ENDOMETRIOSIS IS A RISK FACTOR OF INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME WITHIN SHORT INTERVAL-A NATIONAL POPULATION-BASED STUDY

Hypothesis / aims of study
Interstitial cystitis/bladder pain syndrome (IC/BPS) and endometriosis frequently coexist and elusive. Both diseases share similar symptoms which are common contribute to chronic pelvic pain. This study aimed to evaluate if endometriosis is a risk of IC/BPS.

Study design, materials and methods
From a national insurance database, we identified women newly diagnosed with endometriosis between 2002 and 2013. Those with a history of IC/BPS before endometriosis diagnosis were excluded. All women were stratified into two subgroups based on the propensity scores of 10 confounding factors, including age and nine comorbidities (irritable bowel syndrome, depressive disorder, anxiety, fibromyalgia, stress incontinence, acute cystitis and chronic urinary tract infection) (Figure). All were followed until the end of 2013 to detect the event of IC/BPS diagnosis. The hazard ratio (HR) of IC/BPS in the endometriosis cohort was compared with the non-endometriosis cohort among the two subgroups by Cox regression after adjusting for confounding factors.

Results
In addition to the representative average age, subgroup 2 had similar rates of comorbidities as the general population (Table 1). The study was both externally and internally valid. The risk of IC/BPS in the endometriosis cohort (n=18006) was significantly higher than in the non-IC/BPS cohort (n=389099) in subgroup 2 (HR= 2.091, 95 % CI 1.641–2.663) (Table 2). The mean time to IC/BPS after diagnosis of endometriosis was 3.76 years (Table 3).

Interpretation of results
After adjusting for potential confounding factors, endometriosis was a risk factor of IC/BPS with short occurred interval. Delay diagnosis of IC/BPS in concomitant endometriosis and IC/BPS, or related pathogenesis maybe the possible reasons. Underlying or coexist IC/BPS should be evaluated in women with diagnosis of endometriosis. Further studies to assess the underlying common mechanism of endometriosis and IC/BPS are needed.

Concluding message
Endometriosis has a causal impact on IC/BPS in our database. Caregivers should cautiously evaluate the possibility of IC/BPS in women with diagnosis of endometriosis.
Table 1. Distribution of confounding factors among the two subgroups

<table>
<thead>
<tr>
<th>Variable/Group</th>
<th>Endometriosis cohort</th>
<th>Non-endometriosis cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Subgroup 1 (n=87853)</strong></td>
<td><strong>n=18</strong></td>
<td><strong>n=87835</strong></td>
</tr>
<tr>
<td>Age, mean ± SD (range)</td>
<td>33.08 ± 11.30 (12-52)</td>
<td>3.03 ± 4.95 (0-86)</td>
</tr>
<tr>
<td>Irritable bowel syndrome, outpatient</td>
<td>2.94 ± 8.41 (0-36)</td>
<td>0.08 ± 0.94 (0-175)</td>
</tr>
<tr>
<td>Depressive disorder, outpatient</td>
<td>30.94 ± 63.14 (0-232)</td>
<td>0.09 ± 2.46 (0-357)</td>
</tr>
<tr>
<td>Anxiety, outpatient</td>
<td>96.22 ± 122.74 (0-514)</td>
<td>0.84 ± 10.53 (0-423)</td>
</tr>
<tr>
<td>Anxiety, admission</td>
<td>0.17 ± 0.71 (0-3)</td>
<td>0.00 ± 0.05 (0-12)</td>
</tr>
<tr>
<td>Fibromyalgia, outpatient</td>
<td>38.83 ± 74.26 (0-258)</td>
<td>0.58 ± 6.98 (0-456)</td>
</tr>
<tr>
<td>Stress incontinence, outpatient</td>
<td>6.78 ± 14.52 (0-50)</td>
<td>0.07 ± 2.20 (0-219)</td>
</tr>
<tr>
<td>Stress incontinence, admission</td>
<td>0.06 ± 0.24 (0-1)</td>
<td>0.00 ± 0.01 (0-1)</td>
</tr>
<tr>
<td>Acute cystitis, outpatient</td>
<td>5.17 ± 11.67 (0-46)</td>
<td>0.50 ± 2.22 (0-252)</td>
</tr>
<tr>
<td>Chronic urinary tract infection, outpatient</td>
<td>2.22 ± 7.32 (0-30)</td>
<td>0.03 ± 1.00 (0-109)</td>
</tr>
</tbody>
</table>

**Subgroup 2 (n=407105)**

| Age, mean ± SD (range)                              | 35.15 ± 9.37 (11-102) | 36.27 ± 17.14 (0-102) |
| Irritable bowel syndrome, outpatient                | 0.75 ± 3.81 (0-131)   | 0.59 ± 3.72 (0-285)   |
| Depressive disorder, outpatient                     | 2.54 ± 14.44 (0-449)  | 1.89 ± 12.31 (0-868)  |
| Anxiety, outpatient                                 | 2.66 ± 10.43 (0-200)  | 2.55 ± 10.84 (0-374)  |
| Anxiety, admission                                  | 0.01 ± 0.28 (0-28)    | 0.01 ± 0.24 (0-95)    |
| Fibromyalgia, outpatient                            | 2.52 ± 6.15 (0-175)   | 2.45 ± 7.18 (0-307)   |
| Stress incontinence, outpatient                     | 0.07 ± 0.73 (0-28)    | 0.06 ± 0.68 (0-43)    |
| Stress incontinence, admission                      | 0.01 ± 0.09 (0-3)     | 0.00 ± 0.07 (0-11)    |
| Acute cystitis, outpatient                          | 0.02 ± 0.28 (0-13)    | 0.01 ± 0.26 (0-62)    |
| Chronic urinary tract infection, outpatient         | 2.89 ± 6.64 (0-137)   | 2.25 ± 6.30 (0-269)   |

*SD standard deviation, *Outpatient* total number of times seeking outpatient medical advice for a confounding variable, *Inpatient* total number of admissions for a confounding variable

Table 2. Hazard ratio (HR) of IC/BPS in the endometriosis cohort compared with the non-endometriosis cohort among the two subgroups

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>HR* (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Subgroup 1 (n=329129)</strong></td>
<td></td>
</tr>
<tr>
<td>Endometriosis (yes/no)</td>
<td>27.242 [3.334-222.563]</td>
</tr>
<tr>
<td><strong>Subgroup 2 (n=104382)</strong></td>
<td></td>
</tr>
<tr>
<td>Endometriosis (yes/no)</td>
<td>2.091 [1.641-2.663]</td>
</tr>
</tbody>
</table>

*CI confidence interval,

*Adjusted confounders: age, total number of times seeking outpatient medical advice and total number of admissions for irritable bowel syndrome, depressive disorder, anxiety, fibromyalgia, stress incontinence, acute cystitis and chronic urinary tract infection.

Table 3. Duration of follow-up and the time from study start date to IC/BPS among the two subgroups

<table>
<thead>
<tr>
<th>Duration of follow-up</th>
<th>N</th>
<th>Mean(year)</th>
<th>SD</th>
<th>Min.</th>
<th>Max.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subgroup 1</td>
<td>87853</td>
<td>9.84</td>
<td>2.73</td>
<td>0.003</td>
<td>12</td>
</tr>
<tr>
<td>Subgroup 2</td>
<td>407105</td>
<td>10.78</td>
<td>2.38</td>
<td>0.003</td>
<td>12</td>
</tr>
<tr>
<td>Total</td>
<td>494958</td>
<td>10.61</td>
<td>2.47</td>
<td>0.003</td>
<td>12</td>
</tr>
</tbody>
</table>

| Time from diagnosis of endometriosis to IC/BPS | Subgroup 2 | 70 | 3.76 | 2.80 | 0.003 | 9.860 |

*IC/BPS interstitial cystitis/bladder pain syndrome, SD standard deviation
Disclosures

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Helsinki: Yes
Informed Consent: No