Noninvasive Diagnosis of Bladder Outlet Obstruction in Patients with Lower Urinary Tract Symptoms Using Ultrasound Decorrelation Analysis



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Abbreviations and Acronyms

$\rho_{\text{avg}} = \text{average calculated}$ correlation
B00 = bladder outlet obstruction
BOOI = BOO index
LUTS = Iower urinary tract
symptoms
PFS = pressure flow study
RF = radio frequency
ROI = region of interest
US = ultrasound

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The corresponding author certifies that, when applicable, a statement(s) has been included in the manuscript documenting institutional review board, ethics committee or ethical review board study approval; principles of Helsinki Declaration were followed in lieu of formal ethics committee approval; institutional animal care and use committee approval; all human subjects provided written informed consent with guarantees of confidentiality; IRB approved protocol number; animal approved project number.

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* Correspondence: Molewaterplein 50, Room EE1630 Erasmus MC, 3015 GE Rotterdam, The Netherlands (telephone: +31 10 7043379; FAX: +31 10 7044726; e-mail: <u>a.muhammad@</u> <u>erasmusmc.nl</u>). **Purpose**: We developed a noninvasive method to diagnose bladder outlet obstruction. An ultrasound based decorrelation method was applied in male patients with lower urinary tract symptoms.

Materials and Methods: In 60 patients ultrasound data were acquired transperineally while they were voiding while sitting. Each patient also underwent a standard invasive pressure flow study.

Results: High frequent sequential ultrasound images were successfully recorded during voiding in 45 patients. The decorrelation (decrease in correlation) between subsequent ultrasound images was higher in patients with bladder outlet obstruction than in unobstructed patients and healthy volunteers. ROC analysis resulted in an AUC of 0.96, 95% specificity and 88% sensitivity. A linear relationship was fitted to the decorrelation values as a function of the degree of obstruction represented by the bladder outlet obstruction index, measured in the separate pressure flow studies.

Conclusions: It is possible to noninvasively diagnose bladder outlet obstruction using the ultrasound decorrelation technique.

Key Words: urinary bladder outlet obstruction, male, lower urinary tract symptoms, ultrasonography, diagnostic imaging

BENIGN prostatic enlargement often leads to BOO in elderly men. Nocturia, low urinary flow rate, postvoid dribbling and post-void residual volume are common symptoms of BOO. Urodynamic PFSs are used as the standard procedure to diagnose BOO.¹ A major disadvantage of this method is urethral catheterization, which causes partial obstruction during micturition and may alter diagnostic results. The invasive nature of the procedure also causes patient discomfort and pain, and might result in infection. Therefore, development of a noninvathe sive alternative method of diagnosing BOO is needed. A variety of noninvasive and more patient friendly diagnostic methods for BOO have been proposed, such as the condom catheter method, the penile method, perineal cuff sound recording, ultrasonic measurement of bladder wall thickness and Doppler flowmetry. $^{2-6}$ All of these techniques have some drawbacks and none has been applied routinely in clinical practice.

To develop an accurate clinical urodynamic method to diagnose BOO we applied a noninvasive, US decorrelation based technique to quantify flow velocity and turbulence in urethra models.^{7,8} This technique is based on comparing the scatter pattern in a group of images constructed from sequentially acquired US RF signals due to reflections from small scattering particles. If the particles move slowly, the images are similar, that is they will correlate highly. If the particles move quickly, the images will be less similar and the correlation will be less, that is there will be higher decorrelation.

In urine various types of crystals have been identified, such as calcium oxalate, uric acid and amorphous urates.^{9,10} These crystalline structures can act as small ultrasound scattering particles. In a previous study we found that morning urine contains a sufficient concentration of these scattering materials to be suitable for US of urinary flow using the decorrelation method.¹¹ We subsequently tested and applied the method in healthy volunteers and defined a relation between decorrelation and urinary flow velocity.¹² In a phantom with increasing severity of obstruction we found higher decorrelation values than in unobstructed urethra models at the same flow velocity. This was due to turbulent flow as a result of obstruction.⁸

On this basis we hypothesized that in patients with BOO we would find higher decorrelation values than in healthy volunteers at the same flow velocity. Thus, it might be possible to develop a practical method to noninvasively diagnose BOO in male patients with LUTS. In the current study we applied the decorrelation method in patients with LUTS to diagnose BOO and we compared the results with those of conventional PFSs.

MATERIALS AND METHODS

Population

After receiving institutional research ethics board approval (MEC-2013-419) we recruited 60 male patients with LUTS suggestive of BOO from January to October 2015. All patients provided informed consent. Completing an I-PSS (International Prostate Symptom Score) form to quantify the urological condition was part of routine practice.

Experimental Setup

Each patient voided while sitting with an ultrasound transducer gently placed against the perineum using a specially designed chair with a mechanical transducer manipulator (fig 1, A). Before voiding each patient was asked to void without straining. To adequately visualize the urethra the transducer was manually moved in angular and sidewise directions by the investigator using the vertical handle (fig. 1, B). To acquire RF US data of the urinary stream a Pro Focus UltraView 2202 system (BK-Medical, Herlev, Denmark) with a custom designed RF interface was used. US data acquisition was synchronized with the flow rate signal. Voided volume was measured at each voiding using a measuring jug.

Data Acquisition

From each patient we acquired 4 measurements. The first measurement was a free flow measurement, that is a flow measurement without a transurethral catheter but with US data acquisition. The following 2 measurements were conventional invasive PFSs done with the Andromeda urodynamic system (Medizinische Systeme, Potsdam, Germany) without US data acquisition. Finally, the bladder was refilled with saline solution to which we added approximately 4×10^5 SonoVue microbubbles per L (Braco International, Amsterdam, The Netherlands) to enhance the US reflection by the scattering particles. The catheter was removed and again a free flow measurement with US data acquisition was recorded.

We acquired 5 seconds of US data at different flow rates (maximum and sub maximum) during a complete voiding cycle. Each US frame included 10 sequential US RF data

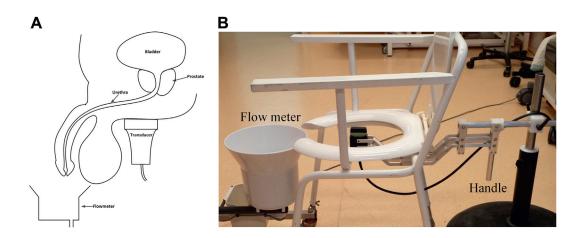


Figure 1. US transducer position was controlled by specially designed manual probe manipulator. A, schematic. B, experimental setup.

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