AIMS Medical Science

AIMS Medical Science, 12(4): 301–311.
DOI: 10.3934/medsci.2025021
Received: 20 June 2025
Revised: 17 September 2025
Accepted: 11 October2025
Published: 21 October 2025

http://www.aimspress.com/journal/medicalScience

Research article

Non-invasive induction of bladder outlet obstruction in adult male rat model has bladder wall events similar to overactive bladder in human adult male

Mohamed Wishahi[1,*], Sarah Hassan[2], Dina Zaki[3] and Nabawya Kamal[3]

[1] Department of Urology, Theodor Bilharz Research Institute, P.O. 30, Cairo, Imbaba, Giza, 12411 Egypt
[2] Department of Pathology and Electron microscopy, Theodor Bilharz Research Institute, Cairo, Egypt
[3] Department of Anesthesia, Theodor Bilharz Research Institute, Cairo, Egypt

* **Correspondence:** Email: wishahi@gmx.net.

Abstract: Objectives: To determine the validity of the non-invasive, novel procedure of partial urethral obstruction in adult male rats to induce bladder outlet obstruction (BOO), this study investigated the reproducibility of non-surgical induction of partial urethral obstruction to induce BOO. Effects in the rat model were compared to those of an overactive bladder (OAB) in real-world adult human males. Previous reports of BOO induction in male rats applied an invasive technique through abdominal incision and dissection of the pelvic urethra, which deviates from real-world events of BOO in men. **Method:** Sixteen adult male Sprague-Dawley rats (16 weeks old, 340 ± 10 g) were randomly divided into three groups: Bladder outlet obstruction group (n = 8), sham group (n = 4), and control group (n = 4). Eight rats underwent induction of BOO with the novel technique. At 8 weeks, the bladders of BOO, sham, and control groups were taken and examined histopathologically. The human study included tissue samples from three patients who had OAB secondary to neurogenic bladder dysfunction and had undergone surgical closure of vesicostomy with excision of the vesicostomy tract; tissue samples were examined histopathologically. Induction of BOO in adult male rats used a non-invasive technique that induces partial urethral occlusion via approaching the urethra at the root of the penis. The subsequent morphological and histological patterns of the male rat BOO were compared to patterns of human OAB. **Results:** All rats survived, were active, and had no complications. Histological examination of tissue samples of the bladder wall with hematoxylin & eosin and Masson's

trichrome stains showed thinner urothelium and condensation of collagen between muscle bundles. Human tissue samples showed similar cytoskeleton events. **Conclusions:** The non-invasive technique to induce BOO in male rats proved to be safe, reproducible, and led to no complications. An increased collagen/smooth muscle ratio in the rat model was similar to that in humans. The results showed that the non-invasive procedure of BOO induction in male rats leads to identical cytoskeleton changes as in human OAB. The results indicate that this model could aid in understanding human male BOO and could be used for experimental studies of BOO in adult men.

Keywords: male rat model; bladder outlet obstruction; overactive bladder; experimental animal

Abbreviations: BOO: Bladder outlet obstruction; OAB: Overactive bladder; HE: Haematoxylin and eosin

1. Introduction

Voiding dysfunctions of micturition and storage are often observed in elderly men with bladder outlet obstruction (BOO) due to benign prostatic hyperplasia (BPH) and neurogenic bladder dysfunction (NBD). Both clinical situations are often resistant to treatment. Ongoing research aims to develop more effective treatments based on underlying anatomical changes and pathophysiological mechanisms.

Female animal models have been used to induce BOO. The standard procedure for the induction of BOO in female rats starts with placing animals under anesthesia; then, an abdominal incision reveals the bladder and proximal urethra. A metal rod of 1.0 mm outer diameter is inserted into the urethra, and a 3/0 monofilament polybutester ligature is placed around the urethra and tied in the presence of an intraluminally placed steel rod. After tying the knot, the steel rod is removed, and the abdominal wall is closed. This technique has been widely performed to induce BOO in female rats; however, it has the disadvantage of not fully replicating the natural events in humans; also, the abdominal surgical procedure itself could alter normal pathophysiological processes [1–7]. Recently, a physiological procedure to establish BOO in female rats was introduced, where the induction of the obstructed element does not require abdominal incision and surgical dissection; instead, the obstruction is applied externally to the urethra [8].

The pathophysiological mechanisms underlying adult male lower urinary tract symptoms due to BOO secondary to BPH are not completely understood and require further extensive studies. Using adult male animal models of BOO would enhance this research. However, male rat animal models for BOO are scarce.

The most reliable method for inducing OAB, with the fewest adverse consequences, is the induction of BOO via partial urethral obstruction by applying partial urethral ligation. This can be performed either by using a retropubic incision with mid-prostatic blockage or a perineal incision with bulbous urethral ligation [9].

The most commonly used surgical procedure for BOO in male rats involves making a lower abdominal incision to expose the urethra, which is then ligated between the bladder neck and a urethral fenestration using a 4-0 silk suture, along with a metal rod with a 1.2 mm outer diameter placed outside the urethra. Then, the metal rod is removed to produce partial urethral obstruction [10,11].

According to reports, open surgical methods used to induce BOO may have potential risks of complications, longer recovery periods, and inflammation at the site of the obstructing suture in the proximal urethra, which increases urethral obstruction. Fibrosis has also been linked to incision sites in the skin and muscle layer, as well as changes occurring due to closure of these layers. These factors reduce the precision and reproducibility of these models and make them less comparable to human conditions, as these events do not occur in real-world human BOO and, consequently, OAB [12].

Previous experimental animal models in rats, mice, and rabbits for OAB induction have classified the subsequent bladder changes into three stages: overactive bladder, decompensated bladder, and fibrotic bladder. These studies defined the time sequence of these events as occurring at 6, 8, and 12 weeks, respectively.

Experimental studies on OAB in animal models showed morphological changes, namely increased collagen in bladder tissues, alterations in smooth muscle, and increased bladder wall thickness. It has been proposed that OAB's higher connective tissue may play a role in maintaining normal physiological function of the bladder. It has been theorized that the increased bladder collagen observed during obstruction, and its subsequent decrease after de-obstruction, are due to the increased functional demands of the bladder in response to BOO. This may be attributed to multiple factors, such as increased tension [13,14].

Purpose: To validate a male rat model of BOO to induce OAB and to demonstrate alterations in smooth muscle and collagen in male rats at 8 weeks. Data from the male rat model are compared with the events observed in human OAB.

2. Materials and methods

2.1. Animal model

Sixteen adult male Sprague-Dawley rats, 16 weeks old, weighing 340 ± 10 g, were acquired and maintained at the Theodor Bilharz Research Institute's animal home in Cairo, Egypt. They were kept in polypropylene cages in groups of two, at a temperature of 20–25 °C, with unrestricted access to water and to a regular chow meal with a 12/12 h light/dark light cycle. Rats were randomly divided into three groups: BOO group (n = 8), sham group (n = 4), and control group (n = 4). Animals were kept under these conditions for 1 week to adapt to the new environment.

2.1.1. Operation

Eight rats underwent induction of calibrated urethral obstruction for the induction of BOO. Rats were anaesthetized with ketamine (10 mg/100 g body weight) administered intraperitoneally. The lower abdominal and penile skin was cleaned with disinfectant solution, and a sterile floppy guidewire (Amecath Medical Technologies US Inc., Wilmington County, Delaware, USA), 0.038 inches in diameter (0.965 mm), was inserted into the urethra and moved to the bladder. Trickling of urine from the urethra indicates the passage of the guidewire to the bladder and confirms that the urethral lumen is wider than the circumference of the guide wire. The penis was pulled forward and degloved from the covering hairy skin by gentle retraction. The guidewire was placed at the root of the penis, and a 4-0 Prolene suture over a curved needle (ETHICON, Inc., Somerville, NJ, USA) was placed around the urethra, guided by the guidewire. A second suture was applied close to the first one. The suture

tension was secured intraoperatively by applying two sutures with 4-0 Prolene and four knots on each suture. The guidewire was then removed, resulting in partial obstruction of the urethra, and the degloved penile skin was brought forward to its normal position (Figure 1). Rats were monitored by a veterinarian and an anesthesiologist; following recovery from anesthesia, they were each transferred to a single cage. Rats were given free water and food and were monitored daily for movements, eating, and micturition by the attendant nurse.

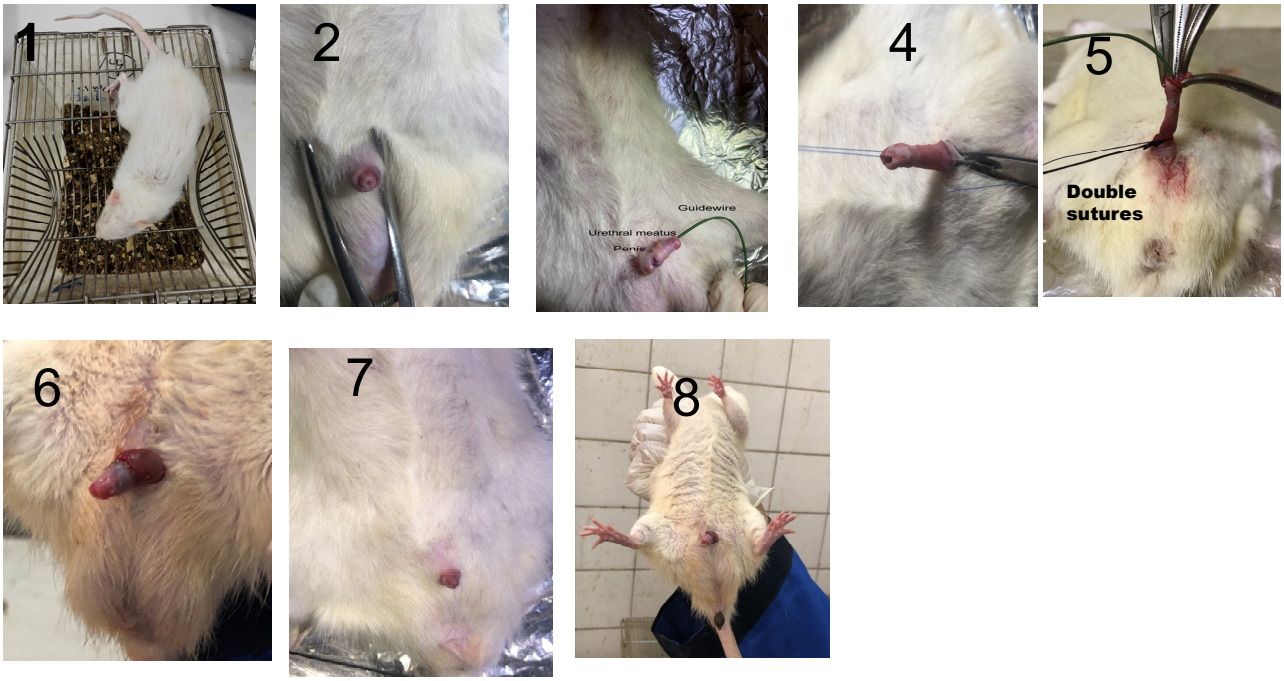

Figure 1. Non-invasive procedure of partial urethral obstruction for induction of bladder outlet obstruction in a Sprague-Dawley adult male rat. (1) Male rat (weight: 340 g) anesthetized with ketamine (10 mg/100 g body weight) via intraperitoneal injection. (2) The glans penis is exposed to visualize the external urethral meatus by applying gentle pressure on the side of the abdominal wall using surgical forceps. (3) A floppy guidewire of 0.038 inches in diameter is passed by the external urethral meatus to the urinary bladder; passing urine through the guidewire confirms its placement in the bladder. (4) The penis is degloved by pushing the skin backward. (5) A 4/0 Prolene thread is passed around the urethral tissue at the root of the penis in the presence of a guidewire at a caliber equal to the caliber of the guidewire. A second suture is applied to secure the first one and to ensure suture tension. (6) End of the procedure with retraction of the penis. (7) The penis is re-embedded in the abdominal wall skin layer. (8) By the second postoperative day, the rat is active, voiding, and eating.

An identical surgical procedure, excluding the urethral sutures, was applied to the four rats in the sham group. The remaining four rats constituted the control group. Following the procedure, rats belonging to the BOO, sham, and control groups were transported to sterile cages with access to regular food and water.

The surgical procedures were conducted by the same surgeon and anesthesiologist. The same procedure steps were repeated in every rat. After anesthesia, the operation time was 5–10 minutes.

The experimental study was divided into three cycles to ensure reproducibility. The first cycle was composed of two rats in the BOO group, one rat in the sham group, and one rat in the control group. The four BOO rats survived the procedure and were healthy and active. Eight weeks later, rats were sacrificed, the bladders were retrieved, and histopathology analysis was conducted; changes in the bladder wall confirmed the existence of BOO. The second cycle was composed of four BOO rats, followed by the third cycle with eight BOO rats.

The 8-week interval between induction of BOO and examination of the bladder wall was based on previous studies that confirmed that changes in muscle layer thickness and detrusor muscle and OAB events occurred in the sixth and eighth weeks and were persistent [3,8].

All 16 rats survived and were active, eating, micturating, and passing stools.

Gross examination: Each rat was weighed before retrieval of the bladder; then, the bladder was weighed. To assess bladder hypertrophy, bladder weight from the BOO group was compared to that of the control and sham groups. Bladder weight in the control and sham groups was 110 ± 7 mg, while in BOO it was 130 ± 15 g. Body weight did not differ between the BOO group and the control/sham groups. The bladder/body weight ratio was also comparable between the 3 groups.

Histological analysis: The wall thickness of each rat's bladder was assessed. Histopathological examination was performed on bladder samples. Tissue samples were fixed in 10% formalin, processed, and embedded in paraffin. For histological analysis, sections of 4 μm thickness were stained with H&E stain; a twin sample was stained with Masson's trichrome staining to evaluate the ratio of smooth muscles to collagen. In each sample, ten fields were inspected at various magnifications.

We adhered to AVMA Guidelines for the Euthanasia of Animals, 2020 Edition.

2.1.2. Statistical analysis

Data analysis was conducted using GraphPad Prism (version 8.0.0, USA). The mean ± standard deviation (SD) of the data was shown. One-way analysis of variance (ANOVA) was used. The different groups were compared using Tukey's multiple-comparison post-hoc test. A p-value < 0.05 was regarded as statistically significant.

2.2. Human OAB

Archival paraffin-embedded tissue samples from three surgical specimens of the urinary bladder were obtained from three adult male patients with neurogenic bladder dysfunction (NBD), representing human OAB. All three patients developed NBD between the ages of 2 and 5 years, presenting clinically with upper urinary tract dilatation and chronic kidney disease with progressive kidney function decline. To eliminate high pressure on the upper tract, all patients underwent abdominal vesicostomy. At puberty (ages 18, 21, and 35 years), all patients were receiving regular hemodialysis. During surgical closure of the vesicostomy, the tract, composed of the dome of the bladder wall, was surgically excised. Tissue samples were processed for histopathology with H&E and Masson's trichrome stain. All patients provided informed consent for the use of their data for scientific reporting.

3. Results

3.1. Male rat model

All rats survived: they were active and moving, and conducted normal daily tasks of eating, drinking, micturition, and defecation. No complications were encountered; still, daily care was provided by nurses. Inspection of the urethral suture site showed no infection or inflammation: the urethral suture was in place, did not fail, and was not disrupted. Gross examination of the bladders in the BOO groups showed a thickening of the bladder wall, while those of the sham and control groups were normal. The ureters and kidneys of all groups were normal.

The first aim of the study was to evaluate whether bladder hypertrophy, assessed by bladder weight, occurs in BOO rats after 8 weeks. The bladder weight of the BOO male rats (130 ± 15 mg) was significantly higher than that of the sham and control groups (110 ± 7 mg). Comparison of body weight between the BOO group and the sham/control groups did not show significant differences. The bladder/body weight ratio was also comparable between the three groups.

Regarding histopathology, the bladders in the BOO, sham, and control groups were examined by H&E and Masson's trichrome staining. Sections of bladder walls of the three groups were stained with H&E, while a corresponding tissue section was also simultaneously examined with Masson's trichrome staining. Histopathology of BOO tissues revealed separation of muscle bundles by collagen condensation and thinning of the urothelium. In contrast, the sham and control groups presented normal urothelium and a few interlacing collagen fibers between the muscle bundles; the muscular layer was condensed and well-organized. The BOO group had a collagen to smooth muscle ratio of 2 and presented muscle bundles that were densely interlaced with collagen fibers, whereas the control group presented normal collagen distribution across muscle bundles (Figure 2).

3.2. Human OAB

Human tissue samples were processed for histopathology with H&E and Masson's trichrome stain. Sections were prepared from the bladder wall of patients with neurogenic bladder and examined with H&E staining, showing a thick urothelium, squamous epithelial metaplasia, and thick submucosal blood vessels with notable congestion. Masson's trichrome stain showed extensive stromal fibrosis with mild chronic inflammatory infiltrate (Figure 2).

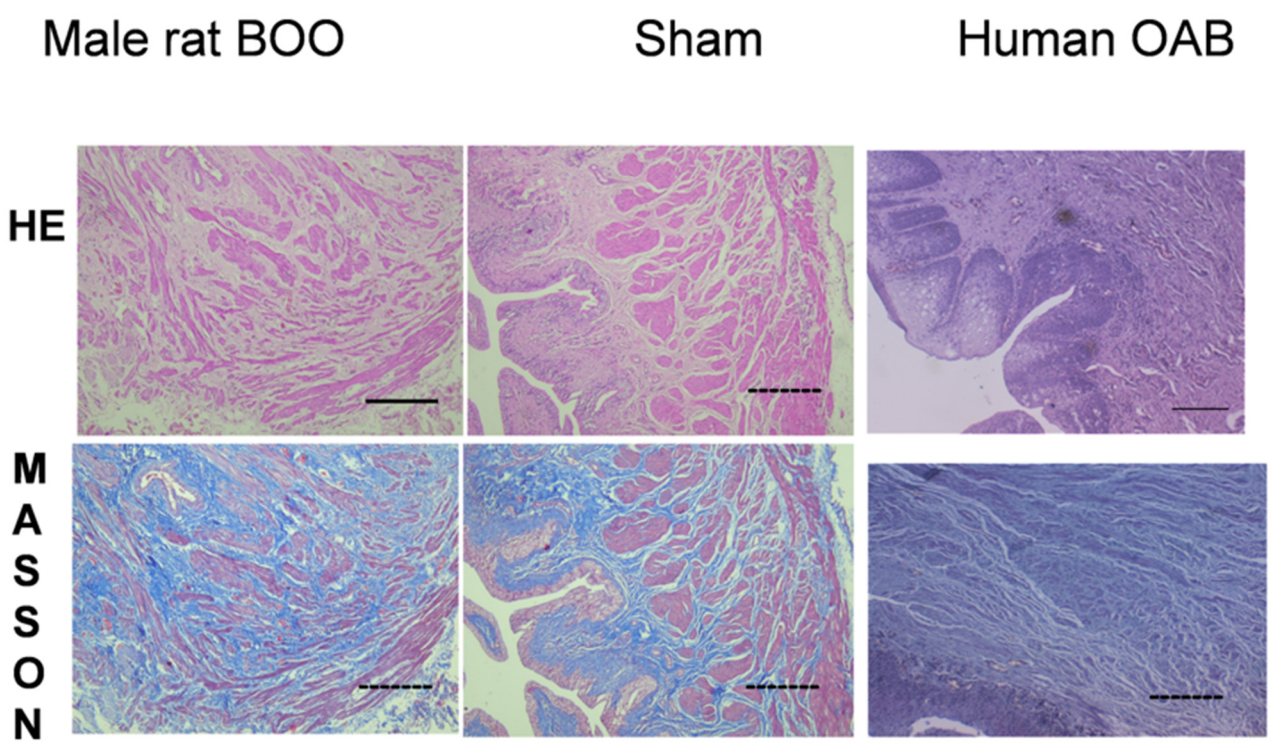

Figure 2. Histopathological analysis of the bladder wall of Sprague-Dawley adult male rats belonging to the bladder outlet obstruction (BOO) and sham groups, and of human patients with overactive bladder (OAB). First column: BOO rat model. HE staining shows thin urothelium and collagen fibers interlacing between muscle bundles; Masson's trichrome staining shows abundant collagen distribution between muscle bundles. Scale bar, 100 μm. Second column: Sham/control rat bladder stained with H&E (top) and Masson's trichrome (bottom) shows normal urothelium and normal arrangement of collagen in the muscle layer. Scale bar, 100 μm. Third column: H&E staining (top) of sections prepared from the bladder wall of patients with neurogenic bladder, showing thick urothelium, squamous epithelial metaplasia, and thick submucosal ectatic blood vessels with notable congestion; Masson's trichrome staining (bottom) showing extensive stromal fibrosis with mild chronic inflammatory infiltrate. Images in the first and second column are attributed to the authors of [8]; that article is open access, published by Spring Nature, and citing is permitted with the agreement of the authors.

4. Discussion

Studies using various approaches on experimental animal models through the induction of BOO have revealed morphological alterations attributed to the pathophysiological changes in OAB. These changes include an increase in collagen tissue, modifications in smooth muscle, and a thickening of the bladder wall. It has been proposed that normalization of bladder function after BOO might be facilitated by the increased connective tissue observed in OAB. Uvelius et al. showed that the amount of bladder collagen increases during obstruction and decreases after de-obstruction, which may be explained by the increased functional demands that obstruction places on the bladder [13,14].

The present study details the thickness changes of the three tissue layers of the male rat bladder at the histological level, showing that the induction of BOO led to OAB events in terms of hypertrophy of the three tissue layers in response to partial BOO. Here, we provide novel information regarding changes in the bladder of adult male rats using a non-invasive technique that simulates natural events of BOO in humans. To the best of our knowledge, this non-invasive procedure for inducing BOO in male rats has not been previously reported. In this study, by employing such a non-invasive approach to induce BOO in male rats, we demonstrated that, following BOO, the bladder wall tissue underwent changes similar to those seen in human OAB. These findings in male rats are similar to those observed in female rat models as demonstrated in previous studies [8–11]. These results highlight the need for understanding tissue mechanics and the distribution among the different anatomical layers, which could have an impact on the development of personalized medicine for men with BOO and OAB.

In the present study, thickening of the muscle layer occurred at 8 weeks, agreeing with a previous study that showed that thickening occurred in the sixth and eighth weeks [8]. This study also highlights the intrinsic mechanical hypertrophy of the different bladder layers in response to BOO after 8 weeks in adult male rats and in human OAB patients. Meanwhile, the control group showed no such increase, indicating the necessity of prompt relief of obstruction in men with BOO. A limitation of our study is that post-obstruction recovery was not evaluated.

The novelty of this non-invasive technique for inducing BOO in animal models is that it avoids tissue manipulation: there is no opening of the abdomen or bladder, and the perivesical and periurethral tissues are not dissected. Such injurious events have been reported in open surgical methods and showed a high rate of complications [8,15,16]. In our non-invasive procedure, all rats survived, had no complications, and presented normal activity for 8 weeks postoperatively. An important aspect in this technique is the utmost care of the experimental animal by applying a minimally invasive procedure and providing appropriate anesthesia during the procedure and at sacrifice. These important points are in accordance with the international agreement on the welfare of experimental animals.

In the present study, animals had a smooth postoperative period without complications. Open techniques reported a longer operation time, while our technique was conducted in 5–10 minutes. The success of our procedure lies in the absence of complications, while the short procedure is due to the use of a sterile guidewire inserted in the urethra, the same instrument used in minimally invasive procedures in urology.

Earlier research in animal models has demonstrated that BOO leads to an increase in muscle mass [6]. Consistent with the findings of other investigations, we observed an increase in bladder weight, muscular hypertrophy, and the predominance of collagen content [2,14].

It has been proposed that a variety of factors, including smooth muscle cells and nerves, may be responsible for the pathophysiology of OAB [15]. A recent study investigated the cytoskeleton and cells in animal models with overactive bladders. Tissues were analyzed using electron microscopy, immunohistochemistry, and light microscopy. According to histopathological analysis, the ratio of muscle to collagen was 0.5:3 [12,17].

The present study demonstrates that bladder hypertrophy in the BOO male rat model at 8 weeks is not comparable to the control group and has similarities to the human male bladder with neurogenic bladder dysfunction regarding the distribution of smooth muscles and collagen. The BOO female rat model has similarities to that of the human OAB [8]. Histopathological and cytoskeletal changes observed in OAB following BOO, such as those due to infravesical obstruction in benign prostatic hyperplasia, urethral strictures, urethral stones, and cystocele in women, are consistent with the

alterations observed at the cellular and cytoskeletal level in our OAB male rat model at 8 weeks [1]. Bladder abnormalities in the real-world clinical presentation of OAB-related lower urinary tract symptoms are stable and rarely decompensate or become fibrotic. After 8 weeks of obstruction in male rats, these alterations remained stable.

According to previous studies, bladder decompensation and consequent fibrosis follow cytoskeletal changes of OAB, usually 4–6 weeks after induction [15]. In the present study, cellular and cytoskeletal features of OAB remained stable at 8 weeks, without evidence of decompensation or fibrosis.

Based on our findings, we propose that the male rat experimental model for OAB, which minimizes surgical injury, accurately simulates real-world events in humans. Further studies are warranted to analyze the mechanisms of hypertrophy and the events following the relief of obstruction in male rats. We suggest that OAB studies in animal models should be designed differently for male or female animals.

The present model should be further extended to include immunohistochemistry, metabolic changes, ultrastructure, and molecular pathways driving collagen deposition or urothelial thinning, including TGF-β signaling for fibrosis, cytokine expression, biochemical markers, and urodynamic parameters. The current data showed changes in the bladder wall after BOO similar to findings in BPH. Further studies are required to determine the optimal timing for relieving the obstruction and evaluate whether medication or early relief of obstruction is recommended.

A limitation of the present study is the lack of post-BOO relief analysis. Still, this study aimed to demonstrate the validity of a non-invasive technique to induce BOO in adult male rats.

5. Conclusions

The non-invasive technique for the induction of BOO in male rats proved to be safe, reproducible, and had no complications, resulting in an increased collagen to smooth muscle ratio. The findings in the rat model were comparable to those in human tissues.

This study shows that a non-invasive male rat model of BOO is possible, with findings after 8 weeks similar to the changes observed in human OAB regarding muscles and collagen distribution. Previous male rat models for the induction of OAB used invasive surgical procedures that does not mimic natural events. The results indicate that this model can aid in understanding human male OAB and could be used for experimental and therapeutic research for adult patients with BOO, to help determine the optimal timing to relieve the obstruction or to continue with medication, as in cases of benign prostatic hypertrophy.

Author contributions

All the authors contributed equally to the work: developed and structured the research, project development, methodology, surgical technique, data interpretation, manuscript writing, and final version editing and review. The final edit was approved by all authors.

Use of AI tools declaration

The authors declare they have not used artificial intelligence (AI) tools in the creation of this article.

Ethical approval of the research and informed consent

The experimental study: The protocol and the study were done according to the requirement of National Research Council 2011 "Guide for the Care and Use of Laboratory Animals: Eighth Edition." Washington, DC: The National Academies Press, and complied with the ARRIVE guidelines, AVMA Guidelines for the Euthanasia of Animals: 2020 Edition and approved by the Research Ethics Committee of Theodor Bilharz Research Institute (Cairo, Egypt) for the conduct of the animal experiments (TBRI- Protocol No: PT636).

The human study: The Research Ethics Committee of Theodor Bilharz Research Institute (Cairo, Egypt) approved the study (TBRI- Protocol No: PT 726). The study was conducted in compliance with the relevant laws and regulations, good clinical practice, and ethical principles as described in the World Medical Association's Declaration of Helsinki. The Patients consented to publish anonymously the data related to their samples.

Conflict of interest

The authors declare no conflict of interest.

References

1. Yokoyama O, Yusup A, Oyama N, et al. (2007) Improvement in bladder storage function by tamsulosin depends on suppression of C-fiber urethral afferent activity in rats. *J Urol* 177: 771–775. https://doi.org/10.1016/j.juro.2006.09.076
2. Vale L, Cruz F, Charrua A (2024) Detrusor overactivity after partial bladder outlet obstruction is associated with high urinary adenosine triphosphate levels in female Wistar rats. *Int Neurourol J* 28: 34–39. https://doi.org/10.5213/inj.2346196.098
3. Kang YJ, Jin LH, Park CS, et al. (2011) Early sequential changes in bladder function after partial bladder outlet obstruction in awake sprague-dawley rats: focus on the decompensated bladder. *Korean J Urol* 52: 835–841. https://doi.org/10.4111/kju.2011.52.12.835
4. Jin LH, Andersson KE, Han JU, et al. (2011) Persistent detrusor overactivity in rats after relief of partial urethral obstruction. *Am J Physiol Regul Integr Comp Physiol* 301: R896–R904. https://doi.org/10.1152/ajpregu.00046.2011
5. Dunton CL, Purves JT, Hughes Jr FM, et al. (2021) BOO induces fibrosis and EMT in urothelial cells which can be recapitulated in vitro through elevated storage and voiding pressure cycles. *Int Urol Nephrol* 53: 2007–2018. https://doi.org/10.1007/s11255-021-02942-3
6. Niemczyk G, Fus L, Czarzasta K, et al. (2020) Expression of toll-like receptors in the animal model of bladder outlet obstruction. *Biomed Res Int* 2020: 6632359. https://doi.org/10.1155/2020/6632359
7. Sezginer EK, Yilmaz-Oral D, Lokman U, et al. (2019) Effects of varying degrees of partial bladder outlet obstruction on urinary bladder function of rats: a novel link to inflammation, oxidative stress and hypoxia. *Low Urin Tract Symptoms* 11: O193–O201. https://doi.org/10.1111/luts.12211

8. Wishahi M, Hassan S, Kamal N, et al. (2024) Is bladder outlet obstruction rat model to induce overactive bladder (OAB) has similarity to human OAB? Research on the events in smooth muscle, collagen, interstitial cell and telocyte distribution. *BMC Res Notes* 17: 22. https://doi.org/10.1186/s13104-023-06681-9
9. Melman A, Tar M, Boczko J, et al. (2005) Evaluation of two techniques of partial urethral obstruction in the male rat model of bladder outlet obstruction. *Urology* 66: 1127–1133. https://doi.org/10.1016/j.urology.2005.06.070
10. Zvara P, Kliment J, Deross AL, et al. (2002) Differential expression of bladder neurotrophic factor mRNA in male and female rats after bladder outflow obstruction. *J Urol* 168: 2682–2688. https://doi.org/10.1016/S0022-5347(05)64244-9
11. Takaoka EI, Kurobe M, Matsuoka K, et al. (2025) Adenosine receptor mechanisms underlying bladder dysfunction in male rats with bladder outlet obstruction. *Neurourol Urodyn* 44: 1370–1377. https://doi.org/10.1002/nau.70080
12. Kitta T, Kanno Y, Chiba H, et al. (2018) Benefits and limitations of animal models in partial bladder outlet obstruction for translational research. *Int J Urol* 25: 36–44. https://doi.org/10.1111/iju.13471
13. Uvelius B, Lindner P, Mattiasson A (1991) Collagen content in the rat urinary bladder following removal of an experimental infravesical outlet obstruction. *Urol Int* 47: 245–249.
14. Uvelius B, Andersson KE (2022) Molecular and morphological characteristics of the de-obstructed rat urinary bladder—an update. *Int J Mol Sci* 23: 11330. https://doi.org/10.3390/ijms231911330
15. Huang J, Li H, Zhang Y, et al. (2023) Excitatory purinergic and cholinergic expression changed in a partial bladder outlet obstruction-induced overactive bladder rat model. *Sci Rep* 13: 18395. https://doi.org/10.1038/s41598-023-45014-5
16. Buttyan R, Chen MW, Levin RM (1997) Animal models of bladder outlet obstruction and molecular insights into the basis for the development of bladder dysfunction. *Eur Urol* 32: 32–39.
17. Kim SO, Song SH, Ahn KY, et al. (2010) Distribution of interstitial cells of cajal in menopausal rat urinary bladder showing detrusor overactivity. *Int Neurourol J* 14: 48–53. https://doi.org/10.5213/inj.2010.14.1.48

AIMS Press