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Systematic Review

Comparison of the Clinical Outcomes and Efficiencies of HIFU (High-Intensity Focused Ultrasound), Da Vinci Robotic Surgery and Laparoscopic Surgery for Uterine Fibroids: A Systematic Review and Meta-Analysis

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Abstract

Background: To compare the clinical outcomes and treatment efficiencies of advanced surgical treatments including High-Intensity Focused Ultrasound (HIFU), robotic surgery and laparoscopic surgery in the uterine fibroid patients. **Methods**: A total of 512 studies from 1995 to 2021 were identified by screening from Science Direct, Cochrane library, Medscape, Willey Online Library, PubMed, and Taylor Francis. From these studies 29 articles were qualitatively included in our systematic review and 24 of them considered quantitively eligible were included in the meta-analysis. Study analyzed by pooling the weighed mean difference (WMD) with the 95% confidence interval (CI) were study provided as a mean + (SD) and pooled risk ratio (RR) was expressed for dichotomous variables. Pooled results were assessed with either a random-effect or fixed-effect model. Heterogeneity was evaluated using the I^2 statistic. **Results**: Comparison of HIFU and robotic surgeries with operation times of 86.13 $\pm$ 36.37 minutes to 120.2 $\pm$ 63 minutes and 166 $\pm$ 48.5 minutes to 278 $\pm$ 67 minutes were higher significant differences (I^2 = 97%, $p < 0.00001$), (WMD –111.88 [–189.68, –34.08]) with statistically significant (p = 0.005). Comparison of HIFU and laparoscopic surgery in operation time of 86.13 $\pm$ 36.37 minutes to 120.2 $\pm$ 63 minutes and 79 $\pm$ 30 minutes to 106.4 $\pm$ 38.5 minutes were not statistically significant (p = 0.75) with higher significant differences heterogeneity (I^2 = 96%, $p < 0.00001$), (5.51 [–27.82, 38.83]). Comparison of between blood losses and fibroid sizes at 154 $\pm$ 75 mL to 278 $\pm$ 164.6 mL and 6.5 $\pm$ 2.9 cm to 13.6 $\pm$ 3.1 cm respectively in laparoscopic surgery was higher significant differences (I^2 = 91%, $p < 0.0007$), (WMD 202.29 [87.77, 316.80]) with statistically significant (p = 0.0005). Between hospital stay and blood loss in laparoscopic surgery at 1.2 $\pm$ 0.9 days to 5.4 $\pm$ 0.2 days and 200 $\pm$ 107 mL to 278 $\pm$ 164.6 mL showed significant differences (I^2 = 90%, $p < 0.0001$), (WMD –269.71 [–361.33, –178.09]) with statistically significant ($p < 0.00001$) while in robotic surgery was not significant. The follow up uterine fibroid symptom & health-related quality of life questionnaire (UF-QOL) at 3 months 45.3 + 26.9 to 70.6 + 26.9 in fibroids group and 61.6 + 41.4 to 79.64 + 17.91 in adenomyosis group and both shows significantly different (I^2 = 83%, p = 0.02), (WMD 14.08 [4.42, 23.75]) with statistically significant (p = 0.0004) and (I^2 = 97%, $p < 0.00001$), (WMD –15.95 [–28.06, –3.84]) with (p = 0.010). SSS follow up 3 months 27.2 + 15.7 to 36.6 + 7.9 in fibroids of HIFU, the heterogeneity test showed significant differences (I^2 = 95%, $p < 0.00001$), (WMD 16.22 [8.33, 24.11]) with statistically significant ($p < 0.0001$). In terms of pregnancy outcome, delivery outcome in live birth between HIFU and laparoscopic surgery 4 (8) within 165 (219) and (7) 23 within 158 (224), the heterogeneity was not significant (I^2 = 0%, p = 0.44), (RR 1.06 [0.97, 1.17]) neither with for risk of delivering was not significant (p = 0.20). **Conclusions**: HIFU treatment reveals more efficient clinical and treatment outcomes than robotic or laparoscopic surgery, including improved symptoms, absence of bleeding, shorter operative time, shorter recovery time, and good benefits in both short-term and long-term quality-of-life.

Keywords: uterine fibroids; HIFU; Da Vinci Robotic; laparoscopic; efficiency; benefits

1. Introduction

High-Intensity Focused Ultrasound (HIFU) is a completely non-invasive ablation technology that is globally recognized for treatment safety, patient satisfaction, and lower cost compared to other surgeries. The advantages of HIFU include the reduction in the uses of anesthesia, bleeding stop guides by ultrasound and real-time imaging. It is also radiation-free, and is associated with reduced risk of infection, absence of scar on the skin, while healing is faster and it is safe with excellent repeatability [1]. HIFU treatment is guided by magnetic resonance imaging (MRI) or ultrasound, and ultrasound waves are absorbed by the body tissues and becomes focused on the tumor, causing coagulant necrosis through mechanical, thermal and cavity effects [2].

Uterine fibroids are the most common among women occurring 20–40% of women of reproductive age [3]. They are also known as myomas or leiomyomas [4]. Several risk factors, including age, skin color, hormonal factors, stress, obesity, physical activity, lifestyle, smoking, diet, and caffeine, can contribute to the increase of uterine fibroids [5]. Environmental toxicants became an immense burden on society, and one of the risk factors to attempt the disease of women including uterine fibroids during the all stages of life. For example, endocrine disrupting chemicals (EDCs) encounter from fetal development through adulthood with early lifetime exposure [6]. EDCs is an act of modulators such as estrogen and androgen receptors at one hormone but an antagonist to another [7]. In recent studies, Vitamin D deficiency, inflammation, DNA repair deficiency and EDCs have been identified as risk factors of uterine fibroids [8]. Although urine concentration of phthalate biomarkers is not associated with high risk of the uterine leimyoma, plasticizer-specific hormonal still develops and influences on uterine leimyoma [9].

Most women diagnosed with uterine fibroids have no symptoms, but some women experience severe pelvic pain and prolonged menstrual bleeding [10]. Estimated cumulative incidence of uterine fibroid tumor develops before menopause at early age. Comparing between white and black women, there were 70% of White women and 80% of Black women detected and diagnosed with uterine fibroids by ultrasound [11].

Treatment of the uterine fibroid tumors with obstetric complications are significant economic burden in the United States. Annually, medical expenses of Uterine fibroid tumors are high and costs up to $5.9–34.4 billion dollars, and with obstetric complications resulted in a cost of $238 million to $7.76 billion in United States [12]. Treatment management should consider fibroid location, size, number of fibroids, age, women who want to have children, optimal treatment, adequate imaging and competent doctor [13]. When patients with uterine fibroids are at high risk for hysterectomy regardless of whether they have received GnRH-agonist therapy, and the symptomatic type of uterine fibroids has a significant impact on quality of life [14,15]. Notably, Multiple interaction of hypovitaminosis D at the myometrial stem cells level can be non-surgical treatment option for uterine fibroids [8].

Currently, no matter what medical treatment does improve fertility or not, fertility preservation becomes the aim of the medical therapy for uterine fibroid patients [16]. Although robotic surgery has many advantages, including reduced blood loss, rare postoperative complications, and shorter hospital stays, robotic surgery is not a cost-effective treatment [17]. Laparoscopic surgery is safe and convenient for treating gynecological cancers, and an alternative surgical technique that safely removes large myomas [18].

Myomectomy increases bleeding and a longer recovery time, and increases the risk of uterine rupture during pregnancy. HIFU is a truly non-invasive, effective and attractive complementary treatment for women who wish to preserve their organs [19]. After USgHIFU treatment, both large and small uterine fibroids are significantly reduced and dysmenorrhea symptoms are improved [20].

Therefore, the aim of our study is to compare clinical outcomes and treatment efficiency of uterine fibroid patients who underwent advanced surgical treatments including HIFU, robotic surgery and laparoscopic surgery.

2. Method

2.1 Study Search

Our study searched SCIENCE DIRECT, COCHRANE LIBRARY, MEDSCAPE, WILLEY ONLINE LIBRARY, PUBMED, and TAYLOR FRANCIS using the following keywords: “Uterine Fibroids” “HIFU”, “Da Vinci Robotic”, “Laparoscopic”, “efficiency”, and “benefits”. Data were collected in the endnote standard software and Microsoft excel. Of the 512 articles that were identified, 29 were included in the systematic qualitative review, of which 24 were quantitively eligible and hence included in the meta-analysis. These English-language articles published during 1995 to 2021 in Taiwan, Hong Kong, China, Korea, USA, Canada, France, Italy, Greece, Israel, UK, Germany and South Africa include 6482 women who diagnosed with uterine fibroids.

2.2 Study Inclusion

Study titles, abstracts, and full text were screened and studies selected as an observational and experimental studies including retrospective studies, cross-sectional study, prospective studies, non-randomized control study, and randomized control studies included in our study. Study population was patients with uterine fibroids who underwent treatments with HIFU, robotic, and laparoscopic surgery.

2.3 Study Exclusion

Not original study, other intervention or other outcomes were excluded.

2.4 Quality Assessment

Observational studies are evaluated by the Newcastle-Ottawa Quality Assessment (NOQA) and experimental-randomized control studies are evaluated by the Critical Appraisal Skills Programme (CASP) (**Supplementary Tables 1,2**). Quality assessment was indicated by a "star systems" as excellent-very good 10–9, good 8–7, satisfactory 6–5, and unsatisfactory 4–0 were given. The CASP was evaluated using 11 questions that were either "yes", "no" or "can't say".

2.5 Outcomes

The primary outcome, clinical outcomes were triaged according to patient compared with patient age, body mass index, operative time (OT), estimated blood loss, uterine fibroid diameter, and length of hospital stay.

Secondary outcomes were treatment efficiencies as measured by the Uterine Fibroid Symptom Health-Related Quality of Life (UFS-QOL) and Symptom Severity Score (SSS).

The final outcome was pregnancy outcome as defined by birth outcomes delineated by live births and between normal spontaneous delivery (NSD) and caesarean section.

2.6 Statistical Analysis

The meta-analysis performed using Review manager (RevMan) Version 5.4. (the Cochrane Collaboration, 2020, London, UK) and analyzes performed by pooling the weighted mean difference (WMD) with 95% Confidence interval (CI) for studies given as (mean + standard deviation [SD]).

For combined variables, pooled results were evaluated using random or fixed effect models, and risk ratio (RR) was expressed for dichotomous variables. Heterogeneity was assessed using the I^2 statistic. A random effects model was performed if the significance value of I^2 was greater than 50% and significantly different. Publication bias using the funnel plots were available for comparing the standard error of the mean difference (**Supplementary Figs. 1–5**).

3. Results

A total of 512 studies from 1995 to 2021 were identified from Science Direct, Cochrane library, Medscape, Wiley Online Library, PubMed, and Taylor Francis. Of these, 29 were articles were included in systematic qualitative review and 24 of them quantitively eligible for meta-analysis (Fig. 1). A total of 6,482 women with uterine fibroids from Taiwan, Hong Kong, China, Korea, the United States, Canada, France, Italy, Greece, Israel, London, the United Kingdom, Germany, and South Africa participated in this study. Detailed characteristics included author's name, year of publication, country, study period, study design, and quality assessment are shown in Table 1 (Ref. [19,21–48]).

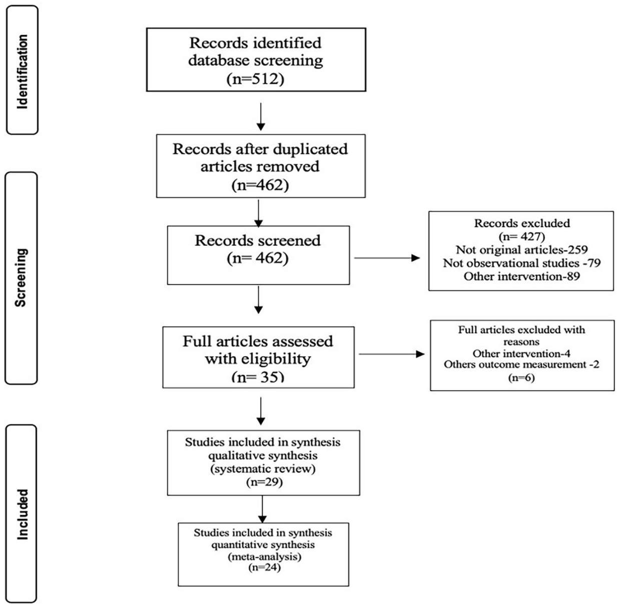

Fig. 1. Flow chart.

3.1 Clinical Outcome

Clinical outcomes were compared according to patient age, body mass index, operative time (OT), estimated blood loss, uterine fibroid diameter, and length of hospital stay. First, a pooled comparison of age and body mass index between HIFU, robotic, and robotic laparoscopic surgery is shown in Table 2.

The patient age of five was HIFU treatment studies [19,21,23,28,30] ranging from 40.7 ± 5.9 to 46.9 ± 3 years and five robotic surgery studies [32–36] ranging from 34 ± 3.8 to 38.26 ± 6.3 years old are of significantly different heterogeneity (I^2 = 85%, p < 0.0001), (WMD 7.58 [5.59, 9.57] with statistically significance (p < 0.00001) (Fig. 2A).

On the other hand, the patient ages of five laparoscopic surgery studies [37,38,43,47,48] ranging from 32.9 ± 4.8 to 38 ± 6.1 years old and five studies robotic surgery studies [32–36] ranging from 34 ± 3.8 to 38.26 ± 6.3 years old showed significantly different heterogeneity (I^2 = 70%, p = 0.010), (WMD 0.06 [–1.91, 2.03], but this was not statistically significant (p = 0.96) (Fig. 2B).

Patient's average body mass index from three studies of HIFU [19,24,28] ranging from 22.4 ± 2.6 to 23.5 ± 2.6 kg/m^2 and three studies of robotic surgery [33–35] ranging from 25.1 ± 4.8 to 27.97 ± 4.8 kg/m^2 showed significantly different heterogeneity (I^2 = 81%, p = 0.005), (WMD –3.26 [–5.30, –1.22] and statistical significance (p = 0.002) (Fig. 2C).

Second, operative times for HIFU, robotic surgery, and laparoscopic surgery were compared. The sizes of fibroids in relation to operative times for robotic surgery and laparoscopic surgery was also compared. A summary of pooled effects is presented in Table 3.

Table 1. Studies included in systematic review.

Study	Location	Study period	Study design	Population size	Treatment method	Patients with fibroids	Main Outcome	Quality assessment NOS/CASP
Jeng *et al*. [19]	Taiwan	2015.04–2018.10	Retrospective Cross-sectional study	500	HIFU	Uterine Fibroids/Adenomyosis	UFS-QOL	9
Cheung *et al*. [21]	Hong Kong	2012.03–2016.06.	Prospective Cohort study	22	HIFU	Uterine Fibroids	Treatment	9
Zhang *et al*. [22]	China	2010.11–2012.06	Retrospective study	202	HIFU	Adenomyosis	UFS-QOL-SSS	8
Cho *et al*. [23]	Korea	2010.04–2010.12	Prospective study	24	HIFU	Uterine Fibroids	Clinical	9
Feng *et al*. [24]	China	2012.01–2015.12.01	Retrospective cohort study	417	HIFU	Adenomyosis	Treatment	8
Lee *et al*. [25]	Korea	2010.02–2017.10	Retrospective study	1807	HIFU	Uterine Fibroids/Adenomyosis	UFS-QOL	9
Zou *et al*. [26]	China	2011.04–2016.03	Retrospective study	406	HIFU	Uterine Fibroids	Pregnancy	8
Liu *et al*. [27]	China	2012.01–2012.12	Retrospective study	302	HIFU	Adenomyosis	UFS-QOL	8
Chen *et al*. [28]	China	NA	Non-randomized clinical trail	107	HIFU	Uterine Fibroids	UFS-QOL	9
Xu *et al*. [29]	China	NA	Prospective study	51	HIFU	Uterine Fibroids	Treatment	8
Zhang *et al*. [30]	South Africa	2015.10–2016.02	Feasibility Study	53	HIFU	Uterine Fibroids	Treatment	8
Liu *et al*. [44]	China	2014.11–2015.11	Non-randomized control study	166	HIFU/Laparoscopy	Uterine Fibroids	Operative	9
Wu *et al*. [45]	China	2009.05.01–2018.05.31	Comparative study	676	HIFU/Laparoscopy	Uterine Fibroids	Pregnancy	7
Cheng *et al*. [31]	Taiwan	2010.10–2012.03	Prospective study	37	Robotic assisted laparoscopy	Uterine Fibroids	Surgical	8
Flyckt *et al*. [32]	USA	1995.01–2009.12	Retrospective cohort study	374	Robotic assisted laparoscopy	Uterine Fibroids	Fertility-Obstetric, Bleeding	9
Nash *et al*. [33]	USA	2008.09–2010.03	Prospective comparative study	27	Robotic assisted laparoscopy	Uterine Fibroids	Clinical	8
Mansour *et al*. [34]	Canada	2008.10–2011.02	Retrospective study	38	Robotic assisted laparoscopy	Uterine Fibroids	Surgical	8
Huberlant *et al*. [35]	France	2009.07–2016.04	Retrospective study	53	Robotic assisted laparoscopy	Uterine Fibroids	Surgical, Obstetric	8
Gunnal *et al*. [36]	USA	2010.05–2013.07	Retrospective study	207	Robotic assisted laparoscopy	Uterine Fibroids	Operative	7
Seracchioli *et al*. [37]	Italy	1996.01–2000.01	Retrospective study	34	Laparoscopy	Uterine Fibroids	Obstetric	7
Prapas *et al*. [38]	Greece	1997.03–2007	Prospective study	116	Laparoscopy	Uterine Fibroids	Operative	8
Mettler *et al*. [39]	Germany	1998.01–2000.11	Retrospective study	216	Laparoscopy	Uterine Fibroids	Surgical	7
Zhang *et al*. [40]	China	2006.01–2009.12	Prospective study	26	Laparoscopy	Uterine Fibroids	Operative	7
Sasson *et al*. [41]	Israel	2012.01–2017.01	Cohort	64	Laparoscopy	Uterine Fibroids	UFS-QOL-SSS	9
Huff *et al*. [42]	London, UK	2012.01–2015.03.31	Prospective study	94	Laparoscopy	Uterine Fibroids	Postoperative job satisfaction	9
Kramer *et al*. [43]	Germany	2012.11.01–2013.06.30	Randomized controlled trails	51	Laparoscopy	Uterine Fibroids	UFS-QOL	8
Palomba *et al*. [46]	Italy	2002.01–2003.03	Randomized control trail	162	Laparoscopy	Uterine Fibroids	Reproductive	8
Alessandri *et al*. [47]	Italy	2002.10.1–2004.10.31	Randomized study	74	Laparoscopy	Uterine Fibroids	Operative	8
Wang *et al*. [48]	Taiwan	2000.01–2002.12	Prospective comparative study	176	Laparoscopy	Uterine Fibroids	Surgical	7

HIFU, High-intensity Focused Ultrasound; LAP, laparoscopic; UFS-QOL, uterine fibroid symptom health-related quality of life; SSS, symptom severity scale; NOS, NEWCASTLE-OTTAWA SCALE; CASP, Critical Appraisal Skills Programme.

Table 2. Summary of pooled comparison of age and body mass index in HIFU, robotic surgery and laparoscopic surgery.

Comparison groups		Number of studies	Total main difference (95% CI)	*p* for heterogeneity test	I^2 (%)	*p* for hypothesis test
AGE						
HIFU	Robotic	5/5	7.58 [5.59, 9.57]	0.0001*	85	0.00001*
LAP	Robotic	5/5	0.06 [–0.91, 2.03]	0.01*	70	0.96
BODI MASS INDEX						
HIFU	Robotic	3/3	–3.26 [–5.30, –1.22]	0.005*	81	0.002*

HIFU, High-intensity Focused Ultrasound; LAP, laparoscopic surgery.

*: $p < 0.05$ statistical significance.

Table 3. Summary of pooled comparison of OT in HIFU, robotic surgery and laparoscopic surgery, and fibroids size and OT in robotic surgery and laparoscopic surgery.

Comparison subgroups		Number of studies	Total main difference (95% CI)	*p* for heterogeneity test	I^2 (%)	*p* for hypothesis test
OPERATION TIME						
OT-HIFU	OT-Robotic	3/3	–111.88 [–189.68, –34.08]	0.00001*	97	0.005*
OT-HIFU	OT-Laparoscopic	3/3	5.51 [–27.82, 38.83]	0.00001*	96	0.75
OT-LAP	OT-Robotic	3/3	–117.64 [–187.15, –48.12]	0.00001*	96	0.0009*
LAPAROSCOPIC						
Fibroid size	Operation time	3	–85.71 [–98.83, –72.58]	0.002*	85	0.00001*
ROBOTIC						
Fibroid size	Operation time	3	–202.54 [–262.00, –143.07]	0.00001*	96	0.0001*

HIFU, High-intensity Focused Ultrasound; LAP, laparoscopic surgery; OT, operation time.

*: $p < 0.05$ statistical significance.

Three studies [19,24,25] of HIFU ranging from 86.13 $\pm$ 36.37 min to 120.2 $\pm$ 63 min and three of robotic surgery [31,34,35] ranging from 166 $\pm$ 48.5 min to 278 $\pm$ 67 min showed significantly different heterogeneity (I^2 = 97%, $p < 0.00001$), (WMD –111.88 [–189.68, – 34.08]) with statistical significance (p = 0.005) (Fig. 3A).

Three studies [19,24,25] of HIFU ranging from 86.13 $\pm$ 36.37 min to 120.2 $\pm$ 63 min and three studies [37,38,40] of laparoscopic surgery ranging from 79 $\pm$ 30 min to 106.4 $\pm$ 38.5 min showed significantly different heterogeneity (I^2 = 96%, $p < 0.00001$), (WMD 5.51 [–27.82, 38.83]) but it is statistically insignificant (p = 0.75) (Fig. 3B).

Comparing between three studies [37,38,40] of laparoscopic ranging from 79 $\pm$ 30 min to 106.4 $\pm$ 38.5 min and three studies of robotic surgery [31,34,35] ranging from 166 $\pm$ 48.5 min to 278.6 $\pm$ 67 min showed significantly different heterogeneity (I^2 = 96%, $p < 0.00001$), (WMD – 117.64 [–187.15, –48.12] with statistical significance (p = 0.0009) (Fig. 3C).

With regard to fibroid size versus operative time in laparoscopic surgery, there were three studies [37,40,47] of laparoscopic surgery with fibroid sizes ranging from 6.2 $\pm$ 0.7 cm to 13.6 $\pm$ 3.1 cm and surgery time ranging from 79 $\pm$ 30 min to 106.4 $\pm$ 38.5 min which showed significantly different heterogeneity (I^2 = 85%, p = 0.002), (WMD –85.71 [–98,83, –72.58] with statistical significance ($p < 0.00001$) (Fig. 3D).

In addition, there were three studies [31,34,35] of robotic surgery with fibroids sizes ranging from 6.9 $\pm$ 1.77 cm to 9.1 $\pm$ 2 cm and surgery times ranging from 166 $\pm$ 48.5 min to 278.6 $\pm$ 67 min showed significantly different heterogeneity (I^2 = 96%, $p < 0.00001$), (WMD – 202.54 [–262.00, –143.07] with statistically significance ($p < 0.00001$) (Fig. 3E).

Finally, comparisons of blood loss and fibrosis rates between robotic and laparoscopic surgeries, hospital length of stay and bleeding between robotic and laparoscopic surgeries are shown in Table 4.

Blood loss compared between three studies [31,34,35] of robotic surgery ranging from 214 $\pm$ 161 min to 235.7 $\pm$ 283.3 min and three studies of laparoscopic surgery [37,38,40] ranging from 154 $\pm$ 75 min to 200 $\pm$ 107 min showed not significantly different heterogeneity (I^2 = 0%, p = 0.85), (WMD 61.23 [14.98, 107.48]) and statistically significant (p = 0.009) (Fig. 4A).

There were two studies [37,40] of laparoscopic surgery was compared between blood loss ranging from 154 $\pm$ 75 mL to 278.2 $\pm$ 164.6 mL and fibroids size ranging from 6.5 $\pm$ 2.9 cm to 13.6 $\pm$ 3.1 cm showed significant difference heterogeneity (I^2 = 91%, p = 0.0007), (WMD 202.29 [87.77, 316.80]) with statistically significant (p = 0.0005) (Fig. 4B).

There were three studies [38,40,48] of laparoscopic surgery compared between length of hospital stay at 1.2

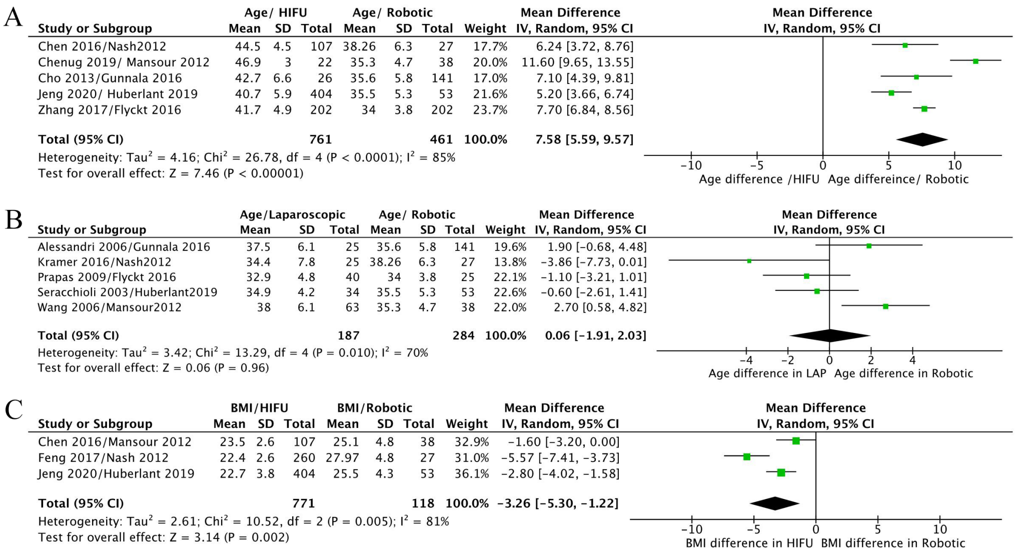

Fig. 2. Forest plot of age and body mass index in HIFU, robotic surgery and laparoscopic surgery. (A) Forest plot of age in HIFU and robotic surgery. (B) Forest plot of age in laparoscopic surgery and robotic surgery. (C) Forest plot of body mass index in HIFU and robotic surgery.

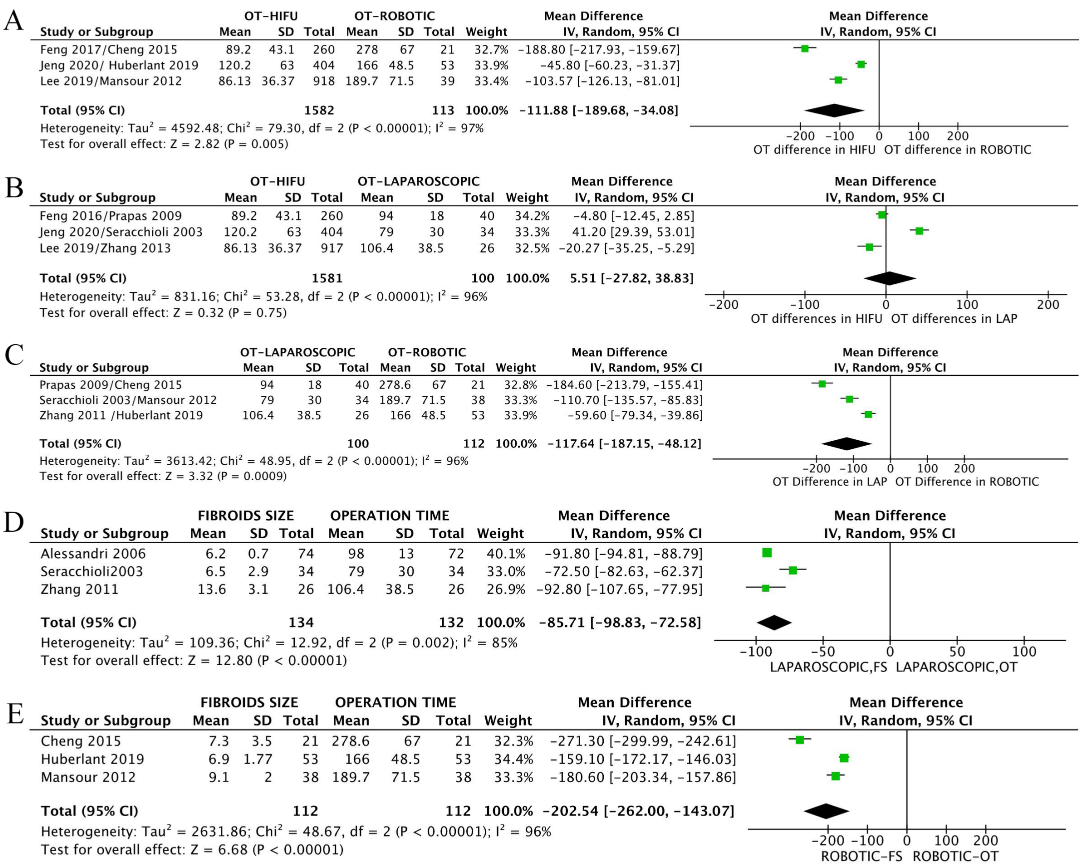

Fig. 3. Forest plot of comparison of operation time between HIFU, robotic surgery and laparoscopic surgery. Fibroids size compared to operation time in robotic surgery and laparoscopic surgery. (A) Forest plot of operation time between HIFU and robotic surgery. (B) Forest plot of operation time between HIFU and laparoscopic surgery. (C) Forest plot of operation time between laparoscopic surgery and robotic. (D) Forest plot of fibroids size and operation time in laparoscopic surgery. (E) Forest plot of fibroids size and operation time in robotic surgery.

Table 4. Summary of pooled comparison of blood loss, fibroids size, and hospital stay in robotic surgery and laparoscopic surgery.

Comparison subgroups		Number of studies	Total main difference (95% CI)	*p* for heterogeneity test	I^2 (%)	*p* for hypothesis test
BLOOD LOSS Robotic	 Laparoscopic	3/3	61.23 [14.98, 107.48]	0.85	0	0.009*
LAPAROSCOPIC Blood loss	 Fibroid size	2	202.29 [87.77, 316.80]	0.0007*	91	0.0005*
Hospital stays	Blood loss	3	–269.71 [–361.33, –178.09]	0.0001*	90	0.00001*
ROBOTIC Blood loss	 Fibroid size	2	–210.52 [165.87, 255.17]	0.66	0	0.00001*
Hospital stays	Blood loss	3	–226.15 [–266.69, –185.60]	0.67	0	0.00001*

*: $p < 0.05$ statistical significance.

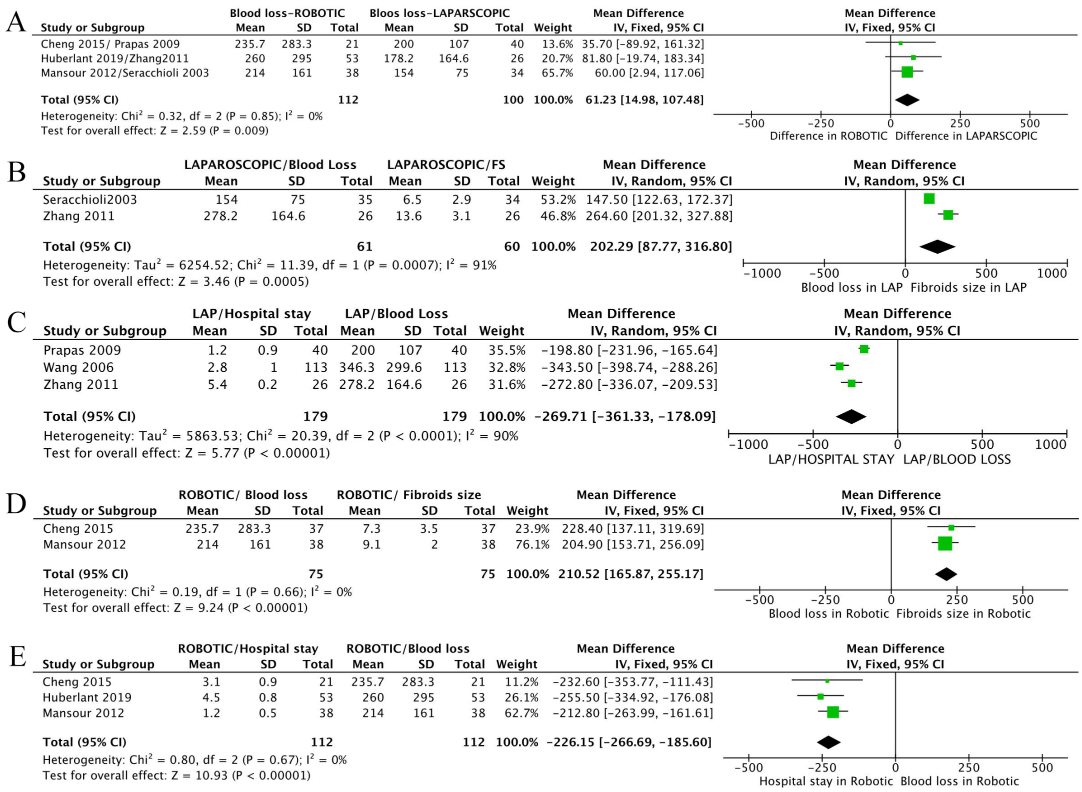

Fig. 4. Forest plot of comparison of blood loss, fibroids size, and hospital stay in robotic surgery and laparoscopic surgery. (A) Forest plot of blood loss between robotic surgery and laparoscopic surgery. (B) Forest plot of blood loss and fibroid size in laparoscopic surgery. (C) Forest plot of hospital stay and blood loss in laparoscopic surgery. (D) Forest plot of blood loss and fibroids size in robotic surgery. (E) Forest plot of hospital stay and blood loss in robotic surgery.

± 0.9 days to 5.4 ± 0.2 days and blood loss ranging from 200 ± 107 mL to 346.3 ± 299.6 mL showed significant differences (I^2 = 90%, $p < 0.0001$), (WMD –269.71 [–361.33, –178.09] with statistical significance ($p < 0.00001$) (Fig. 4C).

There were two studies [31,34] of robotic surgery compared between blood loss ranging from 214 ± 161 mL to 235.7 ± 283.3 mL and 7.3 ± 3.5 cm to 9.1 ± 2 cm showed no differences in heterogeneity (I^2 = 0%, p = 0.66), (WMD 210.52 [165.87, 255.17]) with statistical significance ($p < 0.00001$) (Fig. 4D).

Three studies [31,34,35] of robotic surgery was compared between hospital stay from at 1.2 ± 0.5 days to 4.5 ± 0.8 days and blood loss ranging from 214 ± 161 mL to 235.7 ± 283.3 mL showed insignificant differences heterogeneity (I^2 = 0%, p = 0.67), (WMD –226.15 [–266.69, –185.60] was statistically significant ($p < 0.00001$) (Fig. 4E).

Table 5. Summary of pooled comparison of UF-QOL and SSS in HIFU.

Comparison groups	Number of studies	Total main difference (95% CI)	*p* for heterogeneity test	I^2 (%)	*p* for hypothesis test
HIFU- UFS-QOL					
Uterine fibroids Post-HIFU at 3 months	2	14.08 [4.12, 23.75]	0.02*	83	0.004*
Adenomyosis Post-HIFU at 3 months	3	–15.95 [–28.06, –3.84]	0.00001*	97	0.010*
HIFU- SSS					
Uterine fibroids Post-HIFU at 3 months	4	16.22 [8.33, 24.11]	0.00001*	95	0.0001*

HIFU, High-intensity Focused Ultrasound; LAP, laparoscopic surgery; NSD, normal spontaneous delivery.
*: $p < 0.05$ statistical significance.

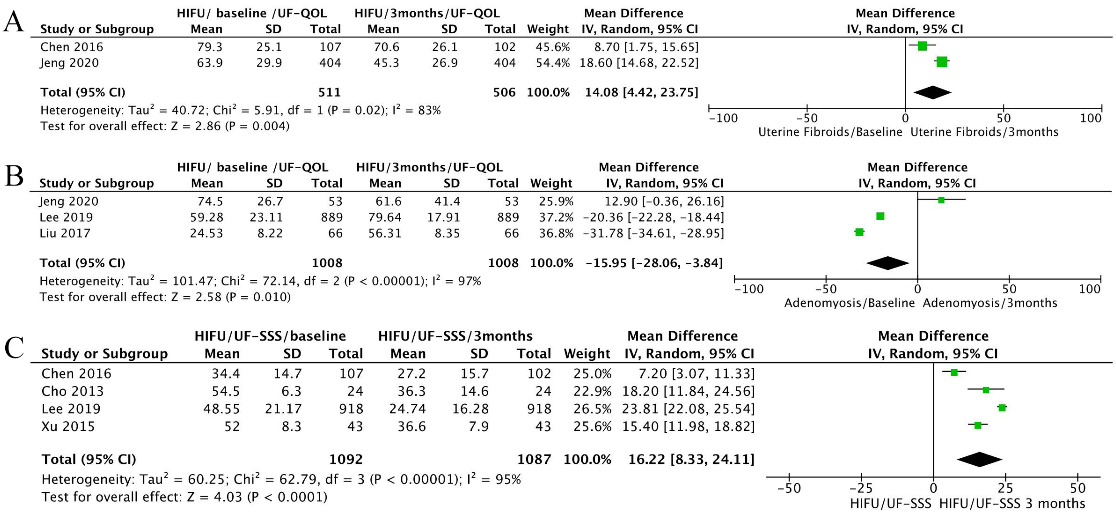

Fig. 5. Forest plot of comparison of UF-QOL score for uterine fibroids and adenomyosis post-HIFU at 3 months. SSS score for uterine fibroids post-HIFU at 3 months. (A) Forest plot of UF-QOL score for uterine fibroids post- HIFU at 3 months. (B) Forest plot of UF-QOL score for adenomyosis post-HIFU at 3 months. (C) Forest plot of SSS score for uterine fibroids post-HIFU at 3 months.

3.2 Treatment Efficiency Outcome

The Efficiency outcomes of HIFU treatment were evaluated by UFS-QOL (Uterine Fibroid Symptom Health-Related Quality of Life) and SSS (Symptom Severity Scale) and are shown in Table 5.

UFS-QOL was analyzed between the fibroid group and the adenomyosis group. Two studies for uterine fibroids [19,28] and three studies for adenomyosis [19,25,27] were compared. For the fibroids group, baseline 79.3 ± 25.1 to 63.9 ± 29.9 and post-HIFU at 3 months ranging from 70.6 ± 26.1 to 45.3 + 26.9 showed significantly different heterogeneity (I^2 = 83%, p = 0.02), (WMD 14.08 [4.42, 23.75]) with statistical significance (p = 0.0004) (Fig. 5A).

For the adenomyosis group, ranging from baseline 74.5 ± 26.7 to 24.53 ± 8.22 and post-HIFU at 3 months ranging from 79.64 ± 17.91 to 56.31 + 8.35 showed significant difference heterogeneity (I^2 = 97%, $p < 0.00001$), (WMD –15.95 [–28.06, –3.84]) with statistically significant (p = 0.010) (Fig. 5B).

SSS score for fibroids group, four studies [23,25,28,29] compared ranging from baseline 54.5 + 6.3 to 34.4 ± 14.7 and at 3 months from 36.6 ± 7.9 to 24.74 + 16.28 showed significantly different heterogeneity (I^2 = 95%, $p < 0.00001$), (WMD 16.22 [8.33, 24.11]) with statistical significance ($p < 0.0001$) (Fig. 5C).

3.3 Pregnancy Outcome

Pregnancy outcomes for both HIFU and laparoscopy were compared according to delivery outcomes between normal spontaneous delivery (NSD) and cesarean section (C-section). Table 6 summarizes the comparison of live births between NSD and C-section for HIFU and laparoscopic surgery.

For delivery outcomes compared between HIFU and laparoscopy, there were three studies [19,26,45] of HIFU from 4 out of 8 live births 4 (8) to 165 out of 219 live births 165 (219) and three studies [37,45,46] of laparoscopic from 7 out of 23 live births 7 (23) to 158 out of 224 158 (224) was showed not significant heterogeneity (p = 0.20), (I^2 = 0%,

Table 6. Summary of pooled comparison of live birth between NSD and C-section for HIFU and laparoscopic surgery.

Comparison groups	Number of studies	Total main difference (95% CI)	p for heterogeneity test	I^2 (%)	p for hypothesis test
Live birth HIFU Laparoscopic	3	1.06 [0.97, 1.17]	0.44	0	0.20
NSD (Normal spontaneous delivery) HIFU Laparoscopic	3	1.38 [0.65, 2.95]	0.05*	66	0.40
C-Section HIFU Laparoscopic	3	0.86 [0.71, 1.04]	0.18	43	0.13
HIFU NSD C-section	3	0.82 [0.22, 3.05]	0.00001*	94	0.76
Laparoscopic NSD C-section	3	0.59 [0.46, 0.75]	0.14	50	0.0001*

HIFU, High-intensity Focused Ultrasound; LAP, laparoscopic surgery; NSD, normal spontaneous delivery.

*: $p < 0.05$ statistical significance.

p = 0.44), (RR 1.06 [0.97, 1.17]) and not statistical significance (Fig. 6A).

For NSD, there were three studies [19,26,45] of HIFU, 3 out of 8 pregnancies 3 (8) and 91 out of 219 pregnancies 91 (219) and three studies [37,45,46] of laparoscopy were 1 out of 23 pregnancies 1 (23) and 63 out of 224 pregnancy 63 (224) were compared and showed significant lower risk heterogeneity (I^2 = 66%, p = 0.05), (RR 1.38 [0.65, 2.95]) with not statistical significance (p = 0.40) (Fig. 6B).

For C-section delivery, three studies [19,26,45] of HIFU from 1 out of 8 pregnancies 1 (8) to 74 out of 219 pregnancies 74 (219) and there three studies [37,45,46] of laparoscopic from 6 out of 23 pregnancy 6 (23) to 95 out of 224 pregnancies 95 (224) were compared and showed insignificant lower heterogeneity (I^2 = 43%, p = 0.18), (RR 0.86 [0.71, 1.04]) neither not statistically significant (p = 0.13) (Fig. 6C).

Comparing between NSD and C-section, three studies [19,26,45] of HIFU, from 3 out of 8 pregnancy 3 (8) to 15 out of 80 pregnancies 15 (80) and from 1 out of 8 pregnancies 1 (8) to 74 out of 219 pregnancies 74 (219) showed significant high heterogeneity (I^2 = 94%, $p < 0.00001$) (RR 0.82 [0.22, 3.05] with statistical insignificant (p = 0.76) (Fig. 6D).

In the comparison between NSD and C-section, there were three studies [37,45,46] of laparoscopic surgery from 1 out of 23 pregnancies 1 (23) to 63 out of 224 pregnancies 63 (224) and from 6 out of 23 pregnancies 6 (23) to 95 out of 224 pregnancies 95 (224) was showed insignificant lower heterogeneity (I^2 = 50%, p = 0.14), (RR 0.59 [0.46, 0.75] was statistically significant ($p < 0.0001$) (Fig. 6E).

4. Discussion

Our study compared the clinical outcomes and treatment outcomes of patients with uterine fibroids who underwent advanced surgical HIFU, robotic surgery, or laparoscopic surgery.

The primary outcome was clinical outcome stratified by patient age and body mass index (BMI). The age of patient in the HIFU group were significantly older than those in the robotic surgery group, while the age of patients in the robotic and laparoscopic surgery groups were similar. There was a significant difference in the BMI of patients who underwent HIFU and robotic surgery. A secondary outcome was clinical outcome relative to operative time. HIFU treatment was shorter than both robotic and laparoscopic surgeries. Overall, OT depends on the diameter of fibroids. The operation time was shortened, and ablation time and total energy were reduced in patients with paracervical block during HIFU treatment [49]. The final finding of clinical outcomes was the link between blood loss and fibroid size. We found that blood loss was related to the diameter of fibroid in the laparoscopic surgery patients, but not in the robotic surgery patients.

In addition, comparison between hospital stay and blood loss revealed a significant difference for laparoscopic surgery while it was not insignificant for robotic surgery. Similar to robotic and laparoscopic surgeries, there were significant differences in hospital stay and bleeding, but no differences in operative complications [50].

In contrast, the advantages of the laparoscopic approach include less blood loss, less adhesions, shorter hospital stay, and a safer approach for multiple and large fibroids [51]. In terms of Lonnerfors study, women who underwent robotic surgery did not display serious complications and had shorter hospital stays [52]. In other words, a similar study showed that not only clinical and surgical outcomes but also fertility and pregnancy outcomes are well known after laparoscopic myomectomy for large fibroids [53]. In Campo's study, which investigated whether the pregnancy rate depended on the age of the patient and the diameter or location of the myoma after laparoscopic surgery [54].

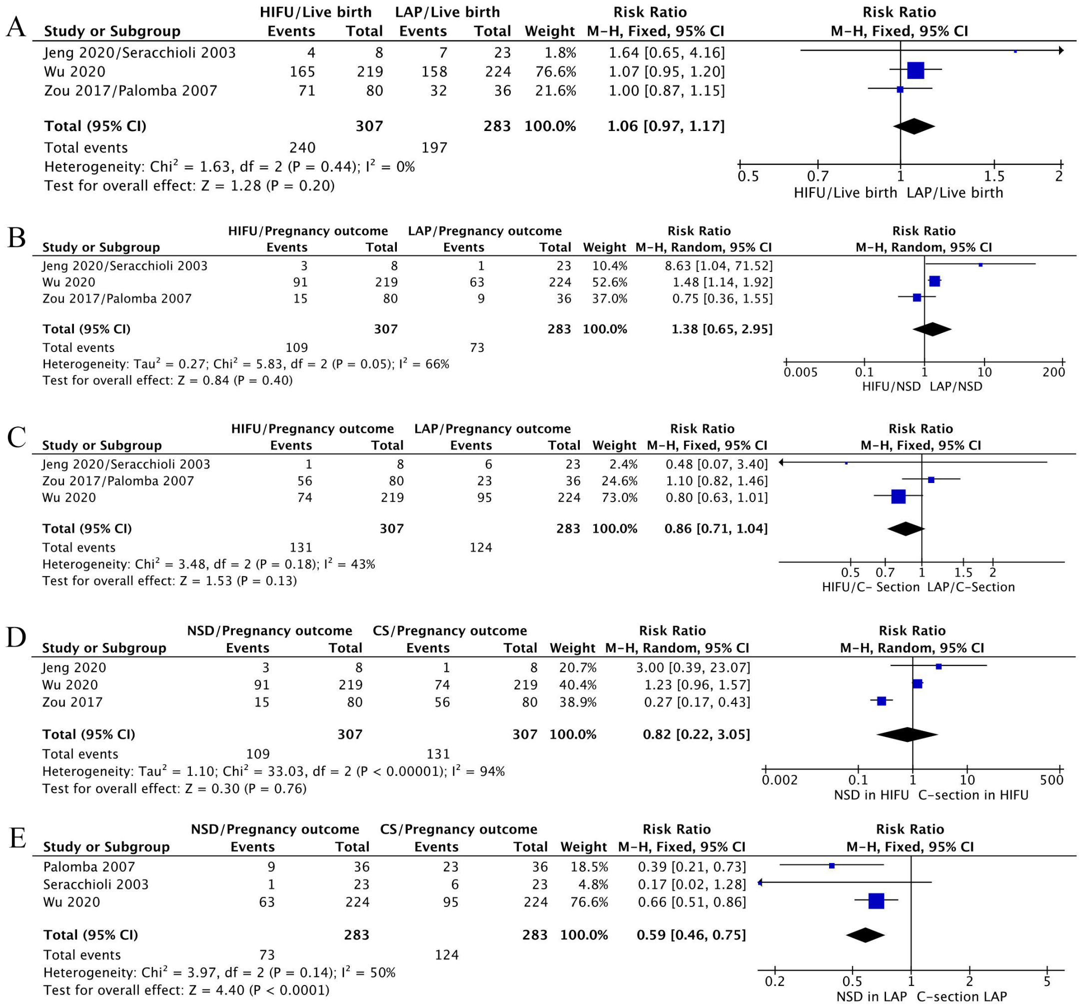

Fig. 6. Forest plot of comparison of forest plot of delivery outcome for HIFU and laparoscopic surgery. (A) Forest plot of live birth in HIFU and laparoscopic surgery. (B) Forest plot of NSD in HIFU and laparoscopic surgery. (C) Forest plot of c-section in HIFU and laparoscopic surgery. (D) Forest plot of NSD and c-section in HIFU. (E) Forest plot of NSD and C-section in laparoscopic surgery.

Fibroids weight, size, location, and number of myoma did not significantly affect the duration of hospital stay [55]. Laparotomic myomectomy was associated with significantly lower complications with improved follow-up symptoms[56]. Laparoscopic surgery has a beneficial effect on reproductive health in pre and postmenopausal patients [57]. Successful HIFU treatment has been shown to significantly reduce uterine size by combining GnRH-a with MRgFUS [58]. In Sinha's study based on the results of blood loss and fewer complications, they found similar clinical results in that laparoscopic surgery was effective and safe in patients with large myomas and multiple myomas [59].

Secondary outcomes treatment efficiency were compared by UF-QoL and SSS. Quality of life scores improved significantly at short-term follow-up in both the uterine fibroid and adenomyosis groups. After 3 months of HIFU treatment, the symptoms of patients with uterine fibroids significantly improved.

The final finding was the pregnancy outcome. HIFU treatment has the amazing advantage of improving pregnancy outcomes and having no risk to fertility.

UFS-QOL score was significantly increased after USgHIFU [60]. In Xie's study, HIFU treatment is more suitable for submucosal fibroids type I, II, and type II is more sensitive [61]. According to Zhang, in women with inverted uterine fibroids, the effect of USgHIFU treatment is milder and transient [62]. MRgFUS is one of the most suitable treatment methods for type 1/2 uterine myomas [63]. In Shui's study, it was found that quality-of-life improvement is significantly improved among adenomyosis patients during two years follow up after HIFU treatment [64]. HIFU is not only safe and effective to treat the uterine fibroids, but also appropriate to treat solid malignant tumors such as breast cancer, soft-tissue sarcoma, renal cancer, pancreatic cancer, malignant bone tumors, primary and metastatic liver cancer [65].

There are several limitations to our analysis. First of all, for the long-term follow-up of HIFU treatment, some studies had the limitation of performing contrast-enhanced MRI after HIFU treatment, which makes it difficult to measure and calculate such as NPV ratio. Therefore, the lack of follow-up data limited us from analyzing both UF-QOL and SSS at long-term follow-up.

Second, the limited number of randomized clinical trials for both robotic surgery and laparoscopic surgery, and the small and limited sample sizes of most studies, where patients were consulted only during medical examinations and were limited to clinical trials, which limited comparative analysis. Finally, therefore, in our study, several pooled efficacy data analyzed the same results by different authors for comparison within the context of HIFU, robotic surgery, and laparoscopic surgery.

5. Conclusions

Although robotic and laparoscopic surgeries are feasible and effective among the patients with uterine fibroids, we found that HIFU treatment results in more efficient clinical and treatment outcomes than robotic or laparoscopic surgeries, including improved symptoms, absence of bleeding, shorter operative time, shorter recovery time, and good benefits in both short-term and long-term quality-of-life.

Author Contributions

C-JJ is corresponding author who was a supervisor and designed the research study. AO is the first author who performed research and wrote the manuscript. T-NW is professional expert who advised and provided help. JS and LTC are professional experts who advised and edited. All authors contributed to editorial changes in manuscript. All authors read and approved the final manuscript.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest. CJJ is serving as one of the Guest editors of this journal. We declare that CJJ had no involvement in the peer review of this article and has no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to SF.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.31083/j.ceog4911248.

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