



Modelling & Simulation

Influence of transurethral catheters on urine pressure-flow relationships in males: A computational fluid-dynamics study

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ARTICLE INFO

Article history:

Received 13 January 2023

Revised 27 April 2023

Accepted 8 May 2023

Keywords:

Computational fluid-dynamics

Lower urinary tract

Male

Pressure-flow study

Transurethral catheterization

ABSTRACT

Background and Objective: In the field of urology, the pressure-flow study (PFS) is an essential uroynamics practise which requires the patient's transurethral catheterization during the voiding phase of micturition to evaluate the functionality of the lower urinary tract (LUT) and reveal the pathophysiology of its dysfunctionality. However, the literature evidences confusion regarding the interference of the catheterization on the urethral pressure-flow behaviour.

Methods: The present research study represents the first Computational Fluid-Dynamics (CFD) approach to this uroynamics issue, analysing the influence of a catheter in the male LUT through case studies which included the inter-individual and intra-individual dependence. A set of four three dimensional (3D) models of the male LUT, different in urethral diameters, and a set of three 3D models of the transurethral catheter, diverse in calibre, were developed leading to 16 CFD non-catheterized either catheterized configurations, to describe the typical micturition scenario considering both urethra and catheter characteristics.

Results: The developed CFD simulations showed that the urine flow field during micturition was influenced by the urethral cross-sectional area and each catheter determined a specific decrease in flow rate if compared to the relative free uroflow.

Conclusions: In-silico methods allow to analyse relevant uroynamics aspects, which could not be investigated in vivo, and may support the clinical PFS to reduce uncertainty on urodynamic diagnosis.

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1. Introduction

The most effective clinical investigation of voiding phase of micturition concerns the relationship between detrusor pressure and urine flow [1–3], which specifies the flow resistance of the urethral duct [4,5]. In detail, urodynamic techniques based on the pressure-flow study (PFS) evaluate urethral resistance, which is correlated with different disorders and/or pathologies, such as strictures, benign prostatic hyperplasia, bladder outlet obstruction, etc. [6,7]. With regard to experimental methods, the engineering measurement of flow resistance is usually performed by monitoring pressure at both the inlet and outlet sections of the duct, and

the corresponding flow by means of pressure and flow sensors, respectively. Considering the lower urinary tract (LUT), the measurement of inlet condition, such as the detrusor pressure, is not simple, because detrusor pressure specifies the difference between bladder and abdominal pressure, and both bladder and abdominal cavity are not directly reachable. The measurement of abdominal pressure usually requires introducing a pressure sensor in the anus of the patient [8]. Similarly, bladder pressure measurement is frequently performed by means of a transurethral catheter [3,4,9–14]. On the other side, the placement of an almost rigid tube, such as a catheter, inside a deformable channel, i.e., the urethra, during urine voiding strongly influences the pressure-flow behaviour of the system [3,15] since the size of the catheter deeply affects the measurements. Typical catheter calibres are usually included between 2.5 and 8 Fr (i.e., about 0.8 mm and 2.7 mm, respectively) [3,4,9–12,14], while male urethral inner diameter usually ranges between 3 and 8 mm [16–19]. The similarity of catheter and urethra dimen-

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Table 1
Diameters (in mm) of urethral sections for A, B, C and D models.

Model	Prostatic region	Membranous region	Bulbar region	Penile region	Navicular fossa	Urinary meatus
A	3.7	3.5	3.7	2.7	3.3	2.1
B	4.0	3.8	4.0	3.0	3.6	2.4
C	4.3	4.1	4.3	3.3	3.9	2.7
D	4.6	4.4	4.6	3.6	4.2	3.0

sions suggests the potentially relevant influence of such a detrusor pressure measurement technique on experimental results and on the subsequent diagnosis.

Computational Fluid-Dynamics (CFD) allows evaluating the influence of catheter sizes on the pressure-flow behaviour of the urethra depending on both urethra and catheter characteristics. The here proposed study aimed at analysing three different sizes of the transurethral catheter, i.e., 1.5, 3 and 6 Fr, depending on urethral dimension of male subjects. Four different three-dimensional (3D) CFD models of the male lower urinary tract were developed, by considering different diameters distributions of the urethra, according to anatomical and anthropometric data. For each model, CFD simulations were performed to analyse the flow from the bladder to the external urinary meatus, considering both the unobstructed urethra and the three different catheterized conditions.

2. Materials and methods

The geometrical conformation of the male LUT was obtained by the investigation of the anatomy and the morphometry of the bladder and the urethra. From average data of bladder and urethra morphometry [16–19], the 3D CAD models of the LUT were obtained (SolidWorks, Dassault Systèmes). Aiming at developing CFD investigations, a fully opened and circular conformation of the urethral lumen was assumed, similar to what occurs in human reality.

In each model, the urethra, along its length from the bladder neck to the urinary meatus, was assumed as subdivided into 25 mm of prostatic region, 15 mm of membranous region, 40 mm of bulbar region, 80 mm of penile region and 10 mm of navicular fossa (Fig. 1a). The actual diameter continuously changed all along the urethral axis according to each section through connection zone of 4 mm, where the mean diameter of the two interfacing sections was assumed.

From [20], four different LUT models were developed by differentiating them in the size of urethral lumen. In Table 1, the diameters adopted for each urethral region are reported for each model. The weighted averages of the urethral diameters, computed in relation to the length of each section, were 3.20 mm (Model A), 3.50 mm (Model B), 3.80 mm (Model C) and 4.10 mm (Model D) (Fig. 1a). The same ellipsoidal conformation of the bladder was assumed in all the models, with a capacity of about 400 mL of urine. The development of the catheterized configurations of the different models required simple 3D CAD Boolean operations, as the subtraction of a 1.5 Fr (Catheter 1), a 3 Fr (Catheter 2) or a 6 Fr (Catheter 3) cylindroid (Fig. 1b,c), which was defined by sweeping a circular shape along the urethral axis. The last two catheter sizes are currently used in male patients, while the first one was added to report about a further potential clinical situation [3,4,9]. Altogether, sixteen CFD configurations were considered, one non-catheterized and three catheterized for each LUT model.

According to the classical CFD discretization of flow regions, the finite volume discretization of the urine domain was performed by means of hexahedral elements within the boundary layer and tetrahedral elements elsewhere. Catheterized models accounted for boundary layers on both the external lumen surface and the catheter wall. Sensitivity analyses led to identify the optimal mesh configuration, aiming to minimize the computational

effort of the models and stabilize the fluid-dynamic solution. The average thickness of the boundary layers ranged between 0.02 and 0.50 mm, while the number of elements resulted on average 300.000 for the non-catheterized configurations and increased up to 3.500.000 for those catheterized. Bladder, urethra and catheter surfaces, defining the mathematical domain of urine flow, were assumed not deformable, thus no effects of the abdominal pressure around the urethra were considered. No slip conditions characterized the interaction between urine and wall domain, while Reynolds-Averaged Navier Stokes equations defined the mathematical problem. Preliminary investigations showed a high Reynolds number characterizing the urine flow, and the $k-\varepsilon$ model was assumed for the description of time-averaged turbulent conditions [20,21]. However, subsequent evaluations required the assumption of a laminar flow for some catheterized configurations, as suggested by the velocity field and related regime in those specific conditions. The fluid characterization of urine assumed incompressible and Newtonian behavior, with density ρ and kinematic viscosity ν at 37 °C of 1020 kg/m³ and 0.83 cSt, respectively [22]. With regard to typical micturition conditions, bladder wall pressure defined the inlet condition, while atmospheric pressure provided for the outlet condition at the urinary meatus. It is necessary to report that bladder pressure includes the contributions from both detrusor and abdominal pressure. Values ranging between 0 and 6 kPa were assumed [23–26] to perform transient CFD simulations: the inlet bladder pressure increased from zero up to the target value according to a 3 kPa/s pressure rate condition, subsequently the bladder pressure was kept constant to achieve a steady state situation. All the simulations have been performed by means of the general-purpose code Comsol Multiphysics 5.4 (Comsol Inc., Burlington, MA, USA).

3. Results

The developed CFD investigations provided detailed information about the influence of catheterization on the pressure-flow measurements that are frequently performed during urodynamic studies. The computational approach to the problem provided a comprehensive characterization of the urine flow field during micturition, depending on both the specific anatomical conformation of the LUT and the calibre of the adopted transurethral catheter. Simulations showed the voiding phase of micturition for an equal detrusor pressure condition. As expected, equal initial condition in different configurations generated different results (Fig. 2). First of all, simulations showed that the voiding phase was influenced by the urethral model considered, in particular urethral diameter along the subsequent sections played a determinant role to define the flow characteristics. Plots of urine velocity field at a bladder pressure of 6 kPa were reported on the middle slice of all non-catheterized configurations (Fig. 2). The corresponding urine flow rates resulted equal to 9.05 ml/s (Model A), 12.17 ml/s (Model B), 15.35 ml/s (Model C) and 18.62 ml/s (Model D) (Table 2). The adoption of four different sized urethral models included also the variability between different individual patients and thus simulated flow rate values within the physiological range (9–23 ml/s) reported in the pertinent literature [14].

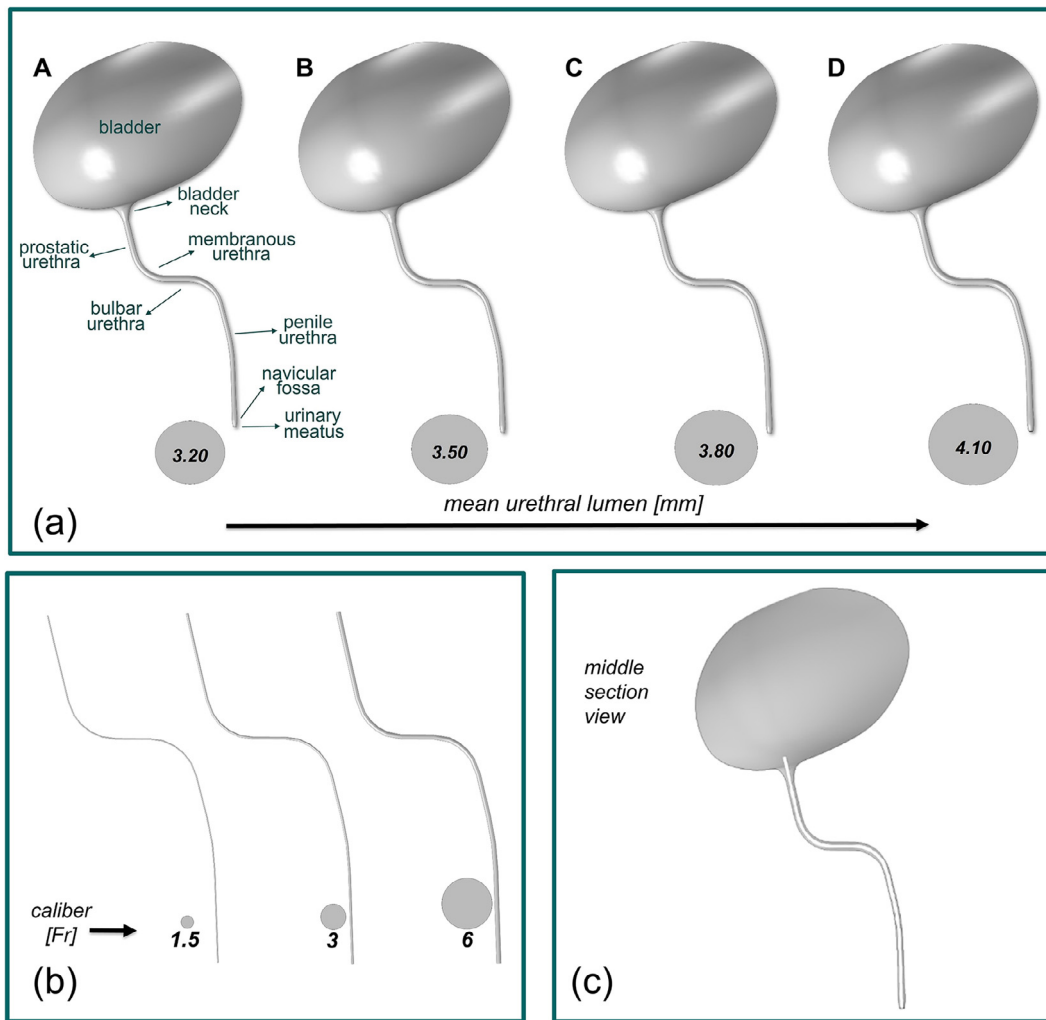


Fig. 1. (a) Morphometrical characteristics assumed for the four 3D LUT models. (b) Set of the three 3D models of transurethral catheter. (c) Example of a catheterized configuration in a middle section view.

Table 2

Regarding the outlet urethral sections, velocity, flow and non-dimensional parameters reported by model and catheter size. Laminar flow highlighted in yellow.

Model	Catheter size (Fr)	Outlet velocity U (mm/s)	Flow (ml/s)	Re	$\frac{2p}{\rho U^2}$	$\frac{L}{D}$
A	-	2683.10	9.05	7043.14	1.67	53.13
	1.5	2309.50	7.54	4619.00	2.25	62.96
	3	2284.40	6.41	3141.05	2.30	77.27
	6	966.60	0.31	120.83	12.84	141.67
B	-	2702.90	12.17	8108.70	1.64	48.57
	1.5	2479.10	10.70	5887.86	1.95	56.67
	3	2376.70	8.86	4159.23	2.12	68.00
C	-	1614.70	2.23	807.35	4.60	113.34
	1.5	2689.50	15.35	9077.06	1.66	44.74
	3	2612.90	14.35	7185.48	1.76	51.52
D	3	2465.90	12.13	5240.04	1.97	60.71
	6	2141.00	5.50	1873.38	2.62	94.45
	-	2704.50	18.62	10141.88	1.64	41.46
	1.5	2649.10	18.12	8278.44	1.71	47.23
	3	2544.10	15.90	6360.00	1.85	54.84
	6	2284.80	8.94	2856.00	2.30	80.95

In addition, these results for each model were compared to those obtained in the catheterized configurations at the same pressure gradient condition. The presence of a catheter within the urethra influenced the urine flow in a more pronounced manner in case of narrower urethral cross-sectional areas (Fig. 2).

The application of three catheters of different calibre introduced the difference in urodynamic parameters not only between the conditions of obstructed flow and free flow, but also between different levels of obstruction. In particular, in terms of urine flow, each catheter determined a decrease strictly sensitive to urethral size and catheter calibre (Table 2). The reduction in urine flow

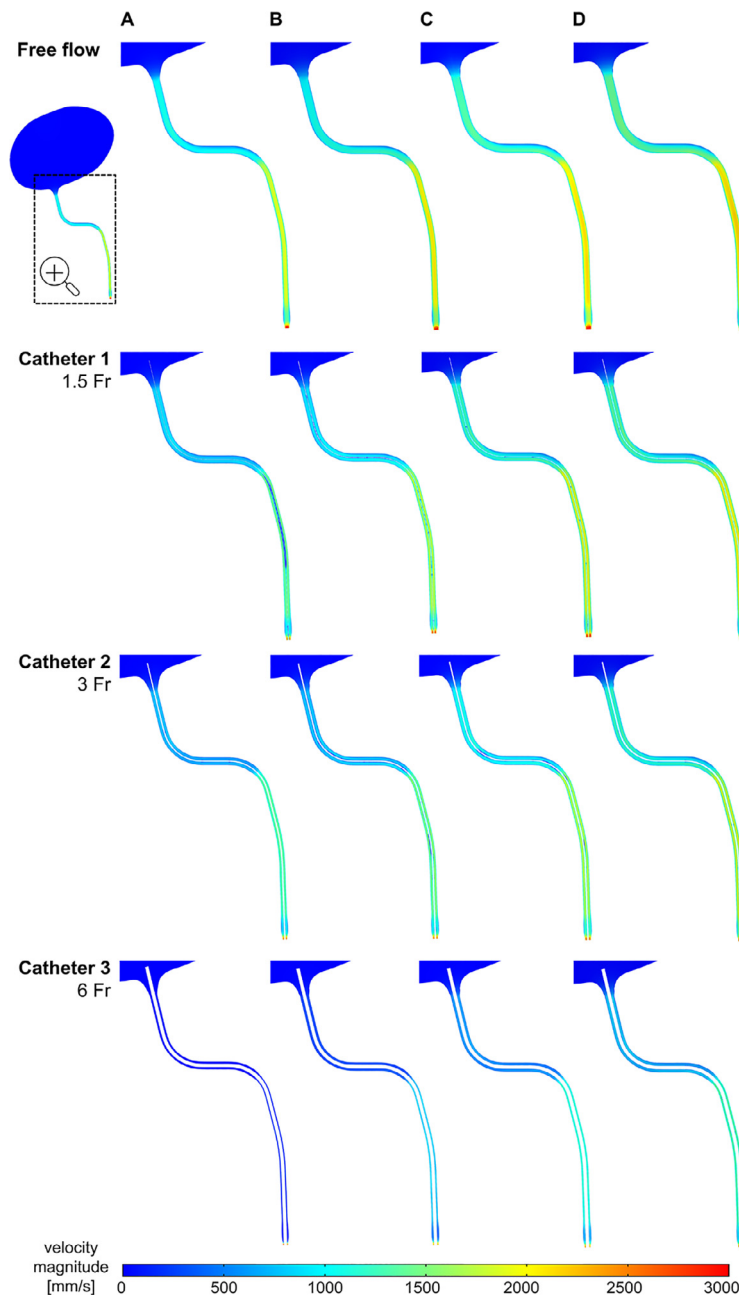


Fig. 2. Urine velocity fields in the middle section view of all non-catheterized and catheterized configurations under a 6 kPa bladder pressure, with a specific focus on the tract of interest from the bladder neck to the urinary meatus.

was computed for all catheterized configurations with respect to each relative non-catheterized ones. When increasing the diameter of the catheter (i.e., decreasing the urethral functional lumen), the decrease in urine flow showed an incremental trend, characteristic for each urethral size. In detail, urine flow decreased by over 90% in the configuration with the major obstructed urethral lumen. Moreover, in Fig. 3 the relationships between bladder pressure and urine flow showed the resulting impact of each catheter on the functionality of the LUT for all the models. Looking at the graphs right to left, a greater slope of the pressure-flow curve corresponded to a higher obstruction level of the urethra. Thus, the normal behavior of the LUT seemed to be not always guaranteed in case of transurethral catheterization.

Then, for all the configurations the Reynolds number Re was computed as $\frac{4R_H U}{\nu}$, where U is the fluid velocity, ν is the kinematic

viscosity (defined in Materials and Methods) and R_H is the hydraulic radius [27]. R_H is expressed as A/P , with A the fluid area and P the wet perimeter of the duct, corresponding to $\frac{1}{2} (R_{outer} - R_{inner})$ for the catheterized configurations (considering R_{outer} as the weighted average radius along the length of the urethra and R_{inner} as the catheter radius), while equal to the $\frac{1}{2} R_{outer}$ for the un-catheterized ones.

A non-dimensional analysis of the results was performed for the urine flow simulations by assuming three non-dimensional parameters: Re , the ratio of the pressure p to the squared velocity U and the flow density ρ , and the ratio of the urethral length L to the hydraulic diameter $D = 4R_H$.

The pressure p was considered in the steady state situation and the term U represented the corresponding average surface velocity of the outlet urethral section of each configuration (Table 2).

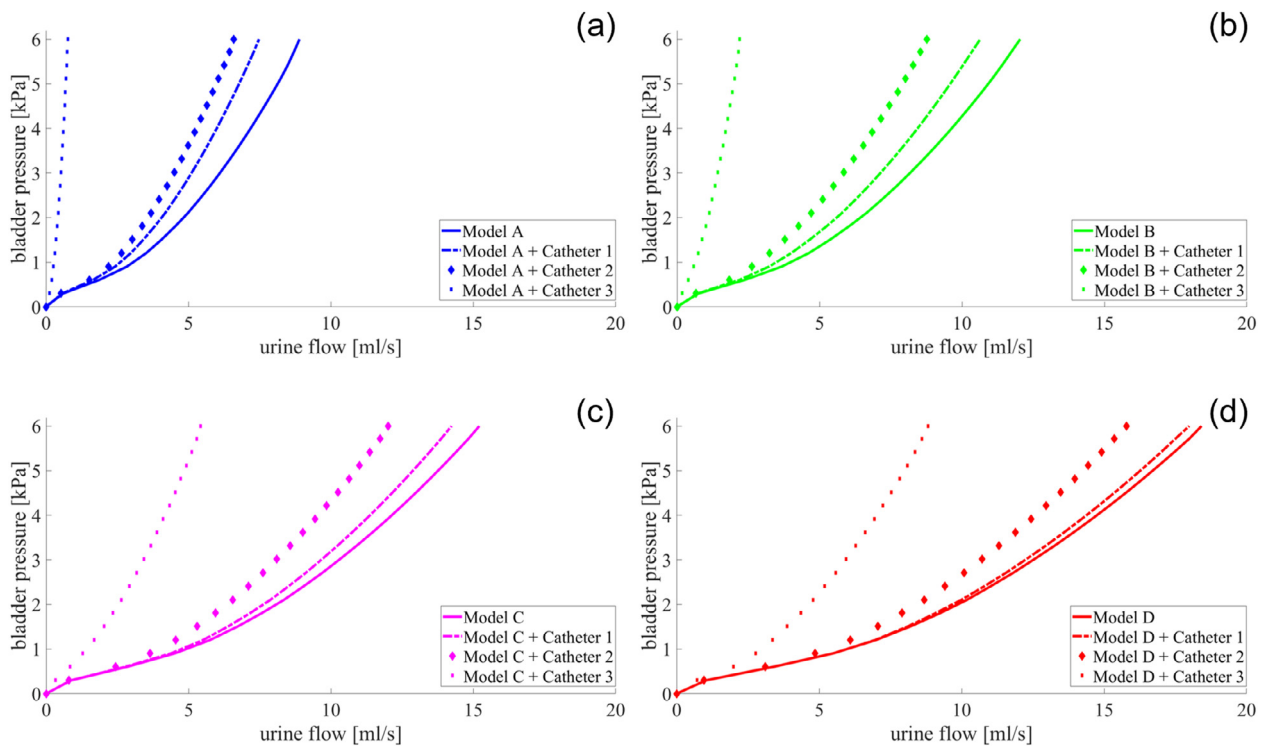


Fig. 3. Relationships between bladder pressure and urine flow resulted for (a) Model A, (b) Model B, (c) Model C and (d) Model D in non-catheterized and catheterized configurations.

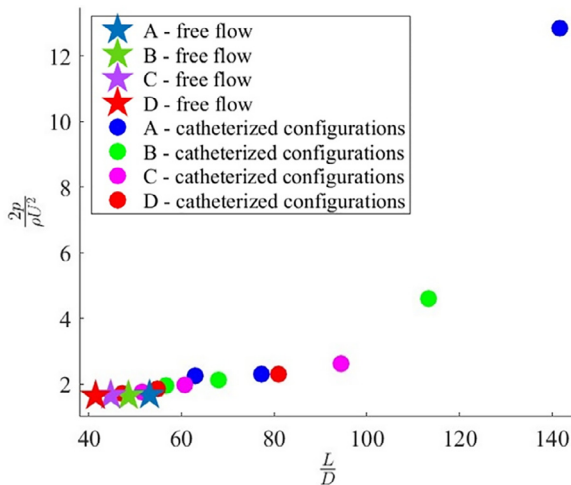


Fig. 4. CFD simulation results in non-dimensional form.

In Fig. 4, the measurement unit-independent results are shown. Points are representative of each configuration and seem to outline the same exponential trend.

4. Discussion

The pressure-flow study is considered the gold standard diagnostic technique for the detection of bladder outlet obstruction (BOO), detrusor underactivity (DU) or detrusor overactivity (DO) in patients with lower urinary tract symptoms (LUTS) [4,9,11]. For instance, to determine the existence and grade of BOO, men are classified as being either obstructed, equivocal or unobstructed according to the International Continence Society (ICS) nomogram. ICS nomogram quantifies the bladder outlet resistance using the

maximum flow rate and the detrusor pressure at maximal flow rate [4]. Clinical results reported that a transurethral catheter could cause more obstruction and weaker detrusor contractility in case of reduced urine flow rate or less obstruction and stronger detrusor contractility in case of increased urine flow rate [9]. However, all pertinent studies stated that further analyses should be mandatory to confirm the obtained results and highlighted the lack of CFD approach to this urodynamics issue. By publications, other CFD modelling approaches to the urological field have been performed, but their application concerned the functionality of LUT in presence of specific diseases, such as urethral strictures [5,20] in adults and obstruction due to posterior urethral valve in children [28]. Hence, the present study represents the first CFD analysis proposing the typical clinical PFS scenario with reference to the urethral size and the catheter calibre, which have shown to be the most influential factors from a clinical point of view.

All the computational simulations were performed by imposing the same idealized bladder pressure, thus avoiding the clinical impasse due to this missing information in absence of catheter. Thanks to this assumption, the CFD simulations provided a comparison of the urodynamic results in non-catheterized and catheterized configurations in the same pressure conditions. In particular, this comparison stressed the intraindividual variability, showing that, for an individual patient, the choice of a catheter size could lead to an important decrease in the urine flow when higher catheter diameters are considered (e.g., a decrease in the flow by over 90% for Model A in presence of 6 Fr catheter). On the other hand, the adoption of various sizes of urethral diameters allowed to include and examine the interindividual variability, showing how the influence of the same catheter size is sensitive to narrower or larger urethral diameters. Moreover, the non-dimensional analysis (Table 2 and Fig. 4) highlighted that, during free flow conditions, $2p/\rho U^2$ remained almost constant independently of the urethral model, while in presence of a catheter it progressively increased according to the decrease in the hydraulic

diameter. The last three points are the cases of the smallest values of the hydraulic diameter (Model A, Model B and Model C in presence of 6 Fr catheter), for which the flow has developed in laminar conditions under a 6 kPa bladder pressure. In literature controversial studies are present about the potential obstructive effect of the transurethral catheterization on the PFS and the accuracy of resulting urodynamics diagnosis. Nevertheless, inconsistent results both in men and in women have been reported and the question is actually not clarified. In general, multiple causes may be responsible for the differences that could be found by comparing uroflowmetry parameters in natural free-flow (FF) and PFS, such as obstruction effect, psychological factors, urethral reflex, irritation and bladder fatigue [4,9]. Due to its peculiar relevance, the obstruction effect to the urine flow represented the main focus of this study. When referring to pertinent clinical investigations, Reid et al. [4] studied the effect of 3.5, 5, 8, and 10 Fr transurethral catheters upon flow and resistance measurements in 8 males. They observed no significant changes by varying sizes in healthy patients, while a trend toward reduction in flow and a progressive rise in resistance resulted in presence of BOO as catheter diameter increased. With particular attention to BOO in men suffering from benign prostatic hyperplasia (BPH), Reynard et al. [10] found that an 8 Fr catheter had no significant influence in voided volume, maximum flow rate and resistance factor and did not change the final urodynamic classification.

Differently, Klingler et al. [11] compared the impact of 5 and 10 Fr filling catheters in addition to the 5 Fr pressure catheter in the urethra. They obtained that the 21.7% of unobstructed control group was erroneously diagnosed as obstructed when the 10 Fr filling catheter was in situ during the measurements. Moreover, the effect of three different sized catheters (4.5, 6 and 7 Fr) on pressure-flow studies was assessed in 60 women [3]. No significant difference in maximum flow rate, average flow rate and flow time resulted between 4.5 and 6 Fr, while statistically significant difference resulted between 4.5 and 7 Fr in those uroflowmetry parameters. In particular, when increasing the catheter size from 4.5 Fr to 7 Fr, a fall in maximum flow rate and a rise in flow time were obtained on average equal to 11.4 and 19.81%, respectively.

In 2012, a retrospective chart review study of 515 men [14] evaluated whether the use of a 6 Fr transurethral catheter affected the maximal flow rate and whether its impact changed the classification of patients on the ICS nomogram. In conditions of similar bladder volume and under the assumption of equal detrusor pressure at a maximal flow rate in both FF and PFS, the presence of the catheter resulted in a significant reduction in maximal flow rate and an upstaging of the BOO grading in up to 24% of cases.

Contrary to the present CFD analyses and previous works, a comparative study of spontaneous and 5 Fr catheterized urinary flow in 60 female patients noted even, in presence of a catheter, an improved voiding with an increase in the maximum flow rate [12]. It should be noted that in these works the direct comparison of the flow rates with or without the catheter under the assumptions of the same pressure conditions is a quite strong hypothesis, as suggested by other studies [9,29,30], due to the potential increase in the bladder pressure for the presence of the catheter.

All the three changing trends (unchanged, decreased and increased) in urine flow rate were observed in the most recent study [9]. The authors screened a quite large sample size (1791 patients) and concluded that the influence of intubation on uroflow and its significance for urodynamic diagnosis depended on the individual patient. The urine flow rate decreased in 72.8% of males and 83.5% of females, while increased in 14.7% of males and 9.5% of females. With a focus on male patients, the urine flow rate in PFS was significantly lower than in FF in cases of BOO and DU diagnosis, while there was no significant difference for DO. By replacing the max-

imum flow rate of PFS by that of FF, the urodynamic diagnosis changed correspondingly in both the reduced and increased flow rate groups.

Overall, the present study is resulted in agreement with the majority of the pertinent studies in literature [3,9,11,14]. Of course, as first computational approach to the reported urodynamics issue, the results have to be interpreted in accordance with its limitations if compared to a clinical study on real patients. First of all, the urethra was assumed as a rigid body, thus neglecting the interaction between the fluid and the tissues. This simplification was adopted to achieve a sufficiently adequate trade-off between accuracy and computational cost. Nevertheless, future analyses will include also the urethra walls deformability and influence with respect to the rigidity of the catheter material, as already realized with the same software but in other contexts such as blood hemodynamics or gastro-oesophageal diseases [31,32]. However, it should be highlighted that the complex distribution of the urethral lumen diameter all along its length was reproduced in all models, avoiding sudden changes along the duct that could affect the urine flow, thus mimicking the real human male body. Moreover, a patient undergoing a urodynamic study is typically affected by disorders of the LUT while in this study only healthy models were considered. Future developments will include also the pathological LUT models, such as in case of BPH.

To date, despite its doubtful invasiveness, the PFS is considered the gold standard for the diagnosis of BOO, DU and DO, as the several non-invasive methods, proposed during the last years, do not exhibit a diagnostic sensitivity and specificity able to replace it [9]. Within this adversarial context, the in-silico simulations may be performed as a valid support method to the clinical PFS in order to improve its effectiveness by considering relevant aspects which could not be investigated in vivo, e.g., bladder pressure for free uroflow. Therefore, additional information related to the voiding phase of micturition may also be beneficial in other urodynamic applications. Quantifying the bladder pressure in free-flow could contribute to overcome the actual problems related to the definition of the occlusive pressure that artificial urinary sphincters have to apply to ensure continence [33].

5. Conclusions

The proposed CFD simulations showed that a transurethral catheterization may negatively impact on uroflowmetry parameters to a greater or less obstructive extent depending on the characteristics of both urethra and catheter. To reflect as far as possible the true functionality of the patient's lower urinary tract, quantifying the influence of the catheter through in silico methods could suggest to clinicians the choice of the catheter size in order to reduce the uncertainties regarding the measured parameters relevant to diagnosis and ensure more efficient clinical support.

Statements and declarations

Statement of ethics

No ethics approval was required since this research does not involve any human or animal subjects.

Ethical review board: not present

Funding sources

This work was supported by MIUR, FISIR 2019, Project n° FISIR2019_03221, titled CECOMES: Centro di studi sperimentali e COmputazionali per la ModEllistica applicata alla chirurgia and by

University of Padova, Project FONT_BIRD2020_01, titled Characterization of Artificial Urinary Sphincters for the identification of new DEVICES (AUS-DEV).

Data availability statement

The raw/processed data required to reproduce these findings cannot be shared at this time due to technical issues, but are available upon direct request to the corresponding author.

Declaration of Competing Interest

The authors have no conflicts of interest to declare.

CRediT authorship contribution statement

Maria Vittoria Mascolini: Conceptualization, Formal analysis, Data curation, Writing – original draft. **Chiara Giulia Fontanella:** Conceptualization, Writing – original draft. **Alice Berardo:** Formal analysis, Data curation, Writing – original draft. **Emanuele Luigi Carniel:** Conceptualization, Writing – original draft.

Acknowledgments

This work was supported by MIUR, FISR 2019, Project n° FISR2019_03221, titled CECOMES: CEntro di studi sperimentali e CComputazionali per la ModelliStica applicata alla chirurgia and by University of Padova, Project FONT_BIRD2020_01, titled Characterization of Artificial Urinary Sphincters for the identification of new DEVICES (AUS-DEV).

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