Ambulatory blood pressure monitoring and renal functions in children with a solitary kidney

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Abstract The aim of this study is to investigate the blood pressure (BP) profile, microalbuminuria, renal functions, and relations with remaining normal kidney size in children with unilateral functioning solitary kidney (UFSK). Sixty-six children with UFSK were equally divided into three groups: unilateral renal agenesis (URA), unilateral atrophic kidney (UAK), and unilateral nephrectomy (UNP). Twenty-two age-, weight-, and height-matched healthy children were considered as a control group. The serum creatinine level and first-morning urine microalbumin and creatinine concentrations were determined by the standard methods. Also, the BP profile was determined by ambulatory blood pressure monitoring (ABPM). We found that the serum creatinine level was higher and creatinine clearance was lower in each patient groups compared to those of the control group ($p<0.05$). Compared with the controls, each group of patients had mean office, 24-h, daytime, and night-time systolic and diastolic BP values similar to those of the controls ($p>0.05$). An inverse correlation was found between the renal size standard deviation scores (SDS) of normal kidneys and 24-h systolic and diastolic BP load SDS in all of the patients ($p<0.05$; $r=-0.372$, $r=-0.295$, respectively). The observed relationship between renal size SDS and 24-h mean arterial pressure (MAP), systolic and diastolic BP load SDS suggests that children with UFSK should be evaluated by using ABPM for the risk of hypertension.

Keywords Blood pressure · Renal function · Solitary kidney

Introduction

Arterial hypertension, proteinuria, and impaired renal functions are potential complications of unilateral functioning solitary kidney (UFSK), including unilateral renal agenesis (URA), unilateral atrophic kidney (UAK), and unilateral nephrectomy (UNP). The reduction of renal mass leads to compensatory hypertrophy of the remaining renal tissue in these patients [1–3]. Functionally, the remnant kidney will partly compensate for the lost function by increasing its workload, which is accompanied by increased glomerular blood flow and blood pressure (BP), so-called hyperfiltration [4]. It has been shown in animal models of unilateral renal ablation that the remaining kidney undergoes accelerated structural renal damage, generally in the form of glomerulosclerosis, with varying degrees of renal insufficiency, partly amenable to a variety of therapeutic interventions [5, 6]. A relatively small number of long-term follow-up studies in humans has documented that the surgical loss of renal functional mass in the presence of a normal remnant kidney rarely leads to renal insufficiency,
although the incidence of mild to moderate proteinuria and hypertension has increased [7–10].

Kasiske et al. [11] reported that UNP does not cause progressive renal dysfunction, but it may be associated with a small increase in BP. On the other hand, Wikstad et al. [8] showed that adults born with URA or UNP in childhood did not have a marked increase in arterial BP or renal insufficiency. Some reports, however, indicate that patients with URA or with an UFSK left after nephrectomy may have proteinuria and focal glomerular sclerosis [5, 12]. Janda et al. [13] recorded marginal diastolic hypertension in one third of their subjects in a study of 40 children and/or adolescents (23 URA, 17 UNP). Although some investigators have reported an increase in the prevalence of hypertension and/or proteinuria, others have failed to document these abnormalities [11]. The discrepancy among the results of these studies may be caused due to a difference in the amount of renal mass removed, the age at the time of renal mass reduction, or unsuspected damage in the remaining kidney.

In the past few years, ABPM has become an accepted method for investigating the BP profile in children with renal disorders [14–16]. Over the years, ambulatory blood pressure monitoring (ABPM) has been increasingly used to investigate hypertension in different pediatric populations [17–20]. A careful review of the literature shows that there are few reports on ABPM, microalbuminuria, and renal functions in children with UFSK [21]. Furthermore, the utility of BP in children with UFSK is not well established. Therefore, the aim of this study was to investigate the BP profile by ABPM, microalbuminuria, renal functions, and relations with remaining normal kidney size in children with UFSK.

### Materials and methods

Sixty-six children with a mean age of 8.32±4.23 and range 0.5 and 18 years with UFSK were equally divided into three groups: URA group (n=22), UAK group (n=22), and UNP group (n=22). Twenty-two Age-, weight-, and height-matched healthy children were considered as a control group (Table 1). Renal ultrasound was normal in all controls. Informed consent was obtained from the children and their parents prior to the testing, and the study was approved by the local ethics committee of the School of Medicine, Çukurova University, Adana, Turkey.

Both renal agenesis and atrophic kidney were established through renal ultrasound and scintigraphy. A non-functioning kidney is caused due to unilateral vesicoureteral reflux (in seven cases), ureteropelvic junction obstruction (in 10 cases), and multicystic dysplastic kidney (in five cases) in the UAK group. In contrast, indications for nephrectomy contained unilateral Wilms’ tumor (in six cases), a non-functioning kidney is caused due to unilateral vesicoureteral reflux (in 10 cases) and ureteropelvic junction stenosis (in two cases), multicystic dysplastic kidney (in two cases), and nephrolithiasis (in two cases) in the UNP group. Patients with Wilms’ tumor have favorable type and they did not receive chemotherapy. The mean time due to nephrectomy was 4.06±3.87 years (range 0.5–17 years) in this group.

All patients had a normal renal function defined as a glomerular filtration rate (GFR) of over 90 ml/min 1.73 m² (as determined by Schwartz et al.’s formula [22]) and normal urinary sediment. The remaining kidney has findings of normal ultrasound and normal scintigraphy in all patient groups. Only children without any anatomical

### Table 1  Demographic data, anthropometric data, and renal functional parameters of the patients and control groups

| Parameters          | URA (n=22)     | UAK (n=22)     | UNP (n=22)    | Controls (n=22) |
|---------------------|----------------|----------------|---------------|-----------------|
| Gender (M/F)        | 11/11          | 12/10          | 10/12         | 10/12           |
| Age (years)         | 8.63±4.50      | 8.03±4.30      | 8.31±4.04     | 8.78±3.49       |
| Weight (kg)         | 28.44±18.07    | 27.01±17.14    | 26.57±10.48   | 29.19±10.92     |
| Height (cm)         | 124.55±27.62   | 126.05±25.22   | 123.96±21.21  | 128.36±26.44    |
| BMI (kg/m²)         | 16.60±2.95     | 17.96±3.14     | 16.77±2.05    | 16.96±1.91      |
| UMA (mg/L)          | 5.46±3.91      | 4.80±2.03      | 4.56±8.11     | 5.18±4.09       |
| UMA/Ucr (mg/mg)     | 0.23±0.72      | 0.17±0.30      | 0.07±0.13     | 0.06±0.06       |
| GFR (ml/dk/1.73 m²) | 121.95±34.19   | 123.66±43.67   | 108.57±26.71  | 155.85±41.27    |
| Serum Cr (mg/dl)²   | 0.59±0.13      | 0.60±0.15      | 0.65±0.10     | 0.47±0.13       |
| Renal size (mm)     | 100.32±18.42   | 91.32±17.56    | 97.23±17.49   | 92.36±16.00     |

Values are expressed as mean±SD, M: male, F: female, BMI: body mass index, UMA: urine microalbumin, UCr: urine creatinine, GFR: glomerular filtration rate

¹ p<0.05 URA vs. controls, UAK vs. controls, and UNP vs. controls

² p<0.05 URA vs. controls, UAK vs. controls, and UNP vs. controls
abnormalities of the remaining kidney and with normal GFR were included in the study. No patient was treated with antihypertensive drugs or drugs interfering with BP. Neither the study patients nor children in the control groups had a positive (first-degree-relative) family history of hypertension. Patients with a renal scar in their solitary kidney or who have other urinary tract anomaly were withdrawn from the study. In all of the study group participants, urinalysis, serum uric acid, creatinine, cholesterol, protein and albumin levels, and first-morning urine microalbumin and creatinine concentrations were determined by the standard methods.

In all subjects, ABPM was performed over 24 h using the SpaceLabs 90217 oscillometric device (Redmond, Washington). The appropriately sized cuff, chosen based on arm width, was placed on the non-dominant arm. The BP was automatically recorded in every 15 min during the day and every 30 min at night. Only ABPM profiles with at least 30 recordings, including at least eight readings between midnight and 06.00 h, were accepted. Daytime was defined as 08.00–20.00 h and night-time as 00.00–06.00 h, according to the study of Soergel et al. [23]. For each subject, the BP values corresponding to the 95th percentile, according to sex and height, was determined [23, 24]. Hypertension was defined as a systolic BP and/or diastolic BP>95th percentile. The percentage of systolic BP and diastolic BP readings above this value constituted a measurement of 24-h systolic and diastolic BP load, respectively. The dipping status was calculated by subtracting the mean night-time BP from the mean daytime BP, and then dividing this value by the mean daytime BP. Dipping was defined as a ≥10% drop in mean systolic BP or diastolic BP between daytime and night-time. Renal size and BP standard deviation scores (SDS) was calculated according the left main stem (LMS) method [24, 25].

The renal size of the normal kidney was evaluated by performing abdominal ultrasound and measuring the lower-to-upper-pole length in the supine longitudinal view by the same observer. Renal size SDS values were correlated to the BP SDS values for each patient. Renal size percentiles were determined and evaluated according to standard length-against-height-nomogram defined by Dinkel et al. [26]. Compensatory hypertrophy was accepted when the measured renal size was found to be greater than the 95th percentile, and its effect on the BP parameters was evaluated.

All data were stored and analyzed using the SPSS statistical package (SPSS Inc., Chicago, Illinois). The normality Kolmogorov-Smirnov test was performed to determine whether continuous variables were normally distributed or not. Differences between groups were analyzed using the non-parametric Kruskal-Wallis test and the Mann-Whitney U test. All values are expressed as mean±SD. The prevalence of hypertension was determined using Fisher’s exact test. The relationships between variables were analyzed with the non-parametric Spearman’s correlation test in each group. A value of p<0.05 was considered to be statistically significant.

Results

The demographic data and renal function parameters of all of the study groups and controls are shown in Table 1. Age, height, weight, BMI, urine microalbumin, urine micro-albumin to urine creatinine ratio, and renal size values are not different between each patient group and the controls (p>0.05). The mean serum creatinine level was higher in all patient groups compared to that of the control group (p=0.006 between URA and control, p=0.004 between UAK and control, p<0.001 between UNP and control) and the GFR was lower in all patient groups compared to that of the control group (p=0.005 between URA and control, p=0.016 between UAK and control, p<0.001 between UNP and control).

Mean heart rates (24 h, daytime, night-time), mean systolic and diastolic BP parameters (office BP, 24 h, daytime, night-time), mean systolic and diastolic BP dipping, and 24-h systolic and diastolic BP loads are all given in Table 2. When compared to the controls, each group with UFSK had mean office, 24-h, daytime, and night-time systolic and diastolic BP, and heart rate values similar to those of the controls (p>0.05). Only the mean 24-h diastolic BP was higher in the URA group than that of the control group (p=0.039). In addition, the diastolic load was higher in the UAK group than that of the control group (p=0.012). There was no significant difference in the mean office, 24-h, daytime, and night-time systolic and diastolic BP, and heart rate between all of the patient groups (p>0.05). The mean office systolic and diastolic BP, respectively, were higher than the mean daytime systolic and diastolic BP in all groups. The prevalence of hypertension in the URA group was 23% (5/22), in the UAK group was 23% (5/22), in the UNP group was 32% (7/22) [in all patients, it was 26% (17/66)], and in the controls it was 5% (1/22). The prevalence of hypertension in patients was higher compared to that in the controls (p=0.035). The prevalence of non-dipping phenomenon in the URA group was 23% (5/22), in the UAK group was 36% (8/22), in the UNP group was 32% (7/22) [in all patients, it was 30% (20/66)], in the controls it was 9% (2/22). There was a statistically significant difference between patients and the controls (p=0.049).

Compensatory hypertrophy (renal size percentile >95%) was seen in 59% (39/66) of patients. Age, height, weight, renal size, and GFR were statistically significantly higher in
patients with compensatory hypertrophy than in patients without compensatory hypertrophy. In contrast, the mean heart rates were lower in patients with >95th percentile of renal size (Table 3).

Renal size SDS was correlated with some BP SDS parameters in the patients and the controls. Statistically significant correlations are shown in Table 4. There was no correlation between the renal size SDS and BP parameters, but an inverse correlation was found between the renal size SDS and 24-h MAP SDS, 24-h systolic and diastolic BP load SDS in all of the patients, but these correlations were not found in the controls.

### Discussion

The UFSK is usually considerably enlarged, this constituting a compensatory diffuse but not partial, lobar enlargement, usually with a larger than normal pelvis [27]. The reduction of renal mass in the rat is associated with hyperfiltration and hypertrophy of the remaining nephrons,

#### Table 3 Some characteristics of the patients with unilateral functioning solitary kidney (USFK) according the percentile of renal size

| Parameters                  | Renal size <95th percentile (n=27) | Renal size >95th percentile (n=39) | p       |
|-----------------------------|-----------------------------------|-----------------------------------|---------|
| Age (year)                  | 5.91±3.16                         | 9.99±4.09                         | <0.001  |
| Height (cm)                 | 113.19±21.24                      | 132.92±23.47                      | <0.001  |
| Weight (kg)                 | 19.80±9.89                        | 32.56±16.41                       | <0.001  |
| Renal size (mm)             | 80.37±11.13                       | 107.31±12.71                      | <0.001  |
| GFR (ml/dk/1.73 m²)         | 107.82±37.31                      | 125.15±33.09                      | <0.05   |
| Av. 24-h HR (beats/min)     | 99.19±15.49                       | 84.87±12.96                       | <0.001  |
| Av. daytime HR (beats/min)  | 102.00±13.81                      | 88.95±13.99                       | <0.001  |
| Av. night-time HR (beats/min)| 88.59±17.05                      | 76.62±13.02                       | <0.05   |

Values are expressed as mean±SD, Av.: average, GFR: glomerular filtration rate, HR: heart rate

#### Table 4 Correlation between renal size standard deviation scores (SDS) and some parameters SDS in patients with UFSK and the controls

| Parameters                  | Patients (n=66) | Controls (n=22) |
|-----------------------------|-----------------|-----------------|
| Av. 24-h MAP SDS            | −0.284 0.021    | −0.011 0.962    |
| Av. 24-h SBP SDS            | −0.175 0.159    | −0.067 0.767    |
| Av. 24-h DBP SDS            | −0.034 0.788    | −0.312 0.158    |
| Av. 24-h SBP load SDS       | −0.372 0.002    | −0.295 0.016    |
| Av. 24-h DBP load SDS       | −0.214 0.002    | −0.148 0.510    |
| Av. 24-h DBP load SDS       | −0.019 0.934    | −0.201 0.971    |

SDS: standard deviation scores, Av.: average, MAP: mean arterial pressure, SBP: systolic blood pressure, DBP: diastolic blood pressure
ultimately resulting in proteinuria, renal failure, and hypertension. Nagata et al. [28] reported that unilateral nephrectomy in young rats leads to a higher incidence of glomerular sclerosis than is observed in adult rats. A study conducted by Regazzoni et al. [29] in a follow-up of UNP in children has reported a decreased renal reserve capacity, but detected no evidence of hypertension or proteinuria.

In our study, subjects were screened with urine microalbumin, urine and serum creatinine, GFR, and urine microalbumin-to-creatinine ratios in first-morning urine for the detection of proteinuria and renal functions. No statistically significant difference was found between the urine microalbumin and microalbumin-to-creatinine ratios in the first-morning urine in all of the patient and control groups. However, the GFR was lower and the serum creatinine level was higher in the subgroups of patients than those of the control group. These results show that a mild renal dysfunction may be detected in patients with UFSK.

Although some investigators have reported an increased prevalence of hypertension, others have failed to document these abnormalities in children with UFSK [11]. Janda et al. [13] recorded marginal diastolic hypertension in one third of their subjects in a study of 40 children and/or adolescents (23 URA, 17 UNP). As we mentioned before, there are few reports which have utilized 24-h ABPM in UFSK children. Mei-Zahav et al. [21] showed that the presence of an UFSK, from whatever cause, leads to an increase in BP. This is particularly manifested in systolic BP and even more so in daytime systolic BP. Kasiske et al. [11] reported that UNP does not cause progressive renal dysfunction, but may be associated with a small increase in BP. On the other hand, Wikstad et al. [8] concluded that adults born with URA or UNP in childhood did not have a marked increase in arterial BP or renal insufficiency. We measured the ABPM in three groups of patient with UFSK and found that they have the same characteristics as in healthy controls. However, in our study, the mean office, 24-h systolic, daytime, and night-time systolic and diastolic BP, mean 24-h, daytime, and night-time heart rate, 24-h systolic BP load, systolic and diastolic BP dipping in all groups of patients were similar to those of the controls. In contrast, mean 24-h diastolic BP was higher in the URA group than those of the control group, but this finding showed no difference between the other patient groups and controls. The 24-h diastolic BP load was increased in the UAK group. In addition, an increased prevalence of hypertension was found in all of the patients groups. According to these results, we suggest that patients with a single kidney have potential risk factors for hypertension in the early childhood period.

Compensatory hypertrophy of the remaining kidney may be seen in patients with UFSK. In adult animals, a compensatory increase in size following UNP is, for the most part, attributable to hypertrophy (an increase in cell size), which is predominantly of proximal tubular origin. In young animals, renal growth is achieved primarily by cell multiplication, that is, hyperplasia [3]. In the present study, an inverse correlation was found between renal size SDS and 24-h MAP SDS, 24-h systolic and diastolic BP load SDS in all of the patients, but was not seen in the controls. Therefore, we think that there is an increased risk of hypertension in children without compensatory hypertrophy.

To this end, we conclude that subtle alterations of renal function might be already present in children with UFSK, while no obvious pathological findings were made for BP or urinary protein excretion in the early period. However, an increased BP load was seen in these patients (particularly in patients without compensatory hypertrophy). Nevertheless, this might not exclude an increased long-term risk for the development of hypertension or impaired renal function in this patient group. Because patients in the present study have a small sample and a shorter follow-up period, further prospective studies with a larger sample size and of longer term are suggested to find the relationship between these parameters.

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