



Evil Twin

Painful bladder syndrome and endometriosis
Not an unusual combination



Presenter

林威霖 醫師

CASE SHARING- clinical course





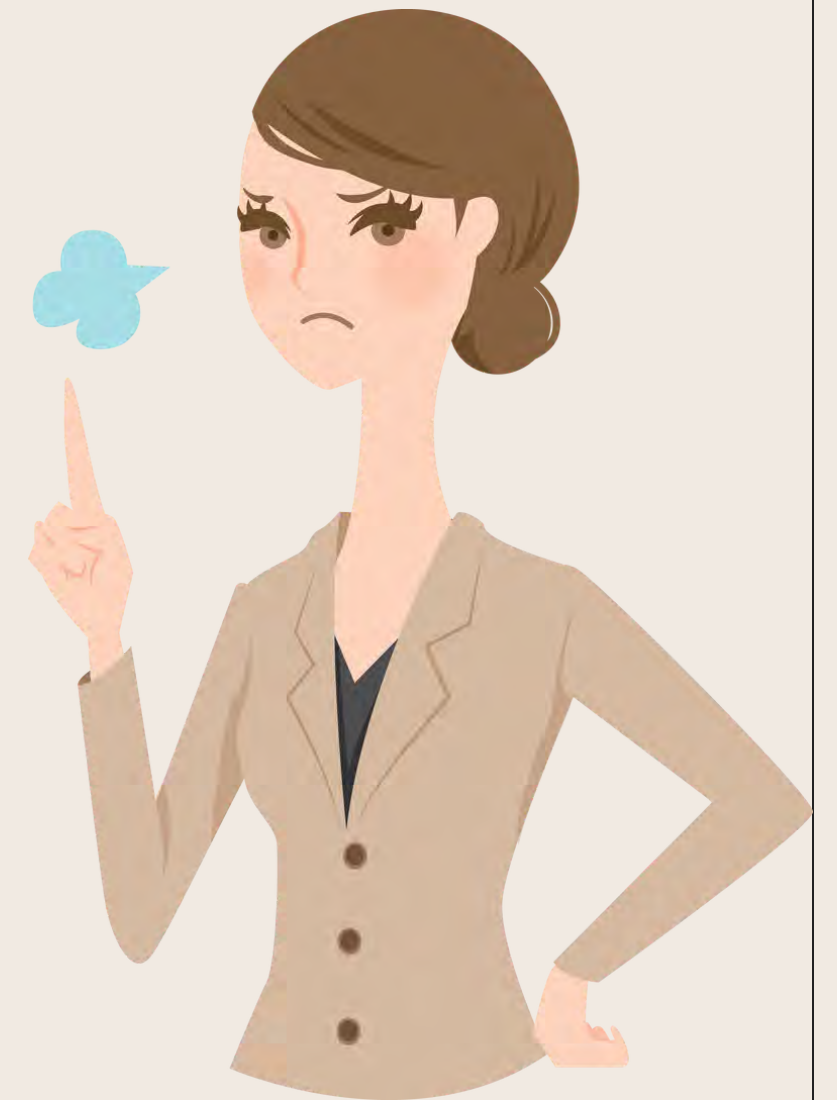
- **45 years old, G4P2SA2 (NSD)**
- **Menarche**
 - 13 years old
- **Menstruation**
 - Interval: 26-32 days
 - Duration: 5 days
 - Dysmenorrhea, VAS 7-8
- **Past history**
 - denied
- **Past surgical history**
 - denied
- **Allergy**
 - nil





Chief Complain -

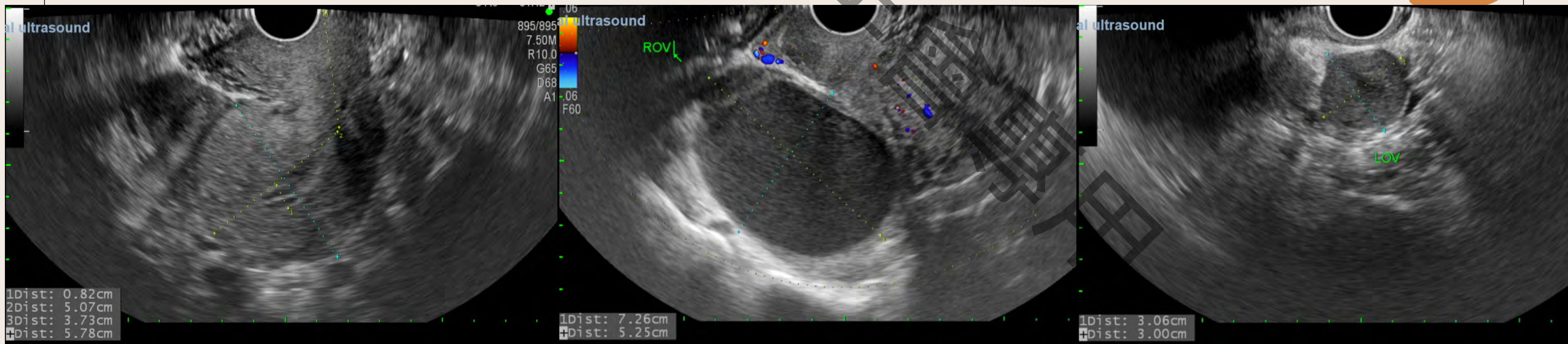
Intermittent **lower abdomen** and **pelvic distension** for more than **6** months





2021. 11. 08 - OPD

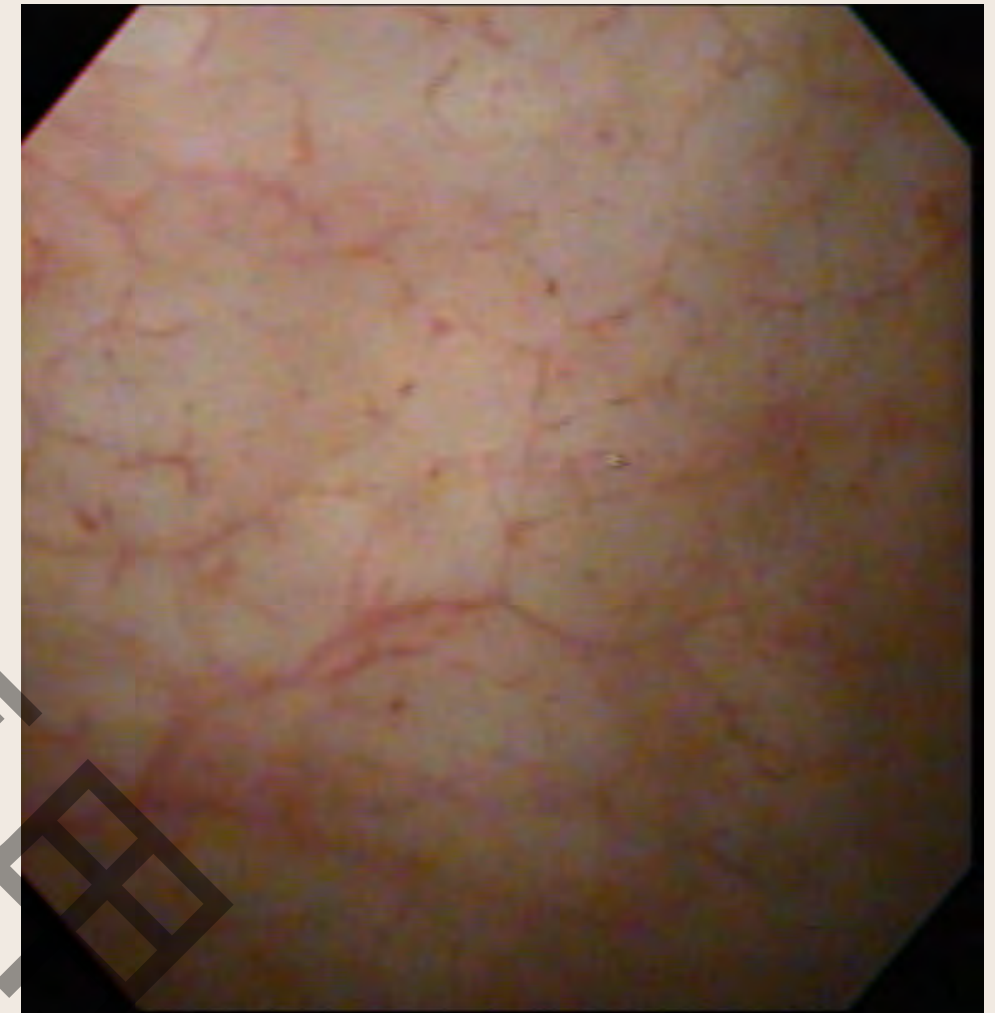
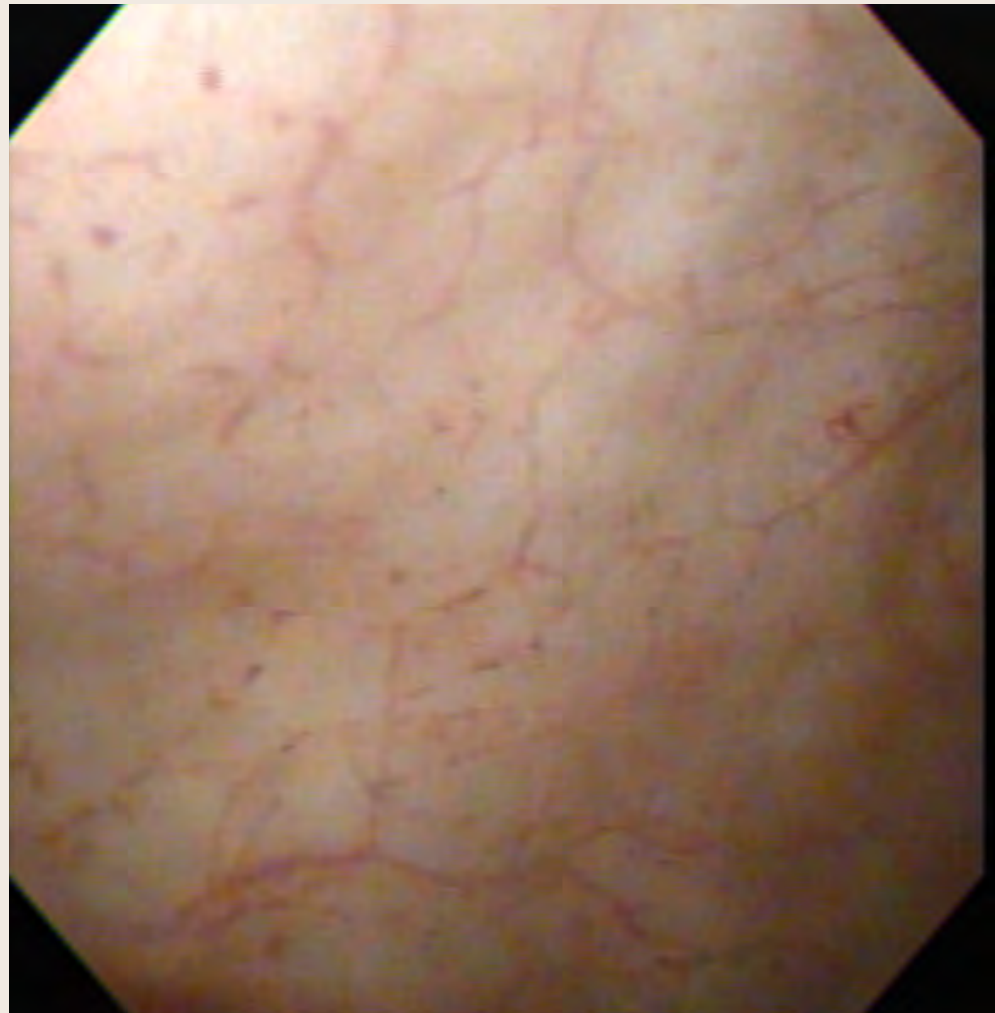
- C.C: lower abdomen and pelvic distension discomfort; **urinary frequency** (every hr) and **nocturia** (5-6 times); dysmenorrhea (VAS: 7-8) with flank soreness
- Pelvic examination:
 - Cervix: no motion tenderness, Uterus: no tenderness
 - Right adnexa: mild dullness; Left adnexa: WNL; CDS: mild dullness
- Ultrasound:





2021. 11. 08 - OPD

- Urine analysis: OB (-), LE (+/-), Bacteria (-), Nitrite (-), WBC (0-5)
- Cystoscopy: suspect interstitial cystitis





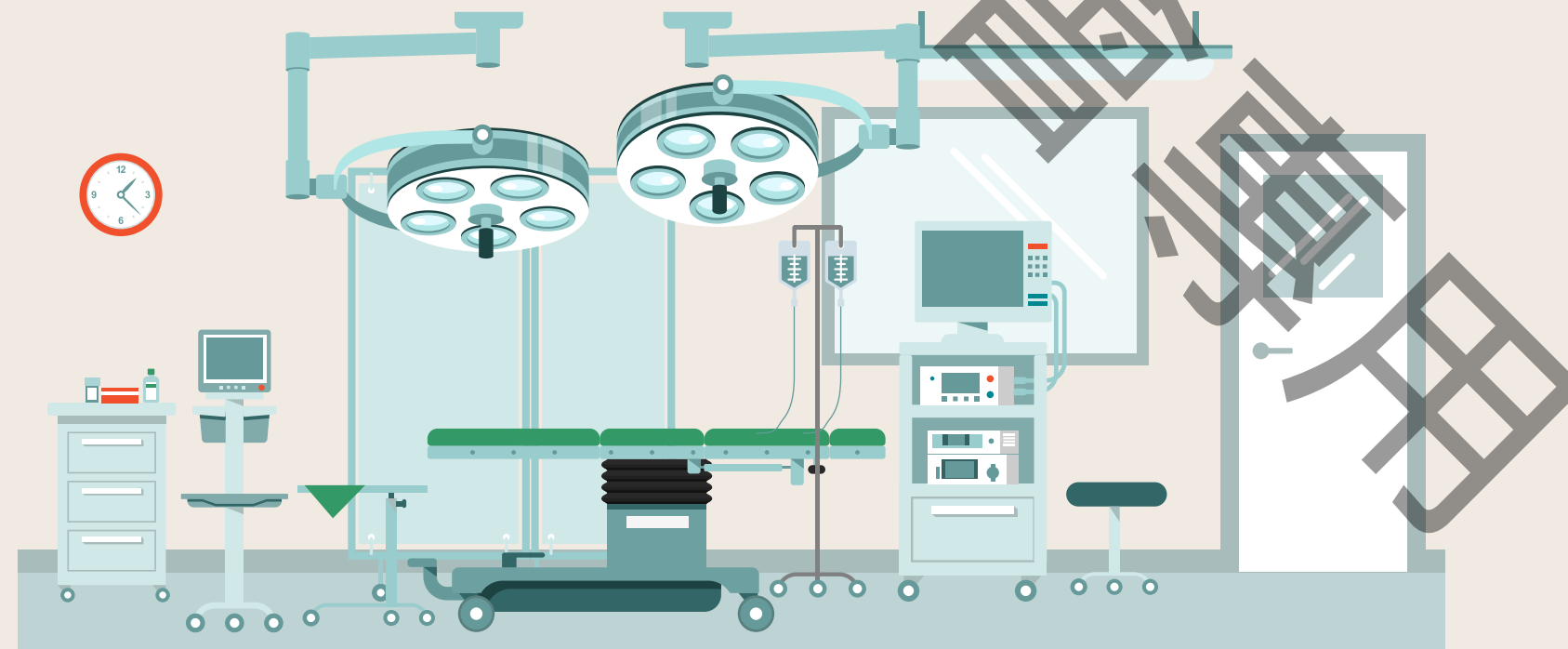
Hospitalization

2021. 11. 15 - **Admission**

- Lab survey: within normal limit; **CA-125: 61.2**
- Urine analysis: OB (+/-)

2021. 11. 16 - **Operation**

- Laparoscopic right ovarian cystectomy + cystoscopic hydrodistension





Operative findings:

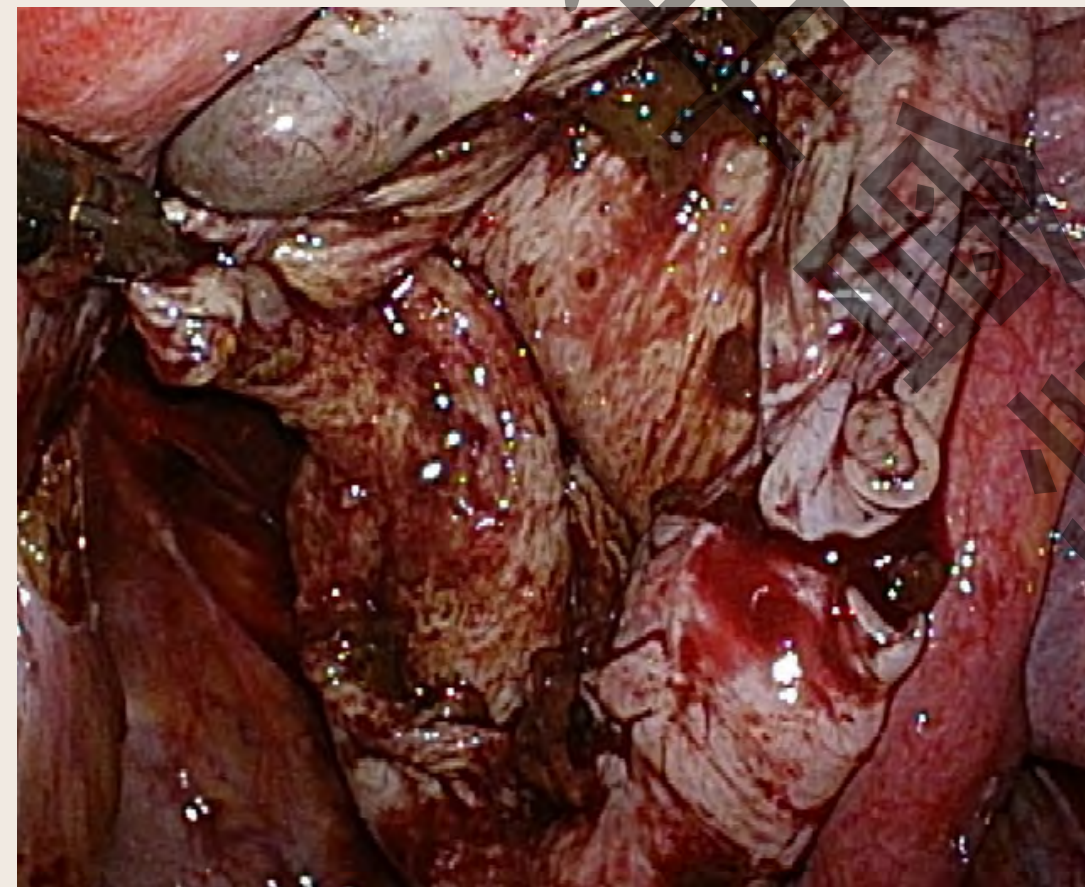
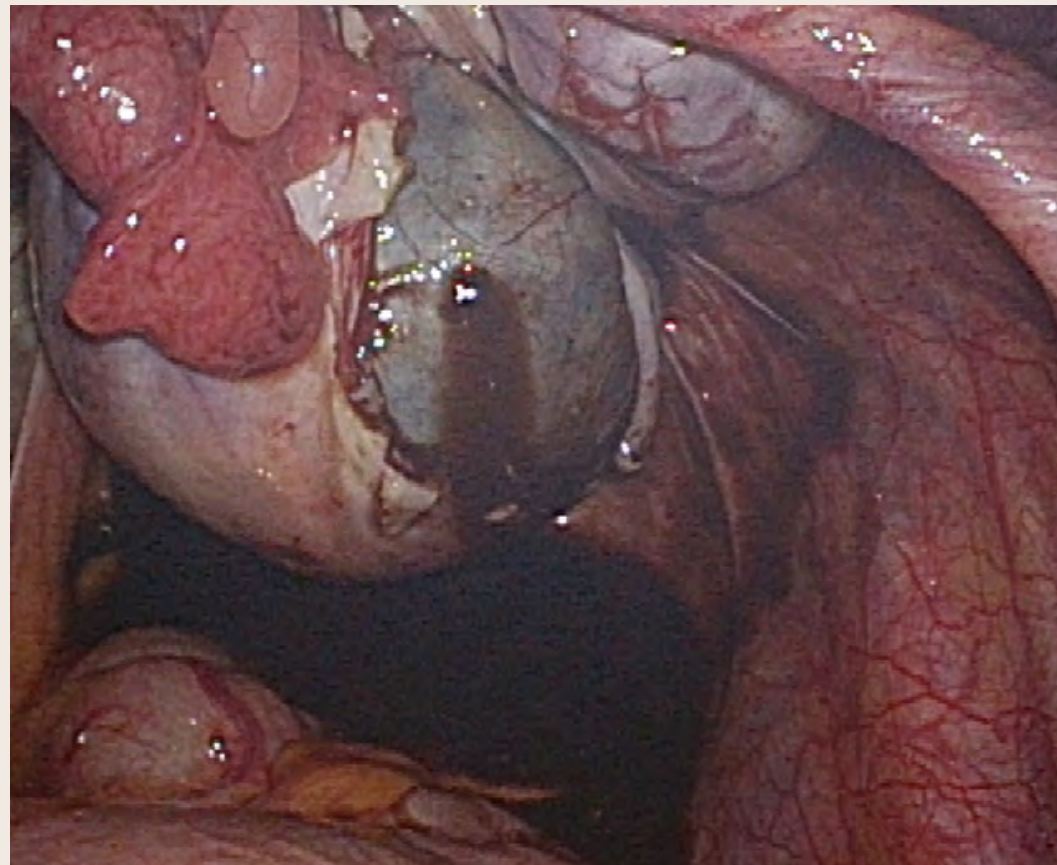
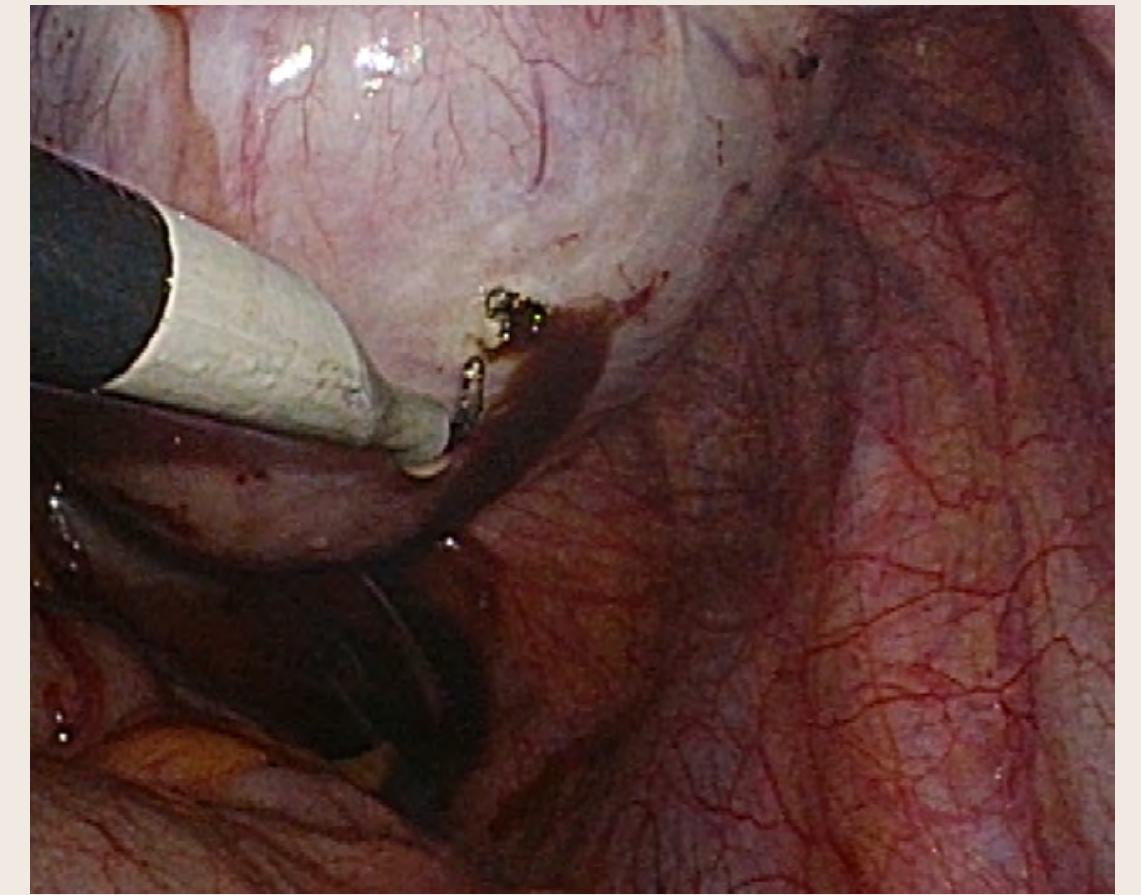
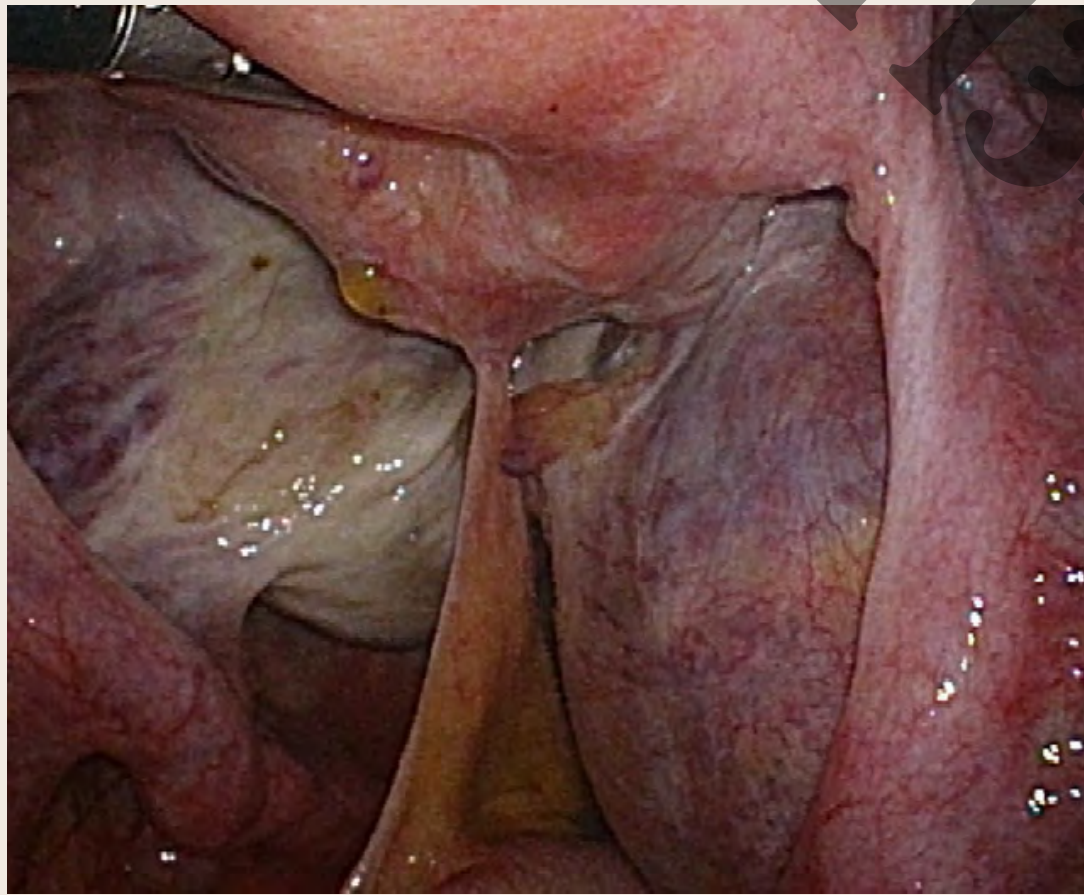
Laparoscopy

- Uterus: RVF, around 7-8 cm
 - Right ovary: ovarian **cystic tumor** with **chocolate content**, 7 cm, densely adherent to ovarian fossa
 - Left ovary: multiple small cystic lesion, favoring endometrioma which densely adherent to ovarian fossa
 - Severe pelvic adhesion between sigmoid colon, uterus, adnexa, CDS and left pelvic wall
 - CDS: obliteration
- # rAFS: **112**

Cystoscopy

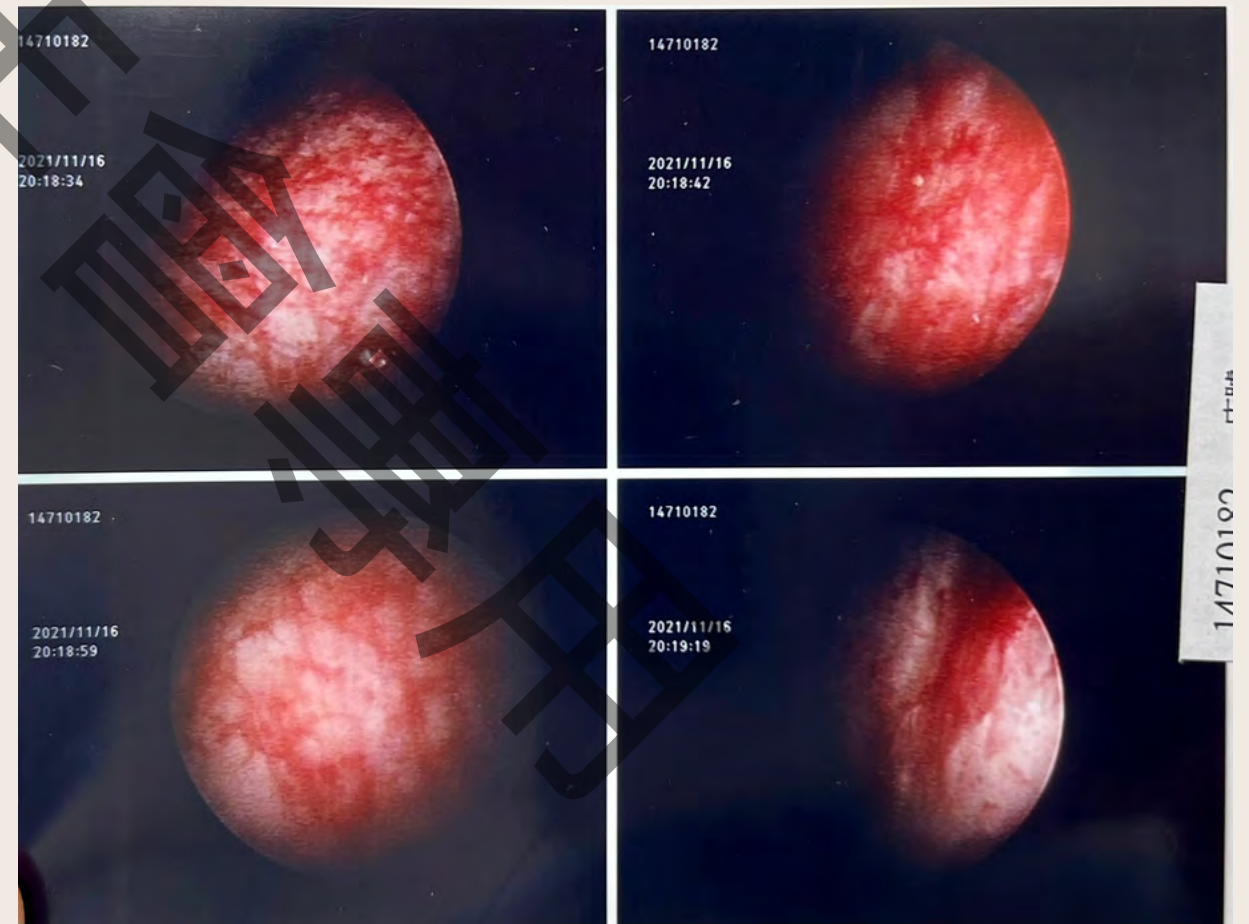
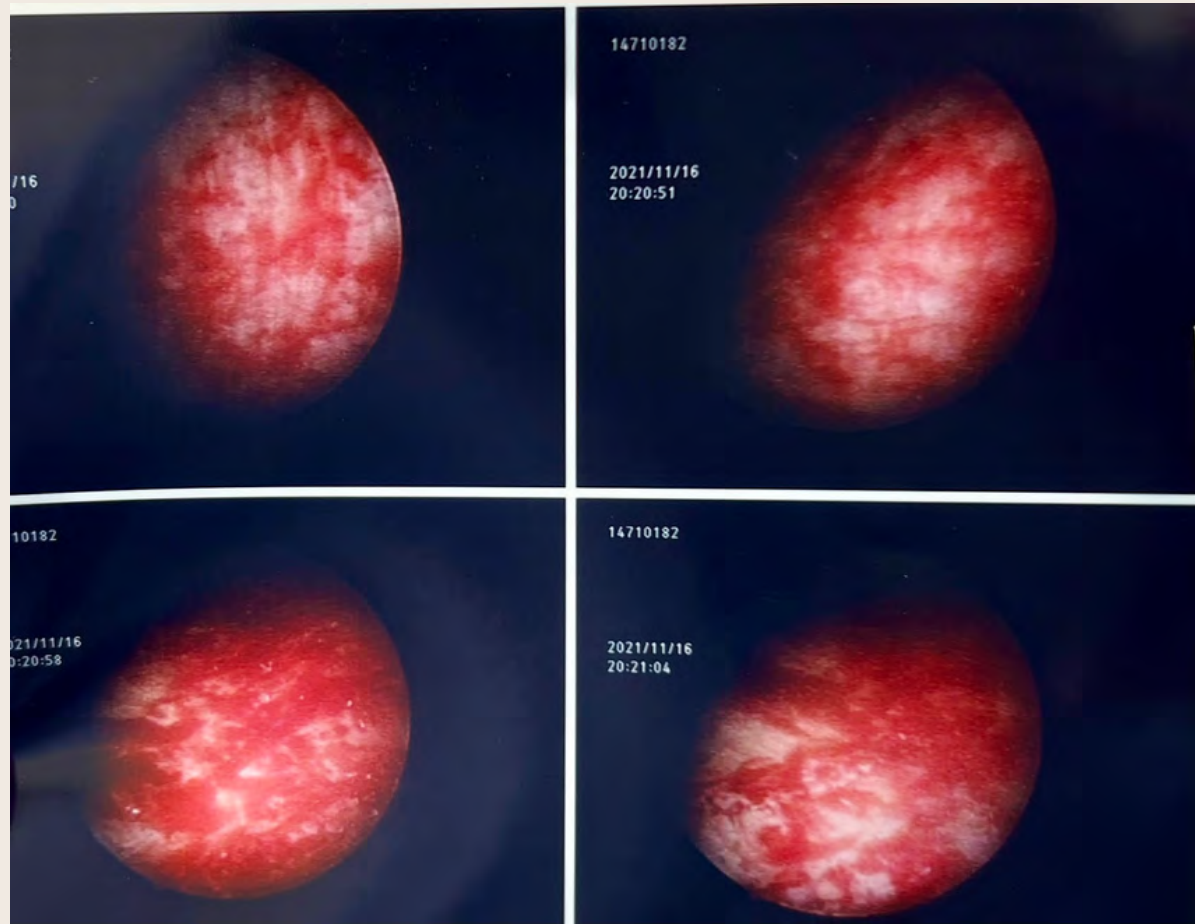
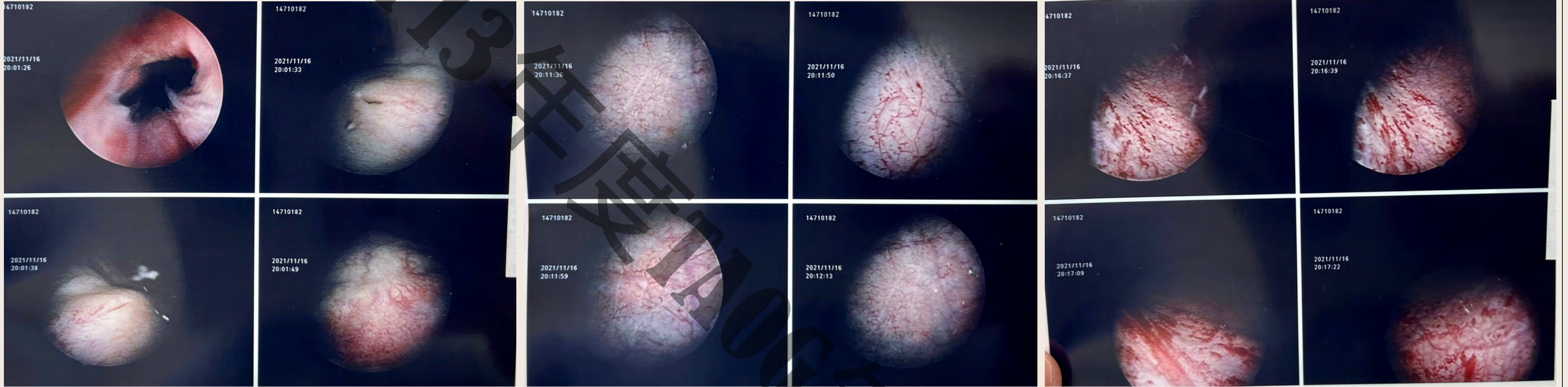
- Normal ureteral orifices, normal urethra
- Mild trabeculation was noted in the urinary bladder
- **Glomerulations:** grade **4** with mucosal tears and erythematous area
- No Hunner`s lesion was noted





PERITONEUM	ENDOMETRIOSIS	< 1cm	1-3cm	> 3cm	
	Superficial	1	2	4	
Deep	2	4	6		
OVARY	R. Superficial	1	2	4	
	Deep	4	16	20	
	L. Superficial	1	2	4	
	Deep	4	16	20	
POSTERIOR CULDESAC OBLITERATION	Partial	40			
	Complete	40			
OVARY	ADHESIONS	< 1/3 Enclosure	1/3-2/3 Enclosure	> 2/3 Enclosure	
	R. Filmy	1	2	4	
	Dense	4	8	16	
	L. Filmy	1	2	4	
	Dense	4	8	16	
	TUBE	R. Filmy	1	2	4
		Dense	4	8	16
		L. Filmy	1	2	4
Dense		4	8	16	

*If the fimbriated end of the fallopian tube is completely enclosed, change the point assignment to 16.





2021. 11. 15 ~ 11. 18 - Hospitalization

- **Pathological report**

- Ovary, right: endometriotic cyst
left: endometriotic cyst
- Peritoneum: chronic inflammation
- Urinary bladder: acute and chronic inflammation
- Urine cytology: absence of abnormal change

- **Final diagnosis**

- Severe endometriosis with bilateral ovarian endometrioma
- Pelvic adhesion
- Interstitial cystitis





- 11/15-11/18 - **Operation**
- 12/01 **Urodynamic study**
 - Diagnosis: Hypersensitivity bladder, suspect IC
 - Cystometry CMG
 - First sensation: 56 mL, First desire: 116 mL
 - Max cystometry capacity: 206 mL
- 11/22-12/29 - **Heparin** installation * 6
- 12-02 - Vaginal laser * 3
- 01/05-05/18 **Cystistat** installation * 9
- 06/15-02/22 **Cystistat** installation * 9





Current patient condition

- reduced dysmenorrhea and chronic pelvic pain
- reduced urinary frequency, urgency, and nocturia
- condition stable without symptoms flare up

2023. 03. 22 OPD

- Bladder instillation with cystistat
- Ultrasound: within normal limit
- **CA-125: 26.0**





Discussion

Chronic Pelvic Pain

Definition

- Lack of consensus
- pain symptoms originate from **pelvic organs/structures**
- lasting more than **6** months
- associated with negative cognitive behavioral, sexual and emotional consequences
- symptoms of lower urinary tract, sexual, bowel, pelvic floor, myofascial or gynecological dysfunction

Box 1. Common Conditions Associated With Chronic Pelvic Pain

Visceral

- Gynecologic
 - Adenomyosis
 - Adnexal mass
 - Chronic pelvic inflammatory disease/chronic endometritis
 - Endometriosis
 - Leiomyoma
 - Ovarian remnant syndrome
 - Pelvic adhesions
 - Vestibulitis
 - Vulvodynia
- Gastrointestinal
 - Celiac disease
 - Colorectal cancer and cancer therapy
 - Diverticular colitis
 - Inflammatory bowel disease
 - Irritable bowel syndrome
- Urologic
 - Bladder cancer and cancer therapy
 - Chronic or complicated urinary tract infection
 - Interstitial cystitis
 - Painful bladder syndrome
 - Urethral diverticulum

Neuromusculoskeletal

- Fibromyalgia
- Myofascial syndromes
 - Coccydynia
 - Musculus levator ani syndrome
- Postural syndrome
- Abdominal wall syndromes
 - Muscular injury
 - Trigger point
- Neurologic
 - Abdominal epilepsy
 - Abdominal migraine
 - Neuralgia
 - Neuropathic pain

Psychosocial

- Abuse
 - Physical, emotional, sexual
- Depressive disorders
 - Major depressive disorder
 - Persistent depressive disorder (dysthymia)
 - Substance-induced or medication-induced depressive disorder
- Anxiety disorders
 - Generalized anxiety disorder
 - Panic disorder
 - Social anxiety disorder
 - Substance-induced or medication-induced anxiety disorder
- Somatic symptom disorders
 - Somatic symptom disorder with pain features
 - Somatic symptom disorder with somatic characteristics
- Substance use disorder
 - Substance abuse
 - Substance dependence



Interstitial Cystitis in Persistent Posthysterectomy Chronic Pelvic Pain

Maurice K. Chung, RPh, MD

Objective

- to investigate the prevalence of IC in patients with posthysterectomy chronic pelvic pain

Methods

- 111 patients (age 34 to 65 years)
- persistent or recurrent pelvic pain who had hysterectomy for treating CPP
- from 1979 to 2001

Discussion

- Patient with CPP of bladder origin are often misdiagnosed and received procedures with little or no symptom relief
- bladder dysfunction may have been the source of pain in posthysterectomy CPP

Results

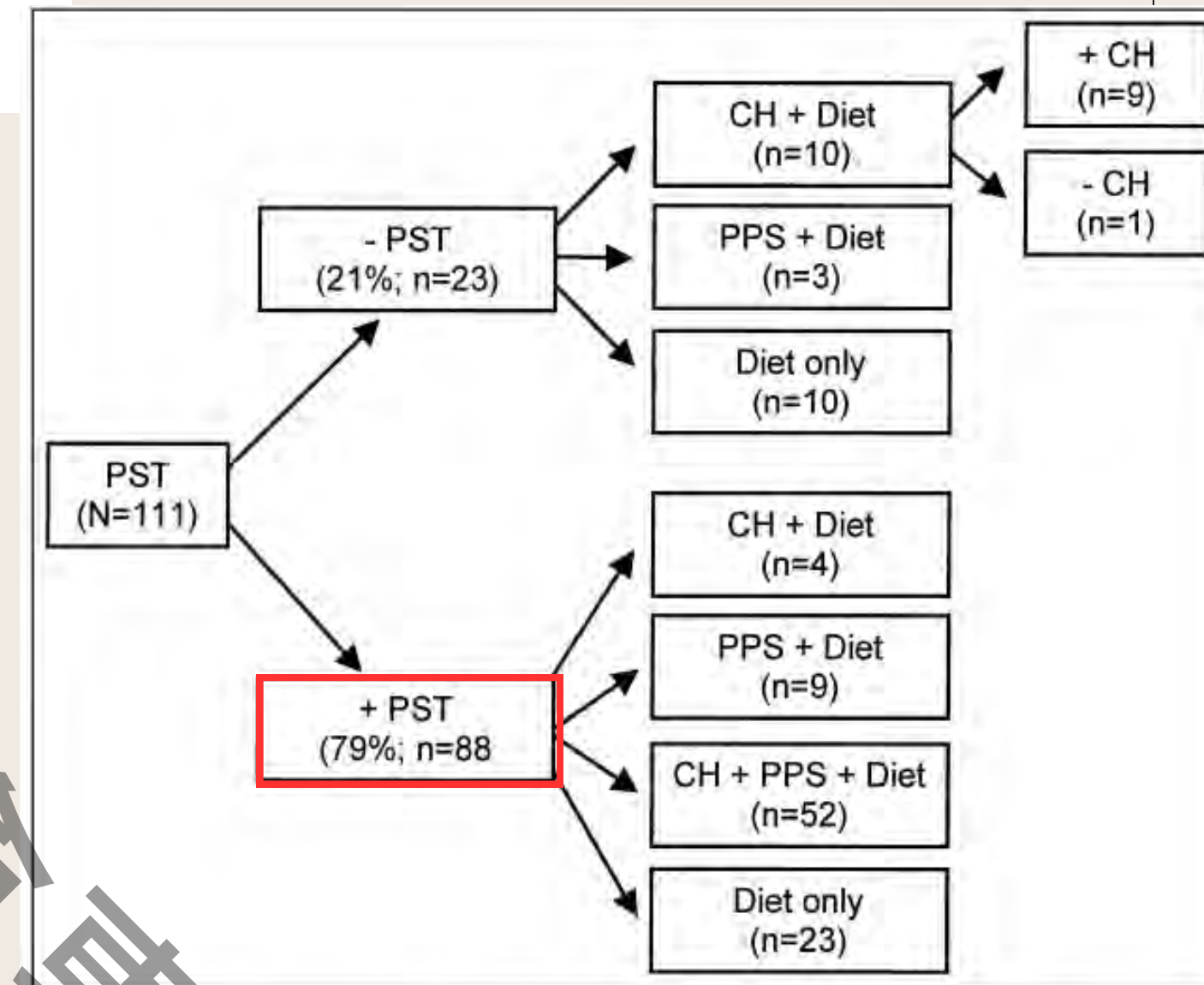


Figure 1. Potassium Sensitivity Test results and treatment decisions. CH=cystoscopic hydrodistention; PPS=pentosan polysulfate sodium; PST=Potassium Sensitivity Test.

- 92%** of PST (+) patient had positive cystoscopic hydrodistention



Interstitial Cystitis and Endometriosis in Patients With Chronic Pelvic Pain: The “Evil Twins” Syndrome

Maurice K. Chung, MD, RPh, Rosemary P. Chung, BSN, PA-C, David Gordon, MD

- Chronic pelvic pain (CPP) may be due to various reasons
 - endometriosis, endosalpingosis, pelvic adhesion, interstitial cystitis, adenomyosis, and uterine leiomyomas

Results

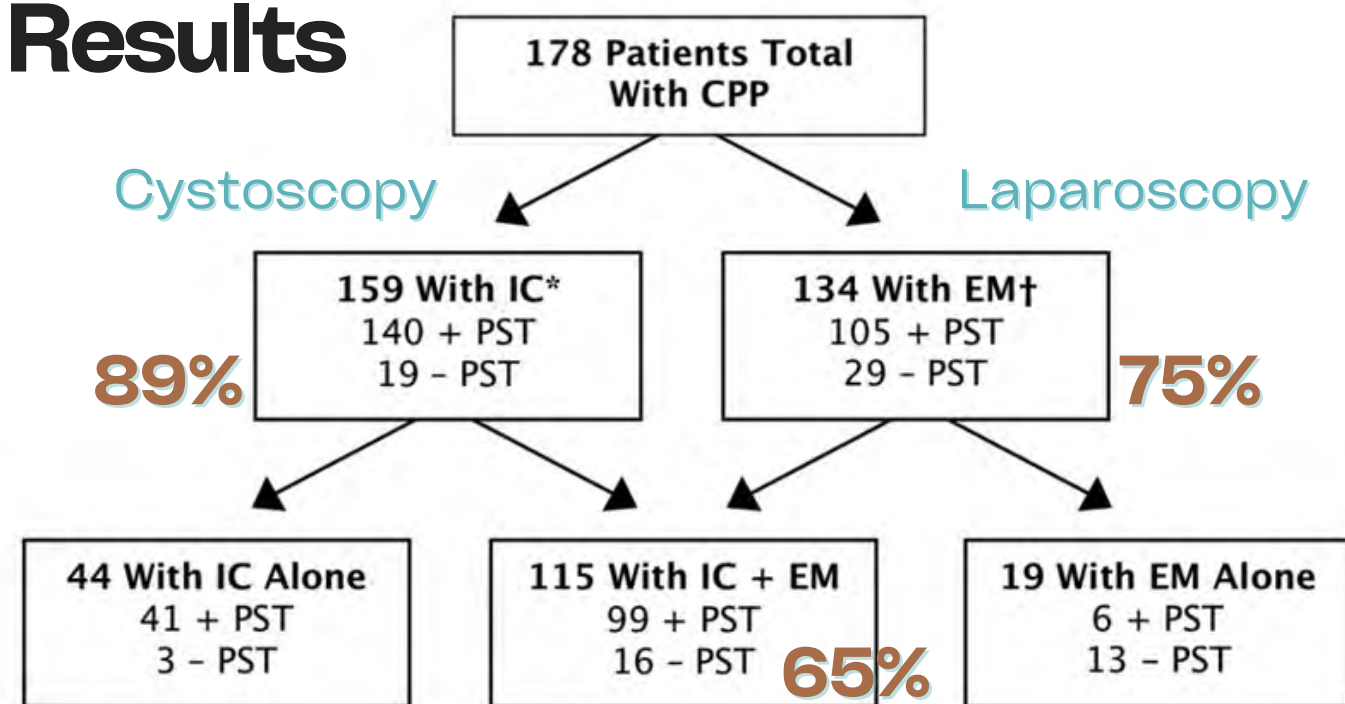


Figure 2. Diagnosis and PST results for patients in this study. CPP=chronic pelvic pain; EM=endometriosis; IC=interstitial cystitis; PST=Potassium Sensitivity Test. *Glomerulations and hematuria according to the National Institutes of Health–National Institute of Diabetes and Digestive and Kidney Diseases guidelines. †Presence of pathologist-confirmed presence of ectopic gland stroma.

Methods

- 178 patient, 18 to 60 years old
- Oct. 2000 to Nov. 2002
- CPP for > 6 months
- Underwent laparoscopy and cystoscopy

Conclusion

- IC and endometriosis are frequently **coexist**
- Cystoscopy with hydrodistention and laparoscopy should be performed concurrently



The Relationship Between Interstitial Cystitis and Endometriosis in Patients With Chronic Pelvic Pain

John D. Paulson, MD, Melissa Delgado, MD

Objective

- to determine the relationship between IC, endometriosis and CPP

Methods

- 162 patient, nonpostmenopausal patients with CPP
- Aug. 2002 to Dec. 2005
- CPP for > 6 months
- Underwent laparoscopy and cystoscopy

Results

Table 1.
Pain Urgency and Frequency (PUF) Scores and Pain Levels (Visual Analog Scale) for Patients With Chronic Pelvic Pain

Patients*	N	%	Mean PUF Score	Initial Pain (0-10)	Dysmenorrhea (0-10)	Dyspareunia (0-10)	Pain After Surgery (0-10)	Pain 6 Months After Surgery (0-10)
All IC patients	133	82	21.2	5.4	8.1	7.3	1.2	3.2
<u>IC and endo</u>	<u>107</u>	<u>66</u>	20.8	5.3	8.0	7.0	1.5	2.7
All endo patients	123	76	19.6	5.2	7.8	6.5	1.3	2.7
IC only	26	16	22.6	5.5	8.0	7.5	1.5	3.2
Endo only	16	10	12.0	5.1	7.6	6.6	1.1	1.9
Other pathology	13	8	7.5	3.2	5.6	2.5	0.5	1.1

*IC = interstitial cystitis patients; endo = endometriosis patients.

The 'evil twin syndrome' in chronic pelvic pain: A systematic review of prevalence studies of bladder pain syndrome and endometriosis

S.A. Tirlapur^{a,c,*}, K. Kuhrt^b, C. Chaliha^c, E. Ball^c, C. Meads^{a,d}, K.S. Khan^{a,c}

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Keywords:

Chronic pelvic pain

Bladder pain syndrome

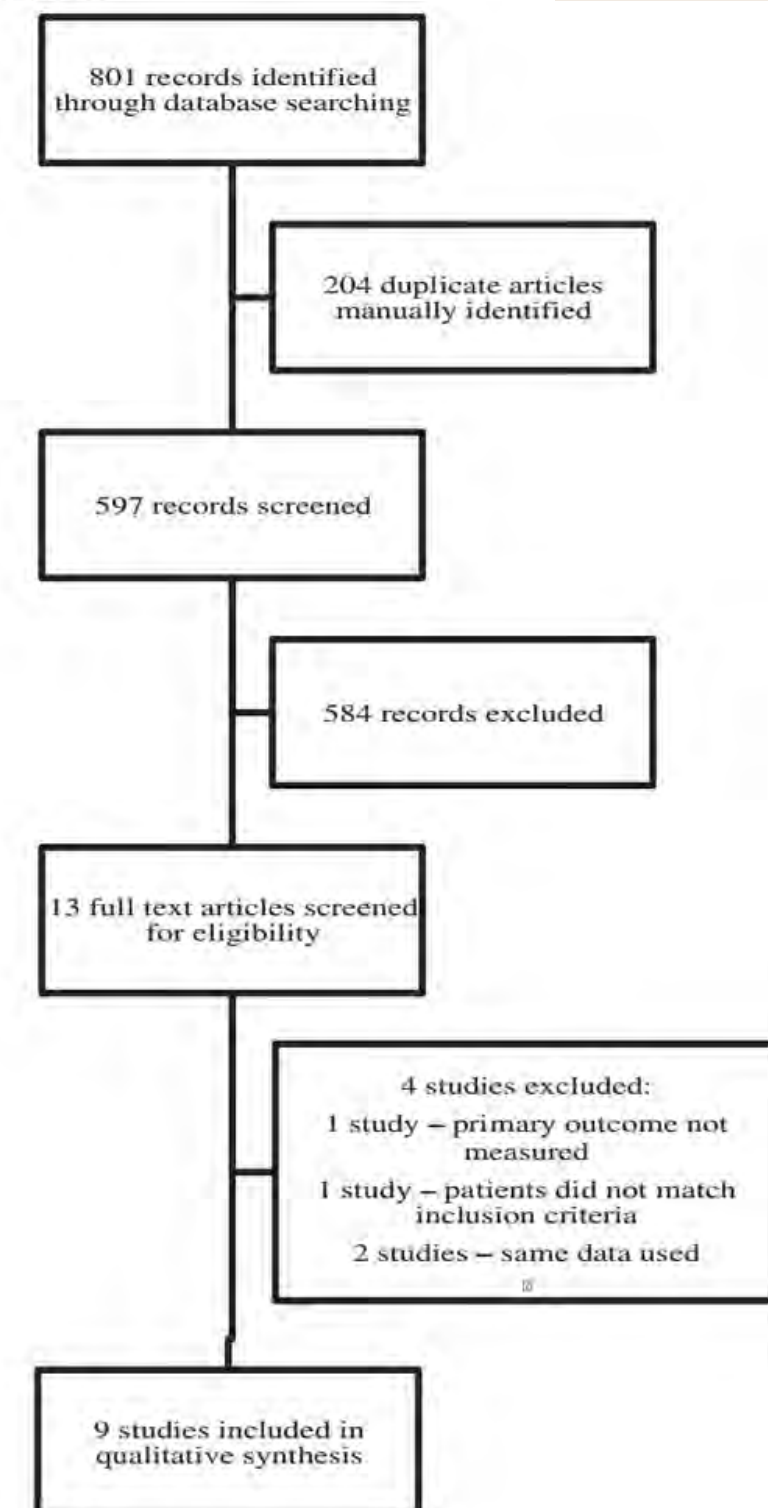
Painful bladder syndrome

Interstitial cystitis

Endometriosis

Prevalence

- **Purpose** of this review: (BPS = IC)
 - to estimate the prevalence of **BPS in CPP** women
 - to estimate the prevalence of **endometriosis** and **BPS**
- **Data sources**
 - Various databases, until March 2012
 - The Cochrane Library, EMBASE, Medline...
 - No language restriction
 - Participants
 - Women with CPP, with or without urinary symptoms suggestive of IC, PBS or BPS
 - received both laparoscopy and cystoscopy examination
- **Results**
 - 9 studies were included, between 1990 to 2011, total **1016** patients



The 'evil twin syndrome' in chronic pelvic pain: A systematic review of prevalence studies of bladder pain syndrome and endometriosis

S.A. Tirlapur^{a,c,*}, K. Kuhrt^b, C. Chaliha^c, E. Ball^c, C. Meads^{a,d}, K.S. Khan^{a,c}

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Prevalence

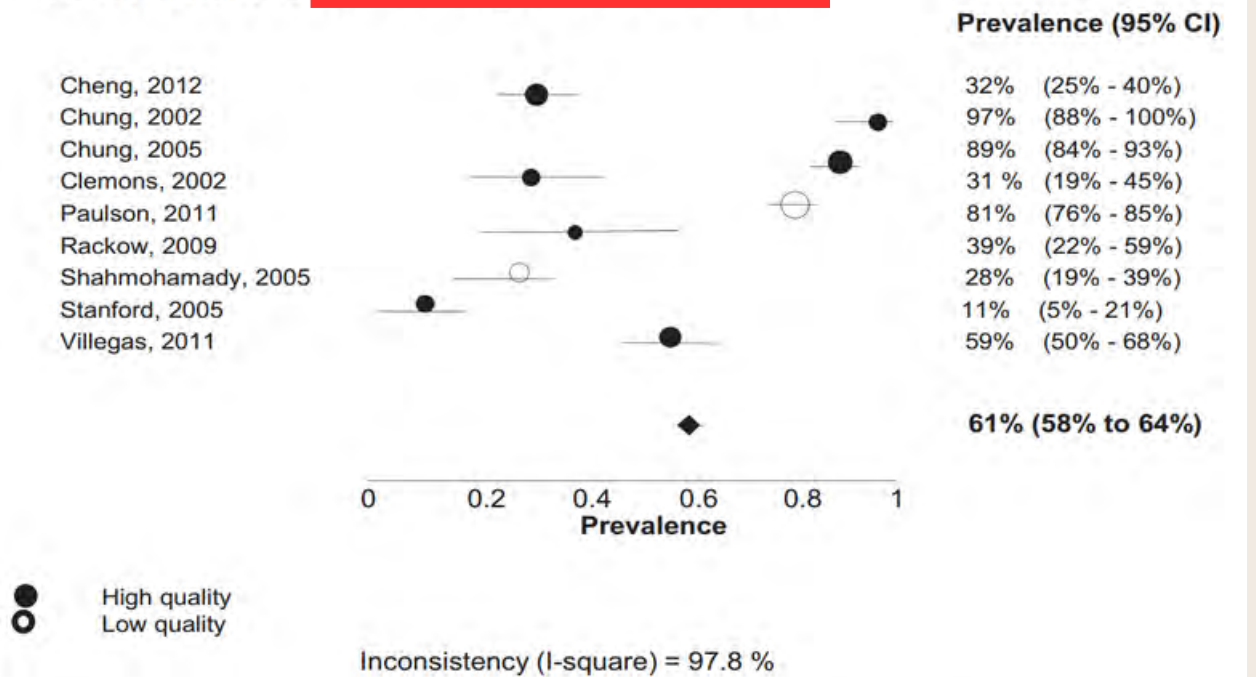
• Results

- diagnosis of BPS with prevalence of **61%**
- prevalence of endometriosis **70%**
- coexistence of endometriosis and BPS **48%**

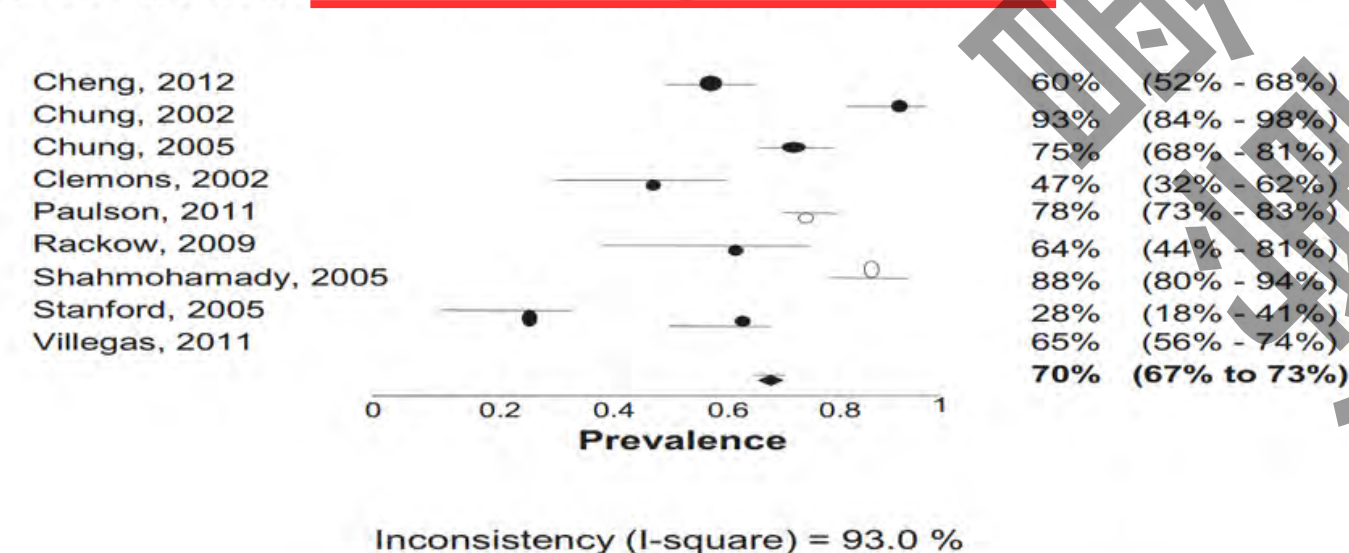
• Conclusion

- almost 2/3 patients presenting with CPP have BPS
- an overlap between BPS and endometriosis
- aware of the **coexistence** and commence active management

3a: Prevalence of **BPS** amongst women with CPP



3b: Prevalence of **endometriosis** amongst women with CPP



3c: Prevalence of **BPS and endometriosis** amongst women with CPP

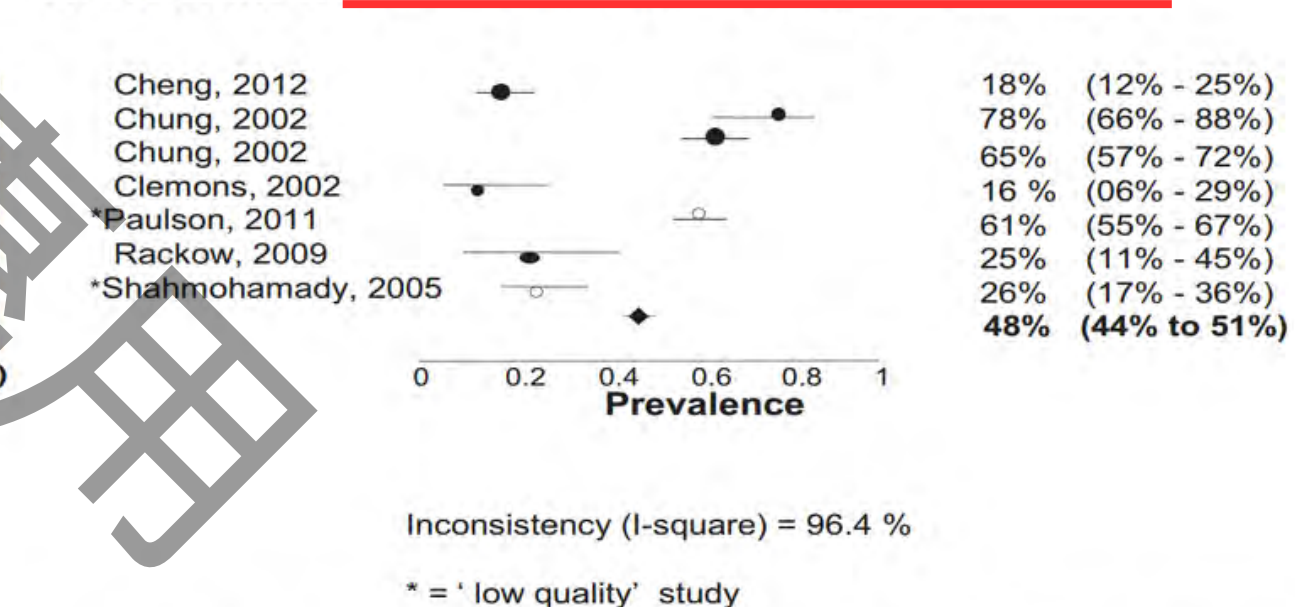


Fig. 3. Prevalences of bladder pain syndrome (BPS), endometriosis and co-existing BPS and endometriosis amongst women with chronic pelvic pain.

Endometriosis increased the risk of bladder pain syndrome/interstitial cystitis: A population-based study

Chia-Chang Wu MD, PhD^{1,2} | Shiu-Dong Chung MD, PhD^{3,4} Herng-Ching Lin PhD⁵ 

- **Aim:** to determine the subsequent risk of developing BPS/IC among women with endometriosis
 - Nationwide population-based study
 - compared to general population for **3** years follow up
- **Method:** Taiwan National Health Insurance (NHI) program
 - Study cohort:
 - 9191 patients, 18 to 50 years, diagnosed with endometriosis
 - Jan. 1, 2001 to Dec. 31, 2006
 - excluded previous BPS/IC

TABLE 1 Demographic characteristics of subjects with endometriosis and comparison subjects ($n = 36\ 764$)

Variable	Subjects with endometriosis ($n = 9191$)		Comparison subjects ($n = 27\ 573$)		P-value
	Total no.	%	Total no.	%	
Age (years)					1.000
18-24	978	10.6	2934	10.6	
25-29	1281	13.9	3843	13.9	
30-34	1555	16.9	4665	16.9	
35-39	1844	20.1	5532	20.1	
40-44	2009	21.9	6027	21.9	
45-49	1524	16.6	4584	16.6	
Monthly income					1.000
0	2627	28.6	7881	28.6	
NT\$1~15 840	1684	18.3	5052	18.3	
NT\$15 841~25 000	3202	34.8	9606	34.8	
≥NT\$25 001	1678	18.3	5034	18.3	
Geographic region					1.000
Northern	4517	49.2	13 551	49.2	
Central	1628	17.7	4884	17.7	
Eastern	2831	30.1	8493	30.1	
Southern	215	2.3	645	2.3	
Diabetes	385	4.2	606	2.3	<0.001
Hypertension	700	7.6	1071	4.1	<0.001
Coronary heart disease	251	2.7	360	1.4	<0.001
Obesity	79	0.9	144	0.6	0.001
Hyperlipidemia	683	7.4	978	3.8	<0.001
Chronic pelvic pain	2786	30.3	4659	17.9	<0.001
Irritable bowel syndrome	488	5.3	687	2.6	<0.001
Fibromyalgia	1689	18.4	3681	14.1	<0.001
Chronic fatigue syndrome	50	0.5	99	0.4	0.037
Depression	523	5.7	879	3.4	<0.001
Panic disorder	63	0.7	123	0.5	<0.001
Migraine	398	4.3	672	2.6	0.015
Sicca syndrome	109	1.2	192	0.7	<0.001
Allergy	105	1.1	282	1.1	0.633
Asthma	361	3.9	828	3.2	0.001
Overactive bladder	395	4.3	409	1.6	<0.001

Endometriosis increased the risk of bladder pain syndrome/interstitial cystitis: A population-based study

• Results

- Mean age: 34.8 years \pm 8.5 years
- Subjects with endometriosis had higher prevalence of other comorbidities
- total 36764 patients, **30** subjects (0.09%) developed BPS/IC in 3 f/u years
 - **18** patients in study cohort (0.2% among endometriosis patient)
 - 12 patients in control cohort (0.05%)

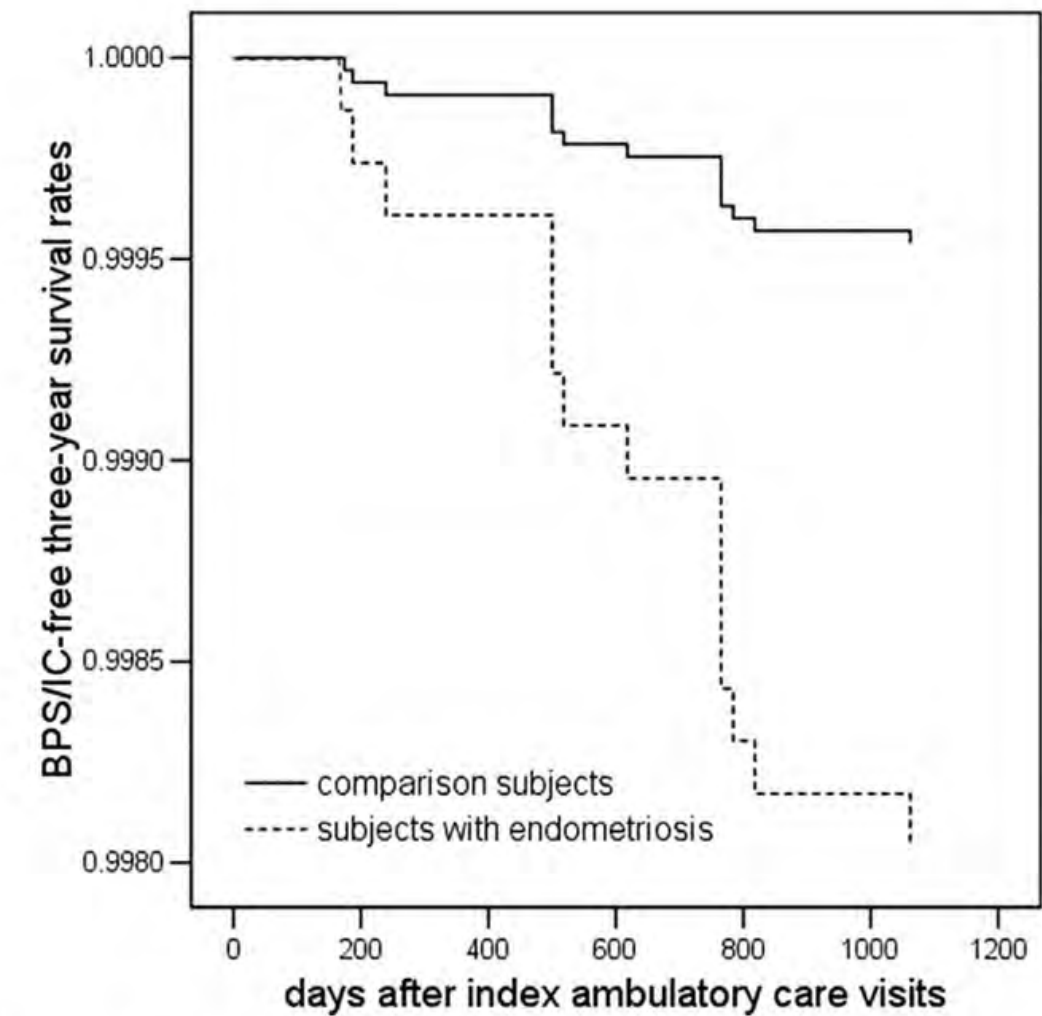


FIGURE 1 Subjects with endometriosis had significantly lower 3-year BPS/IC-free survival rates than comparison subjects

• Discussion

- endometriosis is associated with BPS/IC
- two diseases share common pathomechanisms
 - inflammatory changes via chemokines or cytokines
 - IL-6, TNF
 - chronic inflammation in the pelvis

TABLE 2 Incidence and hazard ratio for bladder pain syndrome/interstitial cystitis among the sampled patients

Presence of bladder pain syndrome/interstitial cystitis	Total (<i>n</i> = 36 764) <i>n</i> , %		Subjects with endometriosis (<i>n</i> = 9191) <i>n</i> , %	
Three-year follow-up period				
Yes	30	0.09	18	0.20
Crude hazard ratio ^a (95%CI)	-		<u>4.43***</u> (2.13-9.23)	
Adjusted hazard ratio ^b (95%CI)	-		<u>3.74***</u> (1.76-7.94)	

****p* < 0.001.

CI = confidence interval.

^aHazard ratio was calculated by conditional logistic regression which was conditioned on age group, monthly income, geographic region, and index year.

^bAdjustments are made for subject's diabetes, hypertension, coronary heart disease, obesity, hyperlipidemia, chronic pelvic pain, irritable bowel syndrome, fibromyalgia, chronic fatigue syndrome, depression, panic disorder, migraine, sicca syndrome, allergy, asthma, and overactive bladder.

Non-bladder centric interstitial cystitis/bladder pain syndrome phenotype is significantly associated with co-occurring endometriosis

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Results

- total 431 patients were reviewed:
 - Group 1: 82 patients
 - Group 2: 349 patients

- Reports suggest **48%-65%** of women with CPP suffer from both endometriosis and IC/BPS
- hypothesized that endometriosis would be more common in non-low bladder capacity (> 400cc)

Method

- Patient recruitment and enrollment
 - IC/BPS patients (18 to 80 years old) - data registry
 - divided into two comparison groups
 - Group 1) IC/BPS patients with known co-occurring endometriosis
 - Group 2) IC/BPS patients **without** known co-occurring endometriosis

TABLE 1. Demographic and medical history data

	Group 1	Group 2	p value
	IC/BPS with endometriosis	IC/BPS without endometriosis	
Total patients	n = 82 (19%)	n = 349	
<u>Age (years)</u>	42.96 ± 11.46	46.44 ± 14.17	0.02
Body mass index	28.80 ± 8.32	29.70 ± 8.10	0.50
<u>Chronic pelvic pain</u>	29 (35.4%)	63 (18.1%)	0.006
<u>Irritable bowel syndrome</u>	43 (52.4%)	135 (38.5)	0.02
<u>Fibromyalgia</u>	38 (46.3%)	88 (25.2%)	0.0002
Depression	34 (41.5%)	122 (35.0%)	0.27
Panic disorder	29 (35.4%)	122 (35.0%)	0.94
<u>Vulvodinia</u>	19 (23.2%)	45 (12.9%)	0.02
Dyspareunia	37 (45.1%)	150 (43.0%)	0.72

IC/BPS = interstitial cystitis/bladder pain syndrome

Non-bladder centric interstitial cystitis/bladder pain syndrome phenotype is significantly associated with co-occurring endometriosis

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Results

Predictors for concurrent endometriosis in IC/BPS patients

Independent predictors of concurrent endometriosis in IC/BPS

TABLE 2. IC/BPS disease characteristics

	Group 1	Group 2	p value
	IC/BPS with endometriosis	IC/BPS without endometriosis	
<u>Non-low bladder capacity</u>	80 (97.6%)	298 (85.4%)	0.003
<u>Hunner's lesion presence</u>	2 (2.4%)	39 (11.2%)	0.02
PUF symptom	16.1 ± 3.04	15.33 ± 4.32	0.17
PUF problem	8.69 ± 1.83	8.24 ± 2.49	0.18
IC symptom index	13.97 ± 2.81	13.57 ± 3.90	0.33
IC problem index	12.77 ± 2.50	12.52 ± 3.18	0.47

IC/BPS = interstitial cystitis/bladder pain syndrome

TABLE 3. Univariate logistic regression analysis

	OR	95% confidence interval	p value
<u>Age (years)</u>	0.98	0.96-0.99	0.03
Body mass index	0.97	0.95-1.02	0.40
<u>Non-low bladder capacity</u>	6.85	1.63-28.73	0.01
<u>Hunner's lesion</u>	0.20	0.05-0.84	0.03
<u>Chronic pelvic pain</u>	2.48	1.46-4.21	0.001
<u>Irritable bowel syndrome</u>	1.77	1.09-2.87	0.02
<u>Fibromyalgia</u>	2.56	1.56-4.21	< .001
Depression	1.32	0.81-2.15	0.27
Panic disorder	1.02	0.62-1.68	0.94
<u>Vulvodynia</u>	2.04	1.12-3.72	0.02
Dyspareunia	1.09	0.67-1.77	0.73

TABLE 4. Multivariate logistic regression analysis

	OR	95% confidence interval	p value
Age (years)	0.98	0.96-1.01	0.22
<u>Non-low bladder capacity</u>	4.53	1.004-20.42	0.049
Hunner's lesion	0.50	0.11-3.34	0.38
<u>Chronic pelvic pain</u>	1.84	1.04-3.24	0.04
Irritable bowel syndrome	1.33	0.77-2.28	0.31
<u>Fibromyalgia</u>	1.80	1.03-3.14	0.04
Vulvodynia	1.63	0.85-3.12	0.14

Low bladder capacity: < 400 cc

Discussion

- **Non-low BC** IC/BPS is significantly associated with endometriosis, IBS, fibromyalgia, and vulvodynia
- CPP-related endometriosis symptom recurrence following menopause should evaluate IC/BPS
 - Age inversely correlate with concurrent endometriosis
- IC/BPS patients don't respond to conventional therapy, a laparoscopic evaluation should be considered



Association of endometriosis with interstitial cystitis in chronic pelvic pain syndrome: Short narrative on prevalence, diagnostic limitations, and clinical implications

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Table 1. Prevalence of non-cyclical chronic pelvic pain as cited by the World Health Organization systematic review determining the prevalence and geographic rates of chronic pelvic pain².

USA	15%
UK	24%
India	5.2%
Pakistan	8.8%
Thailand	43.2%

Take home message

- The rate of concurrent endometriosis and IC reported vary widely
 - prevalence of two condition is high
 - relationship between the two is poorly understood
 - mast cell degranulation
 - neurogenic upregulation with viscerovisceral hyperalgesia
- Simultaneous assessment with cystoscopy and laparoscopy
 - if previous treatment fail
 - presence of endometriosis does not exclude IC as a cause of CPP
- Early referral of patients with CPP for multidisciplinary care is paramount

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THANK YOU!