Medical University – Pleven

Faculty of Health care

Department of Diagnostic imaging and Radiotherapy

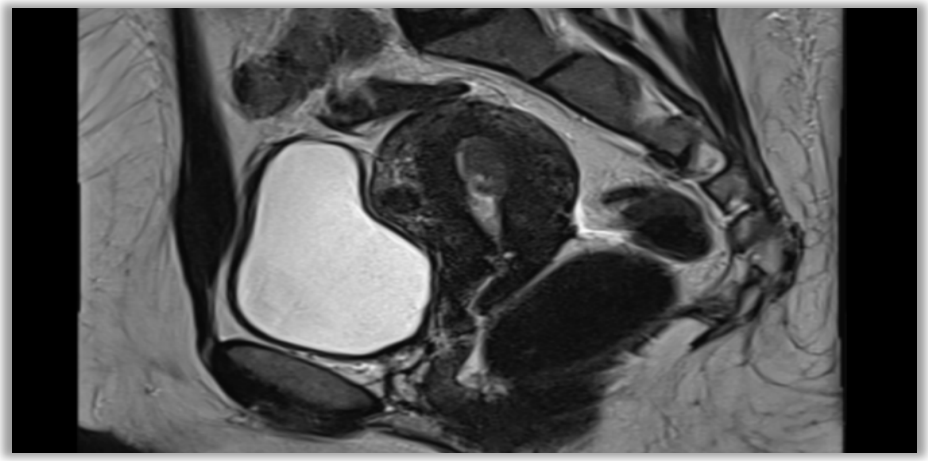
Mirela Veselinova Vasileva, MD

Diagnostic and Therapeutic Value of Magnetic Resonance Imaging for the Preclinical Staging of Early Forms of Endometrial Carcinoma

ABSTRACT

of a dissertation

for the acquisition of an educational and scientific degree „Doctor“



Pleven, 2026 г.

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The dissertation is presented on 196 standard pages and is illustrated with 56 figures, 37 tables, and 3 appendices. The reference list consists of 149 titles, of which 148 are in Latin script and 1 in Cyrillic script.

The author is a regular doctoral student at the Department of Diagnostic Imaging and Radiotherapy, Faculty of Health Care, Medical University – Pleven.

Note: The numbering of figures and tables does not correspond to that in the dissertation.

The dissertation has been reviewed and approved for public defense by the Extended Department Council of the Department of Diagnostic Imaging and Radiotherapy, Faculty of Health Care, Medical University – Pleven.

The public defense of the dissertation will take place on 26.05.2026, at 2 p.m. in Ambroise Pare Hall at "Telec", Medical University – Pleven, in accordance with the Regulations for the Conditions and Procedures for the Acquisition of Academic Degrees and the Occupation of Academic Positions at the Medical University – Pleven, and on the basis of an Order of the Rector No 1311/28.04.2026, before a scientific jury composed of:

Chair:

Prof. Nadezhda Hinkova, MD, PhD

Members:

Prof. Georgi Hadzhidekov, MD, PhD

Prof. Nikoleta Traikova, MD, PhD

Prof. Radoslav Georgiev, MD, PhD

Assoc. prof. Dobrinka Gincheva, MD, PhD

The materials related to the defense are available on the website of MU-Pleven: www.mu-pleven.bg.

CONTENTS

LIST OF ABBREVIATIONS USED:

MRI	Magnetic Resonance Imaging
EC	Endometrial Cancer
BMI	Body Mass Index
EH	Endometrial Hyperplasia
AUB	Abnormal Uterine Bleeding
PCOS	Plycystic Ovary Syndrome
PET/CT	Positron Emission Tomography with Computed Tomography
CT	Computed Tomography
US	Ultrasonography
FIGO	International Federation of Gynecology and Obstetrics
DWI	Diffusion-Weighted Imaging
ADC	Apparent Diffusion Coefficient
T2W	T2-Weighted images
TCGA	The Cancer Genome Atlas
TNM	Tumor, Node, Metastasis
AJCC	American Joint Committee on Cancer
DCE	Dynamic Contrast Enhancement
EN-RADS	Endometrial Cancer Radiology Reporting and Data System
ESUR	European Society of Urogenital Radiology

I. INTRODUCTION

Endometrial carcinoma is the most common gynecological malignancy in developed countries, primarily affecting postmenopausal women. There is a trend toward an increase in its incidence, which is associated with increased life expectancy, obesity, and metabolic syndrome—established risk factors. Accurate pre-operative staging is essential, as it influences treatment planning, the choice of surgical approach, and the overall prognosis. According to current guidelines, assessment is performed using the FIGO (*International Federation of Gynecology and Obstetrics*) classification, which includes depth of invasion into the myometrium, involvement of the cervical stroma, lymphovascular invasion, and the presence of metastases in lymph nodes or distant organs.

The staging system is based primarily on surgical and histopathological data. However, modern imaging techniques offer non-invasive options for assessing the stage of the disease even before surgical treatment. Among these, magnetic resonance imaging (MRI) has been established as the preferred method for local staging of endometrial carcinoma (EC) due to its high resolution and ability to visualize soft tissues and anatomical structures in the pelvis. MRI is particularly effective in assessing the depth of myometrial invasion and involvement of the cervical stroma. In addition, it is used to evaluate regional lymph nodes—key features in the staging system.

With the increasing incidence of this type of cancer worldwide, timely and accurate pre-operative staging has become essential for optimizing the therapeutic approach and the patient's prognosis. The incorporation of MRI into clinical practice provides a non-invasive and reliable tool for determining the depth of invasion into the myometrium, cervical stromal infiltration, and the presence of lymph node metastases—factors of crucial importance for accurate disease staging and risk stratification.

A Upon reviewing the specialized literature on the subject, we identified the following unresolved issues and points of debate:

1. MRI is being established as a leading imaging modality for local staging of endometrial carcinoma due to its high soft-tissue contrast

and its ability to accurately assess the depth of myometrial invasion and cervical stromal involvement. However, diagnostic accuracy may vary depending on imaging protocols, equipment, and examiner experience, highlighting the need for standardization.

2. Functional MRI techniques, such as diffusion-weighted imaging (DWI) and dynamic contrast-enhanced imaging (DCE), significantly improve diagnostic performance and enable more precise risk stratification. Nevertheless, their application in clinical practice is not yet fully standardized and requires further validation through prospective studies.
3. MRI plays a significant role in pre-operative planning by aiding in the selection of the surgical approach and determining the need for lymphadenectomy. Despite its widespread use, there is limited data on its direct impact on final clinical outcomes, which necessitates the conduct of well-structured studies
4. Compared to other imaging modalities such as ultrasound, CT, and PET/CT, MRI demonstrates the highest accuracy in local staging, while the other techniques retain their importance in the assessment of lymphatic spread or detecting distant metastases. This highlights the need for a multimodal diagnostic approach tailored to clinical practice.
5. The integration of radiomics and artificial intelligence in MRI analysis shows significant potential for improving predictive models and personalizing therapeutic decisions. At present, however, these technologies remain primarily in the research sphere due to the lack of standardization and external validation.
6. The lack of unified MRI protocols and standardized interpretation systems leads to variability in diagnostic results and limits comparability across different studies and centers. The use of structured reporting systems could improve both clinical practice and the scientific validity of future research.
7. There are existing gaps regarding the application of MRI in specific patient groups, as well as its integration with new surgical technologies, including robot-assisted systems. This situation outlines promising directions for future research.
8. In Bulgarian clinical practice, despite the presence of individual scientific publications and growing interest in the application of MRI in oncology, there is a lack of sufficiently systematized data and a

standardized approach, which necessitates further research in this field.

The dissertation is dedicated to investigating the diagnostic and therapeutic value of Magnetic Resonance Imaging in patients with endometrial carcinoma, and the significance of imaging findings specifically in the early stages of the disease.

II. AIM, OBJECTIVES AND METHODOLOGY OF THE STUDY

1.Aim

To evaluate the diagnostic value of Magnetic Resonance Imaging in determining the depth of myometrial invasion in patients with endometrial carcinoma, by comparing it with histopathological results as the gold standard, as well as to analyze its association with clinical, morphological, and prognostic factors.

To achieve this aim, the following objectives were defined:

2. Objectives of the study

1. To analyze the main clinical and demographic characteristics of the studied population.
2. To assess the depth of myometrial invasion using Magnetic Resonance Imaging and histopathological examination.
3. To compare the assessment of myometrial invasion obtained by MRI with histopathological findings and to determine the rate of concordance and discordance between the two methods.
4. To analyze cases with discordance between MRI and histopathology in terms of tumor size, histological type, degree of differentiation, and imaging characteristics (T2, DWI, contrast enhancement), and to identify the factors associated with them.
5. To determine the diagnostic performance of MRI (sensitivity, specificity, predictive values, and accuracy).
6. To investigate the relationship between the depth of myometrial invasion and prognostic indicators (lymphatic dissemination, distant metastases, local recurrence, and survival).

3. Clinical cohort – main characteristics

An ambispective clinical-epidemiological study was conducted, including 70 patients with histologically verified endometrial carcinoma. The studied clinical cohort comprised patients treated at the University Hospital "St. Marina", Pleven, in the Clinic of Obstetrics and Gynecology and the Clinic of Diagnostic Imaging, during the period from November 2020 to July 2025.

Inclusion criteria:

• Age over 18 years
• Individuals who had completed informed consent for participation in the study
• Histologically verified endometrial carcinoma following diagnostic curettage
• Patients clinically assessed as having early-stage disease

Exclusion criteria:

• Individuals under 18 years
• Individuals who had not completed an informed consent for participation in the study
• Clinical evidence of advanced disease

4. Methods of the study:

4.1. Documentary and sociological method

4.2. Clinical method

4.3. Imaging method for preoperative staging – Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) was performed using a MAGNETOM Aera system (Siemens Healthineers) with a magnetic field strength of 1.5 T (Fig. 1).

Fig. 1 MAGNETOM Aera (Siemens Healthineers) 1.5 Tesla

The applied protocol included multiplanar imaging in axial, sagittal, and coronal planes, with pulse sequences presented in Appendix 1. The evaluation of imaging findings was performed based on analysis including T2-weighted (T2W) sequences, diffusion-weighted imaging (DWI) with ADC maps, and additional sequences when necessary.

Anatomical orientation and uterine dimensions:

Uterine size was assessed in the sagittal plane using standard measurements, including two main diameters – craniocaudal (including the cervix) and anteroposterior (Fig. 2):

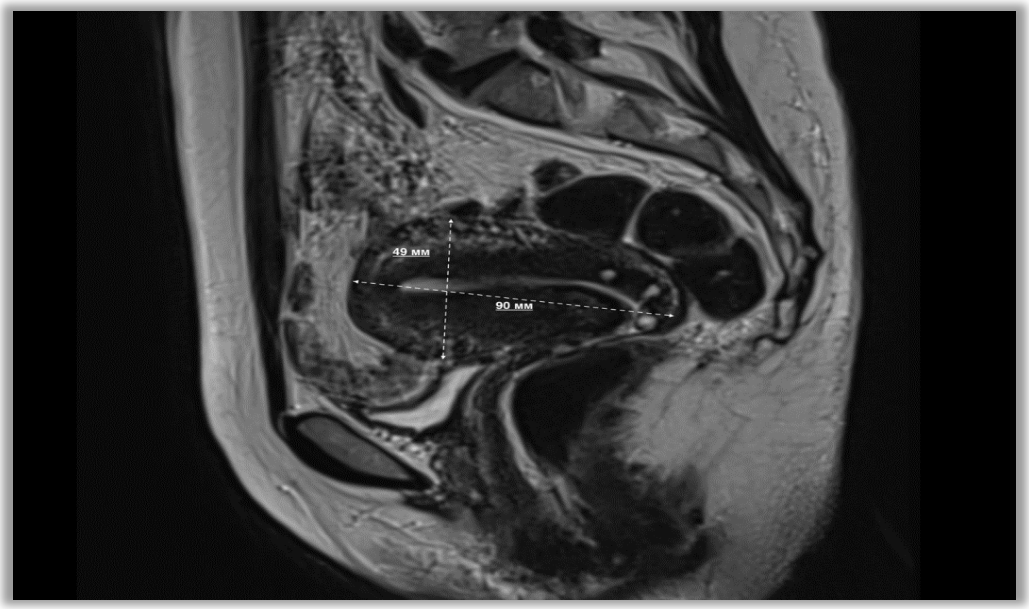

Fig. 2 Uterine size in the sagittal plane; position AVF.

Tumor size:

Tumor size was assessed based on T2-weighted (T2W) imaging, with the maximum lesion diameter measured in the plane in which it was

best visualized (Figs.3 and 4).

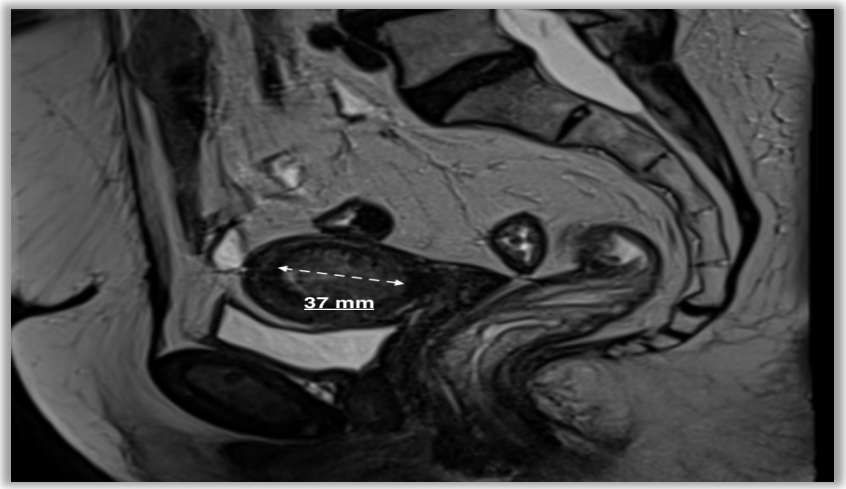

Fig. 3 Measurement of the maximum tumor diameter

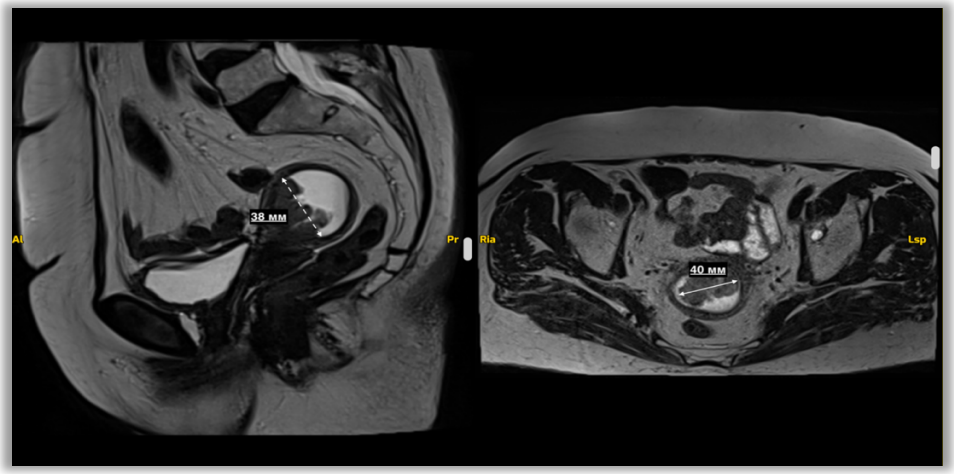

Fig. 4 Measurement of the maximum diameter of an irregularly shaped tumor in different planes

DWI and ADC were used as complementary methods to improve the differentiation of tumor tissue from normal endometrium and myometrium, particularly in heterogeneous or diffuse lesions, as well as as in the presence of concomitant conditions and diseases (Fig. 5):

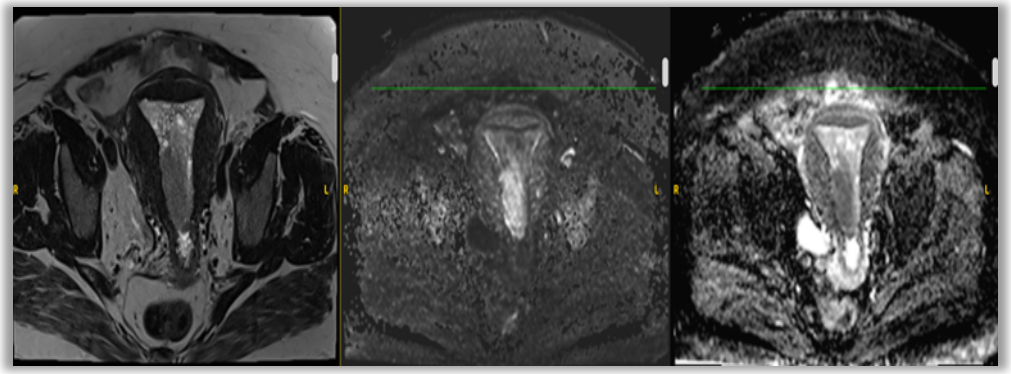

Fig. 5 Comparison of T2W, DWI, and ADC in a patient with EC (endometrioid adenocarcinoma, G1) on the background of endometrial hyperplasia, without myometrial invasion.

Myometial invasion:

The depth of myometrial invasion was determined by comparing tumor infiltration with the thickness of the myometrium at the area of maximum involvement, primarily assessed on T2-weighted images, with additional information from DWI and ADC used to improve differentiation between tumor tissue and normal myometrium, particularly in cases with concomitant changes. It was evaluated in a plane perpendicular to the endometrial cavity by measuring the ratio between the maximum depth of tumor infiltration and the total thickness of the myometrium in the same region (Fig. 6).

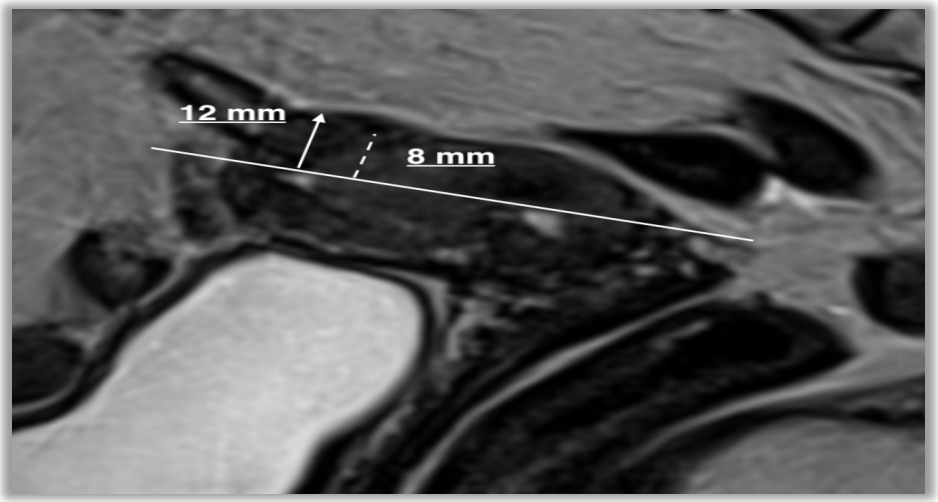

Fig. 6 Determination of myometrial invasion. In the given example, the total myometrial thickness is 12 mm, and the measured tumor invasion is 8 mm (8/12 = 67%); therefore, the case is classified as >50% .

Based on the extent of myometrial involvement, patients were categorized into two groups: invasion of less than 50%, and invasion of 50% or more of the myometrial thickness (Figs. 7 and 8, respectively).

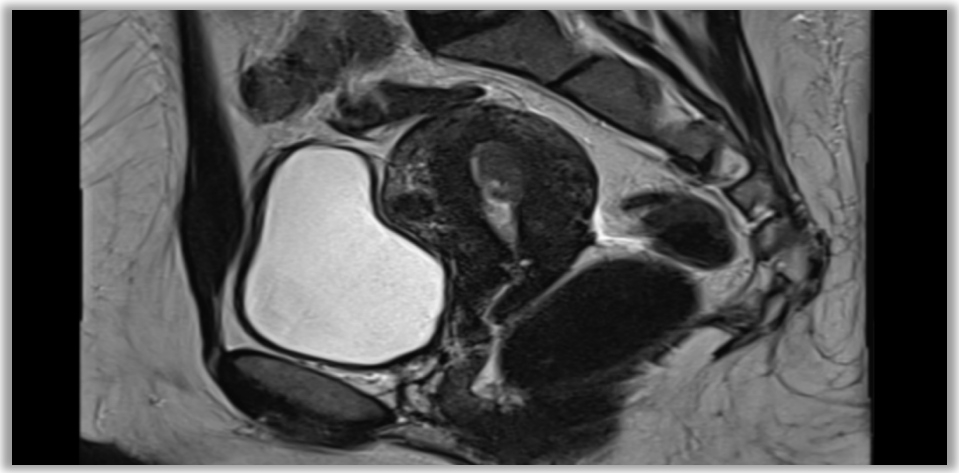

Fig. 7 Example of myometrial invasion less than 50%

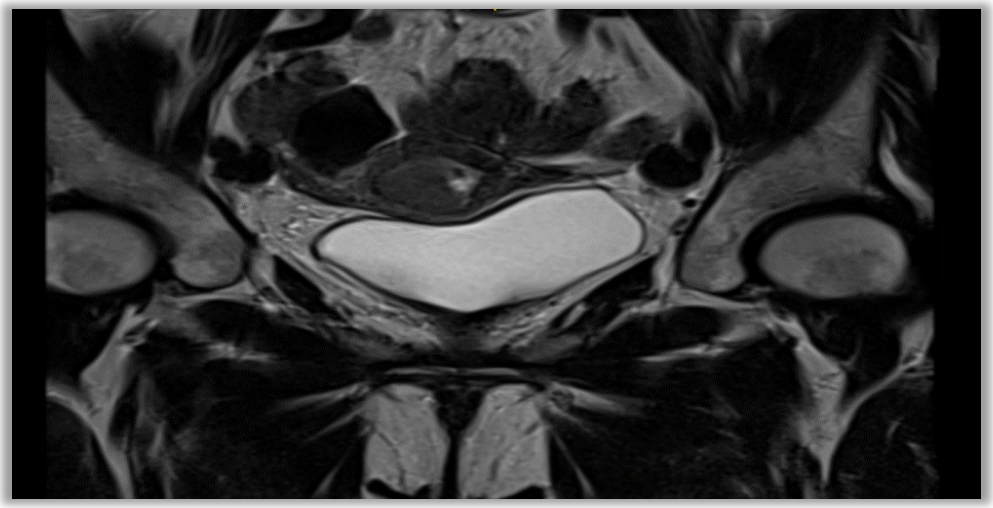

Fig. 8 Example of myometrial invasion ≥50%.

Cervical stromal invasion:

Cervical involvement was assessed based on the presence of tumor infiltration in the cervical stroma, visualized as disruption of the normal hypointense signal on T2-weighted images (Fig. 9):

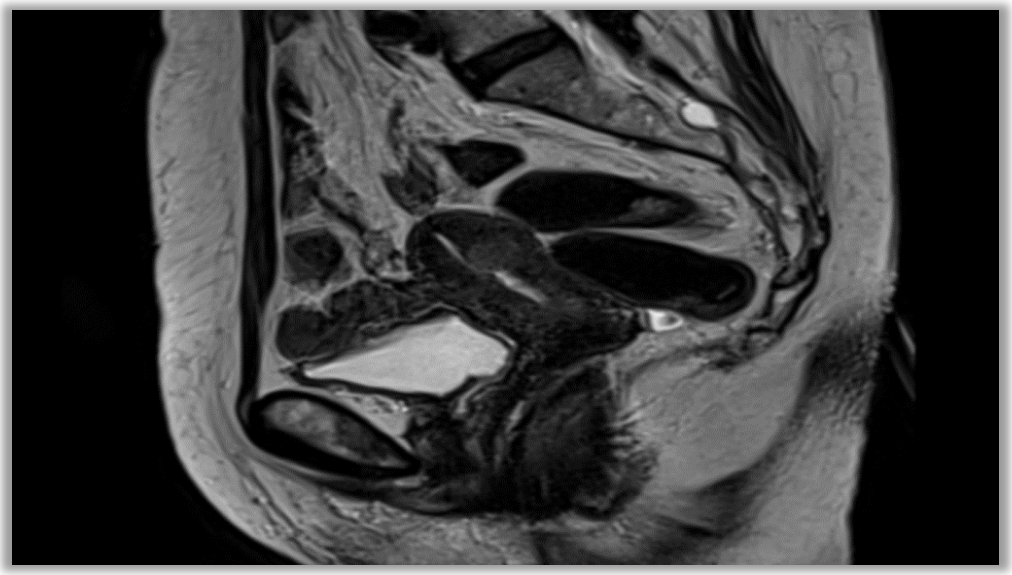

Fig. 9 Patient with cervical stromal invasion

Lymph nodes:

For lymph node assessment, both morphological and functional criteria were used, including increased short-axis diameter, rounded shape, irregular contours, and altered signal intensity, as well as restricted diffusion of water molecules (Fig. 10).

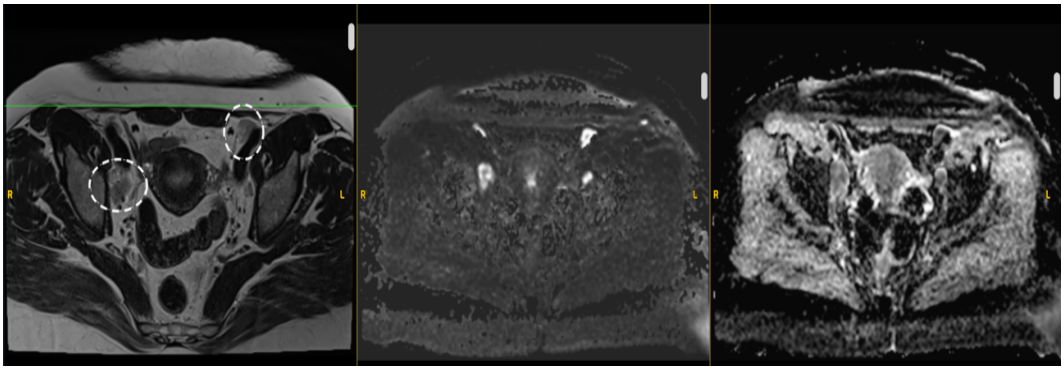

Fig. 10 Pathologically enlarged lymph nodes with altered morphology and functional evidence of restricted diffusion of water molecules (T2W, DWI, ADC).

Extrauterine spread:

The presence of extrauterine spread (serosal involvement, parametrial infiltration, involvement of adjacent organs) was assessed based on disruption of anatomical boundaries and direct tumor infiltration.

4.4. Histopathological method

4.5. Surgical method

All patients underwent surgical treatment. Depending on clinical assessment, disease stage, and intraoperative findings, different types of surgical interventions were performed, including laparoscopic, robot-assisted, and open approaches. The main surgical procedure consisted of total hysterectomy with or without adnexectomy.

In some patients, lymph node dissection was performed, including sentinel, pelvic, or para-aortic, in order to assess lymph node status.

4.5.1. Staging – according to FIGO 2009 and FIGO 2023

Staging of EC in the patients included in the study was performed according to the criteria of the International Federation of Gynecology and Obstetrics (FIGO), using both the 2009 classification and the updated 2023 system in parallel. In clinical practice, the TNM classification (Tumor, Node, Metastasis), proposed by the AJCC, is also used. It is closely related to the FIGO system, with correspondence and overlap between the individual stages. For better illustration of the relationship between the FIGO and TNM classifications, a comparative table is presented in *Appendix 2*.

In the present study, FIGO 2009 was used as the classical reference system, while FIGO 2023 was applied to assess the impact of modern classification criteria on patient stratification. The relationship between MRI imaging characteristics and FIGO staging is of essential importance for preoperative evaluation, and for greater clarity, a summary table is presented in *Appendix 3*.

4.6. Imaging Methods for Follow-up

Follow-up was ambispective, including both retrospective analysis of available imaging studies and prospective follow-up in a subset of patients. In the present study, an analysis of available imaging examinations performed in the postoperative period was conducted, using data from the hospital information system. These examinations included computed

tomography (CT), positron emission tomography/computed tomography (PET/CT), and, in selected cases, Magnetic Resonance Imaging (MRI).

The obtained data were used to analyze disease-free survival, time to recurrence, and the occurrence of distant metastases, as well as to evaluate the relationship between preoperative imaging findings, histopathological characteristics, and clinical outcomes.

In this way, the data obtained from imaging methods used for patient follow-up complement the information from preoperative MRI and allow a comprehensive assessment of the diagnostic and prognostic value of the method.

4.7. Statistical methods

The data were entered and processed using the statistical software packages IBM SPSS Statistics 27.0 and MedCalc Version 23.5.1. Microsoft Excel (Microsoft Office 2021) was also used for figure preparation. A significance level of $p < 0.05$ was accepted for rejection of the null hypothesis.

The following tests and analyses were applied:

1. *Descriptive analysis* – frequency distribution of the studied variables was presented in tabular form, along with standard deviations and ranges for quantitative variables.
2. *Graphical analysis* – for visualization of the obtained results.
3. *Fisher–Freeman–Halton exact test, Fisher's exact test, and chi-square (χ^2) test* – for testing hypotheses regarding associations between categorical variables.
4. *Nonparametric Kolmogorov–Smirnov and Shapiro–Wilk tests* – for assessing the normality of distribution of quantitative variables.
5. *Student's t-test* – for testing hypotheses regarding differences between the means of two independent samples.
6. *Mann–Whitney U test* – for testing hypotheses regarding differences between two independent samples.
7. *Kaplan–Meier method* – for estimating time to the occurrence of the studied event (Kaplan–Meier product-limit estimation of the survival function).
8. *Log-rank, Breslow, and Tarone–Ware tests* – for assessing the impact of the studied factors on the occurrence of the investigated event.

9. *ROC curve analysis* – for determining threshold values of quantitative variables.

10. *Criteria for validation of screening tests* – the following indicators were used to evaluate the validity of the screening (diagnostic) test:

- Sensitivity;
- Specificity;
- Positive predictive value;
- Negative predictive value;
- Accuracy (% of true answers).

III. RESULTS

1. Basic characteristics of the patients

The mean age of the study participants was 57.49 ± 10.05 years, ranging from 28 to 82 years (Fig. 11). The highest proportion (40.0%) belonged to the 50–59 age group, followed by the 60–69 age group with 28.6%.

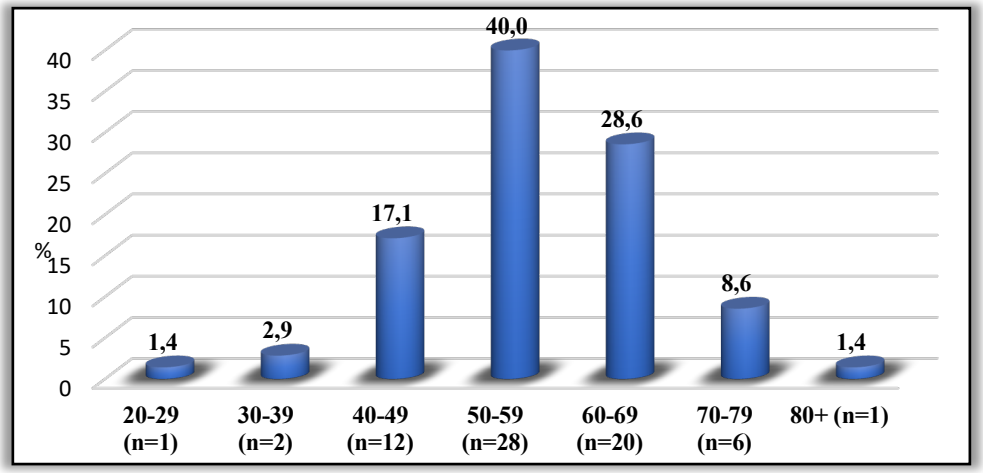

Fig. 11 Distribution of study participants by age groups

Analysis of menopausal status (Fig. 12) showed that the majority of patients were postmenopausal (71.4%), while 28.6% were not:

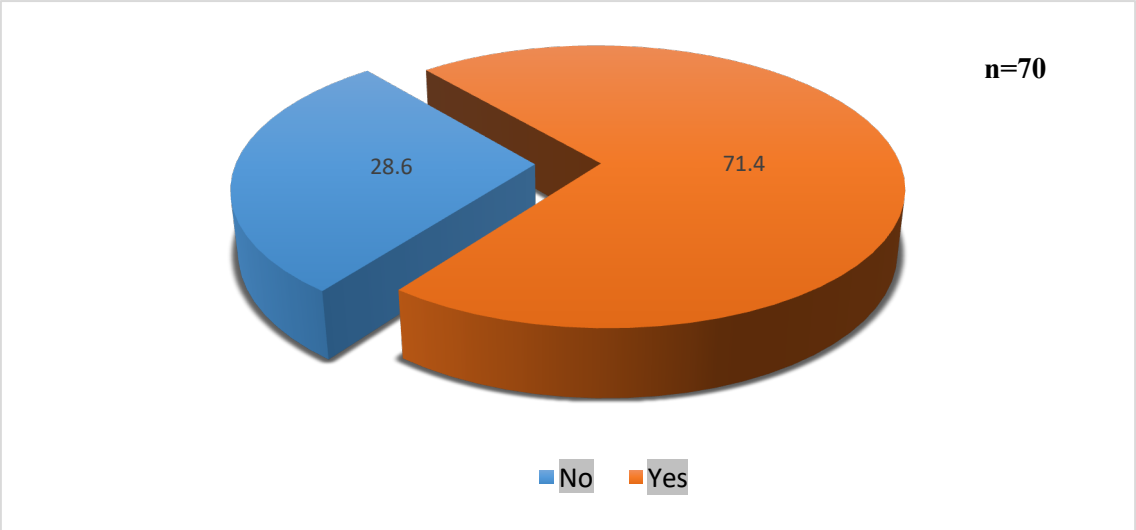

Fig. 12 Frequency distribution of patients according to menopausal status

Regarding body mass index (Fig. 13), 55.7% of patients had a normal BMI, while 44.3% had an elevated BMI:

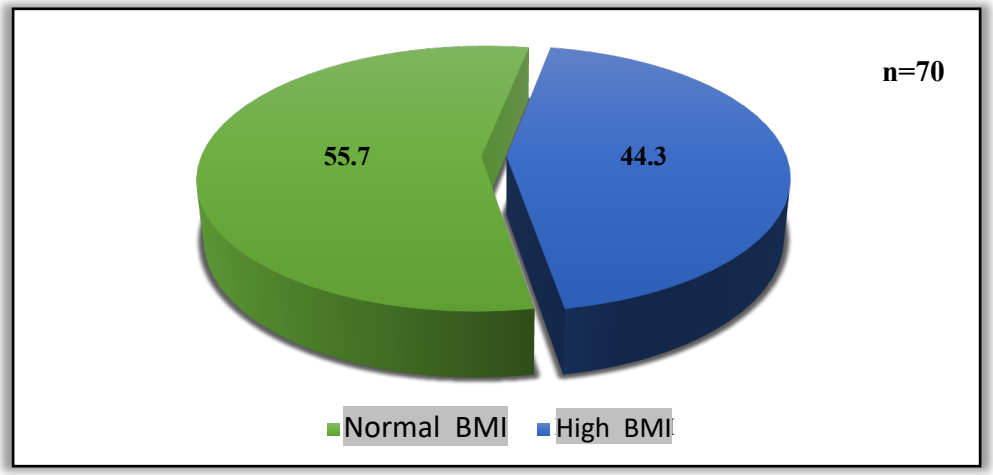

Fig. 13 Frequency distribution of patients by BMI

2. Comparative Analysis of Myometrial Invasion and the Diagnostic Value of MRI

The final assessment of myometrial invasion (Fig. 14) showed that in the majority of patients it was below 50% (81.4%), while in 18.6% it was ≥50%:

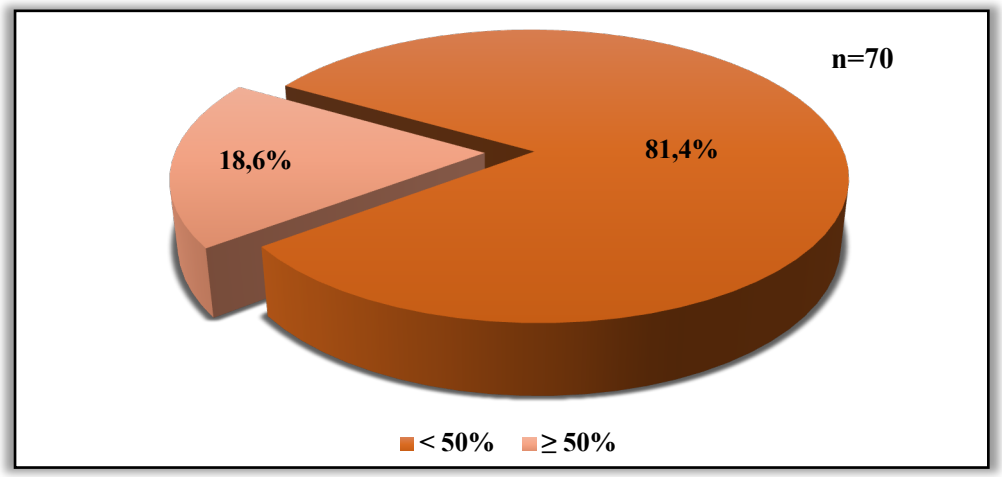

Fig. 14 Frequency distribution of patients according to postoperative, final assessment of myometrial invasion

2.1 Comparison between MRI and histopathological assessment of myometrial invasion

A comparative analysis was performed between preoperatively assessed myometrial invasion by MRI and the final histopathological assessment. In cases with identified discrepancies, additional

characterization was performed regarding tumor grading, tumor size, and imaging features.

The data in Table 1 show that discordance between MRI and histopathological assessment was observed in 8 (11.4%) of the patients:

Table. 1 Association between preoperatively assessed myometrial invasion on MRI and postoperative, final assessment of myometrial invasion (p < 0.001)

Pre-operative MRI-assessed myometrial invasion	**Frequency**	**Postoperative, final myometrial invasion**		**Total**
		< 50%	≥ 50%	
< 50%	n	51	2	53
	%	89,5	15,4	75,7
≥ 50%	n	6	11	17
	%	10,5	84,6	24,3
Total	n	57	13	70
	%	100,0	100,0	100,0

The distribution of these cases according to the degree of differentiation shows a relatively even pattern, with 3 patients (37.5%) each in G1 and G2, and 2 patients (25%) in G3 (Table 2):

Table.2 Frequency distribution of patients with discrepancies between MRI-assessed and histopathologically assessed myometrial invasion according to tumor differentiation

Grading	**n**	**%**	**Sp**
G1	3	37,5	17,1
G2	3	37,5	17,1
G3	2	25,0	15,3
Total	8	100,0	

Analysis of tumor size (Table 3) shows that discrepancies are not dependent on this parameter, as all cases have different sizes, evenly distributed within the range of 7 to 48 mm:

Table 3. Frequency distribution of patients with discrepancies between MRI-assessed and histopathologically assessed myometrial invasion according to tumor size

Tumour size (мм)	n	%	Sp
7	1	12,5	11,7
12	1	12,5	11,7
20	1	12,5	11,7
23	1	12,5	11,7
25	1	12,5	11,7
30	1	12,5	11,7
40	1	12,5	11,7
48	1	12,5	11,7
Total	8	100,0	

Regarding T2W signal intensity, a predominance of hypointense signal was observed (75%), while isointense and hyperintense signals were considerably less frequent, each accounting for 12.5% (Table 4).

Table 4. Frequency distribution of patients with discrepancies between MRI-assessed and histopathologically assessed myometrial invasion according to tumor signal intensity on T2-weighted images relative to the myometrium

Tumour intensity in T 2 time relative to the myometrium	n	%	Sp
Hypointense	6	75,0	15,3
Hyperintense	1	12,5	11,7
Heterointense	1	12,5	11,7
Total	8	100,0	

Analysis of diffusion restriction of water molecules showed that it was present in 62.5% of cases and absent in 37.5% (Table 5).

Table 5. Frequency distribution of patients with discrepancies between MRI-assessed and histopathologically assessed myometrial invasion according to diffusion restriction on MRI

Water molecule diffusion restriction on MRI	n	%	Sp
Yes	5	62,5	17,1
No	3	37,5	17,1
Total	8	100,0	

2.2 Diagnostic value of MRI in the assessment of myometrial invasion

An evaluation of the diagnostic performance of Magnetic Resonance Imaging was performed using histopathological examination as the gold standard. The results presented in Table 6 indicate that:

- Sensitivity (85%), specificity (89%), and overall accuracy (89%) of the method are very good;
- Positive predictive value is satisfactory (65%);
- Negative predictive value is excellent (96%).

Table 6 Values of the validation criteria for screening tests assessing the reliability of Magnetic Resonance Imaging in the evaluation of myometrial invasion (based on final histopathological findings)

Sensitivity	Specificity	Positive predictive value	Negative predictive value	% correct answers
85	89	65	96	89

2.3 Relationship between preoperatively assessed myometrial invasion and clinical outcome

An analysis was performed to evaluate the association between preoperatively assessed myometrial invasion by MRI and indicators such as time to the occurrence of distant metastases, localization of metastases, and time to recurrence.

The data in Table 7 indicate that there is no statistically significant difference in the time to occurrence of distant metastases and recurrence according to the degree of myometrial invasion assessed by MRI.

Table 7. Comparative analysis of time to occurrence of distant metastases and recurrence according to preoperatively assessed myometrial invasion on MRI.

Indicators	**Pre-operative MRI-assessed myometrial invasion**						**P**
	< 50%			≥ 50%			
	n	$\overline{X}$	SD	n	$\overline{X}$	SD	
Time to distant metastasis	41	12,20	13,02	14	10,36	9,04	0,770
Time to recurrence	41	12,20	13,02	14	11,36	11,06	0,675

At the same time, the results in Table 8 demonstrate a statistically significant association between preoperatively assessed invasion and the presence of metastases.

This relationship is reflected as:

- a higher relative proportion of <50% invasion among patients without detected metastases;
- a significantly higher relative proportion of ≥50% invasion among patients with metastases.

Table. 8 Association between preoperatively assessed myometrial invasion on MRI and the localization of metastases (p = 0.001)

Metastasis location	Frequency	Pre-operative MRI-assessed myometrial invasion		P
		< 50%	≥ 50%	
None detected	n	51	11	**<0,001**
	%	96,2	64,7	
Para-iliac lymph nodes	n	0	1	0,077
	%	0,0	5,9	
Para-iliac and para-aortic lymph nodes	n	1	0	0,570
	%	1,9	0,0	
Para-aortic lymph nodes and lung	n	0	1	0,077
	%	0,0	5,9	
Peritoneum	n	0	1	0,077
	%	0,0	5,9	
Lung	n	0	2	**0,012**
	%	0,0	11,8	
Peritoneum and lung	n	1	0	0,570
	%	1,9	0,0	
Peritoneum, lung, and liver	n	0	1	0,077
	%	0,0	5,9	
Total	n	53	17	
	%	100,0	100,0	

3. Lymph node analysis

Regarding lymph node assessment (N status), N1 stage was identified in 81.4% of patients, while N2 stage was observed in 18.6% (Fig. 15):

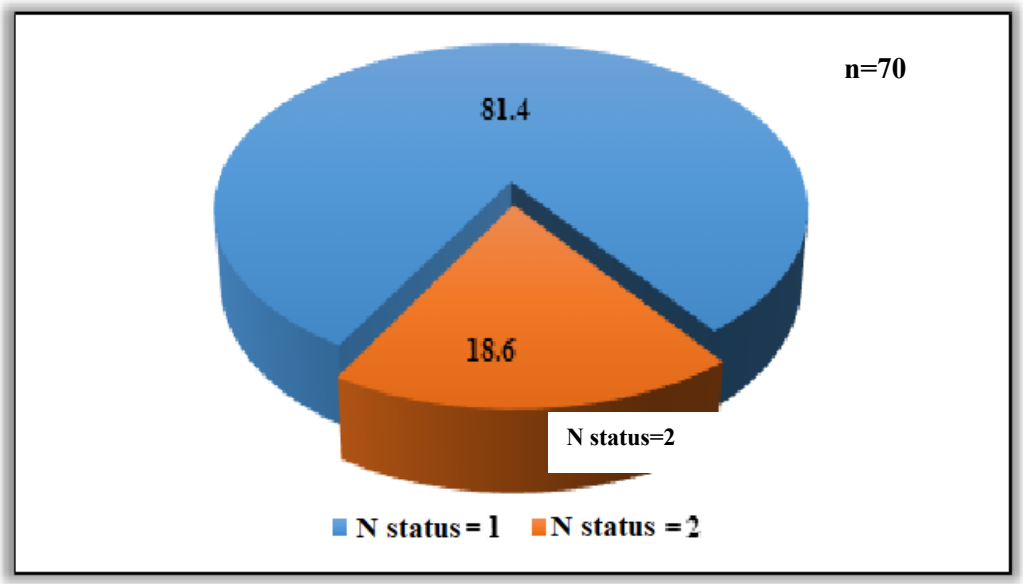

Fig. 15 Frequency distribution of patients according to postoperative N status

4. Analysis of distant metastases

Analysis of patients with metastases (M status) showed that almost all patients had no distant metastases (98.6%), while only one patient (1.4%) had pulmonary metastases (Fig. 16):

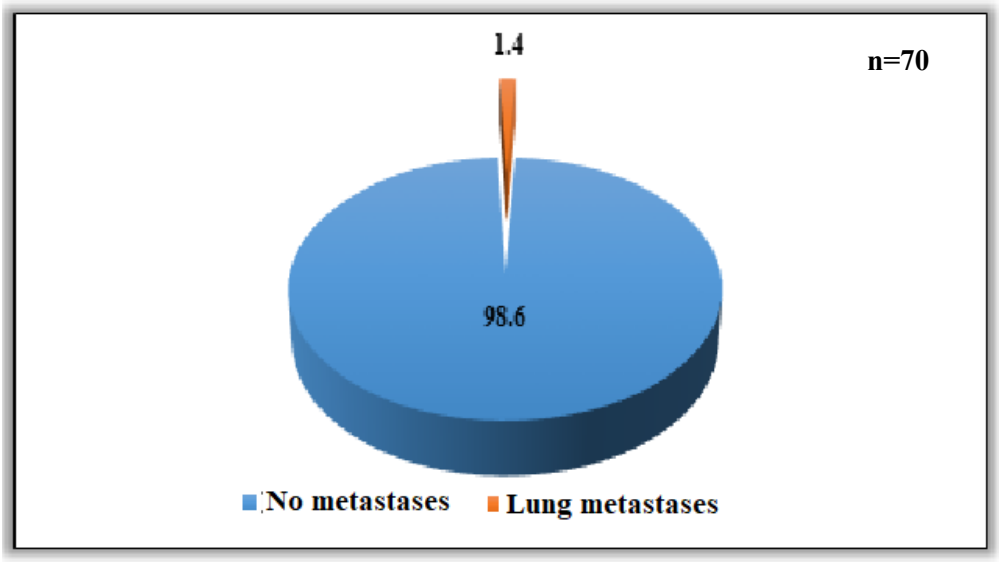

Fig. 16 Frequency distribution of patients according to postoperative M status

The frequency of recurrence was low—observed in 5.5% of patients, while 94.5% showed no recurrence (based on data from 55 patients, Fig. 17):

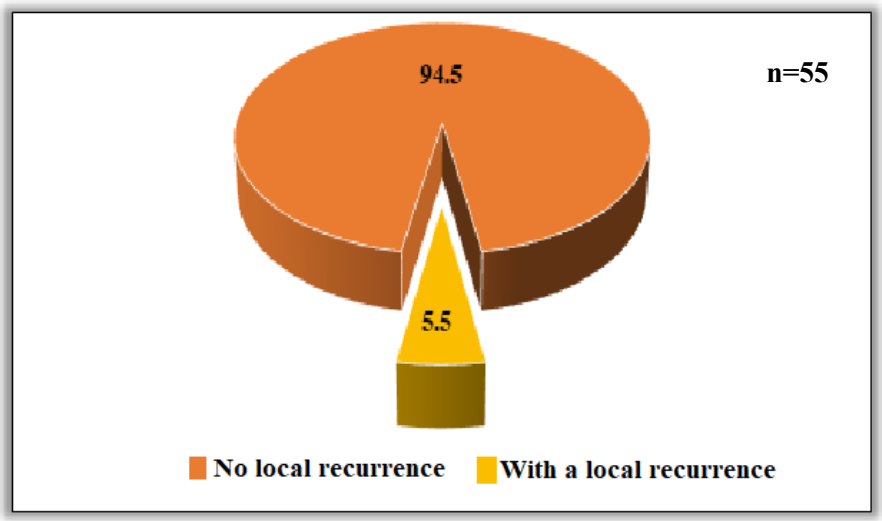

Fig. 17 Frequency distribution of patients according to the occurrence of local recurren

5. Analysis of tumor characteristics (histological type, degree of differentiation, staging)

Evaluation of tumor signal intensity on T2-weighted images relative to the myometrium (Fig. 18) showed that hypointense signal was most frequently observed (47.1%), followed by isointense (21.4%) and hyperintense (12.9%).

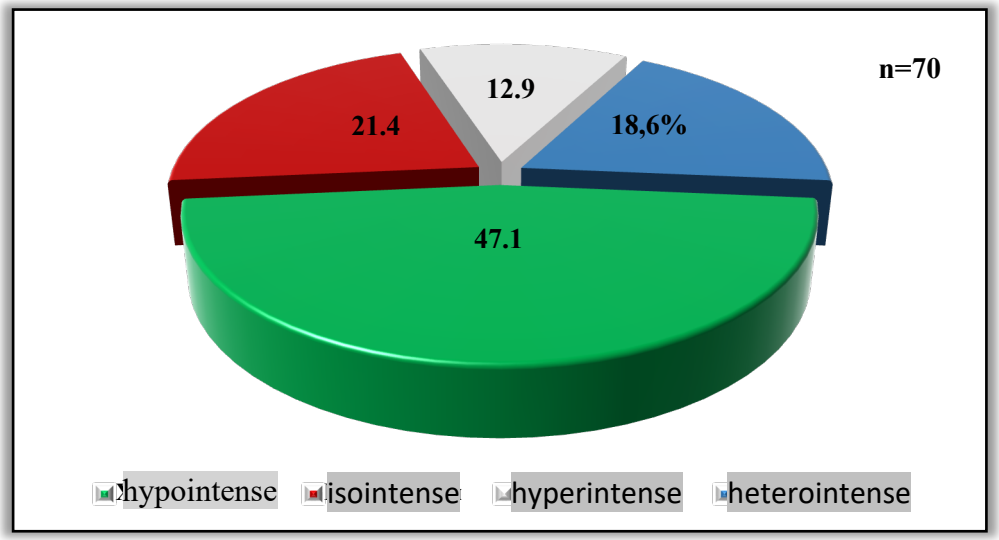

Fig. 18 Frequency distribution of patients according to tumor signal intensity on T2-weighted images relative to the myometrium

Restricted diffusion of water molecules (Fig. 19) was observed in 77.1% of patients, while in 22.9% no such finding was present.

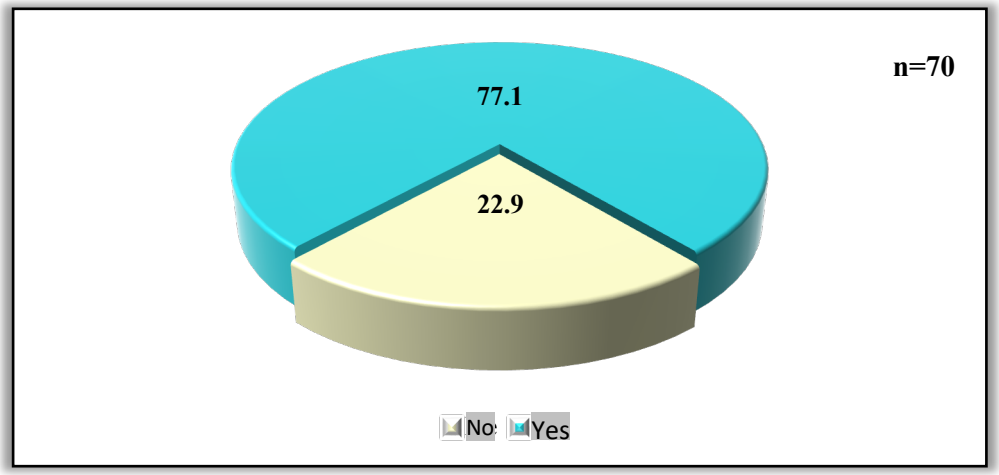

Fig. 19 Frequency distribution of patients according to diffusion restriction on MRI

The distribution of histological variants (Fig. 20) showed a predominance of endometrioid adenocarcinoma (80%).

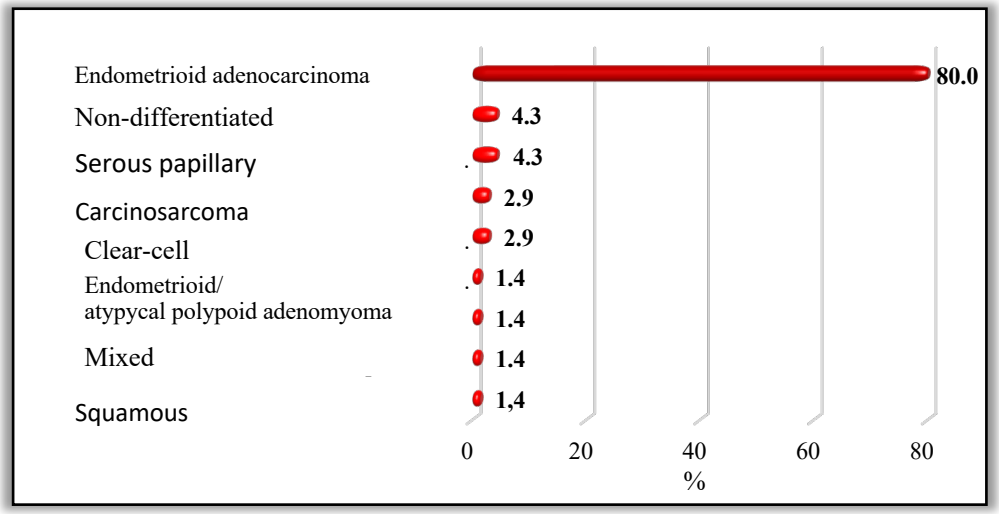

Fig. 20 Frequency distribution of patients according to histological tumor type

Distribution according to the degree of differentiation (G) (Fig. 21) showed the highest relative proportion of well-differentiated tumors (52.9%), followed by moderately differentiated (25.7%) and the lowest proportion of poorly differentiated tumors (21.4%).

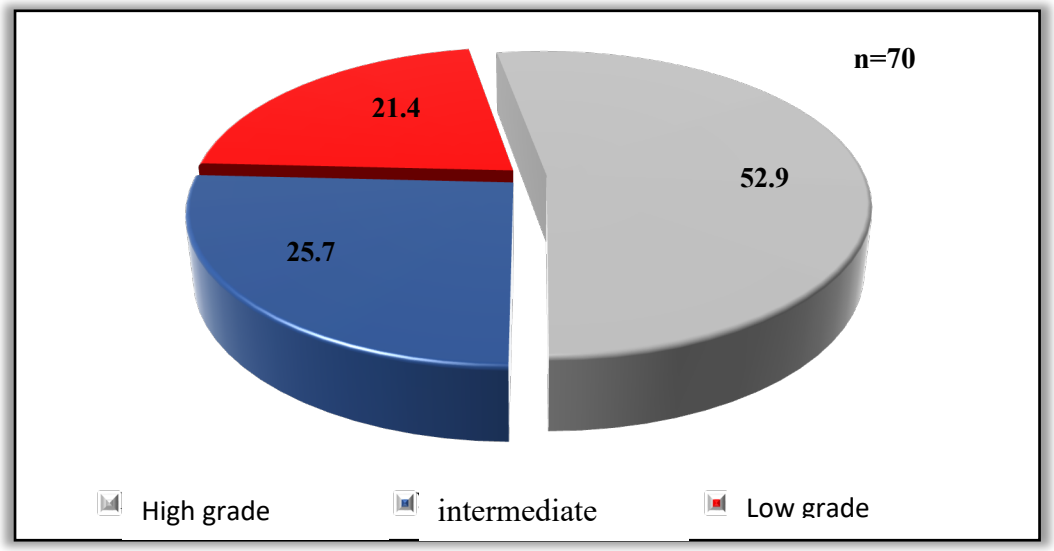

Fig. 21 Frequency distribution of patients according to tumor differentiation

Analysis of surgical treatment (Fig. 22) showed that the most frequently applied surgical method was total robot-assisted hysterectomy with adnexectomy (84.3%). Other types of surgical interventions were significantly less common, with most represented by single cases (1.4% each).

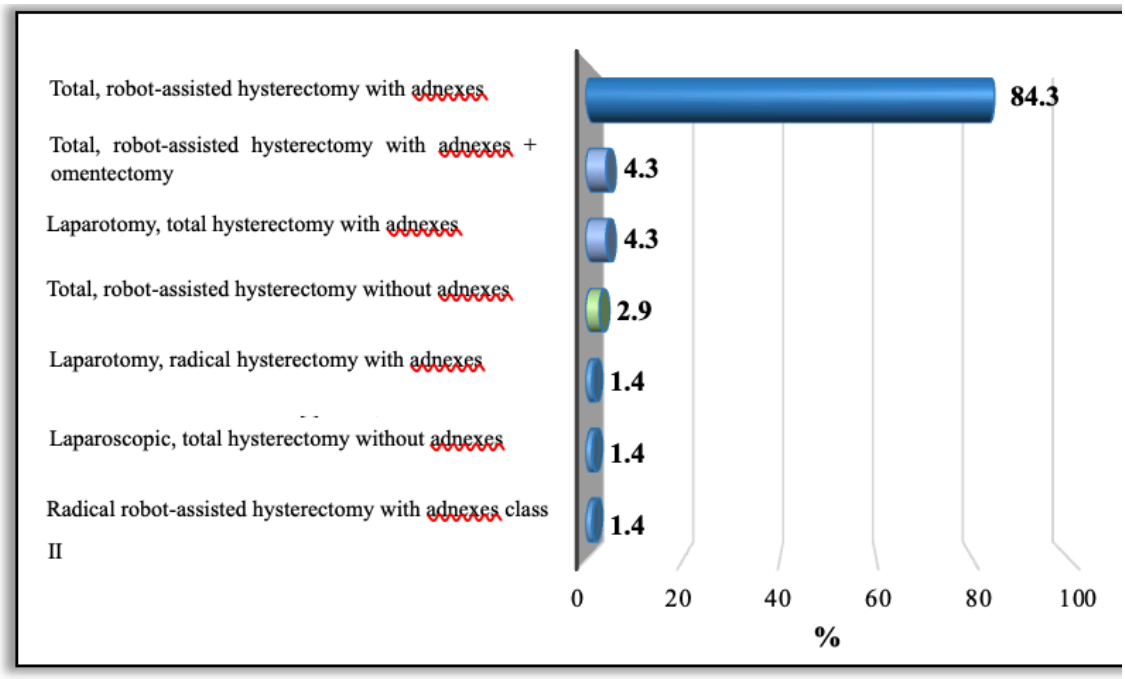

Fig. 22 Frequency distribution of patients according to type of surgery

Staging according to FIGO 2009 (Table 9) showed that stages IA (75.7%) and IB (14.3%) were the most common. According to FIGO 2023 staging (Table 10), the highest relative proportions were observed in stages IA2 (34.3%) and IA1 (27.1%).

Table. 9 Frequency distribution of patients according to disease stage based on FIGO 2009

FIGO 2009 disease stage	n	%	Sp
IA	53	75,7	5,1
IB	10	14,3	4,2
II	3	4,3	2,4
IIIA	0	0,0	0,0
IIIB	0	0,0	0,0
IIIC1	1	1,4	1,4
IIIC2	2	2,9	2,0
IVA	0	0,0	0,0
IVB	1	1,4	1,4
Тотал	70	100,0	

Table. 10 Frequency distribution of patients according to disease stage based on FIGO 2023

FIGO 2023 disease stage	n	%	Sp
IA1	19	27,1	5,3
IA2	24	34,3	5,7
IA3	1	1,4	1,4
IB	9	12,9	4,0
IC	4	5,7	2,8
IIA	1	1,4	1,4
IIB	1	1,4	1,4
IIC	5	7,1	3,1
IICmp53abn	1	1,4	1,4
IIIA1	0	0,0	0,0
IIIB	1	1,4	1,4
IIIC1	1	1,4	1,4
IIIC2	1	1,4	1,4
IIIC1ii	1	1,4	1,4
IVC	1	1,4	1,4
Общо	70	100,0	

6. Analysis of distant metastasis-free survival

The mean follow-up time of patients in the present study was 11.73 ± 12.08 months, ranging from 1 to 55 months. The mean distant metastasis-free survival was 41.57 ± 4.28 months, with a 95% confidence interval of 33.18 to 49.97 months.

Table 11 presents survival to the occurrence of distant metastases, calculated using the Kaplan–Meier method. Analysis of the data showed that out of a total of 55 followed patients, 8 (14.5%) developed distant metastases during the follow-up period.

Table. 11 Kaplan-Meier survival table for time to distant metastasis

Time (months	*Cumulative probability*	*Number with DM*	*Cumulative number with DM*	*Number of dropouts*	*Number remaining*
0	1,000	0	0	0	55
1	0,964	2	2	1	52
6	0,932	1	3	13	28
12	0,863	2	5	4	22
18	0,761	2	7	10	12
24	0,676	1	8	3	8
55	0,676	0	8	8	0

The one-year survival rate without distant metastases was 86.3%, while the two-year, three-year, and four-year survival rates were identical—67.6%. The maximum recorded survival time before the onset of distant metastases reached 55 months (4 years 7 months).

7. Analysis of quantitative variables:

In order to meet the requirements for survival analysis, quantitative variables were transformed into categorical variables using ROC curve analysis to determine optimal threshold values distinguishing patients with and without distant metastases. The Youden index was used as the criterion for selecting optimal cut-off values, defined as follows:

- Youden index = maximum (sensitivity + specificity − 1)

The analysis (Figs. 23–24, Table 12) showed that statistically significant threshold values were identified for age and tumor size, namely ≥ 53.5 years and ≥ 28.0 mm, respectively.

Regarding age, the identified criteria demonstrated excellent sensitivity and negative predictive value (100%); however, low values were observed for positive predictive value, specificity, and overall accuracy (25%, 49%, and 56%, respectively).

For tumor size, the negative predictive value was also high (93%), sensitivity was good (75%), while specificity and accuracy were within acceptable ranges. The positive predictive value remained relatively low (Table 12).

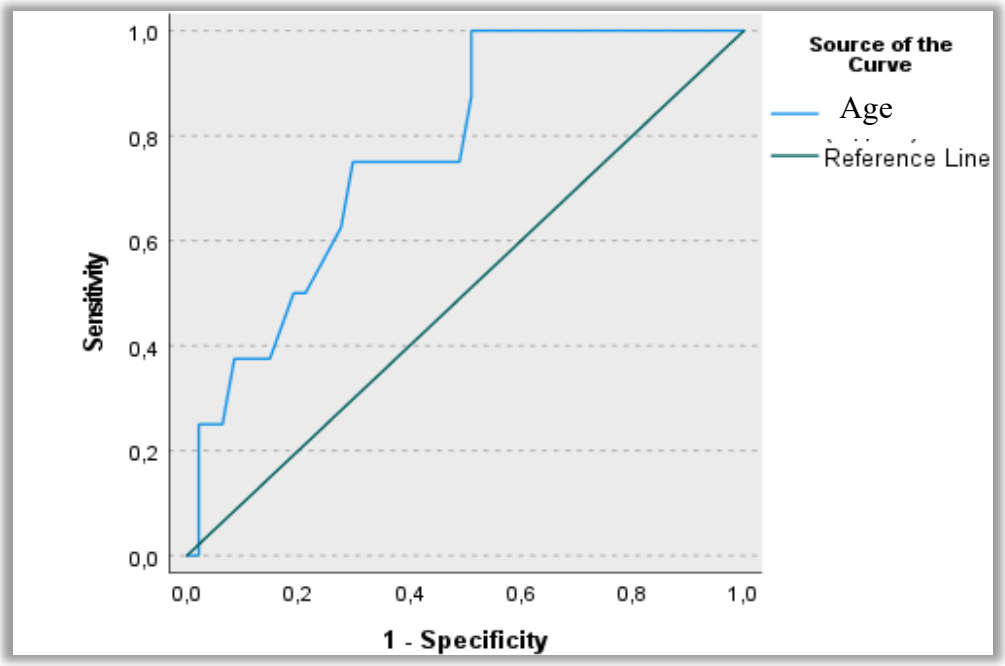

Fig. 23 ROC curve of age for determining the threshold value in distinguishing patients with and without distant metastases (area under the curve 0,771; p<0,001)

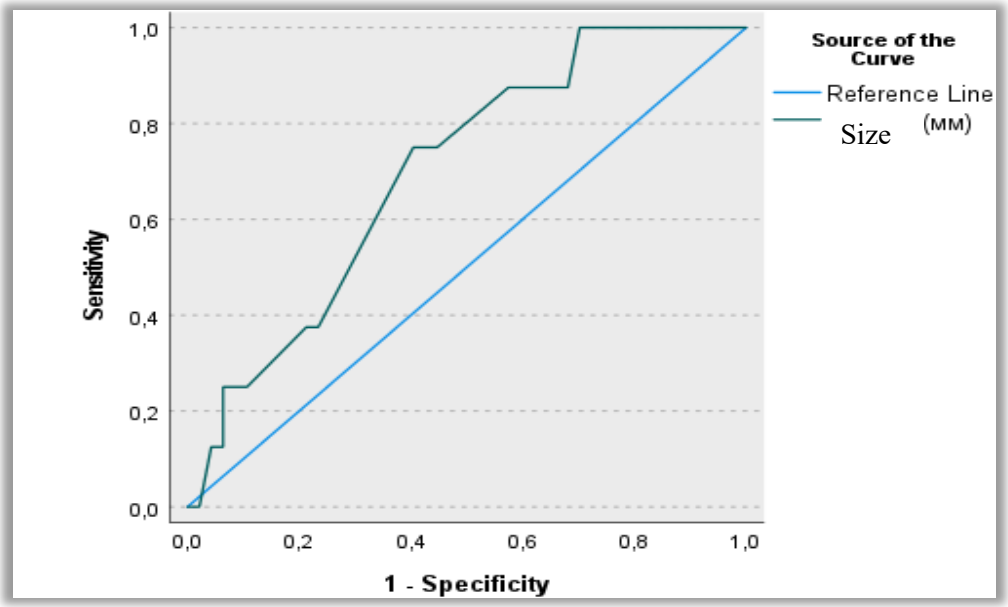

Fig. 24 ROC curve of tumor size for determining the threshold value in distinguishing patients with and without distant metastases (area under the curve0,698; p=0,024)

Table. 12 Age threshold for distinguishing between those with and without DM and validation criteria for screening tests

Indicator	Threshold	Sensitivity	Specificity	Positive predictive value	Negative predictive value	% Correct answers
Age (years)	≥53,5	100	49	25	100	56
Tumour size (mm)	≥28,0	75	60	24	93	62

7.1. Influence of age:

The applied statistical tests (Log-rank, Breslow, and Tarone–Ware) demonstrated a statistically significant difference in survival between groups defined by age (Log-rank (Mantel–Cox) p = 0.009). It was found that patients aged ≥ 53.5 years had significantly lower distant metastasis-free survival, with a mean value of 22.73 months (95% CI: 16.88–28.57), compared to younger patients. Analysis of cumulative risk (Fig. 25) showed that the risk of developing distant metastases in patients aged ≥ 53.5 years increases rapidly and reaches significantly higher values, whereas in younger patients it remains zero.

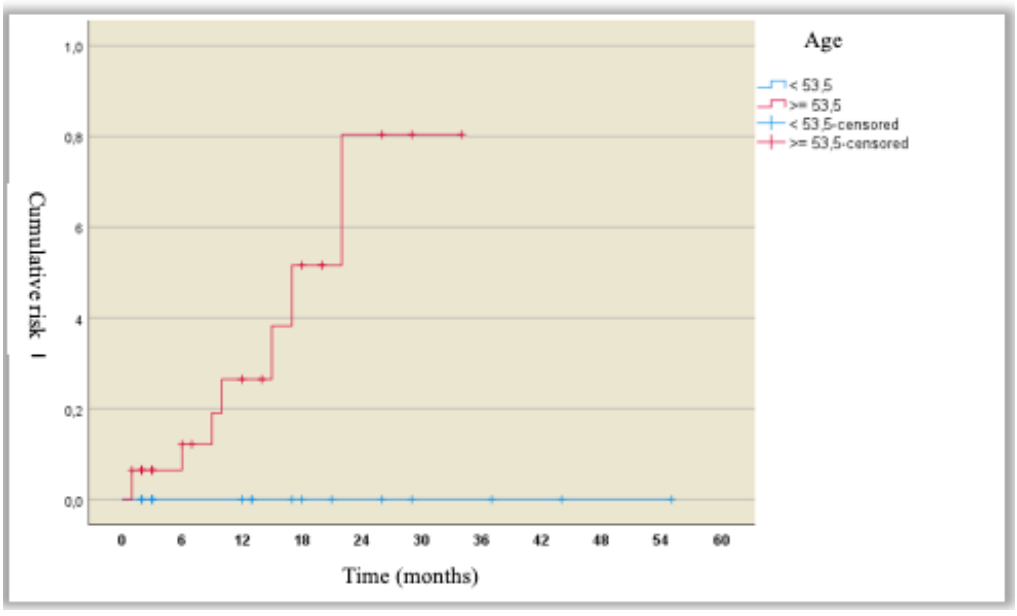

Fig. 25 Risk functions for distant metastases according to the factor age

7.2. Influence of tumor size

Analysis using the Log-rank test showed borderline statistical significance regarding the influence of tumor size on survival (Log-rank

(Mantel–Cox) p = 0.081). A trend toward lower survival was observed in patients with tumor size ≥ 28 mm (Table 13):

Table. 13 Mean survival and 95% confidence interval according to the factor tumor size

Tumour size (мм)	Number of events	Median survival time* (months)	95% confidence	
			Lower Bound	Upper Bound
< 28	2	48,64[a]	39,79	57,50
≥ 28	6	24,38[b]	18,27	30,49

** identical letters indicate no significant difference, while different letters indicate a significant difference (p < 0,1)*

7.3. Influence of myometrial invasion:

Analysis of distant metastasis-free survival according to the degree of myometrial invasion showed borderline statistical significance (Log-rank (Mantel–Cox) p = 0.071). A trend toward lower survival was observed in patients with myometrial invasion ≥ 50% (Table 14).

Table. 14 Mean survival and 95% confidence interval according to the factor myometrial invasion

Myometrial invasion	Number of events	Median median survival time*	95% confidence interval	
			Lower Bound	Upper Bound
< 50%	3	44,41[a]	35,88	52,95
≥ 50%	5	13,96[b]	10,10	17,82

Analysis of cumulative risk (Fig. 26) shows that the risk of developing distant metastases in patients with invasion ≥ 50% increases significantly faster and reaches substantially higher values compared to the remaining patients:

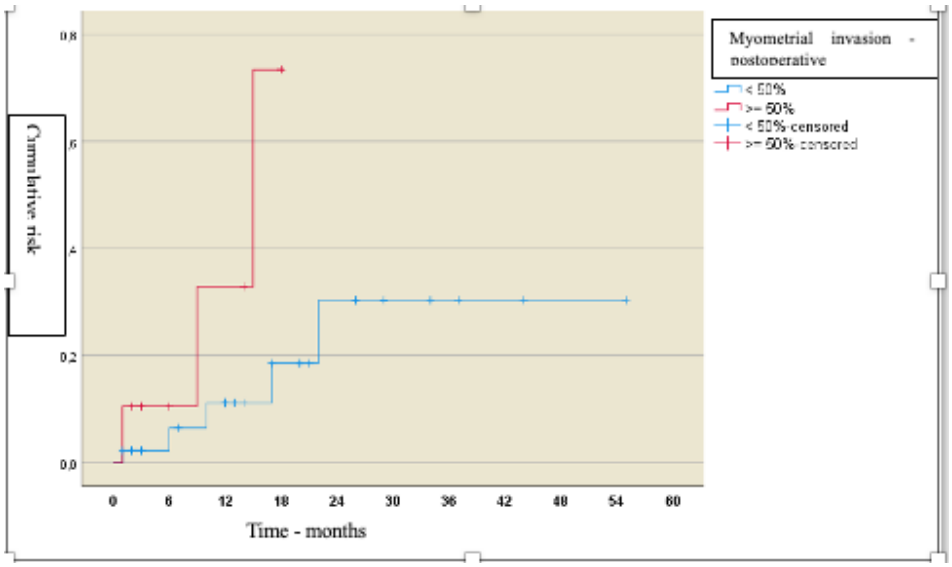

Fig. 26 Risk functions for distant metastases according to the factor myometrial invasion

7.4. Influence of degree of differentiation:

Analysis of survival according to the degree of differentiation (grading) showed that disease progression was observed across all grading categories (Table 15)

Table. 15 Median survival and 95% confidence interval according to the factor grading

Grading	Number of events	Median survival time* (months)	95% confidence interval	
			Lower Bound	Upper Bound
High	1	52,08[a]	46,57	57,58
Intermediate	4	16,43[b]	9,45	23,40
Low	3	19,05[b]	14,57	23,53

* *Identical letters indicate lack of a statistically significant difference, while different letters indicate the presence of such a difference (p < 0,05)*

The applied statistical tests (Log-rank, Breslow, and Tarone–Ware) demonstrated a statistically significant difference in distant metastasis-free survival between the groups ($p < 0.05$). The median survival to the occurrence of distant metastases in patients with moderately and poorly differentiated carcinoma was approximately 33–36 months lower compared to that in patients with well-differentiated tumors.

7.5. Influence of tumor histological type

Since endometrioid adenocarcinoma was the only histological type with sufficient statistical representativeness, the remaining histological variants were grouped into a general category “other”. The statistical tests - Log Rank, Breslow, and Tarone-Ware- did not reveal a statistically significant difference in survival without distant metastasis between the two groups ($p > 0.05$) (Table 16).

Table. 16 Mean survival and 95% confidence interval according to histological tumor type

Tumour histological type	Number of events	Median survival time* (months)	95% confidence interval	
			Lower Bound	Upper Bound
Ендометриоиден аденокарцином	5	37,14[a]	31,51	42,76
Други	3	29,79[a]	10,51	49,06

** - Identical letters indicate lack of a statistically significant difference, while different letters indicate the presence of such a difference ($p < 0,05$)*

The graphical representation (Fig. 27) shows that survival in patients with endometrioid adenocarcinoma reaches higher values compared to other histological types; however, the overall difference between the groups remains statistically non-significant.

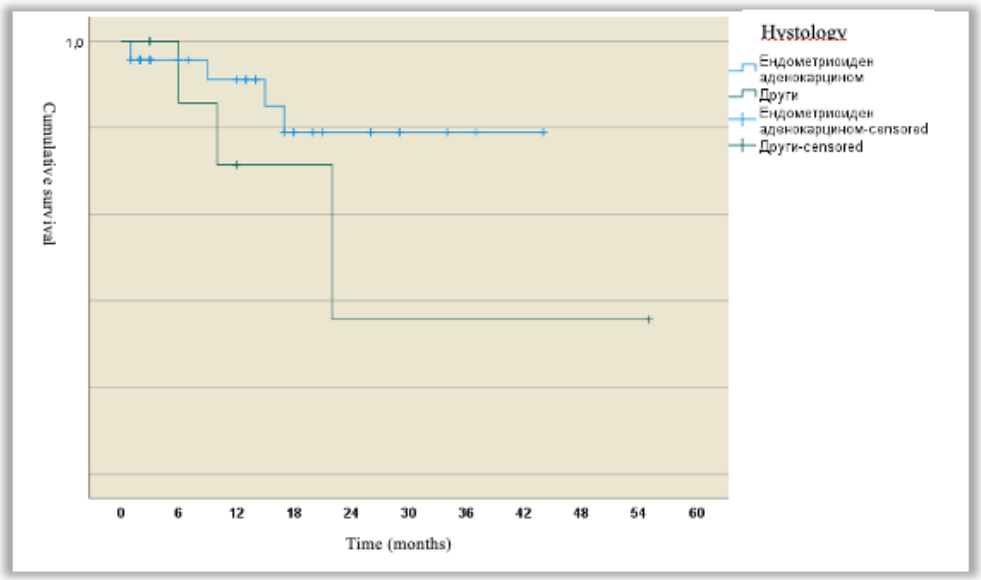

Fig. 27 Progression-free survival according to histological tumor type

7.6. Influence of the presence of local recurrence

Analysis of distant metastasis-free survival in relation to the presence of local recurrence showed a statistically significant difference between the groups (Log-rank (Mantel–Cox) p = 0.011). Patients without local recurrence had significantly higher distant metastasis-free survival, with a difference of approximately 32 months compared to those with confirmed recurrence (Table 17).

Table. 17 Median survival and 95% confidence interval according to the factor occurrence of local recurrence

Local recurrence	Number of events	Median survival time*	95% confidence interval	
			Lower Bound	Upper Bound
No	6	44,28[a]	36,12	52,44
Yes	2	12,00[b]	5,21	18,79

7.7. Influence of the type of hysterectomy:

Due to the limited statistical representation of the individual surgical techniques, all types of surgical interventions other than total robot-assisted hysterectomy with adnexectomy were grouped into the category “Others”. The applied tests (Log-rank, Breslow, and Tarone–Ware) did not demonstrate a statistically significant difference in distant metastasis-free survival between the analyzed groups (p > 0.05) (Table 18):

Table. 18 Median survival and 95% confidence interval according to the factor type of hysterectomy

Postoperative chemotherapy	Number of events	Median survival time* (months)	95% confidence interval	
			Lower Bound	Upper Bound
Other	2	44,20[a]	30,81	57,59
Total robotic with adnexa	6	33,87[a]	27,06	40,68

* - *Identical letters indicate lack of a statistically significant difference, while different letters indicate the presence of such a difference (p < 0,05)*

Cumulative risk analysis (Fig. 28) shows that in patients who underwent total robot-assisted hysterectomy with adnexectomy, the risk of developing distant metastases reaches higher values; however, this difference is not statistically significant:

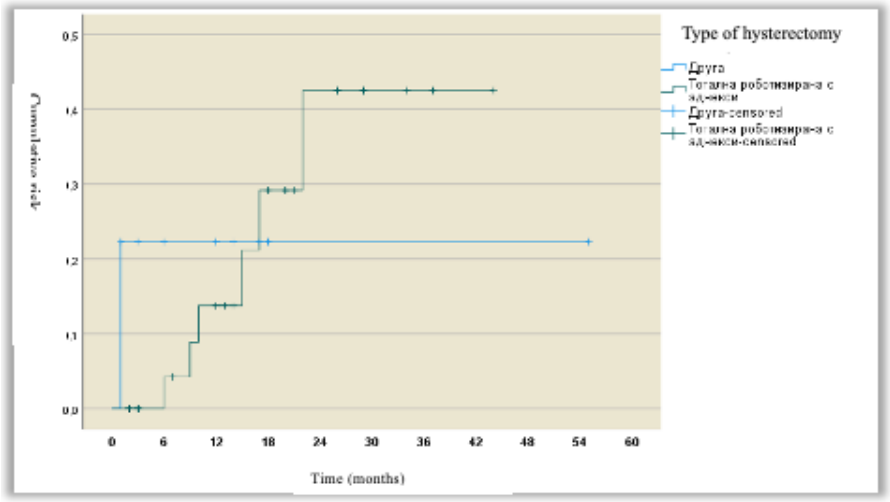

Fig. 28 Risk functions for the occurrence of distant metastases according to the factor type of hysterectomy

7.8. Influence of lymph node dissection:

Analysis of distant metastasis-free survival according to the performance of lymph node dissection did not show a statistically significant difference between patients with and without this intervention ($p > 0.05$) (Table 19):

Table. 19 Median survival and 95% confidence interval according to the factor lymph node dissection

Lymph node dissection	Number of events	Median survival time* (months)	95% confidence interval	
			Lower Bound	Upper Bound
Не	4	42,38[a]	31,82	52,94
Да	4	33,93[a]	25,40	42,46

** - Identical letters indicate lack of a statistically significant difference, while different letters indicate the presence of such a difference ($p < 0,05$)*

7.9. Influence of disease stage (FIGO 2009 and FIGO 2023):

According to FIGO 2023 staging, no groups were identified with sufficient statistical representation and recorded cases of distant metastases.

In contrast, FIGO 2009 staging allowed the formation of three groups that met the necessary conditions for analysis.

The results (Table 20) show that patients with stage IA had significantly higher distant metastasis-free survival compared to those in higher stages, with a difference of approximately 36–39 months.

Table. 20 Median survival and 95% confidence interval according to the factor stage 2009

Stage 2009	**Number of events**	**Median survival time* (months)**	**95% confidence interval**	
			Lower Bound	Upper Bound
IA	2	49,27[a]	41,70	56,85
IB	3	13,70[b]	10,43	16,97
Higher	3	10,90[b]	3,80	18,00

* - *Identical letters indicate lack of a statistically significant difference, while different letters indicate the presence of such a difference* ($p < 0,05$)

These results are also confirmed by the graphical representations (Figs. 29 and 30), which demonstrate both cumulative survival and the risk of developing distant metastases according to disease stage:

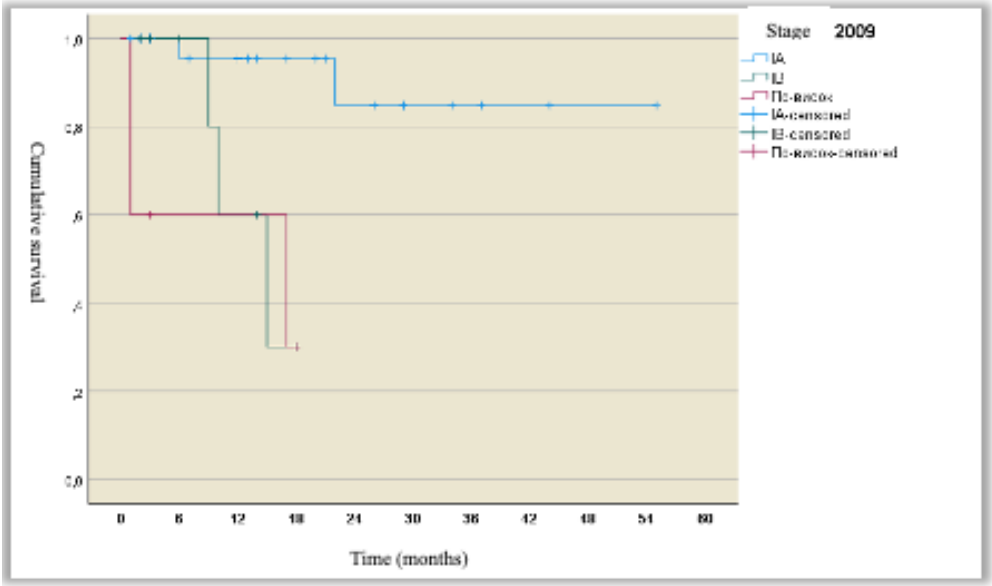

Fig. 29 Distant metastasis-free survival according to the factor stage FIGO2009

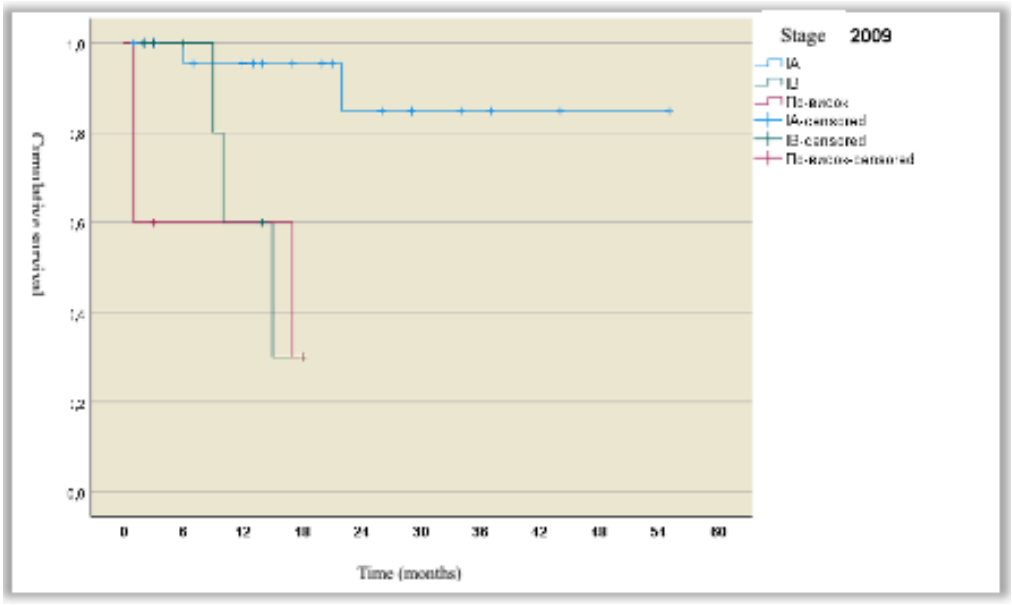

Fig. 30 Risk functions for the occurrence of distant metastases according to the factor stage FIGO2009

7.10. Influence of menopausal status

The analysis showed a statistically significant difference in distant metastasis-free survival according to menopausal status (Log-rank (Mantel–Cox) p = 0.027). Postmenopausal patients had lower survival, with a mean value of 23.79 months (95% CI: 18.20–29.39), compared to non-menopausal patients. The graphical representation (Fig. 31) shows that survival in postmenopausal patients declines more rapidly and reaches lower values, with an overall difference between the two groups of approximately 50%.

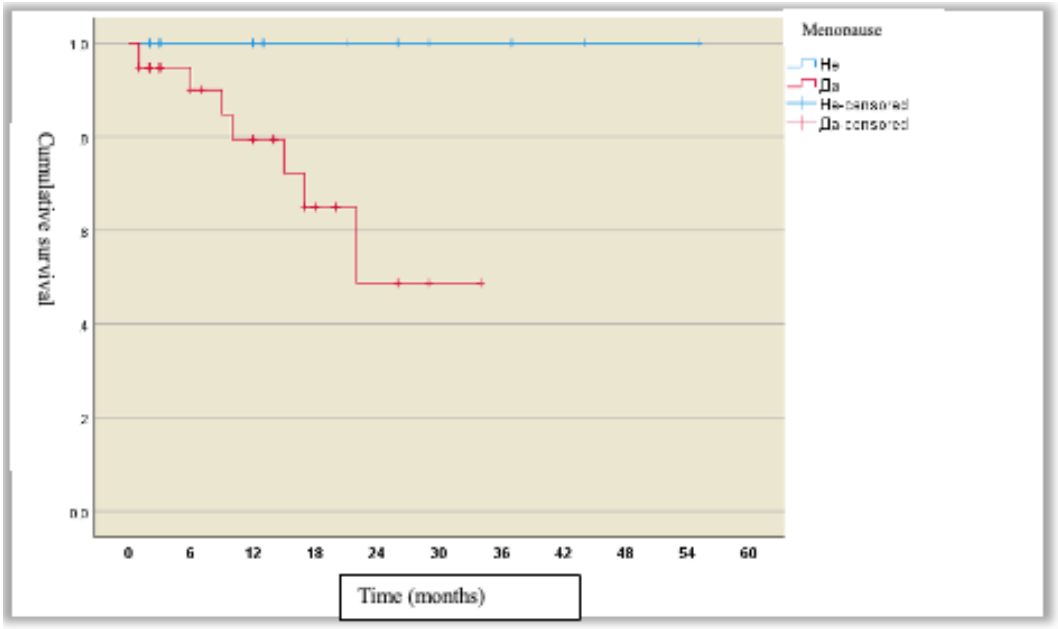

Fig. 31 Distant metastasis-free survival according to menopausal status

Analysis of cumulative risk (Fig. 32) shows a significantly faster increase in the risk of developing distant metastases in postmenopausal patients:

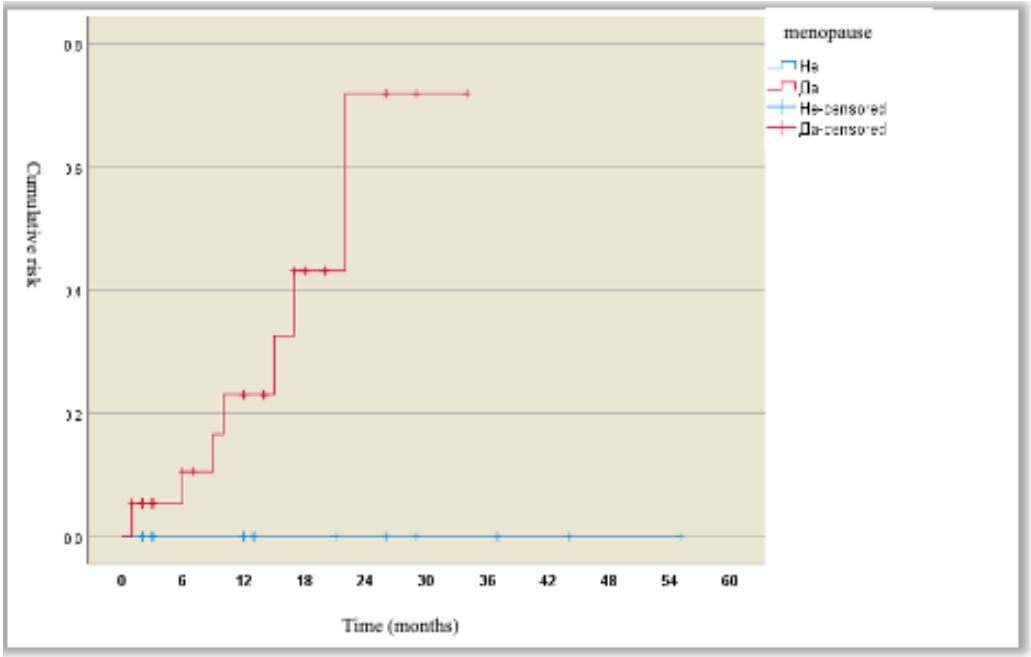

Fig. 32 Risk functions for distant metastases according to menopausal status

7.11. Influence of blood group

Due to the small number of patients with blood group AB (n = 5) and the absence of recorded cases of distant metastases in this group, it was excluded from the analysis. The analysis included patients with blood groups O, A, and B. The applied statistical tests did not demonstrate a statistically significant difference in distant metastasis-free survival among the three groups (p > 0.05) (Table 21).

Table. 21 Median survival and 95% confidence interval according to the factor blood group

Blood group	Number of events	Mean survival time* (months)	95% confidence interval	
			Lower Bound	Upper Bound
0	3	29,15[a]	21,16	37,14
A	3	37,96[a]	23,61	52,32
B	2	34,78[a]	23,56	46,00

8. Analysis of recurrence-free survival

The mean follow-up time in the study group was 11.98 ± 12.46 months, ranging from 1 to 55 months. The mean recurrence-free survival was 48.15 ± 4.09 months, with a 95% confidence interval of 40.13 to 56.17 months. Table 22 presents the results of the recurrence-free survival analysis calculated using the Kaplan–Meier method. The data show that out of a total of 55 patients, 3 (5.5%) developed disease recurrence. The first recorded recurrence occurred as early as the second month from the start of follow-up. The maximum recorded recurrence-free survival reached 55 months, corresponding to approximately 4 years and 7 months.

Table. 22 Kaplan-Meier table of recurrence-free survival table

Time (months)	Cumulative probability	Number of relapses	Cumulative number of relapses	Number of drop outs	Number remaining
0	1,000	0	0	0	55
2	0,981	1	1	15	39
12	0,942	1	2	17	21
24	0,942	0	2	12	9
36	0,753	1	3	5	3
48	0,753	0	3	2	1
55	0,753	0	3	1	0

9. Analysis of associations between tumor type and clinicopathological parameters

Within the scope of the present study, an analysis was performed to assess the relationship between tumor type and a number of clinical and imaging parameters. The statistical analysis demonstrated a statistically significant association between tumor type and grading. In endometrioid adenocarcinoma, the relative proportion of poorly differentiated (G3) tumors was significantly lower compared to well and moderately differentiated forms, whose relative proportions did not differ significantly from each

other. Statistically significant differences were also observed in some other histological types; however, due to the small absolute number of cases, these results should be interpreted with caution (Table 23):

Table. 23 Association between histological tumor type and grading (p<0,001)

Tumour histological type	**Frequency**	**Grading**			**Total**
		G1	G2	G3	
1	n	35	17	4	56
	%	94,6[a]	94,4[a]	26,7[b]	80,0
2	n	0	0	3	3
	%	0,0[a]	0,0[ac]	20,0[bc]	4,3
3	n	0	0	2	2
	%	0,0[a]	0,0[a]	13,3[a]	2,9
4	n	0	1	0	1
	%	0,0[a]	5,6[a]	0,0[a]	1,4
5	n	0	0	1	1
	%	0,0[a]	0,0[a]	6,7[a]	1,4
6	n	0	0	2	2
	%	0,0[a]	0,0[ac]	13,3[bc]	2,9
7	n	0	0	3	3
	%	0,0[a]	0,0[ac]	20,0[bc]	4,3
8	n	1	0	0	1
	%	2,7[a]	0,0[a]	0,0[a]	1,4
9	n	1	0	0	1
	%	2,7[a]	0,0[a]	0,0[a]	1,4
Общо	n	37	18	15	70
	%	100,0	100,0	100,0	100,0

Legend for histological tumor type: 1 – Endometrioid adenocarcinoma; 2 – Serous papillary adenocarcinoma; 3 – Clear cell adenocarcinoma; 4 – Squamous; 5 – Mixed; 6 – Carcinosarcoma; 7 – Undifferentiated

IV. DISCUSSION

Myometrial invasion is one of the most important prognostic factors in endometrial carcinoma and plays a central role in current classifications and treatment algorithms. It is a key component of the FIGO staging system and is directly related to both the risk of lymphatic dissemination and the overall prognosis of the disease. The clinical significance of this indicator is determined by the fact that the 50% myometrial invasion threshold places patients into different risk groups. At ≥50%, a significantly higher incidence of lymphovascular invasion, lymph node involvement, and distant metastases is observed, necessitating a more aggressive therapeutic approach. On the other hand, in cases of superficial infiltration (<50%), the disease often has a more favorable prognosis and allows for a more conservative surgical approach. In this context, precise pre-operative assessment of myometrial invasion is of essential importance. It aids not only in staging but also in deciding on the extent of surgical intervention, including the need for lymph node dissection, as well as subsequent adjuvant therapy.

With the advancement of imaging diagnostics, Magnetic Resonance Imaging has established itself as the method of choice for pre-operative assessment of myometrial invasion. Its main advantage is high tissue resolution, which allows for clear differentiation between tumour tissue, endometrium, and myometrium. Of particular importance is the visualization of the so-called junctional zone, whose disruption or infiltration is a key imaging sign of invasion. An additional advantage of MRI is the possibility of multiparametric assessment using various sequences—T2-weighted images, DWI, and contrast-enhanced series. The combined use of these techniques increases diagnostic accuracy and reduces the likelihood of underestimating or overestimating the depth of invasion.

However, the assessment of myometrial invasion is not always unambiguous. There are a number of factors that can complicate image interpretation. These include the presence of concomitant conditions and diseases—adenomyosis, myomatous nodules, postmenopausal changes, or heterogeneous tumour structure—which can lead to an incorrect assessment of the depth of infiltration.

In the present study, myometrial invasion was assessed preoperatively by MRI and compared with the final histopathological result, considered the "gold standard". The results demonstrated high diagnostic value of the method, with a sensitivity of 85% and a specificity of 89%, as well as an overall accuracy of 89%. The negative predictive value was particularly high (96%), while the positive predictive value was lower (65%). These results are in agreement with data from the literature, according to which the sensitivity of MRI in assessing myometrial invasion ranges between 80% and 90%, and specificity reaches 90–95%. The high negative predictive value observed in our study confirms that the method is particularly reliable in ruling out deep myometrial invasion, which has important clinical significance in planning surgical treatment.

On the other hand, the lower positive predictive value suggests the presence of cases in which MRI overestimates the depth of invasion. This low positivity is also confirmed by the discrepancies between imaging and histopathological assessment found in our study in 11.4% of patients. Similar values have been reported by the other cited authors, who have reported discrepancies in approximately 10–15% of cases.

Further analysis of these cases in the present study did not reveal a correlation between the discrepancies and factors such as tumour size or degree of differentiation. Such a discrepancy is an interesting finding, as some publications suggest that larger and less differentiated tumours are more difficult to assess using imaging. A possible explanation for the observed discrepancies is the influence of concomitant morphological changes in the myometrium, such as adenomyosis or myomatous nodules, which can disrupt the normal anatomical structure and make the image interpretation more complex. Furthermore, the lack of contrast enhancement in a higher percentage of cases in our study may also have contributed to limiting the diagnostic accuracy, as according to many authors, dynamic contrast-enhanced sequences improve the differentiation between tumour and normal tissue.

Regarding the imaging sequences used, our study found that in some cases with a mismatch, there was restriction of water molecule diffusion (as in hypercellular tissues), while in others, there was no such restriction, thus indicating that DWI plays a complementary but not absolute role in assessing invasion. Similar observations have been described in the literature, where it

is emphasized that optimal assessment is achieved by combining T2W and DWI.

In summary, the results of the present study confirm that MRI is a reliable method for assessing myometrial invasion, but there are certain limitations that should be taken into account during interpretation. These limitations are not only related to tumour characteristics but also to the features of the surrounding tissue and the imaging protocol used.

The results related to MRI signal characteristics are also of interest. In most cases of discrepancy (75%), the tumours were hypointense, while the remainder were evenly distributed among the other signal types. These results could be explained by the fact that the hypointense signal on T2-weighted images sometimes makes it difficult to clearly distinguish between tumour tissue and normal myometrium, especially in postmenopausal patients, in whom the physiological reduction in signal intensity in the myometrium leads to lower contrast.

Furthermore, DWI analysis revealed that diffusion restriction was present in 62.5% of cases with mismatch, while it was absent in 37.5%. These percentages indicate that this feature, although a valuable tool, is not sufficient on its own for an accurate assessment of the depth of invasion. Similar observations have been described in other studies, emphasizing that it is a sensitive but not entirely specific marker of tumour infiltration.

In this regard, the results of our study showed that discrepancies between MRI and histopathological assessment of myometrial invasion are relatively rare, yet clinically significant. These discrepancies are not determined by a single factor. Rather, they are attributable to an intricate interaction between tumour characteristics, features of the surrounding tissue, and the imaging protocol used. This interaction underscores the need for a multiparametric approach and careful interpretation of imaging findings.

Myometrial invasion is considered one of the key factors determining the risk of metastatic spread in endometrial carcinoma. The depth of infiltration is associated with the likelihood of lymphovascular invasion, lymph node involvement, and development of distant metastases, which accounts for its place in current prognostic models.

In the present study, the relationship between preoperatively assessed myometrial invasion by MRI and the development of distant metastases and recurrence was analyzed. The results did not demonstrate a statistically significant association between the degree of invasion and the time to occurrence of distant metastases or recurrence. At first glance, this finding appears to contradict some published data suggesting that deep myometrial invasion is associated with poorer prognosis and higher risk of disease progression.

The lack of statistically significant association in our study may be explained by several factors. First, because the number of patients was relatively small, there was a limited number of cases with metastases. Furthermore, the heterogeneity of the group in terms of stage, histological type, and treatment administered may have also masked the influence of the individual prognostic factors.

Nevertheless, a more in-depth analysis revealed a statistically significant association between the degree of myometrial invasion and the location of metastases. Specifically, in patients without established metastases, invasion of less than 50% predominated, whereas in those with lung metastases, a higher relative proportion of invasion ≥50% was found. This observation is consistent with the generally accepted understanding that deep myometrial invasion is an indirect marker of more aggressive tumour behavior.

Another important aspect is the lack of association between myometrial invasion and time to recurrence. This may be explained by the fact that recurrence in endometrial carcinoma is determined by a complex interaction of multiple factors, including histological type, molecular characteristics, and treatment. Therefore, although important, myometrial invasion cannot be considered a single determinant of recurrence.

In summary, although no direct statistically significant association was found between myometrial invasion and time to metastasis or recurrence, a clear trend was observed linking deeper invasion with less favorable disease characteristics, including metastasis localization. This confirms the role of myometrial invasion as an important, but not independent, prognostic factor.

When interpreting the results, it is particularly important to consider myometrial invasion not as an isolated parameter, but also as part of a

comprehensive prognostic profile of the patients. In modern gynecologic oncology, combined risk assessment models that include not only anatomical characteristics but also molecular markers are gaining increasing importance.

In this context, the lack of a direct statistically significant association between myometrial invasion and survival in the present study may be viewed as a reflection of the multifactorial nature of the disease. The literature emphasizes that the prognostic value of myometrial invasion is most pronounced when combined with other factors such as lymphovascular invasion, the histological type, and the molecular profile of the tumour.

Furthermore, it should be noted that current classifications of endometrial carcinoma increasingly include molecular subtypes (POLE-mutated, p53-abnormal, etc.), which may alter the significance of classical morphological indicators. This tendency may partly explain why our study did not find a clear association between myometrial invasion and clinical outcome.

From a clinical perspective, the results highlight the need for an individualized approach in patient assessment. Although myometrial invasion remains an important parameter, it should not be used as the sole criterion for therapeutic decision-making. Instead, it should be interpreted within the context of the overall clinical picture.

The practical significance of these findings is also reflected in the role of MRI as a tool for preoperative risk stratification. The method's high negative predictive value allows deep myometrial invasion to be ruled out with a high degree of certainty, which may support the choice of a less invasive surgical approach in certain patients.

On the other hand, cases of overestimating invasion underscore the need for careful interpretation of imaging findings and, if necessary, further evaluation using other methods or a multidisciplinary approach.

Assessment of lymph nodes and the presence of distant metastases represent essential components of staging and prognostic evaluation in endometrial carcinoma. Lymph node involvement is considered one of the most significant adverse prognostic factors and is associated with increased risk of recurrence and reduced overall survival.

In our study, the majority of patients had no evidence of lymph node metastasis, while a relatively small percentage showed evidence of metastatic involvement. These results are consistent with the expected distribution in early stages of the disease, in which the frequency of lymph node metastases is relatively low.

Of particular importance is the relationship between myometrial invasion and lymphatic dissemination. Although no direct statistically significant association was identified in this study, a trend toward higher frequency of lymph node metastases in patients with deeper invasion was observed. This relationship is widely described in the literature and is explained by the increased likelihood of lymphovascular involvement in cases of deep myometrial infiltration.

In this regard, the assessment of lymph nodes using imaging methods remains a challenge. Magnetic resonance imaging has limited sensitivity in detecting micrometastases, as the primary criterion for a pathological lymph node is an increased short-axis diameter, which does not always correlate with the presence of tumour infiltration. In practice, this means that the absence of enlarged lymph nodes on MRI does not rule out the presence of micrometastases, which is an important limitation of the method.

An interesting observation is the lack of a statistically significant association between the presence of distant metastases and the time to their occurrence. This may be explained by the limited number of cases and the fact that metastasis development results from complex biological processes not solely dependent on local tumor characteristics.

Although MRI provides valuable information on local tumor spread, it has a limited role in the assessment of lymph nodes and distant metastases, especially in early stages. Therefore, in clinical practice, additional imaging modalities such as CT or PET/CT are often used for more accurate evaluation of systemic disease spread. In addition, surgical staging remains the gold standard for lymph node assessment. Despite advances in imaging, final evaluation of lymph node involvement is often based on histopathological examination, which can detect micrometastases not visible on imaging.

In this context, the results of the present study support the concept that MRI plays a leading role in local staging but should be combined with other

diagnostic approaches for comprehensive disease assessment. This is particularly important for treatment planning and determining the extent of surgical intervention.

In conclusion, the analysis of lymph nodes and distant metastases in the present study shows that, despite the lack of statistically significant associations in some parameters, clear trends consistent with patterns described in the literature are observed. This confirms the importance of an integrated approach in the evaluation of patients with endometrial carcinoma.

Survival in patients with endometrial carcinoma is the result of a complex interaction of multiple factors, including disease stage, histological type, degree of differentiation, presence of myometrial invasion, and metastatic spread. In this context, survival analysis represents an important component in evaluating the clinical significance of the obtained results.

In our study, distant metastasis-free survival was analyzed, with a mean follow-up of 11.73 ± 12.08 months and a mean survival of 41.57 ± 4.28 months. These values reflect a relatively favorable clinical course, which can be explained by the fact that the study group consisted primarily of patients with early-stage disease.

The results indicate that most distant metastases occur within the first two years after surgery, with 62.5% of cases recorded during the first year. This observation is consistent with literature data indicating that the risk of progression is highest in the early postoperative period.

An important aspect of the analysis is the assessment of factors influencing survival. In the present study, a statistically significant association was found with regard to age and menopausal status. Patients aged ≥53.5 years showed significantly lower survival compared to younger patients, among whom no cases of distant metastases were observed. A similar trend has been described in the literature, where age is considered an independent prognostic factor associated with a more aggressive disease course and lower tolerance to therapy.

Regarding menopausal status, our study found lower survival rates among postmenopausal patients. These rates could be explained by the fact that they more frequently exhibited more unfavorable histological characteristics.

Tumor size also demonstrated borderline statistical significance, with patients having tumors ≥28 mm showing a trend toward lower survival. This finding is consistent with studies such as that of Mariani et al., which associate larger tumor volume with higher risk of invasion and metastatic spread.

On the other hand, no statistically significant association was found between survival and several other factors, including histological type, type of surgery, and lymph node dissection. These findings may be explained both by study limitations and by the complex nature of the disease, in which the influence of individual factors is difficult to isolate.

From a clinical perspective, the results highlight that survival in endometrial carcinoma cannot be explained by a single factor but rather results from a complex interaction of multiple parameters, including imaging, histological, and clinical characteristics.

In conclusion, survival analysis in the present study shows that, despite the lack of statistically significant associations for some factors, clear trends consistent with those described in the literature are observed. This confirms the importance of a multifactorial approach in prognostic evaluation of patients with endometrial carcinoma.

When interpreting the results of the present study, certain limitations that may have influenced the conclusions drawn should be taken into account. First, the relatively small number of patients included limits the analysis and may explain the lack of statistically significant associations for some of the examined indicators. This limitation is particularly true for analyses related to distant metastases and recurrences, where the number of events is limited.

Another important factor is the lack of contrast enhancement in a substantial proportion of imaging studies. As is well known, dynamic contrast-enhanced imaging improves visualization of the boundary between tumor and normal tissue and may increase the accuracy of assessing myometrial invasion.

Last but not least, the lack of molecular-genetic data on the tumours, which are becoming increasingly important in the current classification of endometrial carcinoma, should also be noted. The inclusion of molecular subtypes could contribute to more precise risk stratification and a more in-depth analysis of prognostic factors.

Despite these limitations, the present study has significant clinical relevance. The results confirm the high diagnostic value of MRI in preoperative assessment of myometrial invasion and highlight its role as the primary imaging modality in staging of endometrial carcinoma.

Of particular importance is the high negative predictive value of MRI, which allows reliable exclusion of deep myometrial invasion. This has direct practical implications for surgical planning, enabling more precise selection of patients who may benefit from less extensive surgical approaches.

On the other hand, the observed discrepancies between imaging and histopathological assessment emphasize the need for careful interpretation of MRI findings and the application of a multidisciplinary approach. The integration of imaging, clinical, and histological data remains essential for accurate staging and optimal patient management.

In a broader perspective, the findings of the present study support the role of MRI as an indispensable tool in modern gynecologic oncology. They also highlight opportunities for future research aimed at optimizing imaging protocols and integrating novel diagnostic approaches, including molecular and functional techniques.

V. CONCLUSIONS, RECOMMENDATIONS AND CONTRIBUTIOS:

1.CONCLUSIONS

1.1. Age and menopausal status were identified as factors influencing survival, with older and postmenopausal patients demonstrating a less favorable prognosis and clinical course.

1.2. MRI is a clinically applicable method for preoperative assessment of myometrial invasion in patients with early-stage endometrial carcinoma.

1.3. A high degree of concordance was observed between MRI assessment of myometrial invasion and histopathological findings. Discrepancy between them is observed in 11.4% of cases, which necessitates a careful interpretation of MRI findings.

1.4. The identified discrepancies showed no association with tumor size or degree of differentiation, suggesting the influence of complex imaging and tissue-related factors.

1.5. MRI demonstrated high diagnostic performance in the assessment of myometrial invasion, with sensitivity of 85%, specificity of 89%, and overall accuracy of 89%.

1.6. The high negative predictive value (96%) of MRI allows reliable exclusion of deep myometrial invasion and is of substantial importance in surgical planning.

1.7. No statistically significant association was found between preoperatively assessed myometrial invasion and time to occurrence of distant metastases or recurrence, confirming the multifactorial nature of disease progression.

1.8. MRI plays a leading role in the preoperative staging of early-stage EK, but optimal assessment requires integration with clinical, histological, and additional imaging data.

2.CONTRIBUTIONS OF THE DISSERTATION

2.1 Contributions of a scientific-theoretical nature

For the first time in Bulgaria, a comprehensive study has been conducted on the diagnostic and therapeutic value of Magnetic Resonance Imaging in the assessment of myometrial invasion in early-stage endometrial carcinoma, with results compared to histopathological findings as the gold standard.

An in-depth analysis of discrepancies between imaging and histopathological assessment of myometrial invasion has been performed, identifying factors potentially influencing the diagnostic accuracy of MRI (tumor size, degree of differentiation, signal characteristics on T2W and DWI).

The role of Magnetic Resonance Imaging as a reliable method for preoperative staging of endometrial carcinoma has been confirmed, demonstrating high sensitivity, specificity, and negative predictive value in the assessment of myometrial invasion.

2.2 Contributions of a scientific-applied nature

1. The diagnostic accuracy of Magnetic Resonance Imaging in the assessment of myometrial invasion in real clinical practice has been determined, allowing optimization of preoperative evaluation in patients with early-stage endometrial carcinoma.
2. The frequency of discrepancies between MRI and histopathological assessment (11.4%) has been established, which has significant practical implications for the interpretation of imaging findings and the determination of therapeutic approach.
3. The relationship between the degree of myometrial invasion and clinical and prognostic indicators, including risk of recurrence and overall survival, has been investigated to improve patient stratification.

4. The lack of significant influence of certain clinical and morphological factors on the accuracy of imaging assessment has been demonstrated, contributing to a more objective interpretation of imaging data.
5. The importance of a multiparametric MRI approach in the assessment of tumor invasion has been emphasized, particularly in settings where contrast enhancement is limited or not applicable.
6. The diagnostic value of Magnetic Resonance Imaging as the primary method for preoperative staging, aiding in the selection of a therapeutic approach and the determination of the extent of surgical treatment, is confirmed.

APPENDICES

Appendix 1:

BASIC MRI PROTOCOL OF THE PELVIS

Sequence	Plane	Purpose	Characteristics
T2-weighted (T2W)	Sag, Ax, Cor	General anatomical assessment, tumor extent, and depth of myometrial invasion	High tissue contrast, good visualization of the uterus, its layers, and the tumor
DWI + ADCmap	Corresponding planes based on T2W	Detection of tumor tissue	Evaluation of diffusion restriction and complementary to T2 findings
T1 TSE Dixon	Ax/oblique	Hemorrhage/blood detection	Additional tissue characterization
Contrast-enhanced sequences (in selected cases)	As indicated	Futher interpretation	Differentiation between tumor and myometrium

Appendix 2

COMPARISON BETWEEN FIGO AND TNM CLASSIFICATION IN ENDOMETRIAL CANCER

FIGO stage	TNM classification	Description
I (IA)	T1a N0 M0	Tumor confined to the uterus with <50% myometrial invasion
I (IB)	T1b N0 M0	Tumor confined to the uterus with ≥50% myometrial invasion
II	T2 N0 M0	Invasion of cervical stroma without extension beyond the uterus
IIIA	T3a N0 M0	Invasion of the serosa and/or adnexa
IIIB	T3b N0 M0	Involvement of the vagina or parametrium
IIIC1	T1–T3 N1 M0	Metastases in pelvic lymph nodes
IIIC2	T1–T3 N2 M0	Metastases in para-aortic lymph nodes
IVA	T4 N0–N2 M0	Invasion of the bladder and/or rectum
IVB/C	Any T, any N, M1	Distant metastases (including intra-abdominal and/or pulmonary)

Appendix 3

MRI IMAGING CRITERIA AND CORRESPONDENCE WITH FIGO STAGE

MRI Finding	FIGO Stage	Description
Lesion confined to the endometrium or with <50% myometrial invasion	IA	Preserved low-signal junctional zone (T2), with minimal disruption
Invasion ≥50% of myometrial thickness	IB	Disrupted or absent junctional zone, deep tumor infiltration
Invasion of cervical stroma	II	Disruption of hypointense cervical stroma (T2), diffusion restriction on DWI
Invasion of serosa and/or adnexa	IIIA	Uterine contour deformity, involvement of serosa or adnexa
Involvement of vagina/parametrium	IIIB	Tumor infiltration beyond uterus involving vagina/parametrium
Pathologically enlarged pelvic lymph nodes	IIIC1	Lymph nodes >10 mm or with abnormal signal (DWI restriction)
Para-aortic lymph nodes	IIIC2	Enlarged lymph nodes along the aorta
Invasion of bladder/rectum	IVA	Disruption of adjacent organ wall
Distant metastases	IVB/C	Lesions in lung, liver, or peritoneum

LIST OF PUBLICATIONS, PARTICIPATION IN SCIENTIFIC EVENTS AND PROJECTS RELATED TO THE DISSERTATION

PUBLICATIONS

FULL-TEXT SCIENTIFIC ARTICLES:

1. **M. Vasileva**, G. Prandzhev, D. Dimitrov, Z. Gorcheva. *"Current state of application of artificial intelligence in preoperative MRI assesment of endometrial cancer a mini review.",* Journal "Series on Biomechanics" ISSN 1313-2458 (2024, vol.38, issue 4, 127-132); Scopus

2. **Vasileva MV**, Gorcheva ZV. *Using magnetic resonance tomography as an imaging method for pre-operative evaluation of early-stage endometrial cancer.* Journal of Biomedical and Clinical Research 2024;17(2): 143-155. ISSN: 1313-9053; Web of Science (CABI)

3. **Vasileva M**, Totsev N, Gorcheva Z, Trifonov R. *Endometrial cancer – classifications, staging system and diagnostic role of MRI.* Jubilee Scientific Conference with International Participation "50 Years of Medical Education and Science in Pleven," 01–03.11.2024, Proceedings, Pleven, Bulgaria;p.92-96. ISBN 978-954-756-346-9

PARTICIPATION IN SCIENTIFIC FORUMS RELATED TO THE DISSERTATION:

1. 16-20 October 2023г. XX International Medical Scientific Conference for Students & Young Doctors, Pleven. "Case report of simultaneous endometrial and cervical cancer – role of magnetic resonance tomography and computed tomography in preoperative and follow-up staging", Abstract book p.127, ***Vasileva M****., Totsev N., Trifonov R., Stanislavova N., Gorcheva* Z. „Second (2nd) prize in PhD Section".

2. 22.07-05.08.2024г. „ Application of Dendritic Cell Therapy in Oncology Patients" – Training course in Tokyo, Japan (Activity 3.3., funded by the European Union – NextGenerationEU, under the Strategic Research and Innovation Program for Development "Medicine for Health," Medical University – Pleven, Bulgaria); *Blazhev A.,* ***Vasileva M****., Blazheva S.*
3. 01-03.11.2024г. Jubilee Scientific Conference with International Participation "50 Years of Medical Education and Science in Pleven". „Endometrial cancer – classifications, staging system and diagnostic role of MRI", Proceedings, p.92-96. ISBN 978-954-756-346-9, ***Vasileva M****, Totsev N, Gorcheva Z, Trifonov R.*
4. 01.11.2024г. Annual Scientific Conference for Presentation of Scientific Progress under the Strategic Research and Innovation Program for Development "Medicine for Health," Medical University – Pleven, Bulgaria. Presentation of scientific results under Activity 3.3. Training course "Application of Dendritic Cell Therapy in Oncology Patients" in Tokyo, Japan. *Blazhev A.,* ***Vasileva M****., Blazheva S.*

PARTICIPATION IN RESEARCH PROJECTS:

1. PhD project "D4/2022," funded by the Medical University – Pleven: "Role of Magnetic Resonance Imaging in the Preclinical Staging of Endometrial Carcinoma."
2. Project "Research University: Medical University – Pleven," within research group 3.1.5 "Artificial Intelligence in Gynecology," No. BG-RRP-2.004-0003, funded by the European Union – NextGenerationEU.