT – warm ischemia time, DRI – donor risk index, IGPF – initial graft poor function

Both lactate levels 15 minutes after reperfusion of the graft (p = 0.002) and at the end of surgery (p = 0.001) were strong predictors for IGPF. CIT and WIT were not. We did not observe any correlations between graft characteristics and lactate level at the end of surgery and only WIT was associated with an increase of lactate 15 minutes after reperfusion (p = 0.005).

Discussion

The main results of our study demonstrate that both high donor age and high DRI have a significant impact on coagulation kinetics both after reperfusion of the graft and on the postoperative day 1 in terms of decreased coagulation kinetics. However, these hemostatic disorders were not associated with increased blood loss and blood products replacement. DRI also strongly correlated with the severity of cholestasis on postoperative day 1 and 2. A longer CIT was associated with an increase in ALT and AST levels during the first three postoperative days. Patients who developed IGPF received a liver graft from an older donor with a higher DRI and although they initially had lower lactate levels after reperfusion of the graft, they showed higher levels of lactate at the end of surgery.

The donor pool in Romania has significantly increased during the last three years in Romania due to the numerous campaigns developed by mass media: „Există viață după moarte!" (There is life after death, after all!), „Donează şi salvează!" (Donate and save lives!) [9]. Secondary to this our donor pool is now characterized by older donors and a higher DRI but these data are similar to those reported by countries with long-standing transplant programs [10, 11]. Matching recipients to liver grafts remains an important and still under debate topic for the Romanian transplant program due to the fact that other possibilities for investigating the liver graft, such as graft steatosis known to be associated with a poorer outcome [12], are scarce.

The drive to use all donor organs available has a major impact on the quality of graft and patient outcome. It is the result of an increasing number of patients on the waiting lists. This is the reason for which every possible deceased donor is thoroughly evaluated by organ procurement associations and transplant physicians. A variety of algorithms have been implemented in order to assess the risk of graft failure after liver transplantation [13] in an attempt to better match grafts and recipients. One of these scores – the donor risk index [4], used in our study, is being extensively used by centers worldwide and incorporates variables regarding the physical status of the patient, the cause of cerebral death, organ allocation and cold ischemic time.

In 2013, 4100 patients are estimated to have died while officially being placed on the waiting lists in 28 states of the European Union (EU). Over a 10 year period, from 2004 to 2013, organ transplants from deceased and living donors have increased significantly in the EU [14]. This happened due to a substantial growth in organ donation. According to these data there was an increase of 18% in deceased donation and an 86% increase in living donation, with a total increase in donations of 33%.

In Romania, ever since the first successful liver transplantation in the year 2000, the number of liver transplants has increased gradually. An overwhelming increase in donors and transplants have taken place in the last 2 years, with a peak of 122 liver transplants in 2013, which represented an almost two-fold increase compared to year 2012 with 75 transplants [9]. However, our results are based only from data collected between January 2013 and December 2014.

A world-wide practice to increase the donor pool in order to cope with the increasing number of patients requiring a LT is the usage of marginal donor grafts. Orman et al. [13] published a study where they analyzed the impact of donor organs by the year 2030 considering the actual trend. They found that the use

will fall from 78% to 44% by 2030, resulting in 2230 fewer LTs. Only the ex-vivo perfusion techniques that would increase marginal donors might settle the number of LT. Physicians will be compelled to use marginal donors and cope with the eventual worse outcomes in order to maintain the number of liver transplants as it is today.

Romero et al. [15] showed that the sexagenarian and septuagenarian donors have demonstrated similar results in comparison to the use of younger donors. Our data are in agreement and we did not find any effects in terms of early postoperative outcome (PACU LoS) but our study was not powered for this result.

The effects of donor age and DRI on early postoperative graft function observed in our study may be short-lived and limited to the first few postoperative days. The same results were observed by both Chapman et al. [16] and Schrem et al. [17].

Hemostasis assessment of liver transplant recipients may prove to be a more reliable way to assess graft function during early postoperative period. Our data suggest that derived ROTEM parameters can better describe the decrease in coagulation kinetics and may offer an earlier diagnosis of impaired graft function compared with the existing criteria we use that allow the diagnosis to be made after several days [7]. Our results have showed the detrimental effect of both patient age and DRI on ROTEM parameters but the current medical literature lacks similar studies to which we could compare our data. Most centers use INR, fibrinogen, bilirubin or other paraclinical markers for postoperative assessment and ROTEM only when there is significant bleed that cannot be explained.

The limitations of our study are due to the relative small sample size and the fact that liver transplantation in Romania is mainly a single center experience. Because our results are presented from an anaesthesiologist point of view we focused mainly on outcome in the early postoperative period. In doing so we intentionally disregarded medium and long term outcome. A subsequent study investigating the effects of one-year graft and recipient survival is required.

Although we cannot change or improve many of the donor parameters analyzed, cold ischemic time was associated with a poorer outcome. A better timing or opening of other LT centers in order to shorten CIT may have beneficial results for Romania.

In **conclusion**, we observed that old donors and those with a high DRI have the most significant impact on coagulation kinetics. A more severe cholestasis was observed in patients with higher DRI and a longer CIT was associated with an increase in ALT and AST levels during the first three postoperative days. Patients who are prone to developing IGPF are those receiving a liver graft from an older donor with a higher DRI and the diagnosis can be confirmed earlier with the aid of derived ROTEM parameters.

Conflict of interest

Nothing to declare

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Impactul calității grefei hepatice asupra evoluției postoperatorii la pacienții transplantați hepatic. Experiență unicentrică

Rezumat

Introducere. Indexul de risc al donatorului (DRI, Donor Risk Index) a devenit principalul scor utilizat la nivel mondial în alocarea grefelor hepatice. Scopul principal al studiului a fost de a evalua influența calității grefei hepatice măsurată prin DRI, TIR (timpul de ischemie rece), TIC (timpul de ischemie caldă), vârsta donatorului asupra hemodinamicii intraoperatorii (sindromul de reperfuzie) şi rezultatele precoce postoperatorii, definite ca proastă funcționalitate primară a grefei (în primele 3 zile de la transplantul hepatic) la pacienții primitori de transplant hepatic de la donatori decedați. Scopul secundar a fost de a aprecia impactul calității grefei asupra hemostazei intraoperatorii şi din ziua 1 postoperator (evaluare ROTEM).

Metodă. Au fost analizate retrospectiv datele obținute de la 135 de pacienți, care au fost supuşi transplantului hepatic de la donator decedat în perioada ianuarie 2013 – decembrie 2014. Au fost luate în calcul următoarele: date demografice (vârstă, sex, cauza patologiei hepatice terminale), date paraclinice preoperatorii (bilirubină totală, creatinină, sodiu seric), scorurile severității patologiei hepatice (Model for End-Stage Liver Disease – MELD, MEDL-sodium), hemoragia intraoperatorie şi transfuziile de produse sangvine, incidența sindromului de reperfuzie, date biochimice postoperatorii (inclusiv bilirubina totală, transaminaze hepatice, niveluri de lactat) şi rezultate (diagnosticul precoce de nefuncționalitate a grefei). Caracteristicile donatorilor au fost notate, inclusiv DRI, TIR, TIC. Coagularea a fost apreciată prin tromboelastometrie rotațională (ROTEM) după reperfuzia grefei şi în ziua 1 postoperator, cu scopul de a determina efectele calității grefei hepatice asupra hemostazei.

Rezultate. Vârsta donatorului s-a corelat semnificativ cu parametrii scăzuți derivați ROTEM: timpul de velocitate maximă de formare a trombului – MaxVt (p = 0,000), aria sub curbă – AUC (p = 0,008) şi elasticitatea maximă a cheagului – MCE (p = 0,018), deşi nu s-au observat diferențe semnificative statistic privind necesitatea de transfuzie. Durata TIR a fost direct proporțională cu nivelurile ALAT şi ASAT din perioada postoperatorie precoce: în ziua 1 ALAT (p = 0,032) şi ASAT (p = 0,008), în ziua 2 ALAT (p = 0,001) şi ASAT (p = 0,001), în ziua 3 ALAT (p = 0,001) şi ASAT (p = 0,010). Nivelurile înalte de DRI s-au corelat cu niveluri înalte de bilirubină cuantificate în ziua 1 postoperator (p = 0,027) şi ziua 2 postoperator (p = 0,001). Pacienții care au dezvoltat inițial funcționalitate scăzută a grefei au fost aceia care au beneficiat de grefe hepatice de la donatori cu vârste avansate (p = 0,05) cu valori DRI mai ridicate (p = 0,002).

Concluzii. Rezultatele acestui studiu sugerează un impact semnificativ al vârstei donatorilor şi al DRI asupra cineticii coagulării, care ar putea determina funcționalitate inițială scăzută a grefei. Deşi TIR şi DRI s-au corelat semnificativ statistic cu severitatea colestazei şi a hepatocitolizei în perioada postoperatorie precoce, aceste rezultate par a nu influența supraviețuirea grefei sau a pacienților pe termen scurt.

Cuvinte cheie: transplant hepatic, grefă hepatică, coagulopatie cirotică, rezultat