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Does polyuria associated with vasopressin V2 receptor antagonism result in an increased ureter diameter in ADPKD patients?

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Introduction

- Tolvaptan, a vasopressin V2 receptor antagonist, has recently been shown to reduce renal function loss in ADPKD patients, but also leads to polyuria because of its aquaretic effect
- Long-term polyuria without frequent voiding can result in ureter dilatation with consequently hydronephrosis and renal function loss

Study Aims

- To investigate the effect of tolvaptan on ureter diameter in patients with ADPKD
- To investigate the associations of 24-hour urine volume, renal function and total kidney volume with ureter diameter at baseline and at the end of treatment

Methods

- Post-hoc single center analysis of the TEMPO 3:4 trial
  - A prospective, blinded, randomized, controlled clinical trial in ADPKD patients with total kidney volume (TKV) ≥ 750 mL and eCrCl ≥ 60 ml/min
  - Patients were titrated to their highest tolerated dose over 3 weeks (45/15 mg, 60/30 mg, 90/30 mg) and treated with tolvaptan (N=32) or placebo (N=19) for 36 months
- TKV was measured by MRI and GFR by continuous infusion of ^{125}I-iothalamate (mGFR)
- The coronal T2-HASTE sequence of the MR images was used to measure ureter diameter 3 cm from the renal pelvis as well as on the level of lumbar 5 (L5)

Conclusions

- **Tolvaptan induced polyuria, but did not lead to an increase in ureter diameter, suggesting that tolvaptan is a safe therapy from a urological point of view**
- **Because of the limited power of our study we still advise other clinicians when prescribing tolvaptan as treatment in ADPKD, to instruct their patients to void frequently**

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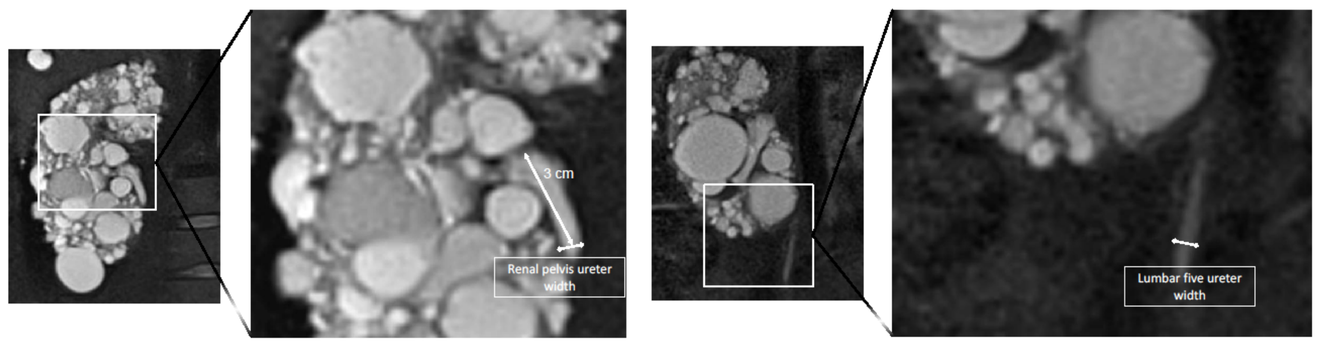
Baseline characteristics

	Placebo (n=19)	Tolvaptan (n=32)	P-value
Age (y)	37 ± 6	40 ± 8	0.2
Male (%)	63.2	78.1	0.2
Length (cm)	181 ± 11	183 ± 8	0.6
Weight (kg)	85 ± 14	89 ± 12	0.3
Body mass index (kg/m^2)	25.7 ± 3.9	26.6 ± 3.0	0.3
Antihypertensive use (%)	78.9	81.3	0.6
Systolic blood pressure (mmHg)	132 ± 11	133 ± 12	0.8
Diastolic blood pressure (mmHg)	82 ± 7	83 ± 10	0.7
Heart rate (per minute)	66 ± 11	69 ± 13	0.4
Plasma creatinine (umol/l)	106 ± 39	100 ± 27	0.5
mGFR (mL/min)	94 ± 27	103 ± 29	0.3
Total kidney volume (L)	1.68 (1.13 – 2.37)	2.00 (1.38 – 2.56)	0.2

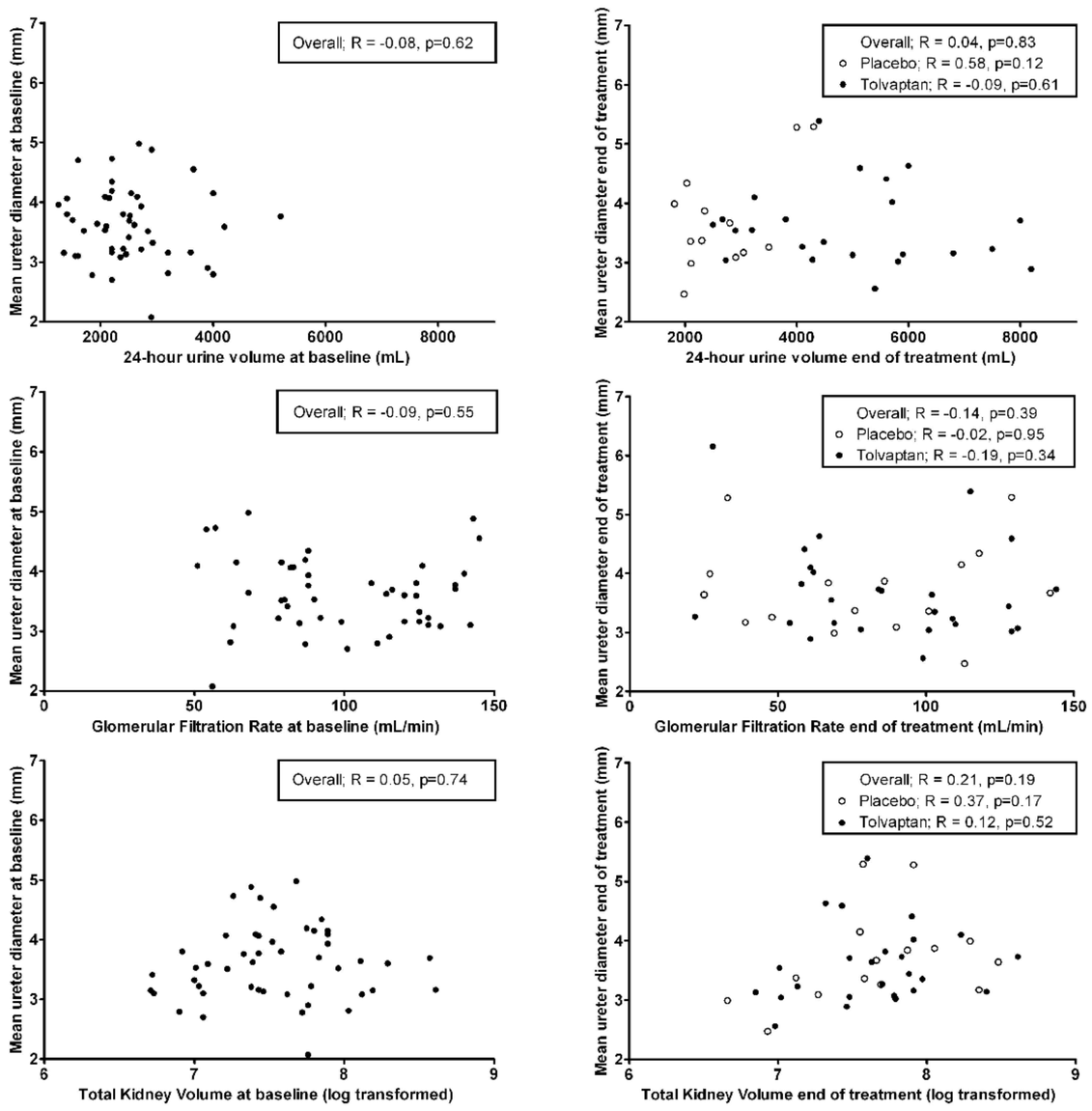
Ureter diameter measurements



	Placebo		Tolvaptan		P-value	
	MRI base	MRI ET	MRI base	MRI ET	P vs. T base	P vs. T ET
24-hour urine volume (L)	2.50 (2.08 – 2.72)	2.33 (2.08 – 2.16)	2.20 (1.85 – 2.90)	5.02 (3.38 – 5.88)*	0.9	<0.001
Renal pelvis left (mm)	4.0 ± 1.0	4.1 ± 0.9	3.8 ± 1.0	3.8 ± 1.1	0.6	0.3
Renal pelvis right (mm)	4.4 ± 1.2	4.7 ± 1.7	4.2 ± 1.2	4.5 ± 1.4	0.6	0.7
Ureter L5 left (mm)	3.1 ± 0.4	3.4 ± 0.8	3.2 ± 0.8	3.2 ± 0.7	0.8	0.5
Ureter L5 right (mm)	3.2 ± 0.5	3.2 ± 0.9	3.0 ± 0.5	3.2 ± 1.2	0.3	0.9

Abbreviations: Base, baseline; ET, end of treatment; P, placebo; T, tolvaptan.
**p < 0.05; MRI baseline versus MRI ET*

Urine volume, mGFR and TKV vs. ureter diameter



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