CLINICAL RESULTS OF COMBINED AND SEQUENTIAL LIVER-KIDNEY TRANSPLANTATION: A SINGLE CENTER EXPERIENCE

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BACKGROUND

Since the model of end stage disease (MELD) score was adopted in the 2002 for liver organ allocation, there was an increase of combined liver-kidney transplantation.
Between January 1995 and December 2011 we performed 38 combined liver-kidney transplantation (CLKT) and 6 sequential liver-kidney transplantation (SLKT).

OBJECTIVES

The aims of this study were:
- to compare the outcomes and the survival of CLKT with SLKT and with the controlateral kidney (KTA1 for CLKT and KTA2 for SLKT).
- to evaluate the correct indications and timing for CLKT.
- to evaluate the potential immunoprotective role of liver allograft on the transplanted kidney.

Recipients characteristics	CLKT	KTA1	SLKT	KTA2	p
Age (range)	47 (3-64)	41 (6-67)	56 (49-72)	57 (45-70)	0.021
Female/Man	20/18	9/21	1/5	0/6	0.027
On dialysis at transplant	73,7%	100%	100%	100%	0.008
Duration of dialysis (months)	21,2	63,6	73,1	57	0,0
Meld score	22,6				
Waiting time (days)	99	659	640	823	0.003
Donor characteristics					
Age (range)	32 (1-65)	32(1-66)	50 (15-71)	50 (15-71)	0.065
Female/Man	12/26	12/26	1/5	1/5	
Serum creatinine (mg/dl)	0,85	0,85	0,85	0,85	
Cold ischemia time (hr)	11,8	16	18	19	
Mean of HLA-A,B,DR mismatch	4,7	3	4	3	

Figure 1. Clinical characteristic of patients and donor.

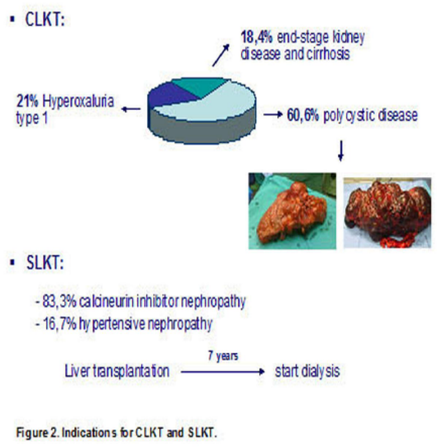


Figure 2. Indications for CLKT and SLKT.

	CLKT	KTA 1	p
DGF	52,6%	38,7%	NS
Infections, bleedings...	86,8%	61,5%	0,034
Surgical complications	42%	11,5%	0,03

In CLKT:
- < cold is chemia time: 11,8 h in CLKT vs 16 h in KTA1

In CLKT recipients with DGF:
- > blood transfusions during transplant (14 U vs 7,8 in patients without DGF)
- > surgical complications

Figure 3. Complications in CLKT and KAT 1.

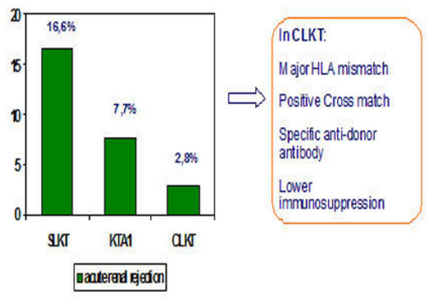


Figure 4. Acute renal rejection.

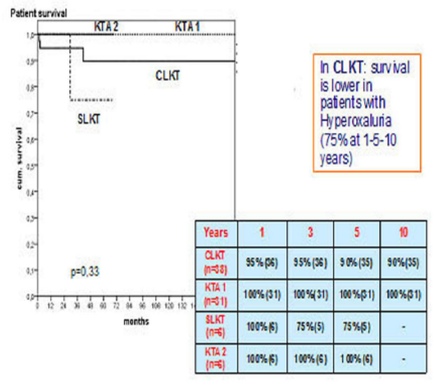
Induction therapy with Basiliximab: 89,5% CLKT
100% SLKT
90% and 100% KTA 1-2

Immunosuppressive protocols:

Protocols:	CLKT	KAT1	SLKT	KAT2
TAC+MMF+st	76,3% (29)	58,6% (17)	50% (3)	66,6% (4)
TAC+st	15,8% (6)	17,2% (5)		
TAC+AZA+st		3,4% (1)		
TAC+mTORi+st			16,6% (1)	
MMF+st				16,6% (1)
CYA+MMF+st		3,4% (1)	33,3% (2)	
CYA+AZA+st	7,9% (3)			
CYA+mTORi+st		10,3% (3		16,6% (1)
CYA+st		3,4% (1)		
mTORi+MMF+st		3,4% (1)		

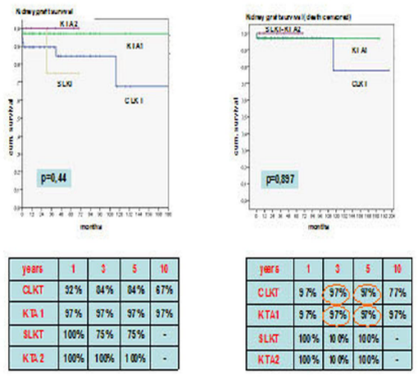
In CLKT recipients: tacrolimus levels were lower and steroid was stopped earlier (13,8 months vs 27,6 months) than in KAT 1

Figure 5. Immunosuppressive protocols.



Years	1	3	5	10
CLKT (n=38)	95% (36)	95% (36)	90% (35)	90% (35)
KTA 1 (n=31)	100% (31)	100% (31)	100% (31)	100% (31)
SLKT (n=6)	100% (6)	75% (5)	75% (5)	-
KTA 2 (n=6)	100% (6)	100% (6)	100% (6)	-

Figure 6. Patient survival.



years	1	3	5	10
CLKT	92%	84%	84%	67%
KTA 1	97%	97%	97%	97%
SLKT	100%	75%	75%	-
KTA 2	100%	100%	100%	-

years	1	3	5	10
CLKT	97%	97%	97%	77%
KTA1	97%	97%	97%	97%
SLKT	100%	100%	100%	-
KTA2	100%	100%	100%	-

Figure 7. Kidney graft survival.

	N° patients	Patient survival (%) 1 year	Patient survival (%) 5 years	Kidney graft survival (%) 1 year	Kidney graft survival (%) 5 years
Turin	38	95	90	92	84
Jeyarajah et al., 1997, Dallas	29	78.6 (2 years)	48,1		
Ruiz et al., 2006, Los Angeles	98	76	70	76	70
Creput et al., 2003, Paris	45	85	82 (2 years)	85	82 (2 years)
Mosconi et al., 2006, Bologna	15		86		86
Fong et al., 2003, UNOS	800	74	64	70	56
Chava et al., 2007, London	39	77	73,7	77	70

Figure 8. CLKT in the literature.

METHODS

We analyzed and compared the outcomes of 38 CLKT, 6 SLKT and the controlateral kidneys (31 of the first group and 6 of the second one) used for the kidney alone transplantation (KTA 1 and 2).

RESULTS

The indications for CLKT were: polycystic disease (60,6%), primary type 1 Hyperoxaluria (21%), end-stage kidney disease and cirrhosis (18,4%).
In SLKT, the major cause of renal failure was calcineurin inhibitor nephrotoxicity (83,3%) and dialysis started in average 7 years time after liver transplantation. Kidney transplantation was performed in average 9 years after liver transplantation. Delayed renal graft function (DGF) occurred in the 52,6% of CLKT vs. 38,7% in the KTA1, despite a minor cold ischemia time in the CLKT group.
Complications, in particular infections and bleedings, were more common in CLKT patients (86,8% vs. 61,5 in KTA1, p=0,034), as well as surgical complications (42% vs. 11,5% in KAT1 p=0,03). The immunosuppressive protocol mostly used was tacrolimus, mycophenolate mofetil and prednisone. In CLKT recipients tacrolimus levels were lower and steroid was stopped earlier than in the KTA1 group. The frequency of acute rejection of the renal graft was lower in CLKT (2,8% in CLKT, 7,7% in KTA1 and 16,6% in SLKT, p = not significant) despite a major HLA mismatch, positive X-match, the presence of DSA (Donor Specific Antibodies) and lower immunosuppression. Mean serum creatinine levels were lower in the CLKT group. At 5 years, patient survival rates in SLKT were lower than those observed in CLKT (75% in SLKT vs 90% in CLKT), and in KTA1-2 (100%). In CLKT we observed the higher mortality rate in the first 3 months after transplant in association with infections or multi organ failure (mainly in patients with primary hyperoxaluria and systemic oxalosis). Kidney graft survival rates at 1, 5 years were 92% and 84% in CLKT, 100% and 75% in SLKT, 97% and 97% in KTA1, 100% and 100% in KTA2, respectively. CLKT and KTA1 kidney graft survival compared using “death censored curves” was the same in both groups (97%) at 1 and 5 years.

CONCLUSIONS

In CLKT we observed lower serum creatinine levels, despite a major incidence of DGF, and a lower incidence of acute renal rejection, despite a less favourable immunological condition and less immunosuppression.
These results seems to confirm that the liver allograft has an immunoprotective effect on the renal allograft from the same donor.
In addiction, in CLKT recipients, although complications and mortality were more frequent in the first three months after transplantation, the patient and kidney allograft survival rates appeared to be superior than those observed in SLKT. In patients with Hyperoxaluria is important to perform the transplant before the occurrence of advanced systemic oxalosis.

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