Chronic prostatitis/chronic pelvic pain syndrome is associated with previous colonoscopy

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Cite as: *Can Urol Assoc J* 2017;11(9):E367-71. http://dx.doi.org/10.5489/cuaj.4279
Published online September 12, 2017

Abstract

Introduction: This study aimed to examine the association between chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) and receipt of a prior colonoscopic examination using a population-based database.

Methods: We used the Taiwan Longitudinal Health Insurance Database 2005 to retrieve the study sample. This study included 3933 patients with CP/CPPS and 3933 age-matched controls. We designated the date of receiving the first diagnosis of CP/CPPS as the index date for cases. We defined the first an ambulatory care visit occurring in the matched year as the index date for the controls. Conditional logistic regressions was used to calculate the odds ratio (OR) and 95% confidence interval (CI) for having previously received colonoscopy between cases and controls.

Results: We found that 349 (4.44%) of the 7866 sampled patients had previously undergone colonoscopy, including 223 (5.67%) cases and 126 (3.20%) controls (p<0.001). A conditional logistic regression analysis revealed that the adjusted OR of receiving a colonoscopy within three years before the index date was 1.77 (95% CI 1.42–2.23) for cases compared to controls. Furthermore, we found that the youngest group of cases (<40 years) had the greatest adjusted OR for having received colonoscopy within three years before the index date compared to controls (OR 2.81; 95% CI 1.45–5.44); however, in contrast, no significant difference in the adjusted odds of having previously received colonoscopy was observed between cases and controls among the oldest age group (≥60 years).

Conclusions: We concluded that there was an association between antecedent colonoscopy and CP/CPPS.

Introduction

Chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) is a condition of chronic pelvic pain among males and accounts for 80–95% of all symptomatic prostatitis cases.[1,2] Characteristics of patients with CP/CPPS include a high prevalence, frequent recurrences, and a substantially impaired quality of life;[3-6] however, the etiology, pathogenesis, and optimal treatment of CP/CPPS remain unknown. Previous reports suggested that trigger factors of the chronic pelvic pain process could be infections, chemical irritation, trauma, genetics, and psychological stress that result in subsequent neurological changes, such as brain microstructural changes, central sensitization, and pelvic floor spasms. A combination of alterations to the nervous system with endocrine, psychosocial, or immunological abnormalities leads to the chronic state of CP/CPPS.[4,7-10]

Colonoscopy is a common procedure for diagnosing a wide range of conditions and symptoms, including chronic abdominal or pelvic pain, neoplasms, and colitis. Numerous studies indicated that the colonoscopic examination itself may induce abdominal pain and transient bacterial infections.[11-13] Therefore, it is reasonable to consider colonoscopy itself as a trigger factor of symptoms in patients with CP/CPPS; however, according to our knowledge, no study has attempted to explore the association between previous colonoscopy and CP/CPPS. This case-control study attempted to examine the association between CP/CPPS and receipt of prior colonoscopy using a population-based database.

Methods

Database

We used the Taiwan Longitudinal Health Insurance Database 2005 (LHID2005) to retrieve the study sample. The LHID2005, which was created by the Taiwan National Health Research Institute, includes data on original medical claims of 1 million subjects who were randomly selected from the 2005 Registry for Beneficiaries (n=25.68 million)

of the Taiwan National Health Insurance (NHI) program. Everyone who was a beneficiary of the NHI program during any period in 2005 is in the population for random sampling. Data from the Taiwan NHI program have been used by many researchers in Taiwan to conduct studies.

This study was exempt from full review by the institutional review board of the National Defense Medical Center since the LHID2005 consists of de-identified secondary data released to the public for research purposes.

Selection of cases and controls

For cases, we first identified 5819 patients who had received a first-time diagnosis of CP/CPPS (ICD-9CM code 601.1) in an ambulatory care visit (outpatient department of a hospital or clinic) between January 2005 and December 2013. We then excluded those CP/CPPS patients who were aged <18 years old (n=13) in order to limit our study sample to the adult population. We further designated the date of receiving the first diagnosis of CP/CPPS as the index date for cases. In addition, we only included those patients who had received two or more CP/CPPS diagnoses, with at least one being made by a certified urologist in order to increase the CP/CPPS diagnostic validity. Ultimately, 3933 patients with CP/CPPS were included as cases.

Controls were also retrieved from the LHID2005. We first excluded all subjects who had a history of CP/CPPS since the beginning of the NHI program in 1995. Thereafter, we selected 3933 controls matched with cases by age group (18–29, 30–39, 40–49, 50–59, 60–69, and >69 years) and index year. We selected the controls by matching them to a given CP/CPPS case simply due to use of medical services in the same index year of that particular case. We further defined the first an ambulatory care visit occurring in the index year as the index date for the controls. In total, this study included 7866 sampled patients.

Exposure assessment

We identified cases that had received a colonoscopy examination by procedure code 28017C in the medical claims data during an ambulatory care visit. This study only counted colonoscopy cases if they had received colonoscopy within a period three years prior to the index date.

Statistical analysis

We used the SAS system (SAS System for Windows, vers. 8.2, SAS Institute, Cary, NC, U.S.) for statistical analyses. Chi-squared tests were conducted to explore differences in monthly income (NT$0–NT$15 840, NT$15 841–NT$25 000, ≥NT$25 001), geographical location (northern, central, eastern, and southern Taiwan), and urbanization level of the patient's residence (five levels, with 1 being the most urbanized and 5 being the least), as well as the prevalence of medical comorbidities (hypertension, diabetes, and hyperlip-

Table 1. Demographic characteristics of patients with chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) and controls in Taiwan (N=7866)

Variable	Patients with CP/CPPS (n=3933)		Controls (n=3933)		p
	Total no.	%	Total no.	%	
Age in years, mean (SD)	55.6 (16.4)		55.2 (16.7)		0.231
Monthly income					<0.001
NT $0–15 840	1427	36.3	1409	35.8	
NT $15 841–25 000	1310	33.3	1073	27.3	
≥NT $25 001	1196	30.3	1451	36.9	
Geographic region					<0.001
Northern	1867	47.5	2325	59.1	
Central	962	24.5	685	17.4	
Eastern	1011	25.7	843	21.4	
Southern	93	2.4	80	2.0	
Urbanization level					<0.001
1 (most urbanized)	1152	29.3	1572	40.0	
2	1106	28.1	994	25.3	
3	644	16.4	507	12.9	
4	567	14.4	435	11.1	
5 (least urbanized)	464	11.8	425	10.8	
Diabetes	639	16.3	582	14.8	0.076
Hypertension	1500	38.1	1347	34.3	<0.001
Hyperlipidemia	1102	28.0	813	20.7	<0.001

Note that the average exchange rate in 2015 was US$1.00≈New Taiwan (NT) $33. SD: standard deviation.

idemia) between cases and controls. We only counted these comorbidities if they were coded prior to the index date. This study also used conditional logistic regressions (conditioned on the study matching factors of age [on a 10-year basis] and index year) to calculate the odds ratio (OR) and 95% confidence interval (CI) for having previously received colonoscopy between cases and controls. The conventional p≤0.05 was used to assess statistical significance.

Results

Table 1 presents the distributions of demographic characteristics and medical comorbidities between cases and controls. After matching for age (on a 10-year basis) and index year, there was no significant difference in the mean ages between cases and controls (55.6 vs. 55.2 years; p=0.231); however, there were significant differences in monthly income, geographical location, and urbanization level of the patient's residence between cases and controls (all p<0.001). In addition, cases were more likely to have a higher prevalence of hypertension (38.1% vs. 34.3%; p<0.001) and hyperlipidemia (28.0% vs. 20.7%; p<0.001) than controls. No significant difference in the prevalence of diabetes between cases and controls was observed.

Table 2 shows the prevalence of a prior colonoscopy between cases and controls. We found that 349 (4.44%) of the 7866 sampled patients had received colonoscopy within the three years before the index date, including 223 (5.67%) cases and 126 (3.20%) controls (p<0.001). A conditional logistic regression analysis (conditioned on age [10-year basis]) and index year) revealed that the OR of having received colonoscopy within the three years before the index date was 1.77 (95% CI 1.42–2.23) for cases compared to controls after adjusting for patients' monthly income, geographical location, urbanization level, hyperlipidemia, and hypertension. Furthermore, Table 2 shows that cases were more likely to have received colonoscopy even within one (adjusted OR 2.03) or two years (adjusted OR 1.90) before the index date compared to controls.

Table 3 further presents the OR of receiving colonoscopy within the three years prior to the index date between cases and controls according to age group. We found that the youngest group of cases (<40 years) had the greatest adjusted OR for having received colonoscopy within the three years before the index date compared to controls (OR 2.81; 95% CI 1.45–5.44); however, in contrast, no significant difference in the adjusted odds of having previously received colonoscopy was observed between cases and controls among the oldest age group (≥60 years).

Discussion

This case-control study shows that 5.67% of patients with CP/CPPS had undergone a colonoscopy within the three years prior to the date of their diagnosis of CP/CPPS. A conditional logistic regression analysis showed that patients who had undergone colonoscopy were significantly associated with CP/CPPS (adjusted OR 1.77; 95% CI 1.42–2.23).

The mechanisms underlying the association between colonoscopy and CP/CPPS still remain unclear. Some patients with CP/CPPS are associated with pelvic floor tension myalgia. Injury to the pelvic floor from surgery or trauma, postural or gait abnormalities, skeletal asymmetry, or prolonged sitting can result in painful and hypertonic muscles that may trigger symptoms in patients with CP/CPPS.[11,12] Previous studies revealed that approximately 33% of patients reported at least one minor, transient bout of abdominal pain or bloating after colonoscopy.[13,14] This could have been caused by gas insufflation, direct trauma to the mucosa by biopsies, or looping and increasing the mucosal

Table 2. Prevalence and odds ratios (ORs) for chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) among the sampled patients

Variable	Total (N=7866)	Patients with CP/CPPS (n=3933)	Controls (n=3933)
Having received colonoscopy within 3 years before being diagnosed with CP/CPPS	349 (4.44%)	223 (5.67%)	126 (3.20%)
Crude OR (95% CI)	—	1.82* (1.45–2.27)	1.00
Adjusted OR[a] (95% CI)	—	1.77* (1.42–2.23)	1.00
Having received colonoscopy within 2 years before being diagnosed with CP/CPPS	254 (3.23%)	167 (4.25%)	87 (2.21%)
Crude OR (95% CI)	—	1.96* (1.51–2.55)	1.00
Adjusted OR[a] (95% CI)	—	1.90* (1.45–2.48)	1.00
Having received colonoscopy within 1 year before being diagnosed with CP/CPPS	142 (1.81%)	96 (2.44%)	46 (1.17%)
Crude OR (95% CI)	—	2.11* (1.48–3.01)	1.00
Adjusted OR[a] (95% CI)	—	2.03** (1.42–2.90)	1.00

The OR was calculated by a conditional logistic regression which was conditioned on 10-year age groups. [a]Adjustments were made for patient's monthly income, geographic region, urbanization level, hyperlipidemia, and hypertension.*p<0.001; **p<0.01. CI: confidence interval.

Table 3. Odds ratios (ORs) for chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) among patients, by age group

Variable	Age group (years)					
	<40		40–59		≥60	
	Patients with CP/CPPS	Controls	Patients with CP/CPPS	Controls	Patients with CP/CPPS	Controls
Having received colonoscopy within 3 year before being diagnosed with CP/CPPS, n (%)	31 (4.2)	13 (1.5)	99 (6.4)	43 (2.8)	93 (5.7)	70 (4.4)
Crude OR[a] (95% CI)	2.78* (1.45–5.36)	1.00	2.32** (1.61–3.34)	1.00	1.30 (0.94–1.79)	1.00
Adjusted OR[a] (95% CI)	2.81* (1.45–5.44)	1.00	2.30** (1.56–3.34)	1.00	1.28 (0.92–1.78)	1.00

The OR was calculated by a conditional logistic regression which was conditioned on 10-year age groups; [a]Adjustments were made for patient's monthly income, geographic region, urbanization level, hyperlipidemia, and hypertension;.*p<0.01; **p<0.001. CI: confidence interval.

permeability to colonic bacteria.[14,15] The high prevalence of prior performed colonoscopy in patients with CP/CPPS could be explained by colonoscopy itself, which may stimulate the pelvic floor resulting in pelvic floor muscle spasms.

In addition, previous studies reported that cytokines play a key role in the inflammatory response of CP/CPPS. These cytokines, including Interleukin-1(IL-1), IL-6, IL-8, IL-10, and TNF-alpha, significantly increased in seminal plasma in men with CP/CPPS when compared with the normal group.[16,17] Some studies also indicated that IL-6 and IL-8 are two of major human cytokines that were rapidly induced in intestinal epithelial cells synergistically with IL-1 or TNF-alpha after mucosal injury, inflammation, or stimulation for repairing damaged mucosa.[18,19] Colonoscopy with biopsy or polypectomy is associated with increased risk of mucosal injury and complications.[20,21] Therefore, colonoscopy with therapeutic procedures itself may increase IL-6 and IL-8 and contribute to the pathophysiology of CP/CPPS.

Apart from direct irritation to the pelvic floor by colonoscopy, infection with atypical bacteria or a sexually transmitted disease has been considered another trigger factor in some patients with CP/CPPS.[4-8,22,23] Previous studies suggested that patients who received colonoscopy, with or with a polypectomy, were complicated with transient bacteremia in approximately 4% of procedures, with a range of 0–25%.[14,24] Therefore, colonoscopy complicated with bacteremia may represent a potential risk factor for CP/CPPS. The bacteremia theory is also plausible in light of the decreasing magnitude of the association between CP/CPPS and colonoscopy with an increasing interval between the first-time CP/CPPS diagnosis and the timing of receiving colonoscopy (adjusted OR 2.03 within one year; adjusted OR 1.90 within two years; adjusted OR 1.77 within three years).

Even though some of the literature has showed that CP/CPPS is an important health issue in elder population,[25-28] the present study failed to observe such an association between CP/CPPS and previous colonoscopy in the elderly (≥60 years old). According to anatomical and physiological changes of the prostate in the elderly, a portion of the pathogenesis of prostate inflammation differs from that in young adults. Benign prostate hyperplasia (BPH) is considered a disease of the elderly, and it is estimated that over 70% of men older than 60 years of age have this disease.[29] In contrast, CP/CPPS is the most common urological diagnosis in male patients under the age of 50 years.[30,31] Previous studies reported that the clinical syndromes of prostatitis and BPH can coexist, but CP/CPPS symptoms improve with age and time.[32,33] Physicians may have difficulty in clinically distinguishing prostatitis from BPH in the older male population.[34] This may explain the lack of a significant association between CP/CPPS and previous colonoscopy in the elderly in the present study.

This study has several strengths. First, a population-based dataset with a large sample size was used to explore the association between colonoscopy and subsequent CP/CPPS during the study period. The large sample size afforded a considerable statistical advantage in detecting a real difference in the prevalences of prior colonoscopy between patients with and without CP/CPPS. Second, the diagnosis of CP/CPPS had a high validity since we only accepted cases that had been diagnosed twice, at least once by a certified urologist.

Nevertheless, the results of this study need to be seen in the light of several limitations. The first limitation is that physicians do not routinely identify the histology of prostatitis in Taiwan. Second, the LHID2005 provides no information on the National Institutes of Health (NIH) category of prostatitis, bacterial species, or white blood cell count of prostatic secretion, semen, or urine specimens, and there are no records of voiding or sexual conditions. Thus, the dataset used in this study did not allow us to differentiate CP/CPPS from chronic bacterial prostatitis, which accounts for only 4.2% of men with prostatitis syndrome.[2] All of these may have influenced the pathogenesis or mechanism of CP/CPPS. Third, the CP/CPPS diagnoses in this study is based on claims data and ICD-9CM code. The diagnoses might be less precise than those made according to standardized diagnostic examinations (including histology and microculture of urine or semen samples). Finally, there may have been a surveillance bias, in that patients who received colonoscopy were more likely to have frequent outpatient clinic visits, which may have led to early detection of CP/CPPS.

Conclusion

Despite the aforementioned limitations, this study demonstrated an association between colonoscopy and CP/CPPS. We suggest that urologists be alert in suspecting CP/CPPS for chronic pelvic pain in patients who previously received a colonoscopy.

Competing interests: The authors report no competing personal or financial interests.

This paper has been peer-reviewed.

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