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Ultrasonography, macroscopy, and frozen section: which is better for predicting deep myometrial invasion in endometrial cancer?

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SUMMARY

OBJECTIVE: The aim of this study was to compare the power of preoperative transvaginal ultrasonography, intraoperative macroscopic examination, and frozen section for predicting deep myometrial invasion in endometrial cancer.

METHODS: This is a retrospective review involving 68 patients who underwent surgical staging for endometrial cancer from 2014 to 2017. Patients with grade 3 endometrial cancer and non-endometrioid tumors were excluded. The findings related to preoperative transvaginal ultrasonography, intraoperative macroscopic examination, and frozen section were compared with definitive histopathological diagnosis.

RESULTS: The mean age, gravidity, and body mass index of the patients were 58.1±8.9 years (range: 30–80 years), 3.2±2.1 (range: 0–9), and 33.5±6.6 kg/m^2 (range: 20–52 kg/m^2), respectively. Only 11 (16.2%) patients were in the premenopausal period, while 57 (83.8%) were in the postmenopausal period. Grade 1 endometrial cancer was found in 29 patients (42.6%) and grade 2 tumors were specified in 39 patients (57.4%). Stage IA disease was found in 45 (66.2%) patients, while stage IB disease was observed in 23 (33.8%) patients. The 5-year survival rate was 91.2%. The sensitivity of preoperative transvaginal ultrasonography, intraoperative macroscopic examination, and frozen section were 56, 34, and 52%, respectively, for predicting deep myometrial invasion. In contrast, the specificity of preoperative ultrasonography, intraoperative macroscopic examination, and frozen section were 86, 100, and 100%, respectively.

CONCLUSION: Transvaginal ultrasonography and intraoperative frozen section were found to have similar sensitivity and specificity for predicting deep myometrial invasion. Preoperative transvaginal ultrasonography appears as an efficient approach for predicting endometrial cancers with deep myometrial invasion.

KEYWORDS: Endometrial cancer. Myometrium. Prognosis. Survival.

INTRODUCTION

Endometrial cancer is the sixth most commonly diagnosed cancer and the 14th leading cause of cancer-related deaths in women worldwide[1]. It is recognized as the most common gynecological malignancy in the United States of America (USA), and the incidence of endometrial cancer in this country is significantly higher than that of other developed countries. The American Cancer Society has estimated that 61,880 new cases would be diagnosed and 12,550 women would die from endometrial cancer in the USA in 2022[2].

Endometrial cancer most commonly affects postmenopausal women. Studies have reported that 3–20% of women with postmenopausal bleeding have endometrial cancer, and endometrial hyperplasia is detected in 5–15% of them[3,4].

The most common type of endometrial cancer is endometrioid adenocarcinoma[5]. Myometrial invasion, lymphovascular space invasion, lymph node involvement, and recurrence have been designated as the most important prognostic factors for endometrial cancer[6]. Among these factors, myometrial invasion appears as an early indicator for the progression of disease, as it has been defined as the invasion of cancer cells into myometrium[7]. Studies have reported that myometrial invasion is associated with lymphovascular space invasion, lymph node involvement, recurrence, and survival of the patients with endometrial cancer. Hence, the depth of myometrial invasion is considered a critical component of surgical-pathological staging[8]. In 2021, the staging system for endometrial cancer has been updated by International Federation of Gynecology and Obstetrics (FIGO). According to this system, stage IA refers to tumors with myometrial invasion less than 50% and stage IB indicates tumors with at least or more than 50% of invasion into myometrium[8,9].

The aim of this study was to compare the power of preoperative transvaginal ultrasonography, intraoperative macroscopic examination, and frozen section for predicting deep myometrial invasion in endometrial cancer.

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METHODS

This is a retrospective review involving 68 patients who underwent surgical staging for endometrial cancer at the gynecological oncology department of Eskisehir Osmangazi University Hospital between 2014 and 2017. The study protocol was approved by the Institutional Review Board and Ethical Committee of Eskisehir Osmangazi University Medical Faculty (grant number: 45425468-32/ 21.08.2017). Written informed consent was obtained from all the participants.

A total of 349 patients were diagnosed with endometrial cancer histopathologically between 2014 and 2017. After excluding 281 patients with non-endometrioid endometrial cancer and/or grade 3 tumors, 68 patients were included for final analysis. Data related to age, gravidity, body mass index, presenting symptoms, menopause, stage, grade, and survival were derived from the patients' records. Body mass index was calculated as weight in kilograms divided by height in meters squared.

Transvaginal ultrasonography was performed in the dorsal lithotomy position after ensuring that the patient's bladder was empty. The uterus was scanned thoroughly, in the longitudinal plane and in the transverse plane, from the cervix to the fundus. Deep myometrial invasion was identified as the infiltration of at least 50% of the myometrial thickness. The endometrial biopsy results were obtained from the sonographer.

All patients who had the histopathological diagnosis of endometrial cancer underwent total extrafascial hysterectomy, bilateral salpingooophorectomy, omental biopsy, and lymph node sampling. Peritoneal cytology was obtained from all patients upon entry into the peritoneal cavity. To specify deep myometrial invasion, the hysterectomy material was transversely cut into two sections and macroscopically examined under the supervision of other gynecological oncology experts and pathologists.

After macroscopic examination was completed, the hysterectomy material was sent to the pathology department for frozen section. The uterus was sliced transversely at 5 mm intervals and stained with hematoxylin and eosin so that the depth of myometrial invasion could be determined microscopically.

Patients with deep myometrial invasion, identified through preoperative transvaginal ultrasonography and/or intraoperative macroscopic examination or frozen section, underwent omentectomy, bilateral pelvic lymph node sampling, and paraaortic lymph node sampling. Staging was conducted based on FIGO criteria[9].

Collected data were analyzed by Statistical Package for Social Sciences version 21.0 (SPSS IBM, Armonk, New York, USA). Continuous variables were expressed as mean or mean±standard deviation (range: minimum-maximum), whereas categorical variables were denoted as numbers or percentages where appropriate. Mann-Whitney U test and chi-square test were used for the comparisons. Sensitivity and specificity values were computed by McNemar's test. Kaplan-Meier curves were drawn to show overall survival with respect to histology, stage, and body mass index. Two-tailed $p<0.05$ were accepted as statistically significant.

RESULTS

The mean age, gravidity, and body mass index of the patients were 58.1±8.9 years (range: 30–80 years), 3.2±2.1 (range: 0–9), and 33.5±6.6 kg/m^2 (range: 20–52 kg/m^2), respectively. The most common presenting symptom was postmenopausal bleeding, which was observed in 55 patients (80.9%). Among all patients, 11 (16.2%) were in the premenopausal period, while 57 (83.8%) were in the postmenopausal period. Grade 1 endometrial cancer was found in 29 patients (42.6%) and grade 2 tumors were specified in 39 patients (57.4%). Stage IA disease was found in 45 (66.2%) patients, while stage IB disease was observed in 23 (33.8%) patients. The overall survival rate was 91.2%. For stage 1a patients, the 5-year overall survival was 97.8%, whereas it was 78.3% for patients between stage 1b and stage 4b (p=0.008). BMI was calculated as weight in kilograms divided by height in meters squared, and participants were categorized into two groups, namely, non-obese (<30.0) and obese (≥30.0)[10], according to the World Health Organization classification. For the patients with BMI<30.0, the 5-year overall survival was 95.7% and for the patients with BMI≥30.0 it was 88.6% (p=0.362). Figure 1 demonstrates the overall survival rates with respect to body mass index and stage.

Table 1 shows the demographic and clinical characteristics of the patients with respect to the depth of myometrial invasion. The patients with myometrial invasion <50% and the patients with deep myometrial invasion were statistically similar in the aspects of age and body mass index. The number of premenopausal patients was significantly higher in patients with histopathologically confirmed myometrial invasion <50% (p=0.012). The number of patients predicted to have deep myometrial invasion by preoperative transvaginal ultrasonography, intraoperative macroscopy, and frozen section was significantly higher in patients with histopathologically confirmed deep myometrial invasion (p=0.001, p<0.001, and p<0.001, respectively). The overall survival rate was significantly lower in patients with deep myometrial invasion (p<0.05). Table 2 shows the performance of ultrasonography, macroscopy, and frozen section for predicting myometrial invasion.

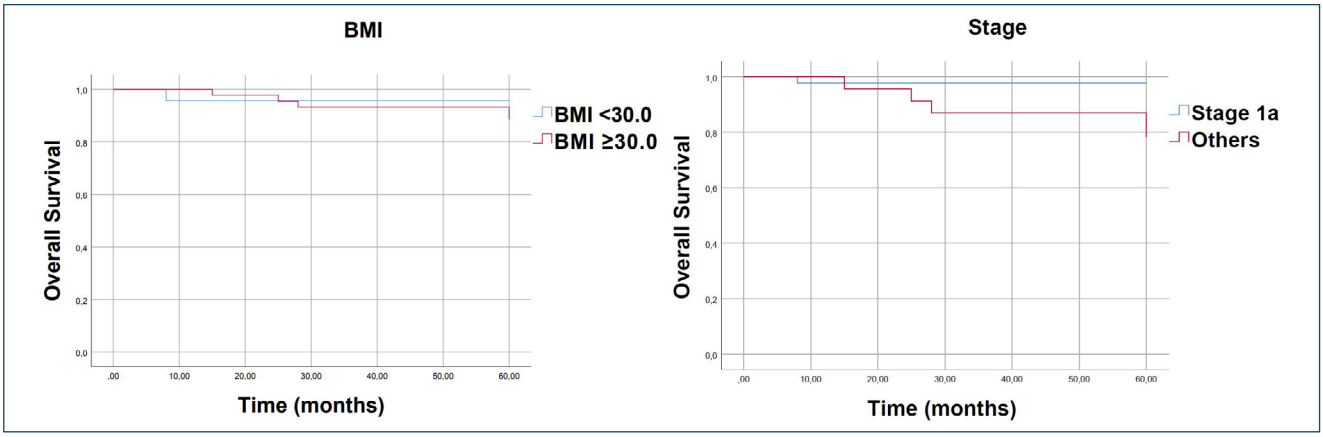

Figure 1. Overall survival rates with respect to body mass index and stage.

Table 1. Demographic and clinical characteristics of the patients with respect to histopathologically confirmed myometrial invasion.

	Myometrial invasion <50% (n=45)	Myometrial invasion ≥50% (n=23)	p
Age (years)	56	60	
Body mass index (kg/m^2)	33.73±7.27	33.73±7.27	0.803
Pre-menopause	11 (100.0%)	0 (0.0%)	0.012*
Post-menopause	34 (59.6%)	23 (40.4%)	
Transvaginal ultrasonography myometrial invasion <50%	39 (79.6%)	10 (20.4%)	0.001*
Transvaginal ultrasonography myometrial invasion ≥50%	6 (31.6%)	13 (68.4%)	
Intraoperative macroscopy myometrial invasion <50%	45 (75.0%)	15 (25.0%)	<0.001*
Intraoperative macroscopy myometrial invasion ≥50%	0 (0.0%)	8 (100.0%)	
Frozen section myometrial invasion <50%	45 (80.4%)	11 (19.6%)	<0.001*
Frozen section myometrial invasion ≥50%	0 (0.0%)	12 (100.0%)	
Five-year survival	97.8%	78.3%	<0.05*

*p<0.05 was accepted as statistically significant.

Table 2. Performance of the methods used for predicting deep myometrial invasion.

	Sensitivity (%)	Specificity (%)
Transvaginal ultrasonography	56	86
Intraoperative macroscopic examination	34	100
Frozen section	52	100

DISCUSSION

Endometrial cancer is usually detected between the ages of 50 and 65 years, with mean age of 60 years during diagnosis[11]. Compatibly, in this study, the mean age of the patients with endometrial cancer was 58.1 years. A Turkish study reported that the mean body mass index of patients with endometrial cancer was 25.8 kg/m^2 [12]. The mean body mass index was significantly higher (33.5 kg/m^2) in this study, and this significant increase might be attributed to the variations in demographic characteristics. It has been claimed that 75% of patients with endometrial cancers are postmenopausal[5,11]. Similarly, in this study, 83.8% of the patients with endometrial cancer were postmenopausal.

Imaging methods such as transvaginal ultrasonography, computed tomography, transvaginal, and magnetic resonance imaging (MRI) are used in the preoperative evaluation of endometrial

cancer[1,4]. The current guidelines put forward by European Society of Gynecological Oncology, European Society for Radiotherapy and Oncology, and European Society of Pathology recommend MRI for predicting deep myometrial invasion in affected patients[13].

Dietz et al. claimed that the sensitivity and specificity of transvaginal ultrasonography were 92 and 50%, respectively, for predicting myometrial invasion in patients with endometrial cancer[14]. Ozdemir et al. yielded the sensitivity and specificity of transvaginal ultrasonography as 86 and 90%, respectively, for predicting myometrial infiltration[15]. Köse et al. assigned the sensitivity and specificity of preoperative transvaginal ultrasonography as 91 and 81.8%, respectively, for predicting myometrial invasion[12]. Savelli et al. found the sensitivity and specificity of transvaginal ultrasonography as 75 and 89%, respectively, for predicting myometrial infiltration[16]. Similarly, in the present study, the sensitivity and specificity of preoperative ultrasonography were 56 and 86%, respectively, for predicting deep myometrial invasion. The relatively lower sensitivity of ultrasonography in this study can be due to the differences in the technical qualities of sonographic equipment.

Intraoperative macroscopic examination can be adopted as an approach for predicting myometrial invasion in endometrial cancer. Pineda et al. stated that the sensitivity and specificity of macroscopy were 78.9 and 90.4%, respectively, for predicting myometrial infiltration[17]. Mavromatis et al. specified the sensitivity and specificity of macroscopic examination as 75 and 92%, respectively, for predicting myometrial invasion[18]. Alcazar et al. found the sensitivity and specificity of macroscopy as 71 and 91%, respectively, for predicting myometrial infiltration[19]. In this study, the sensitivity and specificity of intraoperative macroscopy were calculated as 34 and 100%, respectively, for predicting deep myometrial invasion in endometrial cancer patients. Variations in the professional knowledge and skills of the pathologists might be the underlying reason for the relatively lower sensitivity of intraoperative macroscopic examination in this study.

The sensitivity and specificity of frozen section were designated as 85 and 97%, respectively, for predicting myometrial invasion in endometrial cancer[19]. Another study noted that the sensitivity and specificity of frozen section were 92% for predicting myometrial infiltration[16]. Surprisingly, the sensitivity of frozen section was significantly lower, but the specificity of frozen section was significantly higher than that of MRI for predicting myometrial invasion[20]. In the present study, the sensitivity and specificity of frozen section were 52 and 100%, respectively, for predicting myometrial invasion in endometrial cancer. The inconsistencies in histopathological examination might be the cause for the relatively lower sensitivity of intraoperative macroscopy reported in this study.

The overall survival rate was 85% for endometrial cancer patients[21]. Accordingly, the 5-year disease-free and overall survival rates of these patients were denoted as 95.2 and 96.4%, respectively[22]. Although the 5-year survival rate changed between 74 and 91% for stage 1 and stage 2 tumors, this number decreased to 20 to 26% for stage 4 endometrial cancer[23,24]. In accordance with previous studies, the overall survival rate was 91.2% and overall survival was significantly lowered in endometrial tumors with deep myometrial invasion.

CONCLUSION

This study suggests that transvaginal ultrasonography remains the first-line modality for the assessment of patients with endometrial cancer. The low cost, non-invasive nature, and widespread availability of transvaginal ultrasonography are its major advantages. However, the strength of the present study is limited by its retrospective design, relatively small cohort, relatively shorter follow-up period, and lack of data related to advanced imaging techniques.

Endometrial cancer is the most common gynecological cancer in developed countries. This study aimed to compare the effectiveness of preoperative transvaginal ultrasonography, intraoperative macroscopic examination, and frozen section for predicting deep myometrial invasion in endometrial cancer. Transvaginal ultrasonography and intraoperative frozen section were found to have similar sensitivity and specificity for predicting deep myometrial invasion. Preoperative transvaginal ultrasonography appears as an effective approach for predicting endometrial cancers with deep myometrial invasion.

AUTHORS' CONTRIBUTIONS

CYO: Data curation, Project administration, Resources, Writing – original draft. **EUT:** Data curation, Investigation, Supervision, Validation, Writing – review & editing. **TO:** Formal Analysis, Writing – review & editing. **OTY:** Methodology, Writing – review & editing.

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