Original
ISSN 2521-8492

Advancing Uterine Cancer Care: Transvaginal Ultrasonography in Preoperative Staging Analysis

Kanamatha Reddy Sujana[1*], Sangam Mani Jyothi[1], Lingampelly Pranathi[2]

[1]Department of Radio-Diagnosis, Mallareddy Institute of Medical Sciences, Suraram, Hyderabad, Telangana, India.
[2]Department of Obstetrics and Gynecology, Mallareddy Institute of Medical Sciences, Suraram, Hyderabad, Telangana, India.
*Correspondence to: Kanamatha Reddy Sujana (E-mail: marvelviks@gmail.com)
(Submitted: 19 September 2023 – Revised version received: 27 October 2023 – Accepted: 21 November 2023 – Published Online: 29 December 2023)

Abstract

Objective: To determine the role of transvaginal ultrasonography in the preoperative staging of uterine cancer.

Methods: The research included 110 women who had been diagnosed with endometrial malignancy by histological confirmation, which was achieved through procedures such as dilation and curettage, hysteroscopy, or endometrial biopsy. Additionally, women who had a high suspicion of endometrial malignancy based on imaging results and were scheduled for surgery as their main therapy were also eligible to participate in the study.

Results: A total of 110 individuals satisfied the criteria for inclusion in the research, with an average age of 49.89 ± 2.99 years. In relation to the extent of myometrial invasion, our study yielded sensitivity rates of 81%, 81%, and 69% for the subjective, Gordon, and Karlsson techniques, respectively. The corresponding specificity rates were found to be 67%, 60%, and 81% for the same approaches. The subjective, Gordon, and Karlsson techniques yielded corresponding overall accuracies of 74%, 70%, and 75%. The use of contrast-enhanced MRI yielded a sensitivity, specificity, and overall accuracy of 94%, 72%, and 84%, respectively, in the assessment of myometrial invasion. In the assessment of cervical stromal invasion, the ultrasound subjective technique showed a sensitivity of 33% and a specificity of 99%. On the other hand, the objective method yielded a sensitivity of 52% and a specificity of 92%. The total accuracy for both methods was determined to be 90% and 83% respectively. The use of contrast-enhanced MRI yielded a sensitivity, specificity, and overall accuracy of 69%, 100%, and 96% respectively in detecting cervical involvement.

Conclusion: We concluded that the utilisation of pelvic ultrasound in the preoperative staging of endometrial cancer holds significant value. It demonstrates a notable sensitivity in evaluating myometrial invasion, exhibiting a reasonable to moderate level of concordance with MRI. Furthermore, it exhibits a superior, albeit still moderate, level of agreement with MRI in assessing cervical invasion.

Keywords: Transvaginal ultrasonography, uterine cancer, MRI, preoperative staging

Introduction

Endometrial cancer (EC) is the prevailing gynaecological malignancy in industrialised nations, with endometrioid endometrial carcinoma (EEC) being the predominant histological subtype.[1] The staging of EC follows the guidelines set out by the International Federation of Gynaecology and Obstetrics (FIGO) system. This system suggests the performance of pelvic and para-aortic lymphadenectomy in cases when there are particular risk factors for recurrence.[2,3] Nevertheless, the inclusion of systematic lymphadenectomy in the management of low-risk endometrial cancer (EC) continues to be a topic of discussion and disagreement among experts.[4] The evaluation of tumour extent in women with early-stage endometrial cancer necessitates the use of imaging tools during preoperative assessment. Transvaginal ultrasonography (TVS) and magnetic resonance imaging (MRI) are commonly used methods for preoperative assessment of myometrial invasion depth and cervical stromal involvement (CSI). Nevertheless, the findings of meta-analytical studies have failed to demonstrate any discernible disparity in diagnostic efficacy amongst the aforementioned approaches.[5] Hence, the use of TVS and/or MRI is contingent upon the accessibility and proficiency of these modalities within each respective institution. Historically, endometrial cancer has been approached as a condition that requires surgical staging. Consequently, the customary practise was to forego normal preoperative evaluation aimed at determining the extent of myometrial invasion or cervical involvement. The introduction of the sentinel node approach has made lymph node biopsy a viable substitute for systematic lymphadenectomy in stage I/II, thereby mitigating the morbidity associated with lymphadenectomy.[6] The primary prognostic factors for endometrial cancer include grade, histotype, nodal metastases, and deep myometrial infiltration.[7] Specifically, the infiltration of the myometrium and involvement of the cervix, which may be evaluated by the use of ultrasonography, are important preoperative factors that have the potential to impact the staging and surgical strategy.[8,9] Given the lack of reproducibility associated with the frozen section technique for assessing myometrial invasion, it is now discouraged. In addition, there is a growing trend towards employing sentinel node biopsy for lymph node staging in stage I/II endometrial cancer. Consequently, the selection of an appropriate preoperative work-up is crucial for effective surgical planning and obtaining informed consent. The objective of our research was to assess the accuracy of transvaginal ultrasonography (TVS) in the preoperative staging of endometrial cancer, specifically in relation to the invasion of the myometrium and cervical stroma. We intended to compare these findings with the established gold-standard method of tumour staging, which is the final histological analysis. Our objective also included the assessment of concordance between transvaginal ultrasound (TVS) and pelvic magnetic resonance imaging (MRI), which is widely recognized as the gold standard for preoperative imaging staging.

Materials and Methods

A prospective research was conducted in the department of radio-diagnosis and gynecology at Mallareddy Institute of Medical Sciences and Mallareddy Narayana Multispeciality Hospital during the period from March 2022 to August 2023. The research included women who had been diagnosed with endometrial malignancy by histological confirmation, which was achieved through procedures such as dilation and curettage, hysteroscopy, or endometrial biopsy. Additionally, women who had a high suspicion of endometrial malignancy based on imaging results and were scheduled for surgery as their main therapy were also eligible to participate in the study. Exclusion criteria encompassed cases where there was a suspicion of uterine malignancy but lacked histological confirmation, individuals who were unable to undergo pelvic MRI due to contraindications, technical limitations preventing transvaginal or transrectal ultrasonography, those for whom surgery as the primary treatment was contraindicated, and situations where urgent or emergency life-saving surgery precluded pre-surgical diagnosis and staging. The institutional review board of each centre granted approval for the protocol and consent forms, and before to enrollment, all participants or their legally authorized representative submitted signed informed consent.

Methodology

The recruitment process for the experiment and subsequent data collection was conducted via individual consultations facilitated by the primary investigator. The diagnostic features obtained during TVS were collected according to a predetermined protocol based on previous research.[9] These features included measurements of uterine and tumour dimensions and volume, endometrial thickness, presence of fluid within the uterine cavity, assessment of tumour vascularization, evaluation of the regularity of the endometrial contour and junctional zone, subjective determination of myometrial invasion, and objective assessment using the Gordon and Karlsson methods.[10,11] Cervical involvement was assessed subjectively and objectively by measuring the distance between the outer cervical orifice and the lower margin of the tumour, with a cut-off value of less than 20 mm indicating involvement.[12] Additionally, the presence of invasion into adjacent organs, ascites, and other gynaecological findings that could impact staging were also considered. The radiologist expert established MRI guidelines for endometrial cancer imaging staging, drawing upon worldwide agreement.[13] TVS were conducted by either a resident fellow or a specialist. The used equipment consisted of a GE Voluson E8 US system, which was equipped with a RICS5-9 transducer or a comparable device. The pelvic MRI scan was analysed by a radiologist who had extensive experience of over five years in the field of gynecologic imaging. The clinical and imaging data were blinded for all imaging tests and were systematically conducted according to a predetermined procedure, which was completed by the investigator after each examination. The comprehensive surgical staging protocol includes many procedures such as abdominopelvic washings, complete hysterectomy, bilateral salpingo-oophorectomy, and pelvic and para-aortic lymph node dissection. These procedures are performed based on either intra-operative frozen section staging or preoperative biopsy histologic criteria. The gold standard for evaluating histological changes post-surgery was deemed to be histologic examination. The post-operative staging procedure was conducted by a specialised pathologist who had extensive knowledge in the field of gynecologic cancer. The staging was carried out in accordance with the latest recommendations established by the International Federation of Gynaecology and Obstetrics (FIGO) in 2009.[14]

Statistical Analysis

The study computed sensitivity, specificity, and overall accuracy for each staging technique (transvaginal ultrasound or magnetic resonance imaging) in contrast to the final histopathological examination, which served as the gold standard. Ninety-five percent confidence intervals (95% CI) were also determined for these measures. The aforementioned calculations assessed the extent of myometrial and cervical invasion, since these are critical factors that may significantly influence staging and determine appropriate surgical interventions. The assessment of agreement was conducted by determining the overall and specific Proportions of Agreement (PA) within each category, as well as evaluating dependability using the kappa statistic (K). If the lower boundary of the 95% confidence interval (CI) for the proportion of agreement (PA) is less than 0.50, it will be seen as indicative of poor agreement.

Results

A total of 110 individuals satisfied the criteria for inclusion in the research, with an average age of 49.89 ± 2.99 years. Among these participants, 99 (90%) were postmenopausal, 70 (63.64%) had arterial hypertension, 66 (60%) were obese, 30 (27.27%) had diabetes, and 11 (10%) had high-risk endometrial cancer mutations (Figure 1). The research primarily focused on endometrial malignancies, with the majority of cases (80.91%) being of the endometrioid histological type. Among these cases, 80.91% were classified as well to moderately differentiated, specifically grade 1 or 2. The majority of malignancies were identified at FIGO stage 1 or 2, accounting for 89 cases or 80.91% of the total (Table 1).

In relation to the extent of myometrial invasion, our study yielded sensitivity rates of 81%, 81%, and 69% for the subjective, Gordon, and Karlsson techniques, respectively. The corresponding specificity rates were found to be 67%, 60%, and 81% for the same approaches (Figure 2). The subjective, Gordon, and Karlsson techniques yielded corresponding overall accuracies of 74%, 70%, and 75%. The use of contrast-enhanced MRI yielded a sensitivity, specificity, and overall accuracy of 94%, 72%, and 84%, respectively, in the assessment of myometrial invasion (Table 2).

In the assessment of cervical stromal invasion, the ultrasound subjective technique showed a sensitivity of 33% and a specificity of 99%. On the other hand, the objective method yielded a sensitivity of 52% and a specificity of 92% (Figure 3). The total accuracy for both methods was determined to be 90% and 83% respectively. The use of contrast-enhanced MRI yielded a sensitivity, specificity, and overall accuracy of 69%, 100%, and 96% respectively in detecting cervical involvement, as seen in Table 3.

The inter-rater reliability between magnetic resonance imaging (MRI) and transvaginal sonography (TVS) for the

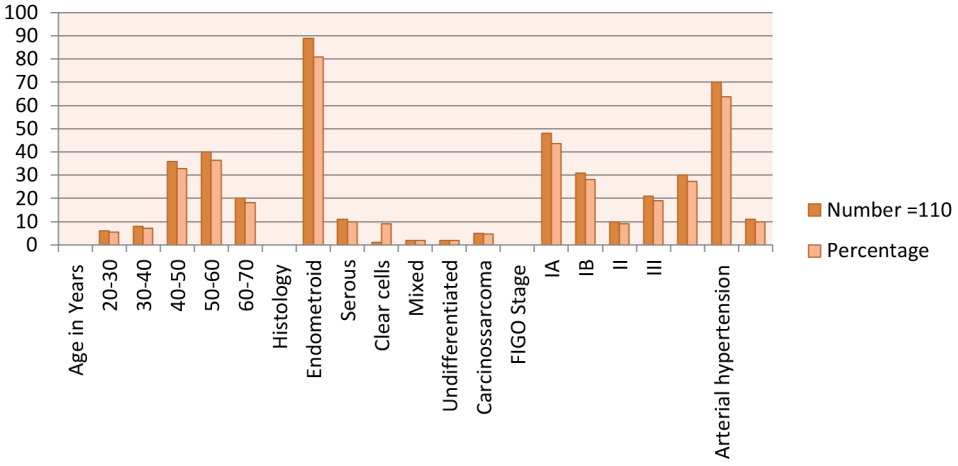

Fig. 1 **Basic parameter of the participants.**

Table 1. **Basic parameter of the participants**

Basic profile	Number = 110	Percentage
Age in years		
20–30	6	5.45
30–40	8	7.27
40–50	36	32.73
50–60	40	36.36
60–70	20	18.18
Age	65.85 ± 3.85	
Age of menopause	49.89 ± 2.99	
Body mass index (kg/m^2)	31.88 ± 2.69	
Histology		
Endometroid	89	80.91
Serous	11	10
Clear cells	1	9.09
Mixed	2	1.82
Undifferentiated	2	1.82
Carcinossarcoma	5	4.55
FIGO Stage		
IA	48	43.64
IB	31	28.18
II	10	9.09
III	21	19.09
Type 2 Diabetes mellitus	30	27.27
Arterial hypertension	70	63.64
BRCA or Lynch mutation	11	10

three ultrasound techniques demonstrated fair to moderate agreement (K = 0.29 to 0.49) in assessing myometrial deep invasion, and moderate agreement (K = 0.47 to 0.60) in evaluating cervical involvement. The level of agreement in the evaluation of cervical invasion was found to be higher for cases categorised as "no" compared to those categorised as "yes" (Table 4).

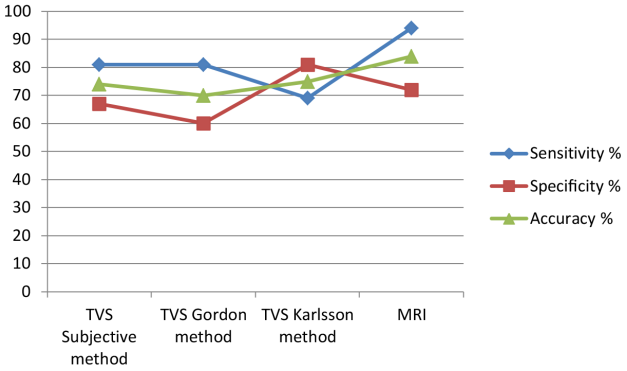

Fig. 2 **Assessment of myometrial invasion.**

When using a combination of methodologies, the assessment of myometrial invasion via the subjective, Gordon, and Karlsson procedures, when paired with MRI for positive deep myometrial invasion, yielded sensitivity rates of 77%, 74%, and 69% respectively. Additionally, the specificity rates for these approaches were found to be 84%, 84%, and 90% respectively. When considering the presence of deep myometrial invasion, our study revealed that if at least one technique is able to classify it as positive, the subjective, Gordon, and Karlsson approaches, when paired with MRI, showed sensitivities of 98%, 100%, and 97% respectively. Additionally, the specificities observed were 52%, 46%, and 67% for the subjective, Gordon, and Karlsson approaches respectively. According to Table 5.

Discussion

TVS and MRI are commonly used imaging modalities for the preoperative assessment of DMI and CSI in EC. At now, a consensus has not been reached about the most appropriate imaging approach for preoperative staging in EC. The selection of an imaging technique is mostly influenced by the availability and expertise within each institution. The efficacy of TVS in the detection of EC in women is shown to be moderate when conducted by a skilled ultrasonographer. MRI has a commendable diagnostic efficacy and is widely regarded as the preferred imaging modality for staging EC by the

Table 2. **Assessment of myometrial invasion**

Myometrial invasion	Sensitivity [95% CI]	Specificity [95% CI]	Accuracy [95% CI]
TVS Subjective method	0.81 [0.62–0.93]	0.67 [0.47–0.81]	0.74 [0.59–0.83]
TVS Gordon method	0.81 [0.61–0.93]	0.60 [0.40–0.75]	0.70 [0.55–0.80]
TVS Karlsson method	0.69 [0.48–0.83]	0.81 [0.62–0.91]	0.75 [0.61–0.84]
MRI	0.94 [0.75–0.99]	0.72 [0.50–0.87]	0.84 [0.69–0.92]

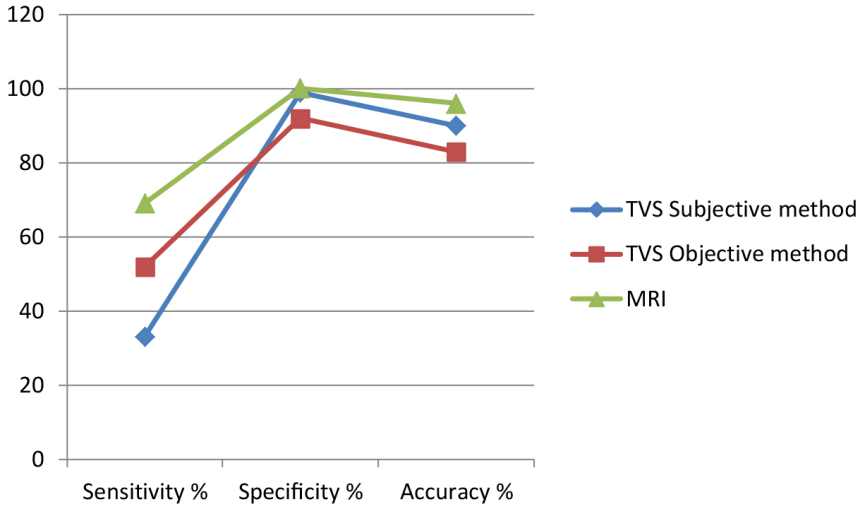

Fig. 3 **Evaluation of cervical invasion.**

Table 3. **Evaluation of cervical invasion**

Cervical invasion	Sensitivity [95% CI]	Specificity [95% CI]	Accuracy [95% CI]
TVS Subjective method	0.33 [0.07–0.63]	0.99 [0.90–1.00]	0.90 [0.77–0.96]
TVS Objective method	0.52 [0.19–0.81]	0.92 [0.75–0.99]	0.83 [0.70–0.92]
MRI	0.69 [0.37–0.92]	1.00 [0.92–1.00]	0.96 [0.84–0.99]

Table 4. **Correlation between TVS and MRI regarding myometrial deep invasion and cervical involvement**

TVS Karlsson method vs MRI	0.49 [0.29–0.69]	0.76 [0.59–0.86]
Superficial		0.59 [0.39–0.69]
Deep		0.63 [0.42–0.69]
TVS Subjective method vs MRI	0.45 [0.19–0.67]	0.75 [0.59–0.79]
Superficial		0.51 [0.29–0.71]
Deep		0.65 [0.51–0.74]
TVS Gordon method vs MRI	0.29 [0.06–0.49]	0.70 [0.57–0.81]
Superficial		0.41 [0.26–0.58]
Deep		0.61 [0.47–0.69]
Cervical invasion		
TVS Subjective method vs MRI	0.60 [0.19–0.91]	0.95 [0.85–0.98]
No		0.94 [0.79–0.98]
Yes		0.46 [0.21–0.81]

(Continued)

Table 4. **Correlation between TVS and MRI regarding myometrial deep invasion and cervical involvement—Continued**

TVS Objective method vs MRI	0.47 [0.11–0.81]	0.79 [0.71–0.89]
No		0.79 [0.59–0.89]
Yes		0.41 [0.21–0.71]
TVS Subjective vs Objective method	0.64 [0.29–0.95]	0.89 [0.81–0.97]
No		0.89 [0.69–0.97]
Yes		0.51 [0.19–0.97]

Table 5. **Sensitivity, specificity and accuracy of combination of TVS and MRI**

"yes" if both approaches classify "yes"			
TVS Subjective method and MRI	0.77 [0.61–0.91]	0.84 [0.63–0.95]	0.81 [0.71–0.91]
TVS Gordon method and MRI	0.74 [0.53–0.88]	0.84 [0.63–0.95]	0.79 [0.64–0.85]
TVS Karlsson method and MRI	0.69 [0.59–0.79]	0.90 [0.69–0.98]	0.81 [0.65–0.87]
"yes" if at least one approach classifies "yes"			
TVS Subjective method and MRI	0.98 [0.83–0.99]	0.52 [0.29–0.69]	0.76 [0.59–0.86]
TVS Gordon method and MRI	1.00 [0.89–0.99]	0.46 [0.31–0.64]	0.75 [0.59–0.85]
TVS Karlsson method and MRI	0.97 [0.79–0.98]	0.67 [0.45–0.79]	0.81 [0.61–0.91]

European Society of Urogenital Radiology. This preference stems from the exceptional picture resolution and soft-tissue contrast that MRI offers.

The use of medical imaging techniques has been recommended for the preoperative assessment and care of individuals diagnosed with uterine corpus cancer. The European recommendations for the care of patients with endometrial cancer, which have been recently revised, recommend the use of expert transvaginal or transrectal ultrasonography or pelvic MRI as part of the pre-operative required work-up.[6] In our investigation, magnetic resonance imaging (MRI) demonstrated the most notable sensitivity (94%) in evaluating myometrial invasion. An overlapping sensitivity of 81% was seen for both the subjective and Gordon approaches. The Karlsson technique, on the other hand, exhibited the lowest sensitivity at 69%, but the greatest specificity at 81%. If both preoperative tests, TVS and MRI, provide positive results for deep myometrial invasion, the combined sensitivity for the subjective, Gordon, and Karlsson techniques is reported to be 77%, 74%, and 69% respectively. The specificity for these procedures is reported as 84%, 84%, and 90% respectively. When at least one technique is able to classify deep invasion as positive, the sensitivity of the subjective, Gordon, and Karlsson approaches coupled with MRI was shown to be greater (98%, 100%, and 97% respectively), but the specificity was lower (52%, 46%, and 67% respectively). It is worth noting that magnetic resonance imaging (MRI) demonstrated a greater overall accuracy in comparison to ultrasonographic procedures, with a reported accuracy of 84% as opposed to a range of 70–75%. A comprehensive examination and statistical analysis of 24 studies were conducted to evaluate the diagnostic precision of TVS in identifying deep myometrial infiltration prior to surgery. The results indicated an aggregated sensitivity of 82% and specificity of 81%, with no significant disparities observed between subjective and objective approaches. Alcazar et al. conducted a clinical trial to evaluate and compare the diagnostic efficacy of six distinct methods for assessing myometrial infiltration in women diagnosed with grade 1 or 2 endometrioid carcinoma.[15] The methods included transvaginal or transrectal ultrasound techniques, namely the examiner's impression, Karlsson's criteria, endometrial thickness, tumor/uterine 3D volume ratio, tumour distance to myometrial serosa, and van Holsbeke's subjective model. The most effective methods for evaluating myometrial infiltration were found to be the impression of examiner and subjective model, with sensitivity rates of 79.5% and 80.5% and specificity rates of 89.6% and 90.3% respectively. These techniques demonstrated much higher sensitivity compared to Karlsson's criterion, which had a sensitivity rate of 31.8%.[16] Frühauf et al. (year) presented comparable findings, documenting a sensitivity, specificity, and overall accuracy of 79.3%, 75.7%, and 75.7% correspondingly for subjective evaluation. For Gordon's ratio, the corresponding values were 69.6%, 65.9%, and 67.3%, while Karlsson's technique yielded results of 56.3%, 76.4%, and 68.1%.[17] The findings of our study provide further support for previous research, indicating that the subjective method demonstrated a considerable level of diagnostic accuracy (74%). Additionally, our results indicate that Karlsson's criteria exhibited lower sensitivity (69%) compared to subjective assessment (81%). In a recent study conducted by Alcazar et al., a systematic review and meta-analysis were performed to assess the effectiveness of MRI and TVS in identifying myometrial infiltration in cases of endometrial cancer. The authors reported a pooled estimated sensitivity of 75% and specificity of 82% for TVS, whereas MRI showed a sensitivity of 83% and specificity of 82%1.[18] The results of our investigation indicate that the accuracies of both preoperative procedures were similar. An observational study was conducted to assess the

concordance between preoperative transvaginal ultrasound and intraoperative macroscopic examination in low-risk endometrioid carcinoma, specifically in relation to deep myometrial invasion. The study included 152 women. The findings revealed that while the agreement between the two approaches was only moderate, both methods demonstrated comparable accuracy when compared to frozen section histology. These results further support the utilisation of preoperative ultrasound by experienced professionals.[19]

Regarding other factors impacting preoperative staging, Fischerova et al.[20] could not substantiate the anticipated association between ultrasound failure and variables such as obesity, uterine position, or the quality of ultrasound imaging. According to a recent retrospective investigation, the primary confounding factor that significantly affects diagnosis accuracy in patients with coexisting benign uterine diseases such as diffuse fibromatosis and adenomyosis is FIGO stage IB.[21] The big multicentre investigation did not find any evidence of enhanced diagnostic accuracy in myometrial infiltration when using 3D transvaginal ultrasound compared to 2D ultrasound. Nevertheless, a recent systematic review has shown that three-dimensional transvaginal ultrasound (3D-TVUS) has equal or even greater performance to MRI in one research, and is mainly equivalent to two-dimensional transvaginal ultrasound (2D-TVUS). This finding highlights the potential of 3D-TVUS in clinical practice.[22,23]

The research used four examiners; however, the limited number of examinations conducted by each examiner hindered the ability to discern subtle variations in the overall diagnostic accuracy rate per examiner and potential disparities between experienced professionals and trainees. There are ongoing concerns over the repeatability of various measurement methodologies in real-time ultrasonography exams. The study conducted by Ericsson et al. revealed a higher level of concurrence with histology and increased consistency across ultrasonography specialists when evaluating cervical stromal invasion. However, this was not seen in the evaluation of deep myometrial invasion.[24]

In relation to cervical stromal invasion, our study findings indicate that MRI had the greatest specificity (69%) in detecting cervical involvement. The sensitivity of the ultrasonic subjective technique was found to be poor, but its specificity was high at 99%. However, the sensitivity of the subjective approach was marginally improved by the use of MRI. On the other hand, the objective methodology yielded identical findings for specificity but shown better sensitivity compared to the subjective approach. The overall accuracy of MRI was found to be greater at 96%, whereas the subjective approach had a very equivalent accuracy rate of 90%. The level of agreement between subjective and objective TVS techniques ranged from fair to moderate. In terms of the agreement between MRI and TVS, it was observed that subjective measurement exhibited somewhat superior performance in comparison to the objective approach. A prior investigation discovered that a threshold of less than 20 mm, measured from the outside cervical ostium to the lower boundary of the tumour, exhibited a correlation with the likelihood of cervical stromal invasion. Nonetheless, it was seen that subjective evaluation yielded much superior results.[14]

One primary limitation of our research is the limited sample size of referred patients who met the specified inclusion criteria, despite the recruiting efforts being conducted throughout three cancer care facilities. The limited size of the sample may pose a risk to the generalizability of the findings and the assessment of repeatability. Moreover, it is worth noting that the study's statistical power may be insufficient to ascertain the precision of pre-surgical staging in relation to cervical invasion. This limitation arises from the scarcity of patients with advanced illness who are deemed inappropriate for surgical intervention.

In relation to the limitations of TVUS, it is important to note that the assessment process is subject to examiner bias and may be influenced by factors such as the quality of the equipment used and the characteristics of the patient being examined. Another limitation is related to the characteristics of the tumour. For instance, a sizable polypoid bulky endometrial cancer can result in an overestimation of myometrial invasion due to the stretching impact it has on the adjacent myometrium. Conversely, a small uterus with an apparently thin, hypoechoic, or poorly defined endometrial stripe may actually exhibit deep infiltration.[8] Ultrasonography is a widely accessible and cost-effective imaging technique that is non-invasive in nature. It serves as a dependable substitute for MRI, particularly in regions with medium and low income levels where immediate access to MRI is limited and financial considerations are significant. Furthermore, the use of this technology has the potential to significantly influence the process of surgical planning, as well as cost and time management inside the operating theatre. This might eliminate the need for frozen section examination and enable the precise identification of patients with low and intermediate risk that are suitable for the implementation of the sentinel lymph node approach. Based on current international recommendations, sentinel lymph node biopsy is considered a viable alternative to systematic lymphadenectomy for the purpose of lymph node staging, especially in cases with high-intermediate and high-risk illness at stage I/II.

Conclusion

We concluded that the utilisation of pelvic ultrasound in the preoperative staging of endometrial cancer holds significant value. It demonstrates a notable sensitivity in evaluating myometrial invasion, exhibiting a reasonable to moderate level of concordance with MRI. Furthermore, it exhibits a superior, albeit still moderate, level of agreement with MRI in assessing cervical invasion.

References

1. Stukan M, Buderath P, Szulczyński B, Gębicki J, Kimmig R. Accuracy of ultrasonography and magnetic resonance imaging for preoperative staging of cervical cancer—analysis of patients from the prospective study on total mesometrial resection. Diagnostics (Basel). 2021;11(10):1749. doi: 10.3390/diagnostics11101749, PMID 34679447.
2. Rei M, Costa-Santos C, Bernardes J, Costa A. Preoperative staging of uterine cancer: can transvaginal ultrasonography play a role? Front Oncol. 2023 Jun 19;13:1089105. doi: 10.3389/fonc.2023.1089105, PMID 37404747, PMCID PMC10315648.
3. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. CA Cancer J Clin. 2020;70(1):7–30. doi: 10.3322/caac.21590, PMID 31912902.

4. Colombo N, Creutzberg C, Amant F, Bosse T, González-Martín A, Ledermann J, Marth C, Nout R, Querleu D, Mirza MR, Sessa C; ESMO-ESGO-ESTRO Endometrial Consensus Conference Working Group. ESMO-ESGO-ESTRO consensus conference on endometrial cancer: Diagnosis, treatment and follow-up. Radiother Oncol 2015; 117: 559–581.
5. Creasman W. Revised FIGO staging for carcinoma of the endometrium. Int J Gynaecol Obstet. 2009;105(2):109. doi: 10.1016/j.ijgo.2009.02.010, PMID 19345353.
6. Koh W-J, Abu-Rustum NR, Bean S, Bradley K, Campos SM, Cho KR et al. Uterine neoplasms. Version 1.2018, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw; 2018. Vol. 16. p. 170–99.
7. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021;71(3):209–49. doi: 10.3322/caac.21660, PMID 33538338.
8. Abramowicz JS, Kossoff G, Marsal K, Ter Haar G, International Society of Ultrasound in Obstetrics and Gynecology Bioeffects and Safety Committee. Executive Board of the International Society of Ultrasound in Obstetrics and Gynecology. Safety Statement, 2000 (reconfirmed 2003). International society of ultrasound in obstetrics and gynecology (ISUOG). Ultrasound Obstet Gynecol. 2003;21(1):100. doi: 10.1002/uog.36, PMID 12528176.
9. Savelli L, Ceccarini M, Ludovisi M, Fruscella E, De Iaco PA, Salizzoni E, et al. Preoperative local staging of endometrial cancer: transvaginal sonograph vs magnetic. resonance imaging. Ultrasound Obstet Gynecol. 2008;31(5):560–6. doi: 10.1002/uog.5295, PMID 18398926.
10. Scaletta G, Dinoi G, Capozzi V, Cianci S, Pelligra S, Ergasti R, et al. Comparison of minimally invasive surgery with laparotomic approach in the treatment of high risk endometrial cancer: a systematic review. Eur J Surg Oncol. 2020;46(5):782–8. doi: 10.1016/j.ejso.2019.11.519, PMID 31818527.
11. Gordon AN, Fleischer AC, Reed GW. Depth of myometrial invasion in endometrial cancer: preoperative assessment by transvaginal ultrasonography. Gynecol Oncol. 1990;39(3):321–7. doi: 10.1016/0090-8258(90)90260-r, PMID 2258078.
12. Karlsson B, Norström A, Granberg S, Wikland M. The use of endovaginal ultrasound to diagnose invasion of endometrial carcinoma. Ultrasound Obstet Gynecol. 1992;2(1):35–9. doi: 10.1046/j.1469-0705.1992.02010035.x, PMID 12797004.
13. Mascilini F, Testa AC, Van Holsbeke C, Ameye L, Timmerman D, Epstein E. Evaluating myometrial and cervical invasion in women with endometrial cancer: comparing subjective assessment with objective measurement techniques. Ultrasound Obstet Gynecol. 2013;42(3):353–8. doi: 10.1002/uog.12499, PMID 23640790.
14. Amant F, Moerman P, Neven P, Timmerman D, Van Limbergen E, Vergote I. Endometrial cancer. Lancet. 2005;366(9484):491–505. doi: 10.1016/S0140-6736(05)67063-8.
15. Alcázar JL, Orozco R, Martinez-Astorquiza Corral T, Juez L, Utrilla-Layna J, Mínguez JA et al. Transvaginal ultrasound for preoperative assessment of myometrial invasion in patients with endometrial cancer: a systematic review and meta-analysis. Ultrasound Obstet Gynecol. 2015;46(4):405–13. doi: 10.1002/uog.14905, PMID 26011665
16. Alcazar JL, Pineda L, Corral M-A T, Orozco R, Utrilla-Layna J, Juez L, et al. Transvaginal/transrectal ultrasound for assessing myometrial invasion in endometrial cancer: a comparison of six different approaches. J Gynecol Oncol (2015) 26(3):201–7. doi: 10.3802/jgo.2015.26.3.201.
17. Frühauf F, Zikan M, Semeradova I, Dundr P, Nemejcova K, Dusek L, et al. The diagnostic accuracy of ultrasound in assessment of myometrial invasion in endometrial cancer: subjective assessment versus objective techniques. BioMed Res Int. 2017;2017:1318203. doi: 10.1155/2017/1318203, PMID 28812010.
18. Alcázar JL, Gastón B, Navarro B, Salas R, Aranda J, Guerriero S. Transvaginal ultrasound versus magnetic resonance imaging for preoperative assessment of myometrial infiltration in patients with endometrial cancer: a systematic review and meta-analysis. J Gynecol Oncol. 2017;28(6):e86. doi: 10.3802/jgo.2017.28.e86, PMID 29027404.
19. Pineda L, Alcázar JL, Caparrós M, Mıńguez JA, Idoate MA, Quiceno H, et al. Agreement between preoperative transvaginal ultrasound and intraoperative macroscopic examination for assessing myometrial infiltration in low-risk endometrioid carcinoma. Ultrasound Obstet Gynecol. 2016;47(3):369–73. doi: 10.1002/uog.14909, PMID 26033260.
20. Fischerova D, Frühauf F, Zikan M, Pinkavova I, Kocián R, Dundr P, et al. Factors affecting sonographic preoperative local staging of endometrial cancer. Ultrasound Obstet Gynecol. 2014;43(5):575–85. doi: 10.1002/uog.13248, PMID 24281994.
21. Capozzi VA, Merisio C, Rolla M, Pugliese M, Morganelli G, Cianciolo A, et al. Confounding factors of transvaginal ultrasound accuracy in endometrial cancer. J Obstet Gynaecol. 2021;41(5):779–84. doi: 10.1080/01443615.2020.1799342, PMID 33063589.
22. Green RW, Valentin L, Alcazar JL, Chiappa V, Erdodi B, Franchi D, et al. Endometrial cancer off-line staging using two-dimensional transvaginal ultrasound and three-dimensional volume contrast imaging: intermethod agreement, interrater reliability and diagnostic accuracy. Gynecol Oncol. 2018;150(3):438–45. doi: 10.1016/j.ygyno.2018.06.027, PMID 30029961.
23. Ziogas A, Xydias E, Kalantzi S, Papageorgouli D, Liasidi PN, Lamari I, et al. The diagnostic accuracy of 3D ultrasound compared to 2D ultrasound and MRI in the assessment of deep myometrial invasion in endometrial cancer patients: a systematic review. Taiwan J Obstet Gynecol. 2022;61(5):746–54. doi: 10.1016/j.tjog.2022.06.002, PMID 36088040.
24. Eriksson LS, Lindqvist PG, Flöter Rådestad A, Dueholm M, Fischerova D, Franchi D, et al. Transvaginal ultrasound assessment of myometrial and cervical stromal invasion in women with endometrial cancer: interobserver reproducibility among ultrasound experts and gynecologists. Ultrasound Obstet Gynecol. 2015;45(4):476–82. doi: 10.1002/uog.14645, PMID 25092412.