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Research Article

Ultrasound Differential Diagnosis of Uterine Leiomyomas

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Abstract

Introduction: Uterine leiomyoma is a common hyperplastic process of the myometrium of women of reproductive age throughout the world.

Objective: To develop a complex of ultrasound criteria for the differential diagnosis of simple and proliferating leiomyomas.

Materials and Methods: A retrospective analysis of the results of a comprehensive ultrasound of 121 women aged 38 - 59 years, operated on for uterine leiomyomas was carried out. According to histological studies, in 67.0% cases, the myomas had a low degree of proliferation, in 19.0% cases, the tumor had a moderate degree of proliferation and in 14.0% cases, the degree of tumor proliferation was high (leiomyosarcoma).

Results: Lobular structure of myomatous node was registered in 7 (8.6 ± 3.1%) cases of non-proliferating myomas, in 4 (17.4 ± 7.9%) cases of moderately proliferating myomas and in 8 (47.1 ± 12.1%) cases of leioyomyosarcomas; an echogenic areas within the node - in 7 (8.6 ± 3.1%), in 8 (9.9 ± 3.3%) and in 9 (52.9 ± 12.1%) cases, respectively.

Peak systolic velocity (PSV) of intranodal arterial blood flow less than 35 cm/s was observed in 62% of patients with simple myoma and more than 55 cm/s - in 68% with leiomyosarcoma. The index of resistance (IR) of intranodal arterial blood flow in 73.4% of patients with simple and in 76.2% of patients with moderately proliferating myoma was in the range of 0.45 - 0.65 (on average 0.54), and in 75.0% of patients with leiomyosarcomas was below 0.45 ($P < 0.001$).

Conclusion: The most significant signs of proliferation of the leiomyomatous node are fuzzy contours of the tumor, the presence of anechoic areas, increased vascularization, peak systolic blood flow velocity in the uterine arteries over 45 cm/s, peripheral resistance index - less than 0.50, and inside the node - over 55 cm/s and less than 0.45, respectively.

Keywords: *Uterine Leiomyoma; Leiomyosarcoma; Ultrasound Diagnostics; Transvaginal Ultrasonography*

Introduction

According to various sources, uterine leiomyoma is detected in approximately 50 - 83% of women of reproductive age worldwide. Among the nodal forms of pathology of the myometrium, leiomyoma occupies a leading position. According to the results of histological studies in leiomyoma, hyperplasia of smooth muscles and connective tissue of the uterus occurs during the proliferation of monoclonal cells. The risk of transformation of leiomyoma into leiomyosarcoma is 0.1 - 0.8% [1,2].

There are three main forms of uterine leiomyomas: simple (non-proliferative), moderately proliferating and leiomyosarcoma. Simple leiomyoma develops according to the type of benign focal muscular hyperplasia, while mitoses are either absent altogether or isolated. Often, morphological signs of simple leiomyoma are dystrophic changes (hyalinosis - 50%, edema - 41%). The greatest difficulties in diagnosis are mitotically active and atypical leiomyoma, since it can have a relatively high mitotic activity and signs of cellular atypism [3]. Thanks to the introduction and widespread use of modern methods for diagnosing tumors, the morphological study and determination of the histological type of leiomyoma has now become more effective. In difficult cases of differential diagnosis of leiomyoma and leiomyosarcoma, it is recommended to use a complex of histological, immunohistochemical and molecular genetic diagnostic methods [4].

Uterine leiomyosarcoma is a rare malignant neoplasm that accounts for 1 - 3% of all uterine cancers and approximately 65% of all uterine sarcomas [5]. In most cases, leiomyosarcoma is detected at a later stage when it becomes inoperable, resulting in a poor prognosis and short life expectancy [6]. Currently, complete surgical resection is the only potentially curative treatment option for leiomyosarcoma when it is the treatment of choice if the tumor is considered resectable [7]. However, the recurrence rate is high in patients who have undergone a potentially curative resection. The risk of recurrence is 50 to 70%, and the 5-year overall survival is < 50% in the early stages, even after radical resection [8].

Ultrasound is an important imaging modality for the primary diagnosis of uterine leiomyomas. It has high sensitivity and specificity. The study can be carried out transvaginally and transabdominally. The imaging quality of transvaginal ultrasound is much better than transabdominal. However, it is difficult to visualize large nodes transvaginally at the same time. For this reason, the measurement of the size of large myomatous nodes is carried out by the transabdominal method, and a detailed study of the internal structure is carried out by the transvaginal method [9].

The presence of clinical symptoms depends on the size and location of the leiomyoma. With Ultrasound, a simple leiomyoma usually looks like a solid rounded lesion, with a clear, even contour, and reduced echogenicity. Often, due to external similarities, it becomes necessary to differentiate between simple leiomyoma and leiomyosarcoma. An erroneous diagnosis of leiomyosarcoma has the most negative consequences, since the five-year survival rate for this tumor is very low [10, 11]. Transvaginal ultrasound has the greatest potential for differential diagnosis of endometrial polyp, adenomyosis, submucosal and intramural uterine leiomyoma [12].

Due to the fact that the treatment tactics for uterine leiomyoma depends on the degree of node proliferation, and ultrasound is an important component of preoperative diagnosis, the development of new criteria for differentiating simple and proliferating leiomyomas, especially leiomyosarcoma using complex ultrasound, is relevant.

Objective of the Study

To develop a complex of ultrasound criteria for the differential diagnosis of simple and proliferating leiomyomas.

Materials and Methods

A retrospective analysis of the results of a comprehensive ultrasound examination of 121 women operated on for uterine leiomyomas was carried out. According to histological studies, in 81 (67.0%) cases, the myomas had a low degree of proliferation (simple or non-

proliferating myoma, group I), in 23 (19.0%) cases, the tumor had a moderate degree of proliferation (proliferating myoma, group II), and in 17 (14.0%) cases, the degree of tumor proliferation was high (leiomyosarcoma, group III). The age of the examined women of group I varied within 29 - 58 years (average 47 ± 6 years), group II - within 38 - 59 years (average 52 ± 5 years), group III - within 51 - 69 years (average 62 ± 4 years). Ultrasound examination was performed transabdominally and transvaginally with a multifrequency transducer using all modes.

Student's t-test was used to assess differences in quantitative indicators between groups. Differences were considered significant at $P < 0.05$.

Results

Table 1 shows the percentage of women within age groups in relation to the number of patients with different types of leiomyomas, taking into account the degree of proliferation. At the age of 39 years, simple non proliferating myoma was diagnosed in 15 (18.5 ± 4.3%), moderate proliferating - in 3 (13.0 ± 7.0%), leiomyosarcoma - none; in the age range of 40-49 years - in 21 (25.9 ± 4.9%), in 9 (39.1 ± 10.2%) and in 1 (5.9 ± 5.7%); at 50-59 years old - in 26 (32.1 ± 5.2%), in 8 (34.9 ± 9.9%) and in 7 (41.2 ± 11.9%); in 60-69 years old - in 19 (23.5 ± 4.7%), in 3 (13.0 ± 7.0%) and in 9 (52.9 ± 12.1%), respectively.

Age	Noproliferating leiomyoma n = 81	Moderately proliferating leiomyoma n = 23	Leiomyosarcoma n = 17
	1	2	3
30-39	15 (18,5 ± 4,3%) P 1-3 < 0,05	3 (13,0 ± 7,0%)	-
40-49	21 (25,9 ± 4,9%) P 1-3 < 0,01	9 (39,1 ± 10,2%) P 2-3 < 0,01	1 (5,9 ± 5,7%)
50-59	26 (32,1 ± 5,2%)	8 (34,9 ± 9,9%)	7 (41,2 ± 11,9%)
60-69	19 (23,5 ± 4,7%)	3 (13,0 ± 7,0%)	9 (52,9 ± 12,1%) P 3-1 < 0,05 P 3-2 < 0,001

Table 1: *Distribution of patients with uterine leiomyoma by age and degree of tumor proliferation.*

As can be seen from the table 1, in the age range of 40-49 years, non-proliferating and moderately proliferating leiomyomas occurred significantly (P1-3 < 0.01, P2-3 < 0.01) more often than leiomyosarcoma, and in 60 - 69 years, on the contrary, leiomyosarcoma more common than non-proliferating (P3-1 < 0.05) and moderately proliferating (P3-2 < 0.001) leiomyomas.

We compared the frequency of ultrasound symptoms in different types of uterine leiomyomas (Table 2). Uterus volume less than 150 cm^3 was registered in 46 (56.8 ± 5.5%) cases of non-proliferating myomas, in 2 (8.7 ± 5.9%) cases of moderately proliferating myomas and with leiomyosarcoma - none; by volume of 151-300 cm^3 was registered in 24 (29.6 ± 5.1%), in 13 (56.5 ± 10.3%) and in 3 (17.6 ± 9.2%) cases respectively; by volume more than 300 cm^3 - in 11 (13.6 ± 3.8%), in 8 (34.9 ± 9.9%) and in 14 (82.4 ± 9.2%) cases, respectively. Lobular structure of myomatous node was registered in 7 (8.6 ± 3.1%) cases of non-proliferating myomas, in 4 (17.4 ± 7.9%) cases of moderately proliferating myomas and in 8 (47.1 ± 12.1%) cases of leioyomyosarcomas; anechogenic areas within the node - in 7 (8.6 ± 3.1%), in 8 (9.9 ± 3.3%) and in 9 (52.9 ± 12.1%) cases, respectively.

Sonographic parameters	Non proliferating leiomyoma n = 81	Moderately proliferating leiomyoma n = 23	Leiomyosarcoma n = 17
	1	2	3
Myomas nodule size < 150 cm^3	46 (56,8 ± 5,5%) P1-3 < 0,05	2 (8,7 ± 5,9%)	-
Myomas nodule size 151 - 300 cm^3	24 (29,6 ± 5,1%)	13 (56,5 ± 10,3%) P2-3 < 0,01	3 (17,6 ± 9,2%)
Myomas nodule size 301 - 600 cm^3	11 (13,6 ± 3,8%)	8 (34,9 ± 9,9%)	14 (82,4 ± 9,2%) P 3-1 < 0,001
Clear contours of the myomatous nodule	68 (84,0 ± 4,1%) P 1-2 < 0,01 P 1-3 < 0,001	12 (52,1 ± 10,4%)	5 (29,4 ± 11,0%)
Lobular structure of myomatous nodule	7 (8,6 ± 3,1%)	4 (17,4 ± 7,9%)	8 (47,1 ± 12,1%) P 3-1 < 0,01 P 3-2 < 0,05
Anechogenic areas within the node	8 (9,9 ± 3,3%)	6 (26,1 ± 9,2%)	9 (52,9 ± 12,1%) P 3-1 < 0,01 P 3-2 < 0,05

Table 2: *Sonographic parameters for different types of uterine leiomyomas.*

As can be seen from the table 2, the volume of the uterus less than 150 cm^3 was significantly more often (P < 0,05) recorded in the I group; 151 - 300 cm^3 - in the II group (P < 0,01) and more than 300 cm^3 - in the III group (P < 0,01). Clear contours of the myomas nodule was significantly more often (P < 0,001) recorded in the first group, lobular structure of myomatous node and anechogenic areas within the node - in the group of women with leiomyosarcoma (P < 0,01).

To differentiate simple and proliferating uterine myomas, in addition to characterizing the structure of nodes in the gray scale mode, we studied the peak systolic velocity (PSV) and resistance index (IR) of blood flow in the uterine and intranodal arteries, the degree of vascularization of leiomyoma nodes.

To assess the magnitude of the peak systolic velocity of blood flow in the uterine arteries in the differentiation of varying degrees of leiomyoma proliferation, we divided this parameter into 3 gradations - up to 30 cm/s, from 31 cm/s to 45 cm/s and more than 45 cm/s. The frequency of occurrence of these speed gradations in various types of leiomyomas was determined in order to highlight the most characteristic blood flow parameters for each group. PSV less than 30 cm/s most often (in 32 - 39.5 ± 5.4% of cases) was observed in the group of patients with simple myoma, and 31 - 45 cm/s - among patients with moderate proliferating leiomyoma, although not statistically. PSV more than 45 cm/s was significantly (P<0.001) more often recorded among patients with leiomyosarcoma (Table 3).

The index of resistance (IR) to blood flow in the uterine arteries is divided into 3 gradations - > 0.70, 0.50-0.69 and < 0.50. As can be seen from table 2, an IR of more than 0.70 was observed in 35 (44.3 ± 5.6%) cases of simple leiomyoma, in 6 (28.7 ± 9.9%) cases of moderately proliferating leiomyoma, and in 3 (18.7 ± 9.7%) cases of leiomyosarcoma; within 0.50-0.69 - in 43 (54.4 ± 5.6%), in 13 (61.9 ± 10.6%) and in 4 (25.0 ± 10.8%) cases; and less than 0.50 in 1 (1.3 ± 1.2%), in 2 (9.5 ± 6.4%) and in 9 (56.3 ± 12.4%) cases, respectively. Thus, a significant difference between the groups was found only in the value of IR less than 0.50 in leiomyosarcoma (P < 0.001).

PSV and IR of uterine artery blood flow	The degree of leiomyoma proliferating		
	Non proliferating leiomyoma n = 81	Moderately proliferating leiomyoma n = 23	Leiomyosarcoma n = 17
	1	2	3
PSV < 30 см/с	32 (39,5 ± 5,4%)	6 (26,1 ± 9,2%)	2 (11,8 ± 7,8%)
PSV - 31-45 см/с	46 (56,8 ± 5,5%)	15 (65,2 ± 9,9%)	6 (35,3 ± 11,6%)
PSV > 45 см/с	3 (3,7 ± 2,1%)	2 (8,7 ± 5,9%)	9 (52,9 ± 12,1%) P 3-1 < 0,001 P 3-2 < 0,001
IR > 0,70	37 (45,7 ± 5,5%)	7 (30,4 ± 9,6%)	3 (17,6 ± 9,2%)
IR - 0,50-0,69	43 (53,1 ± 5,5%)	13 (56,5 ± 10,3%)	5 (29,5 ± 11,0%)
IR < 0,50	1 (1,2 ± 1,2%)	3 (13,1 ± 7,0%)	9 (52,9 ± 12,1%) P 3-1 < 0,001 P 3-2 < 0,01

Table 3: *PSV and IR of blood flow in the uterine arteries in a patients with varying degrees of leiomyomas proliferation.*

We also analyzed the results of PSV and IR of intranodal blood flow among groups of patients with varying degrees of proliferation of uterine leiomyomas. PSV was divided into gradations less than 35 cm/s, 36-55 cm/s and more than 55 cm/s (Table 4).

Intranodal PSV and IR of blood flow	The degree of leiomyoma proliferating		
	Non proliferating leiomyoma n = 81	Non proliferating leiomyoma n = 81	Non proliferating leiomyoma n = 81
PSV < 35 см/с	49 (62,0 ± 5,4%)	5 (23,8 ± 9,3%)	-
PSV - 36-55 см/с	27 (34,2 ± 5,3%)	14 (66,7 ± 10,3%) P 2-1 < 0,05 P 2-3 < 0,001	5 (31,2 ± 11,6%)
PSV > 55 см/с	3 (3,8 ± 2,1%)	2 (9,5 ± 6,4%)	11 (68,8 ± 11,6%) P 3-1 < 0,001 P 3-2 < 0,001
IR > 0,65	21 (26,6 ± 5,0%)	1 (4,8 ± 4,6%)	-
IR - 0,45-0,65	58 (73,4 ± 5,0%)	16 (76,2 ± 9,3%)	4 (25,0 ± 10,8%)
IR < 0,45	-	4 (19,0 ± 8,5%)	12 (75,0 ± 10,8%) P 3-1 < 0,001 P 3-2 < 0,001

Table 4: *PSV and IR of intranodal blood flow in leiomyoma with varying degrees of proliferation.*

PSV less than 35 cm/s was noted in 32 (39.5 ± 5.4%) cases of simple leiomyoma (P 1-2 < 0.001) and in 5 (23.8 ± 9.3%) cases of moderately proliferating leiomyoma, not in one case - leiomyosarcoma; within 36 - 55 cm/s - in 27 (34.2 ± 5.3%), 14 (66.7 ± 10.3%) and 5 (31.2 ± 11.6%) cases; more than 55 cm/s in 3 (3.8 ± 2.1%), 2 (9.5 ± 6.4%) and 11 (68.8 ± 11.6%) cases, respectively. As can be seen from the table, PSV within 36 - 55 cm/s was significantly (P < 0.05) more often recorded with moderately proliferating myoma, and more than 55 cm/s with leiomyosarcoma (P 3-1 < 0.001 and P 3-2 < 0.001).

The resistance index (IR) of intranodal arterial blood flow was divided into gradations of more than 0.65, within 0.45 - 0.65 and less than 0.45. IR over 0.65 in simple leiomyoma was noted in 21 (26.6 ± 5.0%) cases, moderately proliferating leiomyoma in 1 (4.8 ± 4.6%) and leiomyosarcoma in one case; within 0.45 - 0.65 - in 58 (73.4 ± 5.0%), in 16 (76.2 ± 9.3%) and in 4 (25.0 ± 10.8%) cases; and less than 0.45 - with simple myoma not in one case, moderately proliferating leiomyoma - in 4 (19.0 ± 8.5%) and with leiomyosarcoma - in 12 (75.0 ± 10.8%) cases, respectively. As can be seen from table 3, a significant difference between the groups was found in the value of IR less than 0.45 in leiomyosarcoma (P 3-1 < 0.001 and P 3-1 < 0.001).

It should be noted that when differentiating simple, moderately proliferating leiomyoma and leiomyosarcoma, a high systolic intranodal blood flow rate and a low resistance index, as well as the degree of vascularization in color or power Doppler modes, cannot always be combined. The presence of 2 of the 3 main Doppler readings may increase the likelihood of one or the other type of leiomyoma (Figure 1-4).

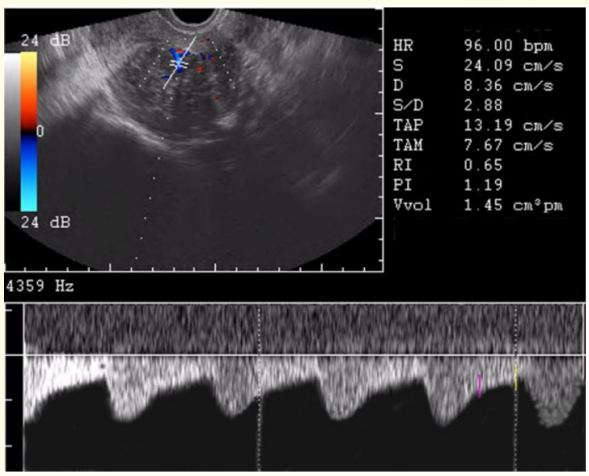

Figure 1: *Simple uterine leiomyoma. In the uterus, an intramurally located hypoechoic formation of a rounded shape, with a clear, even contour, and a homogeneous structure is visualized. The peak systolic blood flow velocity is 24 cm/s, the resistance index is 0.65.*

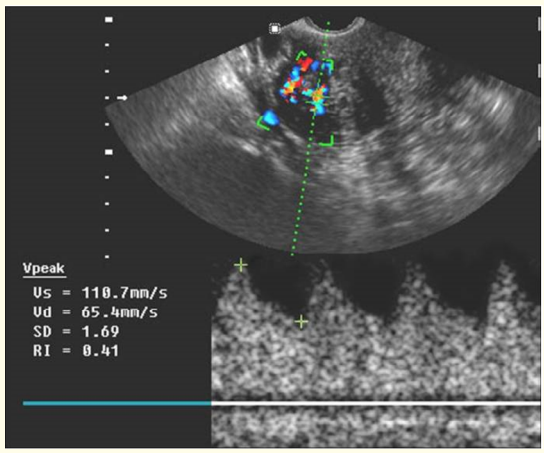

Figure 2: *Moderately proliferating uterine leiomyoma. Enhanced intranodal vascularization of a medium-sized tumor (less than 5 cm), reduced echogenicity. Despite the low blood flow velocity, there is a very low resistance index (0.41), which indicates the proliferating nature of the tumor.*

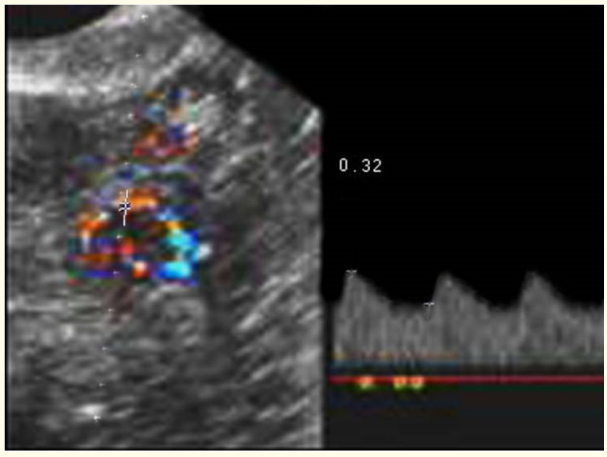

Figure 3: *Leiomyosarcoma. Increased vascularization and a very low blood flow resistance index (0.32) of a myomatous node.*

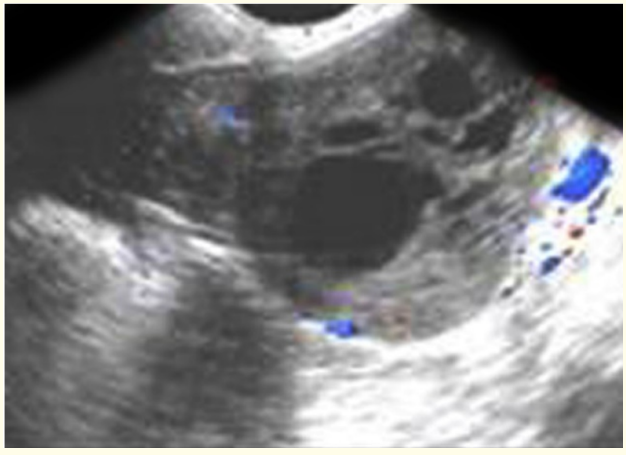

Figure 4: *Moderately proliferating myoma. Anechogenic areas inside the node are visualized.*

Discussion

Leiomyosarcoma is one of the rare tumors of the uterus, in which an incorrect diagnosis leads to the worst prognosis for the patient. It is very difficult to distinguish it from benign simple leiomyoma due to the similarity of both clinical and echographic symptoms. An intermediate variant is a moderately proliferating leiomyoma. In all variants of leiomyoma, central necrosis of the formation, to varying degrees, vascularization with various quantitative parameters of blood flow can occur with varying frequency [9]. Ludovisi M., *et al*. (2017) believe that a large-focal lesion of the myometrium with a heterogeneous echotexture, an uneven surface, the presence of irregularly shaped cystic cavities and no attenuation of ultrasound behind them may indicate a high probability of the presence of leiomyosarcoma [12].

Oh J., *et al*. (2019) in their studies, based on the features of the echostructure and the degree of vascularization of the node, they tried to differentiate various types of uterine sarcoma. In their opinion, a high degree of heterogeneity and vascularization of the node are the most significant signs of leiomyosarcoma [13]. Due to the operator dependence of ultrasound, some specialists in radiological diagnostics admit that magnetic resonance imaging can more objectively assess the internal structure of myometrial nodes. At the same time Minsart AF., *et al*. (2013) revealed many inconsistencies in such an assumption [14]. At the same time, MRI may have an advantage over ultrasonography in that it can better assess the relationship between the uterus and ovaries, and identify metastases in the latter. The results of MRI are based more on assessing the nature of structural changes [15-17]. However, MRI lacks the capabilities of ultrasound, such as assessing the blood supply to small nodes and determining the quantitative parameters of blood flow. We have studied not only the echostructure of various types of leiomyomas, but also the qualitative and quantitative parameters of blood flow in color and spectral Doppler modes.

Conclusion

The most significant signs of proliferation of the leiomyomatous node are fuzzy contours of the tumor, the presence of anechoic areas, increased vascularization, peak systolic blood flow velocity in the uterine arteries over 45 cm/s, peripheral resistance index - less than 0.50 and inside the node - over 55 cm/s and less than 0.45, respectively.

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