Lymph node size detected by magnetic resonance imaging for prediction of lymph node involvement in locally advanced cervical cancer

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Abstract. – OBJECTIVE: To investigate lymph node (LN) size detected by Magnetic Resonance Imaging (MRI) for prediction of LN involvement in locally advanced cervical cancer (LACC).

PATIENTS AND METHODS: A total of 55 cases diagnosed with LACC (IIB-IVA FIGO 2018) between 28 December 2010 and 30 October 2020 were evaluated in this retrospective study. LN involvement was evaluated in patients who underwent surgical staging and MRI. The prediction of LN involvement based on LN size on MRI was calculated statistically.

RESULTS: The mean age of 55 patients was 56 (33-78) years. For the cases, 76.4% were stage IIB, 12.7% were stage III, and 10.9% were stage IVA. Squamous cell histological type was detected with a rate of 90.9%. The cut-off value for pelvic LN diameter on MRI in predicting pelvic LN involvement was 18.5 mm, and the sensitivity and specificity values were calculated as 50.0% and 93.6%, respectively (*p*=0.027). The cut-off value for pelvic and para-aortic LN diameter on MRI in predicting pelvic and para-aortic LN involvement was 17.0 mm with a sensitivity of 41.7% and specificity of 88.4% (*p*=0.081).

CONCLUSIONS: In LACC, prediction of LN involvement by LN diameter detected on MRI has moderate sensitivity and high specificity with a cut-off value of 17.0 mm.

Key Words:
  Cervical cancer, Lymph node, Surgery.

Introduction

Cervical cancer is the most common gynecological cancer in terms of diagnosis and mortality among the female population worldwide. After breast, colorectal and lung cancer, it is the fourth most common cancer[1] and is the second most frequent cause of cancer death among women in developing countries. In 2020, an estimated 604,127 new cases and 341,831 deaths from cervical cancer were reported[2] worldwide. Approximately 85% of these cases occur in developing countries, and more than two-thirds of cases are detected in the advanced stage (FIGO 2009, stage IIB–IVA)[3]. After the publication of the latest FIGO[3] cervical cancer staging in 2009, there have been significant advances in the use of imaging modalities for the evaluation of cervical cancer cases. The cervical cancer FIGO staging system was recently revised[4], and cases with para-aortic LN metastases proven by imaging or histopathology were classified as stage IIIC2 in the new staging. The revised 2018 FIGO[5] staging for pelvic and para-aortic LN metastases classified them into stages IIIC1 and IIIC2, respectively, showing that imaging modalities or surgical pathological confirmation can be used for nodal evaluation. These imaging modalities range from 60 to 88% sensitivity, with specificity as high as 97% for detecting LN metastases[6,7]. LN involvement is, in fact, one of the primary prognostic factors in locally advanced cervical cancer.

There is no gold standard method for the preoperative evaluation of LN status. A major challenge in locally advanced cervical cancer is determining whether there is para-aortic LN metastasis[8] because survival time is affected by LN metastasis. The 5-year disease-free survival is reported to be about 57% in LN-negative patients. However, 5-year disease-free survival decreases to 34% and 12% in patients with metastatic pelvic LN and para-aortic LN, respectively[9]. Among patients diagnosed with locally advanced cervical cancer, 17-24% have para-aortic LN metastasis[10]. Therefore, we aimed to investigate the prediction of

LN involvement by LN size detected on magnetic resonance imaging in locally advanced cervical cancer.

Patients and Methods

The present study received ethical approval from Selçuk University with decision number 2022/305, dated 21.06.2022.

The sample size of the study consisted of cases that were followed up and treated for locally advanced cervical cancer (LACC) at Selçuk University Faculty of Medicine between 28 December 2010 and 30 October 2020. In this retrospective study, a total of 55 patients who were followed up and treated for LACC (FIGO 2018, IIB-IVA) were evaluated. The age, surgical stage, histological types, number of pelvic and para-aortic LNs, and involvement in patients were analyzed. All patients underwent laparotomic extraperitoneal LN dissection (pelvic and para-aortic LNs). Inclusion criteria included: (a) histologically squamous, adenosquamous, adenocarcinoma or undifferentiated cervical cancer with stage IIB-IVA according to the FIGO 2018 system[11]; (b) assessment of tumor extent and LN involvement by MRI; and (c), pathological results evaluated according to pelvic and/or para-aortic LN involvement after extraperitoneal LN dissection. LNs in the abdomen and pelvis on MRI imaging with a short axis diameter measured in mm on cross-sectional images were evaluated. LN involvement was confirmed histopathologically. ROC analysis was performed to predict LN involvement according to the LN diameter detected on MRI. Cut-off value, sensitivity, and specificity were calculated according to ROC analysis, and ROC graphs were drawn.

Statistical Analysis

SPSS version 21 (IBM Corp., Armonk, NY, USA) was used for statistical analyses. Categorical variables were defined as percentages and frequencies, and quantitative variables were defined as mean and minimum-maximum. Categorical variables were compared using the Chi-square test or Fisher's exact test and continuous variables were compared using Mann-Whitney U test. ROC analysis was performed for cut-off, sensitivity, and specificity of the data according to the Youden index. Statistical significance was accepted as $p<0.05$.

Results

The mean age of 55 patients included in this study was 56 (33-78) years (Table I). Of the cases, 76.4% were evaluated as stage IIB, and squamous cell histological type was detected at a rate of 90.9%. LN involvement was detected only in pelvic LNs of 5 cases, in para-aortic LNs of 3 cases, and in pelvic and para-aortic LNs of 5 cases. The cut-off value for prediction of pelvic LN involvement by pelvic LN diameter detected on MRI was 18.5 mm, with a specificity of 93.6% and a sensitivity of 50.0% (Figure 1). However, the cut-off value for prediction of pelvic and para-aortic LN involvement by pelvic and para-aortic LN diameters detected on MRI was 17.0 mm, with a specificity of 88.4% and a sensitivity of 41.7% (Table II, Figure 1 and 2).

Table I. Characteristics of cases according to 2018 cervical cancer staging.

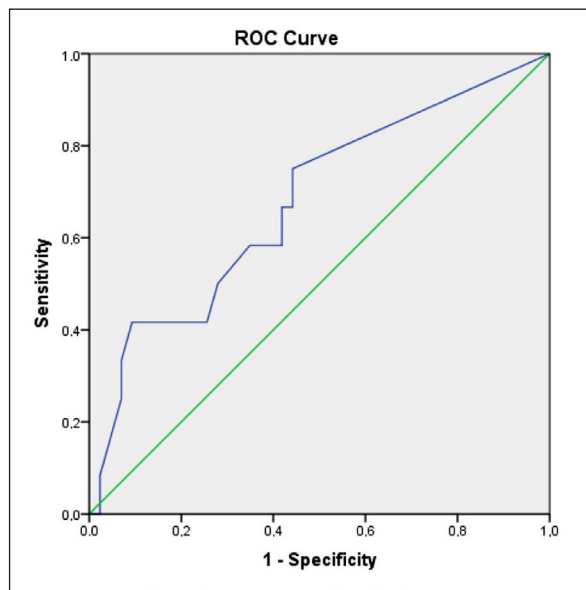| Variables		(N = 55)	(%)
Age, years		56 (33-78)	
Stage distribution	IIB	42	76.4
	IIIB	7	12.7
	IVA	6	10.9
Histologic types	Squamous	50	90.9
	Non-squamous	5	9.1
Pelvic lymph node, n		10	18.2
Total pelvic lymph node number		4 (0-49)	
Para-aortic lymph node, n		8	14.5
Total para-aortic lymph node number		9 (0-35)	
Lymph node involvement, n	Pelvic	5	9.1
	Para-aortic	3	5.5
	Pelvic and para-aortic	5	9.1

N = Number of patients.

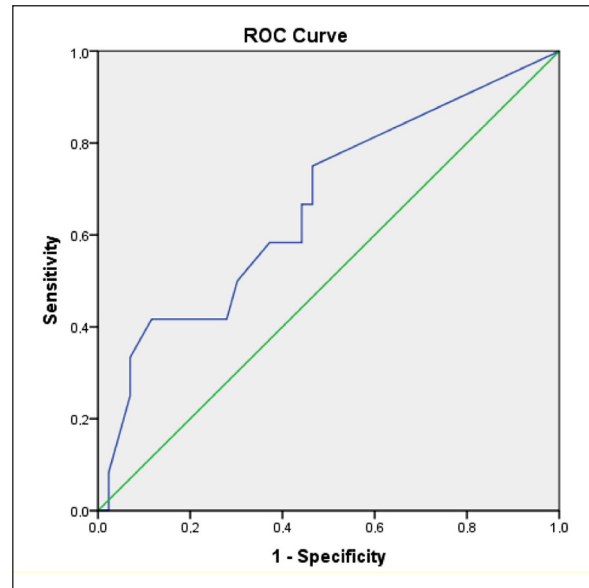**Figure 1.** ROC analysis of pelvic LN diameter and pelvic LN involvement detected on MRI.

Figure 2. ROC analysis of LN diameter detected on MRI according to LN involvement.

Discussion

Nowadays, treatment management for locally advanced cervical cancer is planned according to LN involvement. Either an imaging method or surgical method is used to confirm LN involvement. Starting treatment with imaging methods alone may result in under- or over-treatment. Of the imaging methods, the sensitivity of MRI in evaluating LN involvement ranges from 38% to 89%, and specificity ranges from 78% to 99%[12,13].

In the study by Ayhan et al[14], mean age was 50 years (23-81), 79.1% of all patients had squamous cell histological type, 37% were at stage IIIC, the median number of pelvic LNs was 30.0 (10-97), and the median number of para-aortic LNs was 11.0 (5-52). Only pelvic LN involvement was present in 28%, pelvic and para-aortic LN involvement was present in 9.2%, and isolated LN involvement was present in 0.8%. In a multicenter study[15], the median age was 51 years (42-60), 79%

of cases had squamous cell type, 52% was in stage IIB, and 23.3% in stage IIIB-IVA. Para-aortic LN involvement was reported in 18%, and pelvic LN involvement in 43.2%. In a prospective study[15], the median age of the cases was 53 (32-77) years, 63% of the cases were IIB-IVA, and 70% had squamous cell type. In the study by Ran et al[16], 82.5% of the cases was reported as stage IB, while 4.5% were IIB and IIIB. In this study, the median age of cases was 56 (33-78) years, and 76.4% of cases were recorded as stage IIB, 12.7% were stage III and 10.9% were stage IVA. Histologically, 90.9% of cases were squamous cell type. Pelvic and para-aortic LN involvement rates were at 14.6% and 18.2%, respectively, and isolated LN involvement was present in 5.5% of patients. These different results may arise from different study groups.

The cut-off value for LN diameter detected in imaging methods has been investigated[17-23] for a long time for significance related to LN involve-

Table II. ROC analysis for LN metastasis according to MRI lymph node diameter.

MRI	LN metastasis	Sensitivity (%)	Specificity (%)	AUC	95% CI	*p*-value
Pelvic LN diameter	Pelvic LN involvement	62.5	63.8	0.746	0.559-0.933	0.027
LN diameter	LN involvement	58.3	62.8	0.666	0.486-0.845	0.081

ROC: receiver operating characteristic, LN: lymph node, MRI: magnetic resonance imaging, AUC: Area Under the Curve.

ment. According to the conventional method for identifying metastatic LN on MRI, the short axis diameter of the LN is measured with a cut-off of 10 mm, mainly used[17]. In the study by Klerkx et al[18], LN involvement in cervical cancer had increased specificity but decreased sensitivity when the cut-off value was increased from 5 to 10 mm. Therefore, the cut-off value of 10 mm does not provide a satisfactory result for LN status, while sensitivity for LN involvement can range from 24% to 73%[19]. Song et al[20] found an average short LN diameter of 6.26 mm in their analysis of normal-sized LNs in cervical cancer cases. Metastatic LNs (mm) were found to be larger than non-metastatic LNs. They also reported that approximately 42.4% of MRI-recognizable LNs with short axis diameters between 5-10 mm were metastasized. If the 10-mm criterion is used to evaluate LN involvement, the risk of under-diagnosis increases. Song et al[21] found sensitivity and specificity for LN involvement to be 71.7% and 83.9%, respectively, when the cut-off LN diameter of 6.17 mm was used. Similarly, Liu et al[22] showed that sensitivity was 52% when the cut-off was 10 mm, but this increased to 76% when the short axis diameter of 7.75 mm was accepted as the cut-off, while additionally, the specificity was reduced compared to the 10 mm cut-off. In the retrospective study by Steiner et al[23], sensitivity, specificity, PPV, NPV, and AUC for LN involvement in MRI imaging were calculated as 71%, 75%, 75%, 71%, and 0.73% (0.55-0.91), respectively. The optimal cut-off value for LN was calculated as 10.2. The sensitivity, specificity, PPV, NPV, and AUC of para-aortic involvement were calculated as 50%, 96%, 67%, 93%, and 0.73% (0.41-1.00), respectively[23]. In the present study, we showed that the cut-off value for LN size measured on pelvic MRI was 18.5 mm for detecting pelvic LN involvement with a sensitivity of 50.0% and a specificity of 93.6%. Additionally, the cut-off value for pelvic and para-aortic LN size on MRI for detecting both pelvic and para-aortic LN involvement was 17.0 mm short axis diameter with a sensitivity of 41.7% and a specificity of 88.4%, and this was also not statistically significant. These differences may be due to the advanced stage in this study group, the distribution of cases, and the small number of cases.

Limitations

The limitations of this study are that it was retrospective, single-center, and included a small number of cases. The strength of the study is that while there have been many studies in literature about the use of MRI in the evaluation of LNs with imaging, there are few studies about the cut-off value for LN diameter on MRI for prediction of LN involvement.

Randomized controlled studies are needed to calculate the cut-off value of the lymph node size detected by MRI for the prediction of lymph node involvement in locally advanced cervical cancer. Thus, the use of MRI in patients who are not suitable for the operation without delay in diagnosis[24] of cervical cancer may be useful for the prediction of lymph node involvement and deciding on treatment, in terms of reducing the morbidity and mortality of the cases.

Conclusions

MRI imaging can detect LN involvement with high specificity in locally advanced cervical cancer. The short axis diameter of the pelvic LN of 17.0 mm can be used as a cut-off value in detecting LN involvement.

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