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SIMULTANEOUS LIVER-KIDNEY TRANSPLANTATION IN ADULTS: A SINGLE CENTER EXPERIENCE COMPARING RESULTS WITH ISOLATED LIVER TRANSPLANTATION

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Key words: Simultaneous Liver-Kidney Transplantation, Liver Transplantation, Outcome, Post-Transplant complications

Abbreviations:

BMI – Body Mass Index

BSA – Body Surface Area

D-MELD– Donor Age * Model for End Stage Liver Disease score

GFR – Glomerular Filtration Rate

ICU – Intensive Care Unit

LTx – isolated Liver Transplantation

MELD – Model for End Stage Liver Disease

SLKTx – Simultaneous Liver-Kidney Transplantation

Tables: 1

Figures: 1 (color – No)

ABSTRACT

Background. After introduction of the Model for End-Stage Liver Disease (MELD) score in 2002, a worldwide increasing number of simultaneous liver-kidney transplantations (SLKTx) has been observed. However, organ shortage puts into question the allocation of two grafts to one recipient. This is a retrospective single-center study on SLKTx results compared with isolated liver transplantation (LTx).

Methods: Between 1995 and 2013, 37 SLKTx were performed in adult recipients. Every SLKTx was matched by donor age (± 5 years) and transplantation's date with two LTx (n=74). Pre-transplant, surgical and post-transplant variables were collected; liver graft and patient survivals were calculated.

Results: As expected, donor age was similar in the two groups (median 39.7 years), while serum creatinine level, glomerular filtration rate, MELD and D-MELD (donor age*MELD) were significantly higher in the SLKTx group. SLKTx had longer waiting list time ($p=0.0034$) as well as higher surgical difficulty, testified by more blood transfusions ($p=0.0083$), increased use of classic caval reconstruction ($p=0.0024$) and more frequent need of abdominal packing for bleeding control ($p=0.0003$). Also hospital stay ($p<0.0001$), second-look surgery ($p=0.0082$), post-transplant dialysis ($p<0.0001$) and post-transplant infections ($p=0.04$) were significantly higher in SLKTx group. Instead, liver acute rejection was significantly lower in SLKTx than in LTx (13.5% vs. 41%; $p=0.0045$). Liver graft and patient survival at 10 years after transplantation was similar in the two groups (liver graft: SLKTx=80% vs LTx=77%, $p=0.85$; patient: SLKTx=86% vs LTx=79%, $p=0.55$).

Conclusions. Despite technically challenging, SLKTx allowed excellent long-term results and showed to be an effective use of liver grafts.

ARTICLE

INTRODUCTION.

The first simultaneous liver-kidney transplantation (SLKTx) was successfully performed in 1983 ⁽¹⁾. SLKTx is now an effective therapeutic option in patients with end-stage liver and kidney disease⁽²⁾. After the introduction of the Model for End-Stage Liver Disease (MELD) score in 2002 for organ allocation, a worldwide increasing number of SLKTx has been recorded^(3,4). Nevertheless, the persistent organ shortage combined with a growing transplant demand pushes us to pursue a correct graft allocation. Until now, there are no clinical guidelines on this topic.

This is a retrospective single center study on SLKTx results compared with isolated liver transplantation (LTx), in order to verify the effectiveness of the allocation of a liver graft in combination with a kidney to one single recipient.

METHODS.

Between May 1995 and July 2013, 37 SLKTx (case group) were performed from deceased heart-beating donors in adult recipients at the Liver Transplantation Center of the University of Turin, Italy. Every SLKTx was matched by donor age (± 5 years) and transplantation's date with two LTx from deceased heart-beating donors in adult recipients (n=74, control group). The variables collected and analyzed were: donor features (age, gender, Body Mass Index (BMI), Body Surface Area (BSA), cause of death, serum sodium and creatinine levels, glomerular filtration rate (GFR) obtained with the Cockcroft-Gault formula, allograft steatosis and days of Intensive Care Unit (ICU) stay); recipient features (age, gender, aetiology of liver disease, BMI, BSA, MELD score and serum creatinine levels in waiting list and at transplant, GFR and Modification of Diet in Renal Disease (MDRD) at transplant, waiting list time, pre-transplant hemodialysis); donor-recipient match features (D-MELD, e.g. donor age*MELD); surgical features (total ischemia time, cold ischemia time, warm ischemia time, surgical technique, blood transfusions, use of abdominal packing for bleeding control, use of noradrenaline,

serum lactate levels at the end of transplant); post-transplant features (ICU stay, total in-hospital stay, second-look surgery, need of hemodialysis, liver acute rejection, infections, biliary and vascular complications). Long-term liver graft and patient survival rates were calculated in both groups. Categorical variables were analyzed with χ^2 (chi-square) test or Fisher's exact test, quantitative variables with non-parametric Mann-Whitney test. Kaplan-Meier curves were used for survival analysis and the log-rank test to compare survival curves. The level of significance was placed at p-value <0.05.

RESULTS.

As expected, donor age was similar in both groups (median 39.7 years; range 20.5 – 73.4 in SLKTx vs 18.2 – 75.1 in LTx) due to the matching criteria. No significant differences were observed among any donor feature. **Table 1** summarizes the characteristics of the study population. Leading indications for SLKTx were hereditary diseases involving both organs (polycystic liver and kidney) and metabolic diseases. Serum creatinine level, GFR, MELD and D-MELD were significantly higher in the SLKTx group, because of a selection bias: most of the SLKTx recipients were patients with end-stage kidney disease (89% under hemodialysis treatment at the time of transplant). SLKTx patients had longer waiting list time (median 161 days in SLKTx vs 76 days in LTx; p=0.0034) because optimal donors were generally used for those recipients. SLKTx had also higher surgical difficulty, testified by more blood transfusions (median 2,000 ml in SLKTx vs 1,500 ml in LTx; p=0.0083), increased use of classic caval technique for graft implantation (30% SLKTx vs 7% LTx; p=0.0024) and more frequent need of abdominal packing for bleeding control (38% SLKTx vs 9% LTx; p=0.0003), especially in recipients undergoing transplant for polycystic liver and kidney disease. Also in-hospital stay (median 25 days SLKTx vs 12 days LTx; p<0.0001), abdominal packing (38% SLKTx vs 9% LTx; p=0.0003), second-look surgery (32% SLKTx vs 11% LTx; p=0.0082), post-transplant dialysis (27% SLKTx vs 0% LTx; p<0.0001) and post-transplant infections (38% SLKTx vs 19% LTx; p=0.04) were significantly higher in SLKTx group. Liver acute rejection episodes were instead significantly lower in SLKTx than in LTx

(13.5% SLKTx vs 41% LTx; $p=0.0045$). No difference in 10-year liver graft and patient survival was observed between the two groups (liver graft: 80% SLKTx vs LTx 77%, $p=0.85$; patient: SLKTx 86% vs LTx 79%, $p=0.55$), as shown in **Figure 1**. In the SLKTx group, only four deaths were recorded in the follow-up: two less than 1 year after transplant because of multi-organ failure or sepsis, the other two after more than 4 years of follow-up because of infection or *de novo* cancer.

DISCUSSION.

In our experience, SLKTx showed to be an effective therapeutic option in patients with end-stage liver and kidney disease. The main finding of this study is that long-term patient and liver graft survival are similar in patients undergoing SLKTx compared with a LTx group matched for donor age and transplantation era. Despite a greater complexity of the surgical procedure, moreover performed in sicker patients and therefore entraining more frequent post-transplant complications, the excellent results we obtained in the SLKTx group seem to justify the use of a liver graft in combination with a kidney in patients who would not be served by a LTx alone.

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Table 1. Pre-transplant recipients characteristics, surgical features and post-transplant complications in SLKTx group and LTx group

	SLKTx n: 37		LTx n: 74		<i>p value</i>
RECIPIENT					
Age (years)	49.7	(18.5-64.7)	50.7	(17.2-64.8)	0.77
Gender M:F	16:21	(43%:21%)	53:21	(71%:29%)	0.0065
BMI	23	(18-35)	24	(17-36)	0.25
BSA (m ²)	1.8	(1.4-2.2)	1.8	(1.3-2.2)	0.33
Cockcroft-Gault (ml/min)	16.4	(6.8-106.5)	88.7	(21.7-221.9)	<0.0001
MDRD (ml/min)	10.5	(5.7-65)	77.8	(24.4-185.5)	<0.0001
Serum creatinine level (mg/dL)					
at listing	5.4	(1.0-9.6)	1.0	(0.4-5.9)	<0.0001
At transplant	5.0	(2.6-9.4)	1.0	(0.5-2.1)	<0.0001
MELD					
at listing	25	(8-32)	17	(7-41)	<0.0001
At transplant	24	(9-34)	16	(6-51)	<0.0001
Waiting list time (days)	161	(1-671)	76	(1-674)	0.0034
Dialysis before Tx	33	(89%)	0	(0%)	<0.0001
TRANSPLANTATION					
Warm portal ischemia time (min)	22	(12-41)	23	(11-39)	0.4
Cold ischemia time (min)	477	(183-690)	476	(214-427)	0.18
Total ischemia time (min)	505	(209-715)	505	(233-709)	0.17
D-MELD	921	(258-2350)	617	(137-1784)	0.001
Hemotransfusion (ml)					
Red blood cell	2000	(200-15500)	1500	(0-12500)	0.0083
Plasma	2000	(0-17300)	3000	(0-15750)	0.6
Noradrenaline at the end of Tx (γ/kg/min)	0.1	(0-1)	0.1	(0-1)	0.51
Serum lactate at the end of Tx (mmol/L)	2	(0.9-12)	2.1	(0.8-6.9)	0.87
Surgical technique					0.0024
Piggy Back	23	(62%)	66	(89%)	
Classic	11	(30%)	5	(7%)	
Piggy Back sec. Belghiti	3	(8%)	3	(4%)	
POST TRANSPLANT COMPLICATIONS					
ICU stay (days)	7	(0-100)	3	(0-53)	<0.001
Hospital stay (days)	25	(8-100)	12	(6-59)	<0.0001
Dialysis after Tx	10	(27%)	0	(0%)	<0.0001
Abdominal packing	14	(38%)	7	(9%)	0.0003
Days of packing	3	(2-12)	2	(2-3)	0.17
Second look surgery	12	(32%)	8	(11%)	0.0082
Infections	14	(38%)	14	(19%)	0.04
Biliary complications	6	(16%)	16	(22%)	0.61
Vascular complications	2	(5%)	1	(1%)	0.25
Liver rejection	5	(13.5%)	30	(41%)	0.0045

Quantitative variables are expressed as median (range). Categorical variables are expressed as number (prevalence, %). BMI, Body Mass Index. BSA, Body Surface Area. D-MELD, Donor-Model for End stage Liver Disease. ICU, Intensive Care Unit. MDRD, Modification of Diet in Renal Disease. MELD, Model for End stage Liver Disease. Tx, Transplantation.