Role of preoperative imaging in the diagnosis and planning of surgical radicality of endometrial and cervical cancer

Ph.D. Thesis

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II. Bús D, Nagy G, Vajda G. A preoperatív mágnesesrezonanciavizsgálat klinikai jelentősége az I. stádiumú endometriumcarcinoma myometrialis infiltrációjának és nyirokcsomó-státuszának megítélésében. Magyar Nőorvosok Lapja. 2021, 84:37-41.

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III. Bús D, Buzogány M, Nagy G, Vajda G. Rare virilizing granulosa cell tumor in an adolescent. Molecular and Clinical Oncology. 2017; 6:88-90.

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VI. Husz V, Bús D, Vajda Gy. Subpubicus képlet diagnózisának és terápiájának határterületi kérdései. Interdiszciplináris Magyar Egészségügy. 2017, 7: 47-50. 4.

VII. Goldfinger J, Bús D, Husz V, Nagy Gy, Tóth Z, Vernarelli F, Vajda Gy. Terhességet komplikáló kiterjedt petefészektumor. Interdiszciplináris Magyar Egészségügy. 2017, 7: 44-46. 5.

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1. Abbrevations

18F-FDG	2-deoxy-2-[fluorine-18]fluoro- D-glucose
BMI	Body mass index
CEA	Carcinoembryonal antigene
CIN	Cervical Intraepithelial Neoplasia
CT	Computer tomography
DNA	Deoxyribonucleic acid
DWI	Diffusion weighted imaging
EIC	Endometrial intraepithelial carcinoma
ESMO	European Society for Medical Oncology
ESUR	European Society of Urogenital Radiology
FIGO	International Federation of Gynecology and Obstetrics
HPV	Human papillomavirus
IARC	International Agency for Research on Cancer
ICC	Intraclass correlation coefficient
LEEP	Loop Electrosurgical Excision Procedure
MRI	Magnetic resonance imaging
NCCN	National Comprehensive Cancer Network
NPV	Negative predictive value
PET-CT	Positron emission tomography
PPV	Positive predictive value
SEER	Surveillance, Epidemiology and End Results Program
TNM	Tumor, nodes and metastasis System
TRUFISP	True fast imaging with steady state precession
US	Ultrasound
USA	United States of America

2. Summary of the thesis

Gynecological cancers are the most common tumors among women in the developed world. Due to a more excessive screening, diagnosis is available at an early stage. Furthermore, advanced diagnostic imaging methods allow appropriate preoperative staging, therefore the radicality of surgery and adjuvant therapy can be more tailored to the patient and the tumor-spread.

In this study we analyzed the reliability of preoperative MRI findings in the staging of endometrial and cervical cancer, as well as the clinical characteristics of patients underwent radical hysterectomy and the histopathologic evaluation of their tumor.

The results of the preoperative radiology staging were compared with the final histological analysis of the surgical specimen. The sensitivity, specificity, positive- and negative predictive values of the preoperative assessment were calculated for each endpoint. The percentage of the underdiagnosed or overdiagnosed cases and accuracy rate in terms of stage, local invasion and lymph-node metastases were also evaluated.

In order to analyze the role of the rater's expertise assessing the MRI findings, we divided the specialists into two groups: a radiologist specialized in imaging of gynecological tumors and a subgroup of non-specialized evaluators. Inter-rater agreement was calculated to determine the conformity of pre- and postoperative staging.

Based on our results, we report similar findings as found in international literature. MRI is the method of choice in the terms of evaluating overall staging, as well as myometrial and stromal invasion, as its specificity and negative predictive value is rather high. Our studies showed that the diagnosis of lymph node metastases is difficult with MRI modality, since hyperplastic and metastatic nodes cannot be easily differentiated leading to high percentage of false positive results, therefore other imaging modalities can be used for more accurate evaluation.

We have also found that more experienced raters in gynecological imaging provide more consistent evaluations of staging, local invasion and finding lymph node metastases, however, the difference between inter-rater agreements was not significant between the two groups.

3. Introduction

Gynecological cancers are the most common malignancies among women in industrialized countries.[1] According to the National Cancer Institute SEER[2] and IARC databases, the incidence and mortality of endometrial cancer is slightly increasing in the developing countries. It is estimated to be 3.5% of all cancer cases and 2.0% of all cancer-related deaths in 2019 in the USA. Due to a more excessive screening of cervical cancer, diagnosis is available at an early stage leading to decreased mortality, which is estimated to be 0.7% both in all cancer cases and all cancer-related deaths in 2019 in the USA.

Advanced diagnostic methods and imaging modalities, such as the worldwide available MRI and CT technology, allow staging and treatment to be based on histopathological and magnetic resonance findings. Therefore, the specificity and sensitivity of these diagnostic methods is of great importance in making an appropriate diagnostic choice and in determining the radicality of the treatment.[3]

3.1 Endometrial cancer

Endometrial cancer is the 9th most common cancer among women in developing countries. According to the National Cancer Institute SEER[2] and IARC databases the number of new cases of uterine cancer was 27.5 per 100,000 women per year, and the number of related deaths was 4.7 per 100,000 women per year in the USA – based on 2012-2016 statistics, with the prevalence of an estimated 61,880 new cases in 2019. The incidence is also increasing in Hungary, with an increase of 8% between 2010 and 2014, according to the Hungarian National Cancer Database. Despite the increase of incidence and mortality, the 5-year relative survival rate in the USA is 81.2% overall, with a 95% survival rate in localized tumors – based on data from SEER 18, 2009-2015.

Most cases of endometrial cancer are diagnosed in women aged between 45 and 74. Risk factors include extended hyperestrogenism (due to anovulation, nulliparity, polycystic ovarian syndrome or tamoxifen therapy), obesity (BMI>30), diabetes and hypertension. In rare cases (5% of endometrial cancers), tumors are associated with Lynch-syndrome type II. Symptoms of the cancer are postmenopausal bleeding and premenopausal menstrual disorder.[4]

Based on histopathological characteristics, two types of endometrial cancers have been recognized. Type 1: estrogen-dependent endometrioid adenocarcinomas represent 80% of cases, often strongly associated with endometrial hyperplasia. Type 2: estrogen-independent non-endometrioid forms, generally presenting as serous carcinomas, are often associated with a form of endometrial intraepithelial carcinoma (EIC) as precursor lesion.[5]

Diagnosis is based on dilatation and curettage, minimally invasive methods (endometrial biopsy, hysteroscopy) and vaginal ultrasound scan. MR imaging is the modality of choice for staging, with CT having relatively low specificity (especially for myometrial invasion).[6]

Endometrial cancer is generally staged according to the International Federation of Gynecology and Obstetrics (FIGO)[6] and TNM[7] system which is based on histopathological characteristics, tumor grade, rate of myometrial invasion, the presence or absence of lymph-node and distant metastases. (Table 1.)

TNM	**FIGO**	**Description**
T0	Stage 0	Carcinoma in situ
T1	Stage I	Cancer limited to the body of the uterus (or endocervical glandular involvement only)
T1a	Ia	No invasion or tumor invades less than one-half (≤ 50%) of the myometrium
T1b	Ib	Tumor invades one-half (≥ 50%) or more of the myometrium
T2	Stage II	Cervical stromal involvement
T3 and/ or N1	Stage III	Local or regional spread of the tumor
T3a	IIIa	Tumor invades the serosa of the body of the uterus and/or adnexa
T3b	IIIb	Vaginal or parametrial involvement
T3c	IIIc	Pelvic or para-aortic lymphadenopathy
T3c1	IIIc1	Positive pelvic nodes
T3c2	IIIc2	Positive para-aortic nodes with or without pelvic nodes
T4	Stage IV	Involvement of rectum and or bladder mucosa and or distant metastasis
T4a	IVa	Bladder or rectal mucosal involvement
M1	IVb	Distant metastases, malignant ascites, peritoneal involvement

Table 1. Based on Revised 2009 FIGO staging and TNM Classification of malignant tumours. [6,7]

3.2 Cervical cancer

Cervical cancer is still the 2nd most frequently diagnosed cancer, and the 3rd cause of cancer-related mortality among women in developing countries.[8] However, due to specific screening methods and their increasing availability, a decreasing rate of incidence and mortality is seen in both developing and developed countries. Cervical cancer represents 0.7% of all newly diagnosed cancer cases and of cancer-related deaths in the USA, with a prevalence of estimated 13,170 new cases and 4250 deaths in 2019, according to the to the National Cancer Institute SEER[2] and IARC databases. The incidence is also decreasing in Hungary, with a decrease of 28% between 2010 and 2016, according to the Hungarian National Cancer Database. The 5-year relative survival rate in the USA is 65.8% overall, with a 91.8% survival rate in localized tumors – based on data from SEER 18, 2009-2015.

Cervical cancer is usually diagnosed in women aged between 35 and 74, with a median age of 50. Its main risk factor is human papilloma virus (HPV) infection, with an increased prevalence in groups with certain epidemiologic risk factors, including first intercourse at a young age, sexually transmitted diseases, promiscuity, smoking, multiparity and chronic immunosuppression. The cancer is often asymptomatic in the early stages. The leading symptoms of an advanced cervical cancer are menstrual disorders, abnormal vaginal bleeding or discharge, postcoital contact bleeding or pain, abdominal pain and uraemia.[9,10]

Based on histopathological characteristics, squamous cell carcinoma represents 85% of all cases, while adenocarcinomas are less common, about 10%, and 5% of cases constitute other types, such as neuroendocrine tumors (small cell carcinoma) or other epithelial tumors. Cervical carcinomas usually originate in precursor lesions in the squamous or glandular epithelium, and are highly associated with HPV-derived lesions.[10]

Diagnosis is based on cervical cytology, colposcopy-guided cervical biopsy and HPV DNA testing.[11]

The clinical staging of cervical cancer is determined by tumor size, vaginal/parametrial involvement, or distant metastasis (based on physical examination, histopathology, colposcopy, cystoscopy and MR imaging results of the uterus, kidneys, lung and skeleton. Interpretation is based on FIGO[6] or TNM staging[7]. (Table 2.)[9]

TNM	FIGO	Description
T0	Stage 0	Carcinoma in situ
T1	Stage I	Limited to the cervix (or endocervical glandular involvement only).
T1a	IA	Invasive cancer identified only microscopically. Invasion is limited to measured stromal invasion with a maximum depth of 5 mm and no wider than 7 mm.
T1a1	IA1	Measured invasion of the stroma no greater than 3 mm in depth and no wider than 7 mm diameter.
T1a2	IA2	Measured invasion of stroma greater than 3 mm but no greater than 5 mm in depth and no wider than 7 mm in diameter.
T1b	IB	Clinical lesions confined to the cervix or preclinical lesions greater than Stage IA. (All gross lesions even with superficial invasion)
T1b1	IB1	Clinical lesions no greater than 4 cm in size.
T1b2	IB2	Clinical lesions greater than 4 cm in size.
T2	Stage II	Carcinoma that extends beyond the cervix but does not extend into the pelvic wall. The carcinoma involves the vagina but not as far as the lower third.
T2a	IIA	No obvious parametrial involvement. Involvement of up to the upper two-thirds of the vagina.
T2b	IIB	Obvious parametrial involvement, but not into the pelvic sidewall.
T3 and/ or N1	Stage III	Carcinoma that has extended into the pelvic sidewall. On rectal examination, there is no cancer-free space between the tumor and the pelvic sidewall. The tumor involves the lower third of the vagina. (All cases with hydronephrosis or a non-functioning kidney)
T3a	IIIA	No extension into the pelvic sidewall but involvement of the lower third of the vagina.
T3b and/ or M1	IIIB	Extension into the pelvic sidewall or hydronephrosis or non-functioning kidney.
T4	Stage IV	Carcinoma that has extended beyond the true pelvis or has clinically involved the mucosa of the bladder and/or rectum.
T4a	IVA	Spread of the tumor into adjacent pelvic organs.
M1	IVB	Spread to distant organs.

Table 2. Based on revised FIGO 2009 staging and TNM Classification of malignant tumours.[6,7]

3.3 Therapy and treatment

3.3.1. Endometrial cancer

Surgery is the primary treatment of endometrial cancer.

With a tumor confined to the uterus, total abdominal hysterectomy and bilateral salpingo-oophorectomy are performed. In stage II disease, radical hysterectomy is the treatment of choice.[12] An alternative therapeutic solution for stage II uterine cancer is regular hysterectomy followed with radiation treatment.[13]

In the case of serous-papillary and clear-cell tumors, omentectomy and lymph node extirpation are always performed.

Endometrioid tumors in stage IB with grade 3 are considered high risk with a recurrence rate of about 25%. Adjuvant irradiation to the pelvis reduces the frequency of local recurrences, but do not increase survival.

Serous papillary as well as clear cell tumors have a high risk for recurrence both in stage IA and in stage IB. Adjuvant irradiation to the pelvis reduces the frequency of local recurrences, but do not increase survival.[14]

In the case of patients with grade 3 tumor or more than 50% of myometrial invasion, furthermore for those diagnosed with carcinosarcoma or lymph node metastases, postoperative chemotherapy of carboplatin and paclitaxel should be considered.[14]

In stage II tumors, radical hysterectomy with bilateral salpingo-oophorectomy and pelvic and paraaortic lymph node staging are recommended with postoperative chemotherapy of carboplatin and paclitaxel.[15]

In stage III or IV tumors, radical hysterectomy with bilateral salpingo-oophorectomy and pelvic and paraaortic lymphadenectomy is the treatment of choice after neoadjuvant chemotherapy, and with supplemental postoperative radiotherapy or chemoradiotherapy.[16]

3.3.2. Cervical cancer

The choice of treatment depends on the stage of the disease.

Conisation is the treatment of choice in stage IA1 of the disease, CIN 2-3 lesions and cases with microinvasion with the lack of visible cancer. If fertility is not desired, a total or modified radical hysterectomy may be performed.

The traditional treatment for stages IA2 and IB2 is radical hysterectomy with pelvic lymph node dissection.[17,18] In women desiring future fertility, a radical trachelectomy with pelvic lymph node dissection is also considered to be an adequate treatment. In women with stage IB1, where the tumor is less than 2 cm in diameter, fertility sparing surgery can be considered as well.

Patients with positive lymph nodes, positive margins or parametrial involvement require postoperative treatment with radiation therapy to the pelvis to reduce the risk of recurrence. Radiation therapy is also recommended for patients with negative lymph nodes but with certain pathologic risk factors, including deep cervical stromal invasion, large tumor size or lymphovascular space invasion.[19]

Primary radiation therapy may also be given in cases where surgery is not advisable due to advanced age or other medical comorbidities.

In stages IIB to IVA of the disease, full radiation therapy with neoadjuvant chemotherapy is advisable. Cisplatin and a combination of external radiation therapy and brachytherapy is the method of choice.

In case of lymph node metastases in the common iliac or paraaortal area, radiation is applied to the paraaortal field as well.

In stage IVB cancer, palliative radio- or chemotherapy is considerable.[20]

4. Material and methods

4.1 Design

In the period between January 01, 2010 and December 31, 2019, 254 radical hysterectomies and lymphadenectomies were performed at the Department of Obstetrics and Gynecology of Zala County Saint Rafael Hospital due to endometrial or cervical cancer of the uterus.

Eligibility criteria included: 1. evidence of endometrial or cervical cancer of any type, grade or stage, confirmed by a preoperative endometrial or cervical sample, 2. available documentation on preoperative and postoperative cancer treatment stored in the Medical Network System database of the hospital, 3. achievable information of the preoperative clinical and imaging findings, 4. histological evaluation of endometrial or cervical cancer, 5. intraoperative findings, 6. postoperative histopathological staging and 7. data upon follow-up and treatment until the end of 2019.

Six patients were excluded from data collection due to the lack of preoperative MRI or CT findings, and 12 patients due to their missing data on follow-up.

Patients that underwent radical hysterectomy with a final histopathologic diagnosis of ovarian cancer were excluded from the study due to the low number of cases.

Data collection was approved by the Ethics Committee of the Hospital.

4.2 Diagnostic algorithm

On all patients with abnormal vaginal bleeding or positive Papanicolau-smear dilatation and curettage, cervical biopsy or conisation was performed. Based on a positive histopathological result of endometrial or cervical cancer, a preoperative radiological investigation was performed for local and distant cancer staging. Modalities involved magnetic resonance imaging, chest X-ray, transvaginal ultrasound and computer tomography, when necessary.

Based on radiologic staging, a multidisciplinary tumor board, consisting of an oncologist, a pathologist, a radiologist and a gynecologist, decided on the necessity of neoadjuvant oncological therapy and the radicality of hysterectomy with the possibility of involving a multidisciplinary surgical team in case local intestinal or urological metastases were found.

Staging was re-evaluated by the tumor board postoperatively, based on intraoperative and histopathological findings. A postoperative oncological therapy was designed individually for each patient.

Follow-up visits, conducted in the Department of Oncology and the Department of Gynecology, included routine physical and radiological check-ups.

4.3 Data collection

The following data were obtained from the Medical Network System database of the Hospital:

The age of the patient at the time of surgery, the surgical diagnostic methods (conisation, curettage, biopsy), preoperative MRI or CT findings and staging, the surgical description of the radical hysterectomy and lymphadenectomy, the histopathological type and stage of the tumor, postoperative treatment (irradiation, chemotherapy), recurrence of tumor or metastases in the follow-up period, 1- and 5-year mortality.

4.3.1. Surgical diagnostic methods

Preliminary histological evaluation and grading of the tumors were based on conisation, curettage or cervical biopsy performed at the Hospital.

LEEP (Loop Electrosurgical Excision Procedure) conisation and curettage of the residual endocervical canal were performed on patients with positive cytological screening test, severe cervical dysplasia or cervical cancer.

Cervical punch biopsy was performed in macroscopically visible cervical cancer cases where conisation was contraindicated due to the risk of bleeding.

Dilatation and curettage were performed in patients with abnormal or postmenopausal vaginal bleeding.

4.3.2 Radiology findings

The preoperative MRI was performed using a Siemens Magnetom Area 1.5 Tesla device. Data required for FIGO 2009 staging were collected: the degree of myometrial, cervical, serosal, adnexal and parametrial invasion (Figure 1 and 2.), as well as metastases of pelvic or para-aortic lymph nodes (Figure 3.)

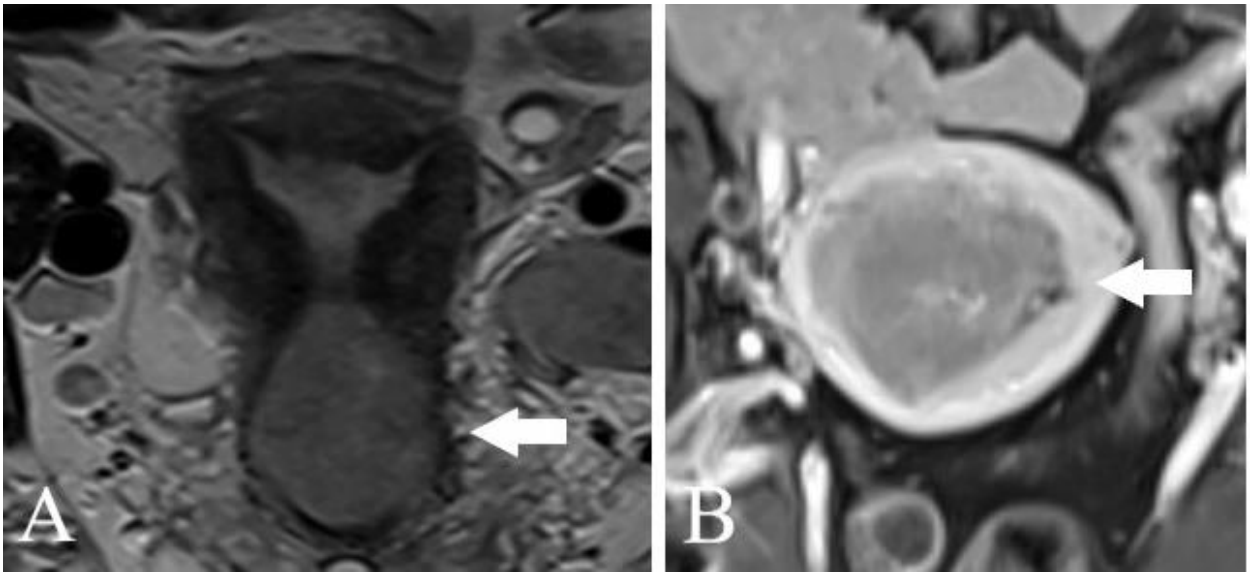

Figure 1. MR imaging. *A. Cervical cancer, stromal invasion (T2 sequence) B. Endometrial cancer, myometrial invasion >50% (T1 sequence)*

Images of the retroperitoneal, parailiacal, pelvic and cervical area were taken with axial oblique fat-saturated T1, sagittal and axial oblique fast spin-echo T2, T2 TRUFISP and DWI sequences, with gadolinium-based contrast medium.

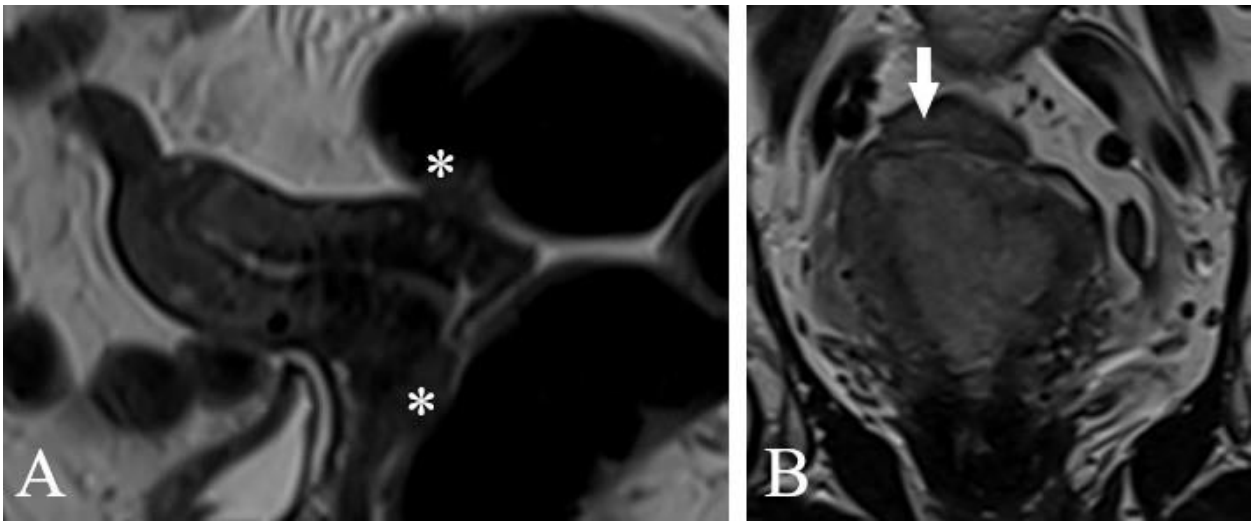

Figure 2 . MR imaging *A. Cervical cancer, tumour spread to upper third of vagina and rectum (T2 sequence, sagittal view)*
B: Endometrial cancer, mass is close to the serosa of the uterus. (T2 sequence, coronal view)

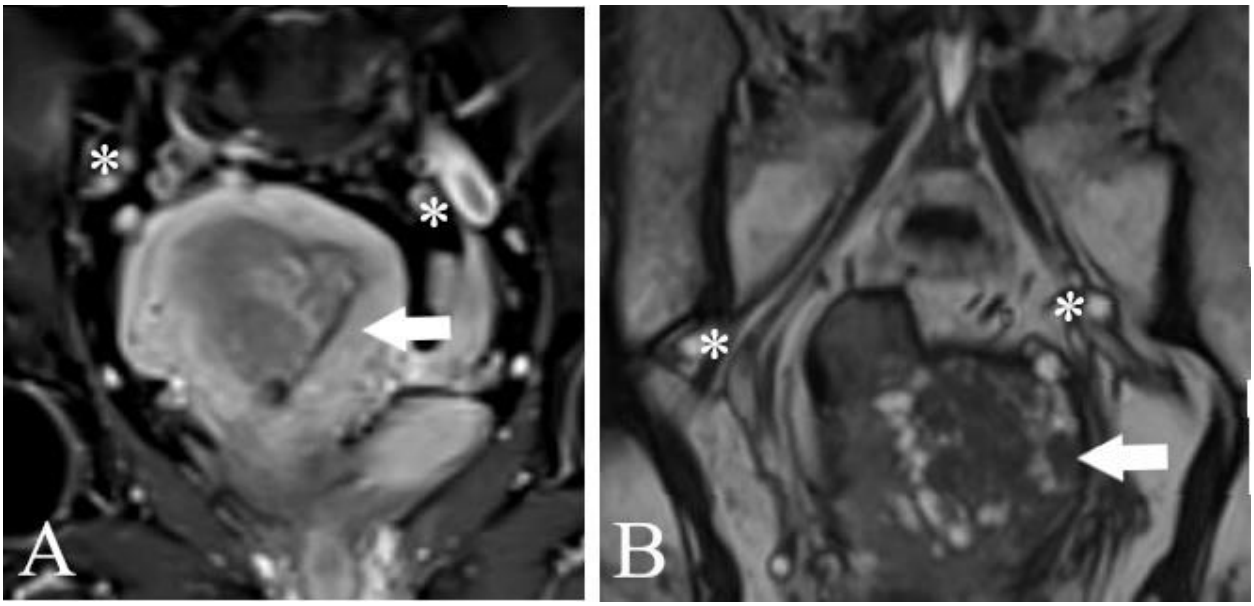

Figure 3 MR imaging. *Evaluation of lymph-node metastases. A.: Endometrial cancer, * enlarged lymph-nodes (T2 sequence, phase 3 of gadolinium enhancement). B.: Endometrial cancer with leiomyomas, * parailacal enlarged lymph nodes (T2 TRUFI sequence)*

Preoperative CT was performed in patients with contraindications for MRI or with extreme obesity using a Siemens Somatom Definition Edge device, with iobitridol as contrast medium. Osseal and pulmonary metastases were evaluated preoperatively for staging of distant tumor-spread.

Transvaginal ultrasound was performed using a GE Voluson E6 device with a multifrequency endovaginal probe (5-8 MHz); it had a role in evaluating cervical stroma infiltration, endometrial thickness and structure, adnexal and parametrial invasion, endometrial color-flow index and vascularization of the masses. (Figure 4 and 5.) Two-dimensional coronal and sagittal planes were used to assess myometrial invasion of the uterine corners, and 3D sampling frame was employed for more accurate evaluation.

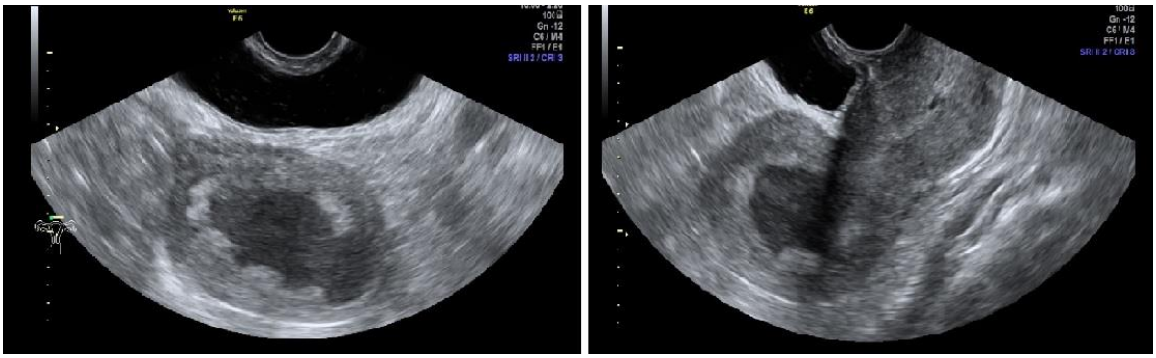

Figure 4. Transvaginal ultrasound*. Enlarged uterine cavity with necrotic mass. 2D imaging.*

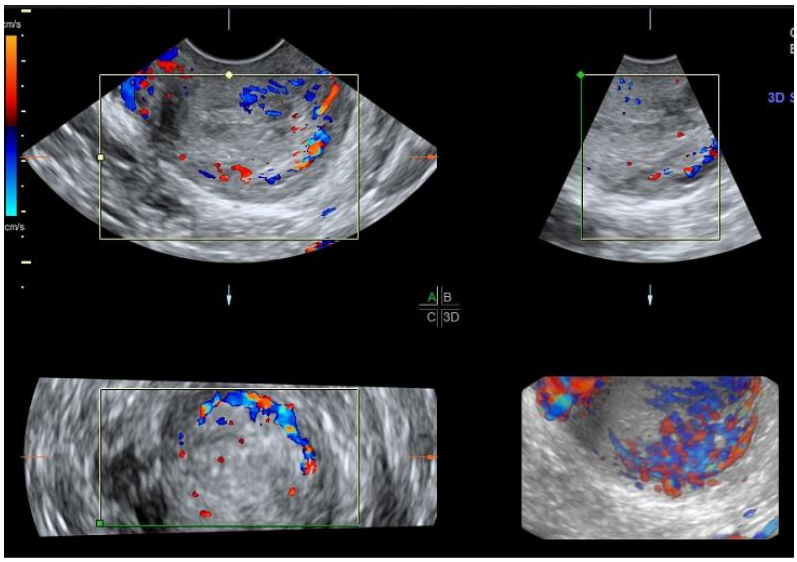

Figure 5. Transvaginal ultrasound. *Cervical cancer, 2D imaging and color-flow.*

4.3.3 Surgical treatment

Indication for surgery was based upon preoperative histological and radiological findings, indicated by the Multidisciplinary Tumor Board of the institution, which involves specialists of radiology, oncology, pathology and gynecology.

Abdominal, laterally extended radical hysterectomy was in all cases performed by a gynecologist and a urologist specialist trained in oncosurgery. Initial steps included catheterization of the ureter, followed by parailiacal and pelvic/obturator lymphadenectomy in the pelvic retroperitoneal space.

Radical hysterectomy included the removal of the cervix and uterus, Fallopian tubes and ovaries, together with the parametries and upper third of vagina. (Figure 6.)

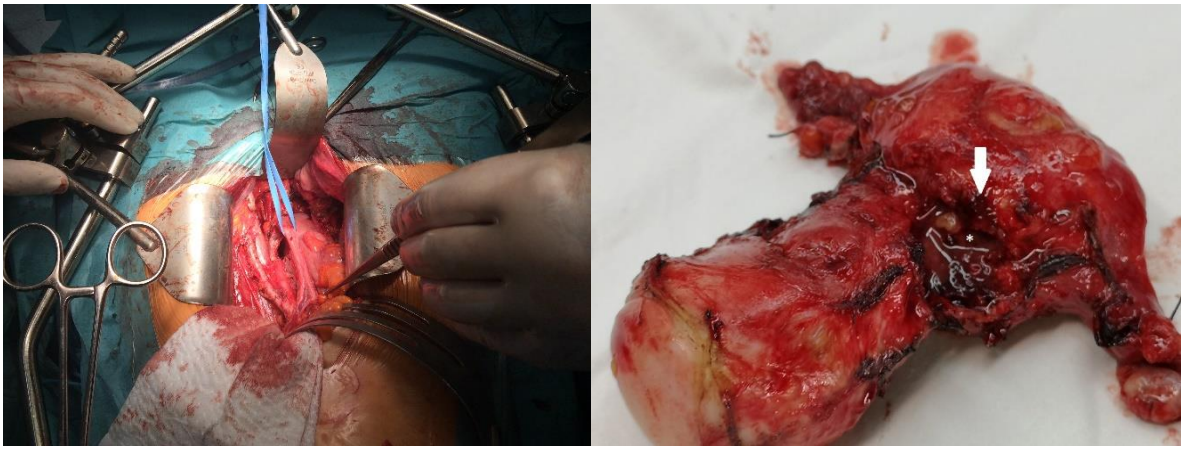

Figure 6. Intraoperative Picture *with preparation and surgical sample of the uterus (arrow: cancer spread beyond the uterinal wall)*

4.3.4 Histopathological evaluation

Macroscopic and microscopic histopathological evaluation of the surgical specimen were performed. Findings included the description of the type of tumor, differentiation, TNM and FIGO staging based on the extent of infiltration, and the presence or absence of parametrian, cervical, adnexal, rectal and urinary bladder involvement, lymph-node and pelvic wall invasion.

4.3.5 Postoperative treatment and follow-up

Method of adjuvant treatment was based on final histopathological staging, and was decided by the institutional Oncology Team as required by ESMO guidelines.

Postoperative irradiation in the form of external beam radiotherapy or brachytherapy was recommended in most cases. In patients with a high-risk of recurrence or with confirmed metastases, chemo- or radiochemotherapy was performed using cisplatin–5-fluorouracil, paclitaxel or carboplatin dublets.

Follow-up visits included a complete physical and pelvic examination performed by an oncologist and a gynecologist specialist, with regular radiology follow-ups to exclude the recurrence of cancer.

4.4 Statistical analysis

The age at the time of surgery, prevalence of different tumor histological subtypes, tumor grades and differentiation were taken into account at analysis. The 1- and 5-year survival rates were calculated accounting for deaths occurring before December 31, 2019.

The results of the preoperative radiology staging were compared with the final histological analysis of the surgical specimen, using $\chi 2$ or Fisher's exact test to compare variables. P-values of < 0.05 were considered to be significant. The sensitivity, specificity, positive- and negative predictive values of the preoperative assessment were calculated for each endpoint, together with 95 % confidence intervals (95 % CI). The percentage of the underdiagnosed or overdiagnosed cases and accuracy rate in terms of stage, local invasion and lymph-node metastases were also calculated.

All data were collected in an Excel database, and they were analyzed using SPSS statistical software. The intraclass correlation coefficient (ICC) and Cohen's kappa value were used to determine the inter-rater agreement of the overall results concerning myometrial invasion and lymph-node metastases, and to evaluate the role of experience between radiologist specialists. ICC and Cohen's kappa below 0.50 were considered as poor, between 0.50 and 0.75 as moderate, between 0.75 and 0.90 as good, respectively, and above 0.90 ICC it was considered as excellent inter-rater reliability. SPSS software (version 25; SPSS Inc., Chicago, IL, USA) was used for the statistical analyses, and p-values < 0.05 were considered to be significant.

5. Results

5.1 Endometrial cancer

A total of 148 patients with a final histopathological diagnosis of endometrial cancer were enrolled in this study. All patients underwent dilatation and curettage for endometrial sampling, those with a positive result were followed by MR staging of the tumor. Based on the decision of a multidisciplinary tumor board, radical hysterectomy with paraaortic and pelvic lymph-node dissection was performed. Pathologists used macroscopic and microscopic evaluations on hysterectomy specimen with a staining of hematoxylin and eosin, vimentin, estrogen, CEA and p16. Tumor histologic subtype, grade, depth of myometrial invasion and lymph-node positivity were examined. The tumor board evaluated the postoperative results and final stages, according to the FIGO 2009 classification to determine the optimal treatment for the patient.

The clinical and histopathological characteristics of the patients are seen in Table 3.

Age of the patients ranged from 37 to 87 years with a mean of 65.09+-9.54 years. of the majority of patients were postmenopausal (93.9%) (Figure 6) and overweight (body mass index > 25 kg/m2; 74.2%).

According to the decision of the tumor board, 1 patient had neoadjuvant chemotherapy (0.7%), 117 patients (79.1%) received adjuvant irradiation and 17 of them (11.5%) had the treatment of chemoirradiation. Fourteen patients (9.1%) were diagnosed with metastases (lung, osseal and lymph-node) and local recurrence occurred in 9 patients (6.1%) during the follow-up period, 96.4% of these patients received chemotherapy.

In the follow-up period, overall 16 patients died, 8 of the deaths were endometrial cancer-related. The overall 1-year mortality rate was 2.7% (0.7% cancer-related), 5-year mortality rate was 10.8% (5.4% cancer-related).

Postoperative histologic assessment revealed histopathologic subtype of endometrioid adenocarcinoma in 87.8 %, serous adenocarcinoma in 8.1 %, sarcoma in 3.4 % and other subtypes in 0.7 % of the cases, respectively. Based on FIGO 2009 classifications, the specimens were evaluated as stadium of IA in 35.1%, IB in 30.4%, II in 18.9%, IIIA in 4.1%, IIIB in 6.1%, IIIC in

0.7%, IVA in 2.0% and IVB in 1.4%, respectively. Seventy seven percent of the cases were diagnosed as high-grade, 23 % as low-grade tumors. (Figure 7.)

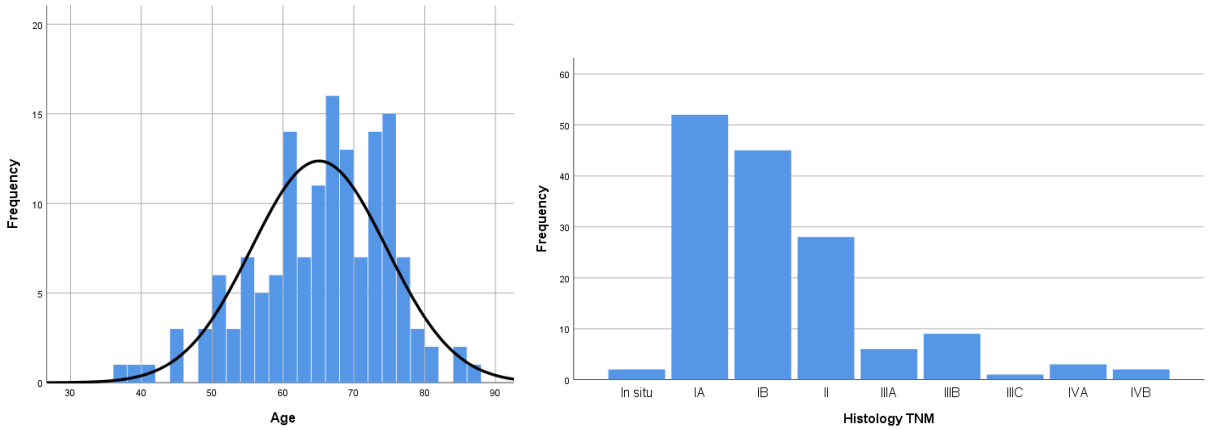

Figure 7 *A. Age of patients with endometrial cancer (years) B. Final stages of endometrial cancer (FIGO 2009 classification)*

Age (year)	65.09+-9.54 (37-87)	Stage (histology)	
Gravidity	2.29 +- 1.33 (0-10)	1	97 (65.5%)
Parity	1.74+-0.88 (0-4)	2	28 (18.9%)
Postmenopause	139 (93,9%)	3	16 (10.9%)
Grade		4	5 (3.4%)
1	34 (23%)	Positive lymph node status	26 (17.6%)
2	114 (77%)	Treatment	
Histologic subtype		Neoadjuvant chemotherapy	1 (0.7%)
Endometrioid adenocarcinoma	130 (87.8%)	Adjuvant irradiation	117 (79.1%)
Serous adenocarcinoma	12 (8.1%)	Adjuvant chemoirradiation	17 (11.5%)
Sarcoma	5 (4.3%)	Adjuvant chemotherapy (due to recurrence or metastases)	14 (9.5%)
Other	1 (0.7%)	Recurrence and/or metastasis	23 (15.6%)

Table 3. Characteristics. *Age, gravidity, parity: mean, SD, range. Postmenopausal state, grade, Histopathologic subtype, Stage, Treatment, Recurrence and metastasis: frequency (%)*

The overall accuracy of MRI evaluating the correct staging was 75%, with the intraclass correlation coefficient of 0.779 (0.695-0.840) and κ-coefficient of 0.474 (both with 95% confidence intervals [CI]; p <0,001). Rates of overdiagnosis were 10.8% and underdiagnosis 14.3% of the cases. (Table 4.)

The accuracy of MRI for the detection of lymph-node in all stages status was 74.3%, and its sensitivity, specificity, PPV, and NPV were 53.8%, 78.7%, 35%, and 88.9%, respectively, with the intraclass correlation coefficient of 0.425 (0.214-0.589) and κ-coefficient of 0.268 (both with 95% confidence intervals [CI]; p <0,001).. False negative results were 8.1%, false positive were 17.6% of the cases.

In stage I cancers, the accuracy of MRI regarding stage was 93.8%, with an underestimation in 6.2% of the cases.

The accuracy of MRI for the detection of myometrial invasion in stage I cancers was 70.1%, and its sensitivity, specificity, PPV, and NPV were 80.0%, 61.5%, 64.3%, and 78%, respectively, with the intraclass correlation coefficient of 0.591 (0.388-0.726) and κ-coefficient of 0.409 (both with 95% confidence intervals [CI]; p <0,001). The rates of overdiagnosis were 20.61%, and that of underdiagnosis were 9.27%.

The accuracy of MRI for the detection of lymph-node in stage I cases was 77.3%, and its sensitivity, specificity, PPV, and NPV were 28.6%, 81.1%, 10.5%, and 93.6%, respectively, with the intraclass correlation coefficient of 0.109 (-0.332-0.404) and κ-coefficient of 0.054 (both with 95% confidence intervals [CI]; p=0.054). False negative results were in 5.2% of cases, false positives in 17.5%, respectively.

In stage II cancers, the accuracy of MRI regarding stage was 32.1%. The MRI staging was underestimated in 11 and overestimated in 8 of the cases.

The accuracy of MRI for the detection of lymph-node in stage II cases was 60.7%, and its sensitivity, specificity, PPV, and NPV were 44.4%, 68.4%, 40%, and 72.2%, respectively, with the intraclass correlation coefficient of 0.223 (-0.680-0,640) and κ-coefficient of 0.125 (both with 95% confidence intervals [CI]; p=0.507). There were 6 false positive and 5 false negativecases with respect to the lymph-node status.

In advanced, stage III and IV cancers, the accuracy of MRI regarding stage was 52.38. The MRI staging was underestimated in 47,61% of the cases.

The accuracy of MRI for the detection of lymph-node in advanced stages cases was 80.95%, and its sensitivity, specificity, PPV, and NPV were 80%, 81.8%, 80%, and 81.8%, respectively, with the intraclass correlation coefficient of 0.764 (0.418-0.904) and κ-coefficient of 0.618 (both with 95% confidence intervals [CI]; p =0.005). There were 2 false positive and false negative cases as well.

	Acc (%, N)	**Sens** (%)	**Spec** (%)	**PPV** (%)	**NPV** (%)	**FP/OS** (%)	**FN/US** (%)	**P**	**ICC**	**κ**
All* **	75 N=111	63.3	93.9	83.8	83.8	10.8 N=16	14.3 N=21	0.000	0.779	0.474
Lymph node status *	74.3 N=110	53.8	78.7	35	88.9	17.6 N=26	8.1 N=12	0.001	0.432	0.268
Stage I *	93.8 N=91					6.2 N=6	7.2 N=7			
Myometrial invasion * **	70.10 N=68	80	61.5	64.3	78	20.61 N=20	9.27 N=9	0.000	0.591	0.409
Lymph node status	77.3 N=75	28.6	81.1	10.5	93.6	17.5 N=17	5.2 N=5	0.534	0.109	0.054
Stage II	32.1 N=9					28.6 N=8	39.3N= 11			
Lymph node status	60.7 N=17	44.4	68.4	40	72.2	21.4 N=6	17.9 N=5	0.507	0.223	0.125
Stage III/IV	52.38 N=11					0 N=0	47.61 N=10			
Lymph node status * **	81.3 N=17	75	87.5	85.	77.8	9.52 N=2	9.52 N=2	0.005	0.764	0.618

Table 4. Results*. Frequency (N) and Percentage (%). Sens: Sensitivity; Spec: Specificity; PPV: Positive predictive value; NPV: Negative predistive value; FP: False positive; OS: Overstaging; FN: False negative; US: understaging. P: significance value, ICC: intraclass correalation coefficient, κ: Cohen's kappa value*

*p<0.05 **moderate to excellent inter-rater reliability (ICC >0.500)

In order to analyze the role of the rater evaluating the MRI findings, we divided the specialists into two groups: a radiologist specialized in imaging of gynecological tumors and a subgroup of non-specialized evaluators. (Table 5.)

A radiologist specialized in the evaluation of gynecological imaging staged 94 cases. The accuracy of overall staging was 75.5%, with the intraclass correlation coefficient of 0.779 (0.790-0.908) and κ-coefficient of 0.514 (both with 95% confidence intervals [CI]; p <0,001), with understaging in 11.8% and overstaging in 12.7%. Sensitivity, specificity, positive predictive value and negative predictive value were 71%, 92.1%, 81.50% and 86.60%, respectively.
The accuracy of the assessment of myometrial invasion was 73.77%, with a sensitivity, specificity, positive predictive value and negative predictive value of 80%, 61.5%, 64.3% and 78%, respectively, with the intraclass correlation coefficient of 0.591 (0.388-0.726) and κ-coefficient of 0.409 (both with 95% confidence intervals [CI]; p <0,001). The rate of myometrial invasion was understaged in 23.5% and overstaged 29.6% of the cases.
The accuracy of MRI for the detection of lymph-node with experienced rater was 69.1%, and its sensitivity, specificity, PPV, and NPV were 53.8%, 78.7%, 35%, and 88.9%, respectively, with the intraclass correlation coefficient of 0.432 (0.214-0.585) and κ-coefficient of 0.268 (both with 95% confidence intervals [CI]; p =0,001). False positive and negative rates were 26.8% and 6.8%, respectively.

In the second rater group, four radiologists of average experience in the evaluation of gynecological imaging staged 54 cases. The accuracy of overall staging was 74.07%, with the intraclass correlation coefficient of 0.546 (0.217-0.736) and κ-coefficient of 0.391 (both with 95% confidence intervals [CI]; p <0,001) with understaging in 9 and overstaging in 4 cases. Sensitivity, specificity, positive predictive value and negative predictive value were 50%, 97.2%, 90% and 79.5%, respectively.
The accuracy of the assessment of myometrial invasion was 69.40%, with a sensitivity, specificity, positive predictive value and negative predictive value of 90.9%, 52%, 45.4% and 90.9%, respectively, with the intraclass correlation coefficient of 0.576 (0.169-0.785) and κ-coefficient of 0.334 (both with 95% confidence intervals [CI]; p =0,015). The rate of myometrial invasion was overstaged in 1 and understaged in 10cases.

The accuracy of MRI for the detection of pathologic lymph-nodes for moderate-experienced raters was 83.3%, and its sensitivity, specificity, PPV, and NPV were 25%, 93.5%, 40% and 87.8%, respectively, with the intraclass correlation coefficient of 0.363 (0.098-0.630) and κ-coefficient of 0.219 (both with 95% confidence intervals [CI]; p=0,096). There were 3 false positive and 6 false negative cases.

	Acc (%, N)	**Sens** (%)	**Spec** (%)	**PPV** (%)	**NPV** (%)	**FP/OS** (%)	**FN/US** (%)	**P**	**ICC**	**κ**
Group 1 * **	75.5 N=71	71	92.1	81.5	86.6	12.7 N=12	11.8 N=11	0.000	0.779	0.514
Myometrial invasion * **	73.77 N=45	80	61.5	64.3	78	13.11 N=8	13.11 N=8	0.000	0.591	0.409
Lymph node status *	69.1 N=43	53.8	78.7	35	88.9	26.8 N=15	6.8 N=3	0.001	0.432	0.268
Group 2 * **	74.07 N=40	50	97.2	90	79.5	7.4 N=4	16.67 N=9	0.000	0.546	0.391
Myometrial invasion * **	69.40 N=25	90.9	52	45.5	92.9	2.8% N=1	27. N=10	0.015	0.576	0.335
Lymph node status	83.3 N=45	25	93.5	40	87.8	5.6 N=3	11.1 N=6	0.096	0.363	0.219

Table 5. Rater-related results. *Frequency (N) and Percentage (%). Sens: Sensitivity; Spec: Specificity; PPV: Positive predictive value; NPV: Negative predictive value; FP: False positive; OS: Overstaging; FN: False negative; US: understaging.*

*p<0.05 **moderate to excellent inter-rater reliability (ICC > 0.500)

5.2 Cervical cancer

A total of 88 patients with a final histopathological diagnosis of cervical cancer were enrolled in this study. Sixty-one patients (69.3%) underwent conisation due to abnormal citology result, or were diagnosed by dilatation and curettage (27 patients, 30.7%). The positive result was followed by MRI staging of the tumor. Based on the decision of a multidisciplinary tumor board, radical hysterectomy with paraaortic and pelvic lymph-node dissection was performed. Pathologists used macroscopic and microscopic evaluations on hysterectomy specimen with a staining of hematoxylin and eosin, p16, direct HPV, Ki-67 and p53 tests. Tumor histologic subtype, grade, depth of stromal and parametrian invasion and lymph-node positivity were examined. The tumor board evaluated the postoperative results and final stages according to the FIGO 2009 classification were determine for optimal treatment of each patient.

The clinical and histopathological characteristics of the patients are seen in Table 6.

Age of the patients ranged from 33 to 73 years with a mean of 53,26+11,06 years. (Figure 8.) Fifty-three patients were in postmenopause (60.2%) and body mass index was between 19–53.2, with only 23% overweight patients (body mass index > 25 kg/m2)

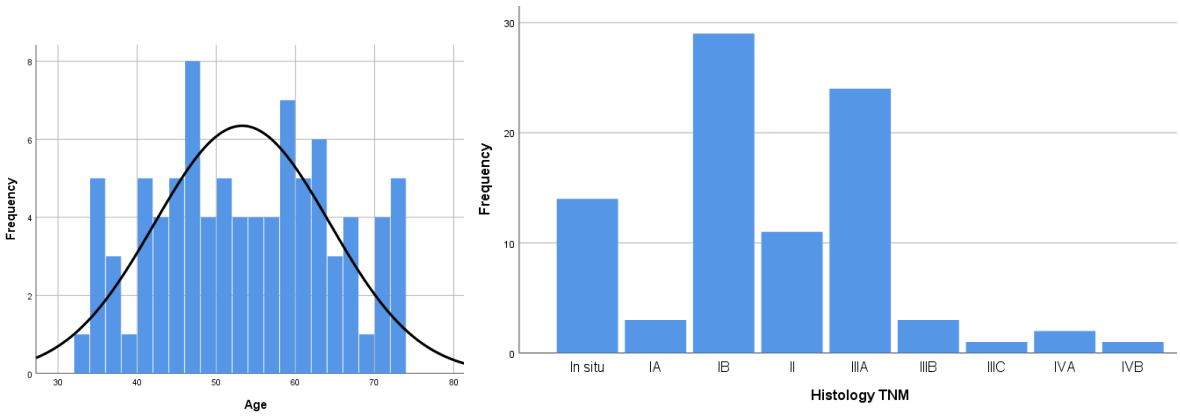

Figure 8 *A. Age of patients with cervical cancer (years) B. Final stages of cervical cancer (FIGO 2009 classification)*

According to the decision of the tumor board, 3 patients had neoadjuvant chemotherapy (3,4%), 58 patients (68,9%) received adjuvant irradiation and 18 of them (20,5%) had the treatment of chemoirradiation. Eleven patients (12,6%) were diagnosed with metastases (lung, brain, osseal and lymph-node) and local recurrence occurred in 6 patients (6,8%) during the follow-up period, 98,2% of these patients received chemotherapy.

In the follow-up period, overall 12 patients died, 5 of the deaths were cervical cancer-related. The overall 1-year mortality rate was 5,7% (4,5% cancer related), 5-year mortality rate was 12,5% (5,7% cancer-related).

Postoperative histologic assessment revealed histopathologic subtype of keratoid squamous-cell cancer in 44,3 %, nonkeratoid squamous-cell cancer in 47,7 %, adenocarcinoma in 5,7 % and other subtypes (adenosquamous and small-cell carcinoma) in 2,3 % of the cases. Based on FIGO 2009 classifications, the specimens classified as stadium of IA in 3,4%, IB in 33,0%, IIA in 12,5%, IIB in 27,3%, IIIA in 3,4%, IIIB in 1,1%, IVA in 2,3% and IVB in 1,1%, respectively. Thirty-nine point eight percent of the cases were diagnosed as well-differentiated, 47,7 % as medially-differentiated and 12,5% as poorly-differentiated tumors. (Figure 8.)

Age	53.26+-11.06 (33-73)	Stage (histology)	
Gravidity	2.55 +- 1.65 (0-8)	In situ cancer	14 (15.9%)
Parity	1.84+-1.15 (0-6)	1	34 (38.6%)
Postmenopause	53 (60.2%)	2	33 (37.5%)
Grade		3	4 (4.5%)
1	35 (39.8%)	4	3 (3.4%)
2	42 (47.7%)	Positive lymph node status	29 (33.0%)
3	11 (12.5%)	Treatment	
Histologic subtype		Neoadjuvant chemotherapy	3 (3.4%)
Keratoid squamous cell	39 (44.3%)	Adjuvant irradiation	58 (65.9%)
Non-keratoid squamous cell	42 (47.7%)	Adjuvant chemoirradiation	16 (20.5%)
Adenocarcinoma	5 (5.7%)	Adjuvant chemotherapy (due to recurrence or metastases)	10 (11.4%)
Other	2 (2.3%)	Recurrence and/or metastasis	12 (11.01%)

Table 6. Characteristics. *Age, gravidity, parity: mean, SD, range. Postmenopausal state, grade, Histopathologic subtype, Stage, Treatment, Recurrence and metastasis: frequency (%)*

The overall accuracy of MRI evaluating the correct staging was 61.4%, with the rates of overdiagnosis in 31.8% and underdiagnosis in 6.8% of the cases, with the intraclass correlation coefficient of 0.824 (0.731-0.885) and κ-coefficient of 0.425 (both with 95% confidence intervals [CI]; p <0,001). Sensitivity, specificity, PPV, and NPV were 87.5%, 68.6%, 70% and 86.8%, respectively. (Table 7.)

The accuracy of MRI for the detection of lymph-node status was 67%, and its sensitivity, specificity, PPV, and NPV were 58,6%, 71,2%, 50%, and 77.8%, respectively, with the intraclass correlation coefficient of 0.447 (0.155-0.638) and κ-coefficient of 0.286 (both with 95% confidence interval [CI]; p =0,007). False negative and positive rates were 13.6% and 19.3%, respectively.

In stage I cancers, the accuracy of MRI regarding stage was 61.8%, with an underestimation in 13 cases (38.2%).

The accuracy of MRI for the detection of stromal invasion was 79.4%, and its sensitivity, specificity, PPV, and NPV were 80%, 75%, 96%, and 33.3%, respectively, with the intraclass correlation coefficient of 0.553 (0.106-0.777) and κ-coefficient of 0.357 (both with 95% confidence intervals [CI]; p =0,019). The rate of overdiagnosis was 2.9%, and that of underdiagnosis was 17.6%.

The accuracy of MRI for the detection of pathologic lymph-nodes in stage I cases was 70.6%, and its sensitivity, specificity, PPV, and NPV were 66.7%, 71.4%, 33.3%, and 90.9%, respectively, with the intraclass correlation coefficient of 0.457 (0.087-0.729) and κ-coefficient of 0.274 (both with 95% confidence intervals [CI]; p =0.076). False negative results were 5.9%, false positives 23.5%, respectively.

In stage II cancers, the accuracy of MRI regarding stage was 72.7%. MRI staging was underestimated in 15.1% and overestimated in 12.2% of the cases.

The accuracy of MRI for the detection of abnormal lymph-nodes in stage II cases was 54.5%, and its sensitivity, specificity, PPV, and NPV were 58.8%, 50%, 55.6%, and 53.3%, respectively, with the intraclass correlation coefficient of 0.163 (0.069-0.586) and κ-coefficient of 0.088 (both with 95% confidence intervals [CI]; p=0.611). False negative results were detected in 21.2%, false positives in 24.2% of the cases.

In advanced, stage III and IV cancers, the accuracy of MRI regarding stage was 85.7%. The MRI staging was underestimated in 14.3% of the cases.

The accuracy of MRI for the detection of lymph-node in advanced stages was 50%, and its sensitivity, specificity, PPV, and NPV were 60%, 50%, 75%, and 33.3%, respectively, with the intraclass correlation coefficient of 0.167 (0.038-0.857) and κ-coefficient of 0.0.87 (both with 95% confidence intervals [CI]; p =0,809). There were 2 false negative and 1 false positive lymph-node detection.

	Acc (%, N)	**Sens** (%)	**Spec** (%)	**PPV** (%)	**NPV** (%)	**FP/OS** (%)	**FN/US** (%)	**P**	**ICC**	**κ**
All* **	61.4 N=54	87.5	68.8	70	86.8	31.8 N=28	6.8 N=6	0.000	0.824	0.425
Lymph node status *	67 N=59	58.6	71.2	50	77.8	19.3 N=17	13.6 N=12	0.007	0.447	0.286
Stage I	61.8 N=21						38.2 N=13			
Stromal invasion * **	79.4 N=27	80	75	96	33.3	2.9 N=1	17.6 N=6	0.019	0.553	0.357
Lymph node status *	70.6 N=24	66.7	71.4	33.3	90.9	23.5 N=8	5.9 N=2	0.076	0.457	0.274
Stage II * **	72.7 N=24					12.2 N=4	15.1 N=5			
Lymph node status	54.5 N=18	58.8	50	55.6	53.3	24.2 N=8	21.2 N=7	0.611	0.163	0.088
Stage III/IV * **	85.7 N=6					0 N=0	14.3 N=1			
Lymph node status	50 N=4	60	50	75	33.3	12.5 N=1	25 N=2	0.809	0.167	0.087

Table 7 Results. *Frequency (N) and Percentage (%). Sens: Sensitivity; Spec: Specificity; PPV: Positive predictive value; NPV: Negative predictive value; FP: False positive; OS: Overstaging; FN: False negative; US: understaging P: significance based on Chi-square or Fisher's exact test, ICC: intraclass correlation coefficient, κ: Cohen's kappa value*

*p<0.05 **moderate to excellent inter-rater reliability (ICC >0.500)

In order to analyze the role of the rater evaluating the MRI findings, we divided the specialists into two groups: a radiologist specialized in imaging of gynecological tumors and a subgroup of non-specialized evaluators. (Table 8.)

A radiologist specialized in the evaluation of gynecological imaging staged 55 cases (62.5%). The accuracy of overall staging was 60%, with the intraclass correlation coefficient of 0.806 (0.668-0.887) and κ-coefficient of 0.406 (both with 95% confidence intervals [CI]; p <0,001). Understaging rates were 7.3% and overstaging 32.7% of the cases. Sensitivity, specificity, positive and negative predictive values were 87.5%, 68.8%, 70% and 86.8%, respectively.
The accuracy of the assessment of stromal invasion in stage 1 was 82.6%, with a sensitivity, specificity, positive predictive value and negative predictive value of 81.8%, 100%, 100% and 20%, respectively, with the intraclass correlation coefficient of 0.486 (0.211-0.782) and κ-coefficient of 0.281 (both with 95% confidence intervals [CI]; p =0.052). The rate of myometrial invasion was understaged in 4 cases and there were no overstaging.
The accuracy of MRI for the detection of pathologic lymph-nodes by an experienced rater was 61.8%, and its sensitivity, specificity, PPV, and NPV were 66.7%, 64.7%, 40% and 84.6%, respectively, with the intraclass correlation coefficient of 0.432 (0.338-0.759) and κ-coefficient of 0.258 (both with 95% confidence interval [CI]; p =0.183). Fourteen cases were false positive (25.5%) and 7 cases false negative (12.7%).

In the second rater group, four radiologists of average experience in the evaluation of gynecological imaging staged 33 cases. The accuracy of overall staging was 63.6%, with the intraclass correlation coefficient of 0.849 (0.694-0.925) and κ-coefficient of 0.457 (both with 95% confidence intervals [CI]; p <0,001). Understaging was found in 2 and overstaging in 10 cases. Sensitivity, specificity, PPV, and NPV were 86.7%, 72.2%, 72.2% and 86.7%, respectively.
The accuracy of the assessment of stromal invasion in stage 1 tumors was 72.7%, with a sensitivity, specificity, positive predictive value and negative predictive value of 75%, 66.7%, 85.7% and 50%, respectively, with the intraclass correlation coefficient of 0.556 (0.140-0.880) and κ-coefficient of 0.377 (both with 95% confidence intervals [CI]; p =0,201). Myometrial invasion was overstaged in 1 and understaged in 2 cases.

The accuracy of MRI for the detection of pathologic lymph-nodes by moderate-experienced raters was 75.8%, and its sensitivity, specificity, PPV, and NPV were 44.4%, 87.5%, 57.1%, and 80.8%, respectively, with the intraclass correlation coefficient of 0.515 (0.018-0.760) and κ-coefficient of 0.343 (both with 95% confidence intervals [CI]; p=0,046). There were 3 false positive and 5 false negative cases with regard to the lymph-node status.

	Acc (%, N)	**Sens** (%)	**Spec** (%)	**PPV** (%)	**NPV** (%)	**FP/OS** (%)	**FN/US** (%)	**P**	**ICC**	**κ**
Group 1 * **	60.0 N=33	87.5	68.8	70	86.8	32.7 N=18	7.3 N=4	0.000	0.806	0.406
Stromal invasion	82.6 N=19	81.8	100	100	20	0	18.2 N=4	0.052	0.486	0.281
Lymph node status	61.8 N=34	66.7	64.7	40	84.6	25.5 N=14	12.7 N=7	0.183	0.432	0.258
Group 2 * **	63.6 N=21	86.7	72.2	72.2	86.7	30.3 N=10	6.1 N=2	0.000	0.849	0.457
Stromal invasion **	72.7 N=8	75	66.7	85.7	50	9.1 N=1	18.2 N=2	0.201	0.556	0.377
Lymph node status * **	75.8 N=25	44.4	87.5	57.1	80.8	9.1 N=3	15.2 N=5	0.046	0.515	0.343

Table 8. Rater-related results. *Frequency (N) and Percentage (%). Sens: Sensitivity; Spec: Specificity; PPV: Positive predictive value; NPV: Negative predictive value; FP: False positive; OS: Overstaging; FN: False negative; US: understaging*
P: significance based on Chi-square or Fisher's exact test, ICC: intraclass correlation coefficient, κ: Cohen's kappa value

*p<0.05 **moderate to excellent inter-rater reliability (ICC >0.500)

6. Discussion

The aim of our study was to evaluate the role and reliability of preoperative imaging and staging in the planning process, regarding the radicality of surgery in gynecological cancers.

According to the 2018 FIGO staging revision, gynecological and pathological examinations, as well as imaging assessments are incorporated in the staging of gynecological cancers. Countries with a developed healthcare system have already been using various imaging modalities at pretreatment and staging, leading to an increased diagnostic accuracy, and therefore to a more tailored surgical and oncological treatment. [21]

The National Cancer Comprehensive Network (NCCN) guidelines for cervical and endometrial cancer recommend pelvic MRI, chest radiography or CT, or whole body PET-CT for primary diagnostics in the evaluation of local tumor extent and metastases.

MRI has been considered the imaging method of choice for the assessment of tumor size, localization, parametrial-, myometrial- and stromal infiltration and lymph-node status.[22] With at least two T2-weighted sequences in sagittal, axial oblique or coronal oblique orientation, local tumor extension and parametrial invasion can be evaluated. An axial T1-weighted sequence is used for the detection of enlarged pelvic or abdominal lymph nodes; however, CT and MRI tend to have low sensitivity for metastatic lymph-node status: since enlarged metastatic and hyperplastic nodes are hard to differentiate, the criteria based on the size often lead to overlooking smaller metastases.[23]

6.1 Endometrial cancer

In the developed world, endometrial cancer is one of the most common malignant gynecological cancer types. Due to the currently available diagnostic modalities and patient education, the early detection of the tumor leads to high overall survival. Prognostic factors include histopathologic subtypes, grade, myometrial invasion and lymph node metastases.

In the detection and staging of endometrial cancer, patients with abnormal vaginal bleeding are candidates for endometrial thickness evaluation by transvaginal ultrasound technique; however, a definitive diagnosis requires endometrial sampling by biopsy or dilatation and curettage for histopathological evaluation.[24]

In the preoperative staging, MRI is considered as the best method of choice to assess myometrial invasion depth, cervical involvement and tumor grade, as well as raise the probability of lymph node metastases. NCCN and ESUR advise MR imaging in type II endometrial cancers, suspected cervical invasions and to identify patients with stage Ia disease.[25] As patients with type I endometrial cancer with myometrial invasion of more than 50%, or with type II endometrial cancer are considered to be intermediate to high-risk of lymph node metastasis, preoperative staging is essential for a tailored pre- and postoperative treatment, and for planning the radicality of the surgical treatment.[26]

6.1.1 Accuracy of pre-and postoperative staging in endometrial cancer

According to our findings, the overall accuracy of MRI in regards of staging and identifying lymph node metastases was 75% and 74.3% with high specificity, high negative predictive value and low sensitivity. (Figure 9.) As the majority of the tumors are detected at an early stage, the high sensitivity of MRI for myometrial invasion, its moderate specificity and high negative predictive value for lymph node metastases in stage I diseases means that this modality plays an essential role in planning the radicality of hysterectomy and lymphadenectomy in localized tumors. However, due to its low sensitivity and low positive predictive value for lymph node detection, a considerable number, 17.5%, of surgeries at an early stage were complemented with lymphadenectomy due to false positive MRI results.[27] In literature reviews of the past few years' studies similar results were reported, showing satisfactory specificity but low sensitivity in regards to lymph node detection due to similar radiological findings of hyperplastic and metastatic lymph-node enlargement.[28]

At advanced stages (stage II-IV) the overall accuracy of MRI was moderate, with relatively high negative predictive value. In terms of lymph-node status, 60.7-80.95% of the metastases were evaluated correctly; however, due to the low number of advanced cases, the results were not considered statistically significant. As the postoperative treatment of endometrial cancer in advanced stages depends on further imaging and pathological findings, such as tumor grade, histopathological subtype and presence or absence of distant metastases, our detection rate of lymph node metastases with MRI modality is satisfactory in order to make the most tailored

decision for post-staging treatment, which leads to only 5.4% cancer-related 5-year mortality at our hospital.

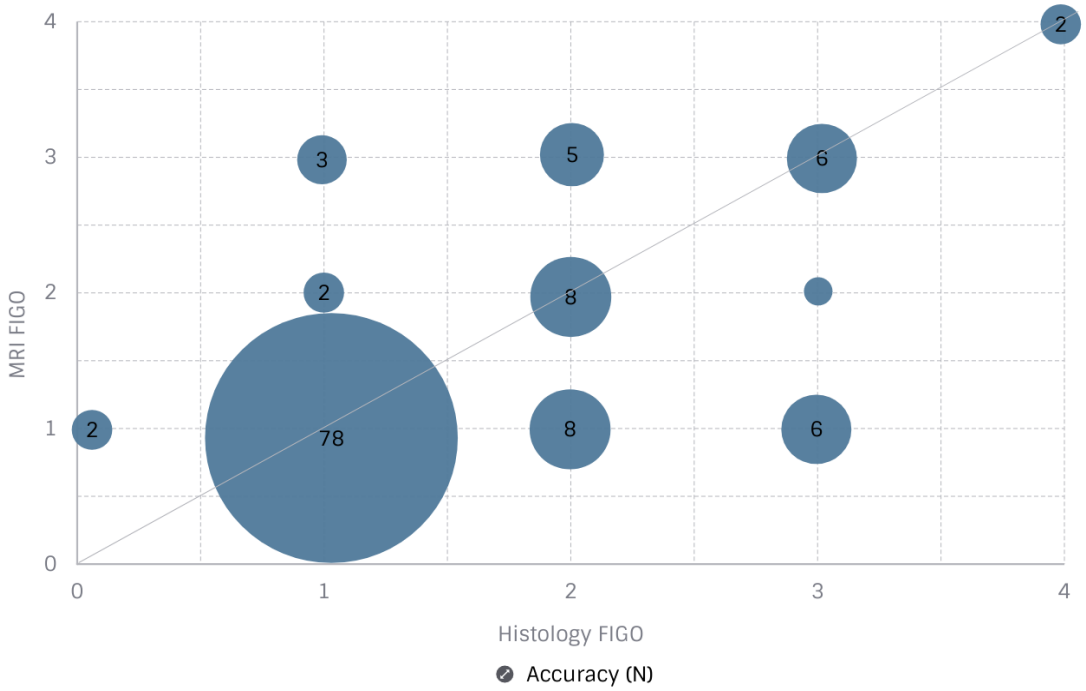

Figure 9. Accuracy *between MRI and histology evaluation.*

Another main objective of our study was to analyze inter-rater agreement. Due to a high BMI in 74.2% of our patients and to the high percentage of stage I disease, which presents difficulty in lymph-node evaluation, we studied, whether there is a significant difference between the findings of a radiologist specialized in gynecological tumors and of a non-specialized radiologist, in endometrial cancer cases.

Overall MRI staging, in comparison with histopathological staging had good inter-rater agreement with ICC of 0.742-0.865, with good to excellent agreement with specialized radiologists and moderate to good agreement with non-specialized radiologists. In terms of accuracy, there was no significant difference between the two groups. In group 1, sensitivity, specificity, positive and negative predictive values were more consistent and satisfactory than in group 2. Findings of radiologists with less gynecological experience showed higher sensitivity for myometrial invasion and higher specificity for lymph node evaluation. Both groups had moderate agreement with

histopathologic staging, when assessing the rate of myometrial invasion and poor to moderate agreement regarding the detection of lymph node metastases, compared to final pathologic results. (Figure 10.)

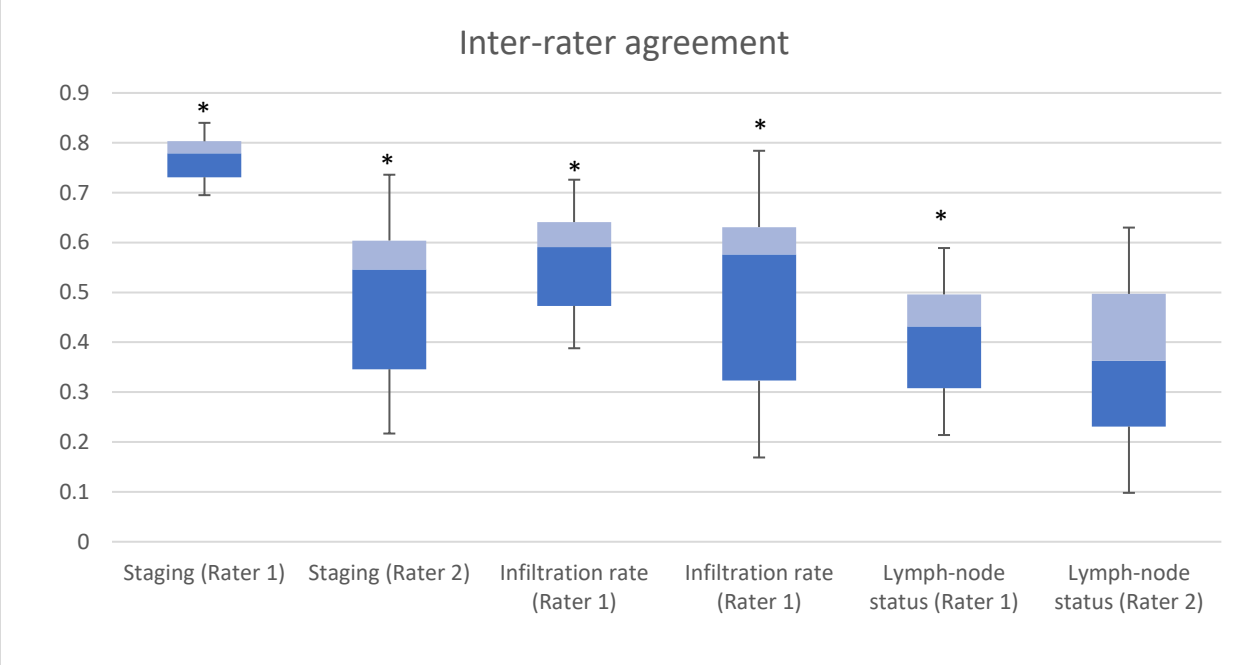

Figure 10. Inter-rater agreement *between MRI and histopathologic staging based on intraclass correlation. *p<0.05*

Compared to CT and MRI studies recommend 18F-FDG PET-CT, which allows more accurate staging and detection of lymph node metastases, as MRI can only find lymph node metastases when the nodes are swollen, with a diameter of >10mm.[29]

Unfortunately, PET-CT for preoperative investigation is still not routinely supported by health insurance in Hungary, and only special cases are evaluated with this imaging technique, such as ovarian cancer cases and investigations of remote metastases.

A 2D and 3D transvaginal ultrasound examination is (routinely) used in preoperative evaluation of staging in middle-income countries. Some studies have shown, that its accuracy and positive predictive value is equal to that of an MRI finding, assuming we can rely on an experienced investigator.[30] In our study, we started using the ultrasound modality only with patients presenting after June of 2017 to improve preoperative diagnostics ; therefore, we have a low number of ultrasound findings. Where transvaginal ultrasound was used for preoperative imaging, the

positive findings propounded the necessity of taking histological samples, such as curettage, and were useful for the early detection and diagnosis of endometrial cancer.

Limitations to the findings are that normal-sized metastatic lymph nodes can be hard to identify during surgery, so samples without metastatic masses can lead to false negative results. As histopathological results were used as endpoints during staging, errors and mis-staging of surgical samples became possible.

6.2 Cervical cancer

Cervical cancer is the most common gynecologic malignancy, with one of the leading causes of cancer-related deaths among women. In developed countries the more attainable screening system allows us to diagnose most of the tumors at an early stage, based on an abnormal Pap-smear, conisation or dilatation and curettage.

Prognostic factors include histopathological subtypes, grade, stromal and parametrian invasion and lymph node metastases.[31]

Similarly to cases of endometrial cancer, MRI is considered as the best method of choice in preoperative staging, due to its high soft tissue resolution and increasing availability.[32]

Primary treatment of cervical cancer is planned with regard to the clinical and imaging staging, and it involves conisation, simple or radical hysterectomy with pelvic lymphadenectomy in stages more advanced than 1a1. Lymph node status is crucial for guiding the target volume of adjuvant chemo-radiotherapy, therefore, paraaortic dissection may be considered in addition to the hysterectomy.[9]

6.2.1 Accuracy of pre-and postoperative staging in cervical cancer

According to our findings the overall accuracy of MRI in regards of staging was 61.4%, with high sensitivity and high negative predictive value, and the accuracy of lymph node evaluation was 67%, with high specificity and high negative predictive value. (Figure 11.) The majority of the tumors were detected in stage I and II, with the accuracy of 61.8% and 72.7%, respectively. The sensitivity and positive predictive value of stromal invasion was high in stage I diseases, with only 6 understaged cases. In the review of literature MRI is considered as the modality of choice in planning the radicality of the hysterectomies, with similar results to ours.[33]

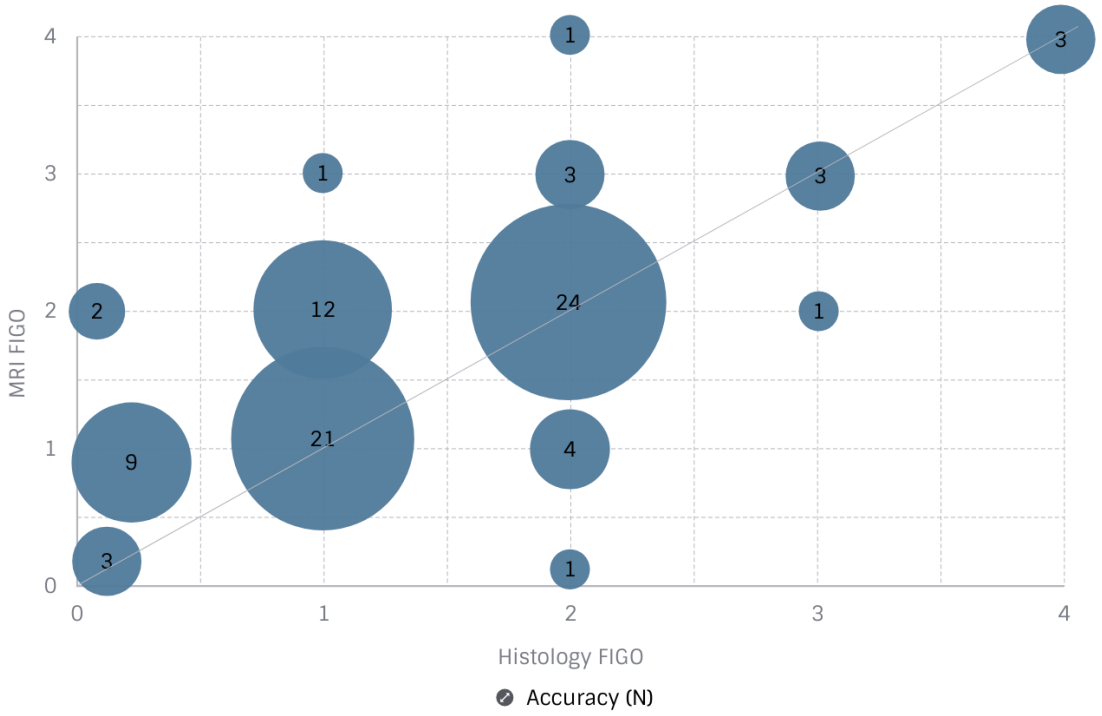

Figure 11. Accuracy *between MRI and histopathologic findings.*

In advanced stages (stage III-IV) the overall accuracy was high, with relatively high sensitivity and positive predictive value in the terms of the lymph-node status; however, due to the low number of advanced cases, it was not considered statistically significant.

Analyzing inter-rater agreement we divided the radiology findings into two subgroups, with one specialized and four non-specialized evaluators. Overall, MRI staging in comparison with histopathological staging had good inter-rater agreement with ICC of 0.668-0.925, both with specialized and non-specialized radiologists, with no significant difference between the two groups. In terms of accuracy there was no significant difference between the two groups. In group 1, specificity and positive predictive values were higher in terms of stromal invasion, than in group 2. Group 2 had higher specificity and higher negative predictive value for lymph node evaluation. Both groups had a moderate level of agreement with stromal invasion and poor to moderate agreement with lymph node metastases. (Figure 12.)

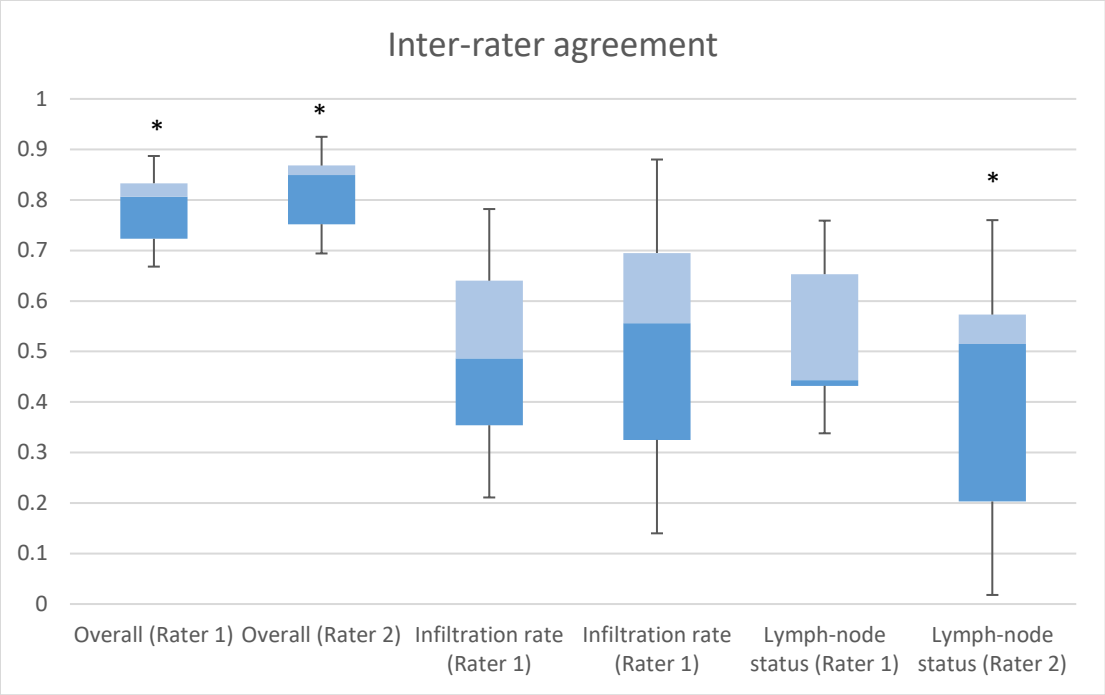

Figure 12. Inter-rater agreement *between MRI and histopathologic staging based on intraclass correlation.*
**p<0.05*

The role of transvaginal ultrasound in the diagnosis of cervical cancer was reported to be comparable to pelvic MRI in the assessment of deep stromal invasions and larger tumor sizes.[14] In our study we also have a low number of cervical cancer cases, where transvaginal ultrasound was used for preoperative imaging; however, for monitoring local recurrence it was used as an adjunct to MRI technique during follow-up studies.

Limitations to the findings are, that we have a low number of cervical cancer cases, and, the fact, that a mis-staging of histopathological samples could not be excluded.

7. Conclusion

Regarding the diagnostic methods, used for the diagnosis of cervical and endometrial cancer, a complex investigation is needed for more accurate staging. Transvaginal ultrasound is readily available in most gynecology departments, and it can be used for preliminary assumptions of cervical and myometrial involvement at low cost; however, its accuracy is highly dependent on the investigator's experience.

Pelvic MRI is considered to be the gold standard for staging gynecologic cancers. In terms of specificity and negative predictive value, our findings were similar that of the data of international literature. Limitations to the modality are that its positive predictive value regarding lymph-node metastases is low, therefore, in cases more advanced than stage Ia, paraaortic and pelvic lymphadenectomy should always be considered beside radical hysterectomy.

However, since an ultrasound modality at the initial phase of examinations proved to significantly improve diagnosis and allows more precise planning, other diagnostic methods are advisable to be considered to complement MRI findings for more accurate preoperative staging.

In conclusion, a combination of imaging modalities are needed for the proper evaluation of tumor size, propagation and staging, so that the radicality of the surgery and the involvement of a multidisciplinary team with a surgeon or an urologist specialist could be planned in advance.

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Clinical Impact of Preoperative Magnetic Resonance Imaging in the Evaluation of Myometrial Infiltration and Lymph-Node Metastases in Stage I Endometrial Cancer

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Abstract: Purpose: In the developed world, endometrial cancer is one of the most common malignant gynecological cancer types. Due to the highly available diagnostic modalities and patient education, the early detection of the tumor leads to high overall survival.

Methods: In this study we analyzed the reliability of preoperative MRI findings in the staging of early stage endometrial cancer, as well as the clinical characteristics of patients underwent radical hysterectomy and the histopathologic evaluation of their tumor, with the retrospective data of radical hysterectomies performed in our hospital between 2010 and 2019.

Results: The accuracy, sensitivity, specificity, negative- and positive predictive value of MRI regarding stage were 94.7, 63.3, 94.8, 83.8, and 83.8%, respectively. The accuracy, sensitivity, specificity, negative- and positive predictive value of MRI for the detection of the myometrial invasion were 69.8, 80.0, 60.8, 64.3, and 77.5%, respectively. The accuracy, sensitivity, specificity, negative- and positive predictive value of MRI for the detection of lymph node metastases were 78.1, 28.6, 82, 11.1, and 93.6%, respectively.

Conclusions: Based on our results, MRI is the method of choice in terms of evaluating overall staging, as well as myometrial invasion, as its specificity and negative predictive value are relatively high. However, systematic lymphadenectomy showed improved cancer-related survival and recurrence-free survival. Our studies showed that the diagnosis of lymph node metastases is difficult with MRI modality since hyperplastic and metastatic nodes cannot easily differentiate, leading to a high percentage of false-positive results. Therefore, other imaging modalities may be used for more accurate evaluation. New findings of our study were that the role of the radiologist's expertise in the evaluation of MR imaging plays an essential role in lowering false-negative and false-positive results. Therefore, findings evaluated by a radiologist with high-level expertise in gynecological imaging can complement the clinical findings and help substantially define the needed treatment.

Keywords: endometrial, MRI, Cancer, Radical hysterectomy, postoperative stage, preoperative stage

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INTRODUCTION

Endometrial cancer is the ninth most common tumor among women in developing countries. According to the National *Cancer* Institute Surveillance, Epidemiology, and End Results (SEER) Program, the International Agency for Research on *Cancer* (IARC) [1], and the Hungarian National *Cancer* databases [2], the incidence and mortality of uterine cancer is increasing. However, the 5-years relative survival rate is still around 81.2% overall, with a 95% survival rate in localized tumors—based on SEER 18 data of 2009–2016 [3].

Most endometrial cancer cases are diagnosed in women aged between 45 and 74.67.2% of the tumors are diagnosed at an early stage. Risk factors include extended hyperestrogenism, obesity, diabetes, and hypertension. Symptoms of the cancer are postmenopausal bleeding and premenopausal menstrual disorder [4].

Diagnosis is based on dilatation and curettage, minimally invasive methods (endometrial biopsy, hysteroscopy), and abnormally thickened endometrium on transvaginal ultrasound scan [5]. Magnetic resonance (MR) imaging is the modality of choice for staging, with computed tomography (CT) having relatively low specificity, especially for myometrial invasion. With relatively high specificity in terms of evaluating locoregional spreading, MRI can diminish the extension of hysterectomy [6].

Endometrial cancer is generally staged according to the International Federation of Gynecology and Obstetrics (FIGO) and TNM system, based on histopathological characteristics, tumor grade, rate of myometrial invasion, the presence or absence of lymph-node and distant metastases [7, 8]. As standard treatment of early stage endometrial cancer is total abdominal hysterectomy and adnexectomy, preoperative staging is crucial to further determine the radicality of surgery and the required neoadjuvant and adjuvant oncologic treatment. Pelvic or pelvic-paraaortic lymphadenectomy performed in early stages is still controversial and discussed in international literature [9].

Our study aimed to examine the accuracy of magnetic resonance imaging in TNM T1 stage cancers in evaluation of myometrial invasion and lymph node metastases compared with final histopathologic results.

MATERIAL AND METHODS

Our results were based on a retrospective, one-institute dataset between the years 2010 and 2019.

In this study, we examined the reliability of magnetic resonance imaging in stage I uterine endometrial adenocarcinoma cases of 9 years, selecting the patients with tumor of TNM stage 1 (TNM T1a or T1b), with or without lymph-node metastases (TNM N0 or N1), based on the final histopathologic evaluation of the surgical specimens. Patients with cervical, vaginal, parametrial, or locoregional involvement (TNM T2-4) or patients with distant metastases (TNM M1) were excluded from the study.

Between 2010 and 2019, 148 radical hysterectomies and lymphadenectomies were performed at the Department of Obstetrics and Gynecology of Zala County Saint Rafael Hospital due to endometrial adenocarcinoma of the uterus. 64.9% of the cases, a total of 96 surgical specimens were evaluated as TNM stage 1 tumors.

The following data were obtained from the Medical Network System database of the hospital: Age of the patient at the time of surgery, preoperative MRI staging, surgical description of the radical hysterectomy and lymphadenectomy, histopathological type of the tumor, postoperative treatment (irradiation, chemotherapy), recurrence of tumor or metastases in the follow-up period (from surgery until December 2019), 1- and 5-years mortality.

On all patients with abnormal vaginal bleeding, dilatation and curettage were performed. Based on a positive histopathological result of endometrial cancer, a preoperative radiological investigation was performed for local and distant cancer staging. Modalities involved magnetic resonance imaging, chest X-ray, transvaginal ultrasound and computed tomography, when necessary.

The preoperative MRI was performed using a Siemens Magnetom Area 1.5 T device. Data required for FIGO 2009 [7] and TNM [8] staging were collected: the degree of myometrial, serosal, adnexal, and parametrial invasion, as well as metastases of pelvic or para-aortic lymph nodes. Measurement of the deepest myometrial tumor invasion was done and classified into stage FIGO IA/TNM T1a (invasion depth less than half of the myometrial thickness) or FIGO stage IB/TNM 1 B tumor (invasion depth more than half of the myometrial thickness). Pelvic or para-aortic lymph node metastases were suspected based on nodal size criterion (short axis >1 cm). Images of the retroperitoneal, parailiac, pelvic, and cervical area were taken, with gadolinium-based contrast medium, sequences seen in **Table 1** (**Figures 1**, **2**).

Based on radiologic staging, a multidisciplinary tumor board, consisting of an oncologist, a pathologist, a radiologist, and a gynecologist, with a distant radiotherapist consultant, if needed, decided on the necessity of neoadjuvant oncological therapy and the radicality of hysterectomy with the possibility of involving a multidisciplinary surgical team was considered in case of local intestinal or urological metastasis.

Abdominal hysterectomy and adnexectomy was in all cases performed by a gynecologist and an urologist specialist trained in oncosurgery, combined with lateral extension in high-risk cases according to the ESMO-ESGO-ESTRO (2010 and 2016 revision) guidelines [9, 10].

Radical hysterectomy involved removing the cervix, uterus, Fallopian tubes, and ovaries, together with the parametria and upper vagina, followed by parailiacal and pelvic/obturator lymphadenectomy in the pelvic retroperitoneal space (**Figure 3**).

TABLE 1 | Imaging protocol of MRI.

Precontrast sequences						
Sequence	**Voxel size (mm)**	**FoV (mm)**	**Slice thickness (mm)**	**Slice number**	**TR (ms)**	**Te (ms)**
Coronal TRUFISP T2	1.0 × 1.0 × 5.0	330	5.0	26	4.17	1.62
Coronal T1 spin echo	0.9 × 0.9 × 4.0	400	4.0	26	589	12
Sagittal T2 spin echo	0.5 × 0.5 × 3.5	240	3.5	48	3,930	97
Axial T2 spin echo	0.5 × 0.5 × 4.0	240	3.5	36	3,080	93
Coronal T2 spin echo	0.5 × 0.5 × 3.5	240	3.5	36	3,080	93
Axial and sagittal DWI	2.0 × 2.0 × 5.5	380	5.5	20	4,700	85
Axial fat-sat T1 spinecho	1.2 × 1.2 × 4.5	300	4.5	32	584	7.8
Axial and coronal fat-sat T1 VIBE (until 2019 January)	1.4 × 1.4 × 1.4	400	1.4	Slices per slab: 144	6.82	2.89
Postcontrast sequences						
Sequence	**Voxel size (mm)**	**FoV (mm)**	**Slice thickness (mm)**	**Slice number**	**TR (ms)**	**TE (ms)**
Axial and sagittal fat-sat T1 spinecho	1.2 × 1.2 × 4.5	300	4.5	28	621	7.8
Coronal fat-sat T1 VIBE (until 2019 January)	1.4 × 1.4 × 1.4	400	1.4	Slices per slab: 144	7.08	2.39
Dynamic fat-sat T1 VIBE (until 2019 January)	1.4 × 1.4 × 1.8	400	1.8	Slices per slab: 104	7.08	2.39

Postcontrast sequences with gadolinium-based contrast medium (TRUFISP, true, fast imaging with steady-state free precession; DWI, Diffusion-weighted magnetic resonance imaging; Fat-sat, Fat suppression; VIBE, Volumetric interpolated breath-hold examination).

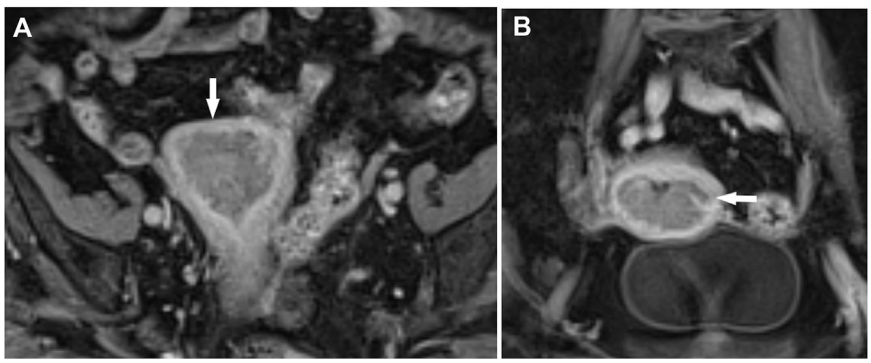

FIGURE 1 | Endometrial cancer, stage T1b. Myometrial infiltration >50%. Post-contrast dynamic fat-sat T1 weighted VIBE image (fat-suppressed Volumetric interpolated breath-hold examination), **(A)** coronal view, **(B)** axial view.

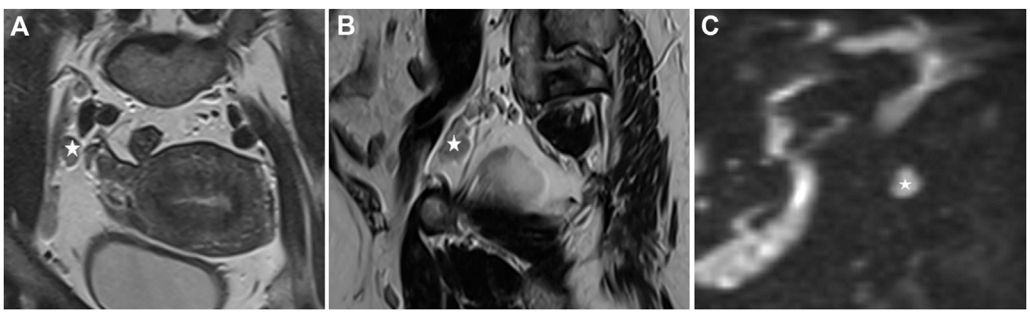

FIGURE 2 | Endometrial cancer, stage T1b. *: Enlarged lymph nodes **(A)**. T2 sequence, coronal view, enlarged lymph nodes near the external iliac artery, **(B)** T2 sequence, sagittal view, an enlarged lymph node near the external iliac artery, **(C)** enlarged lymph node, postcontrast DWI (Diffusion-weighted magnetic resonance imaging, b:800).

Macroscopic and microscopic histopathological evaluation of the surgical specimen was performed. Findings included the description of the type of tumor, differentiation, TNM, and FIGO staging based on the extent of myometrial infiltration (<50%, ≥50%), and the presence or absence of parametrial, cervical, adnexal, rectal, and cystic involvement, lymph-node, and pelvic wall invasion.

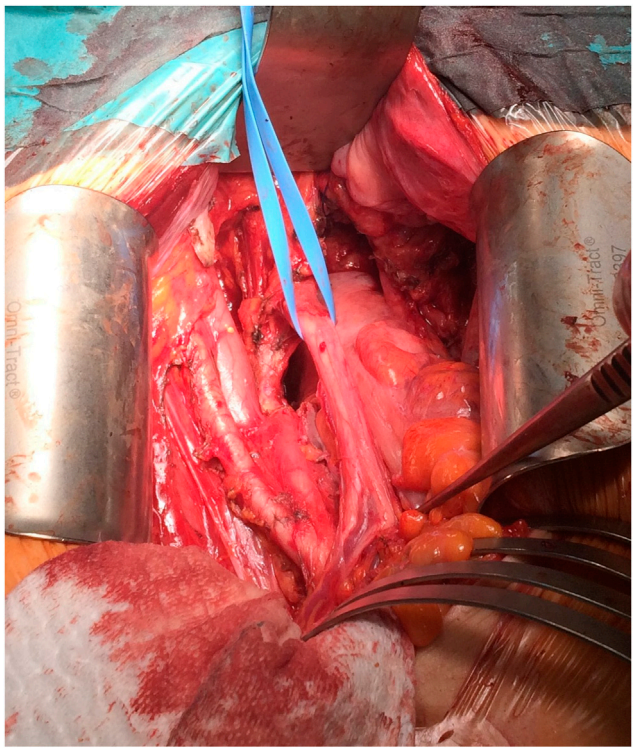

FIGURE 3 | Intraoperative picture, with the preparation of parailiacal and obturator space.

The staging was re-evaluated by the tumor board postoperatively, based on intraoperative and histopathological findings. A postoperative oncological therapy was designed individually for each patient, based on the ESMO Guidelines. Patients with stage 1, low-grade endometrioid endometrial cancer received adjuvant vaginal brachytherapy; high-grade cases were referred to external beam radiation therapy (EBRT). Patients with positive lymph node status received adjuvant systemic, platinum-based chemotherapy, and radiotherapy (EBRT or vaginal brachytherapy) [9, 10].

Conducting follow-up visits in the Department of Oncology and the Department of Gynecology included routine physical and radiological check-ups. The follow-up frequency was six weeks, three months, six months, one year, then annually after surgery. Follow-up data were obtained from surgery until December 2019.

Data collection was approved by the Ethics Committee of the Hospital, according to the Declaration of Helsinki.

STATISTICAL ANALYSIS

The age at the time of surgery, the prevalence of different tumor histological subtypes, tumor grades, and differentiation were taken into account to analyze tumors of the final histopathologic staging as stage I endometrial cancer. The 1- and 5-years survival rates were calculated, accounting for deaths occurring before December 2019 (**Table 2**).

The preoperative radiology staging results were compared with the final histological analysis of the surgical specimen, using $\chi 2$ or Fisher's exact test to compare variables. p-values < 0.05 were considered to be significant. The sensitivity, specificity, positive- and negative predictive values of the preoperative assessment were calculated for each endpoint, together with 95% confidence intervals (95% CI). The percentage of the underdiagnosed or overdiagnosed cases and accuracy rate in terms of stage, myometrial invasion, and the number of lymph node metastases were also calculated.

All data were collected in an Excel database, and they were analyzed using SPSS statistical software. The intraclass correlation coefficient (ICC) was used to determine the inter-rater agreement between the radiologist and the pathologist concerning overall staging, myometrial invasion, and lymph node metastases. ICC below 0.50 was considered poor, between 0.50 and 0.75 as moderate, between 0.75 and 0.90 as good, and above 0.90 ICC, it was considered excellent inter-rater reliability. SPSS software (ver. 25; SPSS Inc., Chicago, IL, United States) was used for the statistical analyses, and p-values < 0.05 were considered significant.

RESULTS

Our results were based on a retrospective, one-institute dataset between the years 2010 and 2019. We analyzed the data of 96 patients with the final histopathologic evaluation of TNM T1 stage endometrial adenocarcinoma tumors, with the follow-up period from their surgery until December 2019. One patient with endometrial sarcoma was excluded from the study.

The patients' age with the final histopathologic result of TNM staged T1 endometrial cancer was from 37 to 84 years with a mean of 63.52±9.4 years. Most of the patients were postmenopausal (94.8%) and overweight (body mass index >25 kg/m2; 76.4%).

According to the tumor board's decision, 87 patients (90.6%) received adjuvant irradiation, and four of them (4.1%) had the treatment of chemoradiation due to local recurrence and distal metastases occurring in the follow-up period. In the follow-up period, five of the patients (5.2%) were diagnosed with metastases (lung, osseal, and lymph-node), and local recurrence occurred in three of the patients (3.1%); three of these patients received chemotherapy.

In the follow-up period, overall, eight patients died; four of the deaths were endometrial-cancer related. The overall 1-year mortality rate was 2.1% (1% cancer-related); the 5-years mortality rate was 8.3% (4.2% cancer-related).

Postoperative histologic assessment revealed histopathologic subtype of endometrioid adenocarcinoma in 92.8%, serous adenocarcinoma in 6.2%, and sarcoma in 1% of the cases. The patient with endometrial sarcoma was excluded from the study. 72.9% of the cases were diagnosed as high-grade, 27.1% as low-grade tumors (**Table 2**).

TABLE 2 | Patient and tumor characteristics.

Age (year)	**63.52 ± 9.4 (37–84)**	**Grade**	
Gravidity	2.28 ± 1.47 (0–10)	Low	26 (27.1%)
Parity	1.69 ± 0.93 (0–4)	High	70 (72.9%)
Postmenopause	91 (94.8%)	Treatment	
Histologic subtype			
Endometrioid adenocarcinoma	90 (93.7%)	Adjuvant irradiation	87 (90.6%)
Serous adenocarcinoma	6 (6.3%)	Adjuvant chemoirradiation	4 (4.1%)
		Adjuvant chemotherapy (due to recurrence or metastases)	3 (3.1%)
Positive lymph node status	26 (27.1%)	Recurrence and/or metastasis	8 (8.3%)

Age, gravidity, parity: mean, SD, range. Postmenopausal state, Histopathologic subtype, Grade, Treatment, Recurrence, and metastasis: frequency (%).

TABLE 3 | Results. Accuracy, sensitivity, specificity, PPV, and NPV regarding TNM staging, myometrial invasion, lymph node metastases, and MRI results were compared with final histopathologic evaluation.

	Overall*	**Myometrial invasion***	**Lymph-node metastases**
Accuracy	94.7%	69.8%	78.1%
Sensitivity	63.3%	80.0%	28.6%
Specificity	94.8%	60.8%	82%
Positive predictive value	83.8%	64.3%	11.1%
Negative predictive value	83.8%	77.5%	93.6%
Intraclass correlation coefficient	0.782	0.576	0.117

*Intraclass correlation coefficient (ICC): <0.50—poor, 0.50–0.75—moderate, 0.75–0.90—good inter-rater reliability (CI 95%) *p < 0.05*

TABLE 4 | Difference between MRI and histology results, myometrial invasion.

	MR imaging		**Histopathologic assessment**	
	N	**%**	**N**	**%**
T1A (<50% myometrial invasion)	40	41.7	51	53.1
T1B (>50% myometrial invasion)	56	58.3	45	46.9

In stage I cancers, the accuracy of MRI regarding stage was 94.7%, and its sensitivity, specificity, PPV, and NPV were 63.3, 94.8, 83.8, and 83.8%, respectively, with the intraclass correlation coefficient of 0.782 (0.697–0.842) (with 95% confidence interval [CI]; $p < 0.001$). Rates of underdiagnosis were 5.2% of the cases (**Tables 3, 4**). Based on the results, MRI is highly accurate and specific in overall staging, with good inter-rater reliability compared to final histopathologic findings.

The accuracy of MRI for the detection of myometrial invasion in stage I cancers was 69.8%, and its sensitivity, specificity, PPV, and NPV were 80.0, 60.8, 64.3, and 77.5%, respectively, with the intraclass correlation coefficient of 0.576 (0.368–0.716) (with 95% confidence interval [CI]; $p < 0.001$). The rates of overdiagnosis were 20.8%, underdiagnosis was 9.4% (**Table 4**). Based on the results, MRI is sensitive in terms of myometrial invasion depth, with high negative predictive value and moderate accuracy, specificity, and positive predictive value. Inter-rater reliability moderate in comparison to final histopathologic findings.

Mean, surgically removed pelvic lymph node count was 10.4 (SD ± 4.1). The accuracy of MRI for the detection of lymph-node in stage I cases was 78.1%, and its sensitivity, specificity, PPV, and NPV were 28.6, 82, 11.1, and 93.6%, respectively, with the intraclass correlation coefficient of 0.117 (−0.394–0.401) (with 95% confidence interval [CI]; $p = 0.026$). False-negative results were 5.2%, false-positive were 16.7% of the cases (**Table 3,**). Based on the results, MRI is moderately accurate and specific in local lymph-node staging, with a high negative predictive value. Results showed poor inter-rater reliability in comparison to final histopathologic findings.

To analyze the initial learning curve's role in evaluating MR images, we compared the results of two rater-group in terms of accuracy, down- and upstaging in regards to myometrial invasion and lymph node spread. A radiologist with high expertize in gynecologic radiology evaluated 60 of the cases, three radiologists with medium-level expertize evaluated 36 cases. A radiologist with higher expertize showed more constant findings and lower upstaging-rate in terms of myometrial invasion than radiologists with no specialization in gynecologic oncology. However, the evaluation of lymph-node metastases was more accurate in the second group, with only four upstaged cases (**Table 5**).

DISCUSSION

In the developed world, endometrial cancer is one of the most common malignant gynecological tumor types. Due to the highly

TABLE 5 | Role of expertize in the evaluation of MR images.

	Myometrial invasion					
	Accuracy		Upstaging		Downstaging	
	N	%	N	%	N	%
Rater 1 (N = 60)	45	75	7	11.7	8	13.3
Rater 2 (N = 36)	23	63.9	12	33.3	1	2.8
	Lymph node spread					
	Accuracy		Upstaging		Downstaging	
	N	%	N	%	N	%
Rater 1 (N = 60)	43	71.7	14	23.3	3	5
Rater 2 (N = 36)	32	88.9	4	11.1	0	0

A radiologist with high gynecological radiology expertize evaluated 60 of the cases, three radiologists with medium-level expertize evaluated 36 of the cases.

available diagnostic modalities and patient education, the early detection of the tumor leads to high overall survival. Prognostic factors include histopathologic subtypes, grade, myometrial invasion, and lymph node metastases [11].

In preoperative staging, MRI is considered the best choice to assess myometrial invasion depth, cervical involvement, and tumor grade. However, its role in the evaluation of lymph node metastases is still controversial [12]. The National Comprehensive *Cancer* Network (NCCN) and the European Society of Urogenital Radiology (ESUR) advise MRI imaging in endometrial cancers with serous histologic subtype, suspected cervical invasions, and identify patients with stage Ia disease. As patients with endometrioid endometrial cancer with myometrial invasion of more than 50%, or with serous-type endometrial cancer are considered to be intermediate to high risk of lymph node metastasis, preoperative staging is essential for a tailored pre-and postoperative treatment and for planning the radicality of the surgical treatment [13].

In this study, we analyzed the reliability of preoperative MRI findings in the staging of early stage endometrial cancer and patients' clinical characteristics who underwent radical hysterectomy and the histopathologic evaluation of their tumor.

The results of the preoperative radiology staging were compared with the final histological analysis of the surgical specimen. The sensitivity, specificity, positive- and negative predictive values of the preoperative assessment were calculated for each endpoint. The percentage of the underdiagnosed or overdiagnosed cases and accuracy rate in terms of stage, myometrial invasion, and lymph node metastases were also evaluated. Inter-rater agreement was calculated to determine the conformity of pre-and postoperative staging.

According to our findings, the overall accuracy of MRI in regards to staging was 94.7% with high specificity, high positive- and negative predictive value, and low sensitivity, with good inter-rater reliability. As most of the tumors are detected at an early stage, the high sensitivity of MRI for the myometrial invasion in stage I diseases means that this modality plays an essential role in planning the radicality of hysterectomy in localized tumors. Based on the decision of the hospital's oncologic team, pelvic lymphadenectomy was carried out in most of our cases for accurate surgical staging; however, due to low sensitivity and low positive predictive value of MR imaging for lymph node detection, a considerable number, 16.7%, of surgeries at an early stage were complemented with lymphadenectomy with false-positive MRI results.

In literature reviews of the past few years' studies, similar results were reported, showing sufficient specificity but low sensitivity regarding lymph node detection due to similar radiological findings of hyperplastic and metastatic lymph-node enlargement (**Table 6**). [14] Our MRI results in terms of myometrial invasion showed average accuracy, sensitivity, and negative predictive compared to studies; however, the positive predictive value was lower. In terms of lymph-node metastases, sensitivity, and positive predictive value of our results were relatively low; even the radiologist with high expertize upgraded 23.3% of the lymph nodes.

Based on our results, MRI is the method of choice in evaluating overall staging and myometrial invasion, as its specificity and negative predictive value are relatively high [15, 16]. The role of lymph-node status is essential in prognosis and guiding adjuvant treatment [17, 18]. Therefore it should be considered based on the preoperative imaging results [19]. In the retrospective ASTEC study, there was no significant better overall survival or recurrence-free survival when pelvic lymphadenectomy was carried out [20]. However, in the large, retrospective SEPAL study, patients with high-risk histology (low-grade endometrial cancer with myometrial invasion ≥50% or high-grade histology) showed better cancer-related survival, recurrence-free survival with standard surgery with lymphadenectomy than with standard surgery with adjuvant radiotherapy [21]. Our results showed similar findings to the SEPAL study as the survival-rate was high with pelvic lymphadenectomy; therefore, systematic lymphadenectomy can be considered in high-risk cases.

Based on our studies, the diagnosis of lymph node metastases is difficult with MRI modality since hyperplastic and metastatic nodes cannot easily differentiate, leading to a high percentage of false-positive results. Therefore, other imaging modalities, such as ultrasound, CT, and PET-CT [10], can be used for more accurate evaluation; however, due to the lack of sufficient data, we did not investigate these methods' accuracy.

Limitations to these findings are that the number of removed lymph-nodes and thoroughness of the histopathological

TABLE 6 | Review of the literature.

Myometrial invasion							
Author	**Year**	**Patient number**	**Accuracy**	**Sensitivity**	**Specificity**	**Positive predictive value**	**Negative predictive value**
Goel et al. [22]	2018	58	74.14%	75%	73.08%	77.2%	70.37%
Tanase et al. [23]	2018	84	88.1%	82.1%	93.5%		
Yu-ting huang et al. [24]	2019	Review of literature	77–90%	85–94%	60–73%		
Shatat et al. [25]	2019	29	75.86–93.1%	66.7–94.7%	60–94.7%	60–94.7%	66.7–94.7%
Yildirim et al. [26]	2018	40	75%	77.8%	72.7%	70%	80%
Gil et al. [27]	2019	44	61–95%	58–96%	58–96%	55–96%	55–95%
Current study	2020	96	69.8%	80%	60.8%	64.3%	77.5%
Lymph node spread							
Author	**Year**	**Patient number**	**Accuracy**	**Sensitivity**	**Specificity**	**Positive predictive value**	**Negative predictive value**
Goel et al. [22]	2018	58	86%	88.64%	66.67%	95.12%	44.4%
Tanase et al. [23]	2018	84		74.4%	82.1%		
Yu-ting huang et al. [24]	2019	Review of literature	77–99%	50–85%	90–99%		
Current study	2020	96	78.1%	28.6%	82%	11.1%	93.6%

Accuracy, sensitivity, specificity, PPV, and NPV of MR imaging regarding Myometrial invasion and lymph node spread.

evaluations can result in false-negative results; however, hyperplastic lymph-nodes can mimic metastases; therefore, the gold-standard size-criterion of positive evaluation should be revised and used cautiously.

CONCLUSION

Based on our results, MRI is considered the best choice to assess myometrial invasion depth, cervical involvement, and tumor grade in preoperative staging. Its role in the evaluation of lymph node metastases is still controversial.

Our study's strength was that our results and examination data were based on retrospective, one-institution data. The limitation of our findings was that the number of patients was relatively low.

New findings of our study were that the role of the radiologist's expertize in the evaluation of MR imaging plays an essential role in lowering false-negative and false-positive results; therefore, findings evaluated by a radiologist with high-level expertize in gynecological imaging can complement the clinical findings and help substantially define the needed treatment.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

All data collection performed in the studies were in accordance with the ethical standards of the institutional and/or national research committee and with the Helsinki Declaration and its later amendments or comparable ethical standards. The research was approved by the ethics committee of Zala County Saint Raphael Hospital. All patients gave informed consent for every diagnostic and/or therapeutic procedure/strategy.

AUTHOR CONTRIBUTIONS

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by DB, GN and GV. The first draft of the manuscript was written by DB and all authors commented on previous versions of the manuscript. RP and GV lectored and commented the final version of the manuscript. All authors read and approved the final manuscript.

CONFLICT OF INTEREST

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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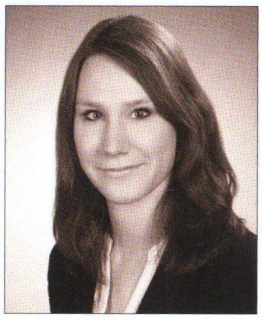
A preoperatív mágnesesrezonancia-vizsgálat klinikai jelentősége

az I. stádiumú endometriumcarcinoma myometrialis infiltrációjának és nyirokcsomó-státuszának megítélésében



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Bevezetés: Az endometriumcarcinoma egyike a leggyakoribb nőgyógyászati tumoroknak a fejlett világban élő nők körében. Az egyre széleskörűbben elérhető és megbízható képalkotó módszereknek, valamint a kiterjedt szűrésnek köszönhetően a daganatok nagy része korai stádiumban kerül felismerésre, jó prognózishoz vezetve.
Célkitűzés: Vizsgálatunk célja a mágnesesrezonancia-vizsgálat, mint preoperatív képalkotó eljárás eredményeinek elemzése a végső, szövettani eredményhez viszonyítva korai stádiumú endometriumcarcinomák esetén.
Módszer: A vizsgálat során kórházunkban 2010. január 1. és 2019. december 31. között radikális hysterectomián átesett páciensek adatait vizsgáltuk. Elemeztük I. stádiumú tumorok esetén a preoperatív mágnesesrezonanciás-vizsgálat megbízhatóságát, a betegek anamnézisét és a tumorok hisztopatológiai karakterisztikáját.
Eredmények: Eredményeink hasonlóak a nemzetközi irodalom nagy esetszámú vizsgálataihoz. Elemzésünk alapján az MR- és a szövettani stádium összehasonlítása esetén a pontosság, szenzitivitás, specificitás, pozitív- és negatív prediktív érték 93,8%, 63,3%, 93,9%, 83,8%, illetve 83,8% volt. Myometrium-invázió megítélésében az MR- és a szövettani eredmény összehasonlításakor a pontosság, szenzitivitás, specificitás, pozitív- és negatív prediktív érték 70,1%, 80,0%, 61,5%, 64,3%, illetve 78% volt. Nyirokcsomó-áttétre gyanús nyirokcsomók MR-leírása, illetve a szövettani lelet alapján a nyirokcsomó-áttét megítélésének pontossága, szenzitivitása, specificitása, pozitív- és negatív prediktív értéke 77,3%, 28,6%, 81,1%, 10,5%, illetve 93,6% volt.
Következtetés: Vizsgálatunk alapján a mágnesesrezonancia-vizsgálat megfelelő specificitásával és negatív prediktív értékével megbízható alapja a műtét előtti stádiummeghatározásnak és a myometrium-invázió megítélésének, ugyanakkor a mágnesesrezonanciás-vizsgálat nem elegendő a kóros nyirokcsomók megítélésére, mivel a gyulladásos és metasztázist felvető nyirokcsomók a modalitással egyértelműen nem elkülöníthetők, így magas álpozitív eredményt adva. Fentieket tekintve a pontos nyirokcsomó-státusz megítéléséhez további képalkotó eljárások bevonása válhat szükségessé.

Kulcsszavak: endometriumcarcinoma, radikális méheltávolítás, mágnesesrezonancia-vizsgálat

Clinical impact of preoperative magnetic resonance imaging in the evaluation of myometrial infiltration and lymph-node metastases in stage I endometrial cancer
Introduction: In the developed world, endometrial cancer is one of the most common malignant gynecological cancer types. Due to the highly available diagnostic modalities and patient education, the early detection of the tumor leads to high overall survival.
Purpose: The aim of our study was to study the role of magnetic resonance imaging in stage I endometrial cancers.in comparison with the final histopathologic evaluation.
Methods: In this study we analyzed the reliability of preoperative MRI findings in the staging of early-stage endometrial

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cancer, as well as the clinical characteristics of patients and the histopathologic evaluation of their tumor, with the retrospective data of radical hysterectomies performed in our hospital between 2010 and 2019.

Results: Based on our results, we report similar findings as found in international literature. The accuracy, sensitivity, specificity, negative- and positive predictive value of MRI regarding stage were 93.8%, 63.3%, 93.9%, 83.8% and 83.8, respectively. The accuracy; sensitivity, specificity, negative- and positive predictive value of MRI for the detection of myometrial invasion were 70.1%, 80.0%, 61.5%, 64.3% and 78%, respectively. The accuracy, sensitivity, specificity, negative- and positive predictive value of MRI for the detection of lymph-node metastases were 77.3%, 28.6%, 81.1%, 10.5% and 93.6%, respectively.

Conclusion: Our studies showed that MRI is the method of choice in the terms of evaluating overall staging, as well as myometrial invasion, as its specificity and negative predictive value is rather high. The diagnosis of lymph node metastases is difficult with MRI modality since hyperplastic and metastatic nodes cannot be easily differentiate leading to high percentage of false positive results, therefore other imaging modalities can be used for more accurate evaluation.

Keywords: endometrial cancer, radical hysterectomy, magnetic resonance imaging

Bevezetés

A méhtestrák a Nemzeti Rákregiszter adatai alapján a kilencedik leggyakoribb daganat a Magyarországon élő nők körében. A Magyar Rákregiszter és az Egyesült Államok Nemzeti Rákkutató Intézetének „Tervezet az Epidemiológia és a Végeredmények Felügyeletének Biztosítására Program" (SEER) [1] 2009 és 2016 közötti adatai alapján a méhtestrák incidenciája és mortalitása enyhén növekszik, ugyanakkor az összes stádiumra vetítve az 5 éves túlélés továbbra is 81,2%, méhre lokalizált tumorok esetén pedig eléri a 95%-ot.

A méhtestrákok nagy része 45 és 74 év közötti nőknél jelentkezik. Legfőbb rizikófaktorai az emelkedett ösztrogénszint (anovuláció, nulliparitás, policisztásovárium-szindróma vagy Tamoxifenkezelés miatt), az elhízás (BMI >30), [2] a cukorbetegség és a magasvérnyomás-betegség [3].

A tumor vezető tünete a menopauza előtti vérzészavar vagy a posztmenopauzális vérzés [4].

A diagnózis felállításához küret, minimálinvazív módszerek (nyálkahártya-biopszia vagy méhtükrözés) és hüvelyi ultrahang áll rendelkezésre [5]. Tekintve, hogy a CT elsősorban a myometriális invázió vonatkozásában relatív alacsony specificitással rendelkezik, az MR-vizsgálat az elsődlegesen választandó modalitás a preoperatív stádium meghatározására [6].

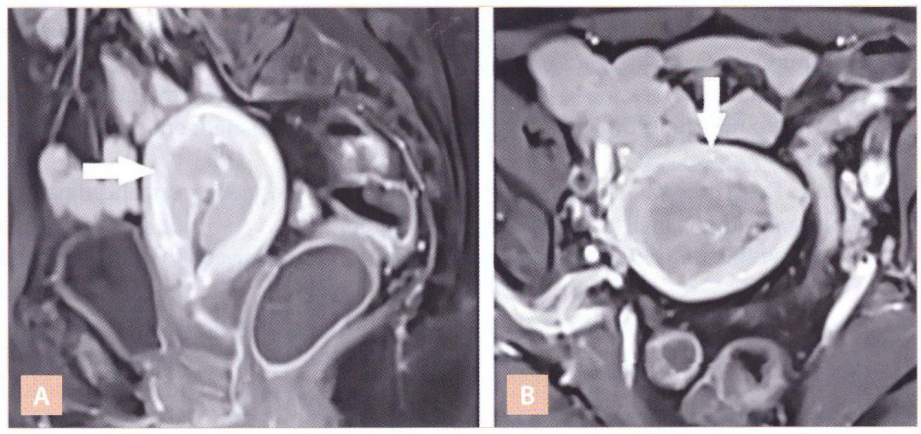
A méhtestrák stádiumbeosztása a FIGO- és TNM-rendszereken alapul, meghatározva a szövettani típust, a tumor grádusát, a myometrium-invázió mértékét és a helyi nyirokcsomó- vagy távoli áttétek jelenlétét [7], amelyek megalapozzák a későbbi onkológiai műtét radikalitását és a neoadjuváns vagy adjuváns kezelés szükségességét [8].

Jelen vizsgálatunk célja volt a mágnesesrezonancia-vizsgálat, mint preoperatív képalkotó eljárás megbízhatóságának elemzése a végső, szövettani eredményhez viszonyítva korai stádiumú endometriumcarcinomák esetén.

Módszer

A Zala Megyei Szt. Rafael Kórház Nőgyógyászati Osztályán 2010 és 2019 között 254 radikális méh- és nyirokcsomó-eltávolítás történt méhtest- vagy méhnyakráknak köszönhetően.

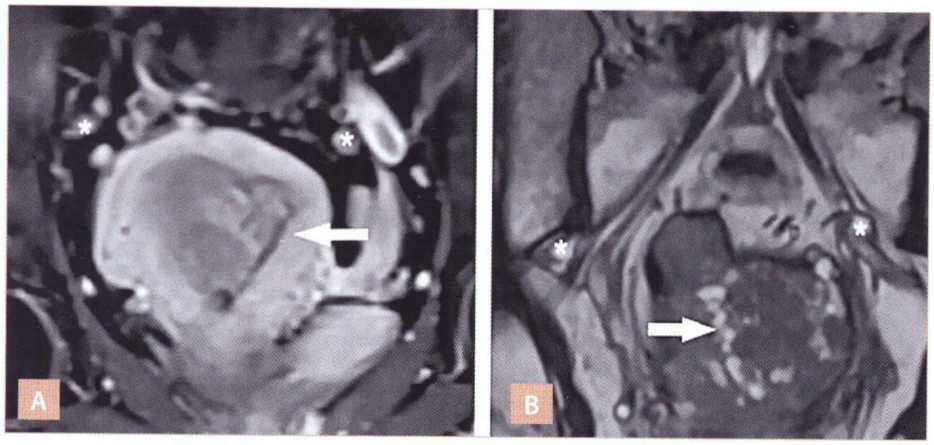
Vizsgálatunk során összesen 97, I. stádiumú méhtestrák szövettani diagnózissal rendelkező beteg adatait elemeztük. Minden páciens esetében frakcionált küret történt a méhnyálkahártya szövettani vizsgálatára, pozitív eredmény esetén MR segítségével preoperatív stádiumbesorolás történt. A preoperatív MR-kivizsgálás Siemens Magnetom Area 1.5 Tesla készülékkel történt *(1. és 2. ábra)*. A FIGO 2009 stádiumbeosztás a myometrium, méhnyak, serosa, adnexumok és parametriumok beszűrtsége, illetve a kismedencei nyirokcsomók áttétjeinek leírásával került meghatározásra. A vizsgálat a retroperitoneumról coronalis síkú T1, T2 TRUFISP, a parailiacalis nyirokcsomókról ferde sagittalis – obturator síkú T1 súlyozott szekvenciákkal, a kismedencéről sagittalis és axialis T2, axialis T1, DWI és zsírelnyomásos T1 súlyozott, majd gadobutrol kontrasztanyagos axialis és sagittalis zsírelnyomásos T1 súlyozott szekvenciás mérésekkel történt. A myometrium-invázió az infiltráció mértékének (<50%, ≥50%), a tubasarkok, a junctionalis zóna és a serosai felszín érintettségének jellemzésével történt. Nyirokcsomó-áttétet



1. ábra: Endometriumcarcinoma, T1b stádium. Myometrialis infiltráció mértéke >50%. T1 TSE (turbo spin-echo) szekvecnia. A: sagittalis sík, B: axialis sík

8 mm-nél nagyobb kismedencei és a 10 mm-nél nagyobb átmérőjű paraaorticus nyirokcsomót vetettek fel, a patológiára gyanús nyirokcsomó inhomogenitása, alakja és esetleges nekrózisa is leírásra került.

A Multidiszciplináris Onkológiai Team döntése alapján radikális méheltávolítást végeztünk a kismedencei nyirokcsomókkal egyetemben *(3. ábra)*. A patológiai és szövettani vizsgálat során a műtéti preparátum makroszkópos és mikroszkópos leírásával a daganat szövettani típusa, grádusa, a myometrium-infiltráció mértéke és a nyirokcsomó-áttétek jelenléte került meghatározásra. A végső, FIGO 2009 stádiumbeosztás alapján az Onkológiai Team meghatározta a megfelelő onkológiai kezelést.



2. ábra: Endometriumcarcinoma. A: T1b stádium. T1 szekvencia, coronalis sík. B: T1b stádium, leiomyomákkal. T2 TRUFI szekvencia, coronalis sík, gadolinium kontrasztanyag. Nyilak: myometrium-infiltráció *: megnagyobbodott nyirokcsomók

Az adatgyűjtést a Kórházi Etikai bizottság az orvosi vizsgálatok etikai elveiről szóló Helsinki nyilatkozattal egyezve engedélyezte.

Az adatgyűjtés során feldolgoztuk a páciensek korát a műtét idején, a különböző daganatos szövettani típusok arányát, a tumorok grádusát és differenciáltságát. Ezeken felül a 2019 végéig bekövetkezett halálozások alapján kiszámoltuk az 1, és 5 éves mortalitást.

A statisztikai analízis során a preoperatív radiológiai stádiumokat hasonlítottuk össze a posztoperatív szövettani stádiumokkal, az összehasonlítást nominális változók esetén a Pearson-féle $\chi 2$ próbával vagy Fischer-teszttel végeztük el, $p<0,05$ értékeket tekintve szignifikánsnak. A pre- és posztoperatív leletek közötti szenzitivitás, specificitás, pozitív- és negatív prediktív érték is meghatározásra került, 95% konfidenciaintervallummal.

Az adatokat Excel tábla alapján SPSS statisztikai szoftver segítségével elemeztük (25. verzió; SPSS Inc., Chicago, IL, USA). A megítélők közötti megbízhatóság vizsgálatára osztályon belüli korrelációs együttható (ICC) került kiszámításra, az egyetértés mértékét a radiológiai- és szövettani leletek között a stádiumbeosztás, myometrium- vagy stromainfiltráció mértékének és a nyirokcsomó-státusz vonatkozásában vizsgáltuk, $p<0,05$ érték esetén tekintve az eredményeket szignifikánsnak. ICC esetén a 0,50 alatti értékeket gyenge, a 0,50 és 0,75 közötti értékeket közepes, a 0,75 és 0,90 közötti értékeket jó, míg a 0,90 feletti értékeket kiváló vizsgálók közti egyetértésnek, azaz konkordanciának tekintettünk.

Eredmények

A páciensek demográfiai adatai, tumorok szövettani típusának és grádusának megoszlása az *1. táblázatban* látható.

Az OnkoTeam javaslata alapján 87 beteg részesült adjuváns sugárterápiában (89,7%), 4 beteg esetében kemoirradiációra volt szükség (4,1%). Az utánkövetés során 5 betegnél áttétet (tüdő, csont vagy nyirokcsomó), 3 betegnél helyi recidívát diagnosztizáltunk.

Az utánkövetési időszakban az 1 éves, daganattal összefüggő mortalitás 1%, az 5 éves, daganattal összefüggő mortalitás 4,1% volt *(1. táblázat)*.

1. táblázat: Statisztikai adatok

Életkor (év)	63,66±9,45 (37–84)	**Grádus**	
Terhesség	2,27±1,47 (0–10)	Alacsony	26 (26,8%)
Szülés	1,70±0,93 (0–4)	Magas	71 (73,2%)
Posztmenopauza	92 (94,8%)	**Kezelés**	
Szövettani típus		Adjuváns besugárzás	87 (89,7%)
Endometrioid adenocarcinoma	90 (92,8%)	Adjuváns kemoirradiáció	4 (4,1%)
Serosus adenocarcinoma	6 (6,2%)	Adjuváns kemoterápia (metasztázis vagy recidíva miatt)	3 (3,1%)
Sarcoma	1 (1%)	**Metasztázis és/vagy recidíva**	8 (8,3%)
Pozitív nyirokcsomó-státusz	26 (17,6%)		

Az MR pontossága a szövettani stádiumhoz képest I. stádiumú daganatok esetén 93,8% volt, szenzitivitása 63,3%, specificitása 93,9%, pozitív- és negatív prediktív értéke egyaránt 83,8%-nak bizonyult. Az osztályon belüli korrelációs együttható (ICC) 0,779 (0,695–0,840, 95% konfidenciaintervallum, p<0,001) volt.

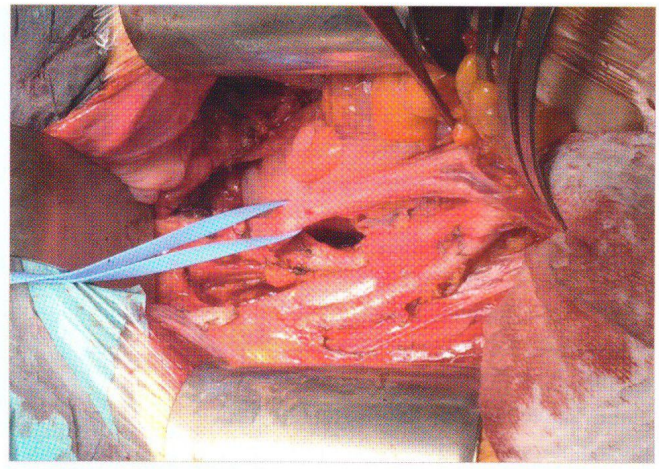
Myometrium-invázió megítélésének tekintetében az MR pontossága 70,1%-nak bizonyult, szenzitivitása 80,0%, specificitása 61,5%, pozitív prediktív értéke 64,3% és negatív prediktív értéke 78% volt, az osztályon belüli korrelációs együttható 0,591 (0,388–0,726, 95% konfidenciaintervallum, p<0,001) volt. Az esetek 20,61%-ában nagyobb fokú, 9,27%-ban kisebb fokú myometrium-invázió került leírásra.

A nyirokcsomó-státuszt tekintve az MR pontossága 77,3%-nak bizonyult, szenzitivitása 28,6%, specificitása 81,1%, pozitív prediktív értéke 10,5% és negatív prediktív értéke 93,6% volt, az osztályon belüli korrelációs együttható 0,109 (–0,332–0,404, 95% konfidenciaintervallum, p=0,054) volt. Az esetek 17,5%-ában álpozitív, 5,2%-ban álnegatív nyirokcsomók kerültek leírásra *(2. táblázat)*.

Megbeszélés

A nemzetközi és hazai ajánlások alapján az MR-vizsgálat az elsőként választandó képalkotó eljárás az endometriumcarcinoma preoperatív kivizsgálásában [9, 10]. A Nemzeti Átfogó Rákbetegségeket Felügyelő Hálózat (NCCN, National Comprehensive Cancer Network) és az Európai Urogenitális Radiológiai Társaság (ESUR, European Society of Urogenital Radiology) ajánlások MR-vizsgálatot javasolnak serosus adenocarcinoma, gyanított méhnyakinvázió és Ia stádiumú betegek kivizsgálása esetén. A nyirokcsomó-áttétek közepes vagy magas rizikója esetén (myometrium-invázió ≥50%, serosus adenocarcinoma szövettani lelete) a megfelelő preoperatív staging különösen fontos a méheltávolítás radikalitásának és az onkológiai kezelés szükségességének mérlegelésében [11].

Vizsgálatunk során elemeztük a kórházunkban az I. stádiumú méhtestrákkal diagnosztizált páciensek anamnézisét, a tumorok szövettani jellemzőit, valamint az MR-vizsgálat megbízhatóságát a preoperatív stagingben. Elemzésünk során a preoperatív, MR-staginget hasonlítottuk a posztoperatív, szövettani staging leleteihez.



3. ábra: Intraoperatív kép, a kipreparált parailiacalis és obturátor-árki régió

Eredményeink alapján az MR-staging 93,8%-ban pontos volt, magas specificitást, pozitív- és negatív prediktív értéket, ugyanakkor alacsony szenzitivitást mutatva. A radiológus és patológus leletező közti 0,779 korrelációs együttható jó vizsgálók közti megbízhatóságot mutatott. Mivel a méhtestrákok többsége korai stádiumban kerül felismerésre, a myometrialis invázió megítélésnek magas szenzitivitása és negatív prediktív értéke megfelelő alapja a műtéti radikalitás tervezésének, ugyanakkor a közepes (ICC: 0,591) radiológus és patológus közti korrelációs együttható alapján mindkét leletező specializáltsága és gyakorlata szerepet játszhat a megfelelő értékelésben.

A nyirokcsomó-státusz megítélésének alacsony szenzitivitása és specificitása miatt az esetek 17,5%-ában álpozitív nyirokcsomók kerültek leírásra, így kétes esetben kiegészítő képalkotó vizsgálatok bevonása megfontolandó.

A nemzetközi irodalomban hasonló eredmények kerültek leírásra, amelyek alapján a nyirokcsomó-áttétek megfelelő specificitással, de alacsony szenzitivitással kerülhetnek diagnosztizálásra, mivel a gyulladásos és áttétet felvető nyirokcsomó-megnagyobbodás a modalitással nehezen különíthető el. Az alacsony (ICC: 0,109), vizsgálók közötti korrelációs együttható elsősorban a nyirokcsomó-áttét megállapításának méretbeli radiológiai kritériumával magyarázható, nőgyógyászati képalkotásra specializálódott radiológus elsősorban az ezen túli kritériumok (inhomogenitás, nekrózis, alak) leírásával segítheti az áttét jelenlétének felvetését [12].

2. táblázat: Eredmények

	Összesen*	Myometrium-invázió*	Nyirokcsomó-áttét
Pontosság	93,8%	70,1%	77,3%
Szenzitivitás	63,3%	80,0%	28,6%
Specificitás	93,9%	61,5%	81,1%
Pozitív prediktív érték	83,8%	64,3%	10,5%
Negatív prediktív érték	83,8%	78%	93,6%
Osztályon belüli korrelációs együttható	0,779	0,591	0,109

Osztályon belüli korrelációs együttható (ICC): <0,50 – gyenge, 0,50–0,75 – közepes, 0,75–0,90 – jó vizsgálók közti egyetértés, (CI: 95%) *p<0,05

Következtetések

Elemzésünk alapján eredményeink hasonlóak a nemzetközi irodalom nagy esetszámú vizsgálataihoz [13]. Magas specificitása és negatív prediktív értéke miatt az MR-vizsgálat megbízható korai stádiumú méhtestrákok esetén a stádiummeghatározás és myometrium-invázió megállapításához [14]. Vizsgálatunk alapján a gyulladásos- és daganatos nyirokcsomó-megnagyobbodás elkülönítésének nehézsége miatt az MR-vizsgálat magas számú álpozitív eredményhez vezethet, így egyéb képalkotó modalitások bevonása szükséges lehet.

Prospektív, randomizált vizsgálatok [15, 16] nem mutattak egyértelmű pozitív prognózist a rutinszerű lymphadenectomián átesett, korai stádiumú méhtestrákkal diagnosztizált betegek körében, ugyanakkor a nyirokcsomó-státusz továbbra is a műtéti terv és onkológiai kezelés alapja [17].

A szerzőknek nincsenek érdekeltségeik.

Irodalom

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