

## SYSTEMIC REVIEW

# Diagnostic Accuracy of Ultrasound in Differentiation Uterine Leiomyosarcoma from Uterine Leiomyoma: A Systematic Review

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## ABSTRACT

**Background:** Uterine leiomyosarcoma is a rare malignant pathology of smooth muscle of uterus which is mostly asymptomatic with a wide range of late onset of symptoms such as post-menopausal bleeding and severe abdominal pelvic pain and abnormal vaginal discharge. Uterine leiomyosarcoma characteristically has structural and clinical similarities with giant uterine leiomyoma because both originate from the smooth muscle cells of the uterus. The diagnosis of uterine leiomyosarcoma through ultrasound is very different difficult due to indistinguishable sonographic features of uterine leiomyoma and leiomyosarcoma but there are certain sonological features which can prove the reliability of ultrasound as the diagnostic tool for differentiating uterine leiomyosarcoma from uterine leiomyoma.

**Aim:** To access the accuracy of ultrasound in differentiating uterine leiomyosarcoma from uterine leiomyoma.

**Methods:** An electronic database search was performed (PubMed, Science direct, Google Scholar) with the data range from 2000 to 2021. All studies included in the research was in English language. Articles which had descriptive studies related to sonographic features of uterine leiomyosarcoma and uterine leiomyoma.

**Results:** Total 15 articles were found regarding the prevalence, clinical manifestation and sonographic findings of uterine leiomyosarcoma and uterine leiomyoma, 10 articles were included in the introduction and technique where as 6 articles were selected for systemic review with the sample size ranging from 20-200 in all different articles and age criteria of the participant in the selected articles was above 40 years with most candidates were investigated in the post menopause period.

**Conclusion:** We identified certain sonographic patterns that can accurately differentiate uterine leiomyoma sarcoma from uterine leiomyoma with moderate sensitivity and specificity.

**Keywords:** Transvaginal ultrasonography, leiomyoma, leiomyosarcoma

## INTRODUCTION

Uterine Leiomyosarcoma (LMS) is one of the most common subtypes of malignant mesenchymal neoplasms and represents approximately 10% to 20% of all newly diagnosed soft tissue sarcomas (STSs). Uterine leiomyosarcoma most commonly exhibit strong resemblance association with a benign tumor known as uterine leiomyomas more specifically known as uterine fibroids are the most commonly benign uterine tumor's, detected in up to twenty to forty percent of reproductive-age women and seventy to eighty percent of peri-menopausal females<sup>1</sup>. According to multiple studies, it is very difficult to differentiate between leiomyosarcoma and leiomyoma because their clinical manifestation and diagnostic features often get entangled with each other due to similar morphological origin of smooth muscle cells of uterus it can only be differentiated via histology.

On histology leiomyosarcoma is differentiated from a leiomyoma by noting the presence of infiltrative margins, nuclear atypia and increased mitotic figures. Leiomyosarcomas are on average 6–9 cm in diameter and the cut surface is typically soft, prominent, fleshy, necrotic and hemorrhagic, with irregular margins. If a leiomyosarcoma is combined with a leiomyoma, the sarcoma is usually the larger mass. Leiomyo-sarcoma is Leiomyosarcomas tend to be larger and softer than leiomyomas.<sup>2</sup> Spectrum on ultrasound shows malignancy of uterine leiomyosarcoma found in patients found 3 to 7% of all uterine pathologies.<sup>3</sup> The most common clinical manifestation associated with the both Benign and malignant pathology is abnormal uterine bleeding, pelvic pain / compression, and pelvic mass is the main symptom and sign of both fibroid and sarcoma, so it is possible to distinguish between the two on this basis. Although problematic, there are certain clinical symptoms. It is associated only with uterine leiomyosarcoma, but not with the general Pyonfargunjeong. At an advanced stage, uterine leiomyosarcoma spreads intraperitoneally, through the lymphatic system or blood circulation pathways. Blood circulation spreads mostly in the lungs. It is necessary to follow techniques that can be slightly invasive for success and treatment of the condition, and it is especially

important to distinguish it from confusing malignancies such as preoperative leiomyosarcoma. Misdiagnosis of LMS in positive leiomyosarcoma is more likely to cause local recurrence and metastasis with poor prognosis, which can improve treatment delays and morbidity.<sup>4</sup> According to a recent study by FIGO (The International Federation of Gynecology and Obstetrics) in 2009, they classified leiomyosarcoma into four-stage pathology. According to up to 68% of LMS, stage I is detected and only up to 22% is detected in stage IV. Uterine LMS, although relatively rare, has a poor prediction even when restricted to the uterus, accounts for deaths due to uterine malignancies, and the 5-year existence rate ranges from 46% to 53%. Additionally, the recurrence rate of LMS is 50 to 70%, with up to 40% found in the lung's and up to 13% in the pelvic region.<sup>5</sup>

Table 1: Representing the figo 2009 staging system.

Stage	Stage characteristics
I	Tumor limited to uterus
I A	<5cm
I B	>5cm
II	Tumor extend beyond the uterus within the pelvis
II A	Adnexal involvement
II B	Involvement of other pelvic structure
III	Tumors invades the abdominal structure
III a	One site
III b	More than one site
III c	Mets to pelvic and paraaortic nodes
IV a	Tumor invades bladder and rectum
IV B	Distant metastases

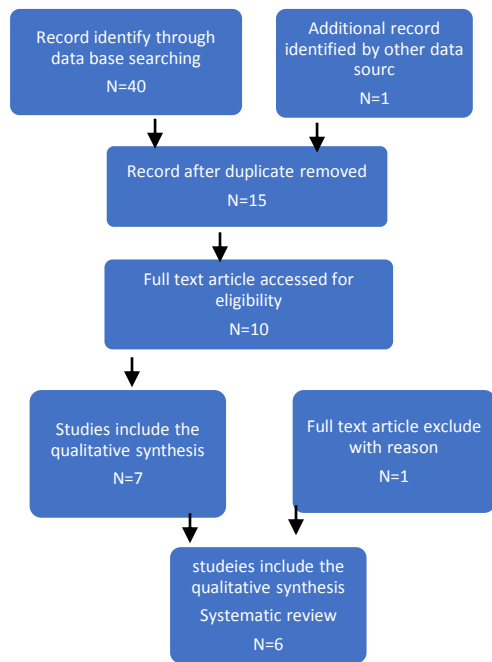
According to a study that was published in 2019 by Lu Denver in which he described the FIGO staging of leiomyosarcoma can be used by comparing the histological finding of uterine leiomyosarcoma with the ultrasonographic features of leiomyosarcoma<sup>6</sup>. The ecogenic classification of cystic contents was different from the first step of the analysis: unscented, low concentration, hemorrhagic, glass, mixed. Ultrasound feature when considered under the light of FIGO staging proved to be an excellent diagnostic reliable tool<sup>7</sup> TVUS is generally preferred for differentiation between uterine leiomyoma and leiomyoma. This is because TVUS post-uterine tilting allows a better assessment of

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patients with significant intestinal gas or obese bladder distension, insufficient bladder distension. Grayscale and color Doppler ultrasonography are readily accessible and radiographic for the evaluation and follow-up of benign uterine leiomyomas. It is in a state of high cost-effectiveness without including it. Ultrasonography reveals that leiomyomas usually appear as masses of well-defined low echoes, and the possibility of calcification shows shadowing. However, it has limited diagnosis in LMS, it has certain functions as a soft indicator of malignancy.<sup>8</sup> The sign that is a prime sign of the accuracy of leiomyosarcoma is raised vascularity on color Doppler ultrasound which it supports malignant tumors. The combination of these results increases the sensitivity of by 75-%, and increases the PPV by 60. Leiomyoma has a statistically significantly lower mean microarterial RI compared to leiomyosarcoma<sup>9</sup>

**MATERIALS AND METHODS**

We performed a systematic search based on the PRISMA statement for systematic review and meta-analysis. MEDLINE and Embase were searched to confirm studies related to ultrasound function uterine fibroid and uterine leiomyosarcoma published in English between 2000 and 2021. It was. Classified as . Data for a systemic study were also obtained for the patient's age, symptoms, menopausal status, childbirth, pre-exposure of pelvic radiation and steps of the International Gynecological and Obstetrics and Gynecology Federation (FIGO) for sarcoma.



**RESULTS AND DISCUSSION**

Many articles have discussed the possible sonographic appearance of uterine leiomyoma and leiomyosarcomas because of their similar origin and anatomy, to differentiate a large leiomyoma and leiomyosarcoma is very difficult, there were many articles written to prove accuracy and reliability of ultrasound to differentiate uterine leiomyoma from leiomyosarcoma.

Kara. G in etal in 2016 conducted a retro prospective case control study with 56 patients ,28 patients were categorized with possible diagnosis of uterine leiomyoma and the other 28 were categorized with uterine leiomyosarcoma, all of the patients were initially investigated with ultrasound as the first line modality. all 56 patients on ultrasound exhibited the same sonographic

appearance and similar vascularity which made ,both uterine leiomyoma and leiomyosarcoma on ultrasound showed a uterine mass with heterogenous echogenicity and necrosis and hypervascularity and compared the imaging features through a imaging scale of both leiomyoma and leiomyosarcoma which statistically deduced that ultrasound does not have much reliability in differentiating both as compare to the magnetic resonance imaging , computed tomography and biopsy but ultrasound can exhibit certain features on color doppler and spectral doppler which does become a soft reliable indicator of malignancy suggesting uterine leiomyosarcoma<sup>10</sup>.

Characteristics	Leiomyoma	Leiomyosarcoma
Margins	2.2 ±0.9	2.5 ±0.9
Necrosis	2.2 ±1.1	2.2 ±1.1
Hemorrhage	1.2 ±0.5	1.2 ±0.5
vascularity	2.9 ±0.6	2.9 ±0.6
calcification	1.3 ±0.7	1.3 ±0.7
heterogeneity	3.3 ±1.0	3.3 ±1.0

Hata .K et al in 2020 conducted prospective study with 44 patient who have previously diagnosed uterine leiomyoma and uterine leiomyosarcoma and performed ultrasound more specifically conducted doppler studies to investigate the differentiating factor on ultrasound of both uterine leiomyoma and leiomyosarcoma. he conducted the doppler studies by dividing the patient on different phases of menstrual cycle . out of 44 patients, 14 were examined in luteal phase and 27 were examined in follicular phase. Both uterine leiomyoma and leiomyosarcoma showed the same RI and PI values with a minimal variation on this parameter with the results of RI values (mean ± SD) ,in luteal phase (0.66 ±0.11), (0.63±0.10) in follicular phase in both uterine leiomyoma and leiomyosarcoma but PSV of uterine leiomyosarcoma showed a little variation in comparison with uterine leiomyoma, uterine leiomyosarcoma showed PSV more than 41 cm/sec (p<0.05).They concluded that PSV can be a diagnostic factor that differentiate the both condition because raised PSV values in leiomyosarcoma is due to cellular changes in the uterine tissue which progress toward malignancy<sup>11</sup>.

	RI values
Uterine leiomyoma	0.64±0.11
Uterine leiomyosarcoma	0.63±0.18

Doppler studies	Histological diagnosis	
	Uterine leiomyosarcoma	Uterine leiomyoma
PSV >41cm/sec	4	1
PSV <41cm/sec	1	40

Caterina. E et al in 2007 performed a unfashionable potential have a look at on girl who had recognized uterine leiomyoma and uterine leiomyosarcoma and feature gone through hysterectomy. She in comparison the ultrasonographic locating of uterine leiomyoma and uterine leiomyosarcoma to show the reliability of ultrasound in differentiating each benign and malignant tumor of uterus. She analyzed preoperative grayscale and CDU outcomes of eight patient's with LMS and 21 with mobileular leiomyoma and three with clean muscle tumors with capacity for faulty malignancies, and evaluated those findings in 225 patient's with tremendous LM. Degenerative cystic versions have been detected in four lesions, and an boom in vascular distribution of the peripheral and relevant vascular changed into determined in 7 lesions. In the analysis of LMS, the sensitivity, specificity, and tremendous predictive values of multiplied relevant and peripheral vascular distribution have been 100%, 86% and 19%, respectively. Combining the superb relevant vascular distribution with different ultrasonographic findings, the tremendous predictive price multiplied via way of means of 60%, however the sensitivity reduced to 75%.<sup>12</sup> I.Sazbo et al. in 2007 performed a

unfashionable potential have a look at to distinguish uterine leiomyoma and leiomyosarcoma thru transvaginal ultrasonography. He performed the studies with 117 sufferers who had histologically demonstrated uterine leiomyoma and 12 sufferers who had histologically demonstrated uterine sarcoma. According to those outcomes, the suggest tumor RI and PI have been extensively lower, and the best intratumor contraction charge (PSV) changed into extensively better in sarcoma sufferers than in uterine leiomyoma sufferers. Substantial discounts in RI and PI and upward thrust in PSV have been visible in 14 instances of leiomyomas with big length and/or necrotizing degenerative inflammatory changes. Considering the cutoff price of RI of 0.5, the detection charge of uterine sarcoma changed into 67% and the fake tremendous charge changed into 11.eight.13 J.H Kim et al in 2019 performed a have a look at to evaluate the sonographic functions of girls who had uterine sarcoma however changed into misdiagnosed as uterine leiomyoma of their post-menopausal They unfashionable prospectively amassed statistics of sixty one girl sufferers preoperatively recognized with uterine leiomyomas thru sonography. Half of the breeding regarded on ultrasound as remoted mass with a median most diameter of  $7.56 \pm$  three.sixty eight cm. Approximately 90% of tumors with regressions confirmed

cystic versions with abnormal cystic walls (87.5%). Calcification changed into determined in handiest approximately 17% of instances, greater than 1/2 of the sarcomas (34 sufferers, 55.7%), and handiest three sufferers without shadows confirmed fan-formed shadows. Internal shadows have been determined in 26 sufferers. Of the sufferers, approximately 88% confirmed an boom in blood vessels however the majority of displaying at least to slight vascularity. Our outcomes are detections sarcoma charges are 20% (n=three) and 53. three% (n=eight), respectively<sup>14</sup>.

Three main characteristics on ultrasound	Sample size 61
≥ 5 cm size, cystic degeneration, heterogeneous echogenicity	27 (44.3)
≥ 5 cm size, heterogeneous echogenicity	19 (31.1)
Cystic degeneration, heterogeneous echogenicity	5 (8.2)

S. Sun et al. in 2019 conducted a retro prospective descriptive review study including about 100 peer reviewed studies to prove the reliability of ultrasound as the first line imaging modality for the recognition of uterine leiomyosarcoma<sup>18</sup>.

Author	Year of publication	Age	Sample size	Sensitivity and specificity and positive predictive value, detection rate	p-value
Kara.G et al	2016	>40 year	56	None	<0.05
Hata.K et al	2020	>40 year	44	None	<0.05
Catarina E et al	2007	>35 year	258	Sensitivity 75%, positive predictive value 60%, specificity 80%	<0.05
Sabzo.I et al	2007	>35 year	117	Sensitivity 67%	none
J.H Kim et al	2019	>40 year	61	Detection rate from 20-53%	none
S. Sun et al	2019	35-55 year	-	Sensitivity 75%, positive predictive value 60%	none

Figure 1: a) Represents leiomyoma on gray scale with size less than 5 cm. b) Represents leiomyosarcoma on gray scale with size more than 5cm.<sup>15</sup>

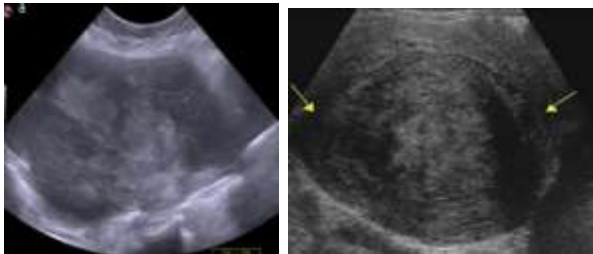


Figure 2: Represents the vascularity pattern of uterine leiomyoma sarcoma on color doppler

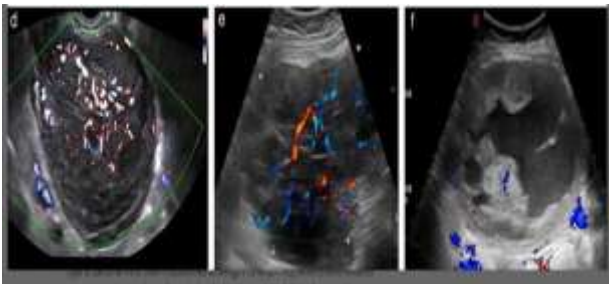
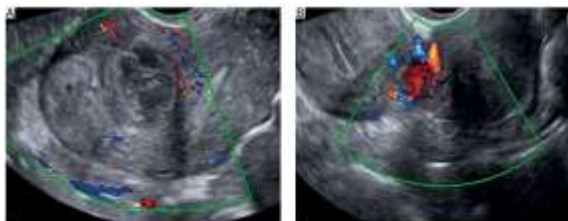


Figure 3: Represents the vascularity pattern of uterine leiomyoma on color doppler.<sup>17</sup>



### CONCLUSION

Ultrasound can provide accurate diagnosis in differentiating malignant uterine leiomyosarcoma from benign uterine leiomyoma after careful analysis of the sonographic feature of the mass that exhibit special features such as necrosis with increased size with increased vascularity, calcification and low resistive indices but the diagnosis should be supported by other modality such as computed tomography and magnetic resonance imaging specially (diffusion weighted imaging).

**Recommendation:** Doppler ultrasonography should be considered as an essential part of the protocol in the case of a mass that exhibit uterine leiomyoma features and has increased size and with slight cystic degeneration and calcification especially in post-menopausal women who has high occurrence of malignancy such as uterine leiomyosarcoma.

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