Received: 6 January 2020 | Accepted: 1 April 2020

DOI: 10.1002/nau.24363

ORIGINAL BASIC SCIENCE ARTICLE

Neurourology Urodynamics ICS SUFU WILEY

Pressure-volume analysis of rat's micturition cycles in vivo

Hsien-Yu Peng PhD[1] | Cheng-Yuan Lai PhD[1] | Ming-Chun Hsieh PhD[1] | Yu-Cheng Ho PhD[1] | Tzer-Bin Lin PhD[2,3,4]

[1]Department of Medicine, Mackay Medical College, New Taipei, Taiwan

[2]Department of Physiology, School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan

[3]Cell Physiology and Molecular Image Research Center, Wan Fang Hospital, Taipei Medical University, Taipei, Taiwan

[4]Department of Biotechnology, College of Medical and Health Science, Asia University, Taichung, Taiwan

Correspondence
Tzer-Bin Lin, PhD, Department of Physiology, Taipei Medical University, No. 250 Wu-Shin St., Taipei 11031, Taiwan.
Email: tblin2@gmail.com

Funding information
Ministry of Science and Technology, Taiwan, Grant/Award Numbers: MOST 105-2628-B-715-003-MY3, MOST 107-2320-B-715-005, MOST 108-2320-B-038-028

Abstract

Aims: Though the pressure-volume analysis (PVA), a method based on thermodynamics, is broadly used for assaying cardiac functions, its potential application on the physiology/pathophysiology of the urinary bladder, which processes resemble thermodynamic cycles to the heart, has not been established.

Methods: Cystometry recording intravesical pressure (IVP) and intravesical volume (IVV) of rhythmic voiding contractions caused by a constant saline infusion (0.04 mL/min) were carried out in forty urethane-anesthetized female Sprague-Dawley rats, and the PVA was established by plotting IVP against IVV.

Results: Pressure-volume points shaped coincident enclosed loops, and loop-associated urodynamic parameters kept stable under a constant infusion rate (0.04 mL/min). Enhancing preload (by elevating infusion rates to 0.08 and 0.12 mL/min) increased the area enclosed by the loop (Apv) and shifted loops to the right and slightly upward. Augmenting afterload (by enhancing resistances using 1/4 and 1/2 urethra clamping) increased Apv and shifted loops markedly to the right and upward. Without affecting Apv, muscarine (0.01 and 0.1 mM)-induced inotropic states shifted loop to the left and upward that was as opposed to the atropine (0.01 and 0.1 mM)-induced anti-inotropic state.

Conclusions: Not only consistently assayed baseline bladder functions, PVA but also validly measured modified bladder functions due to altered extrinsic environment and intrinsic contractility of the bladder itself. In accompanied by cystometry, PVA could provide a clear concept about the relationship between time, pressure, and volume in the voiding activity.

KEYWORDS

micturition, pressure-volume loop, rat, thermodynamics, urinary bladder

Hsien-Yu Peng and Cheng-Yuan Lai contributed equally to this study.

Part of the results of this study has been published as an abstract for the 97th Annual Meeting of the Physiological Society of Japan.

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1 | INTRODUCTION

The urinary bladder collects and stores urine before its disposal by urination.[1] The cystometry, measuring intravesical pressure (IVP) and emptied fluid volume over time, is used clinically to identify urological conditions such as outflow obstruction and stress incontinence. Although rodent micturition differs somewhat from that of humans, rodent cystometry is conducted in preclinical investigations, and has provided important information about bladder physiology/pharmacology.[2]

In addition to well-defined parameters reflecting bladder function, studies based on cystometry have developed novel parameters with the intent of probing specific pathophysiological changes. For example, the time-derived IVP differentiates enhanced IVP caused by active detrusor contraction from that due to passive urine retention,[3] and bladder compliance reveals an altered storage function.[4]

Notably, although cystometry measures pressure and volume events over time, the relationship between pressure and volume during micturition cycles has received scant attention to date. Based on thermodynamics, comprehensive works[5-7] have established the pressure-volume analysis (PVA) of ventricular function (for details see Kuhz-Buschbeck et al[8]). In addition to providing a framework for understanding cardiac function, studies have correlated the areas enclosed by the trajectory in PVA with the oxygen consumption of the beating ventricles; therefore, PVA is a specific means to assess the mechanical work of the heart.[7,9,10]

Given that PVA is informative for ventricular thermodynamics, we questioned if analyzing the pressure-volume relationship obtained from cystometry could extend the utility of cystometry and provide benefit for urology. Fortunately, even though the bladder functions differently from the heart, that is, it stores urine until neurally triggered voiding, while the heart pumps blood to the system according to an intrinsic pacemaker, the thermodynamic processes of these muscular hollow organs are similar; namely both are continuously filling with fluid, resulting in a volume increase with gradual pressure elevation. Then, they contract to develop a marked pressure increment to propel fluid out of the organ against resistance.[11] Moreover, regardless of their muscle fiber types, the mechanics of cardiac[12] and bladder[13] muscles are basically a function of tension-length relationships. The pressure-volume relationship is a specific version of the tension-length relationship found in hollow muscular organs.[11]

In the current study, we aimed to derive PVA of voiding cycles from the cystometry; and its potential application in assaying bladder function was evaluated first by determining whether PVA stably measures baseline conditions. Next, since bladder dynamics depend on the intrinsic contractility of the bladder itself[14,15] and the extrinsic environment, namely the preload[16] and afterload,[17,18] we challenged the bladder with modified contractility and loading conditions to test the validity of PVA in clarifying dynamic bladder functions.

2 | MATERIALS AND METHODS

2.1 | Animal preparations

The animal procuration/husbandry/experiments in this study conformed to the "European Convention for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes." All experiments were reviewed and approved by the Institutional Review Board of Taipei Medical University, Taipei, Taiwan. Forty adult female Sprague-Dawley rats (200-300 g; purchased from BioLASCO, Taipei, Taiwan) were randomly assigned to experiment groups in which the sample size was set before data acquisition based on our previous publication[3]; and the person evaluating data was blinded to the group allocation.

2.2 | Surgical preparations

Animals were anesthetized with subcutaneous urethane (1.2 g/kg), a reagent allows urinary bladder voided rhythmically under continuous infusion.[19,20] Three PE-50 catheters (Portex, Hythe, UK) was placed into the left jugular vein, left femoral artery, and right femoral artery; the former was for anesthetics injection when needed and the latter two were for reagents administration. During experiments, animals breathed spontaneously with an intubated trachea cannula with the body temperature kept at 36.5°C to 37.0°C. If corneal reflex or response to noxious paw presented, a supplementary dose (0.4 g/kg IV) of anesthetics would be given. At the end of the experiments, the animals were killed under deep anesthesia using an injection of overdose urethane.

2.3 | Cystometry

After an abdominal incision, ureters were bilaterally transected and drained freely within the peritoneal cavity to avoid urine accumulation in the bladder. A wide-bore cannula (PE-50) was tied into the lumen of the bladder through an incision on the apex of the bladder dome. The cannula was connected via a three-way stopcock to a

pressure transducer (P23 1D; Gould-Statham, Quincy, IL) and to a syringe pump for recording IVP and saline infusing, respectively. After the bladder was emptied, saline with a constant rate (0.04, 0.08, or 0.12 mL/min) was continuously infused into the urinary bladder to provoke rhythmic voiding contractions; and urodynamic parameters were analyzed when the tracings displayed at least three uniformed contractions. For the specific weight of saline (25°C) is close to 1 g/mL, and our pilot data demonstrated a good correlation between the volume and the weight of saline (data not shown), the accumulated volumes of infused and voided fluid was continuously recorded by measuring the weight of fluid using strain gauges (FT03C GRASS). Rats were tested for steady saline infusion, modified preload/afterload, as well as muscarine/atropine injections. When modifying preload, the infusion rate was stepwise elevated from 0.04 to 0.08 and 0.12 mL/min. When modifying afterload, the outlet resistance was consecutively increased by a quarter (1/4) and a half (1/2) transverse clamping of the urethra at the half-length of genitalia using an artery clip, in which the tip of the clip was localized to the longitudinal line of 1/4 and 1/2 of the urethra width from the right bolder.

2.4 | Pressure-volume analysis

The intravesical volume (Figure 1A, IVV) was calculated by the difference between infused and voided volumes using a build-in function in the software (BSL PRO 3.7; Biopac, Santa Barbara, CA); and PVA was established by plotting IVP against intravesical volume (IVV) (Figure 1B). PVA-associated parameters were: (a) peak pressure: maximal IVP at the end of isovolumic contraction; (b) voiding pressure: IVP difference between the peak pressure and minimal pressures of isovolumic relaxation; (c) end-filling volume: maximal volume at the end of filling; (d) filling volume: volume difference between the end-filling volume and the minimal volume at the beginning of filling; and (e) the area enclosed by the trajectory of a cycle (Apv): measured offline using an image processing program (ImageJ; LOCI, Madison, WI).

2.5 | Statistical analysis

SigmaPlot (Systat Software, Chicago, IL) was used for statistical analyses. All data were averaged from 2 to 3 continuous voiding cycles and were expressed as mean ± SD. For results in the first part of the experiment revealed parameters we analyzed were statistically independent to time, that is, time impact little on the pressure-volume relationship, paired two-tailed Student *t* test was used to compare means of groups. All statistical analyses were specified before the data acquisition. The outcome of all statistical analyses was reported, regardless of *P* values; and significance was set at $P < .05$.

3 | RESULTS

3.1 | Bladder PVA

To establish the PVA of micturition cycles, saline was constantly infused into the bladder (0.04 mL/min) of anesthetized rats to provoke rhythmic voiding that emitted fluid. With respect to time, cystometry displayed the contractions with uniform IVP (IVP, Figure 1C) peaks and IVV fluctuations. By plotting IVP against IVV, we observed a data trajectory that moved counterclockwise and shaped an enclosed loop during a micturition cycle (Figure 1D).

3.2 | Stages in PVA

Based on a PV loop, four phases were characterized. (a) Filling (F, Figure 1D; from the end of the previous to the onset of this voiding contraction): an increasing IVV with a baseline IVP slightly but progressively elevated. (b) Isovolumic contraction (IVC; from the onset of a voiding contraction to the beginning of fluid emission): the bladder contracts without fluid expulsion, which results in an abrupt IVP increase with a relatively constant IVV. (c) Emission (E; from the beginning to the end of fluid emission): because the rodent urethra contracts intermittently to maintain a sufficient pressure gradient to drive urine flow, the IVP oscillates and declines slightly at a plateau level with a marked IVV decrease. (d) Isovolumic relaxation (IVR; from the end of fluid emission to the end of bladder relaxation): the bladder relaxes without fluid expulsion, which results in a marked IVP decline with an almost unchanged IVV.

3.3 | Baseline condition

The consistency of PVA was first tested by examining if it stably measured urodynamic events in baseline cycles. Analogous to cystometry showing rhythmic contractions (Figure 1C), the PVA displayed relatively coincident loops with a period of 30 minutes (Figure 1D). Statistical analyses (Figure 1E) confirmed the consistency by demonstrating no significant differences between the mean values of loop-associated urodynamic parameters measured during the first (0-10), second (10-20), and last

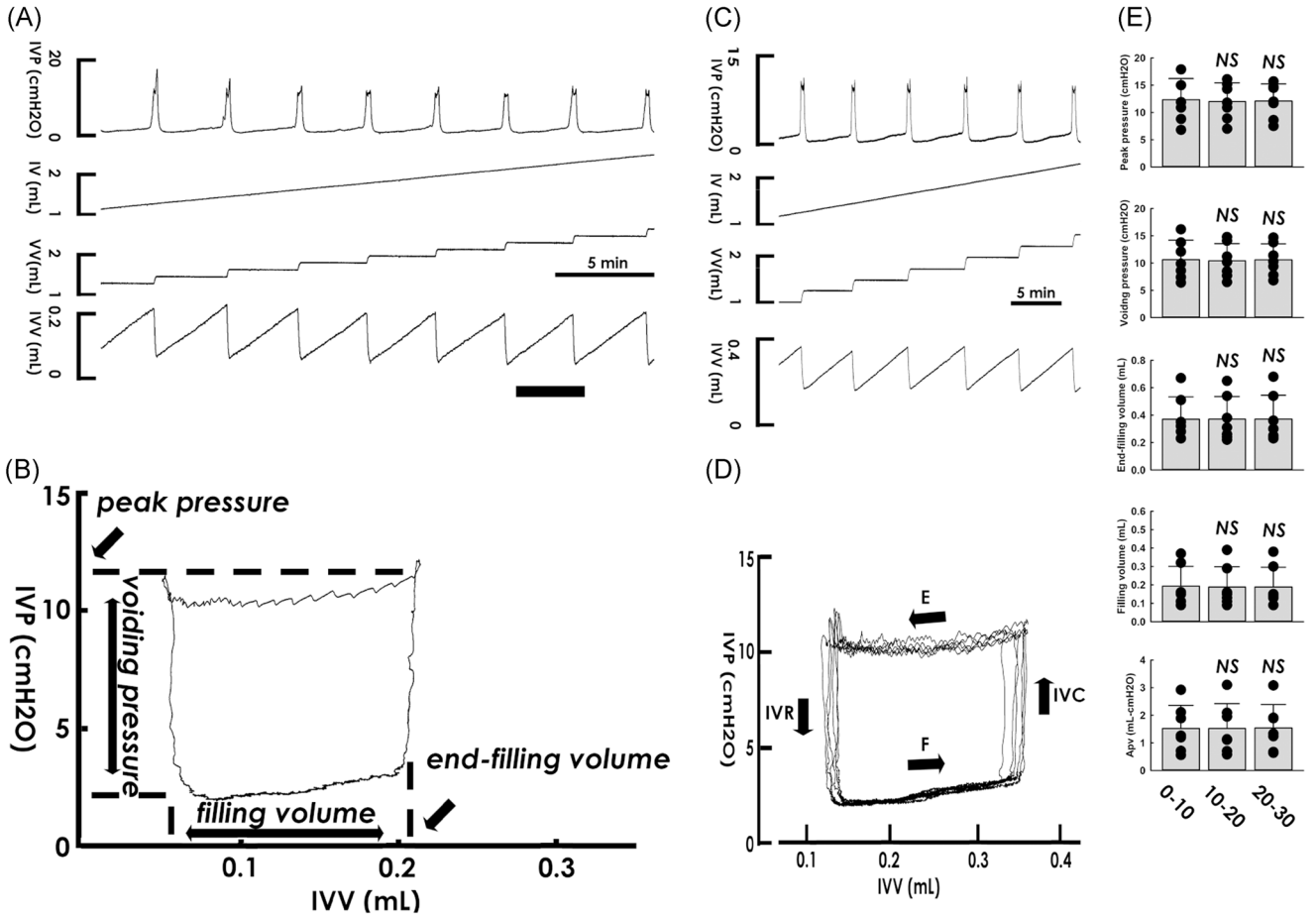

FIGURE 1 Urodynamic parameters of pressure-volume loops derived from micturition cycles. A, Cystometry tracings showing the intravesical pressure (IVP), infused volume (IV), voided volume (VV), and intravesical volume (IVV). The black bar at the bottom marks the cycle displayed in the pressure-volume (PV) diagram. B, A PV relationship of a micturition cycle established by plotting IVP against intravesical volume (IVV). The peak pressure is the maximal IVP at the end of the isovolumic contraction. The voiding pressure is the IVP difference between the peak pressure and the minimal pressure of the isovolumic relaxation. The end-filling volume is the maximal volume at the end of the filling phase. The filling volume is the volume difference between the end-filling volume and the minimal volume at the beginning of the filling phase. C, Cystometry tracings of periodical micturition cycles caused by a constant saline infusion (0.04 mL/min). D, Coincident PV loops at a period of 30 minutes. During micturition cycles, PV data points move counterclockwise as indicated by the arrows and shape enclosed areas in the PV diagram. Four phases are characterized in a PV cycle, that is, the Filling (F), Isovolumic contraction (IVC), Emission (E), and Isovolumic relaxation (IVR). E, Statistical analyses of urodynamic parameters obtained from the PV loop. No statistical difference is evident between the mean values of the parameters measured during the first (0-10) and the second (10-20) or the last (20–30) 10 minutes of the recording period. Apv, the area enclosed by a loop trajectory (NS, no significance vs 0-10, all n = 7)

(20-30) 10 minutes of the infusion period, including the peak pressure, voiding pressure, end-filling volume, filling volume, and the area enclosed by the trajectory (Apv).

3.4 | Altered preloads

After observing that the PVA consistently assayed the baseline condition, we next explored if it validly measured dynamic bladder functions in response to altered environments, which was first evaluated by challenging the bladder with increasing preloads. On cystometry, the stepwise elevation of the infusion rates from 0.04 (control; CON) to 0.08 and then to 0.12 mL/min slightly increased the amplitude of the IVP peaks but markedly increased the scale of the IVV fluctuations (Figure 2A). PVA demonstrated that elevated infusion rates shifted the loops to the right and slightly upward; it transparently increased the end-filling volume but mildly elevated the peak pressure (Figure 2B). The sensitivity of PVA to modified preloads was confirmed, as graded preload increments significantly increased the mean values of the peak pressure, end-filling volume, filling volume, and Apv without affecting the voiding pressure (Figure 2C).

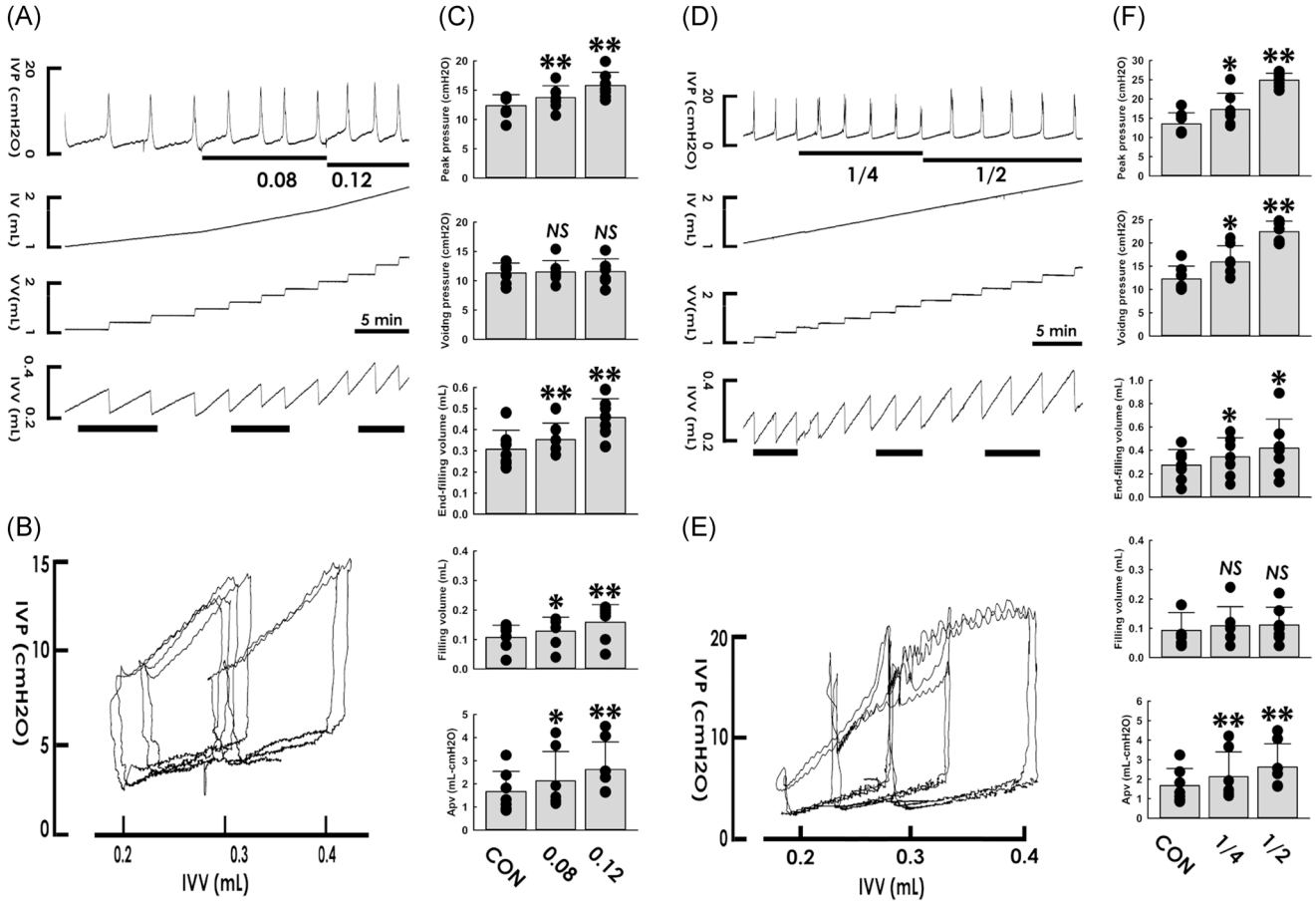

FIGURE 2 Pressure-volume loops in response to altered preloads and afterloads. A, Cystometry tracings of micturition cycles in response to an elevated rate of saline infusion (CON; 0.04 mL/min) to 0.08 and 0.12 ml/min. Black bars at the bottom mark the cycles displayed in the pressure-volume (PV) diagram. B, Representative PV loops under control infusion rates (0.04 mL/min) and rates of 0.08 and 0.12 mLmin. Elevated infusion rates progressively shift loops to the right and slightly upwards. C, Elevated infusion rates significantly increase the mean values of peak pressure, end-filling volume, filling volume, and the area enclosed by the loop trajectory (Apv) without affecting the voiding pressure (*$P < .05$, **$P < .01$, NS vs CON; all n = 7). D, Cystometry tracings of micturition cycles in response to increased outlet resistance by a quarter (1/4) and a half (1/2) urethra clamping. Black bars at the bottom mark the cycles displayed in the PV diagram. E, Representative PV loops under the control condition (CON) as well as 1/4 and 1/2 urethra clamping. Increased outlet resistance progressively shifts loops to the right and upward. F, Enhanced urethra resistance significantly increases the mean values of peak pressure, voiding pressure, end-filling volume, and the area enclosed by the loop trajectory (Apv) without affecting the filling volume (* $P < .05$, **$P < .01$, NS vs CON; all n = 7). IV, infused volume; IVP, intravesical pressure; IVV, intravesical volume; NS, no significance; VV, voided volume

3.5 | Altered afterloads

We next challenged the bladder with increasing afterloads. On cystometry, consecutively increasing the outlet resistance by clamping the urethra at a quarter (1/4) and a half (1/2) urethra clamping at the midpoint of the genitalia using an artery clip markedly increased the amplitude of the IVP peaks and shifted the IVV tracing upward (Figure 2D). In the PVA, enhanced resistance distinctly shifted the loops to the right and upward by considerably increasing the peak pressure and end-filling volume (Figure 2E). Statistical analyses confirmed the sensitivity, as the graded resistance increments significantly increased the mean values of peak pressure, voiding pressure, end-filling volume, and Apv without affecting the filling volume (Figure 2F). Collectively, these data revealed that PVA validly assayed urodynamic events in response to a modified environment, namely the preload and afterload.

3.6 | Inotropic state

Having observed that PVA sensitively analyzed environment-modified bladder functions, we next asked

whether it also validly assayed dynamic functions in response to the altered contractility of the bladder itself, first by focally infusing the animals with muscarine (an M-type cholinergic agonist, 0.01 and 0.1 mM, 0.02 mL/min) through a femoral artery catheter.

Cystometry demonstrated that muscarine dose-dependently increased the amplitude of the IVP peaks but decreased the scale of the IVV fluctuations (Figure 3A). PVA characterized a stepwise left and upward shift, that is, muscarine dose-dependently elevated the peak pressure but decreased the end-filling volume (Figure 3B). Without affecting Apv, statistical analyses confirmed the sensitivity of PVA by demonstrating muscarine significantly increased the mean values of the peak and voiding pressures but decreased those of the end-filling and filling volumes (Figure 3C).

3.7 | Anti-inotropic state

We next conversely reduced bladder contractility by focally infusing the animals with atropine (an M-type cholinergic antagonist; 0.01 and 0.1 mM, 0.02 mL/min, i.a.). On cystometry, atropine dose-dependently decreased the amplitude of the IVP peaks but shifted the IVV tracing upward (Figure 3D). The PVA showed a dose-dependent

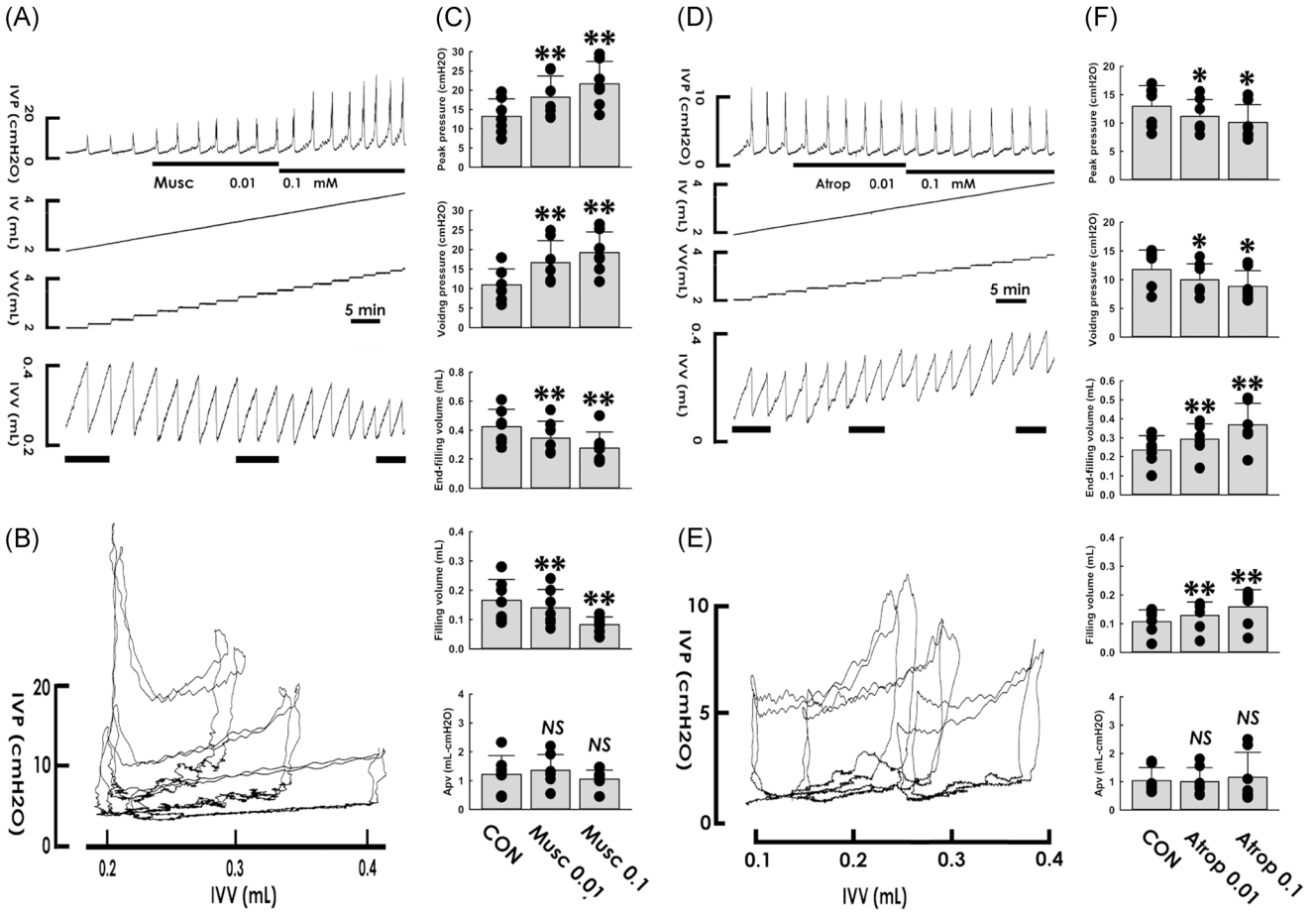

FIGURE 3 Pressure-volume loops in response to modified detrusor contractility. A, Cystometry tracings of micturition cycles in response to focal infusion of muscarine (Musc) with concentrations of 0.01 and 0.1 mM. Black bars at the bottom mark the cycles displayed in the pressure-volume (PV) diagram. B, Representative PV loops before (control, CON) and following cumulative dosages of muscarine infusion. Muscarine progressively shifts loops to the left and upward. C, Muscarine significantly increases the mean values of peak and voiding pressures but decreases that of end-filling and filling volumes without significantly affecting the mean value of the area enclosed by the loop trajectory (Apv) (**$P < .01$, NS vs CON; all n = 7). D, Cystometry tracings of micturition cycles in response to focal infusion of atropine (Atrop) with concentrations of 0.01 and 0.1 mM. Black bars at the bottom mark the cycles displayed in the PV diagram. E, Representative PV loops before (control, CON) and following cumulative doses of atropine infusion. Atropine progressively shifts loops to the right and downward. F, Muscarine significantly decreases the mean values of peak and voiding pressures but increases that of end-filling and filling volume without significantly affecting the mean value of the area enclosed by the loop trajectory (Apv) (*$P < .05$, **$P < .01$, NS vs CON; all n = 7). IVP, intravesical pressure; IV, infused volume; IVV, intravesical volume; NS, no significance; VV, voided volume

right and downward shift, as shown by the reduction of the peak pressure but an increase in the end-filling volume (Figure 3E). Statistical analyses further confirmed the sensitivity by demonstrating that without affecting Apv, atropine significantly decreased the mean values of the peak and voiding pressures but increased those of the end-filling and filling volumes (Figure 3F).

Collectively, these data revealed PVA validly assayed urodynamic events modified by altered bladder contractility itself.

4 | DISCUSSION

Derived from cystometry, which is widely used in preclinical and clinical studies, we developed a novel methodology, PVA, to assay bladder function. For the first time, we defined the stages of a micturition cycle based on the pressure-volume relationships; in addition, our data revealed that PVA consistently and validly analyzed the steady and dynamic functions of a rhythmically voiding urinary bladder in vivo.

4.1 | Consistency and validity

Our conclusion is based on three lines of evidence. For the first, the loop trajectories coincided well over a period of micturition activity and derived urodynamic parameter display no statistical differences under steady-state conditions, revealing that PVA consistently assayed baseline bladder functions. Next, when modifying the extrinsic environment by altering loading conditions, enhanced infusion rates increased the Apv and shifted the loops to the right and slightly upward; the augmented outlet resistance increased the Apv and shifted the loops markedly upward and right, revealing that PVA responded sensitively and specifically to an altered environment. Finally, when modifying the intrinsic contractility of the bladder itself, inotropic muscarine shifted the loops upward and left, while anti-inotropic atropine conversely shifted the loops downward and right, revealing PVA responded sensitively and specifically to reagents-modified bladder contractility. Collectively, these data revealed that PVA not only consistently assayed baseline bladder function but also validly assessed dynamic bladder function in response to an altered extrinsic environment and modified intrinsic contractility. We hence propose that, accompanied by cystometry, PVA could provide a novel dimension to the exploration of bladder functions/diseases.

4.2 | Apv represents micturition work

During the Filling (Figure 4A; F), accumulating fluid gradually increased the bladder volume, and potential energy with an amount represented by the area under the trajectory along the volume change was stored in the bladder.[7] In the subsequent IVC, the bladder actively contracted without fluid elimination, that is, developed tension without muscle shortening; it performed no mechanical work. Instead, the potential energy was enhanced by the contraction-increased stiffness.[10] During the Emission (E), the bladder performed mechanical work equal to the integration of the trajectory along with a volume change to void fluid.[7] Finally, after outlet closure, the bladder isovolumetrically relaxed without

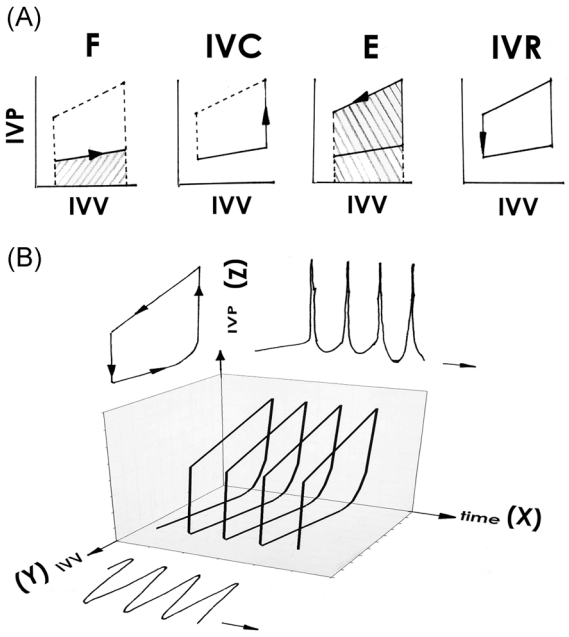

FIGURE 4 The mechanical work of a voiding cycle and the 3D relationship between time as well as bladder volume and pressure. A, Schematic illustration of a thermodynamic cycle of the bladder. During the filling phase (F), potential energy with an amount of the area under the pressure-volume (PV) trajectory is stored (hatched area). In the isovolumic contraction (IVC), the bladder performs no mechanical work but the potential energy is enhanced. During the emission phase (E), the bladder performed mechanical work equal to the area under the PV trajectory (hatched area). In the isovolumic relaxation (IVR), the bladder gains no mechanical work, yet, the potential energy is reduced. B, A 3D plots of time/IVV/IVP curves showing the relationship between the time (*X*-axis), IVV (*Y*-axis), and IVP (*Z*-axis). The IVV and IVP traces in the cystometry are the projections of time/IVV/IVP curves on the *X*-*Y* and *X*-*Z* planes, respectively; and the PV loops are the projection of time/IVV/IVP curves on the *Y*-*Z* plane. 3D, three-dimensional; IVP, intravesical pressure; IVV, intravesical volume

fluid elimination (IVR). Again, there was no muscle elongation and it gained no mechanical work, but the potential energy was reduced by the relaxation-decreased stiffness.[10]

For the area under the trajectory of the filling represents mechanical energy caused by passive fluid stretch rather than active bladder contraction; moreover, this area remained relatively constant and was not liberated during cycles, it was excluded from the total amount of contractile mechanical energy (for details see Suga[7]). These observations collectively indicate that the specific area, Apv, represents the work performed in a micturition cycle. Although this model markedly neglects mechanical work, including the fluid kinetic energy during filling/emission, friction energy throughout the entire cycle, and stress-relaxation during filling, it approximately quantified a simplified but neat model of the mechanical energy involved in a voiding cycle. This proposal is analogous to the basic concept of the Otto cycle, an ideal PV cycle, which defines the Apv in pressure-volume diagrams as the cycle work in thermodynamic engines.[21]

On the other hand, under various conditions, the area of pressure-volume loops is well recognized to precisely represent ventricular work performed in beating cycles because it correlates well with ventricular oxygen consumption, an indicator of ventricular work.[9] For thermodynamic are universally valid in systems involving the energy, entropy, volume, pressure, and temperature; and the thermodynamic processes of the urinary bladder and ventricles are similar, that is, continuously fluid filling increases the volume with a slight pressure elevation, and then actively contract to develop a marked pressure increment that propels fluid, thereby manifestly decreasing the volume.[11] Moreover, even though they have different muscle types, tension and length are the two most basic mechanical parameters of muscles, and the tension-length relationship is the fundamental mechanical property of a muscle regardless of whether it is a cardiac[12] or bladder[13] muscle.

Since the pressure-volume relationship is a modified version of the tension-length relationship in muscular hollow organs,[11] we suggest that the bladder PVA shares a basic mechanical property with the heart; and not restrictively in the heart, Apv, as predicted in the thermodynamics, plays as an index reflecting cycle work also in the bladder. Our proposal is supported by the observation that mechanical overloading induces similar remodeling of cardiac and bladder muscles, despite them being triggered by different pathological conditions, that is, hypertension and outlet obstruction, respectively.[11] Collectively, we suggest that the Apv coarsely represents mechanical work performed in a micturition cycle; nevertheless, potential divergences in the detailed mechanisms used by cardiac and bladder muscles need additional studies, but correlating the energy liberated by the Apv of micturition cycles will clearly define their relationships.

4.3 | Advantages and limitations

Although almost all pressure/volume events in PVA are measured as well or even better by the time-function curves in cystometry, PVA represents a comprehensive summary of the relationship between pressure and volume during micturition cycles, which is beneficial to scientists/clinicians. Moreover, PVA has advantages in assaying bladder functions.

First, PVA visibly illustrates the Apv, which provides a method for conceptual assessment of the mechanical work of voiding contractions; this information cannot be immediately visualized in the cystometry data. Because uniaxial overloading induces reorganization of cultured human smooth cells,[22] PVA offers a platform for quantifying work loadings in vivo for investigating overload-induced bladder adaptations.

Second, PVA has little reference to time, thereby minimizing the potential interference of time-associated variables, such as latency and/or frequency, with the measurements (Figure 4B). For example, elevated infusion rates in this study increased voiding frequency and outlet obstruction decreased voiding frequency in time-domain cystometry. Nevertheless, each cycle shaped a comprehensive loop in PVA, reflecting the PV relationship independent of the frequency (Figure 2). Although this could be a limitation in assaying time-dependent parameters, it reveals that PVA dissects the pressure-/volume-associated urodynamic events with minimal reference to time (Figure 4B). Together with the time-domain cystometry, which illustrates pressure-/volume-time relationships, an additional PVA showing the pressure-volume relationship is really benefit to clearly define the interactions between time, pressure, and volume that are the most important urodynamic parameters.

Third, PVA has the potential to provide a basis for developing techniques/parameters assaying bladder function more specifically, particularly detrusor contractility, because the end-systolic[23] and end-diastolic[24] of ventricular PVA are well established to respectively reflect ventricular contractile and relaxation conditions, and the former is now a recognized standard for monitoring inotropic states of the heart[25] and sensitively reflects responses to resynchronization therapy.[23]

5 | CONCLUSION

Derived from cystometry, PVA provides a method for conceptual assessment of the pressure-volume relationships of bladder activity, and hence could result in new insights into bladder mechanics, dynamics, and energetics. Together with time-domain cystometry, which measures pressure-/volume-time relationships, an additional PVA that illustrates pressure-/volume-associated urodynamic events with minimal reference of time is really benefit to clearly define the interactions between time, pressure, and volume, which are the most important urodynamic parameters.

ORCID

Tzer-Bin Lin http://orcid.org/0000-0002-3833-1951

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How to cite this article: Peng H-Y, Lai C-Y, Hsieh M-C, Ho Y-C, Lin T-B. Pressure-volume analysis of rat's micturition cycles in vivo. *Neurourology and Urodynamics*. 2020;39:1304–1312. https://doi.org/10.1002/nau.24363