European Journal of Gynaecological Oncology

Eur. J. Gynaecol. Oncol. **2022**; 43(2): 278–284
http://doi.org/10.31083/j.ejgo4302035

Original Research

Evaluation of tumor size in cervix cancer patients treated with surgery: ultrasonography or MRI?

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Academic Editor: Enrique Hernandez
Submitted: 13 November 2021 Revised: 16 December 2021 Accepted: 20 December 2021 Published: 15 April 2022

Abstract

Objective: This study aims to compare tumor diameters measured by transvaginal ultrasonography and MRI in cervical cancer. **Materials and methods**: The study includes 127 cervical cancer patients diagnosed and treated at Akdeniz University Faculty of Medicine between January 2002 and December 2019. Data were collected retrospectively using the electronic archive system of the hospital. Patients with pathologically unknown tumor diameters were excluded from the study. Data were tested for normal distribution, and the mean, standard deviation, median, min-max values, and frequencies were used as descriptive statistics. Categorical data were expressed as numbers and percentages (%). The Student's *t*-test, one of the parametric tests, was used to compare tumor diameters. Statistical Package for the Social Sciences (SPSS) 23 software (IBM Corp., Chicago, IL, USA) was used for data analysis. A *p*-value less than 0.05 was considered statistically significant in all tests. **Results**: The mean age of patients included in the study was 49.55 $\pm$ 11.67 years. Of all patients, 79.5% had a normal delivery. 87 (68%) of the patients were not using any contraceptive method, with 0.7%, condom protection was the least. Among the complaints of patients at admission, postcoital vaginal bleeding was the most common complaint with 42.5%, and asymptomatic patients were the second most common with 22%. Human papillomavirus (HPV) status was unknown in the vast majority of patients (91.3%). Regarding the stage status, stage 1b2 was the most frequently seen stage with 29 patients. Tumor histology revealed SCC in 80.3% and adenocarcinoma in 18.1%. The mean tumor diameter measured by transvaginal ultrasonography (TVS) was 3.30 $\pm$ 1.95, by magnetic resonance imaging (MRI) was 3.37 $\pm$ 2.03, and the pathologically measured tumor diameter was 3.17 $\pm$ 1.86. There was no statistically significant difference between the mean tumor diameter measured by TVS and MRI, MRI and pathology, and TVS and pathology (*p*: 0.769, *p*: 0.589, *p*: 0.891, respectively). **Conclusion**: When used by specialists experienced in the field of gynecological oncology, ultrasonography can be considered as effective as MRI, especially in tumor size measurement in cervical cancer, due to its ease of use, cheapness, and easy accessibility in regions with low socioeconomic status.

Keywords: cervical cancer; transvaginal ultrasonography; MRI; postcoital bleeding; tumor diameter

1. Introduction

Treatment in cervical cancer patients varies according to the stage, and staging is the basis of the appropriate treatment. International Federation of Gynecology and Obstetrics (FIGO) staging of uterine cervical cancer dates back to 1958, and tumor size is still one of the main components of staging, maintaining its place in treatment and staging. Recently, almost 60 years after the introduction of the original FIGO staging system, greater emphasis has been placed on the importance of tumor size in uterine cervical cancer. The 2018 FIGO classification further divided stage IB into substages IB1 (<2 cm), IB2 (2–4 cm), and IB3 ($\geq$4 cm). Evaluation in terms of tumor size is crucial in terms of both radical surgery and chemoradiotherapy and ultimately affects prognosis and recurrence in cervical cancer. It has been reported that, as the tumor size increases, the involvement of adjacent and distant organs increases, appearing as a poor prognostic factor in terms of recurrence and overall survival [1–5].

Multiplanar imaging is more sensitive in showing deep pelvic invasion, tumor volume and spread, and nodal involvement. It also reduces the need for other imaging and evaluation methods. The agreement between multiplanar imaging and surgical staging is also high. The fact that cross-sectional imaging modalities such as Computed tomography (CT) and MRI were not included in staging until the revision of staging in 2018 is due to FIGO being incompatible with the principle of the universally widespread availability of any staging method. The other reasons why these imaging methods were not included in the FIGO staging before 2018 can be considered as the inability to perform homogeneous imaging in all centers, the low application rate especially in undeveloped regions where uterine cervical cancer is more common, and their unfeasibility to be widely used due to high fees. Although there are many published articles refuting these hypotheses, these articles either partially include the mentioned reasons or report the results of limited case groups [6,7].

Magnetic resonance imaging is the best imaging modality for determining tumor localization, size, depth of stromal invasion, parametrial extension, and lower uterine segment extension. MRI is recommended because of the increased possibility of parametrial invasion and lymph node metastasis in patients with clinical stage 1B or tumor size greater than 2 cm. The use of MRI compatible with endoscopic surgical staging reduces cost and morbidity [8,9].

In a publication published in 2019, it was seen that there was no difference in the detection of parametrial invasion between USG, MRI and clinical examination under anesthesia in cervical uteri cancer, only MRI and clinical examination under anesthesia had higher accuracy than ultrasonography in terms of diagnosing parametrial invasion. However, in the detection of cervical uteri tumors of 2 cm and above, the diagnostic accuracy of USG was found to be higher than clinical examination and MRI under anesthesia. In addition, in this study, it was revealed that clinical examination under anesthesia is the best method in determining vaginal involvement. It has been stated that the combination of examination and USG under anesthesia may be the most accurate diagnostic tool, but the diagnostic rates will increase with the addition of MRI, especially in large tumors [10].

It has been suggested in many studies that the tumor size and local spread of early stage cervical uteri cancer in the preoperative period have similar diagnostic accuracy with transvaginal ultrasonography and MRI, and that it should be the first diagnostic tool especially because of its low cost and ease of use [11–13].

Today, there are significant inconsistencies and disagreements between the methods and strategies used by gynecologist oncologists, radiologists, and pathologists, especially in the clinical measurement of tumors in the post-surgical specimen, and there is no consensus particularly on the preoperative imaging dependent measurement differences and tumor positivity in surgical margins and other areas.

Thanks to today's technological progress, high-resolution US devices can measure the tumor diameter quite accurately in cervical cancer. It can be helpful in the patient's choice of surgical or radiotherapy treatment, especially since it detects cervical tumors smaller than 2 cm or larger than 4 cm with US as well as MRI. Therefore, US can replace MRI in this regard.

This study aims to compare ultrasonography, which is the most ideal imaging method in our developing country, to magnetic resonance in terms of tumor size assessment measured by pelvic examination, preoperative imaging, and pathology in patients with uterine cervical cancer, and to discuss the importance of ultrasonography, which is an inexpensive and easy-to-apply method, especially in underdeveloped regions, in the light of the literature and to reveal its importance.

2. Materials and methods

The study includes 127 cervical cancer patients diagnosed and treated at Akdeniz University Faculty of Medicine, Antalya, between January 2002 and December 2019. After the approval of the ethics committee of Akdeniz University, the data were collected retrospectively using the electronic archive system of the hospital. Transvaginal ultrasonographic uterine cervical tumor diameter measurements performed by experienced gynecologists and cervical tumor diameters measured on magnetic resonance imaging by experienced gyneco-radiologists were retrospectively analyzed for all patients. Patients with pathologically unknown tumor diameters were excluded from the study. Moreover, patients with stage IA1 microinvasive cervical cancer and stage IVB metastatic tumors and patients who had previously received neoadjuvant chemotherapy were excluded. All patients were restaged according to the lately revised FIGO 2018 classification of cervix uteri. Histopathological diagnosis of all patients was made by experienced gynecological pathologists of our hospital. After a detailed systemic and gynecological examination, each patient was scanned radiologically for metastasis. Then, the diagnosis and treatment of these patients were arranged by gynecological oncology specialists. Patients with stage IA1 were treated with conization or simple hysterectomy. Patients with early-stage (FIGO stage IA2, IB1, IB2, 2A) underwent radical hysterectomy $\pm$ bilateral salpingo-oophorectomy and pelvic-paraaortic lymph node dissection. Depending on the histopathological risk factors, these patients were given either only adjuvant radiotherapy or chemoradiotherapy by a multidisciplinary oncology council. Patients in locally advanced stage (FIGO stage IB3, IIB-4A) received concurrent definitive chemoradiotherapy. Laparoscopic paraaortic lymph node dissection was performed in selected patients with radiologically suspicious paraaortic lymph nodes, and the limits for extended radiotherapy were determined.

In pathological specimens, tumor size was measured macroscopically as the largest diameter and the other largest diameter. And the longest two-dimensional tumor sizes in all ultrasonographic, MRI and pathological examinations were retrospectively included in our study and these were compared with each other in our study.

After the treatment, cervical cytology and pelvic examination were performed every 3 months for the first 2 years, every 6 months for the next 3 years, and annual follow-ups were continued after 5 years. During follow-ups, pelvic examination and transvaginal or transabdominal ultrasonography were performed in all patients, while serum tumor marker evaluations and radiological evaluations (CT and/or Positron emission tomography (PET/CT)) were performed in cases with suspected recurrence. Recurrence diagnosis was established pathologically by biopsies from suspicious sites or clinically or radiologically.

Data were tested for normal distribution, and the mean, standard deviation, median, min-max values, and frequencies were used as descriptive statistics. Categorical data were expressed as numbers and percentages (%). The Student's *t*-test, one of the parametric tests, was used to compare tumor diameters. Statistical Package for the Social Sciences (SPSS) 23 software (IBM Corp., Chicago, IL, USA) was used for data analysis. A *p*-value less than 0.05 was considered statistically significant in all tests.

3. Results

The mean age of patients included in the study was 49.55 $\pm$ 11.67 years. Sixty-six (51.9%) of the cases were illiterate, and among the complaints at admission, postcoital vaginal bleeding was the most common complaint with 42.5%, and asymptomatic patients were the second with 22%. It was noted that 91.3% of the patients were not tested for HPV. The early-stage lesions were 44%, and the locally advanced and metastatic ones were 56%. Regarding the stage status, stage 1b2 was the most frequently seen stage with 29 patients, while the second was 3c1p with 28 cases (22%). Tumor histology revealed SCC in 80.3% and adenocarcinoma in 18.1%. In two rare cases, the tumor was of neuroendocrine type in one, and a clear cell type in the other. While 18 cases were given chemoradiotherapy, one case was given only chemotherapy, 25 early-stage cases were given surgical treatment alone, and 83 cases were given surgical treatment and radiotherapy and/or chemotherapy (Table 1).

The mean tumor diameter measured by transvaginal ultrasonography (TVS) performed by an experienced gynecologist oncologist was 3.30 $\pm$ 1.95, the diameter measured by magnetic resonance imaging (MRI) performed by radiologists experienced in gynecological oncology was 3.37 $\pm$ 2.03, and the diameter measured pathologically was 3.17 $\pm$ 1.86. There was no statistically significant difference between the mean tumor diameter measured by TVS and MRI, MRI and pathology, and TVS and pathology (*p*: 0.769, *p*: 0.589, *p*: 0.891, respectively) (Table 2).

4. Discussion

It has been reported that as the tumor size increases, the involvement of adjacent and distant organs increases, appearing as a poor prognostic factor in terms of recurrence and overall survival [5]. In patients with FIGO 2018 classified uterine cervical cancer, ultrasonography can play a crucial role in assessing and staging tumor size and adjacent organ involvement, as accessing imaging modalities such as MRI or PET/CT is difficult in socio-economically poor countries.

Based on the available literature, the 5-year survival is 91.6% in patients with tumors of 2 cm or less, 83.3% in tumors $>$2 to $\leq$4 cm, and 76.1% in tumors $>$4 cm, and parametrial involvement is detected at 13.2% in patients with tumors larger than 2 cm and 1.3% in patients with tumors below 2 cm. And it has been statistically demonstrated that tumor size above 2 cm is important in terms of parametrial involvement [14,15].

It is crucial to distinguish early-stage (Stage1–2A) cervical cancer with imaging. While early-stage cervical cancer can be treated with surgical methods, Stage 2B and above requires chemotherapy, radiotherapy, and/or combinations.

MRI has long been considered the primary method of choice in the evaluation of patients with uterine cervical cancer [16]. One of the first studies to evaluate the role of MRI in determining uterine cervical cancer staging determined accuracy rates for early-stage tumors to be 79% for clinical staging versus a higher rate of 81% for MRI. Besides, exclusion of the early-stage cases (IB1–IIA1) decreased the accuracy of clinical staging to 53%. The same study found the accuracy rate of MRI in determining tumor location in the cervix as 91% and the accuracy in determining tumor size as 93% [17]. MRI has a high accuracy in determining tumor size with a $<$5 mm difference between pathological evaluation and the largest tumor diameter measured on MRI in 70–90% of cases [18,19].

Carcinoma in situ is the name given to preinvasive cancer, not included in FIGO staging. In stage 1, the tumor is limited to the cervix. Stage 1A1 tumor is too small to be measured on a T2-weighted image, but contrast enhancement can be seen in the early arterial phase on MRI with dynamic contrast [20]. In stage 1A2 (stromal invasion depth $>$3 mm), the histopathological correlation was 76% on T2-weighted images, 63% on T1-weighted contrast-enhanced images and 98% on dynamic contrast images [20]. Stage 1B tumor appears hyperintense within the low-signal cervical stroma on T2-weighted images.

In contrast to computed tomography (CT) and ultrasonography, which are limited by poor tissue contrast and the experience of the practitioner, MRI is significantly more accurate in measuring tumor size, delineating cervical tumor borders, and localizing tumor spread due to its distinctive tissue contrast and multiplanar feature [21]. For patients who are candidates for surgery based on clinical staging, some data suggest that tumor size can be more accurately determined by MRI than clinical examination. For example, a prospective study of 208 women, most of whom had stage IB disease and underwent preoperative MRI and CT, showed more consistent results with postsurgical histopathological findings than MRI, CT or clinical examination. All three imaging modalities overestimated tumor size compared to the pathological evaluation of the specimen after surgery. The results of this study are significant because overestimating tumor size in surgical candidates will probably not alter treatment or prognosis while underestimating tumor size will potentially lead to surgical excision, where chemoradiation is the best option [22].

During the evaluation of tumor size with MRI imaging, false positivity rates increase due to peritumoral edema,

Table 1. Clinical characteristic risk factors of patients.

	Mean ± SD/median (min–max) n = 127	Frequency/Percentage (%)
Age	49.55 ± 11.67	
Education status		
Not literate	66	51.9
Primary/secondary school	29	22.8
High school University	32	25.1
First complaint		
Asymptomatic	28	22
Post-coital v. bleeding	54	42.5
Vaginal discharge	15	11.8
Menometrorrhagia	12	9.4
Pelvic pain	4	3.1
Postmenopausal v. bleeding	14	11.1
HPV status		
Yes	11	8.7
No	116	91.3
Main stage		
Early stage	56	44
Locally invasive	71	56
Stage		
Ia1	2	1.5
Ia2	4	3
Ib1	21	16.5
Ib2	29	22.8
Ib3	11	8.7
IIa1	2	1.5
IIa2	1	0.7
IIb	21	22.8
IIIa	1	0.7
IIIb	2	1.5
IIIc1p	28	22
IIIc2p	4	3
IVa	2	1.5
Tumor histology		
SCC	102	80.3
Adenoca	23	18.1
Others	2	1.6
Type primary treatment		
Surgical	25	19.6
Surgical adj RT	32	25.1
Surgery adj CRT	51	40.1
Primary CRT	18	14.1
Primary CT	1	0.7

SCC, Squamous cell cancer; BMI, Body mass index; Adj RT, Adjuvant radiotherapy; Adj KRT, Adjuvant chemo-radiotherapy; KT, Chemotherapy; NSVB, Normal spontaneous vaginal birth; CS, Cesarean section; OCP, Oral contraceptive pill; IUD, Intrauterine Device.

Table 2. Comparison of tumor diameter between imaging methods.

		ort ± ss	*p* value
Tumor diameter	Pathological	3.17 ± 1.86	0.769
	MRI	3.37 ± 2.03	
	Pathological	3.17 ± 1.86	0.891
	Tv USG	3.30 ± 1.95	
	Tv USG	3.30 ± 1.95	0.589
	MRI	3.37 ± 2.03	

MRI, Magnetic resonance imaging; Tv USG, Transvaginal ultrasonography.

necessitating a careful evaluation in order to distinguish from a true tumor. Especially in recent years, the inclusion of diffusion-weighted imaging in pelvic MRI has helped to overcome this obstacle. Furthermore, this method has facilitated the detection of tumors smaller than 1 cm, and many studies have demonstrated the role of MRI in the staging of uterine cervical cancer [22–25].

In the past years, gynecological ultrasonography has gained great importance especially in the preoperative and postoperative evaluation of uterine cervical cancer patients, as it provides information about tumor presence, size, and local tumor spread with low cost, rapid examination time, and convenient use everywhere when performed by clinicians specialized in the field of gynecological oncology [11,26].

It has been stated that preinvasive lesions of the uterine cervical stiffness are greater than normal uterine cervical structure with 2-D shear wave elastographic application, which is an application based on tissue softness as an ultrasonographic use, and it has been stated that it can be used in the differential diagnosis of high-grade preinvasive lesion [27].

According to the results of transrectal ultrasonography performed prospectively and preoperatively in 95 patients with uterine cervical cancer, the accuracy rate of ultrasonography in tumor diagnosis was 94%, while the accuracy rate of MRI was 83%. The accuracy of detecting 1 cm or less tumor was 91% for ultrasonography and 81% for MRI. Ultrasonographic imaging was considered statistically more valuable ($p < 0.049$). Moreover, the study stated that increased body mass index had no effect on the accuracy of ultrasonography. The correlation analysis according to the tumor sizes obtained as a result of the histopathological examination revealed R: 0.996 for ultrasonography, R: 0.980 for MRI and ultrasonographic examination was determined more valuable statistically [12]. In our study, the comparison of histopathological examination, MRI, and ultrasonography revealed that there was no statistical difference between MRI and ultrasonography and that the two imaging methods and pathological examination were close to each other. However, the only difference in our study is the use of transvaginal ultrasonography.

Another prospective study evaluated the results of patients who underwent primary surgery and 68 patients who underwent surgery after neoadjuvant chemotherapy. Comparison of the histopathologically measured tumor diameters with the measurements made by ultrasonography and MRI determined accuracy rates of 93% for ultrasonography and 88% for MRI. Additionally, the mean difference between histopathological and ultrasonographic measurements of the craniocaudal diameter of the tumor was 0.62 mm, while the difference between histopathological and MRI examinations was higher, with 1.49 mm. Therefore, ultrasonographic examination was considered more compatible with histopathological evaluation [11].

A prospective multicenter study involving 182 women investigated the accuracy rates of preoperative evaluation and MRI and pelvic ultrasonography in terms of tumor size, taking histopathological findings as a reference, and determined concordance rates between ultrasonography and pathology in tumor diagnosis and detection of tumors larger than 4 cm to be as high as 0.84 and 0.82, respectively. However, this rate decreased in tumors smaller than 2 cm, and was around 0.78. Comparison of MRI and pathological examination determined the kappa coefficients of the concordance ratios between tumors below 2 cm and above 4 cm as 0.71 and 0.76, respectively, while the rate of tumor detection was as low as 0.52, and indeed while MRI primary tumor diagnosis rates were around 90%, ultrasonographic diagnosis rates are was as high as 97%. Furthermore, there was a higher and statistically significant agreement between histopathological examination and ultrasonographic evaluation in terms of tumor detection rates in the follow-ups after cervical conization compared to MRI ($p < 0.001$) [26]. This study showed that there is no statistical difference in tumor size between MRI, ultrasonographic evaluation, and pathological examination, but both imaging modalities diagnose a larger tumor size compared to pathological evaluation.

It has been stated that MRI evaluation is important in preoperative evaluation, especially in order to evaluate the involvement of pelvic region lymph nodes before fertility-sparing surgery in early stage cervical uteri cancer [28].

In a recent publication in 2021, it was recommended to use MRI in the preoperative stage, in the evaluation of the response of the tumor to chemotherapy and in the follow-up of the patients after conization, in the cases who were planned for neoadjuvant chemotherapy and then cold conization in patients who wanted fertility-sparing surgery in early stage cervical uteri cancer [29].

In another new prospective study of 2021, transvaginal and transabdominal ultrasonographic examination performed by experienced gynecologists and MRI imaging methods performed by radiologists experienced in the field of gynecological oncology were compared both among themselves and with pathological examination results in the

preoperative and postoperative periods. It has been stated that ultrasonography has the highest accuracy rates in local staging of cervical uteri cancer. It has also been stated that ultrasonography has the same accuracy as MRI imaging in terms of tumor diagnosis, parametrial involvement, uterine corpus involvement and vaginal fornix involvement. With all these results, it has been stated that ultrasonography is superior to MRI imaging in terms of local staging in cervical uteri cancer and because of its ease of use and cheapness [30].

The limitations of our study are its retrospective design and small sample size. Its advantage is being a single-center and long-term study managed by a team experienced in the field of gynecological oncology.

5. Conclusions

Considering the significance of tumor size measurement in diagnosis, staging, treatment, and prognosis in uterine cervical cancer, physical examination, imaging methods, and histopathological evaluation are of great importance. MRI is the best imaging modality for determining tumor size as well as vaginal and parametrial involvement. However, when such imaging modalities are not available in developing or underdeveloped areas, pelvic ultrasonography can provide an equally valuable and effective assessment when performed by specialists with experience in gynecologic oncology.

Author contributions

ÖB, MSB and SS conceived and designed the study; MSB, ÖB, HAT and SD performed the study; SS, HAT and SD analyzed the data; TS contributed materials and evaluation; SS, MSB and ÖB wrote the paper. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Akdeniz University (approval number: KAEK-925 and dated 09.12.2020).

Acknowledgment

We would like to express our gratitude to all those who helped us during the writing of this manuscript. Thanks to all the peer reviewers for their opinions and suggestions.

Funding

This research received no external funding.

Conflict of interest

The authors declare no conflict of interest.

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