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Computational Fluid Dynamic Modeling of Urethral Strictures

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Purpose: Computational fluid dynamics have paradigm shifting potential in understanding the physiological flow of fluids in the human body. This translational branch of engineering has already made an important clinical impact on the study of cardiovascular disease. We evaluated the feasibility and applicability of computational fluid dynamics to model urine flow.

Materials and Methods: We prepared a computational fluid dynamics model using an idealized male genitourinary system. We created 16 hypothetical urethral stricture scenarios as a test bed. Standard parameters of urine such as pressure, temperature and viscosity were applied as well as typical assumptions germane to fluid dynamic modeling. We used ABAQUS/CAE 6.14 (Dassault Systèmes®) with a direct unsymmetrical solver with standard (FC3D8) 3D brick 8Node elements for model generation.

Results: The average flow rate in urethral stricture disease as measured by our model was 5.97 ml per second (IQR 2.2-10.9). The model predicted a flow rate of 2.88 ml per second for a single 5Fr stricture in the mid bulbar urethra when assuming all other variables constant. The model demonstrated that increasing stricture diameter and bladder pressure strongly impacted urine flow while stricture location and length, and the sequence of multiple strictures had a weaker impact.

Conclusions: We successfully created a computational fluid dynamics model of an idealized male urethra with varied types of urethral strictures. The resultant flow rates were consistent with the literature. The accuracy of modeling increasing bladder pressure should be improved by future iterations. This technology has vast research and clinical potential.

Key Words: urethral stricture, male, hydrodynamics, urinary tract physiological phenomena, medical informatics computing

Abbreviations and Acronyms

CFD = computational fluid dynamics

USD = urethral stricture disease

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Further detailed results of the models can be reviewed at https://urology.ucsf.edu/research/adult-non-Cancer/adult-non-cancer-research-programs/breyer-research-program.

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COMPUTATIONAL fluid dynamics have the potential to revolutionize the understanding of the physiological flow of fluids in the human body.[1] CFD uses complex computational and modeling techniques to analyze the motion of fluids and estimate velocity, pressure dynamics and flow rates. These computational techniques have been widely applied in engineering disciplines due to the inherent economic and safety advantages of virtual simulation.[2] More recently bioengineers have begun to apply these principles in the human body.

To date cardiovascular disease treatment has benefited most directly from this technique.[3,4] CFD has already proved useful for understanding dilated cardiomyopathy, hypertrophic cardiomyopathy, left ventricular dysfunction and myocardial infarction.[5–7] These techniques have also allowed for optimal

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intravascular stent and prosthetic valve design prior to human trials.[8,9] CFD may offer clinicians the ability to minimize invasive instrumentation and permit physiological assessments enabling diagnosis and appropriate treatment.

Given the inherent similarities between fluid flow in the cardiovascular system and the urinary tract, CFD may be a useful adjunct to the current understanding of urinary flow patterns for research and clinical practice. Current noninvasive measurement tools to help clinicians gauge the passage of urine include uroflowmetry and ultrasound bladder volume residual measurement, which do not provide information on the dynamic state of flow in the urethra. In uroflowmetry poor bladder function or urethral obstruction may lead to slow flow patterns.[10] Current technical limitations preclude real-time observation of micturition on magnetic resonance imaging. Current noninvasive methods to diagnose and understand obstructive urological processes lack accuracy and usefulness.[11]

We applied CFD to male USD. Urethral strictures are a relatively common and expensive problem faced by many men throughout life with high rates of urinary tract infection, incontinence and resultant surgical treatments.[12] Because USD has a particular length, location and number, it could readily be studied with CFD to gain insight into the disease. Therefore, the aim of this study was to evaluate pressure and flow parameters in a urinary tract model with different hypothetical USD conditions. As proof of principal we applied CFD to assess the practicality and applicability of this technology to model urinary flow.

MATERIALS AND METHODS

A CFD model was prepared using an idealized model of the male genitourinary system. For experimental purposes the bladder was the main source of flow, generating an average force of 25 cm H_2O (0.002451 MPa inlet pressure), including contributions from intra-abdominal pressure. Outlet pressure was assumed to be 0 Pa. This would result in an average urine flow of 20 ml per second in an unobstructed man, consistent with prior literature.[10,13]

The idealized urethra in our model was 25 cm long from bladder neck to meatus. The urethra was divided into 5 cm of prostatic urethra, 7 cm of bulbar urethra and 13 cm of penile urethra. For this simulation we assumed a constant urethral diameter of 30Fr (31.2 mm circumference and 10 mm diameter) without dispensability. We assumed constant sphincteric function and pressure in the prostatic urethra in all scenarios. Tissues were assumed to have no elasticity.

Urethral strictures were then applied to the model to simulate typical clinical presentations while varying stricture location, size and number (fig. 1). Bladder pressure was also altered. In such cases we used bladder pressures of 40 cm H_20 (0.0039 MPa) and 100 cm H_20 (0.0098 MPa). Secondary analysis was performed to garner further details about short proximal urethral strictures as well as multiple strictures in a sequence.

Material property parameters were taken from the literature to best estimate urine behavior, including urine density 1,003 to 1,035 kg/m^3 and dynamic viscosity 0.635 to 0.797 mPa at 37C.[14] Urine was considered a noncompressible and Newtonian fluid. Notably this assumption is typical for simple fluids such as urine as the viscosity of urine does not appreciably change with the physiological shear rate. Studies simulating fluid dynamics of urine flow have commonly used this assumption.[15]

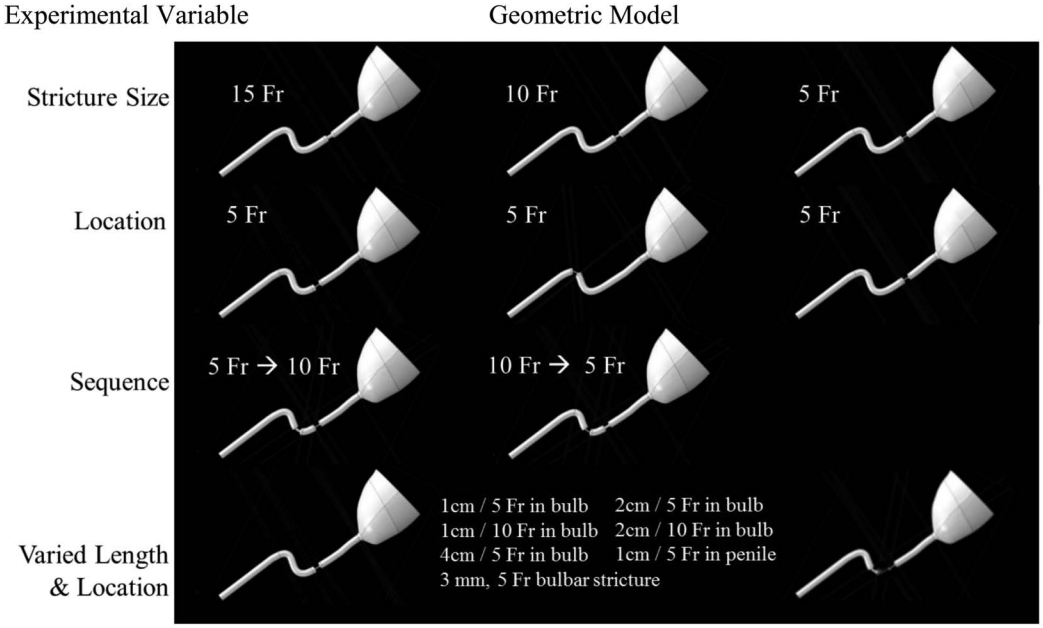

Figure 1. Select urethral stricture models

We assumed no velocity on the wall, which is termed the no slip assumption. The no slip assumption is widely used in fluid dynamics and in particular it was previously used to model blood and urine.[15,16] The assumption is that at the boundary of the urethra the adhesive forces to fluid molecules are stronger than the adhesive forces of fluid molecules to each other. Therefore, urine velocity directly at the urethral mucosa was 0 ml per second.

CFD was used to model pressure and velocity distributions in the lower urinary tract and calculate urine flows in each clinical scenario. Geometry models were derived for each scenario. We used ABAQUS/CAE 6.14 (Dassault Systèmes®) for analysis and a direct unsymmetrical solver with the standard (FC3D8) 3D brick 8Node elements. Areas near the stricture were given higher mesh density, ie a higher degree of detail was calculated in this region. Increased mesh density was a trade-off since it requires additional computational power, which in turn informs simulation time, complexity and cost. Other simple statistics were analyzed with Excel® 2016.

RESULTS

Urine velocity maps were created for all scenarios (fig. 2). Decreased functional urethral diameter due to worsening caliber strictures revealed a corresponding decrease in urine flow when keeping all other variables constant (see table). Urine flow decreased 88% as stricture size decreased from a 15Fr to a 5Fr opening. In contrast, stricture location had a weak impact on urine flow when assuming a 5Fr stricture size with all other variables constant. In this case urine flow decreased to 2.88, 2.45 and 2.44 ml per second when the stricture was located 5, 7 and 15 cm from the bladder neck, respectively.

For multiple strictures urine flow changed 0.21 ml per second overall when the stricture sequence changed. At the nominal caliber urethra further detailed data were obtained on secondary analysis. A 10Fr caliber proximal stricture followed by a more severe 5Fr distal stricture demonstrated worse flow dynamics and an additional 10% loss of flow rate as urine progressed distally. In contrast, a small caliber proximal stricture followed by a less severe distal stricture had an almost identical flow rate through the narrowed portions of the urethra (2.31 and 2.32 ml per second, respectively).

Stricture length had a moderate effect on urine flow, which decreased to 2.25, 1.23 and 0.85 ml per second in 5Fr 1, 2 and 4 cm strictures, respectively. Similarly urine flow decreased to 12.57 and 10.28 ml per second in 10Fr 1 and 2 cm strictures, respectively. On secondary analysis we examined a 5Fr 3 mm proximal stricture in detail to model a short apical recurrence after prior urethroplasty. At the point of minimal lumen caliber we modeled a flow rate of 25.13 ml per second. The urethral pressure drop across the short stricture was 68% (from 24.86 to 7.92 cm H_2O).

Bladder pressure was then varied while assuming a 5Fr stricture 10 cm from the bladder neck. A change in bladder pressure had a strong effect on urine flow. The urine flow increased to 41.98 and 81.13 ml per second as bladder pressure increased to 40 and 100 cm H_2O, respectively, from the baseline assumption of 25 cm H_2O. These flow rates were notably outside the bounds of physiological flow rates. Pressure diagrams of all scenarios were also fully calculated (fig. 3).

The table shows that ultimately the average flow rate in cases of heterogeneous stricture disease incorporating the stricture scenarios would be 5.97 ml per second (IQR 2.2-10.9).

DISCUSSION

These results should be considered proof of concept for the application of CFD to the urological discipline. To our knowledge this pilot study represents

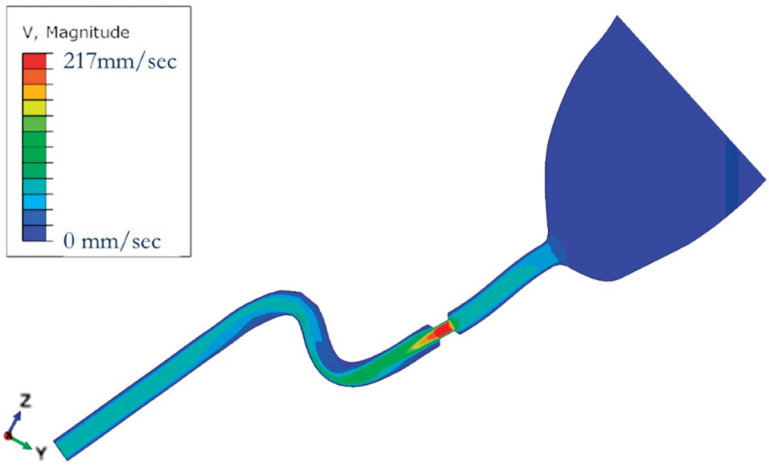

Figure 2. Urine velocity (*V.*) density map of 5Fr stricture in bulbar urethra

Modeled velocity flow dynamics by stricture type

Experimental Variable*	Stricture			Bladder Pressure (cm H_2O)	Mean Velocity (mm/sec)	Flow (ml/sec)
	Size (Fr)	Location (cm)†	Length (cm)			
Stricture size	15	5	1	25	315.8	24.8
	10	5	1	25	177.0	13.9
Location	5	5	1	25	36.7	2.9
	5	5	1	25	36.7	2.9
	5	7	1	25	31.3	2.2
	5	15	1	25	31.1	2.4
Stricture sequence	5, 10	5, 12	1	25	30.6	2.4
	10, 5	5, 12	1	25	28.0	2.0
Bladder function	5	10	1	40	534.6	42.0
	5	10	1	100	1,045.7	81.1
Size, length + location	5	12	1	25	28.7	2.3
	5	15	1	25	30.8	2.4
	10	12	1	25	160.1	12.6
	10	12	2	25	131.0	10.3
	5	12	2	25	15.7	1.2
	5	12	4	25	10.9	0.9

* Other variables constant unless noted.
† Relative to bladder neck.

the first attempt to model the effect of USD on urinary flow in a systematic framework of dynamic fluid effects. The model revealed that stricture size and bladder pressure strongly impacted urine flow while stricture location and length, and the sequence of multiple strictures had a weaker impact. The average flow rate in our heterogeneous modeled strictures was 5.97 ml per second (IQR 2.2-10.9). Flow mechanics changed logically with more severe strictures. Although this is a preliminary study, it reveals the broad applications of CFD in urology. We hope that this report serves to generate further hypotheses and more accurate future computations.

It remains debatable whether uroflowmetry values alone can differentiate stricture disease from other causes of unhealthy flow in males.[17–19] With that limitation aside, the flow rates generated by our model are consistent with uroflowmetry values in the literature. For example, in 75 patients with USD of varied lengths and locations the average flow rate was 5.10 ml per second (IQR 1.20-15.40).[18] Likewise among 57 patients with cystoscopic but not necessarily symptomatic stricture recurrence the maximum flow rate was 9.8 ml per second.[17] It may be that hybrid values derived from uroflowmetry, such as the average flow rate divided by the maximum flow rate squared, better differentiate USD from other causes of a poor stream but the debate about which mathematical derivation is most accurate remains unsettled.[18]

For sequential stricture presentations the smallest and most proximal stricture dictates the

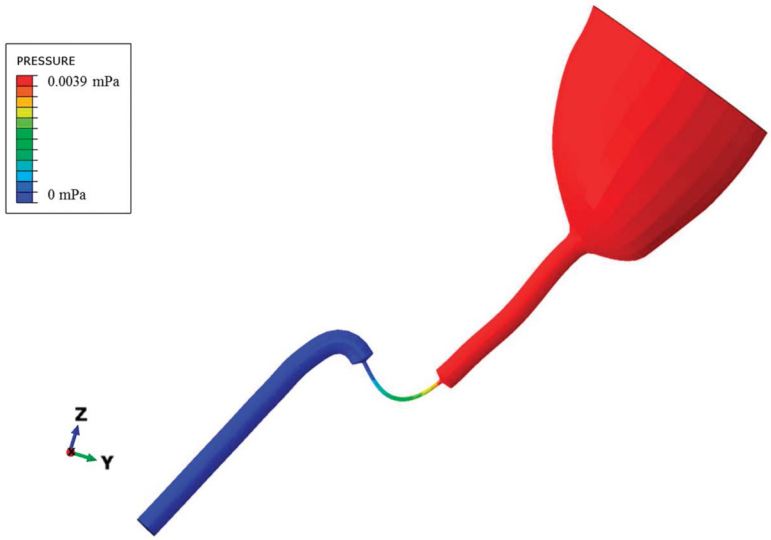

Figure 3. Pressure diagram of 4 cm stricture in penoscrotal region

ultimate flow rate according to our model. The addition of a distal, less severe stricture worsened flow only an additional 10%. Generally this follows clinical practice, in that treatment of the most severe proximal stricture typically provides relief to the patient but may unmask symptoms at an untreated second site. Approximately 6% to 10% of men present with synchronous urethral strictures and 1-stage repair may be safe and effective as long as lithotomy time is minimized.[20] Typically recurrent USD after substitution urethroplasty is focal at the anastomosis site and can be treated with direct vision internal urethrotomy with reasonable 42% success.[21] Our model demonstrates that even patients with a thin stricture require large pressure gradients to maintain flow. This suggests that treatment may be warranted for bladder protection, especially if the patient is symptomatic.

The promise of CFD in urology is evident when we examine its use in cardiology. The computerized tomography derived fractional flow reserve is a form of CFD model used in conjunction with conventional imaging which has been shown to reduce death, nonfatal myocardial infarction and repeat revascularization after percutaneous coronary intervention.[22] Thus, it is the first CFD recommended by clinical guidelines and regularly applied in patient care.[23,24] Estimating the fractional flow reserve permits early diagnosis and treatment since it identifies at risk coronary lesions even when clinical evidence of coronary ischemia is lacking.

CFD has also been a useful research tool. Wall stress is pivotal for the development of atherosclerotic plaque and aneurysm, and it is otherwise not easily estimated or studied by conventional means.[25] Varied cardiac devices have been modeled first using CFD prior to development or to understand the effect in the body.[5–9] The clinical risk of brain aneurysm rupture is actively being studied using similar techniques as well as bioengineering applications such as stem cell growth on a scaffold.[26,27] With increasing higher order computing power available some groups envision that CFD will be as useful an adjunct to clinicians as image processing, which has revolutionized radiology.[1]

As an initial attempt to apply this technique to the genitourinary system, the model has several pertinent limitations which must be addressed. In reality the lumen size of the urethra varies drastically at different locations. Important dynamic changes in urethral shape and elasticity occur during voiding which were not modeled. We also did not model the effect of prostatic obstruction, which may have a large impact on the flow rate. Similarly sphincter function was not incorporated. These parameters were purposefully omitted to create a simplistic model as a first attempt.

There is a constant conflict between keeping a model simple to allow for computation vs a model with so much complexity that errors easily propagate. In our study the model poorly estimated the urine flow rate in the setting of high bladder pressure. Another major problem is validating any model. Given that there is no noninvasive method which the field agrees is best for monitoring stricture disease, it is difficult to compare CFD to a gold standard.[28] Likewise to our knowledge voiding urine velocity, urethral pressure and the urethral flow rate cannot be measured in real time at multiple simultaneous locations in the urethra, making a clinical comparator challenging. Available computing power is also a short-term challenge for real-time applications as supercomputers are still required to create a complex model in timely fashion.[29] Nonetheless, we believe that CFD is currently a viable research tool with the potential for a high clinical impact.

Future steps include more accurately modeling dynamic bladder function and incorporating benign prostatic hyperplasia and meatal stenosis effects. Moreover, clinical correlation with modalities such as videourodynamics, uroflowmetry, cystoscopy or ultrasound should be achieved. Future work could more accurately simulate clinical scenarios and correlate results with intraoperative findings. Using modeling future clinicians could provide a data driven report about individual urethral health based on patient specific information. This digital urological patient could enable simulated surgeries and for stricture disease provide tailored risks and benefits of each treatment option. Large cohorts of digital patients would allow for simulating randomized clinical trials, reducing cost and drastically reducing patient risks.[4] Using complex machine learning it may also be possible one day to know the exact details of a patient stricture, including location, spongiofibrosis degree and length, simply by inputting certain noninvasive parameters into a smartphone.

CONCLUSIONS

We present a preliminary attempt to create a computerized functional model of urine flow in the setting of USD. The model demonstrated that increasing stricture diameter and bladder pressure strongly impacted urine flow while stricture location and length, and the sequence of multiple strictures had a weaker impact. Urinary flow rates of simulated strictures at 25 cm H_2O bladder pressure are consistent with the literature while accuracy is reduced at high bladder pressure. Although the field is in its infancy, CFD may dramatically impact urological diagnosis in the coming decades. Awareness of the potential research and clinical potential of this branch of applied engineering is necessary for clinicians.

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EDITORIAL COMMENT

It is often said that urologists are the plumbers of the medical community. This report is challenging us to become fluid engineers.

The urethra can be reconstructed in many ways and surgeon biases have a large role in which procedure is ultimately chosen. Bias persists and continues to be tolerated, namely due to a lack of randomized, controlled surgical trials. Reasons for the absence of such trials are many but are unlikely to be resolved anytime soon.[1] So to answer the question "What procedure is best?" we have to get creative.

Medicine has been late to the simulation game but computer aided engineering is becoming commonplace in cardiology with so-called in silico trials modeling the flow of blood through the heart and veins, thereby hastening the development of new valves and coronary stents before they ever enter the body.[2] This represents an important departure from the reliance on population averaged data obtained from expensive patient trials, and moves the field towards the "digital patient" to power trials and product development.

Of course, urine flows differently through the urethra than blood flows through the heart and the walls of the urethra differ from those of arteries.

But I have no doubt that urologists of all reconstructive disciplines will be heading in the direction of simulation soon to improve our operations. As the authors suggest, a lot of work still needs to be done to better mimic urine flow but I look forward to the day when questions about "ventral vs dorsal," "flap vs graft" and "excise vs incise" might come with patient specific answers garnered from a computer simulation.

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