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Clinical profiles of 710 premenopausal women with adenomyosis who underwent hysterectomy

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Abstract

Aim: The aim of this study was to determine the frequency of various symptoms and their associated characteristics in women with adenomyosis who underwent hysterectomy, and to determine which symptoms are likely to go with which others in these patients.

Material and Methods: In 2007, 1697 consecutive patients underwent hysterectomy in our hospital. Among them, 734 (43.3%) were histologically confirmed to have adenomyosis, and 710 of them were premenopausal. The medical charts of all 734 patients were retrieved, and their demographic, clinical information and post-operative findings were recorded. We used the Verbal Descriptor Scale to measure the preoperative severity of dysmenorrhea. The Apriori Algorithm was used for mining the association of different symptoms.

Results: Among the 710 premenopausal patients, only 4.5% of them had no symptoms. Dysmenorrhea was the most common complaint, occurring in 81.7% of patients. Dysmenorrhea co-occurred most frequently with menorrhagia. The presence of adhesion, presence of endometriosis, complaint of menorrhagia, longer duration of disease, gravidity, palpable pain during pelvic examination, and diffuse adenomyosis were positively associated with the severity of dysmenorrhea. Age, severity of dysmenorrhea, and complaint of metrorrhagia were positively associated with the risk of menorrhagia.

Conclusions: Dysmenorrhea is the most common complaint in women with adenomyosis, which often goes with that of menorrhagia. Adenomyosis often co-occurs with endometriosis and leiomyomas. Various factors are associated with the risk of having different symptoms.

Key words: adenomyosis, comorbidity, dysmenorrhea, hysterectomy, menorrhagia.

Introduction

Adenomyosis, characterized by the presence of endometrial glands and stroma deep within the myometrium, is a fairly common gynecologic disorder with a poorly understood pathogenesis.[1] Its presenting symptoms in women with symptomatic adenomyosis include menorrhagia, dysmenorrhea, and subfertility.[2] While adenomyosis used to be called endometriosis *interna*[3] and was found fairly recently to be associated with pelvic endometriosis,[4] its exact prevalence, incidence, and causative factors are still poorly understood, let alone its pathogenesis;[5] the symptomatology of adenomyosis is also still vague and appears to be poorly defined due to the lack of a consensus definition and reliable non-invasive diagnostic procedure.[6,7] Perhaps befittingly, adenomyosis has been viewed as an 'enigma'.[8]

For those patients with a histological diagnosis of adenomyosis, made after hysterectomy, there are still enormous variations in the spectrum of symptomatology and severity. It is reported that a sizeable portion

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of patients with adenomyosis are asymptomatic,[9] but little is known about which factors, if any, determine the presence or absence of a particular symptom, such as dysmenorrhea and its severity when present. In an 18-center study of 820 women with benign conditions who underwent hysterectomy, it is found that women with adenomyosis reported more frequently dysmenorrhea and chronic pelvic pain (CPP), but not dyspareunia.[10] While it is known that dysmenorrhea, menorrhagia, CPP, and metrorrhagia can all be complaints from women with adenomyosis, it is unclear which symptom is likely to go with which others.

In this study, from a cohort of 734 consecutive women who underwent hysterectomy and who had histologically confirmed adenomyosis, we sought to determine the frequency of dysmenorrhea, menorrhagia, CPP, and metrorrhagia, the factors associated with the presence of menorrhagia, metrorrhagia, CPP, and the uterus size. We also attempted to determine which symptom is likely to go with which others using an association rule mining method.

Methods

Patients

During the entire year of 2007, 1697 patients underwent abdominal, vaginal or laparoscopic hysterectomy with/without salpingo-oophorectomy at Shanghai OB/GYN Hospital. Among them, 734 (43.3%, 95% confidence interval [CI] = 40.9–45.6%) were histologically confirmed to have adenomyosis. Inclusion criteria were histologically confirmed adenomyosis. The premenopausal status was defined as the occurrence of at least one menstrual period in the 12 months before hysterectomy. Patients with malignant gynecological diseases were excluded.

The medical charts of all 734 patients were compiled and reviewed by the authors (X.L.L. and X.S.L.), and the following details about patients were retrieved and recorded: age, reproductive history, preoperative symptoms, uterus size (measured by ultrasonography), postoperative findings, such as the presence of peritoneal and ovarian endometriosis, and other benign gynecological conditions, such as leiomyomas. The preoperative severity of dysmenorrhea was measured by the Verbal Descriptor Scale as none, mild, moderate, or severe. Abnormally heavy or prolonged menstruation (>7 days) was considered to be menorrhagia, and uterine bleeding occurring at completely irregular intervals (<21 days or >35 days) was considered to be metrorrhagia. History of cesarean section, if any, was recorded. The duration of the disease, that is, the duration of time interval from the appearance of adenomyosis-related symptoms to the diagnosis of adenomyosis, also was recorded.

All histological specimens were evaluated by eight experienced gynecologic pathologists using identical criteria. Namely, the diagnosis was based on the presence of endometrial glands and stroma in the myometrium (>3 mm). In particular, the presence of endometrial glands and stroma distributed locally as nodes or conglobation in the myometrium was diagnosed as focal adenomyosis, while cases in which they were distributed diffusely in the myometrium were diagnosed as diffuse adenomyosis. The uterus size was measured by ultrasonography before surgery with three parameters, and the uterus size was calculated using the formula $v = \pi D_1 D_2 D_3/6$, where D_1 = the distance from fundus to the internal os of the cervix, D_2 = transverse diameter at the level of the cornua, and D_3 = anteroposterior diameter at the level of the cornua.

This study was approved by the institutional ethics review board of Shanghai OB/GYN Hospital.

Statistical analysis

The difference in frequency between two groups was evaluated using Fisher's exact test. The comparison of means between the two groups was made using Wilcoxon's test. Spearman's correlation coefficient was used when one or both variables were ordinal data.

To see which factors were associated with the severity of dysmenorrhea, we first coded the severity of dysmenorrhea as 0, 1, 2, and 3, depending on whether the patient complained of no, mild, moderate or severe dysmenorrhea. We then used a proportional odds model with the logistic link. This model assumes, implicitly, that the data were ordered categorical data, with an underlying order (scale of severity) in the data.[11] To see which factors are associated with the risk of menorrhagia, metrorrhagia, or CPP, a logistic regression model was used. A binary logistic regression model was used to identify which factors were associated with the risk of menorrhagia, metrorrhagia and CPP.

To see which symptom (or complaint) item(s) go with which other symptom(s), we used the Apriori Algorithm as a tool for association rule mining. Association rule mining[12] aims at discovering frequently co-occurring items, called frequent item sets, from a large number of data samples above a certain count threshold (called minimum support).[13] The support of

an item set is defined as the number of data samples where all the items in the item set co-occur. In our case, there were four major complaints: dysmenorrhea, menorrhagia, metrorrhagia, and CPP, which were likely to co-occur frequently among some patients and could be thus identified by association rule mining. Apriori Algorithm proposed by Agrawal *et al*. is a classical approach to determining frequent itemsets.[12]

P-values of less than 0.05 were considered statistically significant. All computations were made with R 2.15.2.[14] R packages *arules* and *stats* were used.

Results

Among the 734 patients who underwent hysterectomy for adenomyosis, 24 (3.3%) of them were menopausal while the remaining 710 (96.7%) patients were premenopausal. The age of the menopausal patients ranged from 49 to 75 years, with a median age of 52 years. The age of the premenopausal patients ranged from 21 to 55 years, with a median age of 45 years. One 21-year-old patient had a rudimentary horn of uterus and the total resection was performed due to pathologically confirmed adenomyosis. The uterus size in the post-menopausal group was significantly smaller than that in the premenopausal group ($P = 0.02$).

Among the premenopausal patients, most of them (83.8%, 95%CI = 81.0–86.6%) had diffuse adenomyosis. Age was negatively correlated with the severity of dysmenorrhea (Spearman's r = –0.28, $P = 2.3 \times 10^{-14}$), but the duration of disease was positively correlated with the severity (Spearman's r = 0.41, $P = 2.2 \times 10^{-16}$). The characteristics of the remaining premenopausal patients are listed in Table 1.

Table 1 Characteristics of the 710 premenopausal patients who received hysterectomy due to adenomyosis

Variable name	Summary statistics
Age (years)	Mean = 44.8 SD = 4.8 Range = 21–55 Median = 45
Duration of the symptoms (years)	Mean = 5.6 SD = 5.8 Range = 0.1–31 Median = 4
Gravidity	
0	24 (3.4%)
1	133 (18.7%)
2	220 (31.0%)
3	183 (25.8%)
4	99 (13.9%)
5	31 (4.4%)
≥6	20 (2.8%)
Parity	
0	40 (5.6%)
1	594 (83.7)
2	60 (8.5)
3	11 (1.5%)
4	5 (0.7%)
Cesarean section	
No	585 (82.4%)
Yes	125 (17.6%)
Severity of dysmenorrhea	
None	130 (18.3%)
Mild	81 (11.4%)
Moderate	173 (24.4%)
Severe	326 (45.9%)
Menorrhagia	
No	358 (50.4%)
Yes	352 (49.6%)
Chronic pelvic pain	
No	594 (83.7%)
Yes	116 (16.3%)
Metrorrhagia	
No	482 (67.9%)
Yes	228 (32.1%)
Type of adenomyosis	
Focal	115 (16.2%)
Diffuse	595 (83.8%)

Frequency of symptomatology

There were four major complaints in the 710 premenopausal patients: dysmenorrhea, menorrhagia, CPP, and metrorrhagia. Among these patients, 580 (81.7%, 95%CI = 78.8–84.6%) of them complained of dysmenorrhea, and 352 (49.6%, 95%CI = 45.8–53.3%), 228 (32.1%, 95%CI = 28.6–35.6%) and 116 (16.3%, 95%CI = 13.5–19.1%) complained of menorrhagia, metrorrhagia and CPP, respectively. The proportion of women complaining of dysmenorrhea was significantly higher than the reported proportion of women with laparoscopically diagnosed endometriosis who complained of pelvic pain (64.4%, $P < 0.00001$).[15] Some patients had more than one complaint, and only 32 (4.5%) patients were free of any of the four complaints. Among those patients who complained of dysmenorrhea, 81 (14.0%), 173 (29.8%), and 326 (56.2%) of them complained of mild, moderate and severe dysmenorrhea.

Dysmenorrhea was found to be frequently associated with other complaints. In fact, only 35.9% of the 580 patients or 29.3% of the entire cohort of premenopausal patients complained of dysmenorrhea alone. The frequency of having any of these complaints alone or in combination is shown in Figure 1. It can be seen

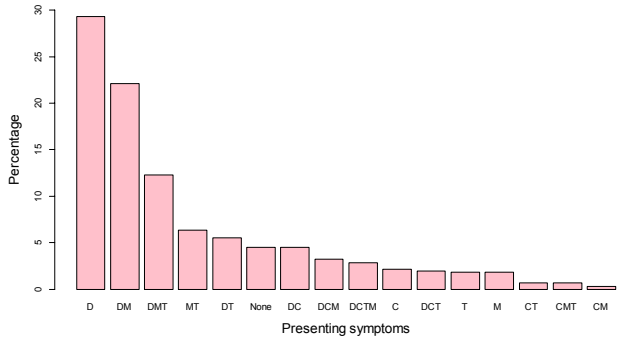

Figure 1 Bar plot of symptom frequencies, in descending order, among the 710 premenopausal patients. C, chronic pelvic pain; D, dysmenorrhea; M, menorrhagia; T, metrorrhagia.

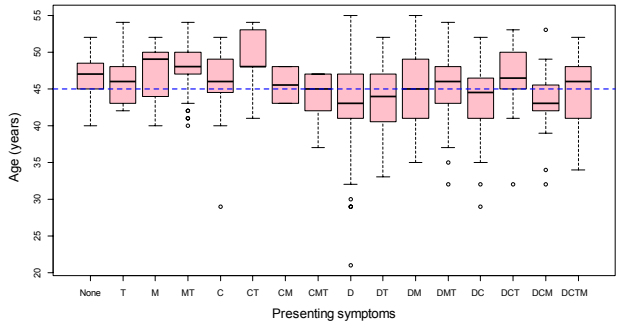

Figure 2 Box plot of age distribution among premenopausal patients who complained of different symptom combinations. The dashed line represents the median age of the entire cohort.

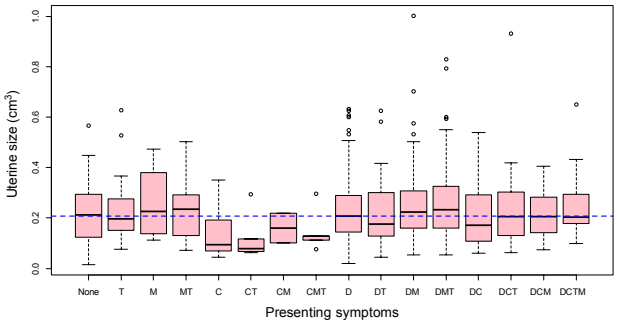

Figure 3 Box plot of uterus size among premenopausal patients who complained of different symptom combinations. The dashed line represents the median uterus size of the entire cohort.

that only 1.8% each of the patients complained of menorrhagia or of metrorrhagia alone. The proportion of patients complaining of CPP and menorrhagia was even lower (0.3%), and so was that of patients complaining of CPP and metrorrhagia (0.7%) and of CPP, menorrhagia and metrorrhagia collectively (0.3%).

As expected, the patients without any complaints were significantly older (median = 47 years, range = 40–52, vs median = 45, range = 21–55, $P = 0.028$; Fig. 2). Although these patients had a higher percentage (96.9% vs 94.2%) of having at least one child than those who had at least one complaint, the difference did not reach statistical significance ($P = 1.0$, Fisher's exact test). There was no difference in uterus size between the two groups, either ($P = 0.53$; Fig. 3).

From Figure 3, it seemed that patients complaining of CPP had smaller uteri. Indeed, patients complaining of CPP had a median uterus size of 180.6 cm^3, which was about 15.3% smaller than that in patients without CPP ($P = 0.0015$).

Co-occurrence of symptoms

Using the Apriori Algorithm, we attempted to find which complaint tended to go with which others. With a support of 0.2 and a confidence of 0.8, we found that menorrhagia went with dysmenorrhea with a confidence of 0.82 and a support of 0.40. Most notably, dysmenorrhea alone had a support of 0.82. That is, in women who had undergone hysterectomy, dysmenorrhea was the most frequent complaint, and the complaint of menorrhagia and, to a lesser extent, metrorrhagia, was often associated with the complaint of dysmenorrhea. These results agree very well with what Figure 1 reveals.

Co-occurrence with endometriosis and/or leiomyomas

In the 710 premenopausal women with adenomyosis, we found that 343 (48.3%), 158 (22.3%), 129 (18.2%), and 80 (11.3%) patients, respectively, had adenomyosis alone, adenomyosis and endometriosis, adenomyosis and leiomyomas, and all three conditions combined (Fig. 4a). Among the four co-morbidity groups, the uterus size distribution was significantly different: the patients with a co-occurrence of endometriosis had smaller uterus size while those with a co-occurrence of myoma had a larger uterus ($P = 8.1 \times 10^{-7}$; Fig. 4b). Similarly, the age distribution in the four groups was also significantly different: the patients with myoma and adenomyosis were older ($P = 8.0 \times 10^{-5}$; Fig. 4c). The duration of symptoms was also different among the four groups: the patients with endometriosis had a

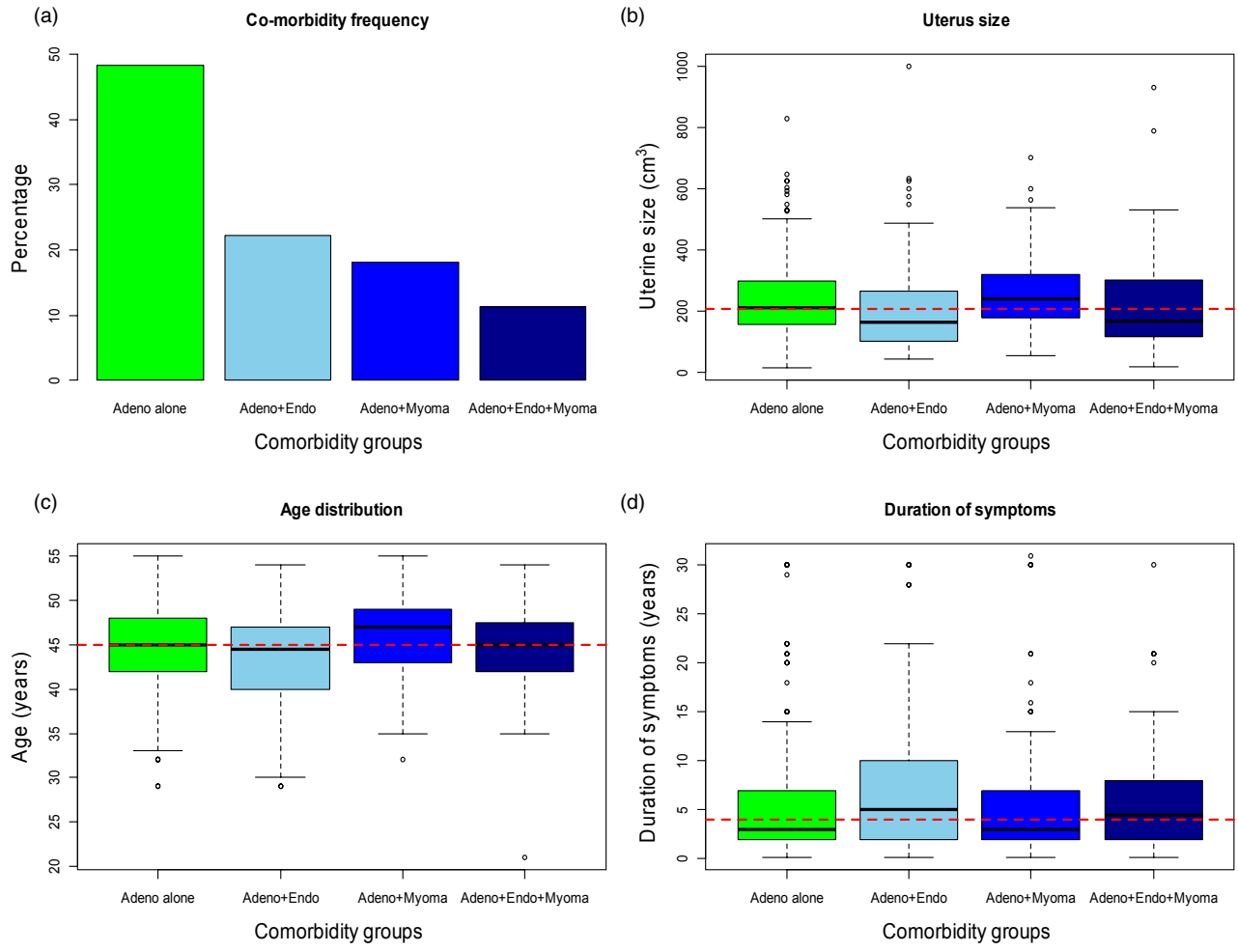

Figure 4 (a) Bar plot of frequency of co-morbidity with endometriosis and/or leiomyomas. (b) Box plot of uterus size in different co-morbidity groups. (c) Box plot of age in different co-morbidity groups. (d) Box plot of duration of symptoms in different co-morbidity groups. In (b–d), the dashed line represents the median of the entire cohort of premenopausal patients. Adeno, adenomyosis; Endo, endometriosis; Myoma, uterine myoma.

longer duration ($P = 0.0009$; Fig. 4d). Further analysis indicated that patients with a co-occurrence of endometriosis had significantly longer duration of complaints than those without (median = 5 years vs 3 years; $P = 0.0008$). In contrast, there was no difference in duration of complaints between patients with and without a co-occurrence of leiomyomas ($P = 0.98$).

Among 238 (33.5%) patients who also had endometriosis, 147 (61.8%) of them had it in a single location, with ovarian endometrioma being the most common (61.2%). Seventy-four (31.1%) and 17 (7.1%) patients had endometriosis at two and three locations, respectively. Overall, focal adenomyosis was found to be associated with higher proportion of endometriosis ($P = 1.4 \times 10^{-7}$), especially with ovarian endometrioma and peritoneal endometriosis (Table 2).

Factors associated with the severity of dysmenorrhea

We found that the severity of dysmenorrhea was inversely correlated with patients' age (Spearman's correlation coefficient r = –0.28, $P = 2.3 \times 10^{-14}$) and also with the parity (Spearman's r = –0.12, $P = 0.0009$). That is, the younger age or lower parity was associated with the complaint of more severe dysmenorrhea. The age of patients was found to be positively correlated with their parity (r = 0.16, $P = 1.4 \times 10^{-5}$). The severity of

Table 2 Distributions of subtypes of endometriosis by subtypes of adenomyosis

Subtype	Focal adenomyosis	Diffuse adenomyosis	*P*-value
Ovarian endometrioma			
No	61 (53.0%)	473 (79.5%)	1.3×10^{-8}
Yes	54 (49.0%)	122 (20.5%)	
Peritoneal			
No	86 (74.7%)	505 (84.9%)	0.013
Yes	29 (25.3%)	90 (15.1%)	
Deep infiltrating endometriosis			
No	113 (98.3%)	591 (99.3%)	0.25
Yes	2 (1.7%)	4 (0.7%)	
Other locations			
No	103 (89.6%)	562 (94.5%)	0.059
Yes	12 (10.4%)	33 (5.5%)	
All locations combined			
No	51 (44.3%)	421 (70.8%)	1.4×10^{-7}
Yes	64 (55.7%)	174 (29.2%)	

dysmenorrhea was also found to be positively correlated with the duration of the disease (Spearman's r = 0.41, $P = 2.2 \times 10^{-16}$; Fig. 5a) and negatively with the age at onset of dysmenorrhea (Spearman's r = –0.44, $P = 2.2 \times 10^{-16}$; Fig. 5c). The median age at onset of symptoms was 40 years (the 25% and 75% quantiles were 35 and 44.35 years, respectively).

Using a proportional odds logistic regression model with age, parity, gravidity, presence of adhesion, presence of endometriosis and/or myoma, uterus size, type of adenomyosis (diffuse vs focal), complaint of menorrhagia or not, complaint of metrorrhagia or not, complaint of CPP or not, palpable pain during pelvic examination, and the duration of the symptoms as covariates, we carried out a multivariate analysis to see which factors are associated with the severity of dysmenorrhea. We found that age and the complaint of metrorrhagia were negatively associated with the severity of dysmenorrhea, while the presence of adhesion, presence of endometriosis, complaint of menorrhagia, longer duration of symptoms, gravidity, palpable pain during pelvic examination, and having diffuse adenomyosis were positively associated with the severity of dysmenorrhea (all *P*-values < 0.027). Individually, the subtype of endometriosis, however, was not associated with the severity. Replacing age and duration of dysmenorrhea with age at onset of symptoms yielded an identical result, with the age at onset being negatively associated with the severity of dysmenorrhea (all *P*-values < 0.027), that is, the earlier the onset, the more severe the dysmenorrhea could be.

Factors associated with the risk of menorrhagia

We found that patients without menorrhagia had significantly lower prevalence of endometriosis than those with menorrhagia (24.1% vs 42.7%, $P = 1.5 \times 10^{-7}$, Fisher's exact test). In addition, patients who complained of menorrhagia were significantly older than those who did not have menorrhagia (median age = 46 vs 45 years, $P = 0.0003$). Using a logistic regression model with age, parity, gravidity, presence of adhesion, presence of endometriosis and/or myoma, severity of dysmenorrhea, complaint of metrorrhagia or not, complaint of CPP or not, uterus size, type of adenomyosis and the duration of the disease as covariates, we found that the presence of endometriosis (or the ovarian endometrioma) and the duration of disease were negatively associated with the risk of menorrhagia, while age, severity of dysmenorrhea, complaint of metrorrhagia were positively associated with this risk (all *P*-values < 0.028).

Factors associated with metrorrhagia

Using a logistic regression model with age, parity, gravidity, presence of adhesion, presence of endometriosis and/or myoma, severity of dysmenorrhea, complaint of menorrhagia or not, uterus size, type of adenomyosis and the duration of the disease as covariates, we found that the severity of dysmenorrhea was negatively associated with the risk of metrorrhagia, while parity, the complaint of menorrhagia and palpable pain during pelvic exam were positively associated with this risk (all *P*-values < 0.044). Endometriosis subtype had no effect.

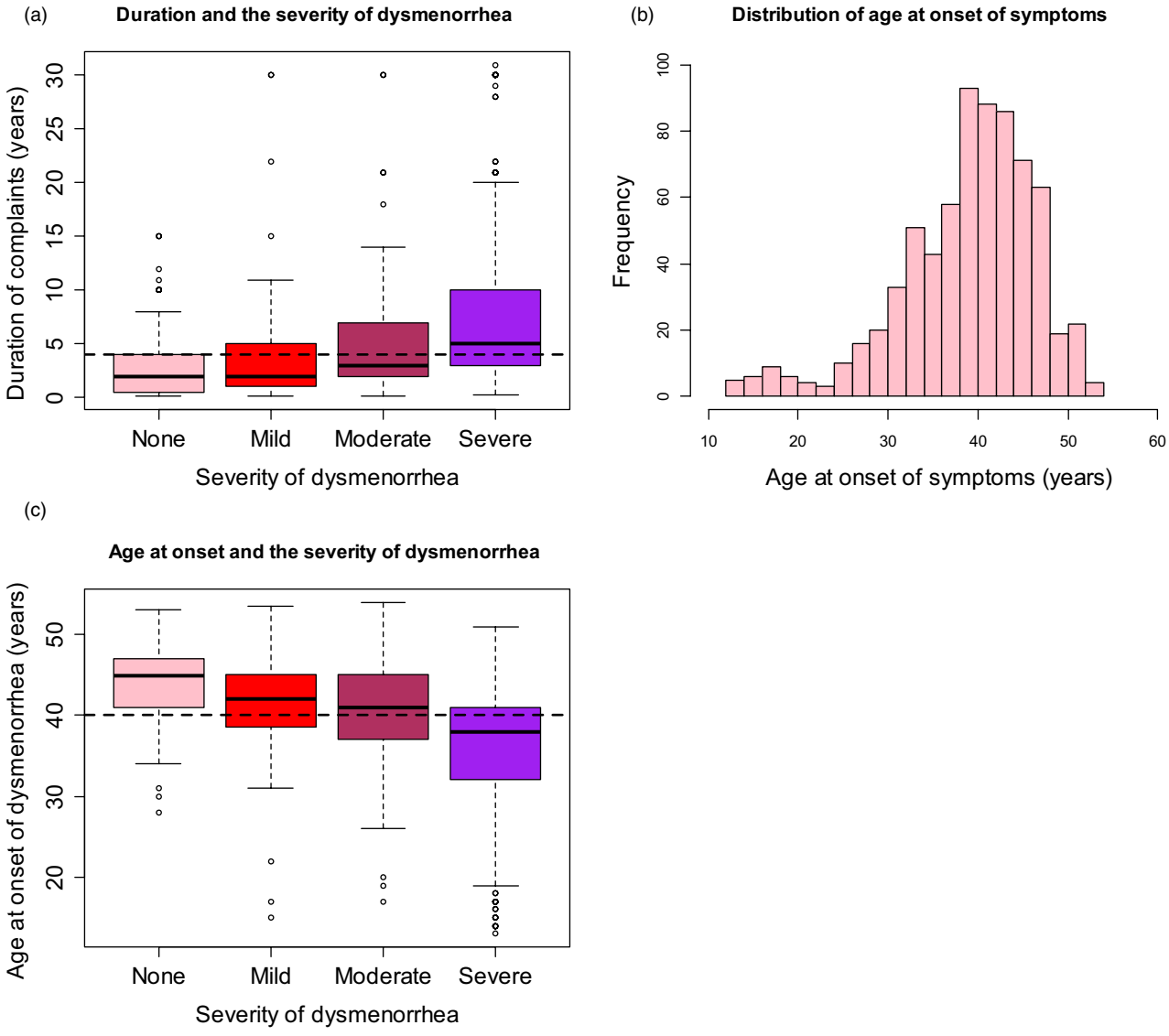

Figure 5 (a) Box plot of the duration of dysmenorrhea among patients with different severity of dysmenorrhea. The dashed line represents the median duration of dysmenorrhea of the entire cohort. (b) Box plot of the age at onset of dysmenorrhea among patients with different severity of dysmenorrhea. The dashed line represents the median age at onset of dysmenorrhea of the entire cohort.

Factors associated with CPP

Using a logistic regression model with age, parity, gravidity, presence of adhesion, presence of endometriosis and/or myoma, severity of dysmenorrhea, complaint of menorrhagia, uterus size, type of adenomyosis, the duration of the disease and the presence of cervix erosion as covariates, we found that gravidity and uterus size were negatively associated with the risk of CPP, while the presence of endometriosis and metrorrhagia were positively associated with this risk (all P-values < 0.048). When all four subtypes of endometriosis were entered as individual covariables, we found that the presence of deep-infiltrating endometriosis and of peritoneal endometriosis, but not metrorrhagia, was positively associated with the risk of CPP (both P-values < 0.029).

Factors associated with the uterus size

Using age, parity, gravidity, presence of adhesion, presence of endometriosis and/or myoma, severity of

dysmenorrhea, complaint of menorrhagia, complaint of metrorrhagia, complaint of CPP, duration of symptoms, and the type of adenomyosis as covariates, we carried out a linear regression analysis to see which factors are associated with the uterus size. We found that age, presence of myoma, duration of the disease, and having the diffuse adenomyosis were all positively associated with the uterus size (all *P*-values < 0.03).

Discussion

The prevalence of adenomyosis in our large cohort of 1697 patients who underwent hysterectomy was 43.3%, which is within the range of reported prevalence[5] but appears to be slightly higher than some recently reported studies.[10,16–19] Difference in race and ethnicity aside, many other factors could be attributed to the difference, such as the difference in the proportion of referral patients, and inclusion criteria for hysterectomy.

In this large cohort series, we found that 3.3% of them were menopausal. While adenomyosis is well regarded as an estrogen-dependent condition[20,21] with elevated expression of estrogen receptors in the adenomyotic uteri[21–24] and menopause results in significantly reduced systemic estrogen level, it is possible that the adenomyotic foci were maintained by increased local production of estrogen, or adipocyte-secreted estrogen. We also found that nearly all patients, in fact 96.6% of premenopausal patients (Table 1) and 91.7% (22 out of 24) of post-menopausal patients, were parous. This is consistent with the report that parity is a risk factor for adenomyosis.[5,25]

While about one-third of patients with adenomyosis are asymptomatic,[6] the vast majority of premenopausal patients (95.5%) in our cohort were symptomatic. Understandably, women who chose to receive hysterectomy may have compelling reasons to adopt such a radical solution. Using association rule mining, we found that in patients who underwent hysterectomy for adenomyosis, the complaint of dysmenorrhea is the most frequent one (82%). This number is significantly higher than the prevalence of pelvic pain in women with laparoscopically diagnosed endometriosis (82% vs 64%).[15] The complaints of menorrhagia and metrorrhagia frequently go with the complaint of dysmenorrhea. Given the sample size of this study, and the firm diagnosis of adenomyosis, we believe that this study provides a better understanding of the symptomatology of adenomyosis, at least in women who have undergone hysterectomy because of the condition.

Adenomyosis is often found to co-occur with other gynecological disorders, such as endometriosis[4] and leiomyomas.[26] In this study, we found 33.5% of premenopausal patients had both adenomyosis and endometriosis, with or without leiomyomas, and 29.5% of them had both adenomyosis and leiomyomas, with or without endometriosis. These results are in broad agreement with published studies,[5,25,27,28] and highlight hyperestrogenemia as the common denominator of all these conditions. In particular, we found that focal adenomyosis is more likely than a diffuse one to co-occur with ovarian endometrioma and peritoneal endometriosis.

We found that presence of adhesion, presence of endometriosis, complaint of menorrhagia, longer duration of disease, gravidity, palpable pain during pelvic examination, and diffuse adenomyosis were positively associated with the severity of dysmenorrhea while age and the complaint of metrorrhagia were negatively associated with the dysmenorrhea severity. Endometriosis and pelvic adhesion have long been regarded as being associated with pelvic pain.[29,30] In endometriosis, the presence of adenomyosis is found to be a risk factor for dysmenorrhea severity.[11] Longer duration may simply signal the prolonged progression of adenomyosis, and thus the worsening of dysmenorrhea. In a mouse model of adenomyosis, the progression of the disease is accompanied by progressive deterioration of pain threshold.[31] Hence our finding is consistent with the animal data.

Palpable pain during pelvic examination may simply be a result of central sensitization found in women with endometriosis.[32] It is also likely in women with adenomyosis, and may be an indication for ongoing inflammation within the myometrium due to the disease. Menorrhagia as a risk factor for dysmenorrhea severity may stem from the fact that in our data, menorrhagia frequently co-occurred with dysmenorrhea. It also may signal more aberrations in the endometrium, which might contribute also to the severity of dysmenorrhea. Diffuse adenomyosis may affect, on average, more areas of myometrium than focal adenomyosis, and may be more likely to contribute to uterine hyperactivity and thus dysmenorrhea severity. That gravidity, but not parity, is associated with the severity of dysmenorrhea may be a proxy measure of the number of endometrial procedures. That age is a negative factor seems to echo the finding by Vercellini *et al*. who found an inverse relation between age at surgery and moderate-to-severe dysmenorrhea in women with endometriosis.[33] Metrorrhagia may have causative

factors that are entirely different from that for dysmenorrhea, and is thus a negative factor for dysmenorrhea severity.

Excessive endometrial bleeding may result in anemia, which may severely impact on daily life. This may explain why shorter duration is associated with the risk of menorrhagia, as the condition may prompt women to seek medical attention earlier. Advancing age as a risk factor is consistent with an earlier report that menorrhagia increases significantly with age.[34]

We found that age, co-occurrence with myoma, duration of the disease, and having diffuse adenomyosis are positively associated with the uterus size in premenopausal women with adenomyosis who underwent hysterectomy. That uterine myoma is a risk factor is easy to understand. Duration of disease may be a surrogate measure for disease progression. Compared with focal adenomyosis, women with diffuse adenomyosis are known to have bulky and heavier uteri, and thus larger uterus size.

Our study has several strengths, with the first being the large sample size of patients with confirmed adenomyosis, in addition to extensive statistical analysis using some sophisticated methods. Small studies tend to report positive findings that may not hold,[35] even those published in high-profile journals.[36] Another strength of our study is the inclusion of all adenomyotic patients who received hysterectomy in 2007 in our hospital. This should remove or minimize any selection bias that may compromise our conclusions.

Our study also has limitations. First, we did not use the wet weight of the removed uteri as a measure for uterus size. Instead, we used ultrasound measurements, which are, at best, a proxy measure for uterus size. Due to the irregular shape in some uteri, the ultrasound-based measurements are inferior to the wet weight. The uteri wet weight was not measured simply due to the very heavy workload and the tradition of our hospital, as the information on uterine wet weight provides no further clinical information once it is removed. However, since we used the measurement across board, it is unlikely that the measurement has introduced any bias that may undermine our conclusions. Second, we did not include patients who underwent hysterectomy due to leiomyomas, which would have given us more information on co-morbidity in patients who had undergone hysterectomy and also provided contrasts between the two conditions. Lastly, we did not perform MRI examination as hysterectomy was performed in 2007, therefore we could not perform a potentially more informative characterization of the 710 patients based on the four subtypes of adenomyosis as proposed by Kishi *et al*.[37] Future studies should remedy these deficiencies.

In summary, we found that in 734 consecutive patients with adenomyosis who underwent hysterectomy, 3.3% of them were menopausal. Among the 710 premenopausal patients, only 4.5% of them did not have dysmenorrhea, menorrhagia, metrorrhagia, or CPP. Dysmenorrhea is the most common complaint, and co-occurs most frequently with menorrhagia. Age and the complaint of metrorrhagia are negatively associated with the severity of dysmenorrhea, while the presence of adhesion, presence of endometriosis, complaint of menorrhagia, longer duration of disease, gravidity, palpable pain during pelvic examination, and diffuse adenomyosis are positively associated with the severity of dysmenorrhea. The presence of endometriosis and the duration of disease are negatively associated with the risk of menorrhagia, while age, severity of dysmenorrhea, and complaint of metrorrhagia are positively associated with this risk. Age, the presence of myoma, duration of the disease, and having diffuse adenomyosis are all positively associated with uterus size. These findings should help, at least in patients with histologically confirmed adenomyosis, to better understand the frequency and severity of adenomyosis-related symptoms and their associated factors, and the association of adenomyosis with other gynecological conditions.

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Disclosure

None declared.

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