***In vivo* oxidized low-density lipoprotein (ox-LDL) aopp and tas after kidney transplantation: a prospective, randomized one year study comparing cyclosporine A and tacrolimus based regiments**

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Aims. Restoration of renal function after kidney transplantation (KT) is expected to improve oxidative stress (OS). However, little is known about the influence of calcineurin inhibitors on oxidized low-density lipoproteins (ox-LDL) after KT. The aim of this study was to evaluate ox-LDLs and related markers of OS, advanced oxidation protein products (AOPP) and total antioxidant status (TAS) in patients after KT on either cyclosporin A (CyA) or tacrolimus (Tac) treatment.

Methods. This was a prospective, randomized, single-center 12 month study evaluating time-dependent changes in biomarkers of OS before and after KT. Twenty nine patients (mean age 54.4 ± 11.1 ; 55% male and 45% female) were treated with CyA (Group A) and twenty four patients (mean age 52.9 ± 9.9 ; 75% male and 25% female) were treated with Tac (Group B). The ox-LDL, AOPP, TAS, lipid metabolism parameters, creatinine and glomerular filtration were assessed on day 1 before KT and on days 1 and 7, and in months 1, 3, 6 and 12 after KT.

Results. Over the 12 months, the ox-LDL for group A changed from 69.2 ± 32.9 to 65.1 ± 17.1 U/L ($P=0.665$), while AOPP significantly decreased from 233.0 ± 159.6 to 156.5 ± 90.1 $\mu\text{mol/L}$ ($P=0.025$) and TAS from 1.87 ± 0.31 to 1.68 ± 0.20 mmol/L ($P=0.030$). For group B the ox-LDL changed from 62.9 ± 29.7 to $\pm 61.4 \pm 14.6$ U/L ($P=0.168$) and TAS from 1.87 ± 0.51 to 1.68 ± 0.20 mmol/L ($P=0.168$), while AOPP significantly decreased from 180.5 ± 90.0 to 123.9 ± 37.7 $\mu\text{mol/L}$ ($P=0.019$).

Conclusion. AOPP is more sensitive than ox-LDL for assessing OS after KT. TAS values appear to be insufficiently sensitive for monitoring OS in patients after KT.

Key words: kidney transplantation, oxidative stress, oxidized low-density lipoproteins, advanced oxidation protein products, total antioxidant status, calcineurin inhibitors

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INTRODUCTION

Enhanced atherosclerosis and subsequent cardiovascular complications are the leading cause of death in patients with chronic kidney disease (CKD). In renal transplant recipients, fifty to sixty percent of deaths are directly related to cardiovascular disease^{1,2}. Besides common risk factors for coronary heart disease such as arterial hypertension, diabetes mellitus, increasing patient age, elevated serum cholesterol, obesity and cigarette smoking, a number of other factors have been found to correlate with cardiovascular complications after kidney transplantation (KT) (ref.³). Potential risk factors contributing to the acceleration of atherogenesis include hyperhomocysteinemia, hyperfibrinogenemia, elevated level of lipoprotein (a), modification of low-density lipoproteins (LDL) and high-density lipoproteins (HDL), elevated C-reactive protein (CRP) level and decreased graft function^{4,5}.

In recent years, substantial attention has been paid

to the possible role of oxidative stress (OS) as a non-traditional risk factor for high cardiovascular morbidity and mortality among renal transplant recipients^{5,6}. OS can be defined as an imbalance between the formation of reactive oxygen species (ROS) and antioxidant defence capacity^{7,8}. The predominance of ROS formation over the cellular antioxidant defence results in the oxidative damage of biomolecules, which leads to tissue damage and organ dysfunction⁹. OS is one of the main factors for enhanced atherosclerosis and is frequently observed in patients with end-stage renal disease. One of the currently recommended markers characterizing OS is the level of oxidized LDL (ox-LDL) (ref.⁴).

Ox-LDL are very biologically active molecules and formation of ox-LDL in the sub endothelial space of the arterial wall is a key step in the development of atherosclerosis¹⁰. Ox-LDL have been recognized as a prognostic marker of transplant-associated coronary artery disease¹¹. Ox-LDL contribute not only to the development of athero-

sclerosis and cardiovascular disease, but also to chronic graft dysfunction (interstitial fibrosis, tubular atrophy) (ref.^{6,7}).

Advanced oxidation protein products (AOPP) were firstly described by Witko-Sarsat in 1996 as the protein biomarkers for OS in uremia¹². Plasma proteins are generally susceptible to OS. The AOPP level is elevated in patients with CKD in comparison with healthy subjects. Plasma AOPP concentration increases with the progression of chronic renal failure and is closely related to advanced glycation end products¹³. AOPP are able to trigger the synthesis of inflammatory cytokines (tumor necrosis factor alpha, interleukine-8) in neutrophil leukocytes and monocytes and seem to act as inflammatory mediators in CKD patients¹⁴.

Cyclosporine A (CyA) and tacrolimus (Tac) are calcineurin inhibitors currently used in immunosuppressive protocols after KT. Both drugs are effective in reducing the incidence of acute rejection after KT, but they differ in their mechanism of action, safety profile, toxicity and side effects^{15,16}. With regard to nontraditional risk factors contributing to high cardiovascular morbidity and mortality in renal transplant patients, little is known about the impact of calcineurin inhibitors on ox-LDL after KT. Further, recent data are based mainly on *in vitro* studies and are controversial¹⁷.

The aim of this study was to describe and to compare the influence of CyA and Tac on ox-LDL, AOPP and total antioxidant status (TAS) in patients after KT over a 12-month period.

PATIENTS AND METHODS

This was a prospective, randomized, single-centre study conducted according to ICH GCP guidelines in the University Hospital Olomouc. The trial was approved by the local ethics committee and all patients gave written informed consent before inclusion in the study.

Kidney transplant recipients from deceased donors followed up for a minimum of 12 months were eligible for the study. The causes of end-stage renal disease in the study population were as follows: chronic glomerulonephritis (n=22; 42%), chronic tubulo-interstitial nephritis (n=16; 30%), autosomal dominant polycystic kidney disease (n=6; 11%) diabetic nephropathy (n=5; 9%), Alport syndrome (n=1; 2%), and an unknown cause (n=3; 6%). No patients had active viral hepatitis B or C. Pregnant or breastfeeding females, patients under 18 years of age, patients undergoing systemic immunosuppressive therapy for reasons other than KT, patients with malignant disease or significant, uncontrolled concomitant infections and those taking vitamin supplements containing folic acid and vitamins C or E were excluded.

The clinical cohort was randomized into two groups receiving two different well-established triple-drug maintenance immunosuppressive regimens. No induction immunosuppression with anti-thymocyte globulin was administered. Patients in the first group (Group A, n=29) were treated with CyA (Sandimmune/Neoral) combined

with mycophenolate mofetil (CellCept) and corticosteroids (Prednisone). The initial daily dosage of CyA was 3 mg/kg (divided into two doses). The blood target CyA level was 200-300 ng/ml at month 1 and 100-200 ng/ml at month 6. The CyA level was measured using fluorescence polarization immunoassay (Abbott Diagnostics). Patients in the second group (Group B, n=24) were treated with Tac (Prograf) combined with mycophenolate mofetil (CellCept) and corticosteroids (Prednisone). The initial daily dosage of Tac was 0.1 mg/kg, (divided into two doses). The blood target Tac level was 5-15 ng/ml at month 1 and 4-10 ng/ml at month 6. The Tac level was measured using microparticle enzyme immunoassay (Abbott Diagnostics). The daily dose of mycophenolate mofetil in both groups was 20 mg/kg. The Prednisone level was progressively tapered to reach daily dose of 20 mg/day at day 15 and 15 mg/day at month 3 and a 5 mg/day maintenance dose at month 6.

Blood for laboratory analysis was collected after overnight fasting on day 1 before KT and days 1 and 7, and months 1, 3, 6 and 12 after KT. The following parameters were studied: urea, creatinine, glomerular filtration rate (GFR) by MDRD, total cholesterol, triglycerides (TAG), LDL cholesterol, HDL cholesterol, ox-LDL, AOPP, TAS, apolipoprotein A-I (Apo AI), apolipoprotein B (Apo B), albumin, hemoglobin, CRP.

Plasma ox-LDL level was measured using the Mercodia Oxidized LDL ELISA test (Mercodia, Uppsala, Sweden) according to the manufacturer's instructions. Recommended normal values for ox-LDL are 26 to 17 U/l.

Determination of AOPP was based on a spectrophotometric assay according to Witko-Sarsat¹³. One milliliter of blood serum diluted 1:5 with phosphate-buffered saline (PBS), 1 ml of chloramine-T (0-100 µmol/l) for calibration and 1 ml of PBS as blank were placed in corresponding tubes. Fifty microliters of 1.16 mol/l potassium iodide and 100 µl of glacial acetic acid were added and absorbance at 340 nm was measured immediately. AOPP levels were expressed in micromoles of chloramine-T equivalents per liter of plasma (µmol/l). The mean AOPP level in the control group of 32 healthy blood donors (19 males and 13 females) with a mean age of 49 ± 11 years (range, 22-64

Table 1. Demographic data of the patient population.

	Group A (cyclosporine A)	Group B (tacrolimus)
Number of patients	29	24
Age (years)	54.4 ± 11.1	52.9 ± 9.9
Gender (M:F)	16 : 13	18 : 6
Time on dialysis prior to KT (years)	2.5 ± 1.9	2.6 ± 1.7
Body mass index	25.9 ± 4.7	26.4 ± 3.2

years) who did not take folic acid, vitamins C or E or any other antioxidants was $81.3 \pm 28.7 \mu\text{mol/l}$.

TAS was determined using the Randox TAS kit (Randox Laboratories Ltd., UK). The assay was carried out according to the kit manufacturer's protocol. The normal value range is 1.3–1.77 mmol/l.

Apo A-I and Apo B levels were measured using an immunoturbidimetric assay (Roche Diagnostics, Germany). The other described biochemical parameters were measured in a certified clinical chemistry laboratory on the Modular Evo analyzer (Roche).

All results are expressed as the mean $\pm$ standard deviation (SD). The SPSS v. 15 (SPSS Inc., Chicago, USA) statistical software was used to analyse the data which were analyzed using the Wilcoxon paired test with Bonferroni correction of significance, Spearman correlation analysis and Mann-Whitney test. Values at a $< 5\%$ level ($P < 0.05$) were considered statistically significant.

RESULTS

Overall, 53 patients (male=34; female=19) after KT were enrolled in the study. The mean age of participants was 54 ± 10 years (range 29–70 years). There were no differences in gender ($P=0.160$), age ($P=0.520$), time on dialysis prior to KT ($P=0.736$) or body mass index ($P=0.612$). The patient demographic data are summarized in Table 1. There were also no statistically significant differences in kidney function parameters (creatinine and GFR), lipid metabolism (TAG, total, LDL- and HDL-cholesterol, Apo AI and Apo B) and OS markers (ox-LDL, TAS and AOPP) in groups A and B before KT (Table 2).

All participants completed the 12-month study. After KT, there was an improvement in renal function and all patients had a stabilized and well-functioning graft. The urea concentration decreased from $15.7 \pm 6.8 \text{ mmol/l}$ at baseline to $8.2 \pm 2.6 \text{ mmol/l}$ at month 12 in Group A ($P < 0.0001$) and from $15.2 \pm 5.3 \text{ mmol/l}$ at baseline to $8.2 \pm 3.0 \text{ mmol/l}$ at month 12 in Group B ($P=0.0001$). The creatinine decreased from $624.5 \pm 186.3 \mu\text{mol/l}$ to $122.0 \pm 28.9 \mu\text{mol/l}$ at month 12 in Group A ($P < 0.0001$).

Table 2. Development of selected laboratory parameters after KT in Group A (cyclosporine) and Group B (tacrolimus).

	Before KT			6 months after KT			12 months after KT		
	Group A	Group B	Statistical significance	Group A	Group B	Statistical significance	Group A	Group B	Statistical significance
Creatinine ($\mu\text{mol/L}$)	624.5 ± 186.3	666.8 ± 161.7	0.381	119 ± 21.7	128.4 ± 30.6	0.274	122.0 ± 28.9	122.7 ± 28.6	0.957
GFR (MDRD) (ml/s)	0.15 ± 0.06	0.15 ± 0.06	1.000	0.92 ± 0.19	0.95 ± 0.35	0.741	0.92 ± 0.22	0.99 ± 0.36	0.688
Ox-LDL (U/L)	69.2 ± 32.9	62.9 ± 29.7	0.487	68.7 ± 33.1	62.6 ± 22.1	0.792	65.1 ± 17.1	61.4 ± 14.6	0.545
AOPP ($\mu\text{mol/L}$)	233.0 ± 159.6	180.5 ± 90.0	0.466	148.7 ± 83.5	124.6 ± 83.4	0.307	156.5 ± 90.1	123.9 ± 37.7	0.123
TAS (mmol/L)	1.87 ± 0.31	1.87 ± 0.51	0.348	1.85 ± 0.24	1.76 ± 0.24	0.087	1.68 ± 0.25	1.68 ± 0.20	0.932
Total cholesterol (mmol/L)	5.3 ± 1.4	4.6 ± 0.9	0.108	5.7 ± 1.0	5.2 ± 1.2	0.091	5.3 ± 1.0	4.9 ± 0.6	0.036
LDL cholesterol (mmol/L)	2.6 ± 1.1	2.4 ± 0.7	0.830	3.0 ± 0.9	2.6 ± 0.9	0.149	2.8 ± 1.0	2.5 ± 0.6	0.140
HDL cholesterol (mmol/L)	1.4 ± 0.6	1.4 ± 0.4	0.844	1.8 ± 0.7	1.6 ± 0.7	0.637	1.6 ± 0.7	1.6 ± 0.5	0.688
Triglycerides (mmol/L)	2.9 ± 2.1	1.9 ± 1.1	0.124	2.2 ± 1.1	2.0 ± 0.9	0.227	2.0 ± 1.1	1.8 ± 0.6	0.442
Apolipoprotein A-I (g/L)	1.48 ± 0.37	1.46 ± 0.32	0.838	1.59 ± 0.39	1.61 ± 0.48	0.917	1.57 ± 0.42	1.54 ± 0.38	0.912
Apolipoprotein B (g/L)	0.91 ± 0.29	0.77 ± 0.19	0.208	0.89 ± 0.22	0.84 ± 0.25	0.290	0.87 ± 0.21	0.78 ± 0.22	0.193

Fig. 1. Ox-LDL levels before KT and 12 months after KT in Group A (cyclosporine A) and Group B (tacrolimus).

Fig. 2. AOPP levels before KT and 12 months after KT in Group A (cyclosporine A) and Group B (tacrolimus).

Fig. 3. TAS levels before KT and 12 months after KT in Group A (cyclosporine A) and Group B (tacrolimus).

and from $666.8 \pm 161.7 \mu\text{mol/l}$ at baseline to $122.7 \pm 28.6 \mu\text{mol/l}$ at month 12 in Group B ($P < 0.0001$). GFR increased from $0.15 \pm 0.06 \text{ ml/s}$ at baseline to $0.92 \pm 0.22 \text{ ml/s}$ at month 12 in Group A ($P < 0.0001$) and from $0.15 \pm 0.06 \text{ ml/s}$ at baseline to $0.99 \pm 0.36 \text{ ml/s}$ at month 12 in Group B ($P < 0.0001$). No significant differences in graft function or other laboratory parameters were found between CyA and Tac (at 6 and 12 month after KT), see Table 2.

The values of selected parameters of lipid metabolism before KT and after KT (at 6 and 12 month) in Group A and Group B including statistical differences between groups are summarized in Table 2. The parameters of lipid metabolism were not statistically different with respect to immunosuppressive treatment regimens. Only total cholesterol was significantly lower in Group B than in Group A ($P = 0.036$) at month 12 after KT.

The time course of ox-LDL, AOPP and TAS over the 12-month study in the groups are shown in Table 3 and Fig. 1-3. The Wilcoxon paired test with Bonferroni correction of significance revealed no significant changes in ox-LDL during the whole 12 months study period after KT in either group in comparison to ox-LDL before KT. There was no significant difference in ox-LDL between patients treated with CyA or Tac (Fig. 1, Table 2).

In whole group of 53 patients the AOPP significantly decreased in each monitored time interval after KT (on day 1 ($P < 0.0001$), day 7 ($P < 0.0001$), at month 1 ($P = 0.007$), at month 6 ($P = 0.001$) and month 12 ($P = 0.007$)) compared to baseline level. The Wilcoxon paired test with Bonferroni correction of significance showed a significant reduction in AOPP on day 1 in Group A ($P = 0.0001$) and Group B ($P = 0.0003$), on day 7 in Group A ($P = 0.002$) and Group B ($P = 0.005$), at month 1 in Group B ($P = 0.037$), at month 6 in Group A ($P = 0.026$) after KT in comparison to level before KT (Table 3). Twelve months after KT, the AOPP significantly decreased in Group A ($P = 0.025$) and also in Group B ($P = 0.019$) compared to level before KT (Fig. 2). The nonparametric Mann-Whitney test showed no statistically significant differences in the AOPP level between patients treated with CyA or Tac at month 6 ($P = 0.307$) and at month 12 ($P = 0.123$), see Table 2.

The significant diminution in TAS on day 1 in Group A ($P = 0.0001$) and Group B ($P = 0.003$), on day 7 in Group A ($P = 0.002$) and Group B ($P = 0.005$), at month 1 in Group B ($P = 0.037$) and at month 6 in Group A ($P = 0.026$) in comparison to levels before KT was found using the Wilcoxon paired test with Bonferroni correction (Table 3). One year after KT, the TAS level significantly decreased in Group A ($P = 0.030$) but not in Group B ($P = 0.157$) compared to level before KT (Fig. 3). The TAS level of all participants was significantly decreased on day 1 ($P < 0.0001$), day 7 ($P = 0.003$), at month 1 ($P = 0.002$) and at month 12 ($P = 0.033$) compared to baseline levels. The Mann-Whitney test showed no statistically significant difference in TAS between patients treated with CyA or Tac either in month 6 ($P = 0.087$) or month 12 ($P = 0.932$), see Table 3.

The Spearman correlation analysis showed no correlation between ox-LDL, AOPP or TAS and other measured biochemical or hematological parameters in either group.

Table 3. Development of ox-LDL, AOPP and TAS after KT in Group A (cyclosporine) and Group B (tacrolimus).

		Before KT	Day 1	Day 7	Month 1	Month 3	Month 6	Month 12
Patients treated with cyclosporine A (Group A)								
ox-LDL (U/L)	Median	57.4	49.4	57.5	70.2	63.9	64.8	61.0
	Mean	69.2	51.3	62.7	76.0	72.0	68.7	65.1
	SD	32.9	29.0	21.4	31.1	29.1	33.1	17.1
AOPP (μmol/L)	Median	178.0	72.7	115.0	160.1	150.4	126.4	144.4
	Mean	233.0	84.0	116.4	203.0	161.2	148.7	156.5
	SD	159.6	62.2	89.1	159.2	82.8	83.5	90.1
TAS (mmo/L)	Median	1.89	1.41	1.67	1.62	1.67	1.85	1.70
	Mean	1.87	1.47	1.61	1.64	1.76	1.85	1.69
	SD	0.31	0.28	0.37	0.33	0.40	0.27	0.25
Patients treated with tacrolimus (Group B)								
ox-LDL (U/l)	Median	54.3	35.0	52.4	62.7	59.7	64.0	61.0
	Mean	62.9	42.0	55.9	64.7	71.4	62.6	61.4
	SD	29.7	18.2	23.3	20.5	32.0	22.1	14.6
AOPP (μmol/l)	Median	173.8	90.4	94.6	128.2	144.2	107.8	123.0
	Mean	180.5	88.2	94.7	130.5	158.1	124.6	123.9
	SD	90.0	50.8	64.6	77.7	105.5	83.8	37.7
TAS (mmol/l)	Median	1.80	1.52	1.58	1.54	1.67	1.76	1.66
	Mean	1.87	1.55	1.65	1.62	1.72	1.76	1.68
	SD	0.51	0.24	0.35	0.32	0.25	0.24	0.20

There was no correlation between ox-LDL, AOPP or TAS and GFR.

DISCUSSION

KT is the treatment of choice for chronic renal failure and is associated with better survival and life quality than hemodialysis or peritoneal dialysis. However, cardiovascular mortality in renal transplant patients remains considerably higher than in the general population. The determinants that lead to atherosclerosis in renal transplant recipients are similar to those in the general population. Many of these factors, such as dyslipidemia/hyperlipidemia, hypertension, hyperhomocysteinemia and diabetes mellitus are exacerbated by the immunosuppressive drugs administered to prevent allograft rejection, but there is a paucity of data concerning the effects of these drugs on oxidative status and ox-LDL after KT. The oxidative modified LDL play an important role in the onset and progression of atherogenesis. Ox-LDL are recognized by a specific receptor on the macrophage surface, which contribute to foam cell generation, endothelial dysfunction and inflammatory processes^{6,10}.

LDLs are sensitive to oxidation and therefore are often used to monitor the antioxidant balance in the body. *In vitro*, it is possible to observe the susceptibility of LDL to oxidation induced by copper ions as lag time. *In vivo* it can be measured as levels of ox-LDL or monoclonal antibodies against ox-LDL in plasma^{4,19,20}.

Investigation of the influence of calcineurin inhibitors

on lipid peroxidation is based predominantly on measurement of *in vitro* LDL oxidability but the results are quite different and controversial. Kandoussi et al. showed that CyA did not change the lag phase of oxidability LDL isolated from healthy volunteers²¹. In studies performed by Ghanem et al. and Sutherland et al. it was found that susceptibility to *in vitro* oxidation of LDL was higher in CyA treated patients than in healthy subjects^{22,23}. Similar results were published by Cofan et al.²⁴ and Bakar et al.²⁵. These authors showed that treatment with Tac and CyA congenerous increases susceptibility of LDL to *in vitro* oxidation in comparison with healthy subjects^{24,25}. On the other hand, it was found that LDL of Tac-treated patients are less susceptible to oxidation than LDL of CyA-treated patients²⁶. However, other authors described no differences in susceptibility to LDL oxidation between Tac-treated patients and the general population²⁷.

Martínez-Castelao et al. and Cofan et al. confirmed that Tac in previously CyA-treated patients increased the resistance to *in vitro* oxidation of LDL (ref.²⁸) and decreased *in vivo* formation of ox-LDL (ref.¹⁸). In contrast, other authors found higher *in vitro* oxidation of LDL in Tac-treated patients compared to patients treated with CyA supplemented with α -tocopherol (Neoral), which is a known antioxidant²⁹. However, this observation was not confirmed by other authors²¹.

To the best of our knowledge, we present the first randomized and prospectively designated study evaluating the influence of the calcineurin inhibitors CyA and Tac on plasma levels of ox-LDL in transplanted patients over a 12-month period after KT. We found no statisti-

cally significant changes in ox-LDL during the monitored period compared to levels before KT. We also found no significant difference in ox-LDL between patients treated with CyA or Tac.

An important role of AOPP in inflammation and atherosclerosis has been demonstrated. The accumulation of AOPP may accelerate ox-LDL formation through enhanced OS, increased plasma TNF- α and other inflammatory mediators, enhanced macrophage invasion and smooth muscle cell proliferation in the arterial wall. Plasma AOPP elevation significantly increases atherosclerotic plaque in hypercholesterolemic rabbits and accelerates progression of atherosclerosis³⁰. Of particular clinical importance is the finding that AOPPs are highly correlated with carotid intima media thickness in end-stage renal disease³¹ and in peritoneal dialysis patients^{32,33}. Moreover, AOPP elevation has been reported as an independent risk factor for coronary artery disease in nonuremic patients³⁴.

In an earlier 6-month study, we described significantly decreased AOPPs in both CyA and Tac treated patients in comparison with those before KT. Nevertheless, AOPP did not reach the normal range even though the graft function was normal³⁵. In this 12-month study, we confirmed our previous results and the AOPP decrease lasted. Our results are not in accord with de Cal et al., who reported that AOPP after KT remained significantly lower during the first postoperative month compared with the levels before KT and then gradually increased to levels similar to those before the KT (ref.³⁶). Likewise, we did not confirm the findings of Antolini et al. that AOPPs are inversely correlated to creatinine clearance and that normalization of parameters of OS after KT is only possible if the graft function is normal³⁷. In our study, normalization of AOPP in patients with normal graft function after successful KT was not observed. We found no significant difference in AOPP between patients treated with CyA or Tac.

In our groups of patients, TAS before KT was higher than the reference values. Immediately after KT, the level of TAS in both treatment groups significantly decreased. The marked decline in TAS on day 1 after KT could be due to the blood loss and hemodilution during the surgery. TAS then slowly increased, but they were still significantly lower 12 months after KT in comparison with levels before KT. The interpretation of elevated TAS values during chronic renal failure needs very careful attention^{9,37}. TAS is a global indirect marker of the antioxidant capacity of organism. It reflects the long-term stress in the organism and the ability of antioxidant defence system to cope with it. TAS is markedly influenced by albumin and may be also affected by decreased excretion of low molecular substance (uric acid) in cases of decreased GFR. TAS values seem to be insufficiently sensitive for monitoring of OS in patients after KT. We found no statistically significant differences in TAS values in relation to treatment regimens.

CONCLUSION

We found no statistically significant changes in ox-LDL during the 12-month period after KT in comparison to levels before transplantation. No statistically significant differences in ox-LDL were found between patients treated with CyA or Tac either. The results demonstrated that after successful KT, the levels of AOPP significantly decreased over a 12-month period compared with those before KT. However, AOPP did not reach the normal range even if the graft function was normal. TAS values seem to be insufficiently sensitive for monitoring OS in patients after KT. We found no statistically significant difference in graft function, OS or other laboratory parameters between patients on CyA and Tac. Our findings suggest that AOPPs are better predictors of OS than ox-LDL in patients after KT.

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ABBREVIATIONS

AOPP, advanced oxidation protein products; Apo AI, apolipoprotein A-I; Apo B, apolipoprotein B; CKD, chronic kidney disease; CRP, C-reactive protein; CyA, cyclosporin A; GFR, glomerular filtration rate; HDL, high-density lipoproteins; KT, kidney transplantation; LDL, low-density lipoproteins; OS, oxidative stress; ox-LDL, oxidized low-density lipoproteins; PBS, phosphate-buffered saline; ROS, reactive oxygen species; Tac, tacrolimus; TAG, triglycerides; TAS, total antioxidant status.

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