The Importance Of Lactate Dehydrogenase Isomers In The Diagnosis Of Uterine Tumors

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1. Introduction

Uterine myomas are the most common benign uterine tumors in women of reproductive age [1]. These lesions rarely appear before puberty, and their incidence decreases with menopause. Factors that increase overall exposure to estrogen throughout life, such as obesity or early first menstruation, among others, increase the risk of uterine myomas in women. On the other hand reduced estrogen exposure found during exercise and increased number of childbirth, have a protectective effect [2]. Heavy menstrual bleeding often leading to patient anemia and a feeling of pressure or distension in the pelvis are the main symptoms associated with myomas [3]. Other symptoms include infertility, increased urinary frequency or incontinence, constipation, abdominal bloating, dyspareunia and fatigue (due to anemia from heavy bleeding) [4,5]. The spectrum and severity of symptoms often depends on the size, location and number of tumors in the uterus. [6] Currently, there are various options for the effective treatment of myomas, ranging from the most conservative approach to the most invasive: symptomatic treatment with oral contraceptive pills or levonorgestrel-releasing IUDs, treatment with ulipristal acetate, HIFU, embolization of the myoma, surgical removal of the lesion (hysteroscopy, laparoscopy, laparotomy) and removal of the affected uterus (laparoscopy,

laporotomy). Various factors will influence a patient's choice: personal preference, age, desire for pregnancy and future fertility, individual symptoms, and medical availability of various treatments. [7]

Uterine sarcomas account for about 1% of all reproductive tract cancers in women and 3-7% of all uterine cancers. Since malignant sarcomas are now classified as metaplastic carcinomas, smooth cell sarcomas remain the most common subtype. [8] The most common symptoms in women with smooth cell myxosarcoma include abnormal uterine bleeding (56%), palpable pelvic tumor or enlarged uterus (54%), and pelvic pressure or pain (22%) [9]. Other nonspecific symptoms such as discharge, frequent urination, constipation and abdominal bloating may also occur. Some patients may present with acute peritoneal hematoma due to tumor rupture or ectopic spread of the tumor. Because these symptoms are not specific and may mimic other more common lesions, such as smooth cell myxoma or gatroenetrological abnormalities, it is difficult to diagnose LMS prior to histopathological examination of the specimen. Lactate dehydrogenase (LDH) is an enzyme that is found in the cells of the human body and is involved in the conversion of glucose. It permeates the blood serum without major complications due to cell death, blood ionic imbalance or increased permeability of the cell membrane. Its elevated levels result from LDH escaping outside the cell when it is damaged. [10] In clinical practice, serum LDH levels are most commonly measured in patients with suspected organ damage or dysfunction, such as myocardial infarction, acute hepatitis or hemolytic anemia. As for cancer, serum LDH levels increase in patients with tumor growth and tissue destruction, determining survival time in patients with Hodgkin's disease and non-Hodgkin's lymphoma [11]. In ovarian cancer, serum LDH levels can serve as a reliable marker to distinguish ovarian cancer from benign ovarian tumors.

Currently, there are no validated fully reliable or tested markers for diagnosing and assessing the malignancy of uterine lesions prior to the implementation of surgical treatment, and in established pathology of this organ. The presence of elevated levels of lactate dehydrogenase, especially its isomers, may be related to the presence of a uterine tumor, the prognosis of the potential malignancy of the lesion, and affect the extent of prognostic surgical treatment[12]. The inability to completely rule out the preoperative presence of a malignant lesion is currently one of the safety concerns regarding the use of morcellation during laparoscopy. Work is underway to find a specific and sensitive marker that will give the possibility of making a confident diagnosis before the implementation of surgical treatment, thus allowing procedures to be performed in a minimally invasive manner. [13,14].While the number of publications on the use of examination of lactate dehydrogenase isomers levels in patients with uterine tumors is considerable, there are few publications describing unequivocally the possibility of confidently using the above-mentioned

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enzymes to differentiate the nature of uterine tumors, which may have implications for the possibility of using minimally invasive procedures to treat the pathology of this organ. Also, the standards for LDH and its isomers for which, a suspicion of a malignant lesion can be raised have not been exhaustively described, so little can be said about their sensitivity and specificity.

2. Aim of the study:

The project aimed to evaluate the usefulness of biochemical tests (LDH and its isomers 3 and 5) in the diagnosis and differentiation of uterine tumors. Lactate dehydrogenase is a cytoplasmic enzyme present in all human cells. It occurs in 5 isoforms. There are reports describing elevated values of lactate dehydrogenase, particularly its isomers 3 and 5, in patients diagnosed with uterine lesions. The purpose of this study is to evaluate the possibility of using the examination of lactate dehydrogenase isomer 3 and 5 levels in the diagnosis of uterine tumors.

3. Material and Methods

The study included 149 patients aged 25-81 years who were the patients of the Department of Maternal and Child Health of the Karol Marcinkowski Medical University in Poznan. Patients referred for surgery to remove the uterus because of established uterine myomas or for extirpation of the myoma/myomas of the uterus and for surgery to repair pelvic organ statics without uterine lesions were included in the analysis. Data on the analyzed patients were obtained from the medical history and questionnaires. The diagnosis was established on the basis of a clinical examination including in each case: history with a detailed analysis of the diagnosis and internal medicine treatment, gynecological examination and ultrasound evaluation. The following parameters were also assessed: age, weight, height, body mass index (BMI), co-occurrence of chronic diseases gynecological and obstetric history, indications for surgical treatment, number of myomas and menstrual cycles. In addition, in each patient, after signing the appropriate consent, blood was drawn for biochemical tests. This was followed by quantification of lactate dehydrogenase isoenzyme 3 and 5. At a later stage, the result of the biochemical tests was matched with the result of the histopathological examination. Approval was obtained from the Bioethics Committee at the Karol Marcinkowski Medical University in Poznan to perform the above procedures. TIBCO Software Inc. (2017), Statistica (data analysis software system), version 13, and Microsoft Excel (version 2019) - Microsoft Office were used for data analysis. Mann-Whitney U test and Kruskal Wallis ANOVA test were used for comparisons between the groups. Using Spearman's R test, Kendall's tau, and the Chi2 of highest reliability test, the relationships between variables were examined. The significance level in all calculations was taken as $p < 0.05$.

4. Results

The analysis included 149 patients hospitalized at the Department of Maternal and Child Health of the Karol Marcinkowski Medical

University in Poznan, Poland, from 2020 to 2022. In the study group, laparoscopic supracervical uterine removal (LASH) was performed in 104 patients (~70%), myomectomy in 22 (~15%), and in the control group, laparoscopic lateral uteropexy using the Dubuisson method was performed in 19 patients (~13%), and hysterolaparoscopy in 4 (~2%).
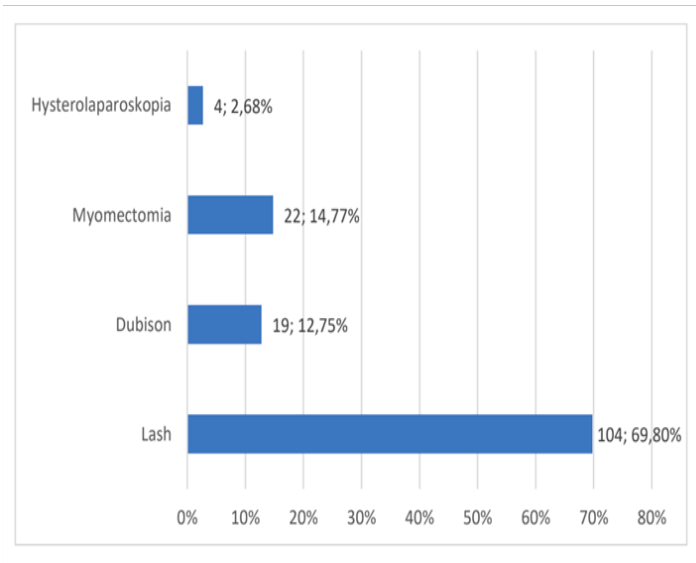
In the study group, the average age of the patients was 45 years, with a BMI of about 25.6. The youngest patient was 25 years old, and the oldest was 81 years old. The lowest BMI was 17.99, and the highest BMI was 39.44. The number of fibroids was also dectermined among the examined patients: without myomas 15 (10.07%), with 1 myoma 53 (35.57%), with 2 myomas 12 (8.05%), with 3 myomas 4 (2.68%), with 4 myomas 5 (3.36%), with 5 myomas and more 60 (40.27%). The study demonstrated that higher body weight was associated with a higher number of myomas ($\tau=0.11$; $p=0.047$).
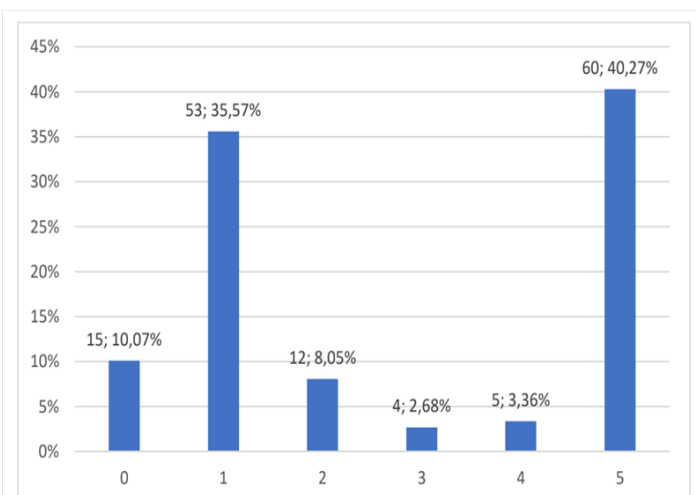
Wykres 2 Liczba mięśniaków

Patients in the Lash group had a significantly higher number of myomas compared to the other groups.

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Grupa		
	Lash	**Inne**
0	2(1,92%)	13(28,89%)
1	32(30,77%)	21(46,67%)
2	10(9,62%)	2(4,44%)
3	3(2,88%)	1(2,22%)
4	4(3,85%)	1(2,22%)
5	53(50,96%)	7(15,56%)
Chi² NW	X²=36,05; df=5; p<0,001	

Table 2: Grupa a liczba miesniakow

In the analysis of the patients, it was also noted that those in the Lash group had a higher number of pregnancies compared to the others.

Tabela 3 Grupa a porody

	Grupa	
	Lash	**Inne**
0	13 (12,5%)	14 (31,11%)
1	26 (25%)	9 (20%)
2	56 (53,85%)	14 (31,11%)
3	5 (4,81%)	6 (13,33%)
4	2 (1,92%)	1 (2,22%)
5	2 (1,92%)	1 (2,22%)
Chi² NW	$\chi^2=12,39$; df=5; p=0,03	

The study demonstrated that patients in the Lash group were significantly less likely to take HRT medications compared to the others.

Tabela 13 Grupa a leki HTZ

	Grupa	
	Lash	**Inne**
Nie	88 (100%)	37 (94,87%)
Tak	0 (0%)	2 (5,13%)
Chi² NW	$\chi^2=4,8$; df=1; p=0,03	

Those in the Lash group significantly more often had Group D diseases, these were patients with a diagnosis of myoma (96.15% vs 64.44% p <0.001). Other diseases including: thyroid diseases, metabolic diseases - diabetes mellitus, cardiovascular disease, gastrointestinal diseases with the exception of liver diseases in the Lash group were more common, but statistical significance was not obtained. There were no differences in the length of the hospitalitation between the study groups, and no differences in the evaluation of menstrual cycles between the study groups. In the study, it was observed that uterine adenomyosis was significantly more common in the Lash group (49.04% vs 14.71%) while myomas were significantly more common among the other subjects (85.29% vs 50.96%).

These results had a statistical significance of p <0.001.

Tabela 14 Grupa a choroby towarzyszące

	Grupa		χ^2	p
	Lash	**Inne**		
C	1 (0,96%)	0 (0%)	0,72	0,4
D	100 (96,15%)	29 (64,44%)	**25,03**	**<0,001**
E	23 (22,12%)	13 (28,89%)	0,77	0,38
F	10 (9,62%)	6 (13,33%)	0,44	0,51
G	2 (1,92%)	1 (2,22%)	0,01	0,91
H	1 (0,96%)	2 (4,44%)	1,73	0,19
I	24 (23,08%)	14 (31,11%)	1,04	0,31
J	1 (0,96%)	2 (4,44%)	1,73	0,19
K	40 (38,46%)	12 (26,67%)	1,97	0,16
L	1 (0,96%)	1 (2,22%)	0,35	0,56
M	2 (1,92%)	0 (0%)	1,45	0,23
N	53 (50,96%)	19 (42,22%)	0,96	0,33
R	3 (2,88%)	3 (6,67%)	1,07	0,3

Tabela 15 Grupa a adenomiosis i mięśniaki

	Grupa	
	Lash	**Inne**
Mięśniaki	53 (50,96%)	29 (85,29%)
Adenomiosis	51 (49,04%)	5 (14,71%)
Chi² NW	$\chi^2=13,85$; df=1; p<0,001	

In the analysis of histopathological results, it was found that Lash subjects were significantly more likely to have Leiomyomata corporis uteri (92.1% vs. 60%; p <0.001), Endometrium cum signisproliferationis (65.5% vs. 2.22% p < 0.001), Adenomiosis (49.04% vs. 11.11% p <0.001).

Tabela 16 Grupa a histopatologia

	Grupa		χ^2	p
	Lash	**Inne**		
I[a]	96 (92,31%)	27 (60%)	**20,98**	**<0,001**
II[b]	65 (62,5%)	1 (2,22%)	**57,42**	**<0,001**
III[c]	77 (74,04%)	2 (4,44%)	**70,54**	**<0,001**
IV[d]	11 (10,58%)	0 (0%)	**8,28**	**0,004**
V[e]	51 (49,04%)	5 (11,11%)	**21,74**	**<0,001**
VI[f]	13 (12,5%)	2 (4,44%)	2,58	0,11
VII[g]	29 (27,88%)	1 (2,22%)	**16,97**	**<0,001**
VIII[h]	4 (3,85%)	0 (0%)	2,92	0,09
IX[i]	16 (15,38%)	2 (4,44%)	**4,16**	**0,04**
X[j]	7 (6,73%)	2 (4,44%)	0,31	0,58
XI[k]	7 (6,73%)	2 (4,44%)	0,31	0,58
XII[l]	6 (5,77%)	1 (2,22%)	1,01	0,32
XIII[m]	10 (9,62%)	2 (4,44%)	1,26	0,26

[a] *Leiomyomata corporis uteri,* [b] *Endometrium cum signis proliferationis,* [c] *Salpinges sine laesionibus,* [d] *Salpingitis chronica,* [e] *Adenomiosis,* [f] *Adnexa sine leasionibus,* [g] *Cystes peripsalpingealis serosa,* [h] *Endometrium atrophicum,* [i] *Endometrium irregularis,* [j] *Polypus glandularis endometrialis,* [k] *Endometrium inactivum,* [l] *Hyperplasia endometrii sine atypia,* [m] *Cystis endometrioides.*

The results of physical and subject tests, including laboratory tests, were also analyzed, it was shown that higher age of the subjects was associated with higher measurements of HGB (r=0.26; p=0.0045), HTC (r=0.2; p=0.03) and LDH (r=0.19; p=0.02) but this result was not statistically significant. As the weight of the subjects increased, there were increases in leukocyte (r=0.3; p=0.001) and LDH (r=0.21; p=0.01) results and decreases in LDH5 (r=-0.18; p=0.025), but the results were not statistically significant. Higher BMI scores were associated with higher levels of leukocytes (r=0.34; p<0.001), platelets (r=0.21; p=0.02), and LDH (r=0.21; p=0.01) and lower LDH5 (r=-0.19; p=0.02), but no statistical significance was found. Statistical significance (p<0.001) was found for HTC values, peripheral blood erythrocyte count (r=0.78; p<0.001) and HGB (r=0.94; p<0.001) for patients in the control group relative to patients in the study group. The study demonstrated a statistically significant relationship between the number of myomas diagnosed by imaging studies - ultrasound, and laboratory analysis of peripheral blood - lower peripheral blood erythrocyte results (τ=-0.13; p=0.04) and higher peripheral blood platelet results (τ=0.13; p=0.03) and elevated LDH3 values (τ=0.16; p=0.005) were significantly more common in patients with myomas; however, these results did not have statistical significance.

Tabela 17 Pomiary laboratoryjne

	N	M ±SD	Min-Max	Me [Q1-Q3]
Leukocyty	118	6,96 ±2,83	3,08-22,21	6,38 [5,18-7,57]
Erytrocyty	118	4,48 ±0,37	3,38-5,36	4,54 [4,3-4,69]
Płytki krwi	118	273,17 ±75,78	137-664	260 [226-309]
HGB	118	7,76 ±1,01	3,1-10,1	7,9 [7,3-8,4]
HTC	118	0,38 ±0,04	0,26-0,47	0,39 [0,36-0,4]
LDH	149	173,85 ±51,94	6-337	169 [149-193]
LDH3	149	203,97 ±195,51	0-657,3	152,25 [36,35-349,19]
LDH5	149	40,65 ±57,28	0,4-585,46	22,4 [11,78-51,88]

Lash subjects were characterized by significantly higher age and height of the subjects - but there were no significant differences between the groups in body weight and BMI.

Tabela 17 Pomiary laboratoryjne

	N	M ±SD	Min-Max	Me [Q1-Q3]
Leukocyty	118	6,96 ±2,83	3,08-22,21	6,38 [5,18-7,57]
Erytrocyty	118	4,48 ±0,37	3,38-5,36	4,54 [4,3-4,69]
Płytki krwi	118	273,17 ±75,78	137-664	260 [226-309]
HGB	118	7,76 ±1,01	3,1-10,1	7,9 [7,3-8,4]
HTC	118	0,38 ±0,04	0,26-0,47	0,39 [0,36-0,4]
LDH	149	173,85 ±51,94	6-337	169 [149-193]
LDH3	149	203,97 ±195,51	0-657,3	152,25 [36,35-349,19]
LDH5	149	40,65 ±57,28	0,4-585,46	22,4 [11,78-51,88]

The study demonstrated that women who did not menstruate were characterized by significantly higher age compared to those with irregular

menstruation (z=5.67; p<0.001) and regular menstruation (z=6.08; p<0.001). The study showed that non-menstruating subjects, compared to subjects with regular monthly cycles, were characterized by significantly lower platelet counts (z=2.51; p=0.04) and significantly lower LDH3 values with concomitantly higher LDH levels (z=2.62; p=0.03).

Tabela 21 Cykle miesiączkowe a pomiary antropometryczne i laboratoryjne

	Cykle miesiączkowe			H	p
	Brak	Nieregularne	Regularne		
Wiek	54 [48-63]	41 [38-47]	44 [40-47]	**44,19**	**<0,001**
Wzrost	165 [160-168]	167 [164-172]	168 [163-170]	4,93	0,08
Masa ciała	70,5 [62-76]	73 [62-81]	67 [62-79]	1,44	0,49
BMI	26,67 [21,88-27,94]	26,49 [22,72-29,74]	24,57 [22,49-27,34]	1,37	0,50
Leukocyty	6,44 [4,87-8,06]	6,55 [5,63-8,83]	6,2 [4,97-7,42]	2,50	0,29
Erytrocyty	4,58 [4,24-4,75]	4,39 [4,26-4,66]	4,55 [4,32-4,68]	0,68	0,71
Płytki krwi	243 [208-262]	262 [218-310]	276 [237-316]	**6,31**	**0,04**
HGB	8 [7,7-8,8]	7,65 [7,2-8,2]	7,8 [7,3-8,4]	4,90	0,09
HTC	0,39 [0,38-0,42]	0,38 [0,36-0,4]	0,39 [0,36-0,4]	2,56	0,28
LDH	180,5 [160-232]	174 [143-190]	164 [144-185]	**6,88**	**0,03**
LDH3	58,95 [7,26-165,28]	231,31 [63,91-363,05]	174,7 [43,17-398,49]	**6,01**	**0,049**
LDH5	21,26 [8-84,29]	19,71 [14,1-48,82]	22,4 [11,58-51,88]	0,06	0,97

In the results of the study, it was found that patients with E group diseases such as: obesity, hypothyroidism, thyroiditis, lipid metabolism disorders and other lipidemias, insulin-dependent diabetes mellitus, and nontoxic goiter, were characterized by statistically significantly higher body weight (76.5 [67.5-85] vs 68 [61-75] p <0.001) and BMI (27.2 [24.67-31.35] vs 24.48 [21.88- 27.24] p<0.001) compared to Patients without E group diseases.

Tabela 23 Choroby towarzyszące E a pomiary antropometryczne i laboratoryjne

	Choroby towarzyszące: E		U	p
	Tak	Nie		
Wiek	46 [42-50,5]	45 [40-49]	1758	0,22
Wzrost	165 [162-170]	167 [163-169]	1936	0,66
Masa ciała	76,5 [67,5-84]	68 [61-75]	**1259,5**	**<0,001**
BMI	27,2 [24,67-31,35]	24,84 [21,88-27,24]	**1263**	**<0,001**
Leukocyty	6,4 [5,15-7,18]	6,38 [5,2-7,7]	1102	0,69
Erytrocyty	4,58 [4,33-4,7]	4,52 [4,3-4,68]	1161	0,99
Płytki krwi	283 [240-316]	258 [223-302]	966	0,20
HGB	7,9 [7,2-8,6]	7,9 [7,3-8,3]	1118,5	0,77
HTC	0,39 [0,35-0,41]	0,39 [0,37-0,4]	1150	0,94
LDH	167 [152,5-197]	169 [147-191]	2006	0,90
LDH3	169,42 [11,77-416,37]	148,55 [43,42-324,73]	2009,5	0,92
LDH5	26,93 [9,35-65,92]	21,39 [13,13-51,14]	1992	0,85

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In the study, it was observed that patients with group I diseases: hypertension, lower extremity varicose veins, ischemic heart disease, other acute forms of ischemic heart disease, non-rheumatic mitral valve disease, portal vein thrombosis, were characterized by significantly higher age, height and BMI. The patients in the group of concomitant diseases N including urinary-genital diseases: prolapse of the female reproductive organs, intrauterine adenomyosis, other abnormal uterine and vaginal bleeding, non-inflammatory diseases of the ovary, fallopian tube and uterine broad ligament, kidney and ureteral stones, female infertility, except cervical, polyp of the female reproductive system, menopause and heavy, frequent and irregular menstruation, were characterized by significantly lower BMI and statistically significantly higher LDH3 levels.

Tabela 26 Choroby towarzyszące N a pomiary antropometryczne i laboratoryjne

	Choroby towarzyszące: N		U	p
	Tak	Nie		
Wiek	45 [40-47]	47 [40-50]	2477,5	0,26
Wzrost	167 [163-170]	165 [162-168]	2531	0,36
Masa ciała	66,5 [60,5-76]	73 [64-79]	2273	0,06
BMI	24,51 [22,1-27,34]	26,49 [23,44-29,69]	**2244**	**0,045**
Leukocyty	6,27 [5,18-7,42]	6,4 [5,39-7,72]	1527	0,26
Erytrocyty	4,54 [4,31-4,67]	4,52 [4,28-4,74]	1683,5	0,77
Płytki krwi	266 [226-316]	249 [223-303]	1589	0,42
HGB	7,8 [7,3-8,3]	7,9 [7,3-8,5]	1550	0,31
HTC	0,38 [0,37-0,4]	0,39 [0,36-0,41]	1654,5	0,65
LDH	168 [146-188,5]	169 [152-204]	2602	0,52
LDH3	221,28 [62,86-400,16]	68,87 [19,16-269,22]	**2124**	**0,01**
LDH5	26,77 [15,57-51,45]	18,1 [7,43-52,21]	2321	0,09

In the study, it was observed that patients with uterine adenomyosis were characterized by significantly higher age, height and body weight compared to patients with myometrium.

Tabela 27 Histopatologia a pomiary antropometryczne i laboratoryjne

	Histopatologia		U	p
	Mięśniaki	Adenomiosis		
Wiek	42,5 [39-47]	47 [42,5-49]	**1668,5**	**0,01**
Wzrost	165 [162-168]	168 [164-172,5]	**1745**	**0,02**
Masa ciała	68 [60-76]	73 [65-80]	**1831**	**0,044**
BMI	24,82 [21,76-27,55]	25,59 [23,02-29,05]	2046	0,28
Leukocyty	6,2 [5,16-7,29]	6,59 [5,78-7,72]	1202,5	0,20
Erytrocyty	4,58 [4,29-4,69]	4,52 [4,3-4,66]	1332,5	0,64
Płytki krwi	259 [225-316]	266,5 [229-297]	1400	0,97
HGB	7,9 [7,3-8,4]	7,85 [7,3-8,2]	1325	0,61
HTC	0,38 [0,36-0,4]	0,39 [0,36-0,4]	1379	0,86
LDH	168 [150-208]	170,5 [147,5-188]	2145	0,51
LDH3	181,65 [33,12-379,51]	154,06 [63,54-382,09]	2188	0,64
LDH5	23,28 [12,61-51,37]	19,28 [9,35-44,78]	2033,5	0,26

The postoperative material showed that patients with the histopathological diagnosis of Endometrium cum signisproliferationis had significantly lower HGB levels. There is a tendency for elevated LDH3 values in the study group, but this correlation did not show statistical significance.

Tabela 28 Endometrium cum signis proliferationis a pomiary antropometryczne i laboratoryjne

	Histopatologia: Endometrium cum signis proliferationis		U	p
	Tak	Nie		
Wiek	45 [41-47]	45 [39-53]	2453,5	0,28
Wzrost	168 [164-171]	165 [160-168]	**2009,5**	**0,005**
Masa ciała	72,5 [63-82]	68 [61-76]	2377,5	0,17
BMI	25,98 [22,68-28,09]	25,16 [22,49-27,55]	2614,5	0,64
Leukocyty	6,33 [5,18-8,06]	6,39 [5,18-7,44]	1712	0,93
Erytrocyty	4,56 [4,26-4,66]	4,52 [4,31-4,74]	1661,5	0,72
Płytki krwi	273,5 [229-337]	258,5 [223-297,5]	1517,5	0,26
HGB	7,7 [7,2-8,2]	8 [7,35-8,55]	**1365**	**0,049**
HTC	0,38 [0,35-0,4]	0,39 [0,37-0,41]	1486	0,19
LDH	167 [152-185]	174 [147-206]	2530	0,43
LDH3	189,79 [35,52-387,33]	78,9 [36,35-322,08]	2502,5	0,37
LDH5	22,26 [14,96-48,82]	22,59 [9,95-55,22]	2702,5	0,89

In the study, it was observed that patients with a postoperative histopathological diagnosis of Adenomiosis were characterized by significantly higher age, height and body weight.

Tabela 30 Adenomiosis a pomiary antropometryczne i laboratoryjne

	Histopatologia: Adenomiosis		U	p
	Tak	Nie		
Wiek	47 [42,5-49]	44 [39-49]	**2103,5**	**0,049**
Wzrost	168 [164-172,5]	165 [162-168]	**1931,5**	**0,01**
Masa ciała	73 [65-80]	68 [61-76]	**2077,5**	**0,04**
BMI	25,59 [23,02-29,05]	24,98 [22,49-27,48]	2353,5	0,33
Leukocyty	6,59 [5,78-7,72]	6,21 [5,11-7,34]	1406,5	0,29
Erytrocyty	4,52 [4,3-4,66]	4,58 [4,3-4,71]	1502	0,60
Płytki krwi	266,5 [229-297]	258,5 [222,5-314,5]	1543,5	0,77
HGB	7,85 [7,3-8,2]	7,9 [7,3-8,4]	1491,5	0,56
HTC	0,39 [0,36-0,4]	0,39 [0,36-0,41]	1527,5	0,70
LDH	170,5 [147,5-188]	167 [149-206]	2498,5	0,68
LDH3	154,06 [63,54-382,09]	143,7 [30,96-336,77]	2360	0,34
LDH5	19,28 [9,35-44,78]	24,8 [12,93-55,25]	2230,5	0,14

5. Discussion

Based on the results of our analysis, the significance of lactate dehydrogenase isomers in the diagnosis of uterine tumors cannot be clearly determined, this requires further analysis in future studies. Referring to medical publications, we can note the significant value of

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lactate dehydrogenase isomers for suspected malignant uterine lesions. Several papers have found statistically higher preoperative serum LDH levels in patients with uterine sarcoma compared to patients with myomas. [15-17] In addition, other studies have shown that the use of serum LDH levels and various imaging modalities (fluor-18-deoxyglucose positron emission tomography (FDG-PET), PET-CT or MRI) increased the sensitivity and specificity of preoperative uterine diagnosis of uterine sarcomas and myomas, respectively. [15,16,18] In the study by Di Cello A et al., LDH isoenzyme levels differed significantly between patients with benign uterine tumors and sarcomas. The LDH3 isoenzyme showed better predictive properties than the other four isoforms. A group in Italy at Magna Graecia University proposed a mathematical index of LDH3 + (24/LDH1), in which elevated ratios correlated with an increased likelihood of uterine sarcoma. LDH isoenzyme levels differed significantly between the patients with benign uterine tumors or sarcomas. The LDH3 isoenzyme showed better predictive properties than the other four isoforms, as confirmed by our study.Combining LDH3 with LDH1 isoenzymes into an inverse algebraic relationship, named the Uterine Mass Magna Graecia Risk score (UMG), the accuracy of the markers in distinguishing between benign and suspicious malignant uterine lesions was significantly increased, with a sensitivity of 100% and specificity of 99.6%, with nine false positives in 2211 benign cases and no false negatives in 43 sarcomas. [17] Goto et al. proposed an association of an increased total LDH activity with suggestive MRI findings, reporting both a positive and negative predictive value of up to 100%. [19] Nagai et al. (2015) proposed a scoring system for the preoperative diagnosis of uterine sarcomas [Preoperative Sarcoma Score (PRESS)] using age at diagnosis, serum LDH levels, MRI findings and endometrial cytology results, and revised it a year later (revised PRESS=rPRESS). [17]

Among the patients undergoing the study, supracervical removal of the uterus by laparoscopy was predominantly performed. In our analysis of the histopathological results, we found no cases of uterine sarcoma. It is worth noting that in our Clinic, due to the lack of a reliable biomarker to differentiate uterine myomas from uterine sarcomas, patients are referred for diagnostic testing prior to surgeries performed in minimally invasive surgery requiring additional morcellation of myomas/ uterus inside the abdominal cavity. In each of these patients, prior to qualification for endoscopic procedures, a hysteroscopy is performed under local anesthesia with the collection of material for histopathological examination: a biopsy from the mucosa of the uterine cavity, a biopsy from the cervical canal and biopsy from the cervical disc, which means that patients qualified for this type of surgery most likely had benign lesions, since overtly malignant cases would be qualified for another type of surgery and would be immediately referred to the gynecological oncology department. Since the Food and Drug Administration (FDA) issued a warning against the use of morcellation in 2014 [20], the risk of sarcoma spread during morcellation of uterine myomas has become a "hot" topic [21,22]. The great importance of determining the preoperative assessment of the risk of sarcoma has been repeatedly emphasized, especially because of the clinical impact and the total ban on minimally invasive surgery. Similar conclusions were reached by Seagle et al. [23]. They write that patients

must be adequately educated before a planned surgical procedure so that informed consent to the proposed surgical procedure is obtained and patient autonomy is preserved. Following the aforementioned guidelines, the thorough histopathological evaluation of the material collected during the qualifying hysteroscopy before the LASH procedure used at our center has a high efficiency for early prediction of an increased risk of uterine malignancy in a patient qualified for endoscopic procedures.

Morcellation of undiagnosed uterine sarcoma without oncologic purity can cause tumor abdominal dissemination and recurrence, so it is important that preoperative evaluation of suspicious uterine tumors consider magnetic resonance imaging (MRI) and total serum lactate dehydrogenase (LDH) activity are identified as the most effective tools, while computed tomography (CT) and LDH isoenzymes are less frequently considered in the literature. [24] Taking into account the effectiveness of the qualification procedure used in our clinic in excluding the risk of uterine malignancy in patients before LASH procedures in the absence of a diagnosis of a malignant process of the uterine corpus in the studied population, as a control group we qualified patients with similar anthropometric parameters undergoing other endoscopic procedures. Therefore, if further work demonstrates that specific serum biomarkers help distinguish uterine myomas from uterine sarcoma, this could potentially improve referral to gynecologists-oncologists for initial uterine cancer surgery and reduce the number of secondary staging procedures, since initial aggressive surgical cytoreduction likely prolongs survival [25] Although the LDH values in the group we analyzed were within the normal range, they were significantly higher in patients with BMI> 30. Ultimately, this may require adjusting the definition of the elevated index in obese patients, so that a false positive result would inappropriately place these women in a high-risk group, which could affect the mode of surgery. This is also confirmed in the results of the study by Spivack and co-authors [26], however, it raises the need and necessity for continued research to develop indicators to eliminate false positives for uterine malignancy risk in overweight and obese patients. The search for a reliable biomarker in differentiating benign and malignant uterine lesions is still ongoing. However, this requires further well-designed prospective studies.

6. Conclusions

Based on the results of the analysis and available literature data, there is still no clear and reliable corrective marker with an increased risk of uterine tumor oncogenesis. The available literature data and the results of our study indicate the diagnostic potential of LDH and its enzymes especially LDH 3. However, it seems reasonable to conduct further analyses and attempt to systematize and correlate the importance of available diagnostic methods in the assessment of the potential malignancy of uterine tumors. In addition, proper preoperative qualification of patients with uterine tumors, preceded by the algorithm used in our center, among others, allows to significantly reduce the risk of intraoperative diagnosis of a malignant proliferative process in uterine tumors, which improves the prognosis for the patient.

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