Uric Acid and Endothelial Dysfunction in Kidney Transplant Recipients

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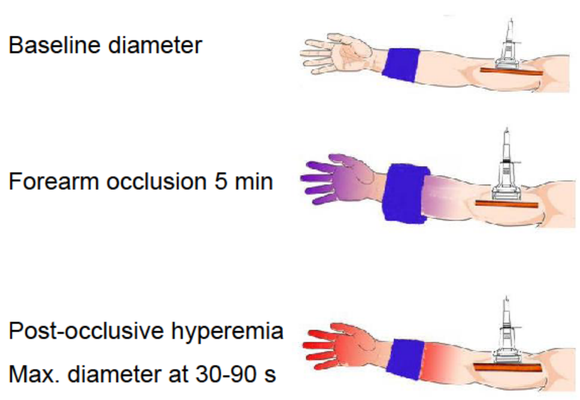
INTRODUCTION

Uric acid is associated with increased mortality in kidney transplant recipients[1]. It has been suggested that uric acid metabolism may induce endothelial dysfunction[2]. We hypothesized 1) that there was an association between uric acid and endothelial dysfunction, and 2) that there was an association between endothelial dysfunction and mortality risk score[3].

PATIENTS AND METHODS

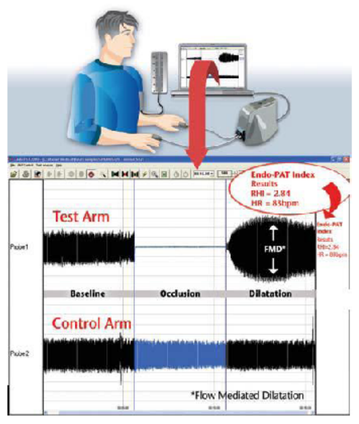
Oslo University Hospital performs all solid organ transplantations in Norway, serves a population of 5 million people and annnually performs 250-300 kidney transplantations. Most patients attend an outpatient clinic for the first 10 weeks. During 2012 we invited adult (ie. >16 yrs) kidney transplant recipients or simultaneous kidney-pancreas recipients at week 9 or 10 after transplantation to this study. 145 of 269 (54%) eligible patients had available endothelial function data, reasons for not participating were 31 declined concent, 37 early discharged, 30 no capacity, 19 other reasons and 7 examinations technically unsuccessful.

Brachial artery flow mediated dilatation (FMD)



FMD% = 100*(Max-Baseline)/Baseline

Fingertip peripheral arterial tone (PAT)



Post-occlusive vasodilatation quantified as log-transformed reactive hyperemia index (**LnRHI**)

Two validated measures of endothelial vasodilatatory function were obtained simultaneously (Figure). After a brief stasis of blood to the forearm (ie 5 min) reactive hyperemia occurs and stimulates endothelial dependent vasodilatation. The response is typically reduced in the presence of traditional cardiovascular risk factors. Brachial artery flow-mediated dilatation (FMD) was measured with a 12 MHz linear array probe (Zonare Medical Systems, California, USA) and the fingertip vasodilatation ("peripheral arterial tone" - PAT) was measured with the EndoPAT 2000 (Itamar Medical, Caesarea, Israel). Mortality risk score was calculated from a validated formula[3], $\sum\beta_i X_i - \sum\beta_i \tilde{u}_i$, where β_i and $\tilde{u}_i$ are the regression coefficient and mean level of risk factor *i* from the prognosis development cohort[3] and X_i the level of risk factor *i* of a patient, including as risk factors age, coronary heart disease, smoking, creatinine, diabetes and time in renal replacement therapy. The association between serum uric acid and endothelial function was analyzed in linear regression models.

Age, yrs	54.9 (12.9)
Women, n (%)	50 (34.5)
Body mass index, kg/m^2	25.0 (3.8)
Coronary vascular disease, n (%)	35 (24.1)
Diabetes or NODAT, (excl SPK), n (%)	41 (28.3)
Simultaneous pancreas tx, n (%)	9 (6.2)
eGFR, ml/min/1.73m^2	55.4 (18.8)
Uric acid, µmol/L	384 (101)
FMD%	4.4 (3.4)
LnRHI	0.83 (0.34)

Table 1. Baseline characteristics, n=145.
Means (SD) or proportions.

	FMD		PAT	
	Unadjusted	Adjusted	Unadjusted	Adjusted
Age, per 10 yrs	-0.96***	-0.88***	0.01	0.01
Female vs. male	1.27*	0.99	0.10	0.12
Uric acid, per 50 µmol/L	-0.39**	-0.22	0.003	0.01
eGFR, per 10 ml/min/1.73m^2	0.40**	0.11	-0.004	0.003

Table 2. Determinants of endothelial function.
Shown are the beta coefficients. *p<0.05, **p<0.01, ***p<0.001.

RESULTS

Baseline characteristics for the 145 patients with available endothelial function measurements are shown in Table 1. Uric acid was associated negatively with FMD in a crude and an age- and gender adjusted model, while not after adjusting for eGFR (Table 2). No association was shown between uric acid and PAT. Both FMD and PAT correlated with mortality risk score in adjusted models (Table 3). There was no correlation between FMD and PAT (r=0.09, p=0.27).

	FMD	PAT
Crude	-0.43***	-0.05
Adjusted age, gender	-0.23**	-0.17*
Adjusted age, gender, eGFR	-0.20*	-0.19*

Table 3. Correlation with mortality risk score.
Pearson's r and partial correlations. *p<0.05, **p<0.01, ***p<0.001.

CONCLUSION

Serum uric acid was neither associated with FMD nor PAT in kidey transplant recipients. There were significant associations between endothelial function indices and mortality risk score.

REFERENCES

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