GAVIN PUBLISHERS

Journal of Urology and Renal Diseases

Denys MA, et al. J Urol Ren Dis 2017: JURD126.
DOI: 10.29011/2575-7903.000026

Research Article

Renal Dilatation in Patients with A Spinal Cord Injury: Both Bladder Pressure and Diuresis Involved? A Pilot Study

Marie-Astrid Denys[1*], Annick Viaene[2], Francois Herve1, Jana Claeys[3], Piet Hoebeke[1], Karel Everaert[1]

[1]Department of Urology, Ghent University Hospital, Belgium

[2]Department of Physical medicine and orthopedic surgery, Ghent University Hospital, Belgium

[3]Department of Gynecology, Ghent University Hospital, Ghent, Belgium

[*]**Corresponding author:** Marie-Astrid Denys, Department of Urology, Ghent University Hospital, De Pintelaan 185, 9000 Ghent, Belgium. Tel: +32 9 332 22 83; Fax: +32 9 332 38 89; E-Mail: marie-astrid.denys@uzgent.be

Citation: Denys MA, Viaene A, Herve F, Claeys J, Everaert K, et al (2017) Renal Dilatation in Patients with A Spinal Cord Injury: Both Bladder Pressure and Diuresis Involved? A Pilot Study. J Urol Ren Dis 2017: JURD126. DOI: 10.29011/2575-7903.000026

Received Date: 06 March, 2017; **Accepted Date:** 30 March, 2017; **Published Date:** 06 April, 2017

Abstract

Background: Dilatation of the upper urinary tract in spinal cord injury (SCI) patients can result from an increased outflow resistance caused by an increased intravesical pressure. However, we suggest that this antegrade obstruction can also result from increased urine production.

Objective: To assess renal dilatation before and after first morning voids (FMVs); explore the link between bladder pressure, renal dilatation and polyuria; and suggest factors to consider in future studies.

Methods: A prospective observational pilot study was performed in adults with a SCI and included measurements of intravesical pressure before FMVs, renal ultrasounds before and after FMVs and completion of a frequency volume chart.

Results: A total of 48 renal ultrasounds, obtained from 4 women and 20 men with a median age of 38 (30-55) years, were analyzed. The mean width of the minor calyces before FMVs was 1.8 mm (1.3-2.1) for the left kidney, 1.6 mm (1.4-2.6) for the right kidney and 1.7 mm (1.5-2.5) in total. These measurements showed a significant decrease after the FMV, with a decrease to 1.0 mm (0.7-1.6; $p<0.001$) on the left side, 0.9 mm (0.7-1.5; $p<0.001$) on the right side and 1.0 mm (0.7-1.6; $p<0.001$) in total. Higher intravesical pressure was correlated with higher differences in width of the minor calyces between pre-void and postvoid ultrasounds ($R^2=0.229$; $p=0.045$).

Conclusions: In adults with a SCI, renal dilatation is significantly lower after the FMV compared to before the FMV. Future studies need to evaluate the association between the volume of FMVs, nocturnal polyuria and hydronephrosis in SCI patients.

Keywords: Spinal Cord Injuries; Neurogenic Bladder; Lower Urinary Tract; Kidney

Introduction

A spinal cord injury (SCI) often causes neurogenic lower urinary tract dysfunction, with signs and symptoms depending on the site of neurologic insult. Adequate treatment is essential to prevent morbidity and mortality and consists of controlling urinary tract infections, maintaining a low-pressure bladder that is both continent and capable of emptying and preventing secondary damage to the upper and lower urinary tract [1-3]. A major cause of renal deterioration is elevated intravesical pressure during bladder filling, either due to a low bladder compliance or detrusor overactivity. Even in the absence of upper urinary tract dilatation or vesicoureteral reflux (retrograde theory), high intravesical pressure can deteriorate pyelocaliceal and ureteral drainage of urine into the bladder. This can be explained by the oblique passage of the ureter through the bladder wall, which results in ureterovesical outflow resistance with increasing bladder filling and pressure. This may lead to obstructive renal dilatation, whether or not intermittent (antegrade theory) [1-3]. The idea to conduct this pilot study is based on our experience and observations in clinical practice. First, we sometimes see SCI patients with important hydronephrosis that reduces or disappears after bladder emptying. Second, we observe

a high nocturnal urine production in the majority of our SCI patients. Therefore, we hypothesize that periods of increased urine production or polyuria contribute to this intermittent obstructive renal dilatation because of the surplus of urine that needs to attend the bladder. Particularly nocturnal polyuria, or increased urine production during nighttime, has been recognized as a highly prevalent condition in SCI patients [4-6]. This may increase the risk of developing obstructive renal dilatation during the night and early morning (Figure 1).

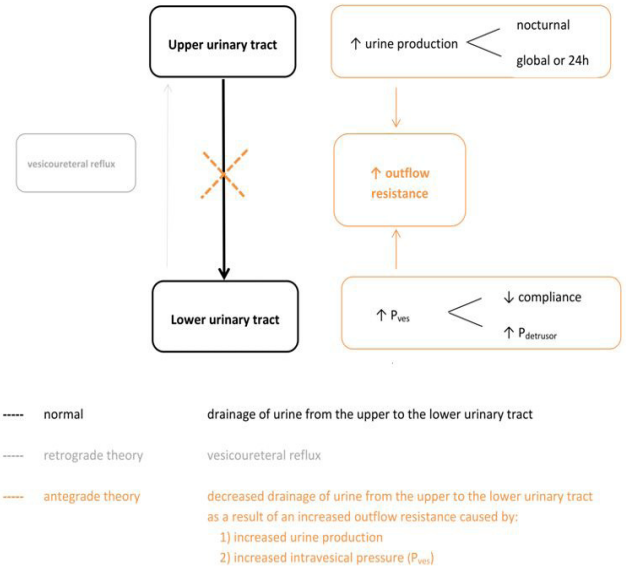

Figure 1: Link between urine production and renal dilatation in patients with a spinal cord injury

We hypothesize that dilatation of the upper urinary tract in patients with N-LUTD can be caused by an increased outflow resistance, regardless of the presence of vesicoureteral reflux (retrograde theory). We suggest that this obstruction of antegrade drainage of urine can result from increased urine production on one hand, and an increased intravesical pressure on the other hand (antegrade theory).

The aim of this pilot study is (1) to assess renal dilatation before and after the first morning void in patients with a SCI, (2) to explore the link between bladder pressure, renal dilatation and polyuria in order to provide insights into a clinical situation that the majority of SCI patients experience and (3) to demonstrate opportunities and pitfalls that need to be taken in consideration by scientists in future studies about this topic.

Methods

Video-urodynamics were performed according to good urodynamic practices using a multichannel urodynamic system as recommended by the ICS Video-urodynamics were performed according to good urodynamic practices using a multichannel urodynamic system as recommended by the ICS

Patient selection

A prospective observational pilot study was designed and carried out in Ghent University Hospital, Belgium. The data were collected from March 2014 to February 2015. Adults with a SCI were asked to participate during their hospitalization at the department of physical medicine and motor rehabilitation or the department of urology, or in an ambulatory setting in the department of urology. For all participants, data from a video-urodynamic examination had to be available in the patients' medical file and bladder management had to remain unchanged in the period between the video-urodynamic examination and study participation. Patients with vesicoureteral reflux, urinary tract infection and severe urinary incontinence were excluded.

Data collection

A renal ultrasound was performed by M.A.D. or J.C. at two different times: before and after patients first morning void. At each time, the width of the minor calyces was measured at 3 different places, both for the left and the right kidney. The ultrasound equipment used was a BK Medical Flex Focus 400 portable apparatus with a 3.5 MHz curved transducer. During the night that preceded these measurement, patients who usually performed nocturnal catheterisation were asked to skip this once and patients with a draining catheter were asked to clamp it in order to be able to evaluate the effect of the overnight urine production. In patients with a known high nocturnal diuresis, we advanced the nocturnal micturition to an earlier time during the night to avoid complications such as urinary tract infections or autonomic dysreflexia. If patients would develop signs or symptoms of autonomic dysreflexia or a urinary tract infection, the bladder had to be emptied immediately.

Patients were asked to complete a frequency volume chart, which is a registration of time and volume of all voids during 24 to 72 hours. Nocturnal urine production comprised the voided volumes of all voids between midnight and the first morning void. Based on this frequency volume chart, nocturnal polyuria was defined as a nocturnal urine production >90ml/h (including the volume of the first morning and considering a night of 8 hours) or as a nocturnal polyuria index >33% (NPi, nocturnal urine production/24h urine production). Patients characteristics and video-urodynamic parameters were extracted from patients medical file. Urodynamic studies were performed according to the standards recommended by the International Continence Society [7]. Intravesical pressure was measured by connecting the patient's catheter to an infusion set, which was connected to a water column. Patients were in supine position and patient's own urine was used as transducing medium. Manometry was performed at the moment of the first morning catheterization and was indicated by the height (in cm H2O) of the urine column from the pubic bone [8]. The study was approved by the Ghent University Hospital review board (EC/2014/0119). The Declaration of Helsinki was followed and written informed consent to study participation was obtained from all subjects.

Statistical analysis

Statistical analysis was performed using SPSS v.22 for Windows (IBM Corp, Armonk, NY, USA). The median, first quartile (Q1, 25th percentile), third quartile (Q3, 75th percentile) and frequency were recorded as descriptive statistical parameters. Non-parametric tests were used to compare unpaired (Mann-Whitney U test) and paired continuous variables (Wilcoxon test) and to explore correlations (Spearman's rank correlation coefficient). A p-value <0.05 was considered statistically significant.

Results

Patients characteristics

A total of 48 renal ultrasounds, obtained from 4 (17%) women and 20 (84%) men with a median age of 38 (30-55) years, were eligible for analysis (Table 1).

	N=24
Mean age (years), median (Q1,Q3)	38 (30-55)
Gender (♀/♂)	4/20
Mean time since spinal cord injury (days), median (Q1,Q3)	228 (154-490)
Cause of spinal cord injury, n (%) - Traumatic - Non-traumatic	19 (79) 5 (21)
Level of spinal cord injury, n (%) - C1-C4 ASIA A - C5-C8 ASIA A ASIA B ASIA D - T1-S5 ASIA A ASIA B ASIA C ASIA D	 4 (17) 4 (100) 7 (29) 3 (43) 3 (43) 1 (14) 13 (54) 5 (38.5) 5 (38.5) 1 (8) 2 (15)
Mode of micturition, n (%) - Suprapubic catheter - Intermittent catheterisation - Spontaneous micturition	 6 (25) 15 (62.5) 3 (12.5)
Bladder management, n (%) - Anticholinergics - Intravesical onabotulinumtoxinA injection - Bladder augmentation	 10 (42) 1 (4) 1 (4)
Urodynamics, n (%) - Detrusor overactivity (Pdet >15 cm H_2O) - Detrusor overactivity (Pdet >40 cm H_2O) - No detrusoroveractivity - Dyssynergia **Urodynamics, median (Q1,Q3)** - Cystometric bladder capacity (ml) - Bladder compliance (ml/cm H_2O)	 7 (29) 3 (13) 17 (71) 4 (17) 502 (389-590) 70 (47-130)
Frequency volume chart (n=20), median (Q1,Q3) - Total 24h voided volume (ml) - Total nocturnal voided volume (ml) - Nocturnal polyuria index (%)	1967 (1578-2435) 947 (671-1188) 50 (39-58)

ASIA = American Spinal Injury Association Impairment Scale grade; Q1 = first quartile; Q3 = third quartile; P_{det} = detrusor pressure

Table 1: Patients characteristics

The cause of the SCI was traumatic in 19 (79%) patients and the median time since the injury was 228 (154-490) days. The level of the injury was C1 to C4 in 17%, C5 to C8 in 29% and T1 to S5 in 54% of patients. Six patients had a suprapubic catheter (25%), 15 (62.5%) performed intermittent catheterisation and 3 (12.5%) patients had a spontaneous micturition. Urodynamic evaluation showed detrusor overactivity in 7 (29%) patients and dyssynergia in 4 (17%) patients. Median cystometric bladder capacity was 502 ml (389-590) and median bladder compliance was 70 ml/cm H2O (47-130).

A frequency volume chart was completed by 20 (83%) patients during 24h (n=4), 48h (n=4) or 72h (n=12). Total 24h urine production was 1967ml (1578-2435) and 2 (10%) patients voided more than 3 liters per 24h. Nocturnal urine production and NPi were 947ml (671-1188) and 50% (39-58), respectively. Based on a NPi >33%, nocturnal polyuria was observed in 17 (85%) patients; based on a nocturnal urine production >90 ml/h, nocturnal polyuria was observed in 14 (70%) patients.

Prevoid and postvoid renal dilatation

To compare the mean width of the minor calyces before and after the first morning void, a total of 48 renal ultrasounds were performed in 24 patients with a SCI. Between the two renal ultrasounds, median voided volume of the frist morning void was 483 ml (350-713), with significantly higher volumes in patients with nocturnal polyuria (540 ml versus 200 ml; p=0.007). The mean width of the minor calyces before the first morning void was 1.8 mm (1.3-2.1) for the left kidney, 1.6 mm (1.4-2.6) for the right kidney and 1.7 mm (1.5-2.5) in total. These measurements showed a significant decrease after the first morning void, with a decrease to 1.0 mm (0.7-1.6; p<0.001) on the left side, 0.9 mm (0.7-1.5; p<0.001) on the right side and 1.0 mm (0.7-1.6; p<0.001) in total (Figure 2).

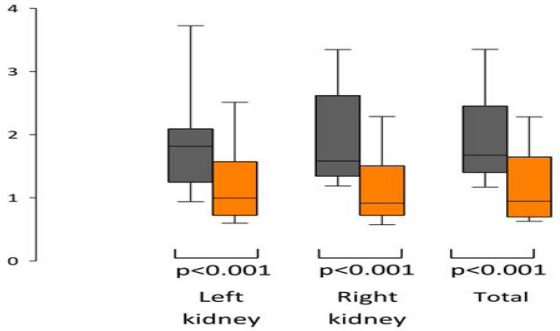

Figure 2: Mean width of the minor calyces (mm) before (grey) and after (orange) the first morning void (n=24)

Between the two renal ultrasounds, intravesical pressure was measured and showed a median pressure of 19 cm H2O (15-31). This intravesical pressure showed a significant correlation (R^2=0.229; p=0.045) with the mean difference in width of the minor calyces (%) between the prevoid and postvoid ultrasound (Figure 3).

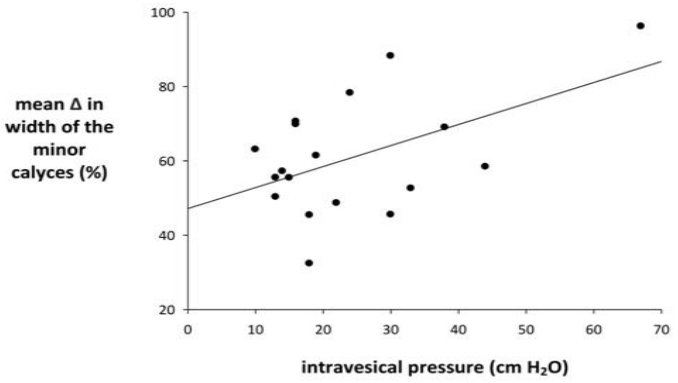

Figure 3: Correlation between the mean difference (Δ) in width of the minor calyces (%) and intravesical pressure (cm H2O), (n=18; R^2=0.229; p=0.045)

No significant correlation was found between the mean difference in width of the minor calyces (%) and the median volume of the first morning void (R^2=0.150; p=0.062), NPi (R^2=0.007; p=0.725), nocturnal urine production (R^2=0.044; p=0.373) or bladder compliance (R^2=0.045; p=0.321) (Figure 4).

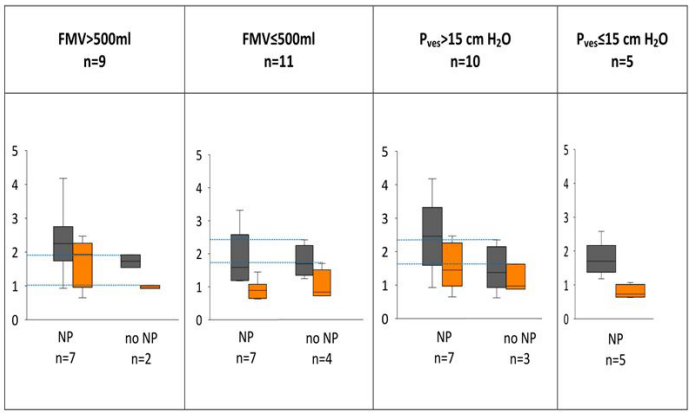

Figure 4: Median width of the minor calyces (cm) before (grey) and after (orange) the first morning void (FMV), according to the volume of the FMV, intravesical pressure (P_{ves}), and presence of nocturnal polyuria (NP, defined as a nocturnal urine production >90ml/h)

Patients with higher volumes of the first morning void (>500ml) and higher intravesical pressures (>15 cm H2O) have wider minor calyces, both before and after the first morning void. Comparison of patients with and without nocturnal polyuria in the group with a first morning void >500ml, showed that 5 of the 7 patients with nocturnal polyuria had a mean width of the minor calyces higher than the maximum width of patients without nocturnal polyuria before the first morning void; 4 of the 7 patients with nocturnal polyuria had a mean width of the minor calyces higher than the maximum width of patients without nocturnal polyuria after the first morning void. In the group with an intravesical pressure >15 cm H_2O, 4 of the 7 patients had a higher value before the first morning void and 3 of the 7 after the first morning void. Statistical analyses were not applicable because of the small sample size.

illustrates that patients with higher volumes of the first morning void (>500 ml) and higher intravesical pressures (>15 cm H2O) have wider minor calyces, both before and after the first morning void. Comparison of patients with and without nocturnal polyuria in the group with a first morning void >500 ml, showed that 5 of the 7 patients with nocturnal polyuria had a mean width of the minor calyces higher than the maximum width of patients without nocturnal polyuria before the first morning void; 4 of the 7 patients with nocturnal polyuria had a mean width of the minor calyces higher than the maximum width of patients without nocturnal polyuria after the first morning void. In the group with an intravesical pressure >15 cm H2O, 4 of the 7 patients had a higher value before the first morning void and 3 of the 7 after the first morning void. Statistical analyses were not applicable because of the small sample size.

Discussion

We measured the width of the minor calyces in SCI patients and showed a significant decrease in dilatation when we compared the measurements before and after the first morning void. In addition, the volume of this first morning void was significantly higher in patients with nocturnal polyuria. This was also described in a prospective study in 67 SCI patients with different grades of renal dilatation, who showed prominently wider diameters of the pyelocaliceal system (graded from 0 to IV) on prevoid renal ultrasound compared to postvoid [3].

We also demonstrated a correlation between intravesical pressure and renal dilatation, with significantly higher differences in renal dilatation in patient with higher intravesical pressures. High residual urine has already been described as a risk factor for upper urinary tract dilatation and deterioration, with higher risk of dilatation with increasing residual urine volumes [9.10]. However, a study in 120 spina bifida patients found that high residual urine was a significant risk factor for renal dilatation only in univariate but not in multivariate analysis, which suggests that high residual urine alone could not explain the development of renal dilatation in these patients [11].

The present pilot study provides opportunities to explore the hypothesis that dilatation of the upper urinary tract in SCI patients can be caused by an increased outflow resistance, regardless of the presence of vesicoureteral reflux (retrograde theory). We sug-

gest that this obstruction of antegrade drainage of urine can result from increased urine production on one hand and an increased intravesical pressure on the other hand (antegrade theory). This hypothesis is supported by the observation that besides volumes of the first morning void and intravesical pressure, also periods of polyuria may contribute to higher renal dilatation. Although future research is necessary to confirm this hypothesis, this pilot study gives an indication that not only detrusor pressure measured during urodynamics, but also actual intravesical pressure and diuresis play a role in the development of hydronephrosis in SCI patients. Future studies need to evaluate the effect of nocturnal polyuria on clinically relevant hydronephrosis, in order to identify patients at risk who need a treatment for nocturnal polyuria as prevention of clinically relevant hydronephrosis, for example by wearing compression stockings, compression therapy, timed diuretics or desmopressin. This pilot study was conducted to evaluate the feasibility of recruitment and assessment procedures, in order to provide valuable insights for future researchers. The main limitation of this study was the small sample size. Ultrasound was used to determine renal dilatation based on the width of the minor calyces since renal dilatation of the pyelocaliceal was only observed in the minority of participants. The lack of radiation and noninvasiveness of ultrasound is an advantage [12], but on the other hand, it is operator dependent and small distances were measured, which is the reason why we calculated the mean of 3 measurement each time.

Large prospective multicentral studies need to be performed to determine the clinical impact of (nocturnal) polyuria and detrusor pressure on renal dilatation and secondary upper urinary tract damage. Discussing the role of (nocturnal) polyuria is challenging, as many clinicians recognize the problem but evidence is lacking. In clinical studies, this can be performed by measuring the voided volume, intravesical pressure and renal dilatation before and after the first morning void. This has to be performed after prohibiting nocturnal micturition, which was one of the practical difficulties of this pilot study because it increased the risk of developing urinary tract infections or autonomic dysreflexia. However, none of the participants developed such complications that would have required immediate bladder emptying. Because of those practical limitations and the high sample size that is required, animal studies could be the first step to conduct those measurements to confirm our hypothesis. Other proposals for future research are measurements of intrarenal pressure in circumstances of standardized fluid intake and diuresis, which can be performed during surgical procedures. Also, evaluation of renal dilatation during standardized variations in intravesical pressure, fluid intake or bladder filling during urodynamic studies can be valuable. Results of such studies could help clinicians to provide advice about importance of prevention and treatment of (nocturnal) polyuria and high detrusor pressure in SCI patients.

Conclusion

In adults with a SCI, renal dilatation is significantly lower after the first morning void compared to the dilatation before the first morning void. The volume of this first morning void is associated with the presence of nocturnal polyuria, which may play a role in the development of obstructive hydronephrosis in this population. This has to be evaluated in future research.

References

1. Verpoorten C and Buyse GM (2008) The neurogenic bladder: medical treatment. Pediatr Nephrol 3: 717-725.
2. Schops TF, Schneider MP, Steffen F, Ineichen BV, Mehnert U, et al. (2015) Neurogenic lower urinary tract dysfunction (NLUTD) in patients with spinal cord injury: long-term urodynamic findings. BJU Int 6: 33-38.
3. Bih LI, Tsai SJ, Tung LC (1998) Sonographic diagnosis of hydronephrosis in patients with spinal cord injury: influence of bladder fullness. Arch Phys Med Rehabil 79: 1557-1559.
4. Ward PJ and Hubscher CH (2012) Persistent polyuria in a rat spinal contusion model. J Neurotrauma 29: 2490-2498.
5. Goh MY, Wong EC, Millard MS, Brown DJ, O'Callaghan CJ (2015) A retrospective review of the ambulatory blood pressure patterns and diurnal urine production in subgroups of spinal cord injured patients. Spinal Cord 53: 49-53.
6. Szollar SM, Dunn KL, Brandt S, Fincher J (1997) Nocturnal polyuria and antidiuretic hormone levels in spinal cord injury. Arch Phys Med Rehabil 78: 455-458.
7. Abrams P, Cardozo L, Fall M, Griffiths D, Rosier P, et al. (2002) The standardisation of terminology of lower urinary tract function: report from the Standardisation Sub-committee of the International Continence Society. Neurourol Urodyn 21: 167-178.
8. Sand PK, Brubaker LT, Novak T (1991) Simple standing incremental cystometry as a screening method for detrusor instability. Obstet Gynecol 77: 453-457.
9. Dromerick AW and Edwards DF (2003) Relation of postvoid residual to urinary tract infection during stroke rehabilitation. Arch Phys Med Rehabil 84: 1369-1372.
10. Takeda M, Tsutsui T, Takahashi H, Hatano A, Komeyama T, et al. (1994) Correlation of upper and lower urinary tract function in patients with neurogenic bladder: evaluation using simultaneous measurement of cystometry and diuresis renography with full and empty bladder. Neurourol Urodyn 13: 243-253.
11. Ma Y, Li B, Wang L, Han X (2013) The predictive factors of hydronephrosis in patients with spina bifida: reports from China. Int Urol Nephrol 45: 687-693.
12. Bueschen AJ and Lockhart ME (2011) Evolution of urological imaging. Int J Urol 18: 102-112.