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REVIEW ARTICLE

Gynecology

Diagnostic accuracy of MRI in the differential diagnosis between uterine leiomyomas and sarcomas: A systematic review and meta-analysis

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Abstract

Background: Differential diagnosis between uterine leiomyomas and sarcomas is challenging. Magnetic resonance imaging (MRI) represents the second-line diagnostic method after ultrasound for the assessment of uterine masses.

Objectives: To assess the accuracy of MRI in the differential diagnosis between uterine leiomyomas and sarcomas.

Search Strategy: A systematic review and meta-analysis was performed searching five electronic databases from their inception to June 2023.

Selection Criteria: All peer-reviewed observational or randomized clinical trials that reported an unbiased postoperative histologic diagnosis of uterine leiomyoma or uterine sarcoma, which also comprehended a preoperative MRI evaluation of the uterine mass.

Data Collection and Analysis: Sensitivity, specificity, positive and negative likelihood ratios, diagnostic odds ratio, and area under the curve on summary receiver operating characteristic of MRI in differentiating uterine leiomyomas and sarcomas were calculated as individual and pooled estimates, with 95% confidence intervals (CI).

Results: Eight studies with 2495 women (2253 with uterine leiomyomas and 179 with uterine sarcomas), were included. MRI showed pooled sensitivity of 0.90 (95% CI 0.84–0.94), specificity of 0.96 (95% CI 0.96–0.97), positive likelihood ratio of 13.55 (95% CI 6.20–29.61), negative likelihood ratio of 0.08 (95% CI 0.02–0.32), diagnostic odds ratio of 175.13 (95% CI 46.53–659.09), and area under the curve of 0.9759.

Conclusions: MRI has a high diagnostic accuracy in the differential diagnosis between uterine leiomyomas and sarcomas.

KEYWORDS
Leiomyosarcoma, malignancy, Myomata, neoplasia, prediction, preoperative assessment, uterus

Paolo Casadio and Maurizio Guida contributed equally to the study.

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1 | INTRODUCTION

Uterine sarcomas are malignant tumors arising from the mesenchymal tissues of the uterus.[1] They are rare among female genital tract malignancies, accounting for 1% of genital tract tumors and 3%–7% of all uterine malignances,[2] with a prevalence of 0.64 per 100000 women.[1]

Different histotypes of uterine sarcomas are known, such as leiomyosarcoma, endometrial stromal sarcoma, adenosarcoma, and undifferentiated sarcoma. Among these, leiomyosarcoma is the most frequently diagnosed, with an incidence of 41%–60%.[3]

Uterine sarcomas show aggressive behavior, with a tendency for fast local growth, distant metastasis, and recurrence, resulting in a poor prognosis.[4]

Recently, the preoperative diagnosis of uterine masses has gained increasing interest among clinicians following the 2020 statement by the US Food and Drugs Administration, which affirmed that laparoscopic power morcellation of myomas should be performed only within a tissue-containing system and only in appropriately selected patients,[5] to avoid unwanted dissemination of occult malignant lesions.[6]

Therefore, an accurate preoperative diagnosis (differentiating uterine leiomyomas and sarcomas) is mandatory to guide physicians to a tailored surgical treatment. In particular, it can help to choose proper surgical route (endoscopic versus laparotomic) and type of intervention (myomectomy for benign masses versus total abdominal hysterectomy, oophorectomy and debulking of the tumor outside the uterus for suspected sarcomas).[7]

Unfortunately, differential diagnosis between uterine sarcomas and leiomyomas is an unsolved issue in daily clinical practice. In fact, uterine sarcomas and leiomyoma can present with similar symptoms, such as abnormal uterine bleeding, palpable pelvic mass or abdominal pain. On the other hand, although serum markers appear to be a helpful and promising tool to exclude malignancy, they lack validation.[8]

Among diagnostic imaging tools, ultrasound and magnetic resonance imaging (MRI) are the most suitable for myometrial lesions. Ultrasound is the first-line imaging technique, as it is non-invasive, cheap, and reproducible. Several studies have assessed its performance in preoperative differentiation between leiomyomas and sarcomas.[9] However, overlapping sonographic characteristics may limit the diagnostic accuracy, particularly in cases of degenerating leiomyoma with heterogeneous echogenicity and central necrosis.[10–12] Moreover, the inability to display large uterine masses in a single ultrasound image and the inter-operator variability of the examination prevents the use of ultrasound as a single diagnostic imaging tool.[11]

Conversely, MRI has shown promising results in the diagnosis of uterine sarcomas.[11] Some features have been associated with these rare tumors, including poorly defined margins, high signal intensity on T1- and T2-weighted images, early heterogeneous contrast enhancement with a central non-enhancing area of necrosis, specific diffusion-weighted imaging characteristics, and texture analysis histogram metrics.[11] Increased signal on T2-weighted images seems to have a limited predictive value as a stand-alone marker of malignancy. Yet, specific diffusion weighted imaging (DWI) characteristics and apparent diffusion coefficient (ADC) values are potentially overlapping for leiomyomas and leiomyosarcomas, and therefore helpful only if combined with signal intensity characteristics.[13–15] Consequently, there is still uncertainty over the diagnostic accuracy of MRI in the differential diagnosis between uterine sarcomas and leiomyomas.

The aim of this study was to assess the overall accuracy of MRI in the differential diagnosis between uterine leiomyomas and sarcomas.

2 | MATERIALS AND METHODS

2.1 | Study protocol

The study followed an a priori protocol, which defined each review step and is registered in the PROSPERO international database of prospectively registered systematic reviews (CRD42023437643). All review stages, including search strategy, study selection, risk of bias assessment, data extraction, and data analysis, were independently performed by two authors. In case of disagreement, consensus was achieved by discussion among all authors.

The Preferred Reporting Item for Systematic Reviews and Meta-analyses (PRISMA) statement and checklist[16] and the Synthesizing Evidence from Diagnostic Accuracy Tests (SEDATE) guidelines[17] were adopted for reporting of the whole study.

2.2 | Search strategy

Search strategy involved searching five electronic databases: MEDLINE, Web of Sciences, Google Scholar, Scopus, and ClinicalTrial.gov, from their inception to June 2023. We searched the following terms: uter* AND (myom* OR leiomyom*) AND sarcoma OR neoplas* OR cancer OR malignancy AND (different* OR distinguis* OR diagnos*) AND (preoperat* OR before surgery OR presurg*) AND magnetic resonance imaging OR MRI; OR resonance.

Reference lists from each eligible study were also screened for missed studies.

2.3 | Study selection

All peer-reviewed studies that allowed calculation of the accuracy of MRI in the differential diagnosis between uterine sarcomas and

leiomyomas were included. In particular, we included English language observational studies or randomized controlled clinical trials that reported an unbiased postoperative histologic diagnosis of uterine leiomyoma or uterine sarcoma and a preoperative evaluation of the uterine mass through MRI or a re-evaluation of preoperatively acquired images.

Literature reviews, case series, case reports, video articles, and studies in a language other than English were a priori considered as exclusion criteria.

2.4 | Data extraction

Data extraction was performed without modification of original data. Two-by-two contingency tables were built for each included study, reporting two qualitative variables:

- MRI diagnosis (index test), dichotomized as "uterine leiomyoma" versus "uterine sarcoma";
- Pathologic diagnosis (reference standard), dichotomized as "uterine leiomyoma" versus "uterine sarcoma".

Cases in which the diagnosis of malignancy at MRI was "indeterminate" or "inconclusive" were considered as "uterine sarcoma" during data extraction.

2.5 | Risk of bias within studies assessment

The risk of bias within studies was assessed using the Quality assessment of Diagnostic Accuracy Studies (QUADAS-2).[18] In particular, each included study was examined according to the following four domains: (1) Patient selection (i.e., if patients were randomly or consecutively selected for inclusion in the study); (2) Index test (i.e., if MRI was unbiased, e.g., examination performed by expert radiologists); (3) Reference standard (i.e., if pathologic examination was unbiased, e.g., blinded evaluation by at least one expert pathologist and clearly defined pathologic criteria); and (4) Flow and Timing (i.e. if all patients were assessed with both MRI and pathologic examination; if interval between MRI and pathologic examination was less than 1 year).

Authors judged each study as being at "low risk", "unclear risk", or "high risk" of bias if data about the domain were "reported and adequate", "not reported", or "reported but inadequate", respectively.

2.6 | Data analysis

Sensitivity, specificity, positive and negative likelihood ratios, diagnostic odds ratio (DOR) and area under the curve (AUC) on summary receiver operating characteristic of MRI in differentiating uterine leiomyomas and sarcomas were calculated as individual and pooled estimates and reported on forest plots with 95% confidence intervals (CI).

We adopted the random effect model of DerSimonian and Laird for all analyses, as recommended for meta-analysis of diagnostic accuracy by the SEDATE guidelines.[17]

We a priori classified the diagnostic accuracy in differentiating uterine leiomyomas and sarcomas as absent for AUC ≤0.5, low for 0.5 < AUC ≤0.75, moderate for 0.75 < AUC ≤0.9, high for 0.9 < AUC < 0.97, and very high for AUC ≥0.97, as previously reported.[19,20]

We estimated statistical heterogeneity among the included studies with the Higgins I^2 statistic; heterogeneity was a priori classified as null for $I^2 = 0\%$, minimal for $0\% < I^2 \leq 25\%$, low for $25\% < I^2 \leq 50\%$, moderate for $50\% < I^2 \leq 75\%$, and high for $I^2 > 75\%$, as previously reported.[21–23]

We used the following softwares for statistical analysis of data: Meta-DiSc version 1.4 (Clinical Biostatistics Unit, Ramon y Cajal Hospital, Madrid, Spain) and Review Manager 5.4 (Copenhagen: The Nordic Cochrane Centre, Cochrane Collaboration, 2014).

3 | RESULTS

3.1 | Study selection

At the end of the databases searches, 2986 studies were identified. Duplicate removal and title screening processes led to 551 and 60 studies, respectively. Abstract screening led to 21 studies, which were evaluated for eligibility, and of them, 13 studies were excluded:

- 10 studies because data about suspicion of uterine sarcoma at MRI were not reported,[24–33]
- One study because it did not report the pathologic diagnosis (reference standard) in cases of expected benign lesion at MRI (expected benign lesions were treated with high-intensity focused ultrasound ablation),[34]
- One study because it included also cases of extrauterine sarcomas and it was not possible to differentiate them from uterine sarcomas,[35]
- One study because it was not possible to extract data about the exact number of suspicious uterine sarcomas at MRI.[36]

Finally, eight studies were included in both qualitative synthesis and quantitative synthesis[37–44] (Figure 1).

3.2 | Studies and patients' characteristics

We extracted data for a total of 2501 women (2334 with uterine leiomyomas and 167 with uterine sarcomas). The included studies were observational, retrospective, cohort studies in seven cases[38–44] and an observational cross-sectional study in one case[37] (Table 1).

Ages of women with uterine leiomyomas and sarcomas ranged from to 21 to 87 years and from 18 to 88 years, respectively. Of all

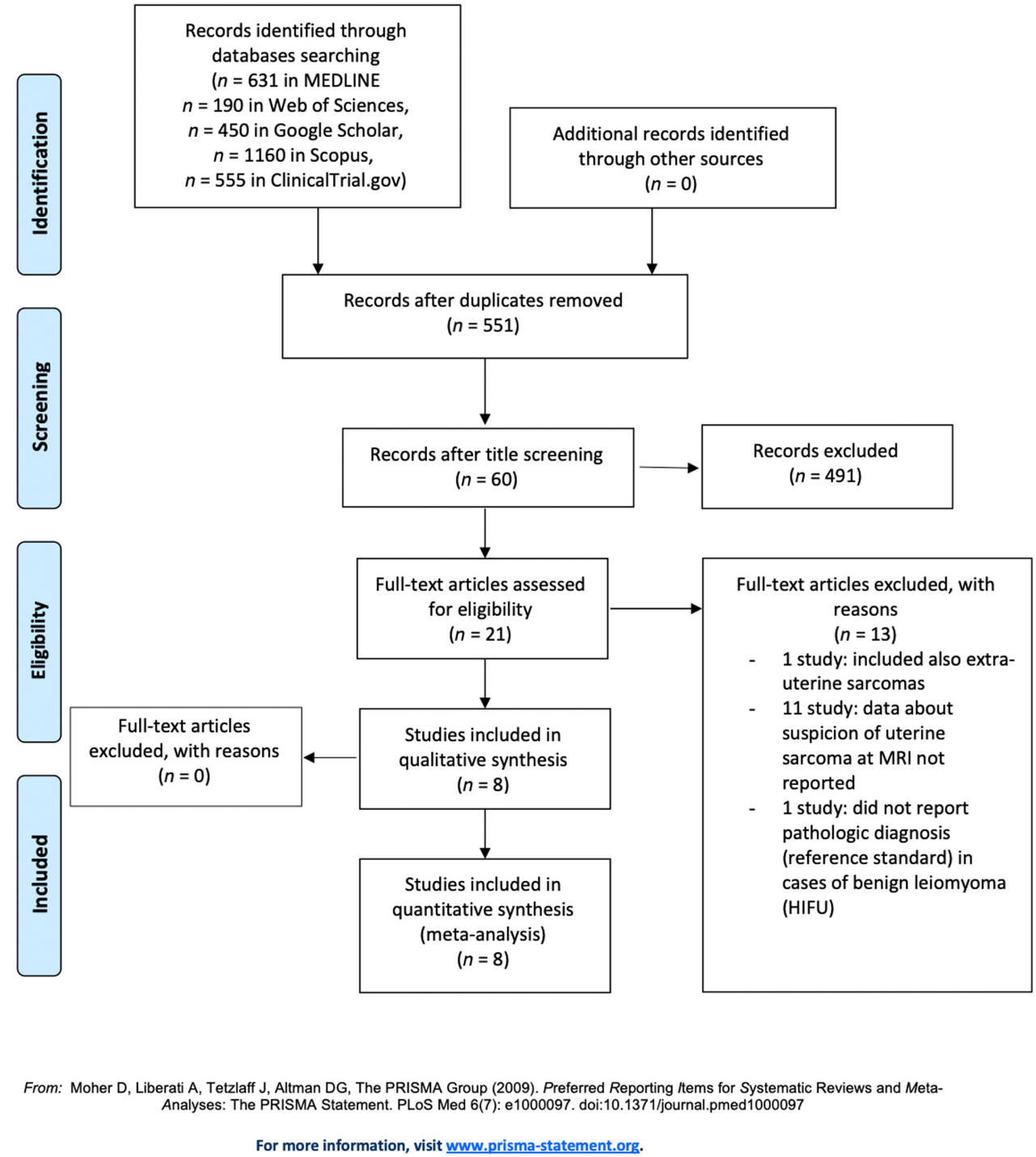

FIGURE 1 Flowchart of study selection step of the systematic review and meta-analysis (Prisma template [Preferred Reporting Item for Systematic Reviews and Meta-analyses]).

the women with uterine leiomyomas and sarcomas, 73.5% (252/343) and 39.7% (54/148) were premenopausal, respectively. About symptoms, 53.3% (96/180) of women with uterine leiomyomas and 63.2% (74/117) of women with uterine sarcoma showed abnormal uterine bleeding, and 32.8% (59/180) and 33.3% (39/117) had pelvic/abdominal pain, respectively (Table 2).

TABLE 1 Characteristics of the included studies.

First author/ year	Country	Setting	Population of interest, n	Leiomyomas, n (%)	Sarcomas, n (%)	Study design	Patient selection criteria[a]	MRI items used	Period of enrollment
2009 Namimoto	Japan	Clinical institution	43	35 (81.4)	8 (18.6)	Single-center retrospective	Surgery for myometrial lesion; preoperative contrast-enhanced MRI; available histologic examination	Intensity of the lesion and myometrium on T2-weighted imaging, DWI TCR, ADC	2007–2008
2013 Sato	Japan	Clinical institution	81[b]	83 (89.2)	10 (10.8)	Single-center retrospective	Surgery for myometrial lesion; preoperative contrast-enhanced MRI; available histologic examination	Fast-spin- echo T1- and T2-weighted images DWI, ADC	2008–2011
2018 Valdes-Devesa	Spain	Clinical institution	19	14 (73.7)	5 (26.3)	Single-center retrospective	Surgery for myometrial lesion; preoperative contrast-enhanced MRI; available histologic examination	Axial gradient echo T1-weighted images, a fat-suppressed T2-weighted image and an immediate and delayed fat-suppressed gadolinium-enhanced gradient echo images, DWI, ADC	2009–2014
2019 Rahimifar	Iran	Clinical institution	101	80 (79.2)	21 (20.8)	Single-center retrospective	Surgery for myometrial lesion; preoperative contrast-enhanced MRI; available histologic examination, weight < 100 kg, no electronic implants	T1- and T2-weighted images, DWI, ADC, MRS lipid peak, MRS choline peak	2014–2015
2019 Tong	USA	Clinical institution	1960	1942 (99)	18 (1)	Single-center retrospective	Surgery for myometrial lesion; preoperative contrast-enhanced MRI; available histologic examination	T1- and T2-weighted images, DWI, and post-contrast T1 sequences	2014–2017
2019 Xie	China	Clinical institutions	78	49 (62.8)	29 (37.2)	Two-centers retrospective	Surgery for myometrial lesion; preoperative contrast-enhanced MRI; available histologic examination; no chemotherapy or radiotherapy or invasive therapy before MRI	Fast-spin- echo T1 and T2-weighted images, DWI, ADC, DCE	2010–2016
2020 Wahab	France	Clinical institution	156	105 (67.3)	51 (33.7)	Single-center retrospective	Surgery for myometrial lesion; preoperative contrast-enhanced MRI; available histologic examination	T1- and T2-weighted images, DWI, ADC, DCE	2000–2017
Najibi 2021	Iran	Clinical institution	63	26 (41.3)	37 (58.7)	Cross-sectional study	Surgery for intrauterine masses assessed using MRI and ultrasound before surgery; available histologic examination	T1- and T2-weighted images, DWI, DCE	2016–2020
Total	–	–	2501	2334 (93.3)	167 (6.7)	–	–	–	–

Abbreviations: ADC, apparent diffusion coefficient; DCE, dynamic contrast enhancement; DWI, diffusion-weighted imaging; MRI, magnetic resonance imaging; MRS, magnetic resonance spectroscopy; TCR, tumor-myometrium contrast ratio.

[a]Structured criteria included: size of the tumor, signal intensity of the lesion and myometrium on T2-weighted imaging, diffusion-weighted imaging, and tumor-myometrium contrast ratio, apparent diffusion coefficient.

[b]In Sato et al., 81 patients with 93 myometrial lesions were included.

3.3 | Risk of bias within studies assessment

For the "Patient selection" domain, all studies were considered at low risk of bias.

For the "Index test" domain, one study was considered at unclear risk of bias because it did not report if MRI was performed by expert radiologists,[39] and another study was considered at high risk of bias because MRI was performed by a junior radiologist with only 1 year of experience in pelvic MRI.[41]

For the "Reference standard" domain, five studies were considered at unclear risk of bias. In particular, one study did not report if pathologic examination was performed by at least one blinded expert pathologist,[44] and three studies did not report defined pathologic criteria.[38,39,42]

For the "Flow and Timing" domain, seven studies were considered at unclear risk of bias because they did not report if the interval between MRI and pathologic examination was less than 1 year.[38–44]

The remaining studies in each domain were considered at low risk of bias (Figure 2).

3.4 | Meta-analysis

In the differential diagnosis between uterine leiomyomas and sarcomas, MRI showed pooled sensitivity of 0.90 (95% CI 0.84–0.94; $I^2 = 79.6\%$; Figure 3), specificity of 0.96 (95% CI 0.96–0.97; $I^2 = 71.8\%$; Figure 4), positive likelihood ratio of 13.55 (95% CI 6.20–29.61; $I^2 = 86.0\%$; Figure 5), negative likelihood ratio of 0.08 (95% CI 0.02–0.32; $I^2 = 83.9\%$; Figure 6), diagnostic odds ratio of 175.13 (95% CI 46.53–659.09; $I^2 = 64.3\%$; Figure 7), and AUC of 0.9759 (Figure 8).

For the study by Namimoto et al.,[42] we included in our analysis only cases that had an histologic diagnosis (43 out of 103 patients).

4 | DISCUSSION

Our study showed that MRI has a very high accuracy (97.6%) in differentiating uterine sarcomas and leiomyomas, with a good sensitivity (90%) and an even better specificity (96%).

In daily clinical practice, the differential diagnosis between uterine myomas and sarcomas is a challenging problem. Ultrasound is the first-line imaging tool due to its low-cost and accessibility.[45,46] However, although several studies have tried to investigate the ultrasonographic appearance of uterine sarcomas,[47,48] the diagnostic accuracy of ultrasound appeared only moderate (89%), with a lower sensitivity (76%) than specificity (89%).[9]

Therefore, additional diagnostic tools appear necessary in order to tailor the surgical approach and avoid misdiagnoses.[49] Following ultrasound, MRI is the second-line diagnostic tool to be performed in case of myometrial masses resembling malignancy.[11]

There are enhanced and non-enhanced versions of MRI. Contrast-enhancement is useful to increase signal to background for small lesions, accentuate vessel structures, and estimate tissue

TABLE 2 Characteristics of the study population.[a]

	Age, y			Premenopausal women			Symptoms					
							Abnormal uterine bleeding			Pelvic/abdominal pain		
First author/year	Total	Myomas	Sarcomas	Total	Myomas	Sarcomas	Total	Myomas	Sarcomas	Total	Myomas	Sarcomas
2009 Namimoto	47.8 (24–78)	nr	nr	68 (66)	nr	nr	nr	nr	nr	nr	nr	nr
2013 Sato	Nr	44.6 (29–75)	55 (50–62)	74 (91.4)	71 (93.4)	3 (60%)	nr	nr	nr	nr	nr	nr
2018 Valdes-Devesa	50.1 (29–88)	45 (29–84)	64.2 (48–88)	nr	nr	nr	nr	nr	nr	nr	nr	nr
2019 Rahimifar	42.1 (1868)	42.8 (2–66)	39.5 (18–68)	40 (61.9)	32 (61.9)	8 (61.9)	nr	nr	nr	nr	nr	nr
2019 Tong	43 (18–87)	43 (19–87)	47 (29–84)	nr	nr	nr	nr	nr	nr	nr	nr	nr
2019 Xie	46.2 (23–77)	38.8 (23–60)	58.7 (38–77)	52 (66.7)	45 (91.8)	7 (24.1)	24 (30.8)	7 (14.3)	17 (58.6)	8 (10.3)	3 (6.1)	5 (17.2)
2020 Wahab	nr	nr	nr	88 (56.4)	80 (76.3)	8 (15.7)	107 (68.6)	70 (66.7)	37 (72.5)	59 (37.8)	44 (41.9)	15 (29.4)
2021 Najibi	nr	nr	nr	52 (82.5)	24 (92.3)	28 (75.7)	39 (61.9)	19 (73)	20 (54)	31 (49.2)	12 (46.2)	19 (51.4)
Total	(18–88)	(21–87)	(18–88)	374 (71.6)	252 (73.5%)	54 (36.5)	170 (57.2)	96 (53.3)	74 (63.2)	98 (33)	59 (32.8)	39 (33.3)

Abbreviation: nr, not reported.

[a]Data are presented as mean (range) or as number (percentage).

Risk of bias

Study	Patient selection	Index test	Reference standard	Flow and timing
2009 Namimoto	+	+	?	?
2013 Sato	+	+	+	?
2018 Valdes-Devesa	+	+	?	?
2019 Rahimifar	+	?	?	?
2019 Tong	+	+	?	?
2019 Xie	+	+	+	?
2020 Wahab	+	–	+	?
2021 Najibi	+	+	+	+

Applicability

Study	Patient selection	Index test	Reference standard
2009 Namimoto	+	+	+
2013 Sato	+	+	+
2018 Valdes-Devesa	+	+	+
2019 Rahimifar	+	+	+
2019 Tong	+	+	+
2019 Xie	+	+	+
2020 Wahab	+	+	+
2021 Najibi	+	+	+

FIGURE 2 Assessment of risk of bias. Summary of risk of bias for each study; +, low risk of bias; –, high risk of bias; ?, unclear risk of bias.

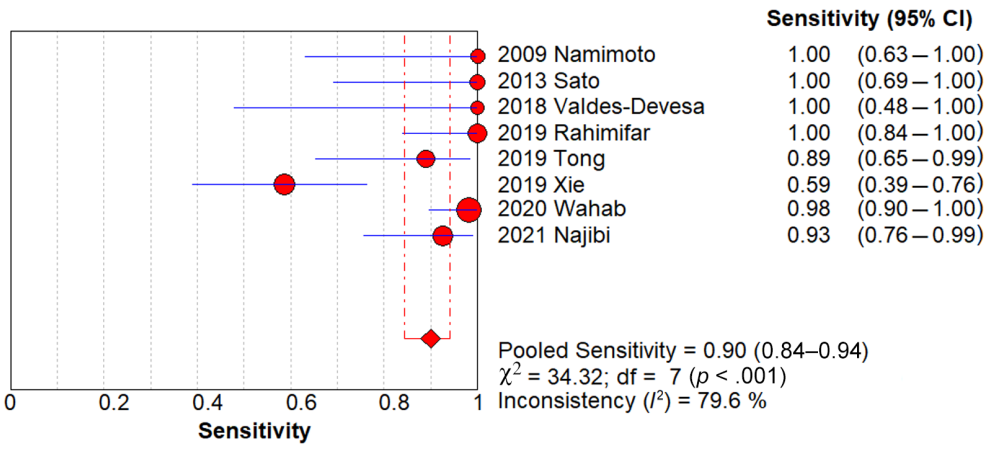

FIGURE 3 Forest plots of individual studies and pooled sensitivity of MRI in the differential diagnosis between uterine leiomyomas and sarcomas.

perfusion. Conversely, new non-contrast-enhanced MRI techniques, such as arterial spin labeling, time of flight, phase contrast, DWI, magnetic resonance spectroscopy (MRS), susceptibility weighted imaging, and amide proton transfer imaging, can offer reliable alternatives.[50] In particular, enhanced MRI techniques described in the literature for the diagnosis of uterine sarcomas are contrast-enhanced MRI,[37,38,41,43] DWI with ADC mapping,[40,42,44] and MRS.[39]

According to traditional MRI items, uterine sarcomas present as solitary, heterogeneous, and poorly demarcated masses. T1-weighted characteristics are variable, but frequently show areas of high signal intensity corresponding to hemorrhage or necrosis.[14]

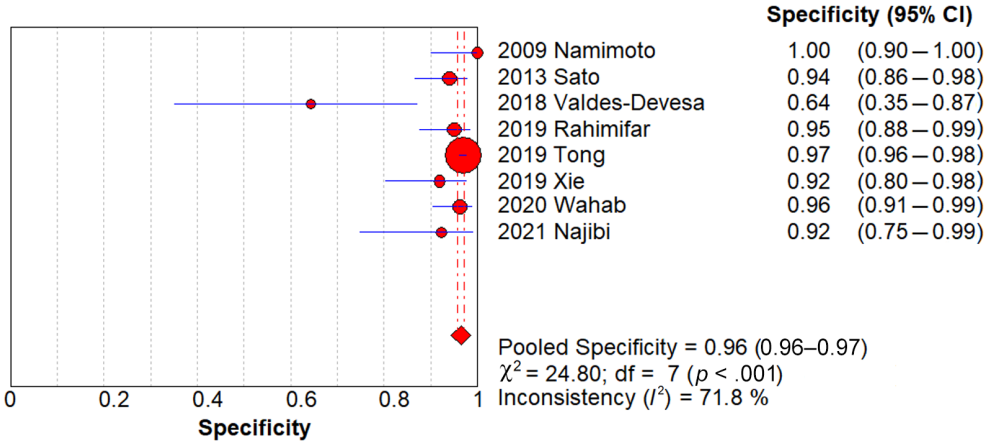

FIGURE 4 Forest plots of individual studies and pooled specificity of MRI in the differential diagnosis between uterine leiomyomas and sarcomas.

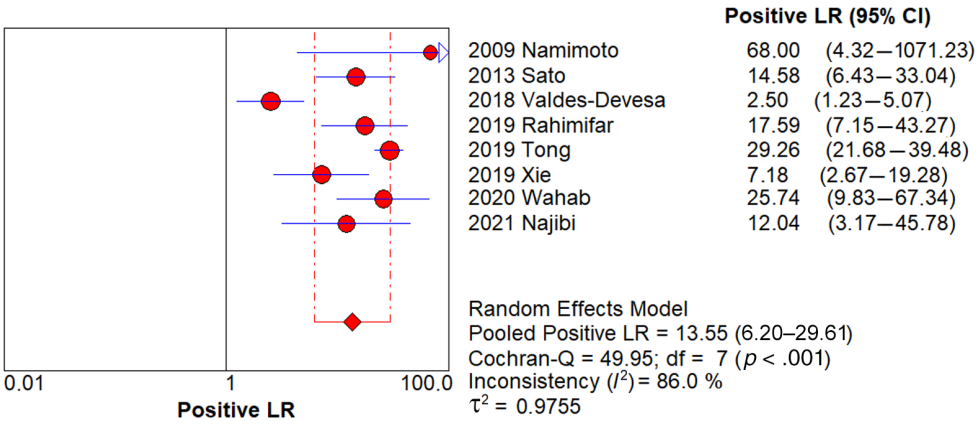

FIGURE 5 Forest plots of individual studies and pooled positive likelihood ratio of MRI in the differential diagnosis between uterine leiomyomas and sarcomas.

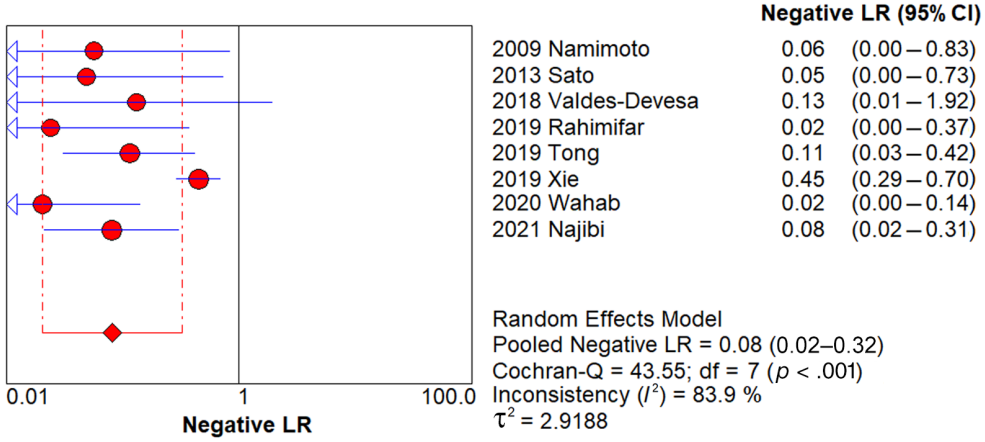

FIGURE 6 Forest plots of individual studies and pooled negative likelihood ratio of MRI in the differential diagnosis between uterine leiomyomas and sarcomas.

On T2-weighted images, uterine sarcomas show intermediate to high signal.[27] On the other hand, DWI is an imaging technique that typically displays tumoral lesions as a hyperintense region with elevated tissue contrast. Moreover, DWI allows the evaluation of ADC, which is a quantitative measurement associated with the nuclear-to-cytoplasm ratio and cellular density of tissue.[39] Although

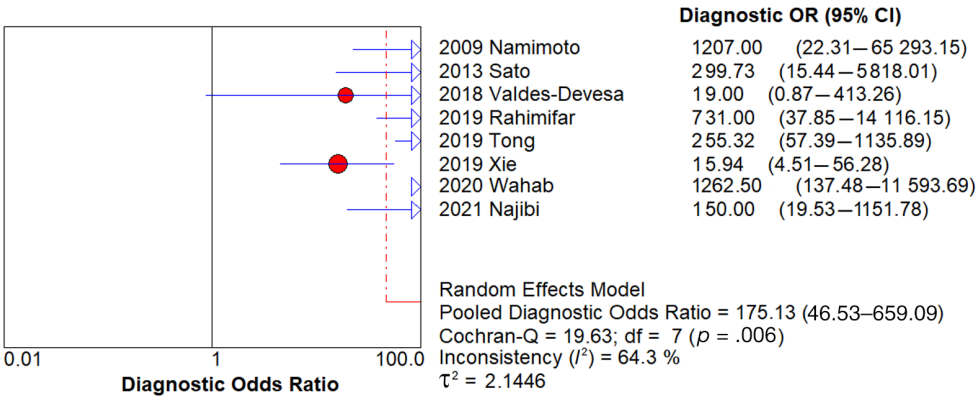

FIGURE 7 Forest plots of individual studies and pooled diagnostic odds ratio of MRI in the differential diagnosis between uterine leiomyomas and sarcomas.

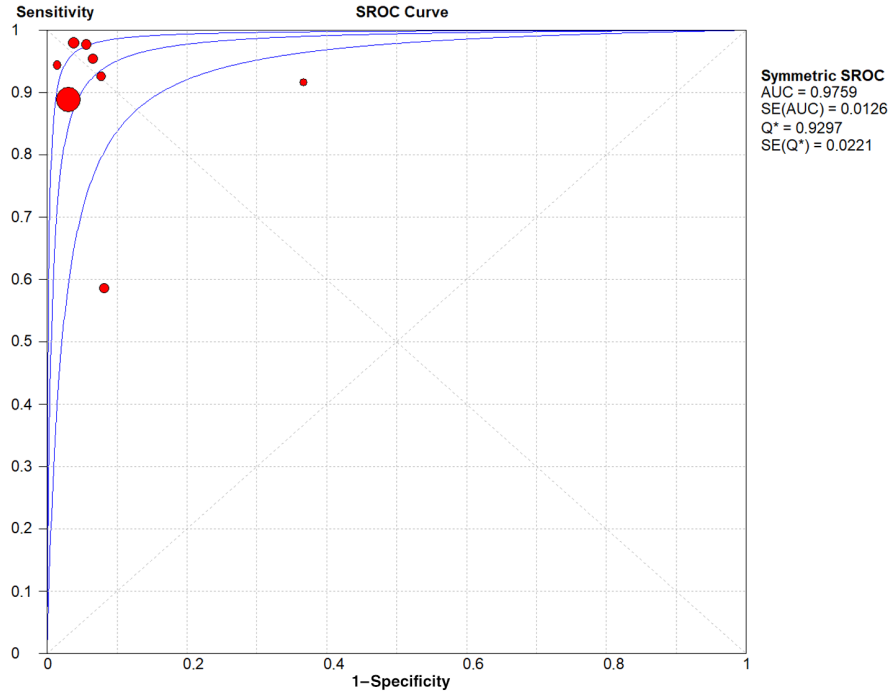

FIGURE 8 Pooled area under the curve (AUC) on summary receiver operating characteristic (SROC) with 95% confidence intervals of MRI in the differential diagnosis between uterine leiomyomas and sarcomas.

ADC values can partially overlap with benign lesions, mean values in uterine sarcomas are lower than degenerated leiomyomas,[30,51] as malignant tissue has histopathologic characteristics, including hypercellularity, enlargement of nuclei, hyperchromatism, and angulation of the nuclear contour, that result in a reduction of diffusional displacement of water molecules.[52]

Non-enhancing areas following gadolinium-based contrast injection demonstrate areas of central necrosis, which usually cannot be seen in non-treated leiomyomas.[11,53] However, the prevalence of each MRI sign of uterine sarcomas is still uncertain[11] and some MRI signs can overlap between uterine sarcomas and leiomyoma.[13,30] For example, high signal on T1-weighted can be detected in benign lipoleiomyomas and red-degenerated myomas. T2-weighted signal may be high also in the case of cystic or myxoid degeneration of leiomyomas. DWI sequences and ADC quantitative mapping are not considered stand-alone parameters for a differential diagnosis between uterine sarcoma and leiomyomas, so they should be combined with signal characteristics on T1- and T2-weighted images. These findings highlight the need for clarification that might result from pooled analyses.

According to our results, MRI showed a very high accuracy, with an excellent pooled specificity, identifying it as a reliable tool in the detection of benign lesions. Notably, small fibroids were excluded in most of the included studies, and in the case of patients with multiple myomas, only the largest was investigated through MRI.[41,42,44,54,55] This screening-like selection may reflect the daily practice that is applied during the differential diagnosis. This process may have even underestimated the specificity and diagnostic accuracy of MRI. However, considering the very low prevalence of

uterine sarcomas, specificity appears less important than sensitivity. Anyway, although MRI sensitivity was lower than specificity from our pooled analysis, it was still higher than that of other diagnostic tools (e.g. ultrasound[9]). Our findings would support the use of MRI as a reliable second-line diagnostic tool (subsequent to ultrasound) in distinguishing uterine leiomyomas and sarcomas.

Notably, our pooled data arose from studies adopting traditional MRI items, such as T1- and T2-weighted images, contrast-enhancement evaluation, DWI and ADC mapping. Hence, MRI diagnostic accuracy might potentially be improved with the integration of additional MRI items or diagnostic algorithms. Recently, several authors have proposed novel instruments to increase MRI accuracy. Namimoto et al.[42] added DWI tumor-to-contrast ratio; Rahimifar et al.[39] proposed the use of MRS, a technique that is able to provide metabolic information related to the transformation of normal to malignant tissue by measuring the presence of several metabolite peaks, such as choline and lipid peaks in uterine sarcoma; Xie et al.[43] evaluated the use of radiomics for the distinction of atypical leiomyoma and uterine sarcoma. Wahab et al.[41] proposed a diagnostic MRI algorithm including visual analysis of T2-weighted images, DWI scans and ADC measurement, with a sensitivity of 98% and specificity of 96%. Lakhman et al.[33] developed an algorithm based on four MRI features (borders, hemorrhage, T2 dark areas, and location of unenhanced areas), with a 98% accuracy, 95%–100% sensitivity and specificity each. The use of positron emission tomography/computed tomography after MRI on patients with suspicious rapidly growing uterine masses was tested in the study by Ho et al.[56] They identified the so-called "hollow ball" sign, a characteristic lesion with uptake of fluorodeoxyglucose, which was associated with leiomyosarcomas and smooth muscle tumors of uncertain malignant potential (STUMPs), with an accuracy of 100%. However, the authors admitted that this sign could be absent in malignant masses lacking areas of tumor necrosis and therefore cannot be considered as a stand-alone marker.

Several authors have proposed the use of artificial intelligence (AI), with different models, some of them showing excellent results. Malek et al.[28] developed a machine learning algorithm that achieved 96.2% accuracy, 100% sensitivity, and 95% specificity. In the study by Toyohara et al.,[57] deep neural network was employed in the evaluation images obtained by MRI. The results indicated that deep neural network not only obtained results better than or comparable to those of radiology specialists (deep neural network: 90.3% accuracy, 89.8% sensitivity, and 91.7% specificity; radiology specialist: 88.2% accuracy, 71.0% sensitivity, and 93.8% specificity), but it also improved the diagnostic skill of radiologists when its support was available. A radiomic multivariable logistic regression model was proposed in 2019 by Xie et al.,[43] yielding a 0.83 AUC, 76% sensitivity, and 73% specificity. Gupta et al.[58] tested the performance of AI in the detection of uterine sarcoma through the analysis of bioimpedance, with an 80% overall accuracy. In 2019, Nakagawa et al.[59] found that a multiparametric machine learning MRI-based method had better results in terms of diagnosis of malignancy than positron emission tomography alone and was comparable to experienced radiologists. However, according to Ravegnini et al.,[60] despite growing interest for the application of AI in the differential diagnosis of uterine masses combined with MRI features, AI systems appear currently too complicated to be readily applied in daily clinical practice.

To the best of our knowledge, this may be the first systematic review and meta-analysis assessing the accuracy of MRI in distinguishing uterine sarcomas and leiomyomas. Furthermore, our findings appear to be supported by a good overall quality of the included studies, as revealed by the risk of bias within studies assessment: in fact, only one included study was considered at high risk of bias in only one domain.[41]

Nevertheless, our study may have some limitations. First, the retrospective design of the included studies and the influence of the study by Tong et al.,[38] accounting for the majority of patients included in our pooled analysis. In fact, given the rarity of uterine sarcomas, prospective studies appear difficult to perform. Second, although MRI was performed by expert radiologists, the subjectivity of the assessment and the absence of clearly defined signs of malignancy might affect our data. Third, although the high expertise of the radiologists improves MRI accuracy, it may limit the generalization of the findings and the wide application of MRI in clinical practice. Lastly, our results might be affected in the generalization by the fact that some of the included studies were carried out in referral oncologic centers which admitted suspected cases.

In conclusion, MRI seems to have a very high accuracy in differentiating uterine sarcomas and leiomyomas, with a good sensitivity and an even better specificity, supporting its use as a reliable second-line diagnostic tool (after ultrasound).

Further studies are necessary to confirm these findings and assess the potential of integration of MRI with other novel tools.

AUTHOR CONTRIBUTIONS

AR, DR, AT, and DN independently assessed electronic search, eligibility of the studies, inclusion criteria, risk of bias, data extraction, and data analysis. MG, LL, FDL, and CC contributed to the elaboration of methods for risk of bias assessment, data extraction, and analysis. AR, DR, AT, DN, MG, PC, RS, EZ, and MG conceived the study; AR, DN, FDL, CC, and LL worked on the design of the study; AR, AT, DN, DR, MG, and PC worked on the manuscript preparation; EZ, RS, PC, and MG supervised the whole study.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflict of interest.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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