



# Prevalence and urodynamic characteristics of detrusor overactivity with impaired contractility in the community-dwelling elderly with non-neurogenic lower urinary tract symptoms: Is it from a single or two independent bladder dysfunctions?

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**Purpose:** To identify the prevalence of detrusor overactivity with impaired contractility (DOIC) in the community-dwelling elderly and explore whether it is from a single or two independent bladder dysfunctions.

**Materials and Methods:** Based on a 10-year urodynamic database of the SEOUL Study Group, elderly patients who met inclusion criteria were selected. Bladder sensation, capacity, and compliance were designated as evaluation elements for storage function, and free maximal flow rate ( $Q_{max}$ ) and post void residual volume, detrusor pressure at maximal flow ( $P_{detQmax}$ ), and bladder voiding efficiency for voiding function.

**Results:** The prevalence rate of DOIC was 18.8% and 5.5% among 2,571 men and 688 women, respectively, and increased significantly with age. In men, patients with DOIC showed no differences in storage parameters and significantly lower free  $Q_{max}$  and  $P_{detQmax}$  among voiding parameters, compared to those with detrusor overactivity (DO) only. Compared to men with detrusor underactivity (DU) only, those with DOIC had worse parameters in the majority of storage and voiding functions. In women, most of the storage and voiding functions were worse in patients with DOIC than in those with DO only. On the other hand, women with DU showed lower  $P_{detQmax}$  and worse voiding functions than those with DOIC, although some parameters did not reach statistical significance.

**Conclusions:** It seems that DOIC is developed from a coincidental combination of two independent DO and DU in men. In contrast, DOIC is likely to be an intermediate step during the process of progression from DO to DU in women.

**Keywords:** Detrusor underactivity; Elderly; Overactive detrusor; Urodynamics

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## INTRODUCTION

Detrusor hyperactivity with impaired contractility (DHIC) is a condition, as its name indicates, in which detrusor overactivity (DO) is combined with impaired detrusor contractile function. DHIC was first introduced to the clinical practice in 1987 [1], recently, it has been stated as a term 'detrusor overactivity with impaired contractility (DOIC)'. For convenience, this term will be used in the manuscript, although 'DO with DU (detrusor underactivity)' would be using standard terms. In real practice, the symptoms of DOIC are not infrequently encountered, especially in the elderly patients, and it is often difficult to expect satisfactory treatment outcome due to the complexity of the disease itself and the heterogeneity of the patients [2].

The specific definition and diagnostic criteria for DOIC have not been standardized yet, although it has been over 30 years since it was first announced. Moreover, its prevalence and clinical characteristics have not yet been clearly identified in the community-dwelling elderly with non-neurogenic lower urinary tract symptoms (LUTS) [3-7] and the debate on the underlying etiology and pathophysiology continues over whether DOIC is developed from a single pathophysiological mechanism or merely reflects the coexistence of independent DO and DU [4,8,9].

Using a large urodynamic database, we aimed to identify the prevalence of DOIC in the community-dwelling elderly with non-neurogenic LUTS and compare urodynamic characteristics of DOIC with those of DO and DU in order to provide background information regarding whether DOIC is developed by a single pathophysiological mechanism or simply represents the complex phenomenon of two independent bladder dysfunctions such as DO and DU. To the best of

our knowledge, the present study is the first to explore the urodynamic association between the elderly with DOIC, DO, and DU.

## MATERIALS AND METHODS

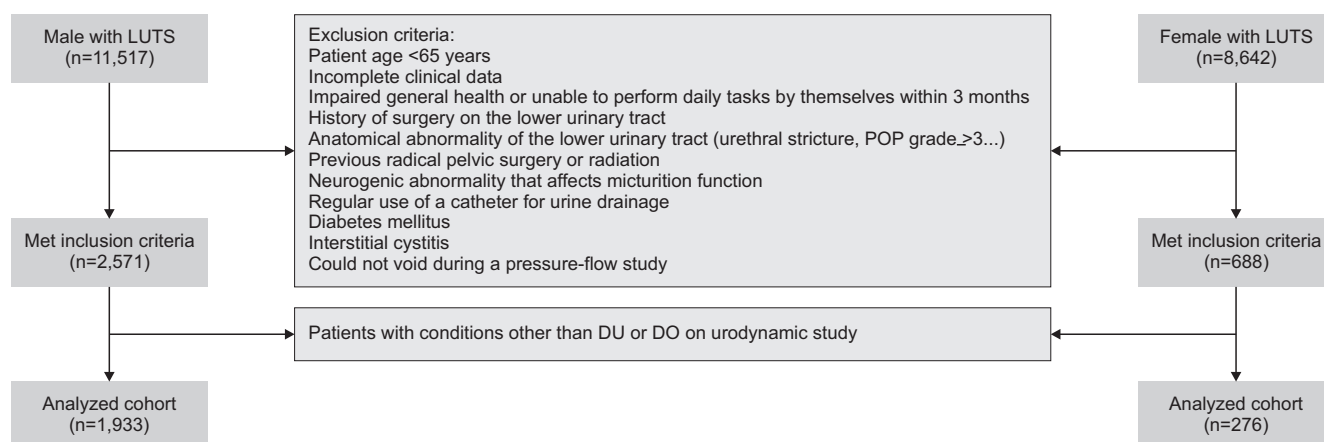
### 1. Patients and clinical data

Using the large-scale consecutive urodynamic database registry from SEOUL (Seoul National University-Experts-Of-Urodynamics-Leading) Study group of three referral centers, men and women cohorts with LUTS who received an urodynamic study between October 2004 and March 2014 was created. The Institutional Review Boards of the Seoul National University Bundang Hospital (approval number: B-2010/642-105) and the Seoul National University Hospital (approval number: 2011-082-1173) approved the research protocol based on the Declaration of Helsinki. All personal identifiers were eliminated from the database and all data were anonymously analyzed.

Fig. 1 depicts the cohort selection process for men and women patients from urodynamic database registry. After eliminating data of patients with the exclusion criteria that are depicted in Fig. 1, 2,571 men and 688 women were enrolled in the initial analyses for the prevalence. Finally, data of 1,933 men and 276 women who were proven to have urodynamic DO and/or DU were entered into the analyses regarding the urodynamic association between the patients with DOIC, DO only, and DU only.

### 2. Practice and urodynamic evaluation

As a routine practice, patients who present with LUTS were interviewed about the detailed history of LUTS/medications and underwent physical examination, free uroflow-



**Fig. 1.** Flow chart of cohort selection process for male and female patients from urodynamic database registry. LUTS, lower urinary tract symptoms; POP, pelvic organ prolapse; DU, detrusor underactivity; DO, detrusor overactivity.

metry and post-void residual (PVR) measurement. For symptom evaluation, they documented an International Prostate Symptom Score, Overactive Bladder Symptom Score, and a 3-day frequency-volume chart. A free uroflowmetry (DABA; Endo tech, Seongnam, Korea) along with a measurement of PVR volume (BladderScan™ BVI-3000; Diagnostic Ultrasound, Bothell, WA, USA) were performed prior to urodynamic evaluation. The result with a higher maximum flow rate ( $Q_{max}$ ) was selected from two sets of free uroflowmetry with a voided volume  $\geq 150$  mL [10]. Data of free uroflowmetry with a voided volume below 150 mL were not included in the present study.

Urodynamic examinations were in accordance with the guidelines of the International Continence Society (ICS) [11] and a multichannel urodynamic measurement (UD-2000; Medical Measurement Systems, Enschede, The Netherlands) was carried out. The medications that could possibly affect voiding function were discontinued for at least 3 days before the examination.

**3. Urodynamic definitions of DOIC, DO, and DU**

DO was considered positive when spontaneous or provoked involuntary detrusor contraction was observed in the filling cystometry regardless of urine leakage and size of amplitude, as indicated by the ICS [11]. With regard to the definition of DU, different urodynamic criteria were used between men and women. Previously, the authors compared several contemporary urodynamic criteria for diagnosing DU, and confirmed that four different urodynamic criteria for men showed considerable variation in the diagnosis of DU [12]. On the other hand, it was identified that the combination of detrusor pressure at maximum flow rate ( $P_{detQ_{max}} < 30$  cmH<sub>2</sub>O and pressure-flow study (PFS)  $Q_{max} < 10$  mL/s [5], and the combination of  $P_{detQ_{max}} < 20$  cmH<sub>2</sub>O and PFS  $Q_{max} < 15$  mL/s and bladder voiding efficiency (BVE; voided volume/[voided volume+PVR volume]×100%)<90% and absence of clinical obstruction [13] showed the significant

concordance and could be appropriately applied to clinical practice when diagnosing DU in women [12]. Based on those results, we defined DU as a formulated bladder contractility index ( $BCI = P_{detQ_{max}} + 5 Q_{max} < 100$  [14] for men because it had been widely used for men patients. For women patients, the combination of  $P_{detQ_{max}} < 30$  cmH<sub>2</sub>O and PFS  $Q_{max} < 10$  mL/s [5] was selected for the diagnostic criteria of DU. DOIC was defined when DO was observed in a filling cystometry and each criteria of DU was proven for men and women in a PFS. For the diagnosis of bladder outlet obstruction (BOO), the BOO Index [14] and the Blaivas and Groutz nomogram [15] were used in men and women patients, respectively.

**4. Statistical analysis**

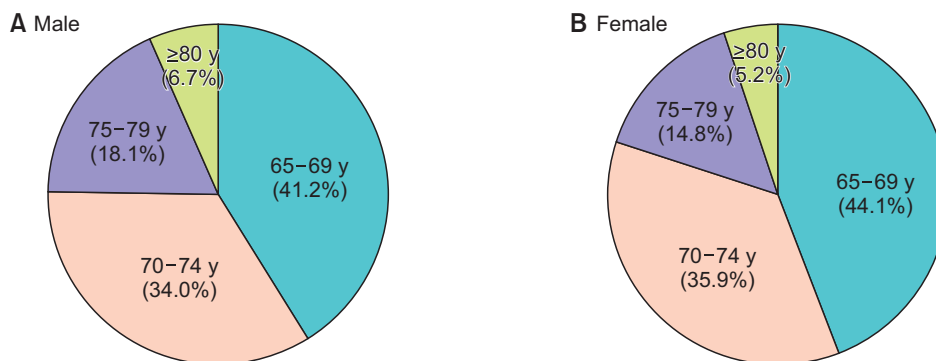
The collected data are presented as mean±standard deviation or as a percentage. The linear by linear association analysis or the chi-squared test for categorical variables and the Student’s t-test for continuous variables were used to identify the significance between groups.

The prevalence rate of DOIC was identified and compared according to the patient age and date of study. The urodynamic characteristics of the elderly with DOIC were compared with those with DO only or DU only. Bladder sensation, capacity, and compliance were designated as evaluation elements for storage function, and free  $Q_{max}$  and PVR volume,  $P_{detQ_{max}}$  and BVE for voiding function.

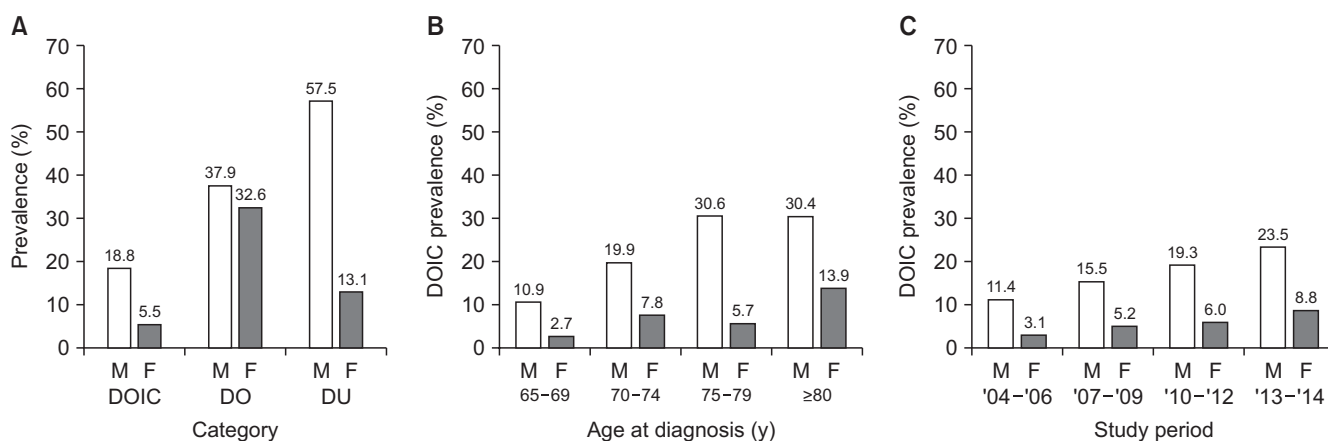
All statistical analyses were conducted with SPSS software package version 20.0 (IBM Corp., Armonk, NY, USA) and MedCalc version 9.6 (MedCalc, Mariakerke, Belgium) and a 2-tailed p-value <0.05 was determined to indicate statistical significance.

**RESULTS**

Of the 2,571 men and 688 women who met inclusion criteria, the distribution of patient age was not statistically different between both sex (Fig. 2). Over 50% of patients were



**Fig. 2.** Distribution of patient age in male and female patients who meet the inclusion criteria. (A) In male patients, 52.1% of patients are in their 70s and 6.7% are aged 80 or over. (B) In female patients, 50.7% of patients are in their 70s and 5.2% are aged 80 or over. The distribution of patient age is not statistically different between both sex.



**Fig. 3.** Prevalence of DOIC according to the patient age and study period in male and female patients. (A) Prevalence of each urodynamic category in male and female patients. (B) Prevalence of DOIC by age group in male and female patients. The prevalence increases with age in both sex ( $p < 0.001$  and  $0.005$ ). (C) Prevalence of DOIC by study period in male and female patients. The prevalence rate increases significantly in male ( $p < 0.001$ ) and tends to increase with study period in female. DOIC, detrusor overactivity with impaired contractility; DO, detrusor overactivity; DU, detrusor underactivity; M, male; F, female.

**Table 1.** Comparisons of patient age and urodynamic characteristics between DOIC, DO only, and DU only groups in male patients

Parameter	DOIC		DO only		DU only	
	Value	Value	Value	p-value <sup>a</sup>	Value	p-value <sup>a</sup>
Age (y)	73.4±5.0	71.8±4.8		<0.001	71.0±4.6	<0.001
Free $Q_{max}$ (mL/s)	8.0±5.1	9.9±6.5		<0.001	8.6±5.0	0.060
Free PVR (mL)	67±97	67±83		0.995	58±94	0.092
First sensation of bladder filling (mL)	167±85	171±82		0.467	204±88	<0.001
First desire to void (mL)	229±107	233±100		0.531	281±103	<0.001
Strong desire to void (mL)	291±125	292±106		0.875	352±106	<0.001
Maximum cystometric capacity (mL)	293±133	304±117		0.162	389±108	<0.001
Poor compliance ( $\leq 20$ mL/cmH <sub>2</sub> O)	15.4	13.5		0.482	5.4	<0.001
$P_{detQ_{max}}$ (cmH <sub>2</sub> O)	46.0±14.9	73.9±28.8		<0.001	42.5±13.4	<0.001
Bladder voiding efficiency (%)	68.5±23.6	69.6±22.6		0.511	76.6±21.6	<0.001

Values are presented as mean±standard deviation or percentage only.

DOIC, detrusor overactivity with impaired contractility; DO, detrusor overactivity; DU, detrusor underactivity;  $Q_{max}$ , maximum flow rate; PVR, post-void residual;  $P_{detQ_{max}}$ , detrusor pressure at maximum flow rate.

<sup>a</sup>:p-value vs. DOIC group.

in their 70s, and 6.7% and 5.2% were aged 80 or over in men and women patients, respectively.

DOIC was identified at 18.8% and 5.5%, DO only at 37.9% and 32.6%, and DU only at 57.5% and 13.1% respectively in men and women population (Fig. 3A). When age was divided into groups of 5 years from 65 years in order of age, prevalence rate of DOIC was 10.9%, 19.9%, 30.6%, 30.4% in men and 2.7%, 7.8%, 5.7%, 13.9% in women, showing a significant increase with age ( $p < 0.001$  and  $0.005$ ; Fig. 3B). The prevalence rate has also increased significantly in men ( $p < 0.001$ ) and tended to increase in women in recent years, depending on the calendar year in which the urodynamic evaluation was conducted (Fig. 3C).

After excluding the patients who had the urodynamic

conditions other than DU and/or DO, in which BOO accounted for 20.6%, followed by normal or inconclusive urodynamic diagnosis, urodynamic associations between groups were analyzed among 1,933 men and 276 women. In men, patients with DOIC showed no differences in storage parameters and significantly lower free  $Q_{max}$  and PFS  $P_{detQ_{max}}$  among voiding parameters, compared to those with DO only (Table 1). Compared to men with DU only, those with DOIC had worse parameters in the majority of storage and voiding functions (Table 1). Free PVR volume did not reflect the characteristics of either of the three conditions.

In women, most of the storage and voiding functions were worse in patients with DOIC than in those with DO only (Table 2). On the other hand, women with DU only

**Table 2.** Comparisons of patient age and urodynamic characteristics between DOIC, DO only, and DU only groups in female patients

Parameter	DOIC	DO only		DU only	
	Value	Value	p-value <sup>a</sup>	Value	p-value <sup>a</sup>
Age (y)	72.8±4.7	71.9±5.2	0.286	71.4±4.7	0.164
Free Q <sub>max</sub> (mL/s)	10.2±8.4	15.3±9.3	0.006	8.5±6.4	0.334
Free PVR (mL)	49±82	41±64	0.537	94±153	0.096
First sensation of bladder filling (mL)	128±68	165±77	0.008	209±117	<0.001
First desire to void (mL)	191±117	228±101	0.076	274±110	0.003
Strong desire to void (mL)	216±119	283±118	0.005	328±117	<0.001
Maximum cystometric capacity (mL)	251±144	326±126	0.001	366±134	<0.001
Poor compliance (≤20 mL/cmH <sub>2</sub> O)	11.1	8.4	0.667	19.0	0.379
P <sub>detQmax</sub> (cmH <sub>2</sub> O)	23.1±12.4	30.4±29.0	0.131	17.3±6.6	0.010
Bladder voiding efficiency (%)	52.2±39.8	72.3±29.8	0.005	54.1±41.7	0.829

Values are presented as mean±standard deviation or percentage only.

DOIC, detrusor overactivity with impaired contractility; DO, detrusor overactivity; Q<sub>max</sub>, maximum flow rate; PVR, post-void residual; P<sub>detQmax</sub>, detrusor pressure at maximum flow rate.

<sup>a</sup>:p-value vs. DOIC group.

showed lower P<sub>detQmax</sub> and worse voiding functions than those with DOIC, although some parameters did not reach statistical significance (Table 2). Free PVR volume did not reflect the characteristics of either of the three conditions in women patients either.

## DISCUSSION

The specific definition and diagnostic criteria for DOIC have not been standardized, and the prevalence and clinical characteristics have not yet been clearly identified in the community-dwelling elderly with non-neurogenic LUTS, although it has been over 30 years since it was first announced. Moreover, DOIC presents a unique clinical dilemma in which therapeutic options targeting one component of the disease may potentially aggravate the other [16].

In the present study, we aimed to identify the prevalence of DOIC in the community-dwelling elderly with non-neurogenic LUTS and compare urodynamic characteristics between DOIC, DO only, and DU only. We think this approach in which the association of each condition is explored using urodynamic parameters may help investigate the possible pathophysiological mechanism of DOIC and lay a foundation for further research on DOIC.

In 1999, it was shown that 11% of 193 men with LUTS and without urodynamic obstruction had DOIC, and the prevalence increased up to 37% in men aged over 70 years and decreased just to 2% in those aged less than 70 [3]. A study by Yamamoto et al. [4] showed the DOIC prevalence at 10% to 18% in patients with various neurological diseases that possibly cause DOIC. In 2007, Abarbanel and Marcus [5] demonstrated that DOIC accounted for 18% of bladder

dysfunction in the elderly and was more commonly observed in men. The prevalence rate of DOIC was 31.7% in men and 6.1% in women. In 2010, Valentini et al. [17] showed that 16% of community-dwelling women with LUTS and aged over 80 years were found to have DOIC. More recently, Stav et al. [7] reported that out of 982 women who received urodynamic studies, 15.4 % had DOIC, and Yang et al. [18] demonstrated that of 1,914 women in which first-line medical treatment failed, 12.0% had DOIC.

Our previous study on the prevalence of DU in 1,179 patients aged over 65 years demonstrated that 40.2% of men and 13.3% of women were classified as having DU and 38.6% of men and 35.6% of women with DU also presented with DO [6]. In consequence, the prevalence of DOIC was calculated as 15.5% and 4.7% in men and women population, respectively. The present study had more population than previous study. As a result, the prevalence of DOIC was 18.8% and 5.5% in men and women population, respectively, and increased significantly with age in both sex. Especially, it exceeded 30% in men over 75 years old. These results are in concordance with our previous research [6]. There were some differences between our study and others in the prevalence rate of DOIC in women population. Although the reason for this finding might not be easily explained, each study adopted different definitions and criteria of DO and DU, possibly resulting in these differences. Thus, additional studies are needed to standardize the urodynamic criteria of DOIC. The prevalence rate of DOIC has increased significantly in men in recent years, and we identified that patient age increased statistically depending on the urodynamic study year, although the difference was small (data not shown). Therefore, the increase in DOIC prevalence in accordance with the

urodynamic study year may be attributed to the increase in the patient age in men population.

The etiology and pathophysiology of DOIC may be heterogeneous and not clearly understood. There are some proposed pathophysiologies of DOIC such as micro-cellular variations, ischemia-induced mechanism, and hormonal causes [2]. Micro-cellular variations [19,20] and ischemia [21] could potentially produce a condition in which the detrusor muscle may be both overactive and poorly contractile as observed in patients with DOIC. Hormonal deviations and deficiency of ovarian hormones may negatively affect the detrusor contractility in women late in life [22], although it has not been proven to induce ultrastructural changes associated with DO. In addition, aging is likely to play a considerable role in the development of DOIC [8].

So far we don't even know whether DOIC is developed from one common cause or from the concurrence of two unrelated bladder dysfunctions such as DO and DU. As DOIC has both two urodynamic components of DO and DU, this question receives attention and this study's approach may help investigate the possible pathophysiological mechanism of DOIC. DOIC may be developed by a coincidental combination of two independent bladder dysfunctions such as DO and DU. Another hypothesis is 'the progression of overactive bladder (OAB) to underactive bladder' in which chronic untreated or treatment refractory OAB may progress to DOIC and, finally, DU [9,23]. In this hypothesis, longstanding DO which presents frequent detrusor contraction, eventually, may cause the structural and functional detrusor changes following gradual accumulation of collagen, interstitial fibrosis, and severe trabeculation. In consequence, DU may develop in the final stage of this hypothesis and DOIC may be an intermediate step during the process of progression from DO to DU. To validate this hypothesis, we did not just use the patient age or disease prevalence, but we used the urodynamic features designated as storage function index and voiding function index. We tried to identify whether these function index have sequential relationship in the degree of deterioration among the patients with DOIC, DO only, or DU only.

According to the present findings, in men, it was identified that urodynamic features of DOIC were similar with those of DO only with regard to the storage function, but were worse than those of DO only regarding the voiding function. Compared to the urodynamic features of DU only, those of DOIC were more aggravated in the storage and voiding functions. Therefore, it seems that DOIC, DO only, and DU only have no sequential relationship when all these urodynamic conditions are arranged in the degree of dete-

rioration of both storage and voiding function index, when compared between groups. Instead, DOIC is likely to reflect the complex condition of two independent bladder dysfunctions such as DO and DU in men. Unlike in men patients, urodynamic features in women patients with DOIC were worse than those in patients with DO only in both storage and voiding functions, and urodynamic features of DU only deteriorated more than those of DOIC regarding the voiding function. Thus, with regard to the voiding function, there was the sequential relationship in the degree of deterioration of urodynamic parameters, in which urodynamic parameters of DOIC deteriorated more than those of DO only, and those of DU only was more aggravated than those of DOIC. It seems that DOIC is likely to be an intermediate step during the process of progression from DO to DU in women. If all these findings are put together, it may be cautiously suggested that, urodynamically, the association of DOIC with DO only and DU only is different between genders.

Several limitations of our study deserve mention. First, patient data of our study were based on the urodynamic database from three affiliated hospitals. These three hospitals have used a unified protocol for the evaluation of patients with LUTS and same urodynamic test format, and have already published the joint researches based on this database for many years. Therefore, there would be no problems with data quality while it was a multi-institutional study. However, the present findings referred to tertiary referral centers and most of study populations were referred for detailed evaluation of lower urinary tract function, thus resulting in selection bias. Second, we adopted BCI criteria as the determinant of diagnosis of DU in men as it had been widely used for men patients. However, BCI criteria tends to overestimate DU and has been criticized that it does not consider conceptually the coexistence of DU and BOO [24]. Previously, the authors studied the DU prevalence of each study. Each study adopted different definitions and criteria of DU in men and average age of the target population varied from study to study, resulting in the prevalence between 25% and 48% [25]. Recently, Gammie et al. [26] reported only 5.5% as the prevalence of DU among 4,618 men when very strict defining criteria was applied. Limitations on these variations can be overcome by the potential future definitions which will be standardized internationally. Third, we did not include the qualitative assessment of various urinary symptoms of each group into the analyses. In routine practice, we used validated questionnaires, but they could not be unified, in part, for the affiliated hospitals and the response rate was not high for a statistical analysis. However, it has not

been clearly identified that types of LUTS are significantly different between patients with and without DOIC [27], and the main purpose of the present study was to compare the urodynamic features of DOIC with those of DO only and DU only. Therefore, the lack of the qualitative assessment of LUTS would have little impact on our results. Finally, we used BOO Index and Blaivas and Groutz nomogram for the diagnosis of BOO in men and women, respectively. It has been suggested that results from these parameters might be overestimated or underestimated for the diagnosis of BOO [28,29]. In addition, Blaivas and Groutz nomogram for the diagnosis of women BOO may be problematic as it was derived from the mixture of free uroflowmetry and PFS. However, our study tried to focus on DOIC, therefore, such errors in BOO diagnosis may not have a significant impact on our findings.

Up to date, DOIC remains a poorly established and unclearly understood bladder dysfunction. Our findings cautiously suggest that the urodynamic association of DOIC with DO only and DU only is different between both sex. We hope our study will promote more researches on the pathophysiological process of DOIC in the future.

## CONCLUSIONS

The prevalence of DOIC in the community-dwelling elderly is not low and increases with age. Urodynamically, the association of DOIC with DO only and DU only may be different between genders. In men, it seems that DOIC is developed from a coincidental combination of two independent DO and DU. In contrast, DOIC is likely to be an intermediate step during the process of progression from DO to DU in women.

## CONFLICTS OF INTEREST

The authors have nothing to disclose.

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## AUTHORS' CONTRIBUTIONS

Research conception and design: Seong Jin Jeong and

Seung-June Oh. Data acquisition: Seong Jin Jeong, Minseung Lee, Sang Hun Song, Hakju Kim, and Seung-June Oh. Statistical analysis: Seong Jin Jeong and Sang Hun Song. Data analysis and interpretation: Seong Jin Jeong, Seung-June Oh, and Min Soo Choo. Drafting of the manuscript: Seong Jin Jeong. Critical revision of the manuscript: Min Soo Choo, Sung Yong Cho, and Seung-June Oh. Administrative, technical, or material support: Seong Jin Jeong. Supervision: Seong Jin Jeong and Seung-June Oh. Approval of the final manuscript: all authors.

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