

Preoperative evaluation of uterine isthmus-cervical infiltration in patient with cervical cancer using nuclear magnetic resonance

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SUMMARY

Background: During the last three decades, fertility preservation has been established as a new treatment modality for young patients with early cervical cancer. In preservation of the uterine corpus in fertility sparing surgery one of the most important factors is evaluation of absence of internal uterine ostium or uterine corpus tumor infiltration. The aim was to evaluate the accuracy of nuclear magnetic resonance (NMR) in detection of infiltration of uterine isthmus-cervical part in cervical cancer patients without fertility preservation.

Methods: In 60 patients with cervical cancer FIGO stage IA-2 – IVA, NMR was performed before the operation. Radical hysterectomy Piver class III was performed in 57 patients and pelvic exenteration in three patients with FIGO stage IVA. The histopathological material was examined at the Department of pathology and cytology and it was used as a gold standard.

Results: The patient average age was 44.7, (range: 25-65 years). Squamous cervical cancer was diagnosed in 53 (88.3%), adenocarcinoma in 4 (6.7%), and adenosquamous carcinoma in 3 (5%) patients. According to NMR findings, 7 (11.7%) patients were with uterine isthmus-cervical infiltration when compared with histopathological examination, which established infiltration in 10 (16.7%) patients. Sensitivity of NMR was 60%, specificity 98%, positive predictive value 85.7%, and negative predictive value was 92.5% with overall accuracy 91.7%.

Conclusion: Sensitivity of NMR was low compared with other studies but with high specificity and overall accuracy. The positive predictive value was relatively acceptable.

Negative findings of NMR for corporal infiltration and precise evaluation of the depth of stromal infiltration and length of the proximal cervix without infiltration are important in preoperative diagnostic for fertility preservation surgery.

Key words: Uterine Cervical Neoplasms; Diagnosis; Magnetic Resonance Imaging; Sensitivity and Specificity; Preoperative Period; Fertility

INTRODUCTION

Cervical carcinoma represents one of the major problems in developing countries where the cervical population-screening program is still not developed (1). Approximately 45% of surgically treated stage IB cancers occur in women under the age of 40 years (2). However, in developed countries, screening enables the detection of cancer in its early phase, which suggests a new approach in comprehension and surgical treatment of early invasive cervical carcinoma. Radical trachelectomy is a surgical method, together with the pelvic lymphadenectomy, for treating invasive forms of cervical carcinoma in its early stage in women who are in their fertile ages and who want to keep their reproductive function (3-8). The general eligibility criteria for radical trachelectomy include the following: women less than 40 years of age who have a strong desire to preserve fertility, no clinical evidence of impaired fertility, lesion size less than 2 cm, International Federation of Gynecology and Obstetrics (FIGO) stages IA –IB-1, no involvement of the upper endocervical canal, and negative regional lymph nodes (9). The absence of metastatic disease in lymph nodes and parametrial involvement allow continuation of the procedure. Another crucial point of the procedure is the level where the cervix has to be incised. In the preservation of uterine corpus in fertility-sparing surgery, the most important factor is the absence of internal uterine ostium or uterine corpus tumor infiltration (10).

When computed tomography (CT) and NMR are compared, NMR is significantly more accurate in the evaluation of tumor volume, local tumor stage, and parametrial invasion due to its distinctive tissue contrast

and multiplanar capability (11). Cervical tumor is best shown in T2W sequence, which gives the most evident difference between normal structures in the body and cervix of the uterus. The same sequence is determined by the integrity of the stromal ring and its deficiency is explained by the penetration of the tumor to the parametrium.

The aim was to evaluate the accuracy of NMR in detection of infiltration of uterine isthmus-cervical part in cervical cancer patients without fertility preservation.

PATIENTS AND METHODS

Sixty patients with cervical cancer FIGO stage IA-2 - IVA were preoperatively examined and conventional NMR before the operation was made. Cervical cancer was confirmed by histopathological specimen obtained by cervix biopsy.

The results of NMR findings for presence or absence of infiltration of uterine isthmus-cervical part, such as diameter of the tumor, were compared with the results of histological examination of the surgical specimens. Radical hysterectomy Piver Class III with pelvic lymphadenectomy was performed in 57 patients and pelvic exenteration in three patients with FIGO stage IVA. The histopathological material was examined at the Department of pathology and cytology of the Oncology Institute of Vojvodina and it was used as a gold standard.

The NMR examinations were performed at the Center for imaging diagnostics of the Oncology Institute of Vojvodina. T2W tomograms

Arch Oncol 2013;21(3-4):87-90.

UDC: 618.146-006:537.635:616-089.8
DOI: <https://doi.org/10.2298/AOQ1304087M>

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Received: 04.03.2013
Provisionally accepted: 01.04.2013
Accepted: 28.04.2013

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targeted perpendicular to the axis of the cervix were used (the technique of multiple-echo (TSE) with 9 intersections of 5 mm thickness and flashover 0.5 mm; field of view 360°; minimum range resolution 259 x 512 pixels and acquisition time 5:50 minutes).

The sagittal T2W images identify the best penetration of the tumor in the body of the uterus and its spread beyond the level of the internal uterine osium. For statistical analysis, T-test and test for sensitivity, specificity, and accuracy were used in SPSS 6.0 statistical program.

RESULTS

The patient average age was 44.7 years (range 25-65 years) (Figure 1).

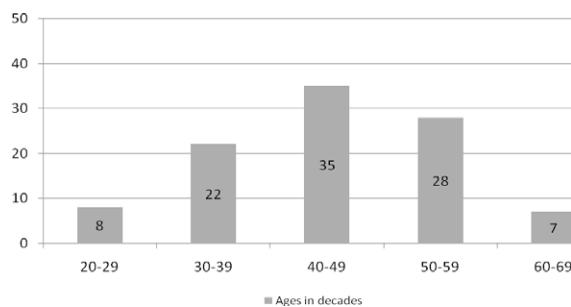


Figure 1. Age of the patients in decades

Squamous cervical cancer was diagnosed in 53 (88.3%), adenocarcinoma in 4 (6.7%), and adenosquamous carcinoma in 3 (5%) patients (Table 1).

Table 1. Histopathological type of the cervical tumor

Tumor	Number of patients (%)
Adenocarcinoma	4 (6.7)
Adenosquamous carcinoma	3 (5.0)
Planocellular carcinoma	53 (88.3)
Total	60 (100.0)

Mean tumor diameter on NMR finding was 31.8mm (range: 5 mm to 60 mm) and mean value found by histopathological examination of the cervical specimen was 27 mm (range: 0 mm to 70 mm). Tumor diameter measured by NMR was greater in comparison with tumor diameter defined by the histopathological examination of the specimen with statistically significant difference of $p=0.0102$ (Table 2).

Table 2. Diameter of the cervical tumor measured by NMR and pathologist

Parameters	Tumor diameter (mm)	
	NMR	PH
Mean value	31.8*	27.1
Standard deviation	14.1	15.5
The smallest diameter	5.0	0.0
The greatest diameter	60.0	70.0

* $p < 0.05$; PH - pathologist

NMR findings showed uterine corpus infiltration in 7 (11.7%) patients when compared with histopathological examination, which established infiltration in 10 (16.7%) patients. NMR sensitivity was 60%, specificity 98%, positive predictive value 85.7% and negative predictive value was 92.5% with overall accuracy 91.7% (Figures 2-4).

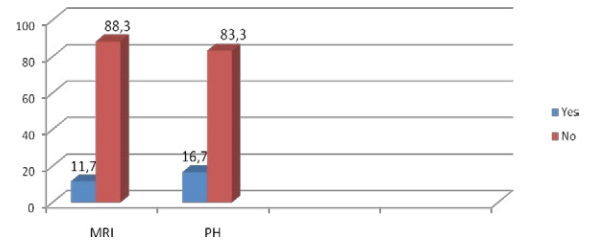


Figure 2. Ratio of infiltration of corpus uteri measured by NMR and pathologist (PH)

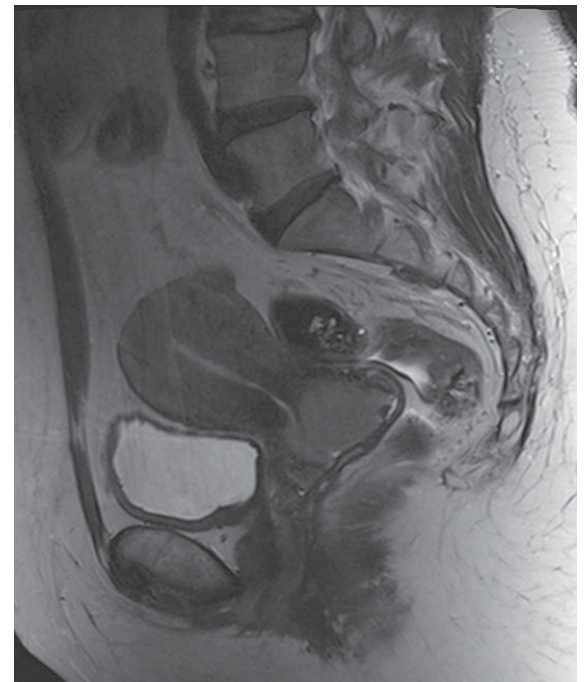


Figure 3. Bulky cervical tumor without parametrial and corpus uteri involvement imaging (T2W sagittal)



Figure 4. Infiltration of corpus uteri by cervical cancer (T2W sagittal).

DISCUSSION

Uterine corpus infiltration was found in 7 (11.7%) patients using NMR when compared with histopathological examination, which established infiltration in 10 (16.7%) patients, in our study. Computed tomography (CT), NMR, or ultrasonography (US), such as PET/CT can be used as pretreatment evaluation of patients with cervical cancer (12-15).

Evaluation of tumor size, stromal infiltration, and cranial border of tumor is essential in the early stages for treatment individualization, including the planning of fertility-sparing procedures. The NMR staging criteria for cervical cancer was first introduced at the end of the 1980s by Hricak and Togashi (16, 17). Today, NMR is widely accepted as a method for evaluation of tumor volume, uterine corpus involvement, parametrial invasion, and metastatic lymph node involvement (18). Exquisite high-resolution images of the female pelvis can be obtained by using current state-of-the-art NMR technology. The routine use of high-resolution, sagittal and axial, T2-weighted, fast spin-echo (FSE) sequences and axial, T1-weighted, spoiled gradient-echo sequences is advocated. The sagittal, T2-weighted images facilitate the evaluation of the primary cervical tumor and of the tumoral extension into the uterine corpus, vagina, bladder, or rectum. The axial images are critical for evaluating the extent of stromal penetration and for detecting parametrial invasion (19).

Despite the results of the accuracy, NMR is not officially incorporated in the International Federation of Gynecology and Obstetrics (FIGO) staging system, but it is already widely accepted as the reliable imaging technique. The reported accuracy of NMR in detecting tumor size within 0.5 cm was 70%–93% (20). In recent study by Manfredi et al. (21), fifty-three patients with biopsy-proven carcinoma of the uterine cervix and eligible for conservative surgery prospectively underwent NMR imaging. In 75% of cases, there was agreement between NMR imaging and histopathology in the assessment of cervical stroma infiltration. NMR imaging had 67% sensitivity, 92% specificity, and 91% diagnostic accuracy in assessing infiltration of the vaginal fornices. In the evaluation of the infiltration of the internal os, NMR imaging had 86% sensitivity, 93% specificity, and 92% accuracy. NMR and histopathology findings in the evaluation of the infiltration of the internal os in our study showed that NMR sensitivity was lower (60%) but specificity was 98%, with overall accuracy 91.7% and they were similar to Manfredi. The magnetic resonance (MR) whole-body diffusion-weighted imaging (WB-DWI) was used in the staging of uterine cervical carcinoma by Chen YB et al. Twenty-six patients received preoperative conventional MR and WB-DWI scans and 30 healthy volunteers were scanned by WB-DWI. Mean ADC value of uterine cervical carcinoma was significantly lower than the 3 layers of normal uterine cervix such as for metastatic nodes compared to benign. An ADC value of $1.28 \times 10^{-3} \text{ mm}^2/\text{s}$ was used as the threshold for cervical cancer and sensitivity was 96%, specificity 100%, and accuracy 98%. When an ADC value of $1.14 \times 10^{-3} \text{ mm}^2/\text{s}$ was used as the threshold for metastasis lymph nodes the sensitivity was 83%, specificity 98% and accuracy 94% (22). Beside the NMR, computed tomography (CT) has also entered into routine practice (23). Although acceptable figures of diagnostic accuracy have been reported for each of these procedures, there is still no general consensus on which represents the best option in the assessment of the extent of the disease (24). During the past decade, several studies have retrospectively compared both methods in the assessment of preoperative

staging of the cervical cancer. In Hricak H et al. study retrospectively were compared diagnostic performance and interobserver variability for CT and NMR imaging in the pretreatment evaluation of early invasive cervical cancer, with surgical pathologic findings as the reference standard. In conclusion NMR imaging was significantly better than CT for tumor visualization ($P < .001$) and detection of parametrial invasion ($P = 0.047$). The modalities were similar for staging, sharing low sensitivity and PPV but relatively high NPV and specificity (25). Bipat et al. published a meta-analysis of 57 studies where the sensitivity of estimation of parametrial involvement was 74% for NMR and 55% for CT (26). This result was not confirmed in the largest to date prospective study conducted by the American College of Radiology Imaging Network 6651 and the Gynecologic Oncology Group 183 (27). NMR was superior to CT in assessing cervical carcinoma size and uterine corpus involvement and the similar staging accuracy were confirmed for both methods, with sensitivities of 42% and 53%, respectively (27). Over the last decade, the quality of gynecological ultrasound has remarkably evolved, which has increased the implementation of ultrasonography as good, the cheapest, widespread available, and relatively quick diagnostic tool in preoperative staging of the cervical cancer. Until then, a small number of the papers were published concerning the use of ultrasound in pretreatment evaluation of patients with cervical cancer (28-30). Fischerova D et al. compared transrectal ultrasound (TRUS) with NMR in the evaluation of tumor volume, early parametrial infiltration, and identification of residual tumor in early-stage cervical cancer. The accuracy for detecting tumor in 95 patients was 93.7% for TRUS and 83.2% for NMR. The accuracy for detection of small tumors $\leq 1 \text{ cm}^3$ was higher by TRUS than by NMR, 90.5% vs. 81.1%. The accuracy of parametrial infiltration detection by TRUS and NMR was 98.9% vs. 94.7%, respectively ($P \leq 0.219$). In the study, authors confirmed TRUS as comparable to the NMR in staging of early-stage cervical cancer with accuracy of TRUS higher than by NMR concerning volumes of the tumor and in detection of residual tumors following conization (31). Tesa et al. (32) presented a prospective study designed to examine patients with invasive cervical cancer by means of ultrasonography and NMR within 1 week before surgery. In her study, transvaginal ultrasound (TVUS) and NMR detected the depth of stromal invasion to be greater than two-thirds with a sensitivity of 100% (16/16) and 94% (15/16) and a false-positive rate of 25% and 15%, respectively. Both ultrasound and NMR provided low sensitivities (60% and 40%, respectively) and the same false-positive rate (11%) for the presence of parametrial infiltration, which are less than in Fischerova study but using the different technical approach transvaginal vs. transrectal (32). Positron emission tomography (PET) scanning with the use of fluorodeoxyglucose (FDG) has some value relative to conventional imaging methods for the detection of nodal metastatic disease and recurrent cervical cancer (33-36).

CONCLUSION

Sensitivity of NMR in our study was lower when compared with the results of other studies regarding the detection of infiltration of isthmic part of the uteri, but specificity and overall accuracy were high. The positive predictive value was relatively acceptable. The evaluation of NMR findings for parameters such as depth of the stromal infiltration, tumor volume, could also be an important issue for fertility preservation surgery

in young patients with early cervical cancer such as evaluation of lymph node status and parametrial infiltration. The importance of ultrasonography as a diagnostic tool must not be ignored.

Conflict of Interest

We declare no conflicts of interest

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