EFFECTS OF RENAL TRANSPLANTATION ON CARDIAC STRUCTURE AND FUNCTION

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INTRODUCTION

Cardiovascular disease is the leading cause of mortality in renal transplant recipients (RTRs). There is conflicting and inadequate data on whether significant regression of LVH occurs after successful renal transplantation (RT). The pathogenesis of LVH in chronic renal failure is multifactorial. Although RT improves some risk factors for LVH of chronic renal failure, some others persist such as anemia, hyperparathyroidism, and hypertension. Furthermor, it has been demonstrated that steroids and calcineurin inhibitor (CNIs) therapy may play a role in maintenance of LVH after RT. The aim of the study was to evaluate the effects of RT on cardiac structure and function and its association with the main cardiovascular risk factors.

SUBJECTS AND METHODS

-77 RTRs who underwent RT > 1 year and with eGRF > 15 ml/min/1.72 m^2 were included in the study.
- All patients had one or two echocardiographic controls performed > 1 year after RT. LV mass was calculated according to American Society of Echocardiography (J Am Soc Echocardiogr 2005; 12: 1440-1463), and indexed to body surface (LVMi). LVH was defined as LVMi > 95 g/m^2 in females and > 115 gr/m^2 in males. Relative wall thickness (RWT) allowed further classification of LVM increase as either concentric hypertrophy (RWT > 0.42) or eccentric hypertrophy (RWT ≤0.42).
- In all patients at the same time was performed ultrasonography on the carotid arteries bilaterally to measure thickness of intima-media layer (CIMT).
- They were also checked for: PTH, Hb, homocystein (Hcy), folic acid, vitamin B 12, C-reactive protein (CPR), HDL and LDL cholesterol, eGFR (CKD-EPI), proteinuria, blood pressure (BP), body mass index (BMI), immunosuppressive, and antihypertensive therapies.

RESULTS

In tables 1 and 2 are reported baseline demographic and clinical data of the RTRs, they have a long graft vintage (> 8 aa), PTH levels meanly twice normal values, homocysteine levels increased, proteinuria < 500 mg/grCr, CIMT high values, presence of LVH in 61% of ourRTRs that was just a little lower than our hemodialysis patients (68%), a lot number of RTRs on steroid therapy un elevato numero di pazienti in terapia steroidea (77%), and few patients on ACEi and/or ARB. LVMi was significantly correlated with systolic blood pressure (SBP; r=.318; P<.001), CIMT (r=.304; P<.01), age (r=.390; P<001), and sCr (r=.218; P<.05), suggesting that the increased artery stiffness can be their hypothetical link. Table 3 shows the main differences between RTRs with LVH compared to RTRs with normal LVMi. Table 4 shows a great number of RTRs with LVH on steroid therapy. In table 5 are reported the main differences among quartiles for LVMi, the higher quartile was characterized by higher values of CIMT and levels of PTH. Table 6 shows not significant differences of LVMi and some others parameters after one year from the first echocardiographic control.

Table 1. Baseline demographic and clinical data of the renal transplant recipients (n=84)

Age, y/o	52 ± 11	25OHD_3, ng/ml	17.0 ± 8.4
Gender (M/F)	52/25	Hematocrit, %	40 ± 5
Dialytic vintage, months	30 ± 24	Hemoglobin, g/dl	13.2 ± 1.7
Graft vintage, months	101 ± 76	Cholesterol, mg/dl	210 ± 43
Diabetes, n° pts	9	HDL, mg/dl	48 ± 14
Cardiovascular events, n° pts	8	LDL, mg/dl	125 ± 34
Serum creatinine, mg/dl	1.6 ± 0,6	C-reactive protein, mg/L	3.9 ± 6.2
eGFR, mL/min/1.73 m^2	50 ± 21	Homocysteine, µMol/L	21.1 ± 7.6
Serum calcium, mg/dl	9.6 ± 0.6	Folic Acid, ng/ml	9.9 ± 10.6
Serum phosphorus, mg/dl	3.1 ± 0.6	Vitamin B12, pg/ml	464 ± 244
Ca x P product, mg^2/dl^2	30 ± 6	Albumin, g/dl	3.9 ± 0.4
PTH, pg/ml	134 ± 116	Proteinuria, mg/L	405 ± 956
Alkaline Phosphatase, mU/ml	83 ± 38	Proteinuria, mg/gr uCr	532 ± 1569

Table 2. Baseline clinical data of the renal transplant recipients (n=84)

Systolic BP, mmHg	130 ± 14	LVH ecc/conc, n° pts	28/19
Diastolic BP, mmHg	79 ± 9	BMI	24.7 ± 3.8
Mean BP, mmHg	96 ± 9	Steroids, %	77
CIMT, mm	1.30 ± 0.56	Cyclosporin, %	47
LVEDD, mm	52 ± 6	Tacrolimus, %	41
LVESD, mm	29 ± 6	Sirolimus, %	14
IVSTd, mm	11.5 ± 1.7	Everolimus, %	14
PWTd, mm	10.1 ± 1.6	Mycophenolate Mofetil, %	64
FS, %	43 ± 8	RAAS blocking agents, %	35
EF, %	61 ± 8	CCBs, %	26
LVM, g	220 ± 65	B-blockers, %	66
LVMi, g/m^2	118 ± 30	Diuretics, %	27
LVH presence, %	61	Statins, %	36

CIMT = carotid artery intima media thickness; LVEDD = left ventricular (LV) end-diastolic diameter; LVESD = LV end-systolic diameter; IVSTd = interventricular diastolic thickness; PWTd = LV postero-lateral diastolic wall thickness; FS = LV fractional shortening; EF = LV ejection fraction; LVM = LV mass; LVMi = LVM index; LVH = LV hypertrophy; LVH ecc/conc = LVH eccentric/concentric; BMI = body mass index; RAAS = renin-angiotensin-aldosterone system; CCBs = calcium channel blockers.

Table 3. Main clinical differences beetwen patients with normal and high LVMi among 77 renal transplant patients

	LVMi normal (n = 34)	LVMi high (n = 50)	P <
Graft vintage, months	68 ± 70	73 ± 88	.05
Dialytic vintage, months	23 ± 14	36 ± 13	.05
Serum creatinine, mg/dl	1.5 ± 0.4	1.8 ± 0.9	.01
eGFR, mL/min/1.73 m^2	54 ± 18	46 ± 22	NS
PTH, pg/ml	109 ± 59	153 ± 133	.05
25OHD_3, ng/ml	16.9 ± 7.8	18.3 ± 12.6	NS
Hb, gr/dl	13.3 ± 1.8	13.1 ± 1.6	NS
Homocysteine, µMol/L	19.7 ± 6.4	21.9 ± 8.1	NS
Proteinuria, mg/gr Cr	199 ± 143	791 ± 1956	.01
Systolic BP, mmHg	125 ± 12	133 ± 14	NS
Diastolic BP, mmHg	75 ± 9	80 ± 9	NS
CIMT, mm	1.18 ± 0.38	1.43 ± 0.67	.01
BMI	23.7 ± 2.9	25.2 ± 4.1	NS

Table 4. Main clinical differences beetwen patients with normal and high LVMi among 84 renal transplant patients

	LVMi normal (n = 34)	LVMi high (n = 50)
Steroids, %	67	78
Cyclosporin, %	47	48
Tacrolimus, %	35	42
Sirolimus, %	12	14
Everolimus, %	18	16
Mycophenolate Mofetil, %	70	56
CCBs, %	29	26
RAAS blocking agents, %	32	46
B-blockers, %	68	66
Diuretics, %	23	30
Statins, %	29	46

Table 5. Main clinical data according to LVMi quartile among 84 renal transplant patients

LVMi, g/m^2 n° patients	< 101 (n = 23)	101 - 116 (n = 25)	117 - 139 (n = 18)	> 139 (n = 18)
Graft vintage, months	61 ± 70	87 ± 87	72 ± 92	96 ± 73
Dialytic vintage, months	22 ± 12	34 ± 31°	39 ± 37*	30 ± 24
Serum creatinine, mg/dl	1.5 ± 0.4	1.5 ± 0.5	2.1 ± 1.29°	1.8 ± 0.7°
eGFR, ml/min/1.72m^2	52 ± 19	54 ± 21	46 ± 25	43 ± 17
25OHD_3, ng/ml	15.8 ± 7.9	16.4 ± 8.0	17.8 ± 10.6	22.1 ± 16.9
PTH, pg/ml	106 ± 50	145 ± 152*	137 ± 114	161 ± 101°
Hb, gr/dl	12.7 ± 1.7	13.5 ± 1.7	13.2 ± 1.7	13.0 ± 1.8
Proteinuria, mg/gr Cr	163 ± 166	453 ± 835*	1169 ± 3182°	631 ± 984^
Systolic BP, mmHg	125 ± 12	125 ± 10	135 ± 8	139 ± 19
CIMT, mm	1.06 ± 0.23	1.33 ± 0.54	1.36 ± 0.63^	1.70 ± 0.74^
Steroids, % patients	62	80	61	89

Table 6. Main clinical data in a group of patients with more than an echocardiographic control in post-transplant period

	1° control (n = 39)	2° control (n = 39)	3° control (n=8)
Graft vintage, months	91 ± 68	106 ± 71	129 ± 75
Serum creatinine, mg/dl	1.6 ± 0.6	1.7 ± 0.7	1.7 ± 0.5
eGFR , ml/min/1.72 m^2	50 ± 22	51 ± 26	46 ± 17
Phosphorus, mg/dl	3.0 ± 0.7	3.1 ± 0.6	4.0 ± 2.3*
PTH, pg/ml	135 ± 127	153 ± 139	127 ± 47
25OHD_3, ng/ml	16.6 ± 8.6	16.8 ± 9.3	12.5 ± 12.1
Hb, g/dl	13.4 ± 1.7	13.1 ± 1.8	12.5 ± 1.3
LDL, mg/dl	125 ± 37	121 ± 26	113 ± 21
Proteinuria, mg/g Cr	346 ± 592	387 ± 601	171 ± 137
Systolic BP, mmHg	130 ± 10	132 ± 9	126 ± 8
Diastolic BP, mmHg	79 ± 7	79 ± 7	83 ± 4
CIMT, mm	1.37 ± 0.58	1.41 ± 0.49	1.30 ± 0.53
LVMi, g/m^2	118 ± 29	124 ± 36	137 ± 60
Steroids, n° of patients	31	27	5

*vs 1° control P < .01

CONCLUSIONS

- Successful renal transplantation does not seem to improve LVH. In fact number of RTRs with LVH in long term follow up remains high.

- Although pathogenesis of LVH in chronic renal failure is multifactorial, in our experience reduced renal function, systolic hypertension, and vascular damage seem to play a key role in its maintenance.

- We cannot say how much steroids and calcineurin inhibitors therapy take part in the persistence of LVH after successful RTx.

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