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## Long-term effects of partial unilateral ureteral obstruction on renal hemodynamics and morphology in newborn rats: a magnetic resonance imaging study

Received: 17 January 2002 / Accepted: 14 May 2002 / Published online: 7 August 2002  
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**Abstract** We assessed the longitudinal changes in renal vein blood flow (RVBF) and kidney volume in response to neonatally induced partial unilateral ureteral obstruction (PUUO) in rats with a magnetic resonance imaging (MRI) technique. During anesthesia, either the upper third or two thirds of the left ureter was embedded into the psoas muscle in newborn rats, creating either a mild ( $n=20$ ) or a severe ( $n=9$ ) partial obstruction. Control groups consisted of sham-operated ( $n=12$ ) and non-operated ( $n=15$ ) rats. During the following 24 weeks, RVBF and kidney volume were measured sequentially every 2–6 weeks with MRI, beginning 9 days after the operation. Both mild and severe obstruction caused a time-dependent decrease in RVBF. At week 24, the mean RVBF had decreased to 79% of the controls in the mildly obstructed kidneys (mean  $\pm$  SE:  $1.45 \pm 0.14$  vs  $1.84 \pm 0.08$  ml/min/100 g body weight,  $P<0.05$ ) and to 57% of controls in the severely obstructed kidneys ( $1.05 \pm 0.10$  vs  $1.84 \pm 0.08$  ml/min/100 g body weight,  $P<0.05$ ). The renal pelvis volume increased and the renal parenchymal volume decreased significantly in the severely obstructed kidneys compared to the mildly obstructed kidneys. A good correlation was found between kidney volume measured in vivo using MRI and that

measured in vitro ( $r>0.8$ ,  $P<0.05$ ), and between RVBF and renal parenchymal volume ( $r=0.758$ ,  $P<0.01$ ). In conclusion, the degree of reduction in RVBF depends on the severity and the duration of the PUUO. MRI can safely and reliably be used to monitor the longitudinal changes in RVBF and kidney volume in rats from early life.

**Keywords** Partial ureteral obstruction · Kidney · Hemodynamics · MR imaging · Rat

### Introduction

Congenital hydronephrosis, predominantly unilateral, is found in about 1% of newborn infants [5]. However, the pathophysiological changes in the kidney in response to partial unilateral ureteral obstruction (PUUO) remain incompletely understood [9]. Data on the effect of post-natal PUUO on glomerular filtration rates (GFR) 5–9 weeks after obstruction are conflicting [1, 2, 8, 9, 10, 16]. In rats, Josephson et al. found that GFR was 16% lower on the obstructed side. In guinea pigs, Chevalier et al. and Taki et al. found that GFR in the obstructed kidney decreased by about 95% over a similar time period. Importantly, the guinea pig studies revealed that both renal blood flow and GFR were reduced in parallel and that the impairment of renal GFR was determined by the severity of the obstruction. The hemodynamic response to partial, long-lasting ureteral obstruction, however, has not been studied longitudinally because most methods are invasive and equivalent to killing the animal.

Recently, the in vivo measurement of renal vein blood flow (RVBF) by magnetic resonance imaging (MRI) was established [13]. The RVBF values obtained from both normal and uninephrectomized rats were comparable to the renal blood flow measured by invasive methods. Furthermore, another study demonstrated that MRI is a reliable method for measuring kidney volume [3]. Consequently, the longitudinal changes in

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RVBF and morphology may accurately be followed by MRI measurements [13].

In a recent study, we have shown that embedding a short segment of the ureter into the psoas muscle produces a mild obstruction, whereas embedding 2/3 of the ureter causes a severe obstruction [20]. In the present study, these procedures were used to create two different degrees of PUUO in neonatal rats, and the longitudinal changes in RVBF and kidney volume were monitored by MRI. Clinically, the course of change in the contralateral kidney in cases of unilateral ureter obstruction is a very important issue. We have chosen to deal with this issue separately [21]. Consequently, the purposes of this study were: (1) to determine how early MRI can be used to measure RVBF in neonatal rats; (2) to compare the changes in RVBF and kidney volume in obstructed kidneys with those in the control kidneys; and (3) to examine whether changes in RVBF correlate with changes in renal parenchymal mass.

## Materials and methods

### Animals

A total of 71 1–2-day-old male/female Wistar rats (Møllegaard, Denmark) weighing 8–10 g were allocated to four groups: (1) mild PUUO ( $n=26$ ); (2) severe PUUO ( $n=18$ ); (3) sham-operated ( $n=15$ ) and (4) non-operated ( $n=16$ ). The initial body weight (BW) did not differ significantly between the groups.

Nineteen rats died from various causes during the study (six from the mildly obstructed group, nine from the severely obstructed and four from the control group). These rats were excluded from the analysis.

### Surgical technique

PUUO was created by a modification of Ulm and Miller's technique [18, 20, 21]. The animals were anesthetized with ether and the left ureter was exposed via an abdominal incision. The left ureter was carefully dissected free under a microscope ( $\times 10$ ). The underlying psoas muscle was split longitudinally to form a groove. To create a mild PUUO, a 3–4 mm long muscle groove was formed. The upper 1/3 of the ureter was placed in the groove and the muscle edges were approximated with two sutures (Ethilon 8–0). To create a severe PUUO, a 13–16 mm long muscle groove was formed. The ureter from the pelvic-ureteric junction down to the level of external iliac vessel was placed into the groove and the muscle edges were approximated with four sutures (Ethilon 8–0). In the sham-operated group, the rats were laparotomized, the left ureter was dissected free and the psoas muscle was split. After the operation, the rats were placed in an incubator with the temperature fixed at 29°C. When the rats woke, they were returned to the cage with their mother and kept in a regular animal care facility. After 4 weeks, the rats were separated from their mother and housed two per cage. The rats had free access to a standard rodent diet (Altromin, Lage, Germany) and tap water with a 12:12-h artificial light cycle, temperature at  $21 \pm 2^\circ\text{C}$  and humidity  $55 \pm 2\%$ .

### Time schedule

The total follow-up time was 24 weeks beginning at 9–10 days of age in both the mildly obstructed and control rats. Due to the larger trauma in the severely obstructed rats, MRI examinations were delayed in these rats until they were 4 weeks old. The

examination intervals were 2–4 weeks during the first 10 weeks and 4–6 weeks during the last 14 weeks. At the end of the studies, the patency of the obstructed ureter was ensured by the injection of Evans blue into the renal pelvis and the observation of the appearance of the dye in the bladder.

### Renal vein blood flow measurements

During general anesthesia with phenobarbital (50 mg/kg i.p.), the changes in RVBF were monitored by a high-field (7 T) MRI scanner with a phase contrast velocity measurement pulse sequence. The scanner was equipped with a 10 gauss/cm field gradient system with a risetime of 0.1 ms. A 35-mm diameter dedicated surface RF-coil was used for optimizing the signal-to-noise ratio. The total measurement time was 8.5 min, the repetition time (TR) and the echo time (TE) were 250 and 3.5 ms, respectively, the slice thickness was 1.25 mm, the acquisition matrix  $256 \times 256$ , the in-plane resolution  $0.23 \times 0.23 \text{ mm}^2$  and the flip-angle  $70^\circ$ . The aliasing velocity was 3 cm/s. After localization of the renal vein by a set of images with different orientations, seven sagittal measurement slices were placed orthogonally to the vessel (Fig. 1A). The measurements were analyzed with a dedicated program [13] that removed offset in the phase images by subtraction of a plane fitted through stationary tissue and removing phase noise from regions with low signal intensity (Fig. 1B, C and D).

### Kidney volume measurement

Following the measurement of RVBF, the total kidney volume (TKV, comprising both the renal parenchyma and pelvis) was measured using MRI without contrast enhancement. At week 24, gadolinium-diethylenetriamine pentaacetic acid (Gd-DTPA) enhanced MRI was used randomly in six rats from both the mildly and severely obstructed groups. At 15 min after the induction of anesthesia, the Gd-DTPA (0.5 mol/l, Schering, Germany) was given to the rats (50  $\mu\text{l}/100 \text{ g BW}$ , i.v.). T1 weighted spin echo images were obtained with TR and TE equal to 80 and 5 ms, respectively. The slice thickness was 1 mm and the slice gap varied from 0.1 to 0.7 mm covering the kidney volume within 16 slices (Fig. 2A). The kidney was manually traced on each slice (Fig. 2B) and the volumes were calculated by linear interpolation of the marked areas. In brief, pelvic volume on each individual slice image in the obstructed kidney was calculated as:

$$\text{PV}_s = \text{PA} \times \text{slice thickness}$$

Where  $\text{PV}_s$  is pelvic volume of each slice, PA is pelvic area and slice thickness is 1 mm. The total pelvic volume (PV) of each kidney was then estimated by simple addition of all the  $\text{PV}_s$ . A reliable estimate of renal parenchymal volume can then be calculated as:

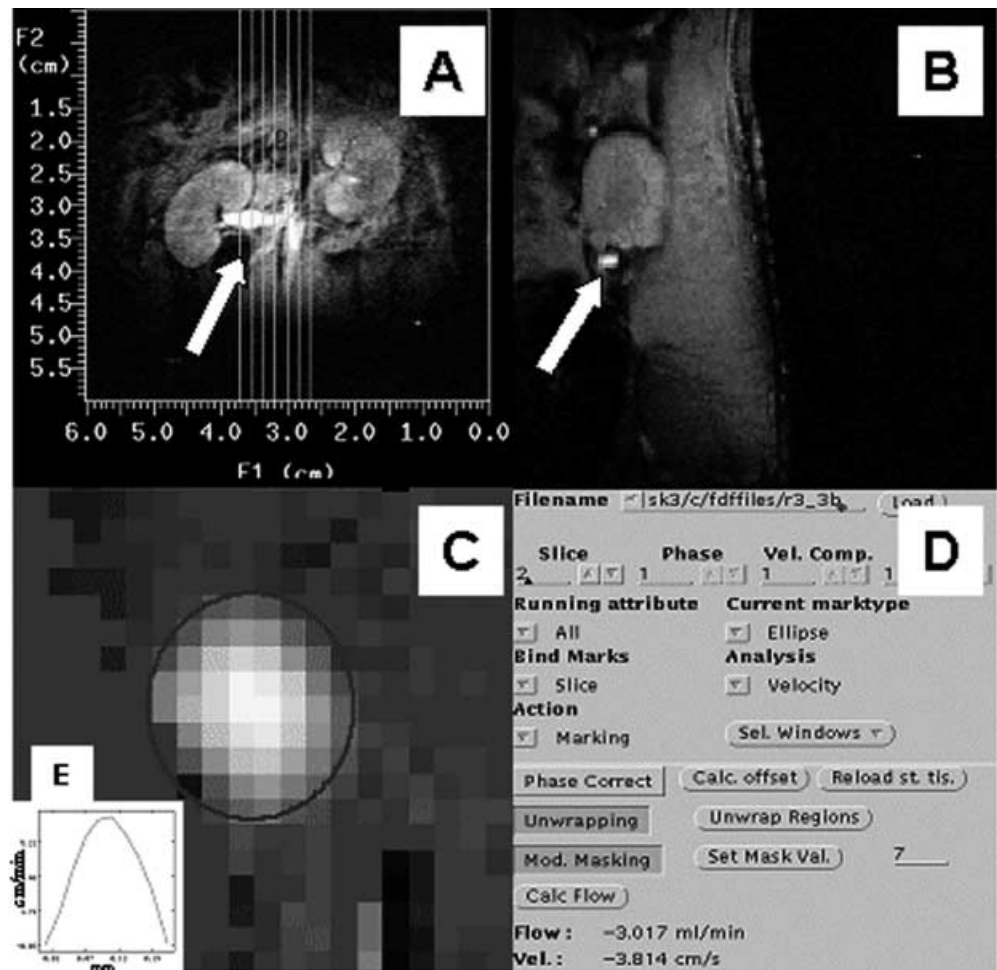
$$\text{RPV} = \text{TKV} - \text{PV}$$

### In vitro volume measurement

In order to verify the MRI volume estimates, six mildly obstructed and six non-operated control rats were randomly sacrificed for kidney volume measurement in vitro after MRI when the rats were 10 days old. In addition, seven mildly and seven severely obstructed rats were sacrificed for in vitro kidney volume measurements at week 24.

Just after the MRI examination, the kidneys were quickly removed and the TKV, the renal pelvis and the renal parenchymal volume were measured immediately in vitro based on the principle of Archimedes [14]. A jar containing isotonic saline (gravity  $\approx 1$ ) was placed on a laboratory balance subsequently adjusted to zero. The kidney to be measured was fixed to a laboratory stand by means of a fine thread and completely submerged in the saline water. The volume of the kidney was expressed by the weight gain registered on the balance. First, the TKV was measured with the pelvis intact. The kidney was then cut into two slices along its longitudinal axis and by

**Fig. 1A–E.** MRI analysis of renal vein blood flow measurement in an 8-week-old sham-operated rat. **A** The positions of seven measurement planes orthogonal to the vein (arrow) for RVBF calculation are indicated with vertical lines. The signal intensity from the renal vein is increased due to flow effects. **B** Sagittal intensity image of the kidney. **C** Velocity image of the kidney. The circle placed on the image indicates the renal vein. **D** The velocity profile corresponding to the cross section of the renal vein which is depicted in **C**. **E** Blood flow and velocity are calculated and in this case RVBF was 3.02 ml/min



this means, the pelvis was completely emptied. Finally, the RPV was measured and the pelvic volume was calculated as:

$$PV = TKV - RPV$$

#### Statistical analysis

Values were expressed as mean  $\pm$  SE. The individual data for TKV and RVBF were plotted against age. ANOVA and linear regression analysis were used for statistical analysis. *F*- and *t*-tests were used to evaluate the difference of the slopes between the different regression lines. To allow a statistical analysis of RVBF and TKV, disparate for different BWs, the values of RVBF and TKV were expressed in ml/min/100 g BW and ml/100 g BW, respectively. The MR image quality did not permit the analysis of RVBF and TKV in all measurements. Therefore, each data point represents the means of 7–14 measurements in each group. Post hoc multiple comparison tests (Bonferroni test) were used to compare the difference in TKV and RVBF between groups at each checkpoint. A paired *t*-test was used to compare the kidney volumes measured in vivo with those measured in vitro. Differences were considered significant when  $P < 0.05$ .

## Results

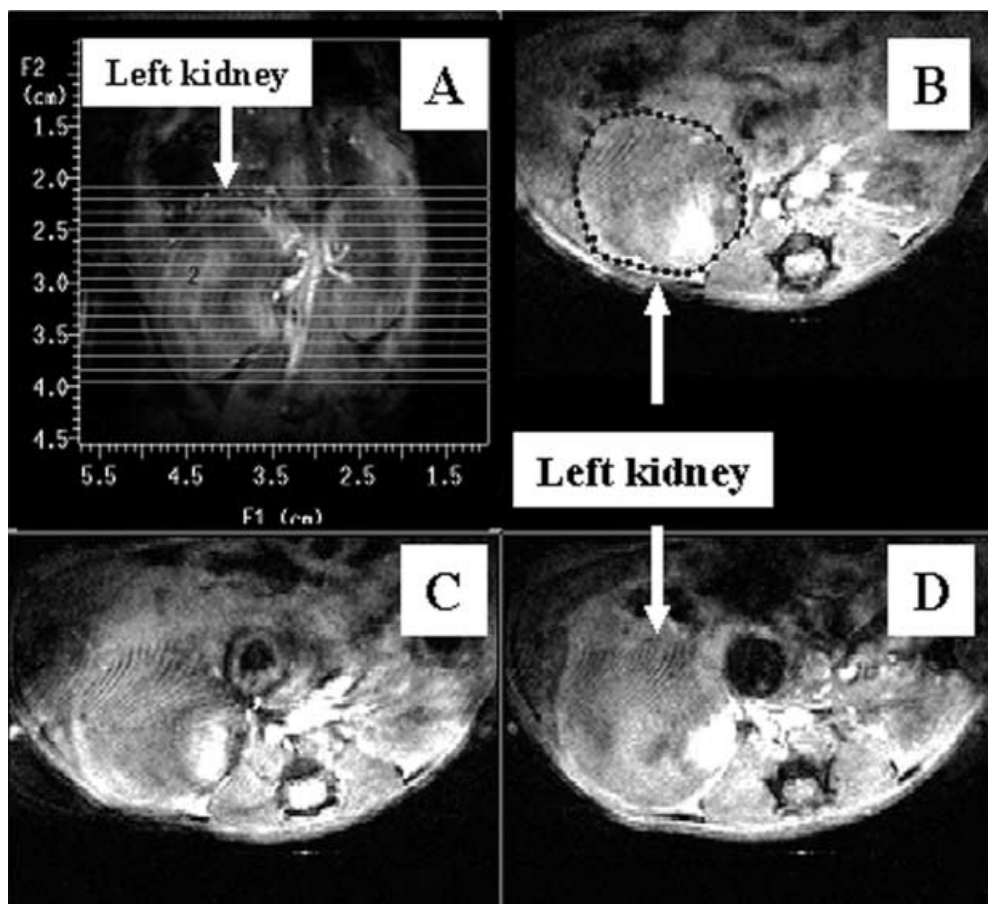
Of the 75 rats included in the study, 19 died from various causes. The remaining 56 rats were all doing well during follow up with a normal body weight development. The weight gain was the same in all groups.

Renal vein blood flow was more reduced with severe than with mild obstruction

Both in the obstructed and the control animals, there was a linear relationship between the RVBF and BW (Fig. 3). The RVBF increase rate was significantly higher in control than in the mildly obstructed kidneys ( $P < 0.001$ ), and in the mildly obstructed kidneys it was significantly higher than in the severely obstructed kidneys ( $P < 0.01$ ). There were no significant differences in RVBF between the intact and sham-operated control groups, and therefore, data from these two groups were combined and are reported as controls.

The relationship between RVBF, expressed relative to BW, and age is shown in Fig. 4. At weeks 10 and 24, the mean RVBF in the mildly obstructed kidneys was 83% and 79% of the controls, respectively ( $1.82 \pm 0.14$  vs  $2.20 \pm 0.11$ ,  $P > 0.05$  and  $1.45 \pm 0.14$  vs  $1.84 \pm 0.08$  ml/min/100 g BW,  $P < 0.05$ ). In severely obstructed kidneys, the RVBF was 68% and 57% of controls, respectively ( $1.50 \pm 0.11$  vs  $2.20 \pm 0.11$ ,  $P < 0.05$  and  $1.05 \pm 0.10$  vs  $1.84 \pm 0.08$  ml/min/100 g BW,  $P < 0.05$ ). The difference between the control kidneys and mildly obstructed kidneys was significant from week 18 on ( $P < 0.05$ ), and between control kidneys and severely obstructed kidneys

**Fig. 2A–D.** MRI of the kidneys in a 4-week-old rat with a severely obstructed left kidney. **A** For kidney volume measurements, 16 measurement planes (indicated with *transverse lines*) were placed over the kidney (coronal section). **B, C** and **D** Representative transverse section images of the kidney. The left kidney is traced (*dotted line*) in one picture (**B**)

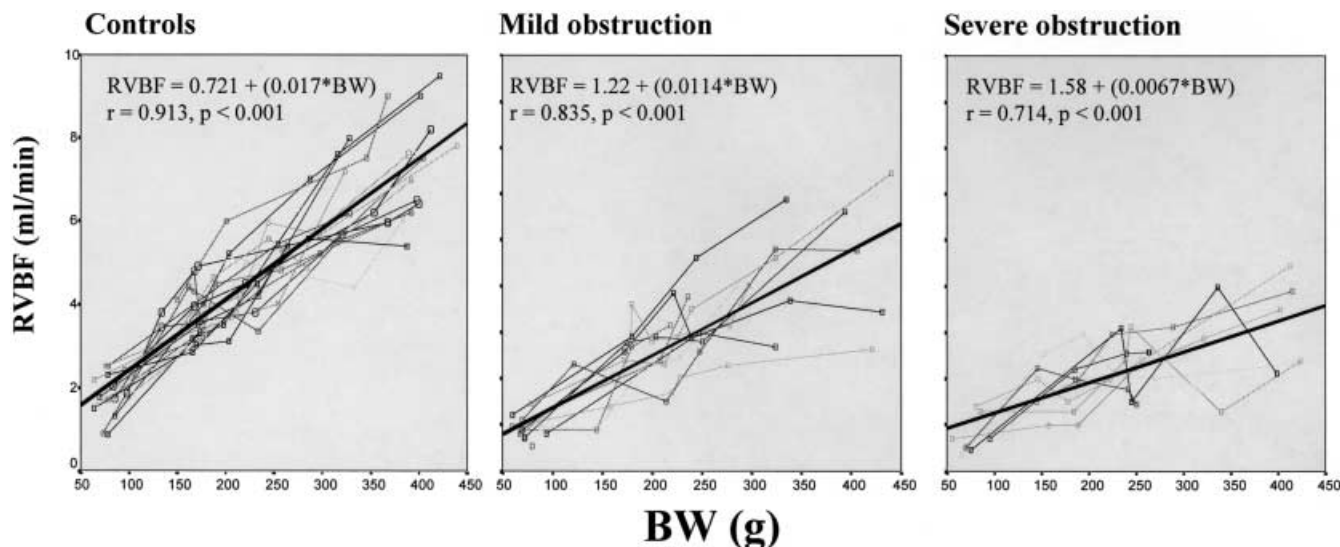


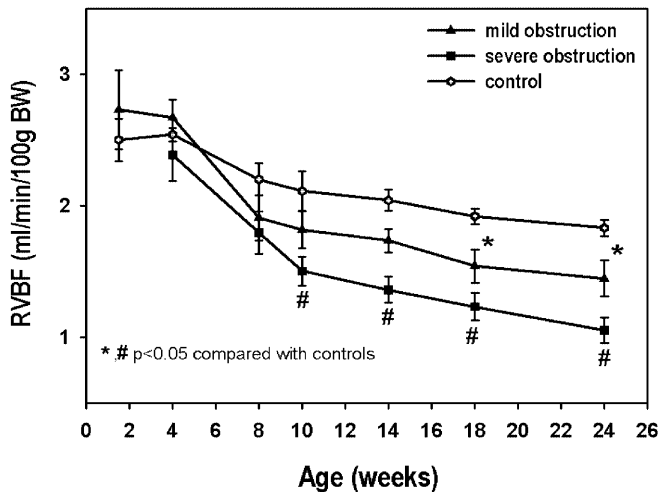
from week 10 on ( $P < 0.05$ ). RVBF differed significantly between the mildly obstructed and the severely obstructed kidneys at week 24.

There was a good correlation between kidney volume measured *in vivo* by MRI and that measured *in vitro*

**Fig. 3.** The relationship between left renal vein blood flow (RVBF) and body weight (BW) in controls, mildly obstructed and severely obstructed kidneys. There was a highly significant correlation between RVBF and BW ( $P < 0.001$ ) in all groups

There was no significant difference between *in vivo* kidney volume and that measured *in vitro* either in the 10-day-old or in the 24-week-old rats. In the 10-day-old rats, there was a good correlation between the *in vivo*





**Fig. 4.** Left renal vein blood flow (RVBF) corrected for body weight vs age. A reduction in RVBF occurred in all groups indicating a relatively higher renal blood flow in the neonatal than in the adult kidney (#, [asteriskmath])  $P < 0.05$  compared to controls). In severely obstructed kidneys there was a significant reduction in RVBF at week 24 compared to week 10, whereas no difference was found between 24 weeks and 10 weeks in mildly obstructed and control kidneys

**Table 1.** Measurement of total kidney volume (TKV) in vivo and in vitro in 10-day and 24-week-old rats, and renal parenchymal volume (RPV) measured in vivo with Gd-DTPA enhanced MRI in 24-week-old rats. Results are presented in ml (mean  $\pm$  SE);  $r$  = correlation coefficient between in vivo and in vitro measurements.  $P1$  indicates the level of significance when comparing in vivo and in vitro measurements.  $P2$  indicates the level of significance of the correlation coefficient

Age and group	TKV		$P1 <$	$r$	$P2 <$
	In vivo	In vitro			
10 days					
Control ( $n=6$ )	0.18 $\pm$ 0.01	0.17 $\pm$ 0.01	NS	0.804	0.05
Mild ( $n=6$ )	0.36 $\pm$ 0.02	0.38 $\pm$ 0.02	NS	0.950	0.01
24 weeks					
Mild ( $n=7$ )	1.91 $\pm$ 0.08	1.92 $\pm$ 0.08	NS	0.98	0.001
Severe ( $n=7$ )	4.18 $\pm$ 0.63	4.82 $\pm$ 0.64	NS	0.98	0.001
24 weeks					
RPV					
Mild ( $n=6$ )	1.03 $\pm$ 0.02	1.04 $\pm$ 0.09	NS	0.95	0.001
Severe ( $n=6$ )	0.83 $\pm$ 0.18	0.85 $\pm$ 0.14	NS	0.87	0.02

and the in vitro measurements (Table 1). Similarly, in the 24-week-old rats, a good correlation was found between the in vivo and the in vitro measurements of TKV in the mildly obstructed kidneys as well as in the severely obstructed kidneys (Table 1). In the 24-week-old rats in vitro RPV measurements did not differ from the in vivo RPV results measured by MRI with Gd-DTPA enhancement. Comparison of in vivo and in vitro measurements showed a very good correlation in both mildly and severely obstructed kidneys (Table 1). From these data it can also be estimated that PV constitutes about 50% of TKV in the mildly obstructed kidneys and 75–80% of TKV in the severely obstructed kidneys.

The in vitro RPV/BW in the severely obstructed kidneys at week 24 decreased to 75% of controls ( $0.25 \pm 0.02$  vs  $0.33 \pm 0.01$  ml/100 g BW,  $P < 0.01$ ), whereas the mildly obstructed kidneys did not differ significantly from the controls ( $0.29 \pm 0.03$  vs  $0.33 \pm 0.01$  ml/100 g BW).

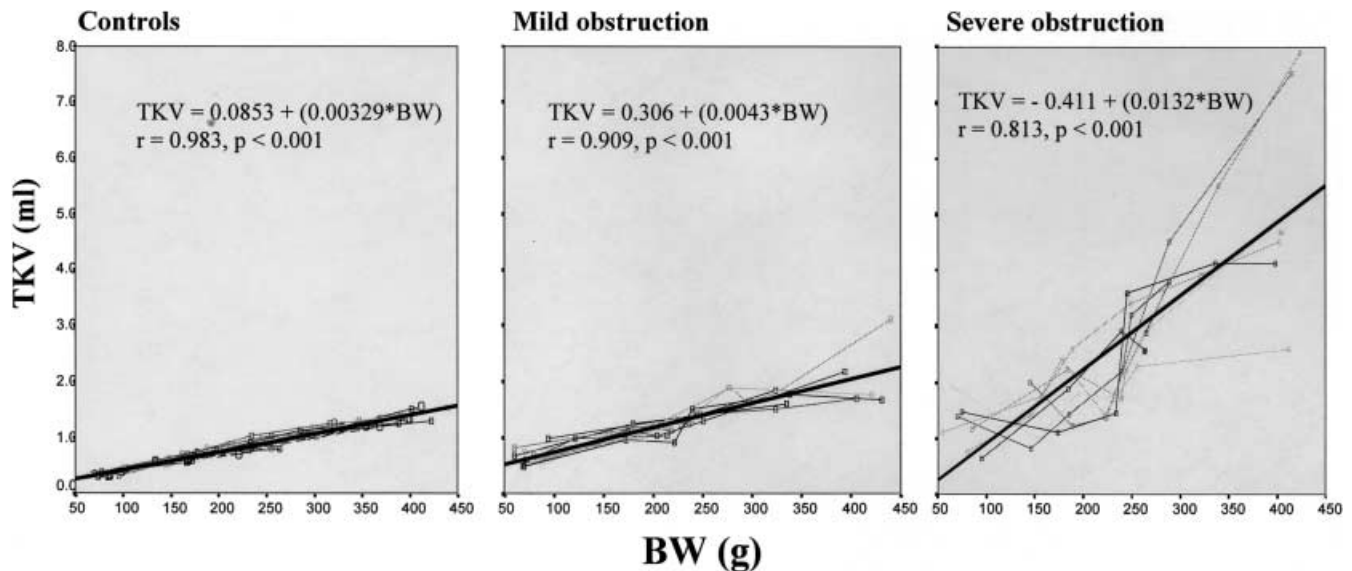
The relationship between RVBF and RPV/BW was examined in order to find out if these parameters changed in parallel. A good correlation was observed in the control group [ $RVBF = 0.425 + (7.013 \times RPV)$ ,  $r = 0.918$ ,  $n = 8$ ,  $P < 0.001$ ] as well as in the combined obstruction groups [ $RVBF = 1.168 + (3.823 \times RPV)$ ,  $r = 0.758$ ,  $n = 13$ ,  $P < 0.01$ ]. In contrast, the relationship between RVBF and TKV was very poor [ $RVBF = 5.775 - (0.291 \times TKV)$ ,  $r = 0.36$ ,  $P = 0.22$ ]. Similarly, the relationship between RVBF and PV was poor [ $RVBF = 5.646 - (0.360 \times TKV)$ ,  $r = 0.463$ ,  $P = 0.11$ ].

Similar trend for TKV and RVBF with regard to severity and duration of obstruction

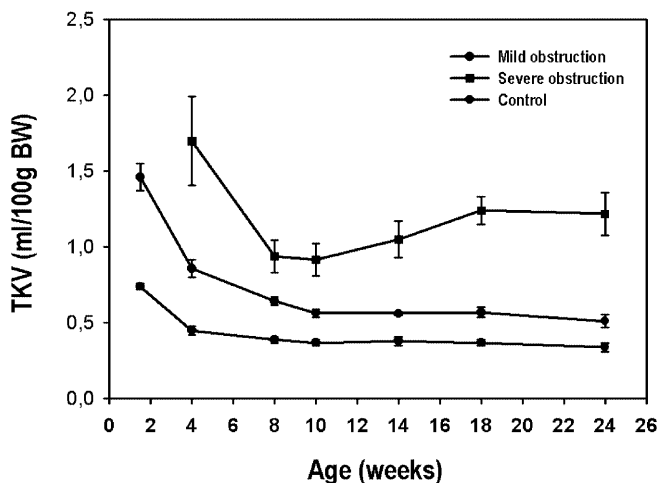
Severe obstruction caused, as expected, a pronounced increase in kidney volume. In all groups, there was a highly significant correlation between TKV and BW ( $P < 0.01$ ) (Fig. 5). The TKV increase rate was significantly higher in the obstructed kidneys (including both mildly and severely obstructed) than in the control kidneys ( $P < 0.002$ ), and in severely obstructed than in mildly obstructed kidneys ( $P < 0.001$ ). The mean TKV of the intact control rats did not differ significantly from that of the sham-operated animals and, therefore, data from these two groups were combined and reported as controls. The left TKV increased consistently in all groups from the beginning to the end of the study (Fig. 5) (Control kidneys: from  $0.19 \pm 0.02$  ml to  $1.38 \pm 0.03$  ml; mildly obstructed kidneys: from  $0.36 \pm 0.02$  ml to  $1.95 \pm 0.21$  ml; severely obstructed kidneys:  $1.20 \pm 0.17$  ml at week 4 to  $4.65 \pm 0.75$  ml).

Body weight corrected TKV was significantly higher in both mildly and severely obstructed kidneys compared with control kidneys immediately after the onset of obstruction (at day 10 and week 4) (Fig. 6). The mean TKV/BW (Fig. 6) of the severely obstructed kidneys was significantly higher than that of the mildly obstructed ones during the 24 weeks of observation. In the severely obstructed kidneys, TKV seemed to reach a stable plateau from week 18 on. Also, the mildly obstructed kidneys differed significantly from the controls during the entire 24-week period. However, TKV/BW in each group did not differ significantly from week 10 to week 24, indicating that within each group TKV/BW did not progress.

TKV measured with Gd-DTPA enhanced MRI did not differ significantly from that without the Gd-DTPA enhancement. The renal pelvic area, however, can be better recognized on the MR images with Gd-DTPA enhancement (Fig. 7).



**Fig. 5.** Left total kidney volume (*TKV*) in relation to body weight (*BW*) in controls, mildly obstructed and severely obstructed kidneys. In all three groups, a linear relationship was found between the left *TKV* and *BW*. In the severely obstructed kidneys *TKV* increase is much more dramatic and shows a larger variation compared to mildly obstructed and control kidneys



**Fig. 6.** Total kidney volume (*TKV*) corrected for body weight decreased during the initial 10 weeks of life indicating a relatively larger kidney volume in the neonatal than in the adult kidney. Furthermore, during the first period the *TKV* was dramatically changed in the obstructed group, indicating a relatively larger kidney volume immediately after the creation of the obstruction. In both obstructed and control kidneys *TKV* became stable from week 10 although *TKV* in both mildly and severely obstructed kidneys differed significantly from that of controls ( $P < 0.001$ ) during the whole course of follow up

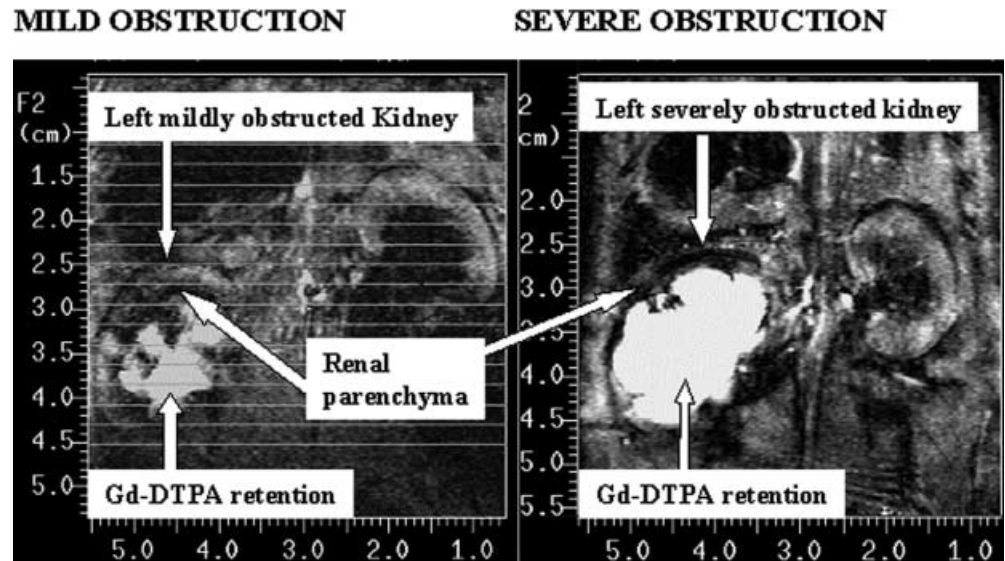
## Discussion

Renal blood flow can be measured quantitatively in rats by laser Doppler flowmetry [6, 15], electromagnetic flowmetry [15], and by radiolabeled microspheres [15].

All of these methods are invasive and do not have clinical applicability. Neither are the invasive methods suitable for repeat studies. Blood flow measurement using MRI was reported in 1982 by Moran who interlaced a velocity-encoding phase modulation field gradient into a conventional MR sequence and thereby obtained quantitative images of velocity [11]. Recently, Ringgaard et al. successfully applied MRI to RVBF measurements in rats [13]. The major advantage of this technique is the elimination of the potential complications of invasive techniques. Blood flow measurements were performed using the renal vein rather than the renal artery for two reasons: first, due to the larger diameter the renal vein it is easier to locate; second, vein blood flow is almost non-pulsatile, and therefore cardiac gating of the measurement is not necessary.

The RVBF, measured by MRI in the present study, was  $5.97 \pm 0.44$  ml/min in the control rats with a BW of 280–350 g ( $306 \pm 5$  g). These renal blood flow values are similar to those measured with electromagnetic flowmetry:  $5.33 \pm 0.41$  ml/min in normal rats with a BW of 280–335 g [11]. Likewise, the RVBF in control rats in the present study averaged  $2.02 \pm 0.08$  ml/min/100 g BW, a value that is similar to the renal blood flow values observed in both anaesthetized [13] and conscious rats [17] (values ranging from 2.0–2.5 ml/min/100 g BW). In addition, to confirm the development of renal blood flow with age, this study also demonstrates that sequential RVBF monitoring by MRI is possible even in the neonatal rat. In vitro flow measurements in the range of 0.5–33 ml/min in an acrylic pipe (diameter: 3 mm) revealed a high accuracy for the MRI method ( $r = 0.997$ ;  $P < 0.001$ ) [13]. RVBF measured in 10-day-old rats was  $0.64 \pm 0.03$  ml/min (i.e. above 0.5 ml/min), thus indicating that the MR technique provides reliable measurements of renal blood flow in most of the 10-day-old rats. A rigid tube, however, might not imitate the renal vasculature sufficiently, therefore, the accuracy of the measurement at this early age needs further validation. Few methods

**Fig. 7.** The left panel shows an MR image with Gd-DTPA enhancement in a mildly obstructed left kidney. The right panel shows an MR image with Gd-DTPA enhancement in a severely obstructed left kidney. Gd-DTPA retention was found in the pelvis of both mildly and severely obstructed kidneys and makes the pelvis more clearly visible



for repeat investigations have been available for following the development of the obstructed kidney. However, the present study shows that the MRI may be the technique that can fulfil the following requirements: it is reliable, can be performed even in neonate rats, and does not necessitate sacrifice and is therefore repeatable in each individual animal.

The effects of complete ureteral obstruction on renal blood flow have been studied in adult animals [22], but there is little knowledge of long-term (more than 3 months), sequential renal blood flow response to neonatal *partial* ureteral obstruction. Our data revealed that both mild and severe PUUO were associated with a time dependent reduction in RVBF. Although the increase in RVBF with BW occurred in the control and in both obstruction groups, a significant difference was found between the slopes, indicating deterioration over time in the obstructed kidneys. In the severely obstructed kidney, RVBF decreased more than in the mildly obstructed group, indicating that the degree of obstruction can be predicted from the renal blood flow measurements. This is in accordance with our previous study of the hydrodynamics in rats with PUUO [19]. In addition, the impairment in RVBF appeared earlier and became more pronounced in the severely obstructed kidneys compared with the mildly obstructed kidneys. These data support the view of Chevalier et al. [1] that the decrease in RVBF is dependent on the severity of the obstruction. The moderate reduction in RVBF observed in the present study in the mildly obstructed kidneys is in accordance with the results obtained by Ichikawa and Brenner [7] that GFR was preserved in kidneys with mild obstruction, at least for a few weeks.

However, Chevalier and Kaiser and Chevalier et al. [1, 2], as well as Taki et al. [16], reported that chronic partial ureteral obstruction early in life results in more substantial decreases in renal blood flow and GFR than those suggested by our results. In their studies the partial

ureteral obstruction was created by surrounding the ureter with a plastic tube [1, 2, 16]. Using this technique, the ureter grows in a rigid cylinder, which automatically leads to progressive obstruction and renal deterioration. In the present study, partial ureteral obstruction was created by embedding the ureter into the psoas muscle. This may explain why the decrease in RVBF did not occur in this study, either in the mildly obstructed kidneys or in the severely obstructed kidneys, until weeks 18 and 10, respectively. In addition, in both degrees of obstruction we observed that after the initial kidney damage RVBF had a tendency to become stable and developed a pattern similar to that of the controls, albeit at a lower level. This may resemble the course of congenital hydronephrosis in humans, in which further progression does not always occur except in cases with complications. However, the progressive RVBF reduction in kidneys with severe obstruction is supported by an absolute renal blood flow that is significantly lower at week 24 than at week 10. Additionally, renal blood flow differed significantly between mildly and severely obstructed kidneys at week 24.

Our study revealed that TKV was significantly enlarged in obstructed kidneys and significantly more enlarged in severely obstructed than in mildly obstructed kidneys. In severe obstruction, TKV progressively increased with age. Our *in vivo* and *in vitro* measurements of the TKV were highly correlated. MRI thus seems reliable for the purpose of measurement of TKV in both neonatal and adult animals. Body weight corrected TKV did not show a similar degree of progression, supporting clinical data showing that TKV of a hydronephrotic kidney rarely progresses during long-term follow-up [5, 9].

In 24-week-old rats, RPV and PV were measured *in vivo* with Gd-DTPA enhancement MRI as well as *in vitro*. A significant correlation was found between these two measurements indicating that Gd-DTPA

enhanced MRI provides a good estimate of TKV, RPV and PV. Furthermore, the results show that the pelvic volume is a major contributor to the increase in TKV, both in the mildly obstructed and the severely obstructed kidneys.

The RVBF correlated well with the RPV in both controls and obstructed kidneys. In contrast, in the same animals there was a very poor correlation between RVBF and TKV and between RVBF and PV. Thus, measurements of RVBF may serve to estimate changes in the renal parenchymal volume in obstructed kidneys. Furthermore, our results indicate that MRI may become an important tool that can provide markers for changes in both RVBF and the size of hydronephrosis in sequential studies of non-operatively treated, antenatally detected cases with hydronephrosis, especially when a differentiated analysis of TKV, RPV and PV is included. Recently, an evaluation of non-operative therapy called attention to degree of dilatation as a sign of the need for surgery [4]. The poor correlation between RVBF and TKV and PV found in the present study indicates that functional changes in the kidney do not correlate with the degree of pelvic dilation or total kidney volume. This view is supported by data from another animal study in which the authors obtained similar results [12], suggesting that the size of the hydronephrosis is a poor marker of renal function. In the present study, there was a good relationship between renal blood flow and in vitro determined parenchymal volume, suggesting that this may be an important parameter for evaluating hydronephrotic patients. The relationship between kidney volume (TKV, RPV and PV) and functional parameters of the kidney needs to be examined in more detail in future studies in order to establish the role of MRI in this important group of patients.

## Conclusion

Both mild and severe PUUO induced a significant decrease in RVBF. The magnitude of the decrease was dependent on the severity and duration of obstruction, which indicates that the removal of the partial obstruction may be important for preserving the renal function in rats with severe obstruction. MRI can be used to follow RVBF and kidney volume from an early age. The reduction in RVBF in the obstructed kidney did not correlate with TKV or PV, but correlates well with the reduction in renal parenchymal volume.

**Acknowledgement** The Danish State Growth and Reproduction Foundation, The Karen Elise Jensen Foundation, The Novo-Nordisk Center For Growth and Regeneration and Aarhus University supported this study. Dr. Yue Chen is thanked for her assistance with the experimental work. Statistician Mr. Niels Trolle Andersen is thanked for his assistance with the statistical analysis. The study complied with the Danish regulations for care and use of experimental animals.

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