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Factors Associated with Lower Urinary Tract Symptoms in Thai Women with Uterine Leiomyomas

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ABSTRACT

Objectives: To identify the associated factors between uterine leiomyoma and lower urinary tract symptoms (LUTS) in Thai women.

Materials and Methods: One hundred and thirty eightwomen presenting with uterine leiomyoma at gynecologic out-patients clinic, King Chulalongkorn Memorial Hospital during August, 2014-March, 2015 were included. International Consultation on Incontinence Questionnaire-Female Lower Urinary Tract Symptoms Module (ICIQ-FLUTS) questionnaires were completed by all patients to identify the presence of LUTS. The LUTS case was defined by the present of any ICIQ-FLUTS questions score more than or equal to 2. The case: control ratio was 1:1. The controls were matched at the same day or within 3 days of the case. The patients' characteristics and the ultrasonographic data were collected.

Results: Among 138 leiomyoma patients were participated (69 cases and 69 controls). The mean age was 43.52 ± 7.4 and 44.86 ± 7.4 years respectively. There was no difference in body mass index and menopausal status. By univariate comparison, the mean of the total uterine volume and the largest leiomyoma volume were significantly different between groups. After the multivariate analysis, only the uterine volume more than 400 cm3 (odds ratio (95% confidence interval) = 2.44 (1.03-5.75)) and the largest leiomyoma volume more than 14 cm^3 (odds ratio (95% confidence interval) = 2.53 (1.02-6.37)) were significantly associated with LUTS.

Conclusion: Uterine volume ≥ 400 cm^3 and largest leiomyoma volume ≥ 14 cm^3 were the risk factors of LUTS in Thai women with leiomyoma.

Keywords: leiomyoma, uterine fibroid, lower urinary tract symptoms, LUTS, ICIQ-FLUTS.

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ปัจจัยที่เกี่ยวข้องกับอาการผิดปกติของทางเดินปัสสาวะส่วนล่างในสตรีไทยที่มีเนื้องอกของมดลูก

สุชาดา เอื้อจงมานี, สุวิทย์ บุณยะเวชชีวิน

บทคัดย่อ

วัตถุประสงค์: *เพื่อศึกษาถึงความสัมพันธ์ของปัจจัยในเนื้องอกมดลูกที่สามารถทำนายการเกิดอาการผิดปกติของอาการทางเดินปัสสาวะส่วนล่าง*

วัสดุและวิธีการ: *ทำการศึกษาในสตรีไทย 138 คน ที่มีเนื้องอกมดลูกที่มารับการรักษาที่คลินิกนรีเวชกรรม โรงพยาบาลจุฬาลงกรณ์ ระหว่างเดือนสิงหาคม พ.ศ.2557 ถึง มีนาคม พ.ศ.2558 ผู้ป่วยจะทำการตอบแบบสอบถาม International Consultation on Incontinence Questionnaire-Female Lower Urinary Tract Symptoms Module (ICIQ – FLUTS) เพื่อสอบถามอาการทางเดินปัสสาวะส่วนล่าง โดยผู้ที่มีคะแนนของแบบสอบถามในข้อใดข้อหนึ่งมากกว่าหรือเท่ากับ 2 จะจัดอยู่ในกลุ่มที่มีอาการผิดปกติของทางเดินปัสสาวะส่วนล่าง โดยสัดส่วน case: control คือ 1:1. ทำการคัดเลือกกลุ่มควบคุมในวันเดียวกัน หรือไม่เกิน 3 วันจากวันที่คัดเลือกกลุ่มที่มีอาการทางเดินปัสสาวะส่วนล่าง พร้อมทั้งทำการบันทึกข้อมูลพื้นฐานของผู้ป่วยและผลการตรวจอัลตราซาวด์*

ผลการศึกษา: *มีจำนวยผู้ป่วยเนื้องอกมดลูก 138 ราย (กลุ่มที่มีอาการ 69 ราย และกลุ่มควบคุม 69 ราย) ค่าเฉลี่ยของอายุคือ 43.52 ± 7.4 และ 44.86 ± 7.4 ปี ตามลำดับ ไม่พบความแตกต่างของดัชนีมวลกาย และภาวะการหมดประจำเดือน จากการเปรียบเทียบแบบ univariate พบว่าค่าปริมาตรของมดลูก และปริมาตรของขนาดก้อนเนื้องอกที่ใหญ่สุด แตกต่างกัน จากการเปรียบเทียบแบบ multivariate พบว่า ค่าปริมาตรของมดลูกมากกว่า 400 ซม.^{3} (odds ratio (95% confidence interval) = 2.44 (1.03-5.75)) และปริมาตรของขนาดก้อนเนื้องอกที่ใหญ่ มากกว่า 14 ซม.^{3} (odds ratio (95% confidence interval) = 2.53 (1.02-6.37)) สัมพันธ์ต่อการเกิดอาการผิดปกติของทางเดินปัสสาวะส่วนล่าง*

สรุป: *จากการเปรียบเทียบแบบ multivariate พบว่า ค่าปริมาตรของมดลูกมากกว่า 400 ซม.^{3} (OR (95% CI) = 2.44 (1.03-5.75)) และปริมาตรของขนาดก้อนเนื้องอกที่ใหญ่ มากกว่า 14 ซม.^{3} (OR (95%CI) = 2.53 (1.02-6.37)) สัมพันธ์ต่อการเกิดอาการผิดปกติของทางเดินปัสสาวะส่วนล่าง*

คำสำคัญ: *เนื้องอก, เนื้องอกในมดลูก, อาการของทางเดินปัสสาวะส่วนล่าง, LUTS, ICIQ-FLUTS*

Introduction

Uterine leiomyoma is the most common benign tumor of smooth muscle of the uterus[1]. The exact prevalence of uterine leiomyoma is unknown. Estimate range is about 60-80 percent in African-American women, which higher than Caucasian women (40-70 percent)[2]. For Asian women, there was report of the overall prevalence of uterine leiomyoma up to 20 percent and about 40 percent was identified in women older than 40 years old[3]. In Thailand, the incidence of the leiomyoma in the total abdominal hysterectomy specimen was 60 % and 18.6 % were associated with adenomyosis[4].

Patients with uterine leiomyomas are usually detected incidentally without symptoms or with symptoms such as abnormal vaginal bleeding, pelvicpain, infertility[7-9], as well as the compressive symptoms which can be divided into two groups, 1) lower urinary tract symptoms (LUTS) such as urinary frequency, nocturia and 2) constipation or difficult defecation. There is evidence that the reduction in size of the uterine leiomyoma volume about 35% by uterine arteries embolization can reduce the symptom of urinary frequency up to 68%[5]. The reduction in size of uterine leiomyomas with GnRH can also decrease the urinary frequency, nocturia and urgency[6]. These evidences suggest the association between uterine size and LUTS. However, there are few reports that specified the details of leiomyoma and the correlations to the LUTS[5, 8], and there is no study about the leiomyoma factors used to predict the presence of LUTS. The aim of this study is to identify factors of uterine leiomyoma and its association to the LUTS in Thai women.

Materials and Methods

A case-control study designed was conducted. After the IRB approval, 138 Thai women who were diagnosed as having uterine leiomyoma by pelvic examination and ultrasonography at Gynecologic clinic at King Chulalongkorn Memorial Hospital (KCMH) during August 2014-March 2015 were recruited. Inclusion criteria were women age 18 and older who diagnosed as having the uterine leiomyoma by clinical symptoms, pelvic examination and ultrasonography. The exclusion were pregnancy, diagnosis of the other concurrent pelvic mass, history or current gynecologic malignancy, history and treatment of a lower urinary tract disorders, chronic urinary tract infection, pelvic organ prolapse, history of pelvic radiation or endocrine disease that can cause polyuria (such as diabetes mellitus, diabetes insipidus). The criteria of leiomyoma diagnosed by ultrasonography were: presence of the well defined, focal masses and solid hypoechoic with posterior acoustic shadowing[10]. The transvaginal or transabdominal ultrasonographic data were collected from the outpatient record (OPD card) if the ultrasonographies were performed within 6 months before recruitment. If not, the ultrasonography was performed at the recruitment day. The total uterine volume, leiomyoma location, size, and number were recorded. Volume of uterus and largest leiomyoma were calculated using the formula for an ellipsoid shape (volume = 0.5236 x length x width x height) and recorded in cubic centimeters (cm^3)[11]. Location of uterine leiomyoma was grouped as anterior, posterior and others. The LUTS were diagnosed as the recommended definition by the International continence society (ICS) terminology[12]. These included eight symptoms (nocturia, urgency, frequency, stress urinary incontinence, urge incontinence, straining, difficulty emptying bladder and delayed urine flow)[12].

LUTS cases were identified by the International Consultation on Incontinence-Female Lower Urinary Tract Symptoms Module questionnaire (ICIQ – FLUTS)[13]. TheThai versions of the ICIQ – FLUTS questionnaires were completed by all patients. The ICIQ-F LUTS (Thai version) was already test for reliability and validity (test retest reliability = 0.8, Alpha cronbach = 0.9) from our pilot study in 130 cases. This questionnaire contained 13 questions. The LUTS cases were defined by the present of any ICIQ-FLUTS questions score equal or more than 2. All cases with LUTS were asked to perform the 3 days voiding diary to confirm the presence of LUTS. The case:control ratio was 1:1. The controls were selected as the next

available after each case recruitment at the same day or within 3 days of the cases. The nocturia, urgency, and urinary frequency were confirmed by voiding diary as these following characteristics according to the ICS definition[12].

Nocturia: presence of night time urination more than one.

Urgency: presence of uninhibited or delayed feeling to void at least 1 episode of urgency with or without incontinence in 3 days.

Urinary frequency: presence of more than 8 times urination per day.

The patients' characteristics and the ultrasonographic data were collected at the day of recruitment. The sample size calculation was done using the previous data of the factors of the uterine size more than 400 cm^3 that related to LUTS (OR= 3.3) from the previous study of Christina et al[14]. With the significant level less than or equal to 0.05, power of 80%, case per control ratio of 1:1. The sample size per group was 69 cases per group.

For statistical analysis, using SPSS version 17.0 with independent t test and a Mann Whitney U test for continuous data and Chi squared test for categorical data. And then multiple logistic regressions were used for odd ratio calculation.

Results

There was no significant difference between demographic data in both groups (Table 1). The median (Interquartile range: IQR) was used for data presentation as the data was not normally distributed. We found that the LUTS in our study comprised of nocturia 42 cases (60.86%), difficult emptying bladder 36 cases (52.2%), urinary urgency 31 cases (44.9%), urinary frequency 17 cases (24.6%), delayed urine flow 9 cases (13.0%),stress urinary incontinence 8 cases (11.5%), urge urinary incontinence 6 cases (8.6%), and straining 6 cases (8.6%).

For leiomyoma factors, the median (IQR) of uterine volume in LUTS group was statistically significant higher than control group (263.33 (137.28-538.87) versus 142.02(83.59-283.29) (Table 2). The median (IQR) of the largest leiomyoma volume (cm^3) in LUTS group was also significantly higher than control group (103.44 (33.05-286.82) versus 49.85 (9.55-125.61) (Table 2). The location, type and number of leiomyoma were not significantly different in both group (Table 2). By using multivariate logistic regression analysis, the uterine volume ≥ 400 cm^3 and largest leiomyoma volume ≥ 14 cm^3, odd ratio (95% CI) = 2.44 (1.03-5.75) and 2.53 (1.02-6.37) respectively, were the significant factors of LUTS (Table 3).

Table 1. Demographic data.

	LUTS group (N = 69)	**No LUTS group (N = 69)**	**p value**
Mean ± SD			
Age (years)	43.52 ± 7.4	44.86 ± 7.4	0.855
BMI (kg/m^2)	24.76 ± 3.1	23.84 ± 4.14	0.454
Premenopause	60 (86.95 %)	58 (84.05 %)	0.854
Postmenopause	9 (13.04 %)	11 (15.94 %)	0.655
Parity	1 (0-4)	0 (0-4)	0.728
Delivery route			
- Vaginal	0 (0-4)	0 (0-4)	0.333
- Cesarean	0 (0-2)	0 (0-2)	0.533
n (%)			
History of pelvic surgery	6 (8.69)	6 (8.69)	1.000

Table 2. Univariate analysis of the Leiomyoma factors.

	LUTS group (N = 69)	No LUTS group (N = 69)	p value
Median (IQR)			
Uterine volume (cm^3)	263.33 (137.28-538.87)	142.02 (83.59-283.29)	0.001*
Largest leiomyoma volume (cm^3)	103.44 (33.05-286.82)	49.85 (9.55-125.61)	0.001*
n (%)			
Number of myoma			
- One	37 (53.62 %)	38 (55.10 %)	0.816
- Two	14 (20.30 %)	11 (15.09%)	0.549
- Three or more	18 (26.10 %)	20 (29.00 %)	0.746
Type of largest myoma			
- Submucous	1 (1.40 %)	2 (2.90 %)	0.564
- Intramural	46 (66.70 %)	48 (69.60 %)	0.837
- Subserous	22 (31.90 %)	19 (27.50 %)	0.639
Location of myoma			
- Anterior	23 (33.30 %)	22 (31.90 %)	0.881
- Posterior	19 (27.50 %)	24 (34.80 %)	0.446
- Other	27 (39.10 %)	23 (33.30 %)	0.572

Table 3. Multivariate analysis of the Leiomyoma factors.

	Odds ratio	95% CI	p value
Uterine volume ≥ 400 cm^3	2.44	(1.03-5.75)	0.04
Largest leiomyoma volume ≥ 14 cm^3	2.53	(1.02-6.37)	0.04

Discussion

Lower urinary tract symptoms are common presenting symptom of uterine leiomyoma, and are one of the indications for treatment. Not all women with leiomyoma presents with LUTS. There are few studies report about the relationship between any lower urinary tracts symptom and leiomyoma[14-18]. There were reports of the cut off level of more than 12 weeks size uterus[14] and largest diameter of leiomyoma nodule of 3 cm^3[17] related to the LUTS in women with leiomyoma uteri. But there is no study defining the risk factors for predicting LUTS symptoms in women with leiomyoma. Our study is the first case-control study that established the leiomyoma factors that can predict the LUTS. We found that the total uterine volume more than 400 cm^3 and largest leiomyoma volume of greater than 14 cm^3 significantly affect the symptoms of lower urinary tract. The reason that we

choose these cut off value, the uterine volume of 400 cm^3, came from the evidence of the study of Goldstein et al[11] (the uterine 12 weeks of gestation had the uterine volume equivalent to 383±29 cm^3[11], so we choose the round number of 400 cm^3 to be the cut off level. And the cut off volume of the largest leiomyoma nodule of 14 cm^3 came from the approximation calculation of the leiomyoma nodule with diameter of 3 cm^3 (the ellipsoidal shape volume formula calculation). We believe that the volume calculation form three dimension measurement is more reliable than using only one dimension to be the cut off value.

Our finding is similar to prior study that reported the uterine size greater than 12 weeks sizes affect LUTS[14]. We found that the number of leiomyoma, type and location of the tumor don't affect on any symptoms of the urinary system. This differs from the study of Candace et al that report of the anterior location of the dominant uterine fibroid was associated with worsening voiding dysfunction[17]. The results from our study can help physicians select the cases that are at the higher chance of developing the LUTS and plan for close follow up of the lower urinary tract symptoms. Moreover these finding are useful information for counseling in leiomyoma patients who are concerned about the risk of developing the LUTS. This study can help giving more information for physicians for taking care of patients in Thai women with leiomyoma.

The strengths of this study – this is the first case control study to identify the factors of uterine leiomyoma and the association to the lower urinary tract symptom. We used the standard questionnaire, ICIQ-FLUTS, to diagnose lower urinary tract symptoms and use the 3 days voiding diary for confirmation. Our study has no time bias because the data from both group were collected at the same or similar period of the sample recruitment.

However, our study focuses at the leiomyoma factors that can have the effect on urinary symptoms. Some other non-leiomyoma factors are not included in this study. For other limitation, we collected patients' data from the outpatient record (OPD card) with inclusion criteria that the ultrasonographies had to perform within 6 months before recruitment. This may cause some deviated of data due to multiple investigator and duration from latest ultrasound. Further study to find out the other non-leiomyoma factors that may be the risk factors for LUTS in Thai women is advocated.

Conclusion

We found total uterine volume more than 400 cm^3 and largest leiomyoma volume greater than 14 cm^3 associated with the lower urinary tract symptoms.

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Potential conflicts of interest

The authors declare no conflict of interest.

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