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Therapeutic effects of high intensity focused ultrasound for in patients with benign uterine tumors with regard to lifestyle and obstetric characteristics

J.Y. Park[1,3], J.H. Jung[2], S. Kim[3*]

[1]Department of Radiology, Incheon Christian Hospital, Incheon, Korea
[2]Department of Biomedical Engineering and Research Institute of Biomedical Engineering, Catholic University, Seoul, Korea
[3]Department of Radiological Science, Gachon University Medical campus, Incheon, Korea

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Corresponding authors:
Kim Sungchul, Ph.D.,
Fax: *+82 32 820 4361*
E-mail: *ksc@gachon.ac.kr*

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ABSTRACT

Background: The present investigation compared the decrease in the volume of benign tumor before and after High Intensity Focused Ultrasound (HIFU) treatment to evaluate the therapeutic effects of HIFU. in terms of Lifestyle and obstetric characteristics of in patients with Benign Uterine Tumors. ***Materials and Methods***: To collect the data on each patients' lifestyle and obstetric characteristics, a survey was conducted on 55 patients with benign uterine tumors who had undergone HIFU treatment for three months. ***Results:*** Regarding obstetric characteristics, the longer the period of discontinuation of contraceptive pills, the higher the therapeutic effects of HIFU. Regarding lifestyle, the decrease in the benign tumor volume was more when the patient did not exercise during the treatment period, and was a non-smoker ($p<0.05$). ***Conclusion:*** The results of the present investigation may provide valuable basic data for increasing the understanding of the factors that heighten the therapeutic effects of HIFU, thereby contributing to the development of novel therapeutic strategies.

Keywords: *High intensity focused ultrasound, benign uterine tumors, life style, obstetric characteristics.*

INTRODUCTION

HIFU (High Intensity Focused Ultrasound) is a minimally invasive procedure in which high intensity ultrasound is focused on a selected lesion leading to a targeted therapy. At present, this procedure is widely used across the globe in the treatment of patients with benign tumor in the uterus. The two most common therapeutic targets are uterine myoma and adenomyosis. HIFU provides a therapy that is safer and more comfortable for patients when compared to the traditional hysterectomy [1, 2]. There has also been a report on higher cost-efficiency of HIFU than other available techniques modalities [3]. The actual cause of benign uterine tumor remains unclear. While many consider this condition to arise under the influence of hormones such as estrogen [4, 5], numerous recent studies have reported other possible causes and mechanisms for the benign growth, including menopause [6, 7], dietary habits (meat-eating or vegetarian) [8] and obstetric characteristics, such as parity, lactation and contraception [9].

Despite diverse research analyzing the cause of benign uterine tumors and the therapeutic effects of HIFU [10, 11], not much attention has been given to the consequences of lifestyle and obstetric characteristics. This study therefore aimed to follow up, monitor and confirm the therapeutic effects of HIFU for benign uterine tumors with regards to lifestyle and obstetric characteristics, and thereby provide higher quality medical treatment to patients.

MATERIALS AND METHODS

Subjects and patients

This study compared the tumor volume before and after HIFU in 55 patients who were under HIFU treatment for three months after being diagnosed to have uterine myoma or adenomyosis at the Department of Gynecology at Hospital A in Incheon, between February 2015 and May 2016. Of the 55 patients, 30 had uterine myoma and 25 had adenomyosis. A detailed survey was also conducted on the 55 patients. We also obtained written consent from all patients and conducted a retrospective study. The research was approved by the IRB (Institutional Review Board) of the Incheon Christian Hospital (Approval #2015-09), and written consent was obtained from all patients prior to the investigations

The survey involving all the 55 patients was carried out using an independently developed questionnaire, which was broadly based on two categories described below. The obstetric characteristics included whether the patient ever had children and the method of childbirth, miscarriages, if any, and how they occurred, use of contraceptive pills with duration, onset of menopause, and whether there was any ongoing hormonal treatment. Lifestyle factors included physical exercise, dietary habits, alcohol intake, coffee intake, and smoking.

Tumor volume estimation

Benign Uterine tumors were treated using the Haifu JC (Chongqing Haifu Technology, Chongqing, China) machine by visualizing real-time change in ultrasound imaging for uterine myoma and adenomyosis and using focus intensity up to 300 ~ 400 Watt depending on the patient's pain. Treatment was ended by the doctor's decision.

To compare the tumor volumes before and after HIFU, transvaginal ultrasonography was performed using the Medison ACCUVIX V10 ultrasound device and an obstetric probe called Vaginal Probe (EC4-9IS). Identical devices and testing methods were employed for the ultrasonography of each patient at both before and after HIFU (three months). The decrease in the tumor volume was estimated in mm^3. The ultrasonography images were used for estimating the longitudinal, anteroposterior, and axial lengths. In patients with more than two lesions, the bigger of the two were used for the estimation. The ellipsoid volume formula was used for a more accurate estimation of the tumor volume [11].

$$\text{Volume} = \pi/6 \times D1 \times D2 \times D3 \quad (1)$$

In the above equation, D1 represents the longitudinal length, D2 the anteroposterior length, and D3 the axial length.

Statistical analysis

The SPSS version 18.0 (IBM Co., Chicago, USA) was used for statistical analysis. ANOVA (Analysis of Variance) and Student's t-test were used to verify the therapeutic effects of HIFU on benign uterine tumors with respect to influences of various patient factors including parity, method of childbirth, details of any miscarriages, administration of contraceptive pills, amount of physical exercise, dietary habits, and frequency and quantity of alcohol intake. The confidence interval was set at 95%, and a p-value of less than 0.05 was considered statistically significant.

RESULTS

Patient's average age was 40.65±6.15, with 30 of 55 patients diagnosed with uterine myoma and 25 of 55 patients diagnosed with adenomyosis. The average treatment time for HIFU and ablation time was 76.23 minutes and 17.35 minutes respectively. The average treatment energy was 385.90 kJ.

Therapeutic effects of HIFU in terms of obstetric characteristics

Regarding obstetric characteristics, patients who were never on contraceptive pills and those who were on the pills for less than a year showed similar results after HIFU treatment;

however, those who were on the pills for a year or more exhibited relatively lower therapeutic effects ($p<0.05$).

Although no statistical significance was found for other obstetric characteristics, relatively higher therapeutic effects were observed in post-menopausal patients than in pre-menopausal patients ($p<0.05$) (table 1).

Table 1. Rate of decrease in the volume of benign tumor according to obstetric characteristics.

Obstetric characteristics	Variables	N	Before treatment volume (mm^3)	3 months after volume (mm^3)	Reduction Rate (%)	SD	p-value
Number of births	No	21	242.19	120.56	48.07	16.36	0.198
	1	10	148.18	73.10	44.15	15.53	
	More than 2	24	180.14	88.12	52.95	9.38	
Method of birth	No	21	246.40	119.08	48.07	16.36	0.781
	Normal delivery	21	172.48	84.59	49.65	10.77	
	Cesarean section	13	167.22	87.11	51.50	14.13	
Method of miscarriages	No	26	206.32	98.50	49.82	12.07	0.877
	Natural	10	157.01	83.60	47.45	19.95	
	Artificial abortion	19	208.25	104.24	50.09	12.66	
Contraceptive pills	No	27	175.36	88.23	50.93	10.40	0.049*
	Less than 1 year	22	222.07	104.66	51.22	13.59	
	Over 1 year	6	211.83	115.50	36.64	21.73	
Hormonal treatment	No	36	179.88	87.41	51.10	13.06	0.233
	Yes	19	232.40	117.41	46.43	14.76	
Menopause	No	52	200.89	99.78	49.26	13.95	0.622
	Yes	3	148.33	63.00	53.33	9.63	

Therapeutic effects of HIFU in terms of life style

Considering the lifestyle of patients, those who did not exercise during the treatment period exhibited higher therapeutic effects ($p<0.05$) following the HIFU treatment.

The lowest therapeutic effects were exhibited by patients who smoked during the treatment period, while the highest effects were exhibited by non-smokers ($p<0.05$).

However, no statistical significances were observed with respect to the dietary habits, coffee intake, or frequency and quantity of alcohol intake per week ($p>0.05$) (table 2).

Table 2. Rate of decrease in the volume of benign tumor according to life style.

Life style	Variables	N	Before treatment volume (mm^3)	3 months after Volume (mm^3)	Reduction Rate (%)	SD	p-value
Exercise during the treatment period	None	37	204.54	94.88	52.81	10.43	0.030*
	Yes	18	184.61	103.72	42.65	17.14	
Dietary habit	Vegetarian	19	215.80	103.47	47.76	16.96	0.759
	Meat - consumer	17	172.40	85.89	49.58	12.17	
	Wheat - consumer	19	203.16	102.72	51.12	11.80	
Alcohol-drinking	None	31	176.92	81.37	51.44	15.53	0.232
	Yes	24	225.27	118.96	46.95	10.74	
Alcohol-drinking per week	None	31	176.92	81.37	51.44	15.53	0.426
	One day	19	217.92	114.95	46.17	11.06	
	2 days or more	5	253.20	134.20	49.93	9.98	
alcohol-drinking per day	None	31	176.92	81.37	51.44	15.53	0.334
	Less than 5 glasses	12	247.96	134.80	44.57	10.52	
	5 glasses or more	12	202.58	103.12	49.34	10.88	
Smoking	Non-smoker	49	200.27	96.24	51.05	13.35	0.014*
	Smoker	6	179.67	110.33	36.69	10.08	
Coffee-drinking	No	11	244.64	113.59	47.83	13.55	0.659
	Yes	44	186.37	93.82	49.90	13.88	

DISCUSSION

Several studies indicate a requirement for retreatment after HIFU. Wang et al. reported that 5.3% patients with adenomyosis who had received HIFU required retreatment [12], and Zhou *et al.* reported recurrent clinical symptoms and increased symptom scores in 13% of the patients whose tumor volume had decreased to varying degrees after HIFU [13]. Although such results indicate that individual patient factors may be the cause for different therapeutic effects of HIFU in each patient, there is currently no study on the correlation between patient factors and the therapeutic effects of HIFU in uterine fibroids.

Hence, the present study was conducted to compare the various risk factors for uterine myoma under the hypothesis that the higher the risk of uterine myoma with an associated patient factor, the lower the therapeutic effect of HIFU.

Park *et al.* [10] reported an improved therapeutic effect of HIFU for uterine leiomyomas in patients with higher parity. The present study also found increased therapeutic effect of HIFU in patients who had childbirth, although it was not statistically significant ($p>0.05$).

Intake of contraceptive pills has also been reported to decrease the incidence of uterine fibroidss [14]; however the present study found a statistically significant correlation between decreased therapeutic effects of HIFU for uterine leiomyomas and long-term (more than a year) administration of contraceptive pills ($p<0.05$). The therapeutic effects observed in patients who were taking pills for less than a year and those who were never administered the pills was similar. Hence, short-term administration of contraceptive pills is regarded relatively safe in HIFU treatment.

A previous research showed that other obstetric factors such as hormonal treatment, number of childbirths, menstruation, miscarriage, etc., increases the chances of adenomyosis. Nevertheless, these factors were ineffective on the outcome of HIFU treatment [6, 15-17].

Considering the lifestyle patterns of patients, two factors were significant. Although regular exercising minimized the chance of adenomyosis in women [18], continuous exercising while undergoing HIFU decreased the effectiveness of the treatment ($p<0.05$). Since adenomyosis has an abundant blood circulation, increased blood flow due to exercising results in decreased

effectiveness of HIFU treatment; conversely, exercising during treatment increased the effectiveness in anaplastic fibroids [19-20]. These results are similar to the observations of this study. In future, additional research is required to understand how factors such as exercise intensity and time affect the treatment results.

A previous research on smoking and adenomyosis showed that smoking decreases the probability of adenomyosis [21-22], while other contrasting researches stated that it increases the disease rate [23], or does not influence the chance of developing adenomyosis [24]. Regardless of these conflicting statements, our study showed that smoking decreases the effectiveness of HIFU treatment ($p<0.05$). Future studies are required to elucidate the association between smoking and the risk of developing adenomyosis, and the influence of smoking on the effectiveness of HIFU treatment.

A limitation of the present study was the small number of subjects. A higher number of subjects could provide more statistically reliable results, and also help distinguish between diverse age groups, environmental factors, and lifestyles. Despite the limitation, the present study analyzes and provides valuable data for effective HIFU treatment, by evaluating various lifestyle and obstetric characteristics of patients.

CONCLUSION

The present study consisted of a multilateral analysis on the therapeutic effects of HIFU treatment in patients with benign uterine tumors, in terms of certain patient factors, namely lifestyle and obstetric characteristics. The results show a decrease in the effectiveness of HIFU when the patient was on contraceptive pills, whereas increased effects are observed when the patient did not smoke or perform physical exercises during the treatment period.

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***Conflicts of interest*:** *Declared none.*

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