Original Article

Efficacy and safety of different thermal ablative therapies for desmoid-type fibromatosis: a systematic review and meta-analysis

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Background: Desmoid-type fibromatosis (DF) is a locally aggressive tumor characterized by peripheral infiltration of neoplastic cells and remote metastasis disability. This systematic review examined the efficacy and safety of thermal ablative therapy for DF tumors.

Methods: A literature search was conducted using PubMed, Web of Science, Cochrane Library, and Embase from January 1, 2000, to November 12, 2022. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement was used to guide literature selection. The inclusion criteria were the following: (I) the patients were diagnosed with aggressive fibromatosis pathologically, (II) the patients were treated by thermal ablations, and (III) a focus on treatment efficacy and safety. Meanwhile, the exclusion criteria were the following: (I) cohorts of patients with hypertrophic scar, Gardner fibroma, or nodular fasciitis; (II) conference abstracts, reviews, case reports, letters to editors, comments, or editorials; (III) number of patients <5; (IV) *in vitro* or animal experiments; and (V) non-English language articles. The inverse variance method with a random effects model was used to obtain the pooled data. Subgroup analyses were performed to identify treatment factors. Egger test was conducted to assess the risk of publication bias.

Results: After literature selection, 694 DF tumors were identified in 23 studies. In terms of modality, 13 studies used cryoablation, 9 studies used high-intensity focused ultrasound (HIFU), and 1 study used microwave ablation (MWA). The pooled symptom relief rate was 90% [95% confidence interval (CI):

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80–97%], with that for HIFU being 100% (95% CI: 85–100%), that for cryoablation being 87% (95% CI: 74–97%), and that MWA being 89% (95% CI). The pooled major complication rate was 3% (95% CI: 1–7%), and that for each modality was as follows: HIFU =2% (95% CI: 0–6%), cryoablation =4% (95% CI: 1–8%), MWA =11%, ultrasound =6% (95% CI: 1–13%), computed tomography (CT) =2% (95% CI: 0–7%), and magnetic resonance imaging (MRI) =3% (95% CI: 0–14%). The pooled nonperfused volume rate (NPVR) was 76% (95% CI: 71–81%), and that for each modality was as follows: HIFU =77% (95% CI: 71–85%), cryoablation =74% (95% CI: 69–79%), ultrasound =75% (95% CI: 67–83%), CT =76% (95% CI: 67–87%), and MRI =78% (95% CI: 70–87%). The pooled local control rate was 88% (95% CI: 79–94%) and that for each modality was as follows: HIFU =99% (95% CI: 96–100%), cryoablation =80% (95% CI: 68–90%), and MWA =78%. The differences in major complication rate (P=0.77) and NPVR between imaging-guided modalities (P=0.40) were not significant, nor were the differences in symptom relief rate (P=0.32) and major complication rate (P=0.61) between ablative techniques; however, the differences in local control rate (P=0.01) were significant between ablative techniques.

Conclusions: Imaging-guided thermal ablative therapies contribute to symptom relief with a duration of more than 6 months and a low major complication rate of DF tumors.

Keywords: Desmoid-type fibromatosis (DF); high-intensity focused ultrasound (HIFU); microwave ablation (MWA); cryoablation; meta-analysis

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Introduction

Desmoid-type fibromatosis (DF), also known as desmoid tumor or aggressive fibromatosis, is a monoclonal fibroblastic proliferation originating from mesenchymal tissue. It is a relatively rare tumor with an annual incidence of 5 to 6 new cases per one million people (1). DF tumors usually occur sporadically in the fourth decade of life of patients (2), about 85–90% of patients acquire this disease with catenin (cadherin-associated protein) beta 1 (*CTNNB1*) gene mutations encoding β-catenin (3), and 5–15% of DF tumors arise in patients with familial adenomatous polyposis (FAP) syndrome.

DF is characterized by local aggressiveness caused by a biological infiltrative growth pattern and, conversely, distant metastases are unable to occur. This disease imposes a persistent mental and physical hardship on patients, and postoperative recurrence frequently occurs (4), with the reported rate being over 40% (5). Even when patients receive macroscopically complete resection with a pathologically negative R0 margin being achieved, over 30% of patients would still experience local recurrence (6). This high recurrence rate of DF makes surgery less than satisfactory in the treatment of symptomatic or asymptomatic DF.

It is worth noting that the treatment standard is shifting, with the generally accepted treatment strategies becoming increasingly conservative (7). In recently published guidelines, active surveillance has become the mainstream recommendation for front-line therapy for DF (7,8). An initial observation over the first 2 years is recommended in patients with the absence of progression, morbidity, or symptomatic DF, as 50% of observed tumors could have spontaneous regression (9). However, a systematic review of 1480 patients who received active surveillance showed that most cases had either stable disease or partial response, while 29% of the patients eventually shifted to active therapy (10). Active therapies include surgery, radiotherapy, systemic therapy, isolated limb perfusion (ILP), and ablation procedures. According to the European Society for Medical Oncology (ESMO) guideline (11), for patients with progressive disease, the optimal strategy is individualized on a multidisciplinary basis, with the option of local active therapy depending on the tumor's origin. Cryoablation is suitable for extra-abdominal DF, ILP is suitable for DF confined to an extremity, and surgery is recommended in favorable locations such as the abdominal wall. Notably, as one type of thermal therapy, cryoablation has been increasingly applied in recent years owing to its accuracy, minimal invasiveness, and cost-effectiveness.

However, besides cryoablation, other imaging-guided

thermal ablative therapies such as high-intensity focused ultrasound (HIFU), microwave ablation (MWA), and radiofrequency ablation (RFA) have also been applied to treat primary or recurrent DF tumors in recent years (12-15). RFA is based on the generation of a high-frequency alternating current through a monopolar electrode tip inserted into a target tumor that induces local heating, reaching a temperature more than 60 ℃, which is necessary for coagulation necrosis. MWA creates an electromagnetic field around an electrode and increases local heating and coagulation necrosis in target tumor. HIFU is based on the ability to precisely concentrate a high-intensity ultrasound beam into a definite target tissue inside the body. The absorption of the acoustic energy by target tissue causes its conversion to heat energy, which may then induce coagulative necrosis at the targeted lesion in a well-defined area. Cryoablation is a minimal invasive thermal technique that uses a device with argon and helium gas or liquid nitrogen to rapidly decrease the temperature of tumors to extremely low level, causing the formation of an ice ball inside and outside tumor cells. This process destroys the cell membrane, resulting in the occlusion of the microvessels in tumor tissue and, in turn, tumor tissue necrosis and ischemia.

Despite inspiring results, debulking or curing thermal ablative procedures remain controversial. The opinions on applying thermal ablation procedures between guidelines and consensuses vary (1,3,7,8). In 2015, the European Organization for Research and Treatment of Cancer (EORTC) suggested that cryoablation should be limited in large tumors or tumors proximal to critical structures and should only be applied to a few locations (extremities and chest wall) (1). Subsequently, cryoablation was not included in the recommendation algorithm in the updated 2017 consensus version (1,3). The National Comprehensive Cancer Network (NCCN) guidelines detailed the situations in which thermal ablation is eligible for treating DF. Only tumors located in the intra-abdominal, retroperitoneal, or pelvic areas were deemed ineligible for ablative procedures (8). Moreover, thermal ablative procedures were not even mentioned in the evidence-based guideline of the Desmoid Tumor Working Group (7). Therefore, this study aimed to evaluate the efficacy and safety of thermal ablation in treating extra-abdominal and intra-abdominal DF using a systematic review and meta-analysis. We present this article in accordance with the PRISMA reporting checklist (available at https://qims.amegroups.com/article/view/10.21037/qims-23-289/rc).

Methods

Search strategy

A detailed search was performed on the PubMed, Web of Science, Cochrane Library, and Embase databases to retrieve original articles published from January 1, 2000, to November 12, 2022, that evaluated the safety and efficacy of imaging-guided thermal ablation for patients with aggressive fibromatosis. "Desmoid-type fibromatosis", "high-intensity focused ultrasound", "cryoablation", "radiofrequency ablation", "microwave ablation", and "laser ablation" were searched in databases as theme words; the detailed search strategy is presented in Appendix 1.

Inclusion and exclusion criteria

The studies included in this analysis fulfilled the following criteria: (I) the patients involved in the studies were diagnosed with aggressive fibromatosis pathologically; (II) the patients were treated with imaging-guided thermal ablation; and (III) clinical outcomes were related to the efficacy and safety of the treatment. The exclusion criteria were (I) patients with hypertrophic scar, Gardner fibroma, or nodular fasciitis enrolled in the cohorts; (II) conference abstracts, reviews, case reports, letters to editors, comments, and editorials; (III) number of patients <5; (IV) *in vitro* or animal experiments; and (V) non-English language articles. Two experienced radiologists (>10 years of experience in diagnostic and interventional radiology) independently performed the literature search and eligibility assessment. Any disagreement between their work was resolved by another senior doctor (>20 years of experience in diagnostic and interventional radiology).

Study selection and data extraction

Two researchers (Luo L, Li Y) independently extracted data according to the PRISMA guidelines (16). Another researcher (Huang K) with abundant experience in meta-analysis checked the consistency between the 2 researchers; if there was difference, this researcher would retrieve the data in relevant articles and obtain the definitive data. (I) Characteristics of the article and procedures, included the following: the first author, the year, nationality, imaging guidance, ablative techniques, number of patients, lesion number, male to female ratio, patient age, follow-up, study purpose, location of the lesion, mean volume and size of the lesion, time spent on the ablative procedure, and the

number of primary treatments; (II) clinical outcomes of the ablative operation, including duration of hospitalization, nonperfused volume rate (NPVR) [the ratio of nonperfused volume to the total volume of the treated lesion in enhanced magnetic resonance imaging (MRI) examination], the relief of symptoms, anesthesia, complete response [defined by the Response Evaluation Criteria In Solid Tumors (RECIST) or modified RECSIST (mRECIST) criteria], repeated treatment (RT); and (III) major complications, which was defined of as the occurrence of adverse events with the possibility of resulting in disability or death of patients such as to require additional medication and prolongation of hospital stay.

Quality assessment and statistical analysis

Two authors (Hong R, Jiang Y) independently performed the extraction and quality appraisal of the articles using the methodological index for nonrandomized studies (17). Eight items were used to evaluate the quality of noncomparative studies. For each item, a study's quality was scored as 0, 1, and 2, representing not reported, inadequately reported, and adequately reported, respectively. A total score >12 was rated as a high-quality study, 8–12 as a medium quality study, and <8 as a low-quality study. Low-quality studies were not retained. The pooled outcomes were major complication rate, symptom relief rate, local control rate, and NPVR. The calculation of pooled proportions was performed using an inverse variance method with a random effects model. Higgins inconsistency index (I^2) was used to evaluate the heterogeneity between the studies. An I^2 value greater than 50% indicated substantial heterogeneity, and subgroup analysis was performed based on the type of ablative methods or the imaging-guided modalities. Egger test was conducted to assess the risk of publication bias of the included articles. All statistical tests were two-sided and were conducted in the "meta" package of R version 4.1.2 (The R Project for Statistical Computing; http://www.r-project.org/).

Results

Literature search

The study selection process is presented in *Figure 1*. A total of 324 articles were retrieved through a preliminary database search, among which 109 articles were identified as duplicates and removed. After the screening of abstracts and titles, 62 reviews, 79 irrelevant studies, 23 case reports, and 19 conference papers were excluded. Meanwhile, 2 animal experiments and 3 studies with fewer than 5 recruited patients were eliminated. After an intensive study of 27 full-text articles, we found 1 study not written in English and 3 articles focused on perspectives other than the efficacy and safety of thermal ablation in aggressive fibromatosis, all of which were excluded. Consequently, 23 articles were ultimately included in this study (12-14,18-37).

Quality assessment

The quality of included studies was assessed according to the Methodological Index for Non-Randomized Studies (MINORS) scale, and the results are presented in *Table 1*. Five studies were rated high-quality, the others were rated medium-quality studies (detail results given in Table S1).

Characteristics of the studies

Table 1 shows the detailed characteristics of the 23 studies: 9 studies used HIFU, 1 used MWA, and 13 used cryoablation. None of the eligible studies used RFA or laser ablation after selection. In terms of imaging modality for guidance, 7 studies chose ultrasound only, 7 studies chose computed tomography (CT) only, 3 studies chose MRI only, 3 studies used ultrasound combined with CT, and 3 studies used CT combined with MRI to guide the ablative processes. A total of 568 patients with 723 tumors were encompassed in the analysis. In 12 studies that reported therapeutic expectation, 240 and 113 patients were treated with palliative and curative intent, respectively. In 11 studies, 75 patients received thermal ablation as the primary treatment, and 353 patients underwent other treatments before thermal ablation, including surgery, chemotherapy, radiotherapy, nonsteroidal anti-inflammatory drugs (NSAIDs), ILP, hormonal therapy, and targeted therapeutics. The sizes of population in the studies ranged from 5 to 111, the mean age of patients ranged from 21.8 to 54.3 years, and the female to male ratio was 2.15. One study (32) was comparative in design, comparing cryoablation therapy with surgery, while all the others were noncomparative.

Thermal ablation

Details of thermal ablation are presented in *Table 2*. The mean time of the ablative process ranged from 20 to 270 min. Moreover, 50.9% of operations were carried

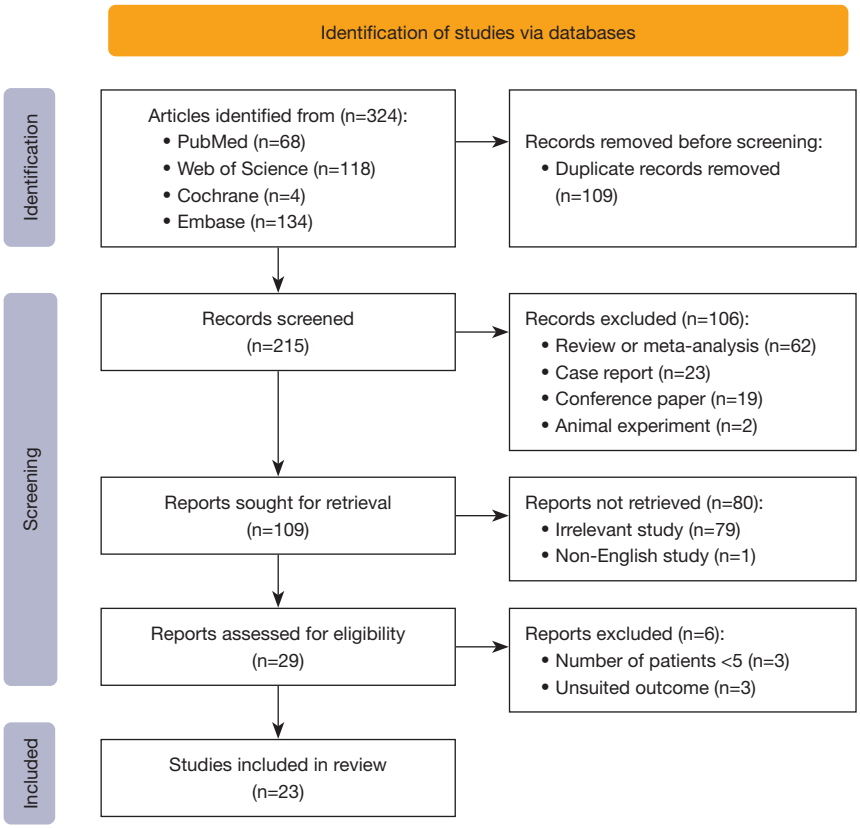

Figure 1 PRISMA schematic diagram of the literature search and selection process. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

out under general anesthesia, while 49.1% used local anesthesia with 1% lidocaine or sedation. The mean days of hospitalization ranged from 0.12 to 7.0, and the mean follow-up after treatment ranged from 3.8 to 53.8 months. A total of 21 studies (12-14,18-32,34,36,37) reported the locations of ablated DF tumors, of which 12 studies used cryoablation, 8 studies used HIFU, and 1 study used MWA. In terms of location, 425 (72.6%) tumors were located in the extra-abdominal area, 69 (11.8%) tumors were located in the intra-abdominal area, and 91 (15.6%) tumors were located at chest wall or abdominal wall.

In the cryoablation group, 67.5% of the tumors were located in the extra-abdominal area, 27.9% of which originated from the trunk, 23.7% from the upper extremity, 32.1% from the lower extremity, and 16.3% from the neck. Additionally, 21.9% of the tumors were located at intra-abdominal area, and 3 studies (13,28,31) reported the definitive locations, all of which originated from pelvis. A further 10.6% of the tumors were located at the chest wall or abdominal wall, and 10 studies (18,20,23,26,28-32,36) reported the definitive locations, 29.4% of which originated from chest wall and 70.6% of which originated from the abdominal wall.

In the HIFU group, 77.5% of the tumors were located in the extra-abdominal area, and 4 studies (19,22,24,25) reported the definitive locations of tumors, 37.5% of which originated from trunk, 9.4% from the upper extremity, and 53.1% from the lower extremity. Finally, 13.7% of the tumors were located at the intra-abdominal area. Only 1 study (37) reported the definitive locations of tumors, 46.7% which originated from the mesentery, 40.0% from the pelvis, and 13.3% from the retroperitoneum. Moreover, 8.8% of the tumors were located at chest wall or abdominal wall, and 3 studies (19,22,24) reported the definitive locations of tumors, 42.9% of which originated from the chest wall and 57.1% of which from abdominal wall.

In the MWA group, all the DF tumors were located in the extra-abdominal area, 55.6% of which originated from the leg and 44.4% from the trunk.

The average size of tumors that received repeated

Table 1 Patient and tumor characteristics in the included studies

Author	Year	Country	Group	Guidance	No. (patient/lesion)	M/F	Age (years)†	Primary treatment (n)	Therapeutic expectation (curative/palliative)	Volume (cm^3)†	Size (cm)†	MINORS score
Kujak *et al.* (18)	2010	USA	Cryo	CT	5/5	2/3	24.2±13.5	0	3/2	NR	6.6±2.9	12
Wang *et al.* (19)	2011	China	HIFU	US	10/25	7/3	21.8±15.8	2	2/8	NR	9.2±2.1	13
Havez *et al.* (20)	2014	France	Cryo	US/CT	13/17	4/9	39.3±17.6	1	9/8	NR	5.7±3.0	12
Schmitz *et al.* (23)	2016	USA	Cryo	CT	18/23	8/10	42.1±18.8	2	NR	NR	6.4±3.1	10
Avedian *et al.* (22)	2016	USA	HIFU	MRI	5/5	3/2	28.6±21.5	2	NR	289.8±405.1	NR	11
Zhao *et al.* (21)	2016	China	HIFU	US	7/7	4/3	31.1±21.1	0	0/7	NR	11.6±5.1	10
Ghanouni *et al.* (24)	2016	USA	HIFU	MRI	15/25	6/9	29.1±17.4	7	NR	211.7±285.5	NR	13
Najafi *et al.* (25)	2019	SWI	HIFU	MRI	5/5	3/2	49.0±16.9	0	NR	24.2±27.4	NR	11
Redifer *et al.* (26)	2019	USA	Cryo	CT	23/30	9/14	40.2±15.8	14	12/11	98.5±126.0	7.1±2.5	9
Bouhamama *et al.* (28)	2020	France	Cryo	US/CT	34/41	9/25	38.1±13.6	0	23/11	104.4‡	5.85‡	10
Saltiel *et al.* (27)	2020	SWI	Cryo	US	10/14	1/9	33.0±18.2	4	8/2	63.6±58.5	NR	11
Mandel *et al.* (32)	2022	USA	Cryo	CT/MRI	22/22	4/18	NR	12	NR	NR	NR	13
Kurtz *et al.* (30)	2021	France	Cryo	CT/MRI	50/50	11/39	40.9±5.72	0	NR	449.4±93.1	8.8±1.8	15
Auloge *et al.* (13)	2021	France	Cryo	CT/MRI	30/30	9/21	40.1±14.8	0	19/11	274.9±352.1	9.1±4.5	12
Zhang *et al.* (12)	2021	China	HIFU	US	111/145	32/79	29.5±1.0	0	NR	294.4±759.7	10.4±6.0	13
Efrima *et al.* (31)	2021	Israel	Cryo	US/CT	11/16	5/6	35.3±13.0	6	NR	258.6±202.1	NR	10
Yan *et al.* (29)	2021	Canada	Cryo	CT	25/55	8/17	NR	11	10/15	153.9±214.3	9.1±5.8	9
Martínez-Martínez *et al.* (14)	2021	Spain	MWA	CT	9/9	3/6	46.6±19.3	0	NR	212.7±213	10.9±5.2	12
Zhong *et al.* (33)	2022	China	HIFU	US	91/122	21/70	29.6±11.1	0	15/107	NR	9.4±6.2	11
Johnston *et al.* (36)	2022	UK	Cryo	CT	10/13	2/8	54.3±23.2	5	6/7	294.9±597.7	NR	12
Colak *et al.* (35)	2022	USA	Cryo	CT	7/7	NR	NR	0	NR	NR	NR	10
Mo *et al.* (34)	2022	China	HIFU	US	42/42	15/27	30.0±11.9	0	6/36	292.1±374.9	NR	10
Yang *et al.* (37)	2022	China	HIFU	US	15/15	5/10	35.2±9.4	2	0/15	632.8±1277	14.1±7.7	12

†, data are presented as mean ± SD; ‡, the SD of the data is not available, and the data could not be included in the analysis. M/F, male/female; MINORS, methodological index for nonrandomized studies; Cryo, cryoablation; CT, computed tomography; NR, not reported; HIFU, high-intensity focused ultrasound; US, ultrasound; SWI, Switzerland; MRI, magnetic resonance imaging; MWA, microwave ablation; SD, standard deviation.

thermal therapy was 6.96 cm (19,24,25,30), and the main reasons for repeated thermal therapy were oversized tumors and unintended residual and/or recurrent tumors. Additionally, 13 studies (12-14,18-21,23,26,29,30,33,37) reported the mean diameter of the ablated DF tumors. The mean diameter of tumors ablated with cryoablation was 7.61 cm (95% CI: 6.62–8.74), the mean diameter of tumors ablated with HIFU was 10.29 cm (95% CI: 9.11–11.63), and the mean diameter of the tumors ablated with MWA was 10.90 cm (14). A total of 14 studies (12-14,22,24-27, 29-31,34,36,37) reported the mean volume of the ablated DF tumors. The mean volume of the tumors ablated with cryoablation was 189.54 cm^3 (95% CI: 111.76–321.45), the mean diameter of the tumors ablated with HIFU was 211.47 cm^3 (95% CI: 92.66–482.63), and the mean diameter of the tumors ablated with MWA was 212.7 cm^3 (14).

Symptom relief

Symptom relief was reported in 12 studies (13,14,18,20, 21,23,24,26,27,29,31,32), with 203 of the 306 (66.3%) patients in the included studies experiencing symptoms of DF and 189 of the 203 symptomatic patients being relieved of discomfort after treatment. Symptom relief rate ranged from 60% (18) to 100% (21,24,32). DF-related symptoms included pain, motor dysfunction, abdominal distension, and pressure, among others. Most studies determined the presence of symptom relief via patients' subjective

Table 2 The treatment characteristic and clinical outcome during follow-up

Author	Follow-up (months)†	Time (min)†	NPVR (%)†	Duration of hospitalization (days), mean	Symptom relief (n)	Complication (n)		Complete response (n)	Local control rate (%)	Repeated treatment (n)	Anesthesia (general/local and others)
						Minor	Major				
Kujak *et al.* (18)	32.4±22.5	NR	NR	NR	3	2	0	2	60.00	NR	NR
Wang *et al.* (19)	29.9±17.9	NR	NR	3	NR	9	1	2	100.00	2	25/0
Havez *et al.* (20)	11.3±7.2	NR	NR	1.5	14	3	0	1	88.24	NR	15/2
Schmitz *et al.* (23)	16.2±20	NR	NR	1.4	4	3	0	10	91.30	NR	NR
Avedian *et al.* (22)	18.2±4.6	270±87	65.2±32.1	NR	NR	5	0	1	60.00	3	3/2
Zhao *et al.* (21)	14.6±2.2	74±31	92.5±3.7	7	7	3	1	0	100.00	1	0/7
Ghanouni *et al.* (24)	17.6±10.6	210±96	79.1±22.1	0.12	6	8	2	5	96.00	7	15/17
Najafi *et al.* (25)	27.0±19.2	NR	NR	NR	NR	4	0	3	100.00	3	0/5
Redifer Tremblay *et al.* (26)	16.8±10.4	173±46	71.3±26.5	0.23	18	4	2	5	86.67	4	13/17
Bouhamama *et al.* (28)	NR	NR	NR	NR	NR	4	0	14	51.22	NR	23/18
Saltiel *et al.* (27)	53.8±23.1	NR	67.3±30.2	NR	NR	0	2	3	85.71	4	NR
Mandel *et al.* (32)	NR	NR	NR	1.3	5	7	1	NR	59.09	5	22/0
Kurtz *et al.* (30)	NR	NR	NR	4	NR	31	11	NR	NR	6	50/0
Auloge *et al.* (13)	31.9±25.6	NR	71.7±27.0	2	29	7	4	13	NR	7	30/0
Zhang *et al.* (12)	NR	116±59	81.9±18.7	3	NR	61	3	NR	NR	8	9/177
Efrima *et al.* (31)	NR	NR	72.1±20.0	3	9	3	0	1	NR	9	16/0
Yan *et al.* (29)	18.5±21.3	132±51	81.5±25.6	1.7	32	3	1	0	88.46	10	37/4
Martínez-Martínez *et al.* (14)	3.8±1.9	NR	NR	NR	8	1	1	2	77.78	11	NR
Zhong *et al.* (33)	32.7±20.3	NR	69.5±23.8	NR	NR	28	7	12	96.70	NR	122/0
Johnston *et al.* (36)	13.9±20.3	112±40	NR	2.0	NR	8	1	1	70.00	NR	NR
Colak *et al.* (35)	≥3.0	NR	NR	NR	NR	0	0	NR	100.00	0	NR
Mo *et al.* (34)	NR	20±11	72.4±22.6	3.0	NR	42	0	NR	NR	NR	3/39
Yang *et al.* (37)	29.2±15.7	NR	71.1±22.9	NR	NR	3	2	1	93.30	15	15/0

Complete response is defined according to the RECIST or mRECIST criteria. †, data are presented as mean ± SD. NPVR, non-perfused volume rate; n, number; NR, not reported; RECIST, Response Evaluation Criteria In Solid Tumors; mRECIST, modified RECIST; SD, standard deviation.

judgement rather than via quantitative or objective scales, and 2 studies used a numerical rating scale (NRS) (24) or visual analogic scale (VAS) (13) to quantitatively assess pain. Ghanouni *et al.* (24) used NRS to compare the changes of pain before and after therapy: they reported 6 patients with pain decrease from a preoperative 6±2.3 points to a postoperative 1.3±2 points, with this difference being statistically significant. The pooled symptom relief rate was 90% (95% CI: 80–97%) with mild heterogeneity (I^2=49%; P=0.03), as presented in *Figure 2*. The symptom relief rate of MWA was 89% (14), that of HIFU was 100% (95% CI: 85–100%), and that of cryoablation was 87% (95% CI: 74–97%). The difference was not statistically significant (χ^2=2.29; P=0.32; *Table 3*). Egger test suggested no risk of publication bias (P=0.2492). The funnel is presented in *Figure 3*.

Major complications

All studies reported major complications after operation. Of the 694 lesions, 40 were associated with major complications, among which severe nerve injury was the most common (26.3%) (*Figure 4*). The pooled major complication rate was 3% (95% CI: 1–7%; I^2=44%;

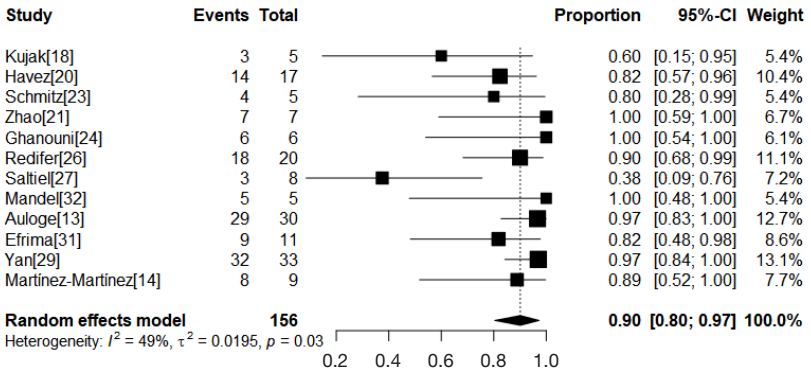

Figure 2 The forest plot regarding the symptom relief rate of the patients (13,14,18,20,21,23,24,26,27,29,31,32). Every study is presented as the first author and reference number, the black box represents individual study point estimate, the size of the black box indicates the contribution to the pooled estimate, horizontal lines signify 95% CIs, and the diamonds below the mark random-effects pooled estimates. CI, confidence interval.

Table 3 Subgroup analysis according to ablative technique and imaging modality

Subgroup	Symptom relief rate			Major complication rate			NPVR			Local control rate		
	Pool proportion [95% CI] (%)	I^2 (%)	P	Pool proportion [95% CI] (%)	I^2 (%)	P	Pool proportion [95% CI] (%)	I^2 (%)	P	Pool proportion [95% CI] (%)	I^2 (%)	P
Ablative technique			0.32			0.61			0.40			0.01
HIFU	100 [85–100]	0		2 [0–6]	35		77 [71–85]	94		99 [99–100]	19	
Cryo	87 [74–97]	60		4 [1–8]	51		74 [69–79]	0		80 [68–90]	68	
MWA	89 [52–100]	NA		11 [0–48]	NA		NA	NA		78 [40–97]	NA	
Imaging modality			0.62			0.77			0.84			0.01
US	76 [60–100]	88		6 [1–13]	53		75 [67–83]	95		98 [95–100]	51	
CT	91 [78–99]	33		2 [0–7]	0		76 [67–87]	53		87 [79–93]	12	
MRI	100 [54–100]	NA		3 [0–14]	0		78 [70–87]	0		93 [68–100]	12	

CI, confidence interval; NPVR, non-perfused volume rate; HIFU, high-intensity focused ultrasound; Cryo, cryoablation; MWA, microwave ablation; NA, not available; US, ultrasound; CT, computed tomography; MRI, magnetic resonance imaging.

P=0.01; *Figure 5*). The major complication rates for MWA, HIFU, and cryoablation were 11% (14), 2% (95% CI: 0–6%), and 4% (95% CI: 1–8%), respectively. However, the difference was not statistically significant (χ^2=0.9; P=0.61; *Table 3*). Egger test suggested no risk of publication bias (P=0.4421). The funnel plot is presented in *Figure 6*. Subgroup analysis showed that the major complication rate with ultrasound guidance was 6% (95% CI: 1–13%), that of CT was 2% (95% CI: 0–7%), and that of MRI was 3% (95% CI: 0–14%); but these were not significant differences (χ^2=0.52; P=0.77). The detailed subgroup data are presented in *Table 3*.

Nonperfused volume rate

Twelve of the included articles (12,13,21,22,24,26,27, 29,31,33,34,37) recorded the NPVR during follow-up, which was calculated in 477 tumors, ranging from 65.2% (22) to 92.5% (21), and the pooled NPVR was 76% (95% CI: 71–81%; I^2=90%; P<0.01; *Figure 7*). In the subgroup analysis, the NPVR was 77% (95% CI: 71–85%) for HIFU ablation and 74% (95% CI: 69–79%) for cryoablation. The difference was not statistically significant (χ^2=0.72; P=0.40). The ultrasound-guided NPVR was 75% (95% CI: 67–83%), that for CT was 76%

(95% CI: 67–87%), and that for MRI was 78% (95% CI: 70–87%), but these differences were not significant (χ^2=0.34; P=0.84). *Table 3* shows the detailed subgroup data. The Egger test showed there to be no risk of publication bias (P=0.0159). The funnel plot is presented in *Figure 8*.

Local control rate

Eighteen studies (14,18-29,32,33,35-37) reported local control rates of tumors, which ranged from 51% (28) to 100% (19,21,25,35). The pooled local control rate was 88% (95% CI: 79–94%; I^2=77%; P<0.01; *Figure 9*). In the subgroup analysis, the rate of local control of MWA was 78% (14), that of HIFU was 99% (95% CI: 99–100%), and that of cryoablation was 80% (95% CI: 68–90%), with these differences being statistically significant (χ^2=17.82; P=0.01). The Egger test showed no risk of publication bias (P=0.4930). The funnel plot is presented in *Figure 10*.

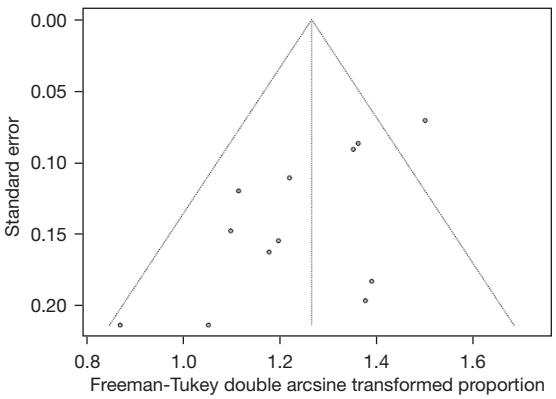

Figure 3 Funnel plot regarding symptom relief rate in thermal ablative procedures according to the Egger test.

Discussion

This review assessed the clinical outcomes of thermal ablative approaches in DF tumors, including HIFU, microwave, and cryoablation, with 23 relevant articles being included. Using meta-analysis, we obtained quantitative data to evaluate the performance of thermal therapies in DF tumors: the pooled symptom relief rate was 90%, the major complications rate was 3%, the pooled NPVR was 76%, and the local control rate was 88%. These pooled data indicated that thermal ablative approaches were suitable treatments for symptomatic DF tumors with impressive safety and efficacy. The treatment paradigm of DF fibromatosis is constantly changing. Many recently published guidelines are consistent in suggesting active surveillance as the front-line therapy for patients with DF, with active treatment only being recommended if active surveillance fails. However, there is substantial divergence regarding the application of thermal ablative procedures. The NCCN guidelines (8) indicate that ablative procedures should be applied in this disease for detailed locations and situations. On the contrary, the guidelines and consensus from other expert panels (1,3,7,9) advise caution concerning the application ablative procedures. This wariness arises from the

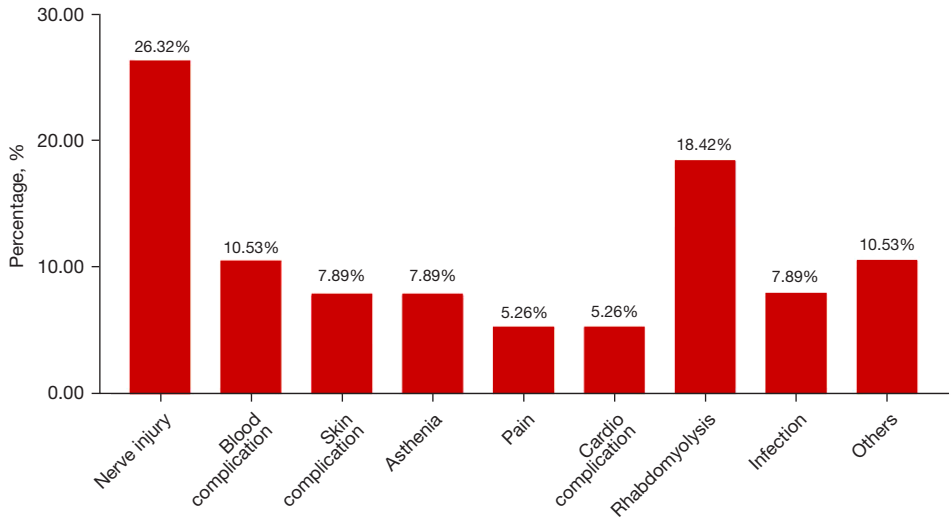

Figure 4 Major complications and the occurrence rate of thermal ablative procedures.

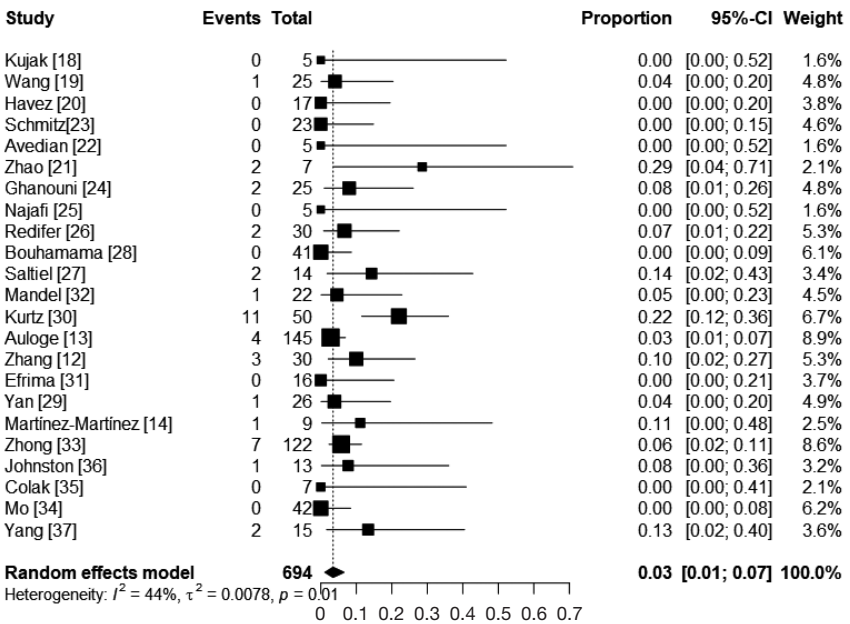

Figure 5 The forest plot regarding the major complication rate of patients (12-14,18-37). Every study is presented as the first author and reference number, the black box represents the individual study point estimate, the size of the black box indicates the contribution to the pooled estimate, horizontal lines signify the 95% CIs, and diamonds below mark the random-effects pooled estimates. CI, confidence interval.

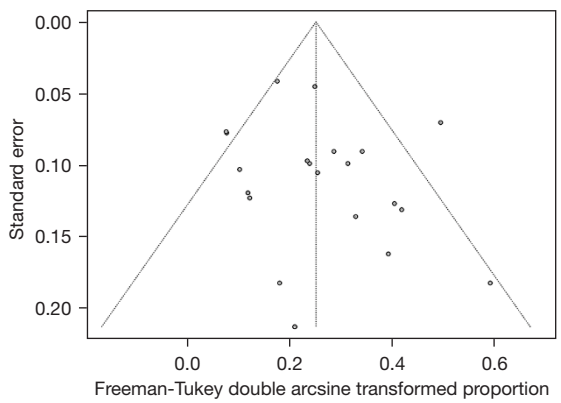

Figure 6 Funnel plot regarding the major complication rate in thermal ablative procedures according to the Egger test.

insufficient efficacy of ablation on tumors and the lack of safety data from long-term and large-sample studies. Hence, the aim of this review was to clarify and possibly quell these concerns regarding the safety and efficacy of thermal ablative procedures. In terms of efficacy, it is unclear if the durability of a symptom or dimensional benefit, particularly in partially treated tumors, is reliable (38). In our study, DF-related pain was present in 88.9% of symptomatic tumors. The pooled symptom relief rate of the ablated tumors was 90%, and most of the symptoms did not recur during the follow-up. The pooled NPVR was 76%, Due to the limited available data, the subgroup analysis based on the extent of tumor ablation was not carried out. However, only 18% of ablated tumors had a complete response (as defined by the RECIST or mRECIST criteria), indicating that most tumors were partially ablated in practice. Consequently, regardless of whether DF tumors were ablated entirely or partially, most patients with thermal ablative treatment benefited from considerable viable spatial dimensional volume changes and symptom relief.

Another concern of ablative procedures is their safety. Although the criteria for the assessment of complications varied between studies, the definition of major complications was clear and consistent. The pooled major complication rate was 3%, which was comparable to that of front-line or alternative therapies. Radiotherapy is usually associated with late toxicity, increased fibrosis, and decreased range of motion (39). Bates *et al.* (40) reported that 37% of DF patients treated with radiotherapy experienced grade 3 or higher toxicity. The major complication rate has been reported to be 6.2% after open surgery (41), with 60% of patients treated in this manner achieving an R0 margin. Systemic therapies are usually associated with bone marrow toxicity, neutropenia, and peripheral neuropathy (4).

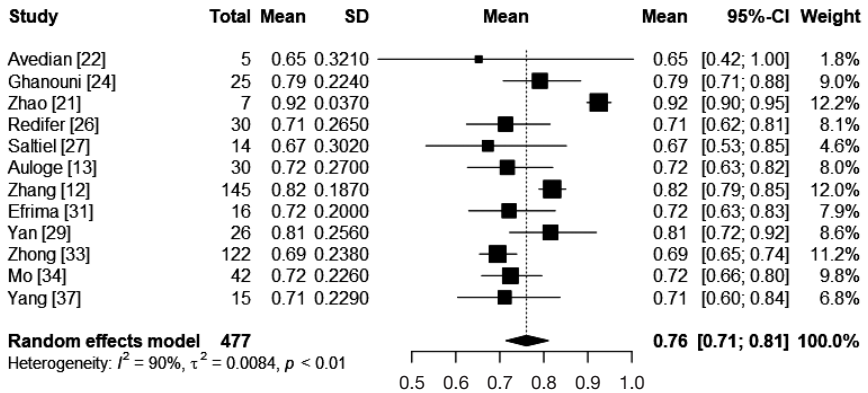

Figure 7 The forest plot regarding the NPVR of the patients (12,13,21,22,24,26,27,29,31,33,34,37). Every study is presented as the first author and reference number, the black box represents individual study point estimate, the size of the black box indicates the contribution to the pooled estimate, horizontal lines signify 95% CIs, and diamonds below mark the random-effects pooled estimates. SD, standard deviation; CI, confidence interval; NPVR, non-perfused volume rate.

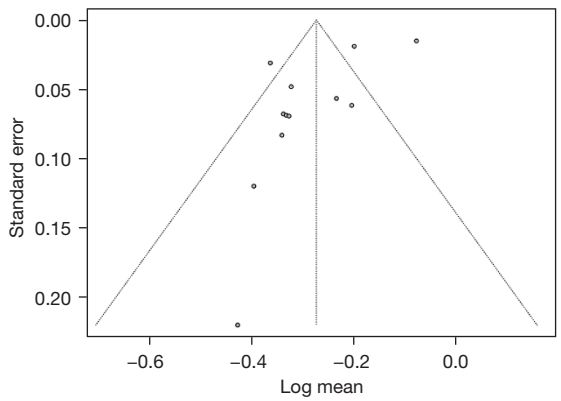

Figure 8 Funnel plot regarding NPVR for thermal ablative procedures according to the Egger test. NPVR, nonperfused volume rate.

A national phase II trial (42) revealed that imatinib administration for unresectable or progressive symptomatic DF tumors caused 45% of the major complications.

Moreover, the locations of DF tumors have large impact on the safety and efficacy of thermal therapies. When important vessels and nerves are encased in tumors, operators usually abandon the complete ablation of the whole tumors. For instance, for DF tumors originating from the popliteal space, popliteal artery and vein are often the obstacles to achieving complete ablation. Zhang *et al.* (12) compared the differences of complications and NPVR between different DF tumor locations. The result revealed that the NPVR of extra-abdominal tumors, abdominal wall tumors, and intra-abdominal tumors was 85.0%, 100%, and 26.2%, respectively, with complication rates of 37.93%, 31.3%, and 27.3%, respectively. When the tumors are located in bowel, the proximal anatomical structure is usually much more complex than that of abdominal wall tumors or extra-abdominal tumors, and a more conservative treatment plan will be more acceptable to operators and patients. For this reason, the NPVR of the intra-abdominal area was markedly lower than that of other locations. In terms of the complication rate, the highest rate was from extra-abdominal tumors, which may be related to the greater abundance and wide distribution of nerve injuries, as temporary pain and nerve dysfunction are not rare postoperative complications.

From the perspective of therapeutic guidance, we conducted subgroup analysis to compare the safety and efficacy between different imaging-guided modalities. As for major complications, when the operations were guided by CT and MRI, the occurrence rate was 2% and 3%, respectively, while the major complication rate of ultrasound guidance was 6%, which was higher than that of CT and MRI. The NPVR of ultrasound, CT, and MRI was 75%, 76%, and 78%, respectively. Ultrasound is characterized by real-time and nonaxial imaging, providing an extensive ablation region and flexible procedure in the ablative treatment (43). This is why the NPVR of ultrasound-guided thermal ablation was similar to that of CT and MRI, while CT and MRI had better resolution in the imaging of soft tissue. However, the contrast resolution of ultrasound is limited in obese patients and the presence of air, and this

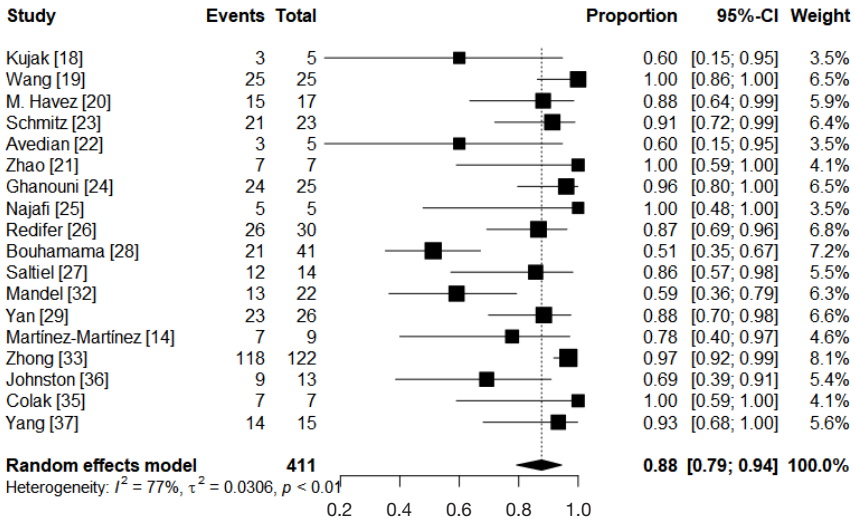

Figure 9 The forest plot regarding the local control rate of the patients (14,18-29,32,33,35-37). Every study is presented as the first author and reference number, the black box represents individual study point estimate, the size of the black box indicates the contribution to the pooled estimate, horizontal lines signify 95% CIs, and diamonds below mark the random-effects pooled estimates. CI, confidence interval.

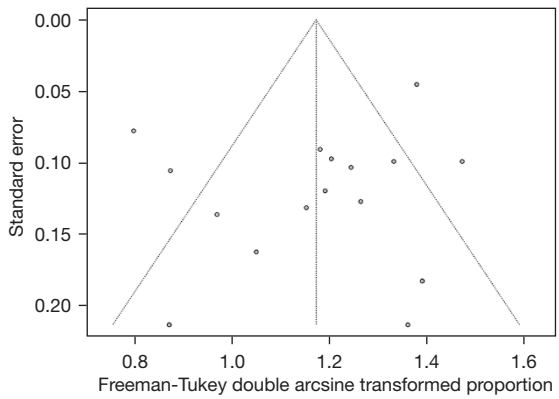

Figure 10 Funnel plot regarding local control rate in thermal ablative procedures according to the Egger test.

may be one reason why ultrasound guidance resulted in a higher major complication rate than did CT or MRI.

The local control of postoperative progression is critical. We found that the local control rate of the included studies was approximately 88%, with a follow-up range of 3.6–53.7 months. This is consistent with the conclusion of a recently published meta-analysis (44), which revealed that when cryotherapy was applied to treat DF tumors, the estimated progression-free survival (PFS) rate for 1 year was 84.5% and that for 3 years was 78.0%. The local control rate of surgical resection for DF tumors varies between 47% and 86% (4), and when tumors are resected with an R0 margin, the rate ranges from 68% to 86% (45,46,47), which is slightly higher. The rate of radiotherapy ranges from 65% to 83% (48,49).

Furthermore, subgroup analysis revealed that when HIFU was applied, the NPVR was higher than that of cryoablation. HIFU is a noninvasive method that involves gathering the ultrasonic power emitted outside the body, with the direction of the power potentially changing according to the tumor outline in a phenomenon known as conformal ablation; meanwhile, the cryoprobes inserted are usually not as flexible as those of HIFU for adjusting the necrotic range during treatment. Meanwhile, as a noninvasive type of thermal therapy, HIFU can be applied safely for the normal tissue in the treatment path, and the possibility of skin hemorrhage is lower than that of MWA and cryoablation. HIFU maybe more suitable for intra-abdominal DF tumors for avoiding direct injury from puncture needles. However, due to its bulky size, HIFU equipment poses challenges in precisely locating certain tumors, leading to incomplete coverage of the entire tumor. Cryoablation has the advantage of skin and tissue cooling during procedures, and when applied to tumors proximal to critical organ or tissue, heat damage can be avoided, which is not the case for HIFU and MWA. However, MWA and HIFU have advantages over cryoablation in bleeding control during procedures. MWA is characterized by a quick heat spread and a high temperature in the ablated region, which can destroy tumor cells more

thoroughly and in less time than can HIFU and cryoablation; indeed, the hemostatic effect of MWA is outstanding. For this reason, MWA may be suitable for treating hypervascular DF tumors.

Some limitations to this study should be addressed. First, this study is restricted by its retrospective nature and a lack of a comparative group with other therapeutic methods, which is an unavoidable deficiency of single-arm studies. Second, despite apparently promising findings concerning the symptom relief rate, the assessment of symptom relief was mainly based on the patients' subjective input rather than objective evaluation such as that provided by the VAS or NRS scale. Additionally quantitative assessments should be taken into critical consideration in future study design of thermal therapy. Finally, the follow-up duration was short in the literature examined, with no included studies with a follow-up duration of more than 5 years.

Conclusions

Imaging-guided thermal ablative therapies contribute to the relief of DF tumor symptoms with a duration of more than 6 months and have a low major complication rate.

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Footnote

Reporting Checklist: The authors have completed the PRISMA reporting checklist. Available at https://qims.amegroups.com/article/view/10.21037/qims-23-289/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-23-289/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Supplementary

Appendix 1

(((((((((Fibromatosis, Aggressive[MeSH Terms]) OR (Aggressive Fibromatoses[Title/Abstract])) OR (Aggressive Fibromatosis[Title/Abstract])) OR (Fibromatoses, Aggressive[Title/Abstract])) OR (Desmoid[Title/Abstract])) OR (Desmoids[Title/Abstract])) OR (Desmoid-type fibromatosis[Title/Abstract])) OR (Desmoid Tumors[Title/Abstract])) AND ((((((((((Radiofrequency Ablation[MeSH Terms]) OR (Ablation, Radiofrequency[Title/Abstract])) OR (Radio Frequency Ablation[Title/Abstract])) OR (Ablation, Radio Frequency[Title/Abstract])) OR (Radio-Frequency Ablation[Title/Abstract])) OR (Ablation, Radio-Frequency[Title/Abstract])) OR (RFA[Title/Abstract])) OR ((microwave ablation[Title/Abstract]) OR (MWA[Title/Abstract]))) OR (((High-Intensity Focused Ultrasound Ablation[MeSH Terms]) OR (High Intensity Focused Ultrasound Ablation[Title/Abstract])) OR (HIFU[Title/Abstract]))) OR (((((Cryosurgery[MeSH Terms]) OR (Cryosurgeries[Title/Abstract])) OR (Cryoablation[Title/Abstract])) OR (Cryoablations[Title/Abstract]))) OR ((((((Laser Therapy[MeSH Terms]) OR (Ablation, Laser[Title/Abstract])) OR (Laser Ablation[Title/Abstract])) OR (Laser Tissue Ablation[Title/Abstract])) OR (Tissue Ablation, Laser[Title/Abstract])) OR (Ablation, Laser Tissue[Title/Abstract])))

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Table S1 Risk of bias in the included cohort studies (according to the MINORS quality assessment tool)

Author	A clearly stated aim	Inclusion of consecutive patients	Prospective collection of data	Endpoints appropriate to the aim of the study	Unbiased assessment of the study endpoint	Follow-up period appropriate to the aim of the study	Loss to follow-up less than 5%	Prospective calculation of the study size	Total quality score
Kujak *et al.* (18)	2	2	1	2	1	2	2	0	12
Wang *et al.* (19)	2	2	2	2	1	2	2	0	13
Havez *et al.* (20)	2	2	1	2	2	1	2	0	12
Schmitz *et al.* (23)	2	1	1	2	1	1	2	0	10
Avedian *et al.* (22)	2	2	2	1	2	1	1	0	11
Zhao *et al.* (21)	2	1	1	2	1	1	2	0	10
Ghanouni *et al.* (24)	2	2	2	2	2	1	2	0	13
Najafi *et al.* (25)	2	1	1	2	1	2	2	0	11
Redifer *et al.* (26)	2	1	1	1	1	1	2	0	9
Bouhamama *et al.* (28)	2	1	1	2	1	1	2	0	10
Saltiel *et al.* (27)	2	1	1	2	1	2	2	0	11
Mandel *et al.* (32)	2	2	2	2	1	2	2	0	13
Kurtz *et al.* (30)	2	2	2	2	2	2	2	1	15
Auloge *et al.* (13)	2	2	2	2	1	1	2	0	12
Zhang *et al.* (12)	2	2	2	2	2	1	2	0	13
Efrima *et al.* (31)	2	1	1	2	1	1	2	0	10
Yan *et al.* (29)	2	1	1	2	1	1	1	0	9
Martínez-Martínez *et al.* (14)	2	2	1	2	2	1	2	0	12
Zhong *et al.* (33)	2	1	1	2	1	2	2	0	11
Johnston *et al.* (36)	2	2	2	2	1	1	2	0	12
Colak *et al.* (35)	2	1	1	2	1	1	2	0	10
Mo *et al.* (34)	2	2	1	2	1	0	2	0	10
Yang *et al.* (37)	2	2	2	2	1	1	2	0	12

MINORS, methodological index for nonrandomized studies.

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