

Retrograde urethrosonography with SonoVue in strictures of the male urethra: a pilot study

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Abstract

Aim: To evaluate the effectiveness of SonoVue urethrosonography in diagnosing the adult male anterior urethral strictures pathology in comparison with retrograde urethrography. **Material and method:** We standardised the method and performed a comparative study evaluating the diagnosis of urethral strictures using retrograde urethrography and retrograde ultrasonographic exploration with SonoVue on 6 male patients. **Results:** In all patients, the existence of urethral stricture, localization and its extension were confirmed. Contrast-enhanced ultrasonographic exploration brought additional categories of information: the degree of spongiofibrosis, the elasticity of the urethral walls and the presence of urethral lithiasis. There were no periprocedural incidents. **Conclusion:** This pilot study demonstrates the feasibility and innocuity of urethral ultrasound with SonoVue. Real-time ultrasound exploration highlights aspects that are not seen in radiological examination, so the method can be complementary or alternative to this procedure.

Keywords: urethral stricture; SonoVue; urethrosonography; retrograde urethrography

Introduction

Urethral strictures represent the reduction of the urethral lumen caused by a process of scarring (by trauma, localized inflammation, iatrogenic/idiopathic pathologies); the congenital form is extremely rare in adults. The urethra presents an anterior and posterior segment. The anterior part is surrounded by the spongious body and is divided into the penile and bulbar segments. The posterior urethra, surrounded by the prostate and urethral sphincter, is divided into prostatic and membranous segments [1-3].

The term “urethral stricture” usually applies to the stricture of the anterior urethra and represents the abnor-

mal narrowing of any segment of the urethra surrounded by the spongious body, secondary to spongiofibrosis; the posterior stricture is due to the fibrotic process that narrows the neck of the bladder and results from a lesion secondary to traumas or surgical interventions (radical prostatectomy) [4]. In the literature the preferred term to describe the narrowing/ obstruction of the urethra is “stricture” and the term “stenosis” is reserved for the narrowing of the membranous and prostatic urethra, not surrounded by the spongious body. The terminology reflects the fact that there may be different damage mechanisms involved, each leading to fibrosis [4]. Urethral stricture is a common cause of presentation to the urologist and could be a complex problem due to the difficulties of diagnosis, treatment and risk of recurrence. Many methods of treatment have been described according to the location, length and density of fibrous tissue in the strictured area [5].

The diagnosis of urethral stricture is based on the history, clinical signs (diminished urinary stream, thin/interrupted jet/urinary retention, or urinary tract infec-

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tions such as prostatitis or epididymitis) and imaging. The methods for diagnosis are retrograde urethrography, voiding cystourethrography, computed tomography (CT) or magnetic resonance imaging (MRI) but also urethral sonography [6-8]. The retrograde urethrography, introduced by Cunningham in 1910, has numerous limitations: it is invasive, it underestimates the length of strictures (due to the patient's positioning/penis traction during injection), it does not provide information about the degree of spongiofibrosis [8] and it contributes with 0.6%-1.6% to hospital-acquired infections. Also, the risk of allergic reaction and the patient/physician exposure to radiation (5-9 MSV = 2.5 years background radiation and 230 X-rays) [7,9] has to be mentioned. CT scans are also radiation-inducing, while MRI of the penis has a higher cost and is recommended only in specific situations (for example, prostatomembranous urethral occlusions secondary to crush injuries of the pelvis) [10].

Contrast enhanced ultrasound (CEUS) is an evolving imaging modality, a non-invasive and non-irradiating method with increasing clinical utility. The most widely used contrast agent is the second generation Sono Vue, namely sulfur hexafluoride. The technique was used for retrograde microbubble enhanced ultrasound urethrogram or contrast-enhanced voiding urosonography for assessing the vesicoureteral reflux, megaureter, ectopic ureter, ureteroceles, vesical diverticulum, urogenital sinus or congenital urethral pathologies (posterior urethral valves, anterior urethral valves, diverticula of prostatic utricle) [11]. In such instances, contrast-enhanced urosonography was able to distinguish between the congenital stricture of Cobb's collar (also known as Moorman ring or Young's type III valve [12]) that requires endoscopic transurethral incision and segmental strictures which ought to be treated with balloon dilation.

The purpose of our study was to evaluate the effectiveness of harmonic ultrasonography with contrast enhancement of the urethra in the diagnosis of adult male anterior urethral pathology. The objectives pursued were: a demonstration of the feasibility of urethronography with contrast enhancement; the identification and characterization of the stricture; the innocuity of the method for the patient and the physician; and comparison of contrast-enhanced urethronography with retrograde urethrography studies which were performed in the same patients.

Material and method

The study was carried out on a series of 6 patients with urethral stricture who presented in the emergency service of Department of Urology between March – May 2018. In all patients, a conventional urological assess-

ment (clinical examination, prostate check, supra-pubic ultrasonography with pre- and postmictional evaluation of the bladder volume) and a radiological exploration – retrograde urethrography – was initially performed. Retrograde ultrasonographic exploration with SonoVue was performed in the same day, after explaining in detail the objectives of the research and the procedure, as well as after obtaining the written patient's consent. The approval of the Ethics Committee of the University was also obtained.

The method of exploration was the same for all the patients: a) the patient seated in the dorsal decubitus and dorsal recumbent position; b) disinfection of perineal and scrotal region; c) CEUS were performed on a General Electric Logiq E9 machine; we used a broad spectrum convex transducer (1.5-6 MHz) suitable for abdominal explorations with contrast; d). the application of the transducer was carried out on the perineal region using as a reference element the medio-sagittal axis with simultaneous and continuous visualization of the penile and prostatic urethra; e) the examination was carried out by a team consisting of an experienced examining physician, an urologist (who injected the contrast agent in conditions of sterility) and a nurse (who ensured the resources necessary to the exploration: ultrasound gel and contrast agent, who filled the syringe with the diluted contrast SonoVue agent and supervised the patient; f) the SonoVue contrast agent used was a small dose (drops) instilled in 10 cc of physiological serum (fig 1).

The ultrasonographic exploration was divided into two stages: a) the initial stage – the overall and indicative assessment of the region for the purpose of identifying the reference anatomical structures; b) the exploration stage: tracking in “hybrid” mode and real-time progression of the contrast agent to the urethral level (fig 2).

The entire urethra was examined by CEUS in order to determine: the presence of the stricture, its site and length but also the presence of other changes: spongiofibrosis, small stones.



Fig 1. Ultrasonographic exploration method of male urethra using transperineal approach (collage) a) Sonovue injection into the urethra; b) distal urethra examination; c) perineal urethra examination

Statistical analysis

A descriptive analysis was performed between the results of the retrograde urethrography and SonoVue urethrosonography.

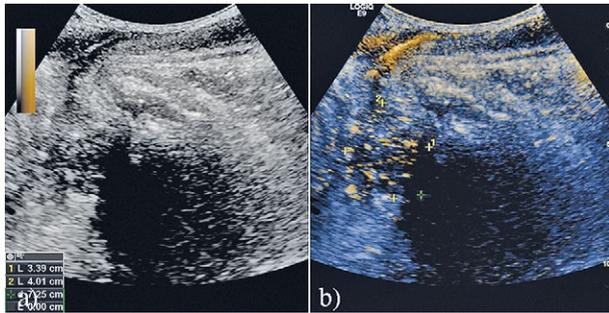


Fig 2. Ultrasonographic exploration of the male urethra using the transperineal approach in grey scale (a) and during the administration of contrast agent (b) using the “hybrid” mode, relevant for a proper assessment of urethral permeability. A marked prostate can be observed (dimensions approx. 4/3 cm). The urethral path appears in the orange color and it is linear.

Results

The average age of patients was 66.16 years (aged between 50 and 75 years). Total duration of exploration was 10 minutes on average. There were no periprocedural incidents.

In table I the diagnosis, the relevant history, the descriptive radiological aspect of the retrograde urethrography, the appearance of ultrasonography with SonoVue and the limitations encountered by the two methods were detailed.

The existence of an urethral stricture and its site were confirmed during urethrosonography in all patients. The length of the stricture was better estimated using this technique (fig 3).

Ultrasonographic exploration also brought additional categories of information: thickening of spongiosum and/or the presence of „garland-like” lithiasis <1 cm disposed on the urethra as well as the elasticity of the urethral walls (fig 4, fig 5).

Table I. Retrograde urethrography and SonoVue urethrosonography – results, advantages and limits

No.	Age (years)	Retrograde urethrography	Retrograde urethrosonography	Advantages and limits of the methods
1	75	Multiple strictures with pseudo-diverticular aspect at bulbar and anterior urethral level	Multiple strictures at the anterior urethra level, on the entire surface of the anterior urethra, with approx. 1.5 cm walls, stricture of the bulbar urethra, with downstream dilatation of the urethral caliber	Urethrosonography was able to identify the posterior bulbar urethra as opposed to standard radiology
2	72	Stricture of the bulbar urethra with minimal reduction of caliber	Urethral stricture on a distance of 2.1 cm, with 1.8 cm spongiofibrosis, and outside the stricture the spongiosum has variable thickness between 3 and 13 mm	Urethrosonography was able to determine spongiofibrosis, as opposed to standard radiology.
3	59	Tight stricture of the bulbar urethra	Urethral stricture at the level of prostate apex of 1.8 cm	Urethrosonography was able to identify the length of the stricture, as opposed to standard radiology, where the passing of contrast media is compulsory.
4	50	Filiform urethra with a caliber of 6 mm, tight posterior bulbar stricture with 1.4 cm prestenotic dilatation on a length of 1.6 cm; a false pathway can be observed	Stricture of the bulbar urethra of approx. 13-14 m; anterior urethra stricture, on a 27 mm distance, with spongiofibrosis	Standard radiology was able to identify a false pathway which was not highlighted in urethrosonography. Spongiofibrosis was only assessed by urethrosonography
5	73	Tight urethral stricture of 1 mm at the half of the penile urethra with 1.3 cm caliber prestenotic dilatation	Penile urethral stricture of approx. 12 mm with spongiofibrosis of 1.7 mm at the stricture level, caliber of 1.9 mm, situated at 4.5 cm from the tip of the penis; small urethral stones with “garland like” aspect	Retrograde urethrography was unable to identify urethral stones – as opposed to urethrosonography which was able to determine spongiofibrosis as well
6	68	Tight urethral stricture of 1 mm at the half of the penile urethra with 1.3 cm caliber prestenotic dilatation	Penile urethral stricture on a 2 cm distance with 2.5 mm spongiofibrosis at the stricture level, caliber 2.3 mm, situated at 6 cm by the tip of the penis	Urethrosonography was able to determine spongiofibrosis and the length of the stricture.

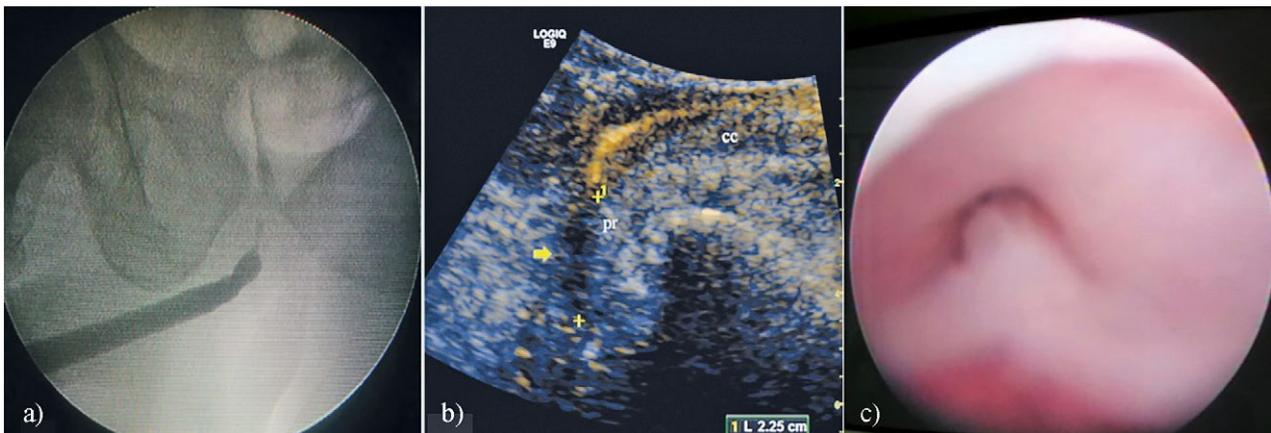


Fig 3. Stricture of bulbar urethra. Radiological (a) and ultrasonographical (b) exploration. In the ultrasonographic assessment, there is a stricture on a distance of 2.25 cm. A tight stricture located at the level of the bulbomembranous urethra was confirmed intraoperatively (c).

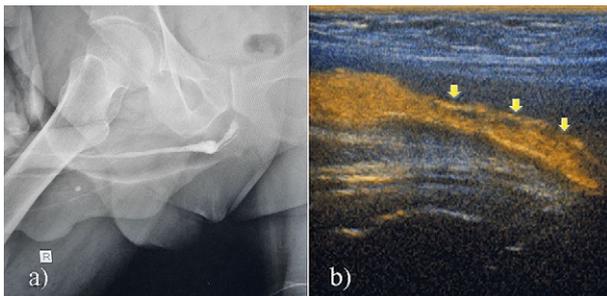


Fig 4. Stricture of the anterior urethra. Radiological exploration (a) and harmonic contrast ultrasonography (b). Ultrasonographic exploration is enlarged and shows in detail the length of the stricture, its degree and the thickness of spongiosum at the level explored (yellow arrows). Suprastenotic dilatation with localized appearance may also be found, similar to radiologically-highlighted dilation.

Discussion

Urethral strictures can have a profound impact on the quality of life, including sexual activity, as a result of a number of complications associated with urinary obstruction (infection, bladder stones, urethral diverticulum, fistula, sepsis) and, finally, with chronic renal failure [13]. The pathology of anterior urethral strictures is a significant part of the work of the urologist.

The choice of an appropriate treatment for anterior urethral strictures requires the evaluation of the entire urethra (proximal/distal versus the strictured area) and depends on preoperative imaging and endoscopic techniques [14,15].

By using retrograde urethrography we could not appreciate the length of the stricture (the contrast substance did not pass the strictures) or the thickness of Spongiosum. The diagnosis of urethral diverticulum/

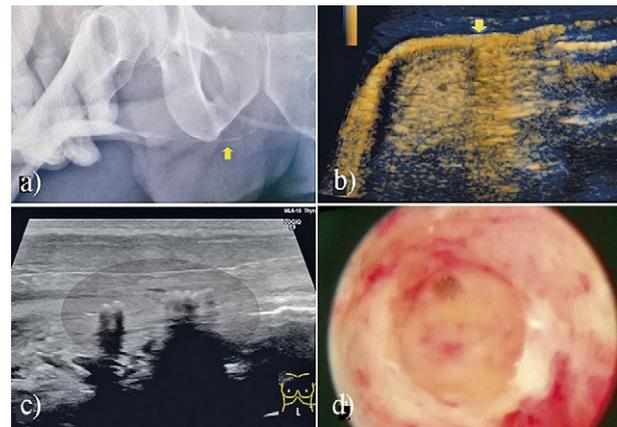


Fig 5. Enlarged urethral stricture at the level of the penile urethra (yellow arrows) associated with prestenotic dilatation. Multiple subcentimetric lithiasis. Radiological exploration (a), contrast enhanced urethrosonography (b) gray-scale ultrasonography (with the visualization of the stones on the path of the penile urethra) (c) and intraoperative appearance with the stricture confirmation (d).

stones/ flexure of the urethra has not been edified (additional incidences of pelvis X-ray are required in these cases). Given the inherent risks of retrograde urethrography (as a routine investigation for urethral strictures), the diagnostic methodology should be revised in order to select less invasive methods such as urethrosonography [7]. Urethrosonography, introduced by McAninch et al in 1988, presents the following advantages: lack of exposure to radiation and hypersensitivity reaction [16], provides a three-dimensional study, it better estimates the length of the stricture, it highlights the degree, the extension of spongiofibrosis and periurethral pathology [14]. However, a limitation of the procedure is represented by the impossibility of assessing the posterior urethra [15].

Different studies have been conducted to compare both techniques. Choudhary et al concluded that retrograde urethrography and urethrosonography are equally effective in detecting anterior urethral strictures, but the latter has greater sensitivity to the additional characterisation of strictures (length, diameters and periurethral pathology such as false pathways and spongiofibrosis) and benefits from a lower incidence of complications [17]. In accordance with the above is the study by Ravikumar et al, which evidenced that urethrosonography was more sensitive and specific in diagnosing urethral strictures comparing with retrograde urethrography. Although the sensitivity and specificity rate were 100% for the identification of anterior urethral strictures, the accuracy of urethral sonography decreased dramatically in the assessment of posterior urethral strictures (75% sensitivity and 50% specificity) [18].

SonoVue urethrosonography was able to determine the degree of spongiofibrosis, in comparison to retrograde urethrography. This information has valuable clinical importance because it has been proven that inpatients with anterior urethral strictures without spongiofibrosis, stricture dilation can be as efficient as internal urethrotomy regarding the recurrence rates [19]. Also, patients with extensive periurethral spongiofibrosis seem to present a worse response after an internal urethrotomy, as they often present early recurrence and have a lower chance of treatment success, thus should be offered urethroplasty [20,21].

Ouattara et al [22] and Gupta et al [23] have also shown that the urethral sonography is a method that allows the diagnosis of urethral stricture, evaluation of periurethral fibrosis and diagnosis of post-infectious stricture, and this method can replace retrograde urethrography and voiding cystourethrography. This procedure is well tolerated and its accuracy has been confirmed by several authors [24].

Shahsavari et al [6] found no superiority of urethral sonography compared with retrograde urethrography. The sensitivity and specificity of urethral sonography in the diagnosis of anterior urethral strictures was 86% and 94% respectively, the negative predictive value being higher than the positive predictive value (96% versus 82%). Also, the authors note that the length of the urethral strictures identified by the urethral sonography was lower than those identified in the retrograde urethrography [6].

The American Urological Association (AUA) and Société Internationale d'Urologie (SIU) state in their Male Urethral Strictures Guidelines that both direct vision internal urethrotomy and dilation can be offered as an initial treatment for strictures with a length less or equal to 2 cm [25,26], while AUA recommend that for longer stric-

tures, multiple, penile or penobulbar, the initial treatment that should be offered is urethroplasty (Grade C). SIU Guidelines mention that urethral reconstruction should be chosen instead of endoscopic treatment in cases of near obliterative strictures or where complete urethral obliteration is present [26].

The study conducted by McAnish et al has shown that, using urethral ultrasonography, the mean length of the anterior urethral stricture was modified from 2 cm (as measured by retrograde urethrogram) to 3.4 cm and, thus, the treatment was switched in 45% of patients (from anastomotic urethroplasty to an onlay urethroplasty) [27].

In this study we found that real-time examination highlights aspects that are not seen in the radiological examination, mainly the distension of the urethra by injection (which constitutes an interesting functional information) and tissue elasticity. Also, we showed that SonoVue ultrasound is a feasible method regarding the assessment of male adult distal urinary tract, which might bring additional information in further studies.

The main limitation of the study is represented by the small number of participants, which, in the end, allow us to draw only preliminary conclusions regarding the method. Additional large-scale studies should take place in order to perform statistical analysis and validate the method. Also, there was no control arm, to ensure the lack of false positive results of the method.

In **conclusion**, SonoVue urethrosonography can identify the anterior urethral strictures, their location and length. Real-time harmonic examination highlights aspects that are not seen in the radiological examination, mainly the distension of the urethra by injection (constituting an interesting functional information) and degree of spongiofibrosis. Larger studies are required in order to evaluate the possibility of the replacement, in selected cases, of retrograde urethrography with SonoVue urethrosonography.

Conflict of interest: none

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