Adipokines and Nutritional Status in Kidney Transplant Recipients

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ABSTRACT

Background. Obesity and disturbances of adipokine concentrations are often recognized in kidney transplant recipients (KTRs). Leptin plays a key role in regulating energy intake and expenditure, including appetite and hunger, metabolism, and behavior. Adiponectin modulates certain metabolic processes, including glucose regulation and fatty acid oxidation, and exerts some weight-reduction effects. Visfatin has various functions, including the promotion of vascular smooth muscle cell maturation and inhibition of neutrophil apoptosis. It also activates insulin receptors and has insulin-mimetic effects, lowering blood glucose and improving insulin sensitivity. The aim of this study was to evaluate the prevalence of leptin, adiponectin, and visfatin and nutritional status abnormalities in stable KTRs.

Methods. Eighty KTRs aged 52.4 ± 14.0 years participated in the study. Nutritional status was determined with the use of the 7-point Subjective Global Assessment (SGA), anthropometric measurements (bioimpedance analysis), and serum concentration. Concentrations of leptin, adiponectin, and visfatin were measured with the use of enzyme-linked immunosorbent assay.

Results. Mean time after transplantation and estimated glomerular filtration rate (eGFR; Modification of Diet in Renal Disease formula) were 82.5 ± 56.5 months and 42.0 ± 15.0 mL/min/1.73 m^2, respectively; 29 (36.2%) of the KTRs, despite high body mass index (BMI ≥25 kg/m^2), presented mild malnutrition (SGA ≤5). BMI, content of body fat, and leptin concentration correlated positively with time from transplantation and negatively with eGFR. Additionally, patients with BMI ≥25 kg/m^2 presented significantly higher leptin-to-adiponectin ratios compared with lean patients (3.5 vs 1.1, respectively; $P < .05$). KTRs with eGFR ≥60 mL/min/1.73 m^2 presented significantly lower leptin concentration and BMI.

Conclusions. Despite high BMI, mild malnutrition was present in one-third of KTRs. Increased BMI, abdominal obesity, and high leptin concentration were aggravated by time from transplantation and deterioration of graft function. Overweight/obesity and incorrect leptin-to-adiponectin ratio could increase cardiovascular risk in KTRs.

WEIGHT gain is quite common in the post-transplantation period. The increase of body weight after kidney transplantation is associated with several factors, such as improvement of appetite, loss of the dietary restrictions of advanced kidney disease, and the effect of immunosuppressive therapy. Mean weight gains seem to fall within the range of ~10% at 1 year and slightly greater thereafter [1]. Overweight and obesity are associated with increased risk of metabolic disturbances, and in consequence hyperglycemia, hypertension, hyperlipidemia, and high risk of cardiovascular diseases (CVDs). The most common cause of allograft loss is death with functioning graft secondary to CVD [2,3].

Adipose tissue is a place of synthesis of several metabolically active proteins called adipokines. Those proteins play an important role in the regulation of metabolic processes, thus having auto- and paracrine functions [4–8].

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Table 1. Basic Characteristics of the Studied Kidney Transplant Recipients

Parameters	All ($n = 80$)	BMI 18.5–24.99 kg/m^2 ($n = 35$)	BMI ≥25 kg/m^2 ($n = 45$)	eGFR <60 kg/m^2 ($n = 55$)	eGFR ≥60 kg/m^2 ($n = 25$)
Age (y)	52.4 ± 13.9	54.2 ± 15.7	54.8 ± 11.9	54.1 ± 14.1	51.7 ± 13.8
M/F	45/35	20/15	25/20	16/9	29/26
BMI (kg/m^2)	25.7 ± 4.2	22.0 ± 1.9	28.6 ± 3.0	24.3 ± 3.6	26.3 ± 4.3
eGFR (mL/min/1.73 m^2)	42.0 ± 15.9	44.6 ± 15.1	44.3 ± 14.6	37.4 ± 12.5	≥60
Time from transplantation (mo)	82.5 ± 56.5	64.9 ± 45.2	88.7 ± 61.2	78.2 ± 58.5	78.1 ± 49.9

Note. Data are presented as mean ± SD.
Abbreviations: BMI, body mass index; eGFR, estimated glomerular filtration rate.

Elevated leptin levels and a decreased level of adiponectin are characteristic for the metabolic syndrome and correlated with high risk of CVDs [9,10]. Adiponectin may lower the risk of CVD by improving insulin sensitivity and blood lipid levels, as suggested by data from nonhuman and human studies [11]. Nicoletto et al [12] showed that leptin levels and homeostasis-model assessment of insulin resistance decrease in the immediate post-transplantation period and remain reduced for at least 1 year. Five years after transplantation, leptin, insulin resistance, percentage of body fat (%F), and lipids have a profile similar to those in the pre-transplantation period. This metabolic profile is possibly associated with the elevated incidence of cardiovascular diseases observed in the late post-transplantation period [12].

Visfatin has various functions, including the promotion of vascular smooth muscle cell maturation and inhibition of neutrophil apoptosis. It also activates insulin receptors and has insulin-mimetic effects, lowering blood glucose and improving insulin sensitivity. Visfatin up-regulates proinflammatory cytokines in monocytes, including interleukin (IL) 1β, tumor necrosis factor α, and IL-6 [13].

Despite the results of the aforementioned studies, the impact of weight changes and adipokines levels on patients and allograft survival remains unclear. The present study aimed to evaluate the prevalence of leptin, adiponectin, and visfatin and nutritional status abnormalities in stable kidney transplant recipients (KTRs).

METHODS

Eighty (45 male, 35 female) stable KTRs aged 52.4 ± 14.0 years participated in the study. They were recruited from the Department of Nephrology, Transplantology, and Internal Medicine in Gdańsk. All patients were clinically stable with no clinical symptoms of infection, 95% were treated with antihypertensive drugs, and 25% suffered from stable ischemic heart disease.

The nutritional status was estimated with the use of the 7-point Subjective Global Assessment (SGA). Results of SGA estimation were scored as: 7–6, good nutrition; 5–3, mild malnutrition; and 2–1, severe malnutrition [12].

Anthropometric Measurements

The following measurements were determined:

Body mass (kg), waist circumference (cm), and hip circumference (cm).

Body mass index (BMI), estimated according to the current body mass/height^2 (kg/m^2). BMI 25–30 kg/m^2 was called overweight, BMI ≥30 kg/m^2 was called obesity.

Waist-hip ratio (WHR), estimated based on waist to hip circumferences ratio.

Body composition, with the use of multifrequency bioimpedance analysis (BIA; Fresenius, Germany).

Laboratory Assay

The blood samples were taken after 12 hours of overnight fasting, and the levels of the following compounds were measured in plasma:

Leptin, with the use of enzyme-linked immunosorbent assay (ELISA; DRG, Germany)

Adiponectin, ELISA (Linco Research, USA)

Visfatin, ELISA (Biovendor R&D, Germany)

C-Reactive protein (CRP), ELISA (DRG)

Serum albumin (s-albumin) with the use of the Hitachi 911 analyzer (Boehringer, Mannheim, Germany).

Statistical Analysis

Statistical analysis was performed with the use of Statistica version 9.0 for Windows (Krakow, Poland). All data are expressed as mean ± SD. Comparisons of the groups were examined with the use of Student test and Mann-Whitney U tests. Pearson correlation test was used to determine the relationship between continuous variables, and Spearman correlation test was used for nonparametric measure of statistical dependence between 2 variables. A P value of <.05 was considered to be statistically significant for all analyses.

RESULTS

The basic characteristics of the studied patients are presented in Table 1. Mean time after transplantation and eGFR were 82.5 ± 56.5 months and 42.0 ± 15.0 mL/min/1.73 m^2, respectively.

Nutritional Status

According to the 7-point SGA score, nutritional status was good (6–7 points) in 48% of the patients; 52% were mildly malnourished (4–5 points).

Mean albumin level in KTRs was 42.0 ± 3.1 g/L (range, 38.0–45.1 g/L); According to the albumin level, 29 (36.2%) of the KTRs, despite high BMI (≥25 kg/m^2), presented mild malnutrition.

SGA score correlated positively with albumin concentration (Spearman $R = 0.36$; $P \leq .05$) and negatively with such parameters as BMI, %F (Spearman $R = -0.3$; $P < .01$), and time after transplantation (Spearman $R = -0.3$;