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The present adenomyosis treatment status in Luzhou, China: a small scope observational cross-sectional survey



Lingling Xie¹, Mengsi Yang², Xinyu Chen², Luxia Yao², Wei Xu^{3†}, Qiuling Shi⁴ and Yuan Yuan^{1*†}

Abstract

Objective To evaluate the current treatment status and management deficiencies of adenomyosis in Luzhou, China.

Materials and methods A small-scale observational cross-sectional study of patients whose imaging suggests adenomyosis from July 2018 to February 2022 at a teaching hospital in Luzhou, China. All participants (1542 patients) completed a questionnaire of 14 items, including basic information, symptoms, treatment options, outcomes, and costs. The patients' treatment options and the hysterectomy rate were evaluated.

Results The treatment options of hormone agents included combined oral contraceptive pills (COCs), gonadotropinreleasing hormone analogues (GnRH-a), levonorgestrel-releasing intrauterine system (LNG-IUS), and dienogest for 2.07, 46.04, 63.49, and 4.67% of patients, respectively. The treatment options under uterus-sparing surgery included adenomyectomy and high-intensity focused ultrasound (HIFU) treatment, presenting in 3.76 and 33.27% of patients, respectively. Finally, 458 (29.70%) patients chose a hysterectomy. The hysterectomy rate between the hormone and uterus-sparing surgery sequential hormone groups (surgery group) was not significantly different (14.8 vs. 12.7%, χ 2 = 0.344, *P* > 0.05). However, for the focal type and patients with > 24 months delayed treatment interval, the hysterectomy rate of the hormone group was significantly higher than that of the surgery group (8.5% vs. 1.3%, χ 2 = 11.722, *P* < 0.01 and 26.7% vs. 18.5%, χ 2 = 4.906, *P* < 0.05, respectively).

Conclusions There were treatment delays and treatment selection bias in managing adenomyosis in Luzhou, China. Popular science education and early individualized hormone therapy are needed. Uterine-sparing surgery should be carefully selected.

Keywords Adenomyosis, Adenomyectomy, High-intensity focused ultrasound, Hysterectomy, Hormone

[†]Wei Xu and Yuan Yuan contributed equally to this study.

*Correspondence: Yuan Yuan yuanyuan413713@163.com ¹Sichuan Provincial Center for Gynaecology and Breast Diseases, The Affiliated Hospital of Southwest Medical University, No.25 Taiping Street, Luzhou 646000, Sichuan, China ²Clinical medical college, Southwest Medical University, No.1, Section 1, Xianglin Road, Longmatan District, Luzhou 646000, Sichuan, China ³School of Public Health and Management, Chongqing Medical University, Chongqing 400016, China ⁴State Key Laboratory of Ultrasound in Medicine and Engineering, College

of Biomedical Engineering, Chongqing Medical University, No. 1 Medical College Road, Yuzhong District, Chongqing 400016, China



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Introduction

Adenomyosis is the aberrant location of endometrial glandular tissue within the uterine myometrium, is a major health issue in women of childbearing age and is associated with severe dysmenorrhea, abnormal uterine bleeding (AUB), chronic pelvic pain, dyspareunia, and infertility [1, 2, 3]. The prevalence and negative impact of adenomyosis on women's quality of life exceeds that of endometriosis, and hysterectomy remains the definitive treatment for adenomyosis. However, there is a growing interest in conservative management to avoid surgical trauma and possible fertility implications, especially for young patients. Indeed, adenomyosis awareness has increased in the recent two decades due to the burden of adenomyosis on patients and the health system. The guidelines for managing this issue suggest several strategies for the conservative treatment and long-term management of adenomyosis [1, 4, 5]. However, people's understanding of adenomyosis may be insufficient, resulting in unsatisfactory management outcomes.

Like endometriosis, adenomyosis is an estrogenresponsive condition, and hormone treatment is always the first line of treatment [6]. Hysterectomy is considered the ultimate treatment for adenomyosis when other, more conservative therapies have failed. A populationbased study in Kaiser Permanente Washington showed that among 3425 adenomyosis patients, <20% used hormone medications, and 82% underwent hysterectomy [2]. The results suggested that patients may not receive standardized hormone therapy management before choosing hysterectomy. China, a populous Asian country, has a wide range of regions, and there are differences in economic development and medical levels among different cities. Thus, the corresponding cognition and management of adenomyosis are also uneven. Luzhou city (China) has relatively poor economic development. Cities with the same medical level as Luzhou account for about one-third of the cities in China. Understanding the treatment mode and management deficiencies in these cities is conducive to adjusting the adenomyosis management strategy and improving the management effect.

Therefore, this study conducted a small-scale crosssectional study in Luzhou to evaluate the current treatment status of adenomyosis and to answer the following questions: What is the patient's cognition and treatment options for adenomyosis? What are the outcomes of treatment? Understanding these problems is helpful for both doctors and patients to pay attention to this disease, adjust the individualized treatment plan, and improve the management of adenomyosis. The ultimate goal is to guide the management of adenomyosis.

Materials and methods Patients

This observational cross-sectional study evaluated adenomyosis in women attending the gynecology department of a teaching hospital in Luzhou, China, from July 2018 to February 2022. The ethics committee of the institutions approved this study, and informed consent was obtained from all participants. The inclusion criteria for the patients were as follows: (1) premenopausal women, 18-50 years of age, married women, (2) symptoms related to adenomyosis, including dysmenorrhea, abnormal uterine bleeding (AUB), chronic pelvic pain, dyspareunia, infertility, and (3) TVUS diagnosis of adenomyosis [8]. The exclusion criteria were as follows: (1) compounded with the following gynecological diseases: endometrial atypical hyperplasia or endometrial carcinoma, endometrial polyps, uterine fibroids, ovarian endometriosis cyst, ovarian tumors, cervical intraepithelial neoplasia or cervical cancer, and ovarian cancer, (2) patients with special types of adenomyosis: uterine cysticadenomyosis, adenomyomatous polyp of the endometrium, and atypical polypoid adenomyoma, (3) asymptomatic patients, and (4) adenomyosis patients who underwent hysterectomy due to gynecological diseases other than adenomyosis.

Data collection methods and measures

The research indicators for each patient were extracted through paper, telephone, or an online questionnaire. The questionnaire included the following 14 items: age, height, weight, hobbies of tobacco and alcohol, adolescent dysmenorrhea, pregnancy times, delivery times, diagnosis time, delayed treatment interval, adenomyosisassociated symptoms, treatment options, symptom relief, hysterectomy, and treatment cost. The delayed treatment interval refers to the time gap from adenomyosis diagnosis to treatment using hormonal agents or surgery.

The diagnosis and classification of adenomyosis were based on 2-dimensional (2D) transvaginal ultrasound (TVUS) images, assessed independently by two sonographers with >10 years of work experience. The adenomyosis types in this study included focal and diffuse types only [7]. Diffuse adenomyosis was diagnosed using one or more of its morphological sonographic criteria as follows: the uterus with diffuse adenomyosis is uniformly enlarged and boggy; asymmetry of anterior and posterior uterine walls; heterogeneous myometrium, presence of hyperechogenic islands with intramyometrial hyperechogenic areas within the myometrium that have no connection with the endometrium (regular, irregular, or ill-defined); poorly delineated junctional zone (JZ) [7, 8]. Focal adenomyosis was defined as a heterogeneous nodular mass with ill-defined borders. Focal adenomyosis that is demarcated distinctly and surrounded by hypertrophic myometrium is an adenomyoma. Thus, Adenomyoma is classified as a focal type. In case of inconsistent adenomyosis type, the two sonographers discussed and decided accordingly.

Adenomyosis-associated symptoms included dysmenorrhea, AUB manifesting mainly as heavy menstrual bleeding (HMB) and bradymenorrhea (menstruation that lasts > 7 days), chronic pelvic pain, dyspareunia, and infertility. The degree of dysmenorrhea was evaluated by visual analogue score (VAS). Infertility was defined as failure to achieve pregnancy within 12 months of unprotected intercourse or therapeutic donor insemination in women younger than 35 years or within 6 months in women older than 35 years [9].

All treatment options received by patients in the past were recorded, including medical treatments, uterinesparing surgery, and/or hysterectomy [1, 4, 5]. Patients needed to recall the treatments they have received for adenomyosis in the past. Medical treatments included non-hormone drugs (refer to non-steroidal anti-inflammatory drugs (NSAIDs) for managing dysmenorrhea) and hormone agents, including combined oral contraceptive pills (COCs), progesterone pills, levonorgestrel-releasing intrauterine system (LNG-IUS), gonadotropin-releasing hormone analogues (GnRH-a), dienogest, and danazol. Uterine-sparing surgery includes non-excisional techniques and excisional techniques. Non-excisional techniques for adenomyosis treatment include endometrial ablation, electrocoagulation, uterine artery embolization (UAE), and ablation techniques (including radiofrequency, microwave, and high-intensity focused ultrasound (HIFU)). Excisional techniques refer to adenomyectomy, including complete or partial excision, whether performed by laparoscopy or laparotomy. Hysterectomy includes laparotomy, laparoscopy, and transvaginal surgery.

Outcome indicators

Hysterectomy was the primary outcome indicator of this study, whose primary aim was to evaluate the hysterectomy rate of different treatment options. The secondary outcome indicators were the symptom relief rate and treatment cost. The study design did not support validated measures of adenomyosis symptomatology, for instance, the SF-36 questionnaire, to acquire more accurate information on symptom relief [3]. Therefore, selfreported symptom amelioration was categorized as relief and no relief. The treatment cost was collected to evaluate the adenomyosis medical burden and the costs of different treatment options. The treatment cost was divided into three levels, including < 2000 dollars, 2000-4000 dollars, and >4000 dollars, because patients could not accurately record treatment costs during the questionnaire survey.

Sample-size calculation

This cross-sectional study employed a one-sample proportion test to determine the precision of the findings with a 1534 sample size. The study also included a previous report indicating a 28% prevalence of adenomyosis (both diffuse and focal types) as detected by MRI, anticipating a <5% precision rate. Therefore, the study revealed a 4.5% precision rate based on the above prevalence, assuming a 0.95 confidence level (corresponding to a Type I error rate of α = 0.05). This approach ensures a high degree of confidence in the prevalence estimates, contributing to the reliability of the research outcomes.

Statistical analysis

SPSS 26.0 software (SPSS Inc., IL, USA) was used for statistical analysis. Normally distributed data were presented as mean ± standard deviation. Data with skewed distribution were presented as the median and interquartile range (IQR). The weighted Kappa test was used to assess the consistency of the two sonographers' judgment on the classification of adenomyosis type. A kappa value between 0.75 and 1 indicated consistency. Comparative analysis between groups was statistically analyzed using two-sample t-tests, Mann-Whitney U, or chi-square tests. In the comparative analysis of the treatment results between the hormone group and the uterus-sparing surgery sequential hormone group, when the baseline data between the two groups was significantly different, linear regression analysis was used to evaluate the effect of this difference in baseline data on treatment outcomes. All Pvalues were calculated from 2-sided tests, and P < 0.05was considered statistically significant.

Results

Participant and baseline data

A total of 5408 patients had imaging studies suggestive of adenomyosis. The Kappa value of the Weighted Kappa test was 0.857, suggesting consistency of the two sonographers' judgment on the classification of adenomyosis type. Among these patients, 4471 (82.7%) had adenomyosis-related clinical symptoms, 2624 met the inclusion criteria, and 1542 patients were enrolled in this study and completed the questionnaire (Fig. 1). The enrolled patients included 435 (28.2%) cases of focal and 1107 (71.8%) diffuse types. The mean age was 42.96 ± 5.38 years, and the mean body mass index (BMI) was 23.84 ± 11.62 kg/m². 863 (56.0%) patients had adolescent dysmenorrhea, 34 (2.2%) had no history of pregnancy, and 90 (5.8%) had no history of delivery.

Distribution of adenomyosis-related symptoms

The adenomyosis-associated symptoms collected in this study include dysmenorrhea, AUB manifesting as HMB and menometrorrhagia, chronic pelvic pain, dyspareunia,

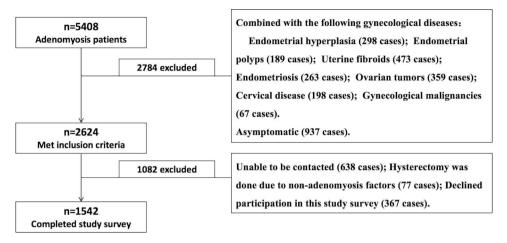


Fig. 1 The study participant flow

Table 1 The treatment cl	hoices of	patients
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Variable	Value
n	1542
Medical treatment	
NSIDS, n (%)	467 (30.3)
COCs, n (%)	32 (2.1)
GnRH-a, <i>n</i> (%)	709 (46.0)
LNG-IUS, n (%)	979 (63.5)
Dienogest, n (%)	72 (4.7)
Uterus-sparing surgery	
Lesion resection, M	59(3.8)
HIFU	863 (33.3)
Hysterectomy, n (%)	458 (29.7)
Without history of medical or uterus-sparing surgery	185 (12.0%)
With failed medical or uterus-sparing surgery	273 (17.7%)

NSIDS: non-steroidal anti-inflammatory drugs; COCs: combined oral contraceptive pills; GnRH-a: gonadotropin-releasing hormone analogues; LNG-IUS: levonorgestrel-releasing intrauterine system; HIFU: high-intensity focused ultrasound

and infertility. Dysmenorrhea and AUB were presented in 99% of patients. However, 513 (33.3%) patients had dysmenorrhea, but no AUB, 268 (17.4%) had AUB but no dysmenorrhea, and 761 (49.4%) had combined symptoms of dysmenorrhea with AUB. The other clinical symptoms (coexisting with dysmenorrhea and/or AUB) included dyspareunia, chronic pelvic pain, and infertility in 3.31, 6.70, and 9.27% of patients, respectively.

Treatment choices of patients

Table 1 shows the treatment options for patients with adenomyosis. Hormone-agent selections included COCs (32 cases), GnRH-a (710 cases), LNG-IUS (979 cases), and dienogest (72 cases) in 2.07, 46.04, 63.49, and 4.67% of patients, respectively. No patient selected dydrogesterone and danazol. Among the patients who chose LNG-IUS, 518 (52.91%) were pretreated with GnRH-a, and 113 (11.54%) chose hysterectomy due to the LNG-IUS-related AUB or LNG-IUS shedding. Uterus-sparing

surgery included adenomyectomy (58 cases) and HIFU treatment (513 cases), presenting in 3.76 and 33.27% of patients, respectively. Of patients who chose uterussparing surgery, 545 (95.44%) chose sequential hormone therapy after surgery. Meanwhile, 468 (30.35%) used NSAIDs intermittently to temporarily control dysmenorrhea symptoms, and 185 (12.0%) received no treatment before choosing hysterectomy. Besides HIFU and adenomyectomy, other uterus-sparing operations were not selected. Further, 196 (12.7%) patients immediately chose hormone agents or uterus-sparing surgery when they were diagnosed with adenomyosis. The remaining 1346 (87.3%) began treatment or directly chose hysterectomy when the adenomyosis-related symptoms were severe. The median delayed treatment interval was 24 (9, 60) months.

Treatment outcomes

After treatment, 827 (53.63%) patients experienced symptom relief, and 530 (34.37%) experienced symptom persistence. Finally, 458 (29.70%) chose hysterectomy. Therefore, 36.8, 42.4, and 20.8% of patients spent < 2000 dollars, 2000–4000, and >4000 dollars for treating adenomyosis, respectively.

Comparative results of the hormone group and the uterussparing surgery sequential hormone group

Patients who chose hormone treatment agents were analyzed further. Based on whether a uterus-sparing surgery was chosen, the patients were classified into the hormone group (675 cases) and the uterus-sparing surgery sequential hormone group (surgery group) (545 cases). The two groups had significantly different basic characteristics, including BMI, pregnancy times, delivery times, adenomyosis type, diagnosis time, and delayed treatment interval (P < 0.05). The linear regression analysis included significantly different baseline data between the two **Table 2** The basic characteristics of the hormone group and the uterus-sparing surgery sequential hormone group (surgery group)

Variable		Hormone group	Surgery group	χ2	р
n		675	545		
Age, Y		42.17 ± 5.63	42.17 ± 4.92	-	0.997
BMI, Kg/m2		22.99 ± 3.09	23.78 ± 3.54	-	0.000*
Times of pregnar	ncy, n (%)			18.893	0.013*
1	None	4 (0.6)	23 (4.2)		
1	l time	65 (9.6)	44 (8.1)		
2	≥2 times	606 (89.8)	478 (87.7)		
Times of delivery	r, n (%)			27.967	0.000*
1	None	23 (3.4)	56 (10.3)		
1	l time	324 (48.1)	273 (50.3)		
2	≥2 times	327 (28.5)	214 (39.4)		
Diagnosis time, N	Λ	54 (36,82)	61 (37,96)	-	0.000*
Delayed treatme val, M	nt inter-	15 (7,38)	24 (6,51)	-	0.006*
Adenomyosis typ	oe, n (%)			65.879	0.000*
F	ocal type	142 (21.1)	232 (42.6)		
-	Diffuse :ype	532 (78.9)	312 (57.4)		
Adolescent dysm n (%)	nenorrhea,	323(47.9)	230 (42.5)	5.238	0.073
Symptoms, <i>n</i> (%)				5.895	0.052
F	Pain▲	221 (32.8)	207 (38.1)		
ŀ	AUB★	102 (15.2)	92 (16.9)		
	Both pain and AUB	350 (52.0)	245 (45.0)		

*P<0.01;BMI: Body mass index; \blacktriangle Pain: including dysmenorrhea, pelvic pain and dyspareunia; \bigstar AUB: abnormal uterine bleeding manifesting mostly as heavy menstrual bleeding (HMB) and bradymenorrhea

groups to determine their effects on hysterectomy rates. The results showed that the adenomyosis type (R2:0.067, B:0.196, t:7.024, r: 0.179, 95%CI: 0.993–1.007, P < 0.01) and delayed treatment interval (R2:0.067, B:0.158, t:5.652, r: 0.372, 95%CI:0.004–0.005, P < 0.01) affect the hysterectomy rate. The proportion of focal type was significantly higher in the surgery group than in the hormone group (42.6 vs. 21.1%, $\chi 2 = 65.879$, P < 0.01. The median delayed treatment interval was significantly shorter in the hormone than in the surgery group (15 vs. 24 months, P < 0.01). The BMI, pregnancy times, delivery times, and diagnosis time did not affect the hysterectomy rate (P > 0.05) (Table 2).

There was no significant difference between the symptom relief rate in the hormone and the surgery group (74.7 vs. 76.7%, $\chi 2 = 0.626$, P > 0.05). The hysterectomy rates of the hormone and surgery groups were 14.8 and 12.7%, respectively. The two groups were not significantly different ($\chi 2 = 1.168$, P > 0.05). Nevertheless, the treatment cost of the surgery group was significantly higher than that of the hormone group ($\chi 2 = 269.69$, P < 0.05) (Table 3).

Table 3 The treatment outcomes of different adenomyosistypes between the hormone group and the uterus-sparingsurgery sequential hormone group (surgery group)

Variable	Hormone	Surgery group	χ2	р
Total				
n	672	544		
Symptoms change, n (%	6)		0.626	0.431
Relief	502 (74.7)	417 (76.7)		
No relief	170 (25.3)	127 (23.3)		
Hysterectomy, n (%)	100 (14.8)	69 (12.7)	1.168	0.280
Treatment cost, n (%)			269.69	0.000*
≤ 2000 USD	396 (58.8)	71 (13.0)		
2000–4000 US	6D 178 (26.4)	277 (50.8)		
>4000 USD	99 (14.7)	197 (36.1)		
Focal type				
n	142	232		
Symptoms change, n (%	6)		5.694	0.017*
Relief	111 (78.2)	203 (87.5)		
No relief	31 (21.8)	29 (12.5)		
Hysterectomy, n (%)	12 (8.5)	3 (1.3)	11.722	0.001*
Diffuse type				
n	530	312		
Symptoms change, n (%	6)		2.609	0.063
Relief	391 (73.8)	214 (68.6)		
No relief	139 (26.2)	98 (31.4)		
Hysterectomy, n (%)	88 (16.5)	66 (21.2)	2.805	0.094
*P<0.01				

The patients were divided into two subgroups according to the adenomyosis type: focal and diffuse, and the symptom relief and hysterectomy rates were further analyzed accordingly. In the focal type, the results showed that the symptom relief rate of the surgery group was significantly higher than that of the hormone group (87.5 vs. 78.2%, $\chi 2 = 5.694$, P < 0.05), and the hysterectomy rate was significantly lower than that of the hormone group (1.3% vs. 8.5%, $\chi 2 = 11.722$, P < 0.01). In the diffuse type, the symptom relief and hysterectomy rates of the hormone and surgery groups were 73.8% vs. 68.6% ($\chi 2 = 2.609$, P > 0.05) and 16.5% vs. 21.2% ($\chi 2 = 2.805$, P > 0.05), respectively. There was no significant difference between the two groups (Table 3).

Further, the patients were divided into three subgroups according to delayed treatment interval: ≤ 12 months, 12–24 months, and >24 months, and their symptom relief and hysterectomy rates were further analyzed accordingly (Table 4). In the ≤ 12 -month group, the symptom relief and hysterectomy rates of the hormone and surgery groups were 87.2 vs. 83.0% ($\chi 2 = 1.819$, P > 0.05) and 7.4 vs. 6.1% ($\chi 2 = 0.344$, P > 0.05), respectively. The two groups had no significant differences. In the 12–24 months group, the symptom relief and hysterectomy rates of hormone and surgery groups were 85.7 vs. 75.0% ($\chi 2 = 3.340$, P > 0.05) and 8.9 vs. 13.9% ($\chi 2 = 1.113$, P > 0.05), respectively. The two groups were

Table 4 The treatment outcomes of different delayed treatment intervals between the hormone group and the uterus-sparing surgery sequential hormone group (surgery group)

Variable	Hormone	Surgery group	χ2	р
Total	672	544		
Delayed treatment in	terval≦12 m	onths		
n	312	230		
Symptoms change, n	(%)		1.819	0.177
Relief	272 (87.2)	191 (83.0)		
No relief	40 (12.8)	39 (17.0)		
Hysterectomy, n (%)	23 (7.4)	14 (6.1)	0.344	0.558
Delayed treatment in	terval: 12–24	months		
n	112	72		
Symptoms change, n	(%)		3.340	0.068
Relief	96 (85.7)	54 (75.0)		
No relief	16 (14.3)	18 (25.0)		
Hysterectomy, n (%)	10 (8.9)	10 (13.9)	1.113	0.291
Delayed treatment in	terval > 24 mo	onths		
n	251	243		
Symptoms change, n	(%)		15.139	0.000*
Relief	135 (54.2)	173 (71.2)		
No relief	114 (45.8)	70 (28.8)		
Hysterectomy, n (%)	67 (26.7)	45 (18.5)	4.906	0.030*
*P<0.05				

not significantly different. In the >24 months group, the symptom relief rate of the surgery group was significantly higher than that of the hormone group (71.2 vs. 54.2%, $\chi^2 = 15.139$, *P*<0.01). In contrast, the hysterectomy rate of the hormone group was significantly higher than that of the surgery group (26.7% vs. 18.5%, $\chi^2 = 4.906$, *P*<0.05).

Discussion

This study revealed the substantial healthcare burden for adenomyosis patients in Luzhou, China. Essentially, 82.7% of the patients had adenomyosis-related clinical symptoms, mainly with AUB and/or menorrhagia (99.9% of the patients). Further, 63.2% of the adenomyosis patients spent over \$ 2,000 on treatment, with 37.03% receiving uterus-sparing surgery. However, only 53.63% of patients experienced symptom relief. The total hysterectomy rate was 29.7%. Adenomyosis is a chronic disease that requires early treatment. In this study, 87% of the patients had delayed treatment after diagnosis of adenomyosis. Therefore, the management of adenomyosis in the Luzhou area in China needs to be improved.

Studies demonstrated that women referred with benign gynecological diseases have a preference for uterus preservation [10, 11]. The quality of life is impacted by a number of hysterectomy-related effects on females. physical, psychological, environmental, and social relations are some of these impacts [11]. Postoperative pelvic floor function and sexual function are main concerns for many women and their partners [12]. The results of this study also found that only 12.0% adenomyosis patients give up conservative treatment and choose hysterectomy directly, suggesting that Chinese women also have a high demand for retaining uterus for benign gynecological diseases. Like endometriosis, adenomyosis is an estrogen-responsive condition, and hormone treatment is always the first line of treatment [6]. The proposed hormone treatments for adenomyosis mainly include COCs, progesterone (dienogest, dydrogesterone), LNG-IUS, GnRH-a, and danazol [1, 4, 5]. Among the 3425 adenomyosis patients, 82% underwent hysterectomy, and very few (16%) used hormonal agents [2]. In this study, 79.1% of patients chose hormone therapy, and the hysterectomy rate was 29.7%, significantly lower than in the literature [2], probably due to the higher usage of hormone agents. Nevertheless, there was more preference for GnRH-a and LUG-INS (46.04 and 63.49%, respectively) and extremely low preference for COCs and dienogest (2.07 and 4.67%, respectively). No patient selected dydrogesterone and danazol. There is a noticeable preference in the choice of hormone agents. GnRH-a sequential LNG-IUS management is an effective, comprehensive long-term management for adenomyosis, especially for patients with HMB or a large uterine volume [5, 13]. Of the 508 patients who chose GnRH-a sequential LNG-IUS management, 113 cases chose hysterectomy as a last resort due to AUB or LNG-IUS shedding, suggesting that the indications for GnRH-a and LNG-IUS in this study may be inappropriate [14, 15].

Dienogest effectively alleviates dysmenorrhea, relieves pelvic pain dyspareunia, and reduces menstrual flow in patients with adenomyosis, with few adverse effects and a high safety profile [16, 17]. Moreover, 6-12 months of dienogest treatment significantly controlled the menstrual volume compared to LNG-IUS [18]. Continuous use of COCs adequately treats AUB and/or dysmenorrhea and is being used for long-term adenomyosis treatment. Overall, COCs had a lesser impact on pain scores and bleeding than LNG-IUS and dienogest but effectively decreased pain and heavy bleeding. Therefore, COCs can be considered another option for patients with symptomatic adenomyosis [16, 19]. In this study, the usage rates of COCs and dienogest were extremely low, possibly because of their side effects, the requirements of patient compliance, and costs for long-term usage. However, COCs and progesterone pills are effective alternative treatment options, especially for patients with LNG-IUS treatment failure or LNG-IUS shedding [16, 18].

Medical treatment is usually the first choice, although surgery is a viable option for refractory adenomyosis. Many surgery procedures spare the uterus and relieve symptoms, including non-excisional and excisional techniques. In this study, 571 patients chose uterus-sparing surgery, with 513 and 58 cases of non-excisional and

excisional measures, suggesting that patients are more inclined to surgical techniques with less trauma to the body. There are several non-excisional techniques for treating adenomyosis, including endometrial ablation, electrocoagulation, uterine artery embolization (UAE), and ablation by radiofrequency, microwave, and highintensity focused ultrasound (HIFU) [1, 4, 5]. In this study, patients in the Luzhou area only chose HIFU treatment (among all non-excisional techniques). This noninvasive ablation technique, HIFU, has the advantage of rapid postoperative recovery with few complications and has become an interesting treatment option for patients [20, 21]. Previous studies have confirmed the safety and efficacy of HIFU in treating adenomyosis [21, 22]. Nonetheless, any uterus-sparing surgery should be individualized due to the extensive variation in patients' age, clinical presentations, location and extent of the lesion, socioeconomic status, and fertility requirement. Therefore, individualized non-excisional techniques may bring greater benefits to patients than a single choice.

The plane between adenomyoma and normal myometrium is not well demarcated; thus, it is difficult to completely remove adenomyosis lesions by non-excisional or excisional techniques [23]. Therefore, combined treatment is recommended after uterus-sparing surgery as a long-term management strategy for adenomyosis [24]. In this study, sequential hormone management was also performed after uterus-sparing surgery. However, the treatment strategy does not reduce the symptom relief and hysterectomy rates compared to hormone-only therapy. In contrast, the cost of uterus-sparing surgery sequential hormone therapy significantly exceeds that of hormone-only therapy. Therefore, the role of uterussparing surgery in managing adenomyosis is not ideal [25]. Some studies have shown that patients with excised adenomyosis reported improvement in pain, menorrhagia, and uterine volume reduction [26]. Comparative systemic reviews revealed the lowest recurrence rate after complete excision and the highest after non-excisional techniques [23, 27]. The proportion of excisional techniques in this study was significantly lower, probably underestimating the management effect of uterus-sparing surgery on adenomyosis.

Meanwhile, this study suggests that uterine-sparing surgery has a good impact in managing focal adenomyosis and faces challenges for diffuse type. This type of adenomyosis lesion is a key determinant of the recurrence rate of uterus-sparing surgery procedures, and focal lesions have overall better follow-up outcomes than diffuse lesions [22, 23]. Due to the limited distribution of focal adenomyosis lesions, uterine-sparing surgery can minimize the lesions and achieve better therapeutic effects than hormone-only therapy. In this study, 87% of patients had delayed treatment after diagnosis of adenomyosis. The consensus was that adenomyosis needs early treatment and long-term management [1, 4, 5]. Delayed treatment may lead to larger adenomyosis lesions and more obvious symptoms, and hormone-only therapy may not achieve the desired therapeutic effect. The results of this study showed that, for patients with a delayed treatment interval of over 24 months, the followup outcome of the uterus-sparing surgery sequential hormone group was significantly better than that of patients with the hormone-only group. Uterine-sparing surgery may achieve a better therapeutic effect than single hormone therapy by reducing adenomyosis lesions, reducing uterine volume, and reducing drug load. Therefore, the indications for uterine-sparing surgery are diffusedtype adenomyosis and delayed treatment interval < 24 months. Uterine-sparing surgery should be carefully selected to reduce the wastage of medical resources and avoid unnecessary trauma for patients.

However, several factors limited this study. First, the single-center research may bias the results, but the data represented the patients residing within the various regions of Luzhou. Second, the uterine volume was not included in the analysis, and the results of the comparative analysis of the treatment outcome may be biased. Third, this study failed to analyze the pregnancy outcome of adenomyosis patients after treatment, as most patients had completed the fertility plan. Further multi-center prospective studies incorporating these factors are recommended, to analyze the influencing factors of delayed treatment, the long-term effects of different hormone agent on the management of adenomyosis, and the management effects of uterine uterus-sparing surgery for different types of adenomyosis.

Conclusions

The individualized and comprehensive management of adenomyosis in the Luzhou area of China is not standardized and needs further optimization. The delayed treatment and bias in treatment choice require more attention. Gynaecologists need to strengthen the popular science education on the characteristics and treatment options of adenomyosis, implement early individualized hormone therapy and regular long-term management. Uterine-sparing surgery should be carefully selected. For focal type and patients with >24-month delayed treatment interval, uterus-sparing surgery sequential hormone treatment showed advantageous in the comprehensive management of adenomyosis.

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Author contributions

All authors contributed to the study conception and design. The integrity of the entire study was guaranteed by Yuan Yuan and Wei Xu, Lingling Xie and

Yuan Yuan provide supervision and guarantee for the implementation of study executing. Mengsi Yang, Xinyu Chen, Luxia Yao and Lingling Xie executed the study and collected the data. Wei Xu and Yuan Yuan performed the data analysis. Qiulin Shi conducted the quality control of data analysis. Lingling Xie and Yuan Yuan were responsible for the manuscript which was reviewed by all the other authors. All authors read and approved the final manuscript.

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Data availability

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Declarations

Competing interests

The authors declare no competing interests.

Chinese clinical trial registry

This trial was approved by the institutional review board of the three participating hospitals and registered in the Chinese Clinical Trial Registry (Registration Date September 24, 2020, registration number ChiCTR2000038590).

Ethics approval

This study was performed according to the guidelines of the Helsinki declaration and was approved by the Ethics Committee of Southwest Medical University (approval number: 23135). Informed consents were obtained from all participants.

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