



# A comparison of the cost–utility of ultrasound-guided high-intensity focused ultrasound and hysterectomy for adenomyosis: a retrospective study

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**Objective** To evaluate cost-effectiveness of ultrasound-guided high-intensity focused ultrasound (USgHIFU) and open hysterectomy for adenomyosis.

**Design** A retrospective analysis.

**Setting** Gynaecological department in a single centre in China.

**Population** Patients with symptomatic adenomyosis.

**Main outcome measures** Cost difference between patients with adenomyosis treated with USgHIFU and open hysterectomy.

**Methods** Three hundred and sixty-eight patients with adenomyosis were retrospectively reviewed. Among them, 302 patients were treated with USgHIFU and 66 patients with open hysterectomy. All of them had 1-, 3-, 6- and 12-month follow ups. The patients' quality of life (QOL) was evaluated and the utility scores were obtained from a rating scale to conduct a cost–utility analysis (CUA).

**Results** No significant differences were found at any follow-up time point in the QOL between the two groups ( $P > 0.05$ ). After treatment, the QOL scores significantly increased in both groups ( $P < 0.05$ ): the quality adjusted life year (QALY) for patients treated with USgHIFU was US\$5256.48, whereas it was US\$7510.03 for patients treated with open hysterectomy. Both incremental cost and sensitivity analysis showed that USgHIFU was less costly than open hysterectomy.

**Conclusions** The QOL of patients with adenomyosis can be significantly improved by either USgHIFU or open hysterectomy, but USgHIFU is less costly.

**Keywords** Adenomyosis, cost–utility analysis, high-intensity focused ultrasound, open hysterectomy.

**Tweetable abstract** USgHIFU can safely be used to treat patients with adenomyosis and significantly improved the quality of life of patients after treatment. The cost of USgHIFU is less than that of surgical treatment.

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## Introduction

Adenomyosis originates within the uterine muscle from endometrial tissue. It is common in women of reproductive age and its exact prevalence is unknown; it is generally reported as anywhere from 8.8 to 31%.<sup>1,2</sup> The diagnosis of adenomyosis is often strongly suspected from a patient's initial history and ultrasound examination and magnetic resonance imaging (MRI) can help to confirm the diagnosis. Pelvic pain during menstrual cycle is the cardinal symptom and infertility is often seen in these patients.<sup>3,4</sup> Hysterectomy, hormonal therapy and high-intensity focused

ultrasound (HIFU) have been used for the treatment of adenomyosis.<sup>5–7</sup> Of these, hysterectomy is still the only definitive treatment for patients with adenomyosis. However, hysterectomy cause many adverse effects and is not suitable for patients who wish to remain fertile. Hormonal therapies are effective in relieving adenomyosis-related symptoms, but the effects are limited because of the side-effects and recurrence of symptoms.<sup>8</sup> As a non-invasive treatment, ultrasound-guided HIFU (USgHIFU) has been widely used in treating uterine fibroids and adenomyosis.<sup>9,10</sup> Many studies have shown that USgHIFU is safe and effective in treating these benign uterine diseases.<sup>10–12</sup>

A few studies have compared the cost-effectiveness of hysterectomy and magnetic resonance-guided focused ultrasound surgery (MRgFUS) for uterine fibroids.<sup>13–15</sup> However, no study has yet compared the cost-utility of USgHIFU and hysterectomy for the treatment of adenomyosis. The advantages of USgHIFU over MRgFUS are a shorter treatment time, lower cost, and higher non-perfused volume ratio. In comparison with surgery, previous studies have also demonstrated that USgHIFU could yield comparable clinical symptom relief and facilitate faster recovery.<sup>10,12</sup> Thus, we designed a retrospective study to compare the cost-utility of USgHIFU and hysterectomy for adenomyosis.

## Material and methods

This retrospective study was approved by the ethics committees at our institutions. All patients signed an informed consent before each procedure.

### Patients

From January 2012 to December 2012, 66 patients with adenomyosis underwent open hysterectomy and 302 patients underwent USgHIFU.

The patients in the open hysterectomy group received preoperative ultrasound examination to determine the size of the uterus, and the patients in the HIFU group received pretreatment magnetic resonance imaging examination.

### Pre-HIFU treatment preparation

Starting 2 days prior to HIFU treatment, every patient was required to have a specific bowel preparation. These patients were advised to ingest liquid food without meat, popcorn, beans, vegetables, milk or fruits for 2 days. On the day prior to the treatment, every patient drank a single dosage of bowel preparation solution. Following a 12-hours fast, an enema was performed in the morning of the treatment day.

The hair on the abdominal wall from the umbilicus to the upper margin of the pubic symphysis was shaved, and the area then degreased and degassed before treatment.

To optimise the therapeutic acoustic pathway, a urinary catheter was inserted to control the bladder volume with a saline injection. A degassed water balloon was prepared for each patient with the purpose of compressing and pushing bowels away from the acoustic pathway to prevent intestine toxicity.

### USgHIFU treatment

USgHIFU treatment was performed using the JC HIFU system (Chongqing Haifu Medical Technology Co., Ltd. Chongqing, China) equipped with an ultrasound device (MyLab 70; Esaote, Genova, Italy) for real-time ultrasound

imaging guidance of the procedure. The therapeutic ultrasound beams were produced by a transducer with a 20-cm diameter, 15-cm focal length, operated at a frequency of 0.8 MHz. A 1.0–8.0 MHz diagnostic ultrasound probe was located at the centre of the therapeutic transducer.

During treatment, every patient was positioned prone on the HIFU bed. The abdominal wall was in contact with cold degassed water. A degassed water balloon was placed between the transducer and the abdominal wall of the patient to push the bowel away from the acoustic pathway. USgHIFU treatment was performed under conscious sedation to minimise discomfort and prevent movement. The respiration, heart rate, blood pressure, and oxygen saturation level were monitored. In addition, the patients were asked to report any discomfort during the procedure.

Sagittal ultrasound scanning was used for observing of the positional relation between the uterine lesion and the bladder. Sonication at 350–400 W was delivered to the target, with the sonication terminating when the grey-scale change at the target region was observed. The focal point was then moved to the next point to achieve complete ablation of the planned treatment volume. Patients were discharged from the HIFU unit 30 minutes after HIFU treatment.

### Hysterectomy

Open hysterectomy was performed under general anaesthesia in a standard protocol. Briefly, a 4- to 8-inch transverse incision was made on the lower abdominal wall, and the entire uterus and the cervix were removed.

### Follow up

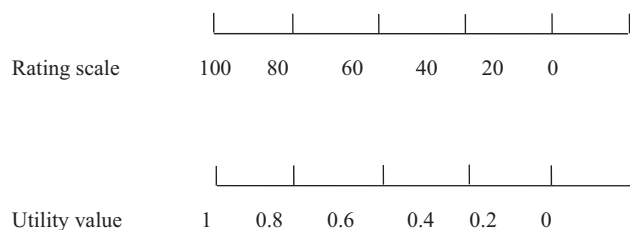
All patients were followed up 1, 3, 6, and 12 months after HIFU treatment or surgery. The quality of life (QOL) of the patients in both groups and the size of the uterus in the HIFU group were evaluated.

### Cost-utility analysis

Both direct and indirect costs were analysed in this study. The direct costs included the cost of medication, cost of patient care, cost of treatment procedure, cost of nursing, cost of ward, material cost and the non-medical costs, such as transportation and meals. Indirect costs included loss of working time of the patients and accompanying persons.

Utility was analysed using the quality of life (QOL) scale. The QOL scores of 0, 20, 40, 60, 80, and 100 were transferred to a utility value of 0, 0.2, 0.4, 0.6, 0.8, and 1.0, respectively, by rating scale measurement (Figure 1).

The quality adjusted life year (QALY) was calculated.<sup>11</sup> The follow-up time was 1 year (365 days). QALYs = utility value × 365, and required QALYs = Posttreatment QALYs – pretreatment QALYs. Therefore, QALY = QALYs/365.



**Figure 1.** The transformation diagram of utility value and QOL score.

The cost–utility of the two treatments could be analysed through QALY, comparing the economic benefits.

### Statistical analysis

SPSS 17.0 software was used for data analysis. Data were reported either as the median and interquartile range or as the mean and standard deviation (SD). Repeated measures analysis of variance and a randomised block analysis of variance test were used for between- or inter-group comparisons of pretreatment and post-treatment results. A *P*-value <0.05 was considered to indicate a significant difference.

## Results

### Demographic characteristics of the patients

The baseline characteristics of the patients are shown in Table 1. The average age was  $42.15 \pm 5.08$  years in the patients treated with USgHIFU and  $45.41 \pm 4.29$  years in the patients treated with open hysterectomy. Menstrual volume, the menstrual period, and the degree of dysmenorrhea were 64.3 ml (range: 40.9–107.4), 6 days (range: 2–11), and 2–3 points in the patients treated with USgHIFU, and 78.4 ml (range: 35.0–110.0), 8 days (range: 3–15), and

2–3 points, in the patients treated with open hysterectomy, respectively. Based on MRI, the uterine volume was  $186.96 \text{ cm}^3$  (range: 146.34–255.35) in patients treated with HIFU, and  $187.88 \text{ cm}^3$  (range: 137.22–241.65) in patients treated with open hysterectomy. No significant difference in baseline characteristics between the two groups was observed (*P* > 0.05) (Table 1).

### Improvement in symptoms and change in adenomyotic lesion volume after HIFU treatment

Table 2 shows that the menstrual volume, menstrual period, and dysmenorrhoea significantly improved at the 12-month follow up after HIFU treatment, and the adenomyotic lesion volume was reduced from  $186.96 \text{ cm}^3$  (range: 146.34–255.35) to  $157.35 \text{ cm}^3$  (113.13–205.64) after HIFU treatment. A statistically significant difference was observed (*P* < 0.05).

### Changes in QOL score in HIFU group and hysterectomy group

Table 3 shows that the QOL score significantly increased in both groups (*P* < 0.05). No significant difference was observed between the two groups (*P* > 0.05).

### Adverse events in HIFU group and hysterectomy group

The HIFU-related adverse effects included leg pain (0.33%), sciatic pain (0.66%), an uncomfortable ‘hot’ skin sensation (3.3%), and pain in the treated areas. All these adverse effects were mild and subsided within 3 days after HIFU treatment. No major adverse effects occurred in this study.

For hysterectomy, all patients complained skin incision pain or discomfort in the lower abdomen after surgery. The patients were given medication or physical therapy for symptom control.

**Table 1.** The baseline characteristics of patients treated with HIFU or surgery

Variables	HIFU ( <i>n</i> = 302)	Hysterectomy ( <i>n</i> = 66)
Age	$42.15 \pm 5.08$	$45.41 \pm 4.29$
Menstrual volume, ml	64.3 (40.9, 107.4)	78.4 (35.0, 110.0)
Menstrual volume, days	6 (2, 11)	8 (3, 15)
Dysmenorrhoea degree	2–3	2–3
The uterine volume, $\text{cm}^3$	186.96 (146.34–255.35)	187.88 (137.22–241.65)
Abdominal wall thickness, cm	$3.6 \pm 0.56$	$4.4 \pm 0.72$
Haemoglobin, g/l	$112.5 \pm 15.6$	$98.0 \pm 12.0$

**Table 2.** Symptom improvement and the adenomyotic lesion changes after USgHIFU

Variables	Pretreatment	12 months post-HIFU
Menstrual amount, ml	64.3 (40.9–107.4)	43.7 (30.6–88.7)
Menstrual period, days	6 (2, 11)	5 (3, 10)
Dysmenorrhoea degree	2–3	0–1
The uterine volume, $\text{cm}^3$	186.96 (146.34–255.35)	157.35 (113.34–205.64)*

\**P* < 0.05.

**Table 3.** QOL score changes of patients treated with USgHIFU and hysterectomy

Variable	Pretreatment	1 month	3 months	6 months	12 months
HIFU	24.53 ± 8.22	43.79 ± 9.55*	56.31 ± 8.35*	71.07 ± 11.21*	66.24 ± 9.85*
Hysterectomy	27.90 ± 9.36	40.82 ± 11.59*	51.80 ± 11.91*	63.06 ± 10.36*	60.52 ± 8.24*

\* $P < 0.05$ .

## Cost-utility analysis

### Cost analysis

The analysis results showed that the percentage of direct medical costs in HIFU was 44.83% of the total cost, whereas it was 64.01% in the hysterectomy group. We further compared the indirect costs between the two groups and found a statistical difference between the two groups, which was higher in the hysterectomy group ( $P < 0.05$ ). We also found that the direct medical costs and total costs of hysterectomy group were higher than those in HIFU group ( $P < 0.05$ ) (Table 4).

### Cost-utility, incremental cost-utility and cost-sensitivity analysis

The cost-utility of patients treated with USgHIFU was lower than that of patients treated with hysterectomy. In this study, one patient spent US\$2253.55 more to acquire 1 QALY in the hysterectomy group. The direct medical cost was the main factor in the cost differences between the two groups. Our results further showed that one patient spent US\$2450.42 more to acquire 1 additional QALY after subtracting the direct non-medical cost and indirect cost.

## Discussion

USgHIFU has been used in the treatment of adenomyosis for years.<sup>16–18</sup> Recently, more and more gynaecologists in

China have considered USgHIFU to be a routine treatment for patients with adenomyosis. The 3- to 12-month follow-up results showed that the clinical effective rates for dysmenorrhea or menorrhagia were around 80%.<sup>17</sup> As a non-invasive treatment technique, HIFU offers patients another choice. The advantages of USgHIFU over hysterectomy for the treatment of adenomyosis are that the adenomyotic lesions can be selectively ablated to achieve symptom relief without removing the uterus and, if the symptoms recur, USgHIFU could be performed again. In this study, all 302 patients with adenomyosis completed the USgHIFU treatment. The follow-up results showed that the menstrual volume was significantly decreased, and the menstrual period and dysmenorrhea significantly improved after HIFU treatment. In comparison with the pretreatment size, the adenomyotic lesions were significantly smaller 12 months after HIFU treatment. Currently, hysterectomy is still the only definitive treatment for patients with symptomatic adenomyosis. In this study, 66 patients with adenomyosis received hysterectomy and our results showed that the QOL score significantly increased in both the HIFU and hysterectomy group. The patients with adenomyosis who completed USgHIFU achieved similar symptom relief to those who had hysterectomy. Therefore, our results demonstrated that both USgHIFU and hysterectomy are effective in treating symptomatic adenomyosis.

In clinical practice, we realised that adenomyosis carries not only spiritual and economic costs for the patients,<sup>19,20</sup> but also losses of health resources. Approximately 600 000

**Table 4.** Cost analysis of USgHIFU treatment and hysterectomy [median (P25,P75)]

Variable	HIFU	Hysterectomy
Direct medical cost	US\$824.81 (766.22, 901.27)	US\$1297.89 (1134.50, 1416.20)*
Medication cost	US\$174.68 (135.18, 254.49)	US\$560.21 (406.83, 688.29)*
Non-medication cost	US\$631.64 (592.29, 680.90)	US\$713.86 (644.15, 821.85)
Adverse event cost	US\$0.00 (0.00, 0.00)	US\$0.00 (0.00, 8.91)*
Non-medical cost	US\$39.50 (31.60, 41.47)	US\$252.78 (227.50, 303.34)
Indirect cost	US\$126, 39 (101.11, 132.71)	US\$236.98 (227.50, 303.41)*
Total cost	US\$1839.77 (1771.36, 1943.57)	US\$2027.71 (1855.07, 2305.43)*

According to the exchange rate of RMB and US\$ in 2012.

\* $P < 0.05$ .

hysterectomies are performed annually in the United States, of which over 90% for benign conditions.<sup>21</sup> This high rate has led to a major controversy that hysterectomies are being largely performed for unwarranted and unnecessary reasons. Our results suggest that USgHIFU is likely to be a reasonable alternative and also cost-effective. In our study, USgHIFU is significantly less costly than hysterectomy. On average, one patient spent US\$2253.55 less to gain 1 QALY per year in this group. To obtain the same QALY per year, the average total cost of hysterectomy was 1.10 times that of USgHIFU. We further performed cost-sensitivity analysis and found that the cost per QALY gained is more sensitive to the cost of USgHIFU relative to hysterectomy. When we subtracted the direct non-medical cost and indirect cost, the incremental cost-utility value demonstrated that the additional cost of society and patients was relatively higher for every 1 QALY in the hysterectomy group.

We also found that the costs for adverse effects and complications played a major part. After hysterectomy, the loss of reproductive function, damage to the integrity of the pelvic anatomy, and damage to the neural network system and gonadal endocrine axis were the main consequences. In contrast, the HIFU-related adverse effects were mild, e.g. uncomfortable sensation of 'hot' skin, sciatic pain, leg pain, and pain in the treated areas, and incurred minor costs.

## Conclusions

In summary, we conclude that USgHIFU and hysterectomy were both cost-effective. However, the costs of hysterectomy were higher than that of USgHIFU within 1 year. Therefore, the overall benefit and risk should be evaluated rationally to achieve the maximum benefit for an individual. USgHIFU treatment for adenomyosis is safe and effective and the cost was lower than hysterectomy.

## Disclosure of interests

There are no conflicts of interest to declare.

## Contribution to authorship

Data acquisition, analysis and interpretation, drafting the article and final approval of the version to be published (Xiaofang Liu). Data acquisition, analysis and interpretation, final approval of the version to be published (Liu Hai Huang, Cai Zhang, Guohua Huang, Limei Yan). Responsible for the initial concept, design of study and final review of the manuscript (Jia He).

## Details of ethics approval

This study was approved by the ethics committee at Suining Central Hospital.

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