RENAL DISEASE AND LIVER TRANSPLANTATION IN FAMILIAL AMYLOIDOTIC POLYNEUROPATHY

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INTRODUCTION AND AIMS

Portuguese familial amyloidotic polyneuropathy (FAP) type I is a systemic amyloidotic disease due to an amyloidogenic transthyretin (TTR) protein, in which an amino acid substitution of methionine for valine at position 30 of TTR molecule is present[1].

Although peripheral nervous system is primary affected, renal involvement is common. In this disease, all patients had amyloid deposits in the kidney, but only one third will develop CKD and 10% will progress to stage 5[1].

Because more than 90% of the mutant protein is produced in the liver, orthotopic liver transplantation (OLT) is the definitive treatment for the disease.

The aims of this study was to evaluate the incidence of renal dysfunction post OLT and its impact on patient's survival.

POPULATION AND METHODS

This was a retrospective study of 185 FAP patients submitted to 217 OLT in our unit, between September 1992 and March 2007.

Clinical data: age at transplantation, gender, weight, presence of diabetes mellitus, hypertension, hepatitis B and C infection, renal dysfunction pre transplant (RD pre), immunosuppression (ISS) and necessity for acute renal replacement therapy (RRT).

Laboratorial data: serum creatinine (Scr) values and/or glomerular filtration rate (GFR), determined by Cockcroft-Gault equation, at the last observation pre transplantation and at days 1, 7 and 21, month 6 and every year post transplantation.

RESULTS

185 OLT recipients:

- Male gender 59%
- Mean age: 36.8±9.5 years
- Diabetes in 2 patients; Hypertension in 17 patients
- Mean follow up time 3.6±3.7 years, 28.6% > to 5 years
- Retransplanted: 32 recipients (14.7%)

RD PRE-OLT

n=31 (14.3%)

GFRe < 60 ml/min or Scr >1.5 mg/dl

Logistic Regression	CKD development			
	β	CI 95%	p	R^2
RD pre OLT	3.5	8.2 – 127.6	<0.001	0.6
Age	0.7	1 – 1.1	0.003	
Gender	0.2	0.5 – 2.8	0.6	
AKI post OLT	2.8	6.5 – 37.7	<0.001	

Renal dysfunction pre OLT, adjusted for age, gender and AKI post OLT, was correlated with development of CKD post OLT.

AKI

n=57 (26.3%)

Defined by RIFLE criteria

- RRT in 28% (n=16)
- Death in 23% (n=13)
- Renal recovery in 3.5% (n=2)

Spearman Correlation	r	p
Women	0.2	0.02
RRT *(16)*	0.4	<0.001
CKD stage 3 *(25)*	0.3	<0.001
CKD stage 4 *(9)*	0.3	<0.001
CKD stage 5d *(8)*	0.2	<0.0001
Mortality *(13)*	0.1	0.04

Logistic Regression	CKD development			
	β	CI 95%	p	R^2
AKI	2.8	6.7 – 38.3	<0.001	0.6
Age	0.7	1 – 1.1	0.002	
RD pre OLT	3.5	8.5 – 131.2	<0.001	

AKI pos OLT: more common in women, and associated with acute RRT necessity, CKD development, and high mortality.
In multivariate analysis, adjusting for age and for presence of renal dysfunction pre OLT, AKI was correlated with development of CKD.

CKD

n=75 (34.6%)

- CKD stage 3 in 23.5% (n=51)
- CKD stage 4 in 6% (n=13)
- CKD stage 5 in 5% (n=11)

Spearman Correlation	R	p
Age	0.3	<0.001
RD pre OLT	0.5	<0.001
AKI post OLT	0.5	<0.001
Tacrolimus use	-0.2	0.03
Mortality	0.19	<0.0001

Logistic Regression	Mortality			
	B	CI 95%	P	R^2
CKD	1.9	1.2 – 38.2	0.02	0.3
Age	0.04	0.9 – 1	0.2	
RD pre OLT	0.6	0.5 - 6	0.4	
AKI post OLT	1	0.9 – 9.2	0.08	

Age, renal dysfunction pre OLT and AKI post OLT were risk factors for CKD development in all the 3 stages. Tacrolimus seemed to have a beneficial effect.
In multivariate analysis, adjusting for age, renal dysfunction pre OLT and AKI post OLT, CKD was correlated with mortality.

Mortality

n=32 (14.7%),

Mean follow up time 1.8±3.2 years

Spearman Correlation	r	p
Age	0.3	<0.001
Re transplatation	0.2	0.004
RD pre OLT	0.3	<0.001
AKI post OLT	0.2	0.04
CKD development	0.2	0.001

Mortality was associated with age, retransplantation, and with any kind of renal dysfunction namely renal dysfunction pre OLT, AKI post OLT (specially F class), and CKD development (particularly stage 5).

CONCLUSIONS

These results demonstrate that renal complications are important prognostic tools in FAP patients submitted to OLT. Careful assessment of pre transplant renal function is essential. Combined liver kidney transplantation should be proposed for patients at higher risk of renal dysfunction post transplant.

References:

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