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Comparison between gynecologic oncology ultrasound and magnetic resonance imaging in the assessment of early-stage cervical cancer: A local experience in cancer imaging

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Abstract:

OBJECTIVE: This study aimed to compare the diagnostic accuracy of gynecologic oncology ultrasound and magnetic resonance imaging (MRI) in the assessment of early-stage cervical cancer.

METHODOLOGY: This was a prospective, cross-sectional study of patients with early-stage cervical cancer eligible for radical hysterectomy in a tertiary government institution from November 25, 2020, to August 2, 2022. Preoperative gynecologic oncology (transabdominal/transvaginal/transrectal) ultrasound and MRI measurements were obtained and compared with histopathologic findings. Sensitivity, specificity, positive predictive value, negative predictive value, and positive likelihood ratio were used to check for the diagnostic accuracy of each modality.

RESULTS: A total of 27 patients were enrolled in the study. Four were stage IB1 (14.81%), 10 were stage IB2 (37.03%), nine were stage IB3 (33.33%), two were stage IIA1 (7.40%), and two were stage IIA2 (7.40%). Ultrasound has a comparable diagnostic accuracy with MRI to assess tumor size length, width, and height with an area under the curve of 0.789, 0.753, and 0.806, respectively. Both modalities can predict the absence of parametrial invasion and nodal involvement with a specificity of 100% and a negative predictive value of 88.89% and 81.48%, respectively. The results of the gynecologic oncology ultrasound showed good agreement with MRI.

CONCLUSION: Ultrasound has comparable diagnostic accuracy with MRI in assessing tumor size, parametrial invasion, and nodal involvement in patients with early-stage cervical cancer. It is a good alternative imaging modality to MRI in staging cervical cancer, especially in low- to middle-income countries.

Keywords:

Early-stage cervical cancer, gynecologic oncology ultrasound, magnetic resonance imaging

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Introduction

Cervical cancer ranks as the second-most frequent gynecologic cancer among Filipino women. About 2.9% of women in the general population are estimated to harbor high-risk human papillomavirus (HPV) 16/18 infection at a given time, and 58.6% of invasive cervical cancers are attributed to these high-risk HPV types.[1] The majority of these women who eventually develop invasive cervical cancer are diagnosed in the advanced stage. Precise knowledge of the tumor stage allows the physician to tailor the treatment, whether chemoradiation or radical surgery, to what is optimal for a particular patient, and at the same time, minimizing the inherent treatment-related

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effects as well as avoiding giving two radical procedures to an individual. Staging classification for cervical cancer was initially based on clinical assessment of tumor size, vaginal and/or parametrial involvement, and bladder/rectum tumoral extension. In 2018, the International Federation of Obstetrics and Gynecology incorporated imaging as a complement to clinical assessment in the staging of cervical cancer. Magnetic resonance imaging (MRI) has been recommended as the best modality to assess tumor size and volume, parametrial invasion, and adjacent organ invasion.[2] It is available in the majority of tertiary institutions in the country; however, its use and acceptance have been limited by its cost. In recent years, ultrasound has gained increased attention in the preoperative staging of cervical cancer. Prospective studies have shown that the accuracy of transrectal or transvaginal ultrasound is comparable to MRI.[3,4] Furthermore, ultrasound is affordable and accessible, and the results are immediately available, in contrast to MRI. It is also more acceptable to patients since there are no preprocedure preparations needed. Ultrasound, therefore, is the best alternative method to MRI, especially in low- to middle-income countries like the Philippines. To the best of our knowledge, there are no local data published comparing ultrasound and MRI in the assessment of tumor volume and parametrial and nodal invasion in early-stage cervical cancer.

Objective

General

The objective was to compare the diagnostic accuracy of gynecologic oncology ultrasound and MRI in the assessment of early-stage cervical cancer.

Specific

1. To determine the sensitivity, specificity, positive predictive value, negative predictive value, and likelihood ratio of gynecologic oncology ultrasound in the assessment of tumor size, parametrial invasion, and nodal involvement in patients with early-stage cervical cancer
2. To determine the sensitivity, specificity, positive predictive value, negative predictive value, and likelihood ratio of MRI in the assessment of tumor size, parametrial invasion, and nodal involvement in patients with early-stage cervical cancer.

Methodology

Study design and setting of the study

This was a prospective cross-sectional study done among women diagnosed with early-stage cervical cancer (Stage IA2-IIA2) between November 25, 2020, and August 2, 2022, in a tertiary government institution. The study was approved by the Institutional Review Board last November 19, 2020.

Study participants/target population

Consecutive patients with histopathologically confirmed cervical cancer, diagnosed through clinical examination by a trainee and confirmed by a consultant to have Stage IA2, IB1, IB2, and IIA1 cervical cancer and Stage IB3 and IIA2 postneoadjuvant chemotherapy using paclitaxel and cisplatin for three cycles who were eligible for radical hysterectomy, with good surgical risk, and who read and signed the informed consent were included in the study.

Women excluded from the study were the following:

1. Those with associated pregnancy or with poor surgical risk
2. Those who refused radical surgery or with prior radiotherapy
3. Those diagnosed with other malignancies
4. Those with poor histologic types such as carcinosarcoma, neuroendocrine, and leiomyosarcoma.

Sample size collection

In the sample size, the sensitivity used was based on a study titled "Transrectal ultrasound (TRUS) and MRI in the evaluation of tumor size following neoadjuvant chemotherapy for locally advanced cervical cancer" by Pinkavova *et al*.[5] According to the study, the posttreatment MRI and TRUS images showed evidence of a tumor with a sensitivity of 96.3% (26/27). Thus, the sensitivity used was 96.3%, the *Z*-score was 1.96 (for a 95% confidence level), the error rate was 10%, and the prevalence used was 50% with a computed sample size of 27 [Figure 1].

Data collection

All patients underwent gynecologic oncology ultrasound (transvaginal/transrectal and transabdominal) and pelvic MRI not more than two weeks before surgery. A maximum of 7 days of procedure interval between ultrasound and MRI was allowed. Transabdominal/transvaginal/TRUS examination was performed by one sonologist trained in doing gynecologic oncology ultrasound. The machine used was Samsung WS80 with curved array transducer models CV1-8A, EV2-10A, and LA3-16A. Tumor size and parametrial and nodal involvement were assessed as shown in Figures 2-4.

A standardized MRI examination technique with contrast medium was used, including T2-weighted [Figure 5] sequences in the sagittal and axial planes (perpendicular to the long axis of the cervix) and axial T1-weighted [Figure 6] sequences to assess tumor size, extension to parametria, and nodal metastasis. One radiology resident interpreted the result, and this was confirmed by the consultant in charge.

After a radical hysterectomy, specimens were properly labeled and measured by one dedicated

$$n \geq \frac{z^2_{1-\alpha/2} \times Sensitivity \times (1 - Sensitivity)}{d^2 \times (1 - Prevalence)}$$

$$n \geq \frac{1.96^2 \times 0.963 \times (1 - 0.963)}{0.10^2 \times 0.50}$$

$$n \geq \frac{0.13688005}{0.005}$$

$$n \geq 27.37600992$$

$$n \geq 27$$

$$n \geq \frac{z^2_{1-\alpha/2} \times Sensitivity \times (1 - Sensitivity)}{d^2 \times (1 - Prevalence)}$$

$$n \geq \frac{1.96^2 \times 0.963 \times (1 - 0.963)}{0.10^2 \times 0.50}$$

$$n \geq \frac{0.13688005}{0.005}$$

$$n \geq 27.37600992$$

$$n \geq 27$$

Figure 1: Formula of computed sample size

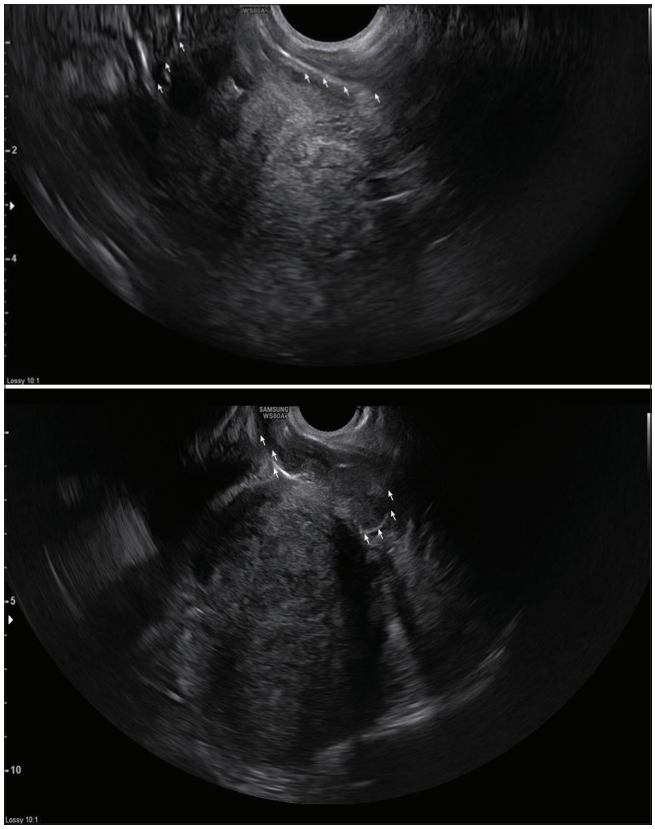

Figure 3: Determining pericervical fascia (no parametrial invasion)

pathology rotator. Specimens were fixed in buffered formalin and sent to the pathology department for histopathologic examination. A dedicated resident

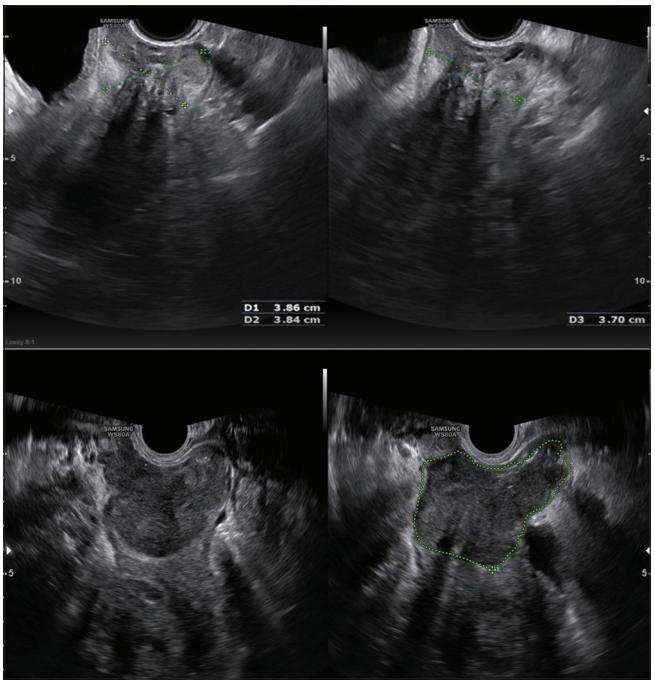

Figure 2: Determining tumor size

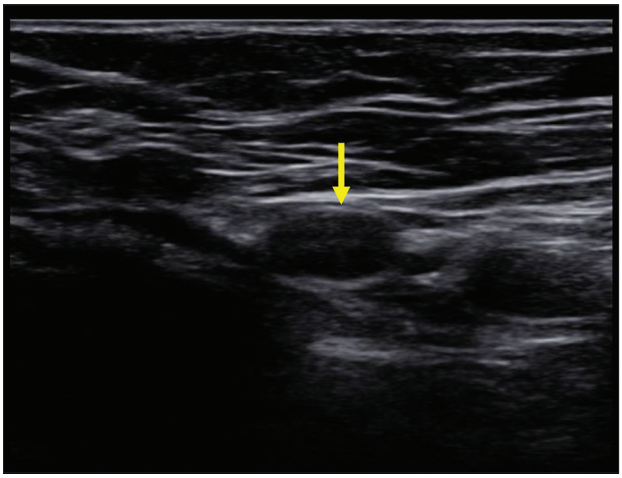

Figure 4: Determining nodal involvement (Arrow points to the reactive lymph node)

pathologist assessed the specimens with approximate sectioning of 2 mm intervals. Each specimen was measured and described macroscopically (pre- and postformalin) and microscopically with the following parameters: size and location of the lesion, distance from margins and gross depth of invasion, extension to other areas, and nodal involvement. Results were confirmed by the consultant in charge. The sonologist, radiologist, and pathologist were all blinded to the clinical and imaging findings. The results of the sonographic and radiologic (MRI) findings were compared to the histopathologic findings as the gold standard. The preformalinized specimen was used for tumor comparison and the formalinized specimen for parametrial and nodal involvement.

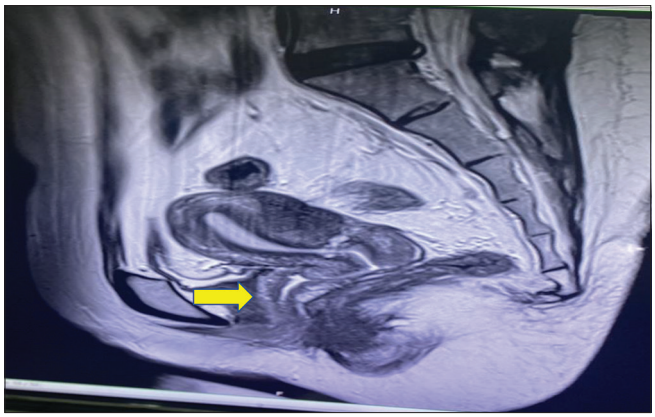

Figure 5: T2-weighted image of the cervix

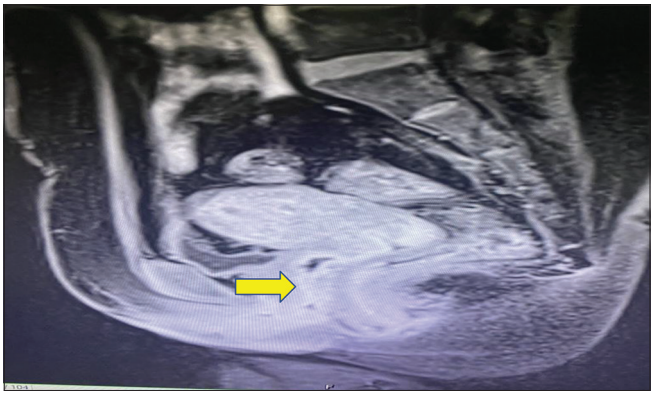

Figure 6: T1-weighted image of the cervix

Statistical analysis

The following parameters were evaluated by ultrasound, MRI, and histopathology report: the presence of tumor size in three dimensions (height, weight, and length), parametrial invasion, and nodal involvement. Descriptive statistics such as median, interquartile range, frequency, and percentage were used to summarize the demographic and clinical characteristics of the patients. Sensitivity, specificity, positive predictive value, negative predictive value, and positive likelihood ratio were used to check for the diagnostic accuracy of each modality. To summarize the overall diagnostic accuracy of the test, the area under the curve (AUC) was used with the histopathologic result as the gold standard. AUC above 0.500 indicates that ultrasound has a good predictive ability to assess tumor size and parametrial and nodal involvement in early-stage cervical cancer. Kappa statistics were used to check for interobserver variability. $\kappa > 0.75$ was considered excellent agreement beyond chance. >0.40–<0.75 was considered good agreement. κ <0.40 was considered poor agreement beyond chance. SAS program on demand and MedCalc were used for data analysis, and MS Excel was used for data encoding.

Results

A total of 27 patients were enrolled in the study [Table 1]. Four were stage IB1 (14.81%), 10 were stage 1B2 (37.03%), nine were stage IB3 (33.33%), two were stage IIA1 (7.40%), and two were stage IIA2 (7.40%). The median age was 46 years, and the most common histologic type was squamous cell carcinoma (70.37%). The comparison of the diagnostic accuracy of ultrasound and MRI in terms of tumor size assessment is shown in Table 2. Of the eight patients with tumor size of more than 2 cm, all were predicted on ultrasound and MRI. These findings translate to a sensitivity and specificity of ultrasound to detect more than 2 cm tumor size as follows: tumor size length sensitivity of 100% (63.06%–100%) and specificity of 57.90% (33.50%–79.35%), tumor size width sensitivity of 81.82% (48.22%–97.72%) and specificity of 68.75% (41.31%–88.89%), and tumor size height sensitivity of 100% (66.37%–100%) specificity of 61.11% (35.75%–82.70%). The sensitivity and specificity of MRI, on the other hand, to evaluate more than 2 cm tumor size are as follows: tumor size length sensitivity of 100% (63.06%–100%) and specificity of 31.58% (12.58%–56.55%), tumor size width sensitivity of 90.91% (58.72%–99.77%) and specificity of 37.50% (15.20%–64.57%), and tumor size height sensitivity of 77.78% (39.99%–97.19%) and specificity of 38.89% (17.30%–64.25%). There were 19 patients with tumor size less than or equal to 2 cm. Eleven (57.90%) of these patients were predicted on ultrasound, and 6 (31.58%) were noted on MRI. Overall, ultrasound has a comparable diagnostic accuracy with MRI to assess tumor size length, width, and height with an AUC of 0.789, 0.753, and 0.806, respectively. Its ability to predict tumor size $\leq$2 cm is better than MRI.

Table 1: Profile of patients (*n*=27)

Demographics	Number of patient
Age	46 (36–53)
Stage	
IB1	4 (14.81)
IB2	10 (37.03)
IB3	9 (33.33)
IIA1	2 (7.40)
IIA2	2 (7.40)
Histopathology	
Squamous cell carcinoma	19 (70.37)
Adenocarcinoma	7 (25.92)
Endometrioid adenocarcinoma	1 (3.70)

Table 3 shows that ultrasound and MRI have high specificity but low sensitivity to detect parametrial invasion. The specificity of both modalities is 100% (85.75%–100%) with a negative predictive value of 88.89% and AUC of 0.500. False-negative findings for both modalities were noted in one-stage 1B3 and two-stage IIA2 patients who underwent neoadjuvant chemotherapy. Overall, sufficient evidence is still needed

Table 2: Comparison of the diagnostic accuracy of ultrasound and magnetic resonance imaging in terms of presence of Tumor size >2

	Surgical Outcome vs Ultrasound			Surgical Outcome vs MRI	
	>2	≤2		>2	≤2
Tumor size <2					
Length (*n*=8, 19)					
>2	8 (100%)	8 (42.11%)		8 (100%)	13 (68.42%)
≤2	0 (0%)	11 (57.89%)		0 (0%)	5 (31.58%)
Kappa coefficient	0.449			0.215	
Diagnostic test					
Sensitivity	100% (63.06 to 100%)			100% (63.06 to 100%)	
Specificity	57.90% (33.50 to 79.75%)			31.58% (12.58 to 56.55%)	
PPV	50.00% (37.12 to 62.89%)			38.10% (31.20 to 45.51%)	
NPV	100%			100%	
+ Likelihood ratio	2.38 (1.40 to 4.02)			1.46 (1.08 to 1.98)	
- Likelihood ratio	-			-	
AUC	0.789			0.658	
Coefficient of variation	UTZ: 49.6% I SO: 61.6%			UTZ: 49.6% I SO: 61.6%	
P-value (UTZ vs MRI)			0.064		
Width (*n*=11, 16)					
>2	9 (81.82%)	5 (31.25%)		10 (62.5%)	10 (62.5%)
≤2	2 (18.18%)	11 (68.75%)		1 (9.09%)	6 (37.5%)
Kappa coefficient	0.485			0.252	
Diagnostic test					
Sensitivity	81.82% (48.22 to 97.72%)			90.91% (58.72 to 99.77%)	
Specificity	68.75% (41.37 to 88.98%)			37.50% (15.20 to 64.57%)	
PPV	64.29% (45.25 to 79.68%)			50.00% (39.58 to 60.42%)	
NPV	84.62% (60.07 to 95.26%)			85.71% (45.48 to 97.74%)	
+ Likelihood ratio	2.62 (1.20 to 5.70)			4.13 (0.57 to 29.67)	
- Likelihood ratio	0.26 (0.07 to 0.97)			0.69 (0.45 to 1.05)	
Coefficient of variation	UTZ: 60.9% I SO: 63.3%			UTZ: 41.5% I SO: 63.3%	
P-value (UTZ vs MRI)			0.117		
Height (*n*=8, 19)					
>2	9 (100%)	7 (38.89%)		7 (77.78%)	11 (61.11%)
≤2	0 (0%)	11 (61.11%)		2 (22.22%)	7 (77.78%)
Kappa coefficient	0.512			0.133	
Diagnostic test					
Sensitivity	100% (66.37 to 100%)			77.78% (39.99 to 97.19%)	
Specificity	61.11% (35.75 to 82.70%)			38.89% (17.30 to 64.25%)	
PPV	56.25% (41.88 to 69.65%)			38.89% (27.69 to 51.39%)	
NPV	100%			77.78% (47.51 to 93.12%)	
+ Likelihood ratio	2.57 (1.44 TO 4.59)			1.27 (0.77 TO 2.11)	
- Likelihood ratio	-			0.57 (0.15 to 2.21)	
Coefficient of variation	UTZ: 53.6% I SO: 70.6%			UTZ: 38.7% I SO: 70.6%	
P-value (UTZ vs MRI)			0.002		

Formalinized Coefficient of Variation=L: 69.4% W: 59.8% and H: 64.3%, PPV: Positive predictive value, NPV: Negative predictive value, AUC: Area under the curve, MRI: Magnetic resonance imaging

to prove the diagnostic capability of ultrasound and MRI in predicting parametrial invasion.

Table 4 shows that both MRI and ultrasound were not able to detect a true positive finding in nodal involvement (0%). Of the five patients with confirmed nodal involvement on histopathology report, none were identified by both imaging modalities preoperatively. Three of these patients were stage IB2 and two were stage IB3. Alternatively, 100% of these patients with negative nodal involvement findings in pathology were correctly detected by both ultrasound and MRI. The specificity of both ultrasound and MRI was 100% (84.56%–100%), the negative predictive value was 81.48%, and the AUC was 0.500. More evidence is also needed to prove the diagnostic capability of ultrasound and MRI in predicting nodal involvement correctly. No kappa coefficient was computed due to the absence of true positive findings for parametrial and nodal involvement.

Table 3: Comparison of the diagnostic accuracy of ultrasound in terms of presence of NODAL INVOLVEMENT

	Pathology vs Ultrasound		Pathology vs MRI	
	With findings	Without findings	With findings	Without findings
Nodal Involvement (*n*=5, 22)				
With findings	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Without findings	5 (100%)	22 (100%)	5 (100%)	22 (100%)
Kappa Coefficient	0.000		0.000	
Diagnostic Test				
Sensitivity	0%		0%	
Specificity	100% (84.56 to 100%)		100% (84.56 to 100%)	
PPV	-		-	
NPV	81.48%		81.48%	
+Likelihood Ratio	-		-	
-Likelihood Ratio	1.00		1.00	
AUC	0.500		0.500	
P (UTZ vs MRI)	-			

Table 4: Comparison of the diagnostic accuracy of ultrasound and MRI in terms of presence of Parametrial Invasion

	Pathology vs Ultrasound		Pathology vs MRI	
	With findings	Without findings	With findings	Without findings
Parametrial Invasion (*n*=2, 25)				
With findings	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Without findings	3 (100%)	24 (100%)	3 (100%)	24 (100%)
Kappa Coefficient	0.000		0.000	
Diagnostic Test				
Sensitivity	0%		0%	
Specificity	100% (85.75 to 100%)		100% (85.75 to 100%)	
PPV	-		-	
NPV	88.89%		88.89%	
+Likelihood Ratio	-		-	
-Likelihood Ratio	1.000		1.000	
AUC	0.500		0.500	
P (UTZ vs MRI)	-			

Discussion

Imaging now plays a significant role in the staging of cervical cancer. Staging using gynecologic oncology ultrasound, either by transabdominal, transvaginal, or transrectal route, is the most practical approach, especially in our country. The comparable accuracy of ultrasound in assessing the tumor size in early-stage cervical cancer with MRI may be due to the improved and detailed visualization of the cervix and the blood flow seen through the use of two-dimensional ultrasound with color enhancement. The dynamic nature of the ultrasound examination, the use of different probes (such as transabdominal, transvaginal, and transrectal probes), the movement of these probes in relation to the other structures, its proximity to the cervix, and the enhancement by color Doppler also allow the sonologist to thoroughly evaluate the cervix. A cervical tumor is also more rigid than its surrounding tissue, enabling the detection of tumor tissue when using a dynamic examination technique, especially in an experienced sonologist. Although intravenous contrast administration was routinely employed during MRI in this study, its use did not improve the detection rate of lesions 2 cm or less. A tumor size more than 2 cm for Stage I and II disease is one of the pathologic prognostic risk factors for cervical cancer. Its presence may predict prognosis, risk of recurrence, and use of postoperative adjuvant treatment, especially if this is associated with more than 1/3 stromal invasion and the presence of lymphovascular space invasion and parametrial and nodal involvement.

Fischerova *et al*.[3] showed that ultrasound was significantly superior to MRI in estimating tumors with histologic concordant rates of 93.7% versus 83.2% ($P < 0.006$). Our study, on the other hand, showed that both modalities have comparable diagnostic accuracy in assessing tumor size and parametrial and nodal involvement. The relative performance of MRI with ultrasound in evaluating tumor size and parametrial invasion may stem from the inherent inflammation that occurs with the disease. This may cause stromal and parametrial

edema that may affect the interpretation of the results. Postbiopsy changes may also lead to inflammation and overestimation of the size at baseline MRI.[4]

Correct identification of parametrial involvement in imaging is vital in the proper staging of patients. Patients with evidence of parametrial invasion are staged with locally advanced disease and become a candidate for chemoradiation instead of surgery. Several studies[4,5] have shown that the sensitivity of ultrasound and MRI was 60%–83% and 40%–69%, respectively, and the specificity was 98%–100% and 92%–98% for the detection of parametrial invasion. These findings are similar to our study, in particular, the high specificity for parametrial invasion. All of the false-negative findings for parametrial invasion for both imaging modalities were noted in those patients who underwent neoadjuvant treatment. The limited ability of ultrasound to correctly identify parametrial invasion in this subset of patients may be due to the fibrosis and necrotic changes brought about by the treatment to the tumor and surrounding tissues. These changes may disrupt the normal architecture of the cervix and the parametrial tissues, thereby affecting the interpretation of the sonologist. A meta-analysis done comparing MRI and ultrasound also showed comparable results when assessing parametrial infiltration in cervical cancer. The pooled estimated sensitivity and specificity of ultrasound were 78% (95% confidence interval [CI]:48%–93%) and 96% (95% CI = 89%–99%), respectively, while for MRI, the pooled sensitivity and specificity were 68% (95% CI = 54%–80%) and 91% (95% CI = 84%–95%), respectively.[6] Furthermore, Chiappa *et al*.[7] showed that the percentage concordance between the three-dimensional ultrasound and MRI was 79% ($\kappa = 0.508$), thus confirming the utility of ultrasound in the assessment of parametrial invasion.

The accurate detection of lymph node metastases is one of the most important challenges in cancer imaging today, for the presence of nodal disease portends a poor prognosis. The presence of nodal involvement on imaging upstages a clinically diagnosed early-stage disease. Enlarged lymph nodes, however, do not always equate to metastasis. In some instances, normal-sized lymph nodes may actually have metastatic focus. In a local study by Cu and Reforma,[8] the sensitivity and specificity of ultrasound in detecting pelvic lymph node invasion were 29.4% and 96.4% with an overall accuracy rate of 91.5%. Likewise, the study by Stukan *et al*., in 2021,[9] mentioned that ultrasound and MRI had similar sensitivity and specificity with regard to regional lymph node assessment. In another study by Mamsen *et al*., the prediction of nodal metastasis was also low at 23% sensitivity and concluded that ultrasonography cannot be used to detect lymph node metastasis preoperatively in this group of patients with early cervical cancer.[10] The findings of these studies were consistent with our study. MRI and ultrasound were not able to detect nodal metastasis in five patients with histopathologic findings of nodal involvement. This may be due to the similar appearance and character of early cervical cancer with normal tissue in both modalities. MRI, however, was able to correctly identify all true negatives or those without nodal involvement.

Ultrasound is a widely available and affordable imaging technique that does not require a contrast medium to enhance its capability to assess certain parameters in cervical cancer staging. The prohibitive costs of MRI should be considered with its potential as a diagnostic tool when evaluating patients with cervical cancer. The proven benefits of ultrasound in precise tumor delineation, including assessment of parametrial invasion and nodal involvement, in the hands of a specially trained examiner, may help justify its use for individual treatment planning, especially in our local setting.

Conclusion

Ultrasound has comparable diagnostic accuracy with MRI in assessing tumor size, parametrial invasion, and nodal involvement in patients with early-stage cervical cancer. It is a good alternative imaging modality to MRI in staging cervical cancer, especially in low- to middle-income countries.

Limitation of the study

The data were obtained in a small population of women in a single institution by one sonographer and one machine. The specimen used to compare parametrial and nodal involvement was formalinized. Formalin causes tissue shrinkage, which may affect the results. Thus, a good agreement between the modalities may not be achieved.

Recommendations

It is recommended that a larger sample size and multicenter study be employed in future studies for us to make a better generalization of the results and consider its clinical impact in the management of patients with cervical cancer.

Authorship contributions

Martha Parroco - involved in the conceptualization, methodology,investigation, data curation, writing of the original draft, visualization, project administration, funding acquisition.

Dr. Genalin Amparo - involved in conceptualization, methodology, writing - review and editing of the draft, supervision.

Dr. Leilani C. Coloma - involved in conceptualization, methodology, writing - review and editing of the draft, supervision.

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Nil.

Conflicts of interest
There are no conflicts of interest.

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