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# Cardiometabolic Risk Factors in Pediatric Kidney Transplant Recipients

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## What is already known on this topic?

- *Kidney transplantation reverses uremic abnormalities, but cardiovascular disease remains a concern for clinicians due to obesity, hypertension, diabetes, and metabolic syndrome. The prevalence of obesity, and consequently metabolic syndrome, is common among patients receiving kidney transplants. Only limited evidence supports the notion that pediatric kidney transplant recipients are at increased risk for cardiometabolic complications.*

## What this study adds on this topic?

- *Pediatric kidney transplant recipients are at increased risk for metabolic syndrome and for left ventricular hypertrophy. Left ventricular hypertrophy is more prevalent in pediatric kidney transplant recipients with metabolic syndrome. After transplantation, the increase in body mass index contributes significantly to the development of the metabolic syndrome as well as left ventricular hypertrophy.*

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## ABSTRACT

**Objective:** There is an increased risk of obesity and metabolic syndrome among kidney transplant recipients, which adversely affects cardiovascular and renal outcomes in these patients. The present study aims to investigate the prevalence of metabolic syndrome in pediatric kidney transplant recipients and the associations of metabolic syndrome with cardiovascular disease and graft function.

**Materials and Methods:** This cross-sectional, single-center study included 52 kidney transplant recipients (27 males) transplanted before 18 years of age. All subjects underwent a comprehensive assessment that included anthropometric and blood pressure measurements and laboratory tests. Metabolic syndrome was defined based on the recent recommendations of the Pediatric Renal Nutrition Taskforce. Left ventricular hypertrophy was assessed as a risk factor for cardiovascular disease, and estimated glomerular filtration rate was assessed to determine graft function.

**Results:** The median age of patients was 15.9 (13.8;18.4) years, and the median follow-up time was 35.5 (20.0;62;0) months after transplantation. Nineteen patients (36.5%) were obese or overweight, 43 (83%) had hypertension or controlled hypertension, 23 (44%) had dyslipidemia, and 9 (17%) had hyperglycemia. Ten patients (19.2%) were diagnosed with metabolic syndrome. Twenty-eight patients (54%) had left ventricular hypertrophy. The prevalence of left ventricular hypertrophy was higher in patients with metabolic syndrome than in those without metabolic syndrome (90% vs. 45%, $P = .014$), whereas estimated glomerular filtration rate did not differ between the 2 groups.

**Conclusion:** Cardiometabolic risk factors are common in pediatric kidney transplant recipients. Approximately one-fifth of patients have metabolic syndrome, and left ventricular hypertrophy is much more common among patients with metabolic syndrome. However, there is no relationship between metabolic syndrome and graft dysfunction.

**Keywords:** Cardiometabolic, cardiovascular disease, children, kidney transplantation, left ventricular hypertrophy, metabolic syndrome, pediatric, obesity

## INTRODUCTION

Metabolic syndrome (MS) is a common problem after kidney transplantation and is mainly related to post-transplant weight gain. There is evidence that immunosuppressive drugs, especially tacrolimus and mammalian target of rapamycin inhibitor (mTORi), have a significant impact on the pathophysiology of MS.[1] Steroid use after kidney transplantation is strongly associated with the development of MS.[2] In addition, specific kidney diseases

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such as cystinosis and cystic kidney disease may contribute to abnormal glucose metabolism.[1]

The prevalence of MS in pediatric populations varies according to study populations and diagnostic criteria. In pediatric patients who have received kidney transplant (KTx), the prevalence has been reported to be 25%-38%,[3,4] which is higher than the prevalence of 4%-10% in healthy children.[5,6] Evidence of the deleterious effects of obesity on kidney function and the association between obesity and cardiovascular mortality even in healthy children and adolescents underscore the importance of managing the components of MS as modifiable treatment targets.[7,8] Therefore, MS is of particular concern because it has been associated with cardiovascular disease and worsening graft function in KTx recipients.[9]

The aim of the present study is to investigate the prevalence of MS in pediatric KTx recipients based on the most recent recommendations of the Pediatric Renal Nutrition Taskforce (PRNT) in 2022.[10] The secondary endpoints of the study are to determine the association of MS with cardiovascular disease and graft function.

## MATERIALS AND METHODS

### Study Design and Population

For this cross-sectional, single-center study, 73 KTx recipients transplanted before the age of 18 years between 2011 and 2019 and followed up in the Department of Pediatric Nephrology, İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, İstanbul, Turkey, were reviewed. The exclusion criteria were as follows: (i) patients less than 10 years old or older than 21 years old at the time of the study, (ii) patients with a glomerular filtration rate (GFR) of less than 30 mL/min/1.73 $m^2$ calculated according to the modified Schwartz formula,[11] (iii) patients with a follow-up time of less than 1 year after transplantation, (iv) patients with known cardiovascular disease, (v) patients with no valid measurements or examinations, or (vi) patients or their parents who did not agree to participate in the study. Finally, 52 KTx recipients were eligible for enrollment in the study. The cross-sectional evaluation of the study was carried out between 2018 and 2020 after the Ethics Committee of the University of İstanbul University-Cerrahpaşa approved the study (51437/07.02.2018). All examinations of the patients were performed in accordance with good medical and laboratory practices and the recommendations of the Declaration of Helsinki on Biomedical Research Involving Human Subjects. Informed consent was obtained from each eligible patient or their parents/caregivers.

### Definitions

Metabolic syndrome was defined based on PRNT recommendations for the assessment and management of MS in children with chronic kidney disease (CKD), including children on chronic dialysis and children living with a KTx.[10] Accordingly, the definition of MS was as follows: overweight [body mass index (BMI) > +1 SD for height–age) or obese (BMI > +2 SD for height–age) plus at least 2 of the following cardiovascular risk factors: (i) office systolic and/or diastolic blood pressure (BP) ≥90th percentile for age, sex, and height or ≥130/80 mmHg or use of antihypertensive medication, (ii) fasting triglycerides (TGs) ≥100 mg/dL, (iii) fasting high-density lipoprotein (HDL) <40 mg/dL, and (iv) fasting plasma glucose (FPG) ≥100 mg/dL or known new-onset diabetes mellitus after transplantation.[10]

### Data Collection

Anthropometric and BP measurements and laboratory tests were performed simultaneously in each patient. The anthropometric indices (weight and height) of the subjects were measured using standard techniques. The BMI of each subject was calculated by dividing the body weight in kilograms by height in meters squared (kg/$m^2$). Waist circumference was measured in the standing position using a non-elastic, flexible tape measure between the lowest rib and the top of the iliac crest. The SD values for weight, height, BMI for height–age, and waist circumference of a single measurement were calculated based on the references for Turkish children and adolescents.[12,13] Office BP was measured with an appropriately sized cuff using the auscultatory method. The mean of 3 measurements of systolic and diastolic BPs was calculated for each patient, and then SD scores (SDS) were calculated based on normal values adjusted for age, gender, and height.[14]

The following biochemical parameters were measured by routine laboratory methods: FPG, fasting TGs, HDL, LDL, creatinine, 25-OH vitamin D, and insulin. Based on FPG and insulin levels, the homeostasis model assessment of insulin resistance (HOMA-IR) was calculated as an estimation of insulin resistance [HOMA-IR = FPG (mg/dL) × fasting plasma insulin (μU/mL)/405].[15] Patients' medical records were reviewed for data, including age, sex, primary kidney disease, modality and duration of dialysis, donor and transplant characteristics (donor type and age, number of HLA mismatches, age at transplantation, follow-up time after transplantation, and history of rejection), and medications.

The presence of left ventricular hypertrophy (LVH) as a risk factor for cardiovascular disease was assessed by an echocardiogram performed within the 3 months to the study period. M-mode measurement at the left ventricular minor axis was used to determine the left ventricular mass (LVM) using left ventricular end-diastolic dimension, interventricular septal thickness, and posterior wall thickness. The LVM was corrected by dividing it by the patient's height$^{2.7}$ and called the LVM index.[16] The LVH was defined as an LVM index greater than the 95th percentile.

### Statistical Analysis

Statistical analyses were performed using the Statistical Package for Social Sciences version 21.0 for Windows (IBM Corp.; Armonk, NY, USA). The characteristics of the study population were described using descriptive statistics. The Shapiro–Wilk test was used to test whether a continuous variable followed a normal distribution. Continuous data were then presented as median (25th, 75th percentile) and compared with the Mann–Whitney *U*-test. The categorical variables were presented as numbers (percentages) and compared using the chi-square test. Fisher's exact test was used in analyses where the chi-square assumptions were not met. Binary logistic regression analyses were performed to evaluate the risk factors for MS and LVH, using the variables that had $P < .2$ in the univariate analyses. A 2-tailed *P* value of less than .05 was considered statistically significant.

## RESULTS

### Study Population

The median (25th, 75th percentile) age of 52 pediatric KTx recipients was 15.9 (13.8, 18.4) years, and 52% of patients (n = 27) were male. Primary kidney diseases were congenital abnormalities of the kidney and urinary tract in 20 patients (38.5%), glomerular disease in 8 (15.4%), cystic kidney disease in 6 (11.5%), cystinosis in 7 (13.5%), neurogenic bladder in 4 (7.7%), hemolytic uremic syndrome in 1 (1.9%), and others in 6 (11.5%). The median age at transplantation was 12.0 (9.5, 15.2) years, and the median post-transplant follow-up time was 35.5 (20.0, 62.0) months. Two of the patients had a second transplant. Sixteen patients (30.8%) received a kidney from a deceased donor. All patients, except 2, were on maintenance immunosuppressive therapy that included steroids. At the time of the study, 45 patients (87%) were taking calcineurin inhibitors, of which 42 were on tacrolimus. A total of 9 patients (17%) were taking mTOR inhibitors.

In the entire cohort, 8 patients (15.4%) were obese and 11 (21.2%) were overweight. Forty-three patients (82.7%) had hypertension; of these, 33 had normal BP with antihypertensive medication, called as controlled hypertension. Twenty-three patients (44%) had dyslipidemia; of these, 17 (32.7%) had hypertriglyceridemia, and 10 (19.2%) had a low level of HDL. Nine patients (17.3%) had an elevated FPG level.

### Metabolic Syndrome and Its Risk Factors

Ten patients (19.2%) were identified as having MS based on the PRNT. All patients with MS were overweight or obese, all were hypertensive or on antihypertensive medications, 70% had high TGs, 40% had low HDL, and 20% had high FPG. As shown in Figure 1, patients with MS had a significantly higher prevalence of overweight/obesity ($P < .001$) and a higher prevalence of elevated TG ($P = .009$) than patients without MS; however, there were no differences in the prevalence of hypertension, low HDL, or elevated FPG between the 2 groups. In addition, there were significant differences between patients with and without MS in the values of BMI SDS and TG but not in BP SDS, HDL, or FPG (Table 1).

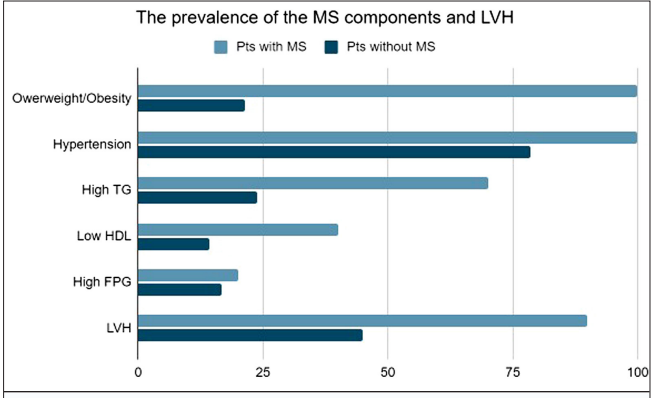


**Figure 1.** The prevalence of the components of metabolic syndrome (MS) and left ventricular hypertrophy (LVH) in patients with and without metabolic syndrome. There were significant differences between patients with and without MS in the prevalence of overweight/obesity (100% vs. 21%, $P < .001$), hypertriglyceridemia (70% vs. 24%, $P = .009$), and LVH (90% vs. 45%; $P = .014$), but no differences were observed in the prevalence of hypertension (100% vs. 79%, $P = .18$), low HDL (40% vs. 14%, $P = .09$), or a high FPG (20% vs. 17%, $P = .80$). FPG, fasting plasma glucose; HDL, high-density lipoprotein; LVH, left ventricular hypertrophy; TG, triglycerides.

**Table 1.** Clinical and Laboratory Components of Metabolic Syndrome (MS)

| | All Patients (n = 52) | Patients With MS (n = 10) | Patients Without MS (n = 42) | *P* |
|---|---|---|---|---|
| BMI SDS at study time | 0.51 (−0.22, 1.41) | 1.90 (1.22, 2.56) | 0.31 (−0.34, 0.87) | **<.001** |
| Systolic BP SDS | 1.17 (0.38, 1.93) | 1.41 (0.90, 2.28) | 0.98 (0.18, 1.89) | .16 |
| Diastolic BP SDS | 0.96 (0.32, 1.53) | 1.10 (0.74, 1.58) | 0.91 (0.20, 1.50) | .19 |
| Fasting TG, mg/dL | 100.0 (75.0, 145.5) | 176.0 (103.3, 227.5) | 95.0 (75.0, 126.8) | **.003** |
| Fasting HDL, mg/dL | 48.0 (41.3, 60.5) | 42.5 (35.3, 53.0) | 52.0 (45.0, 61.5) | .12 |
| FPG, mg/dL | 92.0 (84.3, 98.0 | 95.0 (92.0, 99.3) | 89.0 (82.5, 97.3) | .06 |

Data presented as median (25th, 75th) and compared with the Mann–Whitney *U*-test between patients with and without metabolic syndrome. BMI SDS was adjusted to height–age. $P < .05$ was considered statistically significant.
BMI, body mass index; BP, blood pressure; FPG, fasting plasma glucose; HDL, high-density lipoprotein; SDS, SD score; TG, triglycerides.

When possible risk factors for MS were assessed (Table 2), patients with MS showed a higher ΔBMI SDS ($P = .045$), a higher waist circumference SDS ($P = .015$), and a higher HOMA-IR ($P = .031$) compared with patients without MS. However, there were no significant differences between the 2 groups in age, sex, primary kidney disease, transplant age, BMI SDS at transplant, post-transplant follow-up time, rejection episode, cumulative steroid dose, or tacrolimus/mTORi use.

A binary logistic regression analysis that included parameters with a *P* value of less than .2, as shown in Table 2 (ΔBMI SDS, waist circumference SDS, cumulative steroid dose, HOMA-IR, and 25-OH vitamin D levels), revealed that the presence of MS was independently associated only with the ΔBMI SDS ($\beta$= 3.359, 95% CI: 1.189-696.280, $P = .039$).

### Association of Metabolic Syndrome with Left Ventricular Hypertrophy and Graft Function

The median LVMI was 39.2 (33.1-54.3) g/m$^{2.7}$, and a total of 28 patients (54%) had LVH. The median eGFR was 95.0 (66.5-121.8) mL/min/1.73 m$^2$. Patients with MS had a significantly higher rate of LVH than those without MS (90% vs. 45%; $P = .014$) (Figure 1); however, current eGFR or change in eGFR did not differ between the 2 groups (Table 2).

Regarding the factors influencing LVH, the frequency of male sex was significantly higher in patients with LVH than in those without LVH (64% vs. 29%, $P = .012$). In addition, patients with LVH tended to be older ($P = .08$) and had a higher ΔBMI SDS ($P = .08$) than patients without LVH; however, there were no significant differences between the 2 groups in terms of current BMI SDS, systolic or diastolic BP SDS, FPG or lipid levels, eGFR, or transplant-related factors. A binary logistic regression analysis that included age, male sex, and ΔBMI SDS showed that

**Table 2.** Clinical and Laboratory Characteristics of Patients With and Without Metabolic Syndrome (MS)

| | Patients With MS (n = 10) | Patients Without MS (n = 42) | *P* |
|---|---|---|---|
| *Demographics and anthropometric characteristics* | | | |
| Age, years | 15.2 (13.2, 18.3) | 16.2 (13.8, 18.5) | .34 |
| Male sex, n (%) | 5 (50) | 20 (47.6) | .89 |
| Prepubertal, n (%) | 1 (10) | 3 (7.5) | 1.00 |
| Height SDS at study time | −2.25 (−4.27, −1.70) | −2.31 (−3.18, −1.27) | .63 |
| BMI SDS at transplantation | −0.50 (−1.11, 1.78) | 0.01 (−1.39, 0.92) | .73 |
| ΔBMI SDS | 0.95 (0.14, 1.84) | 0.40 (−0.15, 0.86) | **.045** |
| WC SDS at study time | 1.72 (0.52, 3.05) | 0.75 (−0.45, 1.07) | **.015** |
| *KRT and transplant characteristics* | | | |
| Modality of pretransplant KRT, HD/PD/preemptive | 4/6/0 | 20/15/7 | .31 |
| Age at the initiation of KRT, years | 11.0 (5.7, 15.0) | 8.6 (5.2, 10.9) | .31 |
| Age at transplantation, years | 12.9 (9.3, 15.1) | 12.0 (9.6, 15.3) | .94 |
| Deceased donor, n (%) | 6 (60.0) | 30 (71.4) | .48 |
| Number of HLA mismatch | 3 (3, 4.5) | 3 (2, 3) | .41 |
| Follow-up time after transplantation, months | 31.2 (10.5, 60.6) | 40.8 (28.8, 63.9) | .21 |
| History of rejection, n (%) | 2 (20) | 9 (21.4) | 1.00 |
| Cumulative steroid dose, g/kg | 0.13 (0.07, 0.22) | 0.20 (0.11, 0.29) | .12 |
| Tacrolimus use, n (%) | 9 (90) | 33 (78.6) | .66 |
| mTORi use, n (%) | 2 (22.2) | 7 (16.7) | 1.00 |
| *Laboratory features* | | | |
| HOMA-IR | 3.8 (3.1, 5.1) | 2.6 (1.9, 4.1) | **.031** |
| 25-Hydroxyvitamin D3, ng/mL | 21.7 (19.9, 26.3) | 19.3 (15.0, 24.5) | .13 |
| eGFR at study time, mL/min/1.73m$^2$ | 95.0 (68.8, 122.5) | 89.0 (52.6, 116.3) | .53 |
| Change in eGFR, % | 1.5 (−30.2, 22.3) | 19.0 (−14.3, 45.0) | .22 |

Continuous data presented as median (25th, 75th) and compared with the Mann–Whitney *U*-test. Categorical variables compared with Fisher's exact test. BMI SDS adjusted to height-age. $P < .05$ was considered statistically significant.
BMI, body mass index; eGFR, estimated glomerular filtration rate; HD, hemodialysis; HLA, human leukocyte antigen; HOMA-IR, homeostatic model assessment of insulin resistance; KRT, kidney replacement therapy; MS, metabolic syndrome; mTORi, mammalian target of rapamycin inhibitor; PD, peritoneal dialysis; SDS, SD score; WC, waist circumference.

LVH was independently associated with male sex ($P = .004$) and ΔBMI SDS ($P = .044$) (Table 3).

## DISCUSSION

This cross-sectional study, which assessed MS using a very recent standardized criterion for the pediatric CKD population, shows that the prevalence of MS in children and adolescents with a functioning KTx is approximately 20%. This study also demonstrates a high prevalence of LVH of 54 % in children with KTx, and LVH is more prevalent in patients with MS. Finally, this study highlights that the increase in BMI after transplantation contributes to the development of MS as well as LVH.

The MS is of particular interest to KTx recipients. Several consensus reports have offered definitions of MS for both adults and children and adolescents.[17-19] In adult studies, the National Cholesterol Education Program Adult Treatment Panel III has mostly been used,[20] whereas definitions used in pediatric studies are inconsistent.[2-4,18,21-25] Although diagnostic criteria for MS vary from study to study, an increased incidence of MS and cardiometabolic risk factors has been reported. Wilson et al[4] evaluated 234 post-transplant children for MS and showed a prevalence of 37.6% using the modified Weiss criteria.[18] The current 2022 PRNT report recommends the use of obesity or overweight as an obligatory criterion for defining MS in addition to 2 of the 4 cardiometabolic risk factors, including hypertension,

**Table 3.** Factors Related to Metabolic Syndrome (MS) and Left Ventricular Hypertrophy (LVH)

| | MS | | | LVH | | |
|---|---|---|---|---|---|---|
| **Factors** | *β* | **95% CI** | ***P*** | *β* | **95% CI** | ***P*** |
| Age, years | | | | −0.157 | 1.488-23.578 | .239 |
| Male sex | | | | 1.957 | 1.838-27.251 | **.004** |
| ΔBMI SDS | 3.359 | 1.189-696.280 | **.039** | 0.560 | 1.015-3.018 | **.044** |
| WC SDS | 0.347 | 0.522-3.834 | .496 | | | |
| Cumulative steroid dose, mg/kg | −19.377 | 0.001-181.900 | .122 | | | |
| HOMA-IR | 1.457 | 0.819-22.504 | .085 | | | |
| 25-Hydroxyvitamin D3, ng/mL | 0.019 | 0.891-1.164 | .785 | | | |

BMI, body mass index; HOMA-IR, homeostatic model assessment of insulin resistance; SDS, SD score; WC, waist circumference. P < .05 was considered statistically significant.

high TG, low LDL, and elevated FPG in children with kidney disease.[10] The group emphasizes the potential impact of adiposity on the cardiometabolic risk profile and recommends using BMI, especially BMI to height–age rather than waist circumference or waist-to-height ratio, which may not represent true visceral adipose tissue in children with CKD and kidney transplantation. In the present study, we used the PRNT criteria to define MS and BMI SDS adjusted to height–age because short stature is common in our cohort. Based on these criteria, the prevalence of MS in our cohort was approximately 20%. To the best of our knowledge, this study is the first report to assess the prevalence of MS in pediatric KTx recipients using the specific PRNT recommendations criteria, which ensures a standardized approach to the diagnosis.

The obesity epidemic throughout the world also affects children with kidney diseases, including dialysis, and KTx recipients. The risk of obesity and MS in children is influenced by genetic, environmental, and perinatal factors. In KTx recipients, the use of steroids after kidney transplantation is another important risk factor for the development of obesity and MS.[23] Discontinuation of steroids in pediatric KTx recipients is associated with a significantly lower incidence of MS.[2] Treatment with mTORi may cause severe dyslipidemia in pediatric KTx recipients.[1] There is also evidence that some primary kidney disorders may contribute to the development of MS. In particular, cystinosis, cystic kidney disease, and hemolytic uremic syndrome may increase the risk of developing abnormal glucose metabolism as well as the development of new-onset diabetes.[1] Our study revealed a significant association between MS and an increase in BMI after transplantation. On the other hand, in our cohort, in which almost all of the patients were taking steroids and a majority were receiving tacrolimus, no relationship was found between MS and steroid dose, tacrolimus or mTORi use, or primary kidney disease. Therefore, further studies with a larger sample size are needed to identify the effect of steroids and other immunosuppressives.

Chronic kidney disease is a significant risk factor for cardiovascular disease in children. Although kidney transplantation reduces uremia-related risk factors, the risk of cardiovascular disease remains, particularly due to obesity, hypertension, and dyslipidemia. Midwest Pediatric Nephrology Consortium studies from 6 centers showed that MS was associated with a 2.6-fold increment in post-transplant LVH, as well as a 3-fold increase in eccentric LVH after transplantation.[4] It is consistent with a large, single-center prospective study of approximately 2000 patients who received KTx that indicated that MS was associated with a higher incidence of cardiovascular events.[26] The Chronic Kidney Disease in Children Study (CKiD) Cohort including non-dialysis CKD children showed that for each 1-unit increase in BMI *z*-score, the risks of developing LVH were 3.1-fold higher in girls and 1.5-fold higher in boys.[27] Our study showed that pediatric KTx recipients with MS had 2-fold higher LVH as an early marker of cardiovascular disease than KTx recipients without MS. As a result, our data support the conclusion that MS is associated with an increase in LVH. Moreover, our results show that the increase in BMI after transplantation seems to be an important risk factor not only for the development of MS but also for LVH. Therefore, it is important to prevent BMI increase after transplantation to reduce cardiovascular risk in this group of individuals.

There is a well-established link between obesity and kidney disease in adults, even in otherwise healthy obese adolescents.[7] It has also been demonstrated by Meier-Kriesche et al[28] that an increased BMI is associated with graft survival in a study of 51 927 KTx recipients. In a pediatric study of 472 children with CKD, it was found that MS is more prevalent among children with CKD, as well as a more rapid decline of kidney function in children with MS.[22,25,29] Our study found no significant difference in GFR between patients with and without MS after approximately 3 years of follow-up. A larger cohort with a longer follow-up is clearly necessary to evaluate the impact of obesity and MS on kidney function.

The cross-sectional nature of our study and the use of the most recent definition of MS contribute to its strength. One of the major limitations of our study is the small sample size. Another limitation is that only 2 patients did not receive steroids, making it difficult to assess the effects of steroids on the development of MS. In addition, we were unable to investigate whether environmental factors such as diet, salt consumption, exercise, screen time, or immobility contributed to the development of MS. Finally, in this study, we did not investigate all possible factors that may influence LVH, such as anemia and hypoalbuminemia.

In conclusion, cardiometabolic risk factors are common in pediatric KTx recipients. The most common risk factors are obesity, hypertension, and dyslipidemia. Metabolic syndrome as a composite risk factor accounts for approximately 20%. Left ventricular hypertrophy is present in 54% of patients, and the risk of developing LVH is significantly increased in patients with MS. In addition, the increase in BMI after transplantation appears to be a significant contributing factor for the development of MS and LVH. Therefore, it is crucial to prevent an increase in BMI following transplantation to reduce cardiovascular risk in this patient group.

**Ethics Committee Approval:** This study was approved by the Ethics Committee of İstanbul University-Cerrahpaşa (Approval No: 07/02/2018-51437).

**Informed Consent:** Written informed consent was obtained from the patients who agreed to participate in the study.

**Peer-review:** Externally peer-reviewed.

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**Declaration of Interests:** The authors have no conflict of interest to declare.

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