Tension-free trans-obturator tape enhanced thermodynamic efficacy of the bladder in stress urinary incontinence patients: a retrograde observational study

HUI-HSUAN LAU[1], Cheng-Yuan Lai[2], Hsien-Yu Peng[2], Ming-Chun Hsieh[2], Tsung-Hsien Su[1], Jie-Jen Lee[3], and Tzer-Bin Lin[4]

[1]Affiliation not available
[2]Mackay Medical College
[3]Mackay Memorial Hospital
[4]Taipei Medical University

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Abstract

Objective In contrast to the well-recognized benefit of trans-obturator tape (TOT) to urine continence, if the TOT-enhanced urethra resistance results in modified voiding functions in stress urinary incontinence (SUI) patients is not adequately investigated. Design and setting Urodynamic investigations were retrograde analyzed in a tertiary referral hospital. Population A total of 26 female SUI patients Methods The area enclosed by the loop trajectory (Apv) in a pressure-volume analysis (PVA) which represent the work performed in each voiding cycle was retrospectively analyzed Main outcome measures The Apv of female SUI patients before and after the TOT were analyzed. Results When compared with the pre-operative control, the Apv was significantly increased post-operatively. The TOT-enhanced Apv was accompanied by increments in the mean urethra resistance (Rv) and mean voiding pressure (Pv) but unaffected voided volume (Vv) and voiding time (Tv). Moreover, the TOT-induced Apv increase (ΔApv) displayed moderate correlations with the changes in Rv and Pv (ΔRv and ΔPv, respectively) but no correlation with the changes in Vv or Tv (ΔVv and ΔTv, respectively). Notably, the TOT-induced ΔRv displayed a strong correlation with the ΔPv. Conclusions: The thermodynamic efficacy of the bladder was enhanced after the TOT; that could be attributed to that bladder develops an elevated pressure gradient in response to the TOT-enhanced outlet resistance during urine emission. Keywords: mid-urethra sling, trans-obturator tape, stress urinary incontinence, urethra resistance, thermodynamics, pressure-volume analysis Tweetable abstract The bladder developed an elevated pressure gradient to the TOT-enhanced outlet resistance; and herein enhanced the voiding efficacy.

Tension-free trans-obturator tape enhanced thermodynamic efficacy of the bladder in stress urinary incontinence patients: a retrograde observational study

Hui-Hsuan Lau, MD[1,3]*, Cheng-Yuan Lai, PhD[4]*, Hsien-Yu Peng, PhD[3]*, Ming-Chun Hsieh, PhD[3]*, Tsung-Hsien Su, MD, PhD[1,3], Jie-Jen Lee, MD, PhD[2,3], Tzer-Bin Lin, PhD[5,6]

[1]*Division of Urogynecology, Department of Obstetrics and Gynecology,* [2]*Department of Surgery, Mackay Memorial Hospital, Taipei, Taiwan*

[3]*Department of Medicine, Mackay Medical College, Taipei, Taiwan*

[4]*Institute of Biomedical Sciences, Mackay Medical College, New Taipei, Taiwan*

[5]*Institute of New Drug Development, College of Medicine, China Medical University, Taichung, Taiwan*

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

*These authors contributed equally to this study.

Short title: TOT enhances voiding efficacy in SUI patients

Please send corresponding to:

Tzer-Bin Lin, Department of Physiology, Taipei Medical University, No. 250 Wu-Shin Street Taipei 11031, Taiwan

ABSTRACT

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Design and setting Urodynamic investigations were retrograde analyzed in a tertiary referral hospital.

Population A total of 26 female SUI patients

Methods The area enclosed by the loop trajectory (Apv) in a pressure-volume analysis (PVA) which represent the work performed in each voiding cycle was retrospectively analyzed

Main outcome measures

The Apv of female SUI patients before and after the TOT were analyzed.

Results When compared with the pre-operative control, the Apv was significantly increased post-operatively. The TOT-enhanced Apv was accompanied by increments in the mean urethra resistance (Rv) and mean voiding pressure (Pv) but unaffected voided volume (Vv) and voiding time (Tv). Moreover, the TOT-induced Apv increase (ΔApv) displayed moderate correlations with the changes in Rv and Pv (ΔRv and ΔPv, respectively) but no correlation with the changes in Vv or Tv (ΔVv and ΔTv, respectively). Notably, the TOT-induced ΔRv displayed a strong correlation with the ΔPv.

Conclusions: The thermodynamic efficacy of the bladder was enhanced after the TOT; that could be attributed to that bladder develops an elevated pressure gradient in response to the TOT-enhanced outlet resistance during urine emission.

Keywords: trans-obturator tape, SUI, thermodynamics, pressure-volume analysis

Tweetable abstract

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This study was registered in ClinicalTrials.gov (NCT05255289)

INTRODUCTION

Weakness in muscle and/or tissue surrounding the urethra results in stress urinary incontinence (SUI) characterized by involuntary urine leakage on effort, physical exertion, sneezing, or coughing.[1] SUI is a common problem affecting women's daily life in physical, social, and hygienic aspects.[2]Conservative options, such as strengthening of the pelvic floor musculature[3] and bladder training,[4]are prescribed for SUI patients; and for those who have failed conservative therapies, a mid-urethral sling is a preferred treatment recommended.[5] In 1996, the first mid-urethral sling, tension-free vaginal tape, was launched;[6] and subsequently, the trans-obturator tape (TOT) was developed in 2001.[7] For TOT exhibits a satisfied cure rate and a relatively diminishes invasiveness,[8,9] it is increasingly accepted as a treatment of choice worldwide in the last decade.[10]

The procedure of TOT positions a narrow band of synthetic tape under the urethra;[11] and together with the scar tissue that grows following the sling implantation, the tape adds-on an exogenous urethra resistance to maintain the continence during urine storage.[12] Notably, in contrast to the well-recognized therapeutic benefit of the enhanced resistance to the bladder continence during urine storage,[13] if the voiding function of the bladder adapts to the TOT-enhanced outlet resistance has not been adequately investigated.[14-16] Particularly, to the best knowledge of ours, there is so far no study exploring if the thermodynamic efficacy of the bladder is modified following the TOT. Because an insufficient work output in response to an enhanced loading caused by the TOT-enhanced resistance could be a risk factor leading to un-compensated bladder functions,[17] we investigated the change in the thermodynamic efficacy of the bladder in response to the TOT to clarify the potential adaptation of the bladder to the enhanced outlet resistance.

Interestingly, a recent study demonstrated the pressure-volume analysis (PVA) of voiding cycles specifically assays the voiding work of the bladder and thereby quantifies the thermodynamic efficacy of bladder emptying.[18] We hence explored the potential modifications in the thermodynamic efficacy of the bladder in response to the TOT using the PVA.

2 MATERIALS AND METHODS

2.1 Patients

Pressure-flow studies of 30 female SUI patients ($<$ 70 years old) who had a TOT procedure following the Delorme's description of the obturator route[19] in the Mackay Memorial Hospital were retrospectively reviewed. 4 patients whose urodynamic data failed to shape complete pressure-volume loops were excluded, thus there was a total of 26 patients in the statistical analysis.

2.2 Pressure-flow study and pressure-volume analyses

Our protocols of cystometry complied with the guidelines of the International Continence Society (ICS).[20] Briefly, a multi-channel urodynamic study, in which warm saline (37 °C) was infused (80 ml/min) into patients' bladder, was recorded (MMS UD-200, Medical Measurement System, Enschede, Netherlands) and analyzed (Biopac MP36, Biopac Systems, Santa Barbra, US) using computer systems. The vesical pressure (Figure 1A Pves), abdominal pressure (Pabd), detrusor pressure (Pdet), urethral flow (Flow), voided volume (Vvod), infused volume (Vinf), and intra-vesical volume (Vive) were online recorded; and the mean voiding pressure (Figure 1B Pv; the mean Pdet during fluid emission), the voided volume (Vv; the volume of emitted fluid), the voiding time (Tv; the time latency of fluid emission), and the mean voiding resistance (Rv; calculated by Pv/(Vv/Tv)) were off-line analyzed.

Derived from the cystemetry (Figure 2A), the pressure-volume analysis (PVA) of the voiding cycle was established by plotting Pdet against Vive (Figure 2B);[18,21] and the trajectory-enclosed area (Apv) was analyzed using an image processing program (Image J, LOCI, Madison, WI, USA).

Although cough and Valsalva tests markedly interfere Pves and Pabd, a previous publication[22] and our data (Figure 1A) demonstrated these tests displayed little effect on the Pdet in the cystometry. Moreover, our data discovered cough and Valsalva maneuver impacted trivially on the trajectory of PVA. In addition, cough and Valsalva tests were carried out during the storage phase in our protocol that would hardly affect the voiding dynamics. Therefore, cystometry data of SUI patients who underwent stress tests (coughs and/or Valsalva) were pooled together with those cystometry data without these tests.

2.4 Statistical analyses

All data in this study were expressed as mean $\pm$ SEM. Student's t-tests were used to assess the difference in values between groups. A significance in difference was set at $p<0.05$.

RES1ULTS

3.1 Database of patients

This study analyzed a total of 26 female SUI patients (mean age=54.59±1.27 years old). Urodynamic evaluations were respectively carried out at a mean of 52.84±20.29 days before and 177.80±23.26 days after the TOT surgery.

3.2 Pressure-flow/volume analyses

In the cystometry, saline infusion into the pre-emptied bladder of patients provoked a voiding (Figure 2A). The pressure-volume analysis (PVA), which was established by plotting the detrusor pressure (Pdet) against the intra-vesical volume (Vive), demonstrated the trajectory of pressure-volume data moved counterclockwise and shaped an enclosed loop representing a voiding cycle (Figure 2B). Four phases were identified in the loop, namely (1) Filling (F; from the infusion began to the voiding contraction onset): an increasing Vive in accompanied by a slightly but progressively elevated baseline Pdet. (2) Iso-volumic contraction (IVC; from the voiding contraction onset to the emission began): the bladder contracted without fluid expulsion that resulted in an abruptly elevated Pdet with a nearly constant Vive. (3) Emission (E; from the beginning to the end of fluid emission): a plateau Pdet that slightly elevated at the end of this stage with a marked Vive decrease. (4) Iso-volumic relaxation (IVR; from the end of emission to the end of bladder relaxation): the bladder relaxed without fluid expulsion that resulted in a marked Pdet decline with an almost constant Vive.

3.3 TOT increases the loop-enclosed area

To investigate the potential impact of TOT on the thermodynamic efficacy of bladder voiding, we compared and contrasted the area enclosed by the trajectory in the PVA (Apv) measured pre- and post-operatively for it represents the work performed by the bladder in a voiding cycle.[18]

Derived from the pressure-flow data measured before (Figure 3A PRE) and after (Figure 3B POST) a TOT operation, the illustrative loops in the PVA demonstrated while TOT failed to markedly shift the left, the lower, or the right boundary, it obviously elevated the upper border of the loop post-operatively that resulted in an increased Apv compared to the pre-operative control (Figure 3C and D). Inspecting individual Apv change in each patient revealed TOT increased Apv in most patients (20 out of 26, 77%; Figure 3E); and the TOT-associated Apv increment was confirmed by the summarized data showing the mean value of Apv was significantly increased after operation compared to the pre-operative control (Figure 3F).

3.4 TOT increases voiding resistance

For TOT is well-recognized to increase the resistance of the urethra during urine storage,[23] we examined if TOT also affects outlet resistance during urine voiding by assaying if TOT affect the mean urethra resistance (Rv).

As anticipated, TOT increased individual Rv in most patients (21 out of 26, 80%; Figure 4A) as well as significantly increased the mean value of Rv of patients when compared with the pre-operative control, indicating TOT did increase the outlet resistance during voiding.

3.5 TOT increases voiding pressure

Because the mean resistance during voiding was defined as the mean voiding pressure (Pv) divided by the mean urethral flow (Fv; Rv=Pv/Fv); and the Fv can be further calculated by dividing the mean voided volume (Vv) by the voiding time (Tv; Fv=Vv/Tv). Thereby, the relationship between the mean urethra resistance and the derived parameters can be described as Rv=Pv/[Vv/Tv]. We hence further assayed the changes in Pv, Vv, and Tv in response to surgery to specify the impact of TOT. When compared with pre-operative controls (Figure 4B PRE), TOT post-operatively increased individual Pv in most patients (POST; 21 out of 26, 80%) and significantly increased the mean value of Pv of patients. In contrast, individual data demonstrated that neither Vv (Figure 4C; 9 patients, 34% increased; 16 patients, 62 % decreased; 1 patient, 4% unchanged) nor Tv (Figure 4D; 8 patients, 31% increased; 17 patients, 65 % decreased; 1 patient, 4% unchanged) displayed a majority change (>75%). Moreover, no statistical significance was evidenced in the mean values of Vv and Tv of patients. These results indicated that in accompanied with an increased outlet resistance, TOT post-operatively elevated bladder pressure during voiding.

3.6 Correlated increments in Apv with Pv and Rv

We next assayed the relationship between the TOT-enhanced Apv and changes in urodynamic parameters by analyzing the correlation between the change in Apv (ΔApv) and those in Rv, Pv, Vv, and Tv (ΔRv, ΔPv, ΔVv, and ΔTv, respectively). Though the strength was not very strong, the TOT-induced ΔApv displayed moderate correlations with the ΔRv and ΔPv (both $r>0.5$, Figure 5A and 5B). Nevertheless, no correlation was evidenced between the ΔApv and ΔVv or ΔTv (both $r<0.3$, Figure 5C and 5D). Moreover, the potential association between the TOT-induced ΔRv and ΔPv was also assayed; and the ΔRv displayed a strong correlation with the ΔPv ($r>0.7$, Figure 5E). Together, these results indicate the TOT-enhanced Apv was accompanied by a syncytial change of Rv and Pv.

4. DISCUSSION

Main Findings

In contrast to studies investigating the urine storage,[24] this study explored if the voiding function adapts in response to the TOT by specifically focusing on the thermodynamic efficacy of the bladder. Our results reveal the word performed by the bladder was increased post-operatively; that could be attributed to that bladder develops an elevated pressure gradient in response to the TOT-enhanced outlet resistance during urine emission.

Our conclusion is based on lines of evidence. First, in consistent with studies showing TOT adds-on outlet resistance during storage to restore adequate continence,[12,25] our data demonstrated TOT post-operatively increased the Rv (mean resistance) during voiding. While no change was evidenced in the Vv (voided volume) or Tv (voiding time), Pv (mean voiding pressure) was elevated post-operatively in accompanied by the Rv increment. Considering the Rv was defined by the Pv divided by the Fv (mean voiding flow; Rv=Pv/Fv), and the Fv was further calculated as the Vv over the Tv (Fv=Vv/Tv); the relationship between the Rv, Vv, and Tv can be described as Rv=Pv/[Vv/Tv]. Based on this equation, unchanged Vv and Tv means the TOT-increased Rv is accompanied by a corresponding Pv elevation. Since TOT is well-accepted to add-on outlet resistance,[12,25] these data imply bladder develops an elevated voiding pressure in response to the TOT-increased resistance.

Moreover, though the sample size is not very large, the TOT-increased Apv statistically correlated with the changes of Rv and Pv (ΔRv and ΔPv, respectively) but rather than that of Vv (ΔVv) or Tv (ΔTv), indicating the TOT-enhanced thermodynamic efficacy is ΔRv and ΔPv dependent. Notably, when examining the relationship between the TOT-induced ΔRv and ΔPv, the ΔRv was highly correlated with the ΔPv. Considering the above data showing bladder develops an elevated voiding pressure in response to the TOT-increased resistance, these findings together imply that the enhanced Apv during voiding is resulted from the ΔRv-associated ΔPv, i.e., the enhanced thermodynamic efficacy during voiding is resulted from the elevated bladder pressure in response to the TOT-increased outlet resistance.

This proposal is further supported by the PVA showing that instead of the left, right, and bottom boundaries, the upper bolder of the loop trajectory representing the pressure during the emission was markedly shifted upward post-operatively; and thereby increased the Apv. For the Pv was the mean bladder pressure during urine emission, this results imply the increased Apv is attributed to an elevated Pv. Collectively, these several lines of evidence reveal that after the TOT, the bladder compensatory develops an elevated pressure during the voiding to overcome the enhanced outlet resistance that as a result to increase Apv.

We suggest that before TOT, the bladder of SUI patients fail to develop a sufficient pressure gradient not only because the increment of bladder pressure results in leakage during urine storage but also it possibly causes premature urine flow that brings about an early pressure decline during voiding.[26] Whereas, not restrictively to the storage, TOT-increased outlet resistance also prevents urine leakage during the early voiding that allows the bladder to develop an acceptable pressure gradient thereby ensures an adequate driving force for the urine flow during the whole voiding period.

An issue need to be concerned about is "Dose the elevated pressure is sufficient to overcome the TOT-enhanced outlet resistance during voiding?". Our data reveal TOT affected neither Vv nor Tv post-operatively, indicating, at least not inferior to the pre-operative condition, the bladder is capable to void an acceptable urine volume within a satisfactory time period. Nevertheless, for we measured urodynamic parameters short after TOT, if the bladder is able to maintain sufficient contractility and thereby persistently develops adequate pressure gradient to overcome the everlasting resistance increment needs longer following-up.

Interpretation

Patients in this study displayed an unchanged Vv after TOT. Because the Vv was the difference between the pre-emptied volume and maximal bladder capacity, this result implies an un-modified volume threshold triggering/initiating a voiding, i.e., our TOT protocol exhibits little effect on the sensory afferents, namely the pelvic and the hypogastric nerves,[27] and integration centers regulating voiding activity. Moreover, rather than the pudendal nerve innervating the urethra, the motor impulse provoking bladder contractions is also mainly transmitted by the pelvic and the hypogastric nerves.[27] We thereby suggest our TOT procedure exhibits trivial damage on the afferent/efferent pathways and the centers mediating voiding activity. Thereby, the post-operative effects in this study could be attributed to the biomechanical modifications occurring in the bladder itself.

We propose two possible causes could underlie the TOT-associated Pv increment. First, below the failure threshold, detrusor could adapt itself to an inotropic situation following enhanced outlet resistance.[28] Alternatively, the bladder is inherently to develop higher tension to the enhanced outlet resistance for its length-tension relationship is distinctive and relatively linear,[29] nevertheless, the precise mechanisms wait for final proof

Strengths

In accompanied by the well-accepted cystometry, this study for the first time establishes the PVA of voiding cycles in human subjects. Stepwise analysis of the thermodynamic processes reveals that during the filling (F; Figure 6A); accumulating fluid gradually increases bladder volume with a slightly but progressively elevated baseline pressure; thereby an amount of potential energy represented by the area under the trajectory along the volume change is stored in the bladder.[30]Next, in the isovolumic contraction (IVC; Figure 6B), the bladder contracts without fluid elimination. For there is no shortening in the detrusor, the bladder performs no mechanical work; instead, it gains potential energy caused by contraction-increased stiffness.[31] In the subsequent emission (E; Figure 6C), the bladder performs a mechanical work characterized by the integration of the trajectory along the volume change to repulse fluid.[30] Finally, the bladder isovolumically relaxes without fluid elimination (IVR; Figure 6D). For the detrusor length remains unchanged, the bladder gains no mechanical work. Nevertheless, the potential energy of the bladder is reduced by the relaxation-decreased stiffness.[31]

Despite this model obviously neglects the kinetic energy of fluid moving and the friction energy between fluid and the bladder, we suggest the trajectory-enclosed area coarsely quantifies a simplified but neat mechanical work performed by the bladder in a voiding cycle (net; Figure 6E);[30] and in accompanied with a cystometry assaying time-domain events, an additional PVA which represents the voiding work, will benefit to clinicians because lasting increased work loading could be a risk factors causing un-compensatory bladder functions.[17]

Limitations

This study has inherent limitation due to its retrospective design; and the sample size is relatively small. Moreover, for a significant percentage of patient experiences voiding dysfunctions at 12 months after TOT,[14] a longer following-up is needed to confirm the lasting benefit of TOT.

Conclusion

Collectively our results reveal TOT post-operatively enhanced the thermodynamic efficacy of the bladder; that is attributed to that bladder develops an elevated pressure gradient in response to the TOT-enhanced outlet resistance during urine emission.

Disclosure of interests

None declared.

Contribution to authorship

HH L and TB L: design study. HHL, TH Su, and JJ Lee: collect data. HH L and HY P: draft the manuscript. CY L, HY P, and MC H: analyze data, statistical analysis. TB L: finalize the manuscript.

Details of ethic approval

This study was registered in ClinicalTrials.gov (NCT05255289); and all the protocols were reviewed and approved by the ethics committee of Mackay Memorial Hospital, Taipei, Taiwan, which waived the requirement for informed consent (20MMHIS410e; 2021/03/08).

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Data availability statement

The data that support the findings of this study are available from the corresponding author, upon reasonable request.

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LEGENDS

FIGURE 1. Pressure-flow study and derived voiding parameters.

Representative cystometry tracings showing the vesical pressure (Pves), abdominal pressure (Pabd), detrusor pressure (Pdet), urethral flow (Flow), voided volume (Vvod), infused volume (Vinf), and intra-vesical volume (Vive). Although coughs (arrows) and Valsalva maneuvers (triangles) induce marked fluctuations in the Pves and Pabd, they exhibit trivial effect on the Pdet. The Pdet, Flow, Vvod, Vinf, and Vive marked by the red bar at the bottom are displayed using a faster time-base below. **(B)** Derived voiding parameters including the mean voiding pressure (Pv), the voided volume (Vv), and the voiding time (Tv).

FIGURE 2. Pressure-flow/-volume analyses of a voiding.

(A) A representative cystometry of a SUI patient. Arrows on the top indicate coughs. Pves: vesical pressure, Pabd: abdominal pressure, Pdet: detrusor pressure, Flow: urethral flow, Vvod: voided volume, Vinf: infused volume, and Vive: intra-vesical volume. **(B)** A pressure-volume analysis established by plotting the Pdet against Vive. The trajectory of pressure-volume data moves counterclockwise and shapes an enclosed loop representing a voiding cycle. Four phases are identified in the pressure-volume loop, namely (1) Filling (F), (2) Iso-volumic contraction (IVC), (3) Emission (E), and (4) Iso-volumic relaxation (IVR). Although coughs induce marked fluctuations in the vesical and abdominal pressure in the cystometry, they exhibit trivial influence on the pressure-volume trajectory.

FIGURE 3. Pressure-flow/-volume analyses in response to the TOT surgery.

(A) and (B) Representative cystometry of a SUI patient measured pre- and post-operatively (PRE and POST, respectively). Pves: vesical pressure, Pabd: abdominal pressure, Pdet: detrusor pressure, Flow: urethral flow, Vvod: voided volume, Vinf: infused volume, and Vive: intra-vesical volume. **(C) and (D)** Pressure-volume analyses measured before and after the TOT surgery, respectively. **(E)**The loop-enclosed area (Apv) of each SUI patient measured pre- and post-operatively. **(F)** Summarized Apv of SUI patients before and after the TOT surgery (** $p<0.01$ vs. PRE; N=26).

FIGURE 4. Individual and summarized data of voiding parameters in response to the TOT surgery.

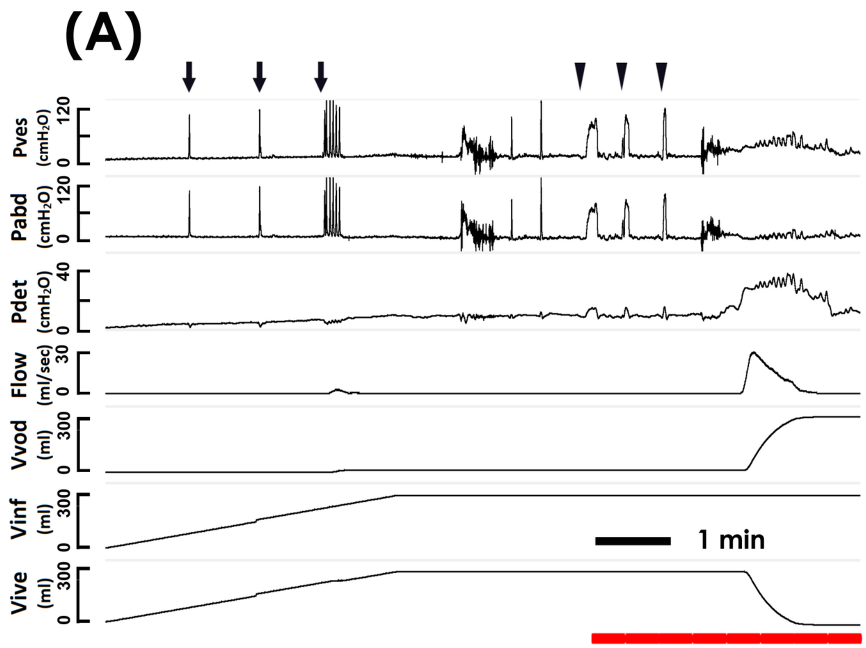
(A)-(D) Individual (left) and summarized (right) data of the mean voiding resistance (Rv), mean voiding pressure (Pv), voided volume (Vv), and voiding time (Tv), respectively. (** $p<0.01$, NS $p>0.05$ vs. PRE; N=26).

FIGURE 5. Correlation analyses of the TOT-associated change in Apv and changes in voiding parameters.

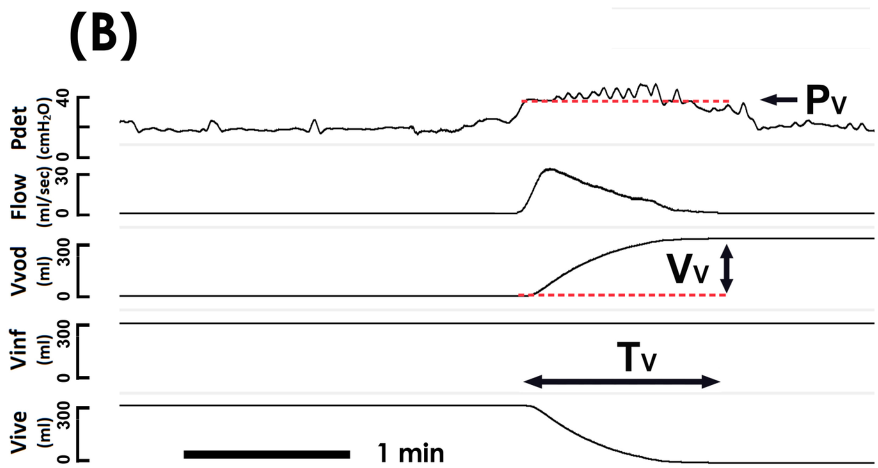
(A)-(D) Correlation analyses of the TOT-associated change in the loop-enclosed area (ΔApv) and changes in the mean voiding resistance (ΔRv; $r>0.5$, N=26), the mean voiding pressure (ΔPv; $r>0.5$, N=26), the voided volume (ΔVv; $r<0.3$, N=26), and the voiding time (ΔTv; $r<0.3$, N=26), respectively.**(E)** Correlation analysis of the ΔRv and ΔPv ($r>0.7$, N=26).

FIGURE 6. Thermodynamic processes in a pressure-volume loop of a voiding.

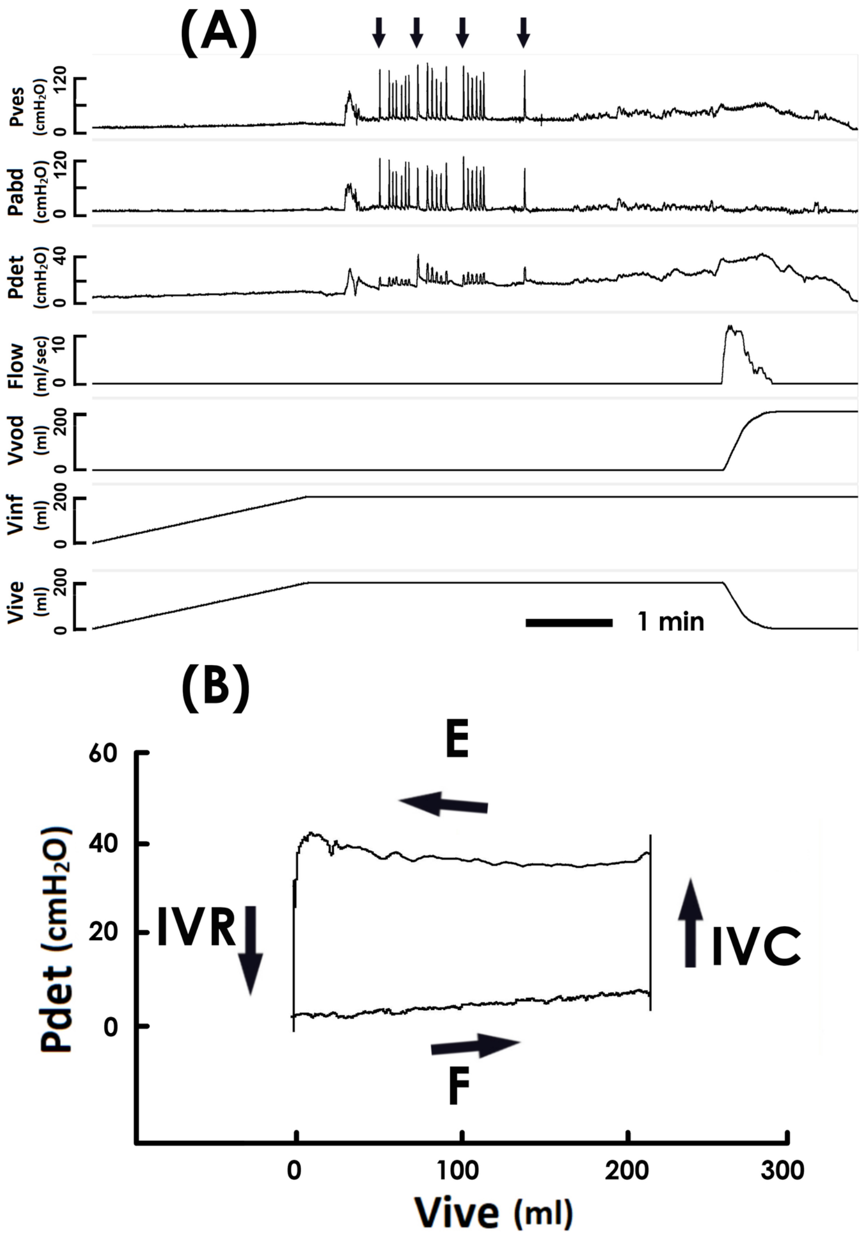
During the filling (F), an amount of potential energy represented by the area under the trajectory along the volume change is stored, i.e., the output work is negative (-; red). **(B)** In the isovolumic contraction (IVC), the bladder performs no mechanical work, i.e., the output work is zero (0). **(C)** In the emission (E), the bladder performs a mechanical work characterized by the integration of the trajectory along this stage to repulse fluid, i.e., the output work is positive (+; green). **(D)** In the isovolumic relaxation (IVR), the bladder gains no mechanical work, i.e., the work output is zero (0). **(E)** The net work done in the entire cyclic process is given by the area enclosed by the loop trajectory of a voiding cycle (net; green).



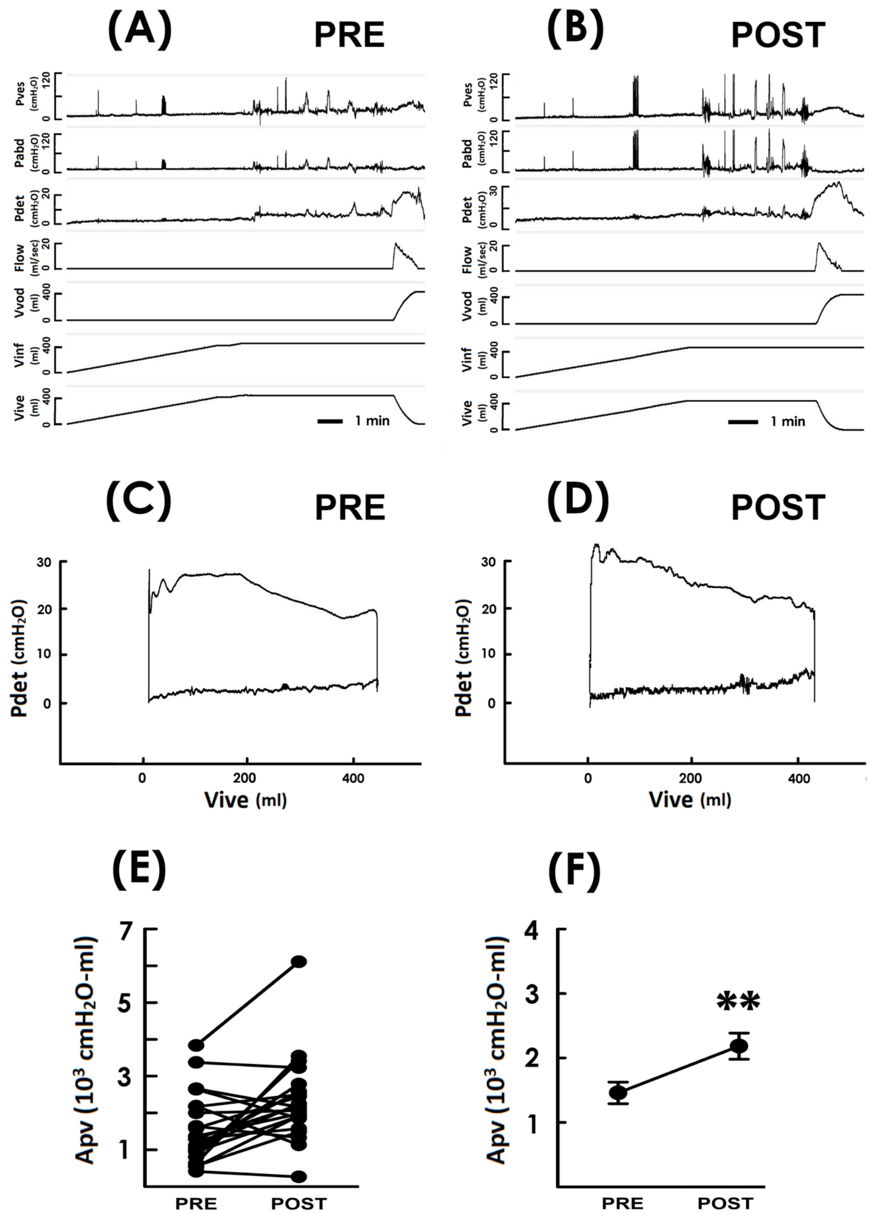
(A)
Pves (cmH2O)
0
60
120
Pabd (cmH2O)
0
60
120
Pdet (cmH2O)
0
20
40
Flow (ml/sec)
0
15
30
Vvod (ml)
0
150
300
Vinf (ml)
0
150
300
1 min
Vive (ml)
0
150
300



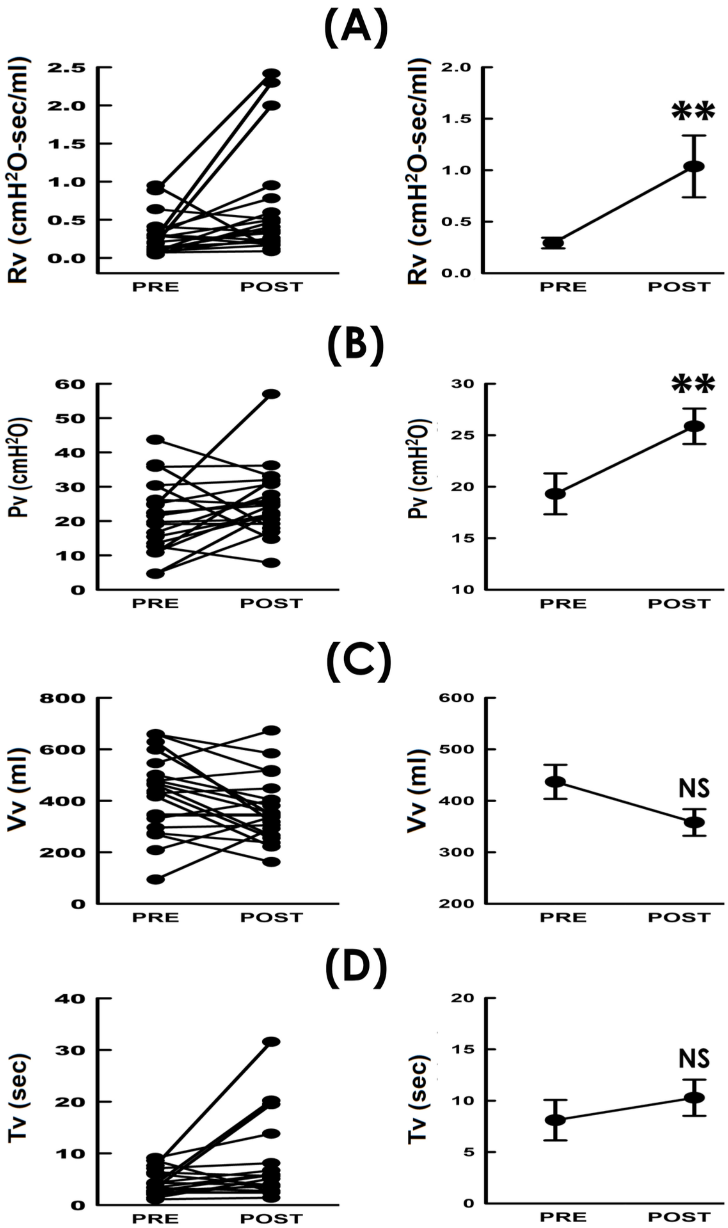
(B)
Pdet (cmH2O)
0
20
40
PV
Flow (ml/sec)
0
15
30
Vvod (ml)
0
150
300
VV
Vinf (ml)
0
150
300
TV
Vive (ml)
0
150
300
1 min

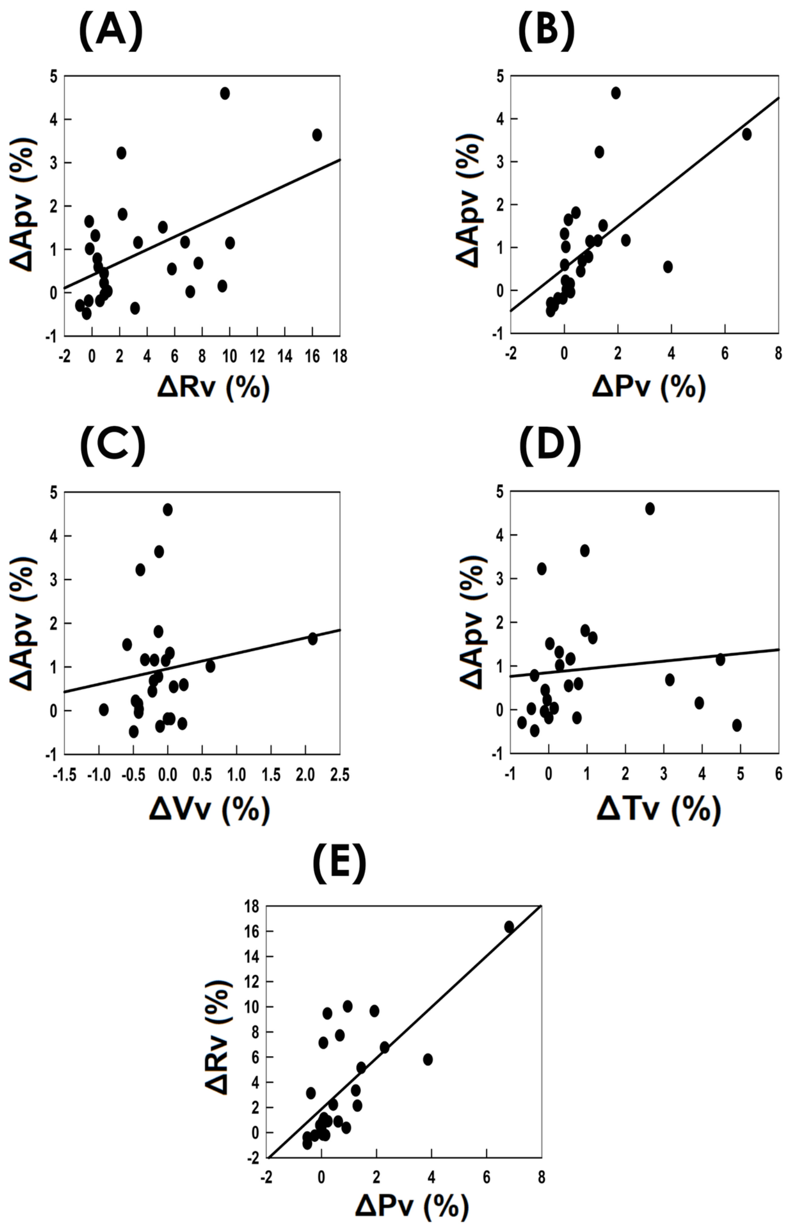


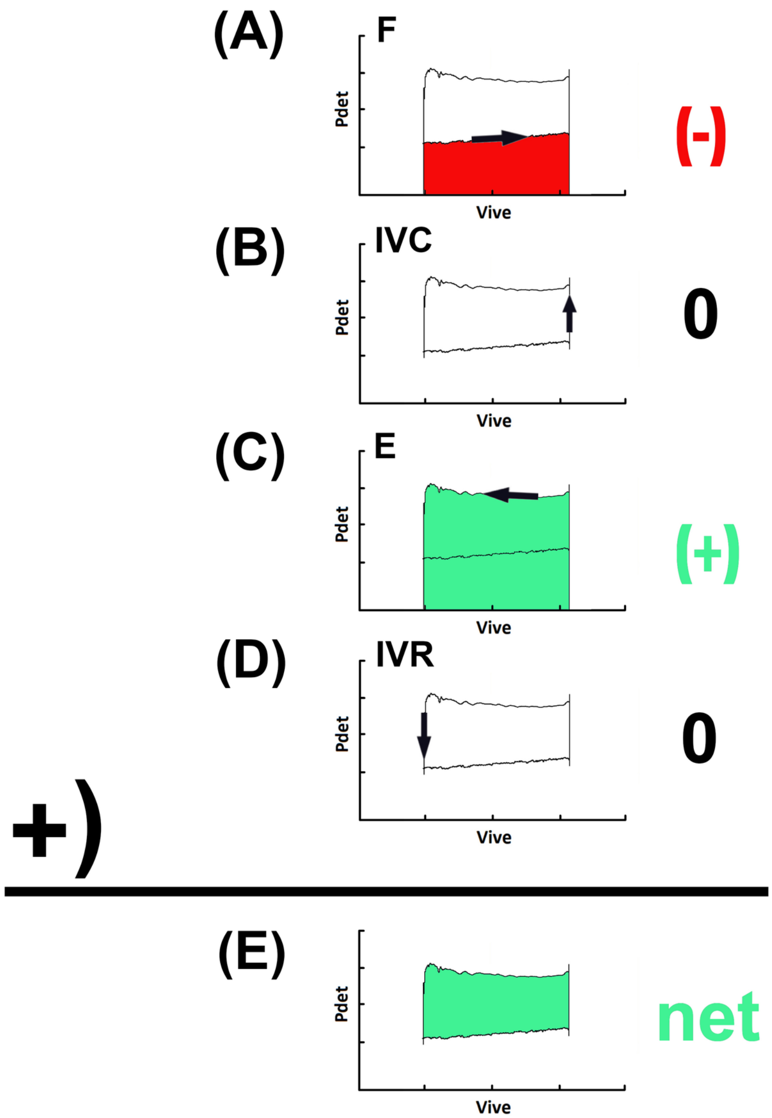
(A)
Pves (cmH2O)
120
0
Pabd (cmH2O)
120
0
Pdet (cmH2O)
40
0
Flow (ml/sec)
10
0
Vvod (ml)
200
0
Vinf (ml)
200
0
Vive (ml)
200
0
1 min
(B)
Pdet (cmH2O)
60
40
20
0
E
F
IVR
IVC
0
100
200
300
Vive (ml)



(A)
PRE
(B)
POST
Pves (cmH2O)
Pabd (cmH2O)
Pdet (cmH2O)
Flow (ml/sec)
Vvod (ml)
Vinf (ml)
Vive (ml)
1 min
(C)
PRE
(D)
POST
Pdet (cmH2O)
Vive (ml)
(E)
(F)
Apv (10³ cmH2O-ml)
PRE
POST
**


(A)
Rv (cmH2O-sec/ml)
2.5
2.0
1.5
1.0
0.5
0.0
PRE
POST
**
(B)
Pv (cmH2O)
60
50
40
30
20
10
0
25
15
NS
(C)
Vv (ml)
800
600
400
200
500
300
(D)
Tv (sec)
5


(A)
ΔApv (%)
ΔRv (%)
(B)
ΔApv (%)
ΔPv (%)
(C)
ΔApv (%)
ΔVv (%)
(D)
ΔApv (%)
ΔTv (%)
(E)
ΔRv (%)
ΔPv (%)


(A)
F
Pdet
Vive
(-)
(B)
IVC
Pdet
Vive
0
(C)
E
Pdet
Vive
(+)
(D)
IVR
Pdet
Vive
0
+)
(E)
Pdet
Vive
net