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Comparison of imaging features and diagnostic values of MRI, CT and contrast-enhanced ultrasonography in the diagnosis of cervical carcinoma staging

L. YU[1], H.-F. ZHANG[1], D.-W. JIANG[1], D.-Y. ZHAO[2], H. LIU[3], L.-M. SHEN[1]

[1]Department of Ultrasonography, People's Hospital of Dongying, Dongying, P.R. China
[2]Department of CT, People's Hospital of Dongying, Dongying, P.R. China
[3]Center of Disease Prevention and Control, Dongying District, Dongying, P.R. China

L. Yu and H.-F. Zhang contributed equally to this study

Abstract. – OBJECTIVE: This study aimed at exploring and contrasting the clinical significances and values of MRI, CT and contrast-enhanced ultrasonography in FIGO staging of cervical carcinoma.

PATIENTS AND METHODS: The contrast-enhanced ultrasonography, CT and MRI imaging data of 348 patients with cervical carcinoma confirmed by clinical pathology were analyzed retrospectively and contrasted with pathological findings.

RESULTS: The total accuracy of MRI in cervical carcinoma staging was 79.89% (278/348), and the diagnostic accuracy of MRI in stage IB, stage II, stage III and stage IV of cervical carcinoma was 74.29% (26/35), 75.74% (153/202), 85.25% (52/61), 94.00% (47/50), respectively. The total accuracy of CT in cervical carcinoma staging was 73.28% (255/348), and the diagnostic accuracy of CT in stage IB, stage II, stage III and stage IV of cervical carcinoma was 60.00% (21/35), 69.80% (141/202), 78.69% (48/61), 94.00% (45/50), respectively. The total accuracy of contrast-enhanced ultrasonography in cervical carcinoma staging was 57.47% (200/348), and the diagnostic accuracy of contrast-enhanced ultrasonography in stage IB, stage II, stage III and stage IV of cervical carcinoma was 37.14% (13/35), 50.99% (103/202), 70.49% (43/61), 82.00% (41/50), respectively. The accuracy of MRI in the diagnosis of stage IB, stage II of cervical carcinoma was higher than that of CT and contrast-enhanced ultrasonography ($p<0.05$), and the diagnostic accuracy of CT was higher than that of contrast-enhanced ultrasonography ($p<0.05$). The differences among the three methods were statistically significant.

CONCLUSIONS: According to the results of pathological sections, there were statistically significant differences among the sensitivity and specificity of MRI, CT and contrast-enhanced ultrasonography in the diagnosis of stage IB and stage II ($p<0.05$). MRI has high diagnostic values in the differentiation and diagnosis of cervical carcinoma staging.

Key Words
MRI, CI, Contrast-enhanced ultrasonography, Cervical carcinoma, FIGO staging.

Introduction

Cervical carcinoma is a common carcinoma of reproductive organs in Chinese women, accounting for about 12.4% of female carcinomas[1]. The fatality rate of cervical carcinoma is second only to breast cancer, accounting for 19.67% of the mortality rate of female malignant tumors, second only to gastric cancer, breast cancer and liver cancer[2,3]. Most of the patients with cervical carcinoma are 40 or 60 years old middle-aged women, but in recent years, cervical carcinoma tends to develop in younger women. According to the research data of Li et al[4], 133800 new cases of cervical carcinomas in the world were under 35 years old in 2017, accounting for 21.67%. The clinical manifestations of cervical carcinoma were irregular vaginal bleeding, postmenopausal vaginal bleeding, and contact bleeding. Early cervical carcinoma was mainly screened by pathological sections and diagnosed by cervical endoscopic technique. However, according to the statistics of Romm et al[5], the rate of medical errors and disputes caused by immaturity of medical treatment, sequelae of invasive screening and insufficient health knowledge of patients was 29.76%. In recent years, with the improvement of imaging techniques such as the contrast-enhanced ultrasonography, CT and

Corresponding Author: Limei Shen, MD; e-mail: shenlimei819@163.com

MRI, a new shortcut has been added for the treatment of cervical carcinoma, as locating the target area is the most important step in the treatment of cervical carcinoma[6]. Although contrast-enhanced ultrasonography has the characteristics of no allergic reaction, low cost, good safety and strong convenience[7], it is not intuitive enough, resulting in a lot of errors. At present, CT tomography is temporarily used to locate the target area and to calculate the chemoradiometric measurement. In the diagnosis of cancer, MRI is characterized by high tissue resolution, multi-azimuth and multi-sequence imaging, which has high clinical values in the differentiation and diagnosis of cervical carcinoma staging and is very popular in recent years[8]. The clinical staging of cervical carcinoma is based on the clinical staging classification[9,10] developed by the International Society for Gynecological Oncology (IGCS) and the International Gynecology and Obstetrics Association (FIGO). Because of the strong subjectivity of clinical staging, there is great difference between clinical staging and imaging staging. Imaging provides precise, convenient and stable reference values for the diagnosis and staging of cervical carcinoma, and the incidence and fatality rate of cervical carcinoma have decreased significantly in recent years[11]. Therefore, we intend to contrast and explore the values of MRI, CT and contrast-enhanced ultrasonography in the diagnosis of cervical carcinoma staging, and to provide a more effective and more accurate diagnostic method for clinical staging of cervical carcinoma.

Patients and Methods

Patients

A retrospective analysis of 348 patients with cervical carcinoma was performed. Those patients were diagnosed in People's Hospital of Dongying from July 2010 to September 2015. They underwent MRI, CT and contrast-enhanced ultrasonography in radiology department of People's Hospital of Dongying. They were 25-76 years old with an average age of 53.7±8.4 years. The pathological diagnosis was the following: 249 cases (71.55%) of squamous cell carcinoma, 81 cases (23.28%) of adenocarcinoma and 18 cases (5.17%) of adenosquamous carcinoma. According to FIGO clinical staging classification, there were 35 cases of stage IB, 202 cases of stage II, 61 cases of stage III and 50 cases of stage IV. The details of patients' basic information were shown in Table I.

Table I. Clinical data table of 348 patients with cervical carcinoma.

Factors	[n (%)]
Total Cases	348 (100)
Age	
<40	39 (11.21)
≥40, <60	238 (68.39)
Married or Not	
Unmarried	41 (11.78)
Married	307 (88.22)
Pregnant or Not	
Not pregnant	64 (18.39)
Pregnant	284 (81.61)
Types of Pathological Diagnosis	
Squamous cell carcinoma	249 (71.55)
Adenocarcinoma	81 (23.28)
Adenosquamous carcinoma	18 (5.17)
FIGO Staging	
Stage Ib	35 (10.06)
Stage II	202 (58.05)
Stage III	61 (17.53)
Stage IV	50 (14.37)

Inclusion and Exclusion Criteria

Inclusion criteria: the clinical pathological results of the selected cases were consistent with the findings of cervical carcinoma; the patients did not receive relevant treatment in other hospitals. Exclusion criteria: patients who did not cooperate with the examination; patients who refused to receive treatment in People's Hospital of Dongying; patients who had a history of allergic examination by imaging; patients with hereditary diseases; patients with neoplastic diseases other than cervical carcinoma. All subjects and their families signed informed consent and this study was approved by the Ethics Committee of People's Hospital of Dongying.

Examination Methods

MRI examination method of pelvic cavity

In this study, Philips Ingenuity TF PET/MR (Philips Healthcare, Cleveland, OH, USA) was used. Patients were told to drink 500 ml water 2 hours before the examination, to fill the bladder and to hold the urine. From 2 cm above the symphysis pubis, 4.0-5.0 mm thick slice scanning was performed. The sequence of examination was: T1WI, T2WI and DWI were scanned, gadolinium-diethylenetriamine penta-acetic acid (Gd-DTPA) was injected into the vein and then the dynamic enhanced scanning was performed.

CT examination method of pelvic cavity

In this study, Somatom Definition AS+4016 CT (Siemens Healthineers USA) was used. Patients were advised to eat less, take 1% -3% (150 ml) of water reinforcements of meglumine diatrizoate 0.6 hour before scanning and then drink 500 ml water to hold the urine. The scanning conditions were 300 ma, 120 kv, 5 mm interval and 4 mm thickness, and the range was from the symphysis pubis to the third lumbar vertebra. Then, enhanced scan was performed and 100 ml of iopromide were injected into the cubital vein. The injection was performed with a pressure injector at a rate of 3 ml/s, with a delay of 65 s, a scanning interval of 5 mm, a thickness of 5 mm and a reconstruction interval of 0.8 s.

Contrast-enhanced ultrasonography examination method of vagina

In this study, GE Voluson S8 Doppler ultrasound diagnostic apparatus (Boston, MA, USA) was used. Patients were told to drink 500 ml water before the examination and hold the urine. In supine position, routine abdominal gynecological ultrasonography examination was performed before contrast-enhanced ultrasonography, the general situations of uterus and appendages were recorded, and conventional ultrasound diagnosis was made. Then, Contrast- enhanced ultrasound (CEUS) suspension of 1 ml was injected quickly to the cubital vein and the clearest section was selected to show the lesion and to be converted to the imaging mode. At the same time, the timer was started to store and observe the image continuously and in real time for 120 s -3 min.

Without knowing the results of clinical and pathological examinations, MRI, CT and contrast-enhanced ultrasonography images were read independently by four chief physicians, respectively, who had more than 20 years working experience in imaging, in double blind method and without interfering with each other. According to the results of reading, the FIGO classification was used to confirm the stages of cervical carcinoma.

Statistical Analysis

SPSS 19.0 (Asia Analytics Formerly SPSS China) software system was used to count and analyze. The counting data was expressed as [n (%)] and the diagnostic accuracy of different stages of cervical carcinoma was compared and detected by x^2. When $p<0.05$, it was considered that the difference was statistically significant.

Results

Imaging Findings and Clinical Staging of Pelvic MRI, Pelvic CT, and Vagina Contrast-enhanced Ultrasonography in Cervical Carcinoma

Findings of pelvic MRI images in different stages

278 cases of cervical carcinoma were diagnosed by MRI. The stage IB of cervical carcinoma presented with T2WI sagittal cervical canal enlargement or hyperintense lump, but it was easy to miss diagnosis because of the complete display of T2WI axial cervical low signal matrix ring and normal para-uterine signal. There were only 26 cases detected by MRI in 35 cases diagnosed by staging. Of the 156 cases with stage II detected by MRI, 64 cases showed T2WI sagittal hyperintense, more than two-thirds of vagina infiltrated. 89 cases showed that normal low signal disappeared in T2WI cervix and diffuse or focal abnormal information was seen in para-uterine area. In stage III, 52 cases of MRI images showed that T2WI changed from low signal to hyperintense and one third of them were invaded under vagina. In stage IV, 47 cases of MRI images showed low signal in the wall of bladder or rectum and T2WI sagittal lump. The details were shown in Table II.

Findings of pelvic CT images in different stages

In stage IB of cervical carcinoma, the edge of the cervix was blurred or slightly adherent to the surrounding tissues, and the size and shape of the tumor (long diameter < 4 mm) were not abnormal with the edge of the surrounding normal tissues and organs, so it was easy to miss diagnosis. There were only 21 cases of stage IB of cervical carcinoma detected by CT in 35 cases diagnosed by staging. Of the patients with stage II detected by CT, 27 cases showed irregular, enlarged and blurred soft tissues in the margin of cervix and para-uterine, and 114 cases showed partial thickening of the inner wall of the vagina and infiltration of cervical lump into the vagina cavity. In stage III, 48 cases of CT images showed lump or stripe infiltrating the inner wall of the pelvic cavity, piriformis muscle, obturator internal muscle, or infiltrating uterine main ligament, broad ligament, sacral ligament. In stage IV, 45 cases of CT images showed pelvic lymphadenopathy with effusion after an obvious infiltration of the rectum, bladder, or abdominal cavity. The details were shown in Table III.

Table II. Imaging findings of 278 patients with cervical carcinoma by pelvic MRI.

Staging	Imaging Findings of MRI	Number of Cases
Stage Ib	T2WI sagittal cervical canal enlargement or hyperintense lump	26
Stage II	T2WI sagittal hyperintense, more than two-thirds of vagina infiltrated	64
	Normal low signal disappeared in T2WI cervix and diffuse or focal abnormal information was seen in para-uterine area	89
Stage III	T2WI changed from low signal to hyperintense and one third of them were invaded under vagina	52
Stage IV	Low signal in the wall of bladder or rectum and T2WI sagittal lump	47

Findings of vagina contrast-enhanced ultrasonography images in different stages

In stage IB of cervical carcinoma, no abnormal perfusion area was found in contrast-enhanced ultrasonography, or the abnormal perfusion area was confined to the cervix, so it was not possible to make a complete judgment. Due to the lack of specificity, contrast-enhanced ultrasonography was of little values in the diagnosis of stage I of cervical carcinoma. There were only 13 cases detected by contrast-enhanced ultrasonography in 35 cases diagnosed by staging. In stage II, 103 cases showed that the boundary between the lesions and tissues and organs around para-uterine was unclear or adhesive. In stage III, 39 cases showed that the lesions were immersed in the lower margin of the vagina, and the boundary between the lesions and tissues and organs around para-uterine was unclear or adhesive, and 4 cases showed that lymphadenopathy was seen on the right or left side of para-uterine. In stage IV, 40 cases presented with lump infiltrating bladder mucosa and 1 case presented with adhesion of the rectal mucosa with lump. The details were shown in Table IV.

Diagnostic Results of Different Stages of Cervical Carcinoma by MRI, CT and Contrast-enhanced Ultrasonography

The total accuracy of MRI in cervical carcinoma staging was 79.89% (278/348), and the diagnostic accuracy of MRI in stage IB, stage II, stage III and stage IV of cervical carcinoma was 74.29% (26/35), 75.74% (153/202), 85.25% (52/61), 94.00% (47/50), respectively. The total accuracy of CT in cervical carcinoma staging was 73.28% (255/348), and the diagnostic accuracy of CT in stage IB, stage II, stage III and stage IV of

Table III. Imaging findings of 255 patients with cervical carcinoma by pelvic CT.

Staging	Image Findings of CT	Number of Cases
Stage Ib	The edge of the cervix was blurred or slightly adherent to the surrounding tissues	21
Stage II	Irregular, enlarged and blurred soft tissues in the margin of cervix and para-uterine	27
	Partial thickening of the inner wall of the vagina and infiltration of cervical lump into the vagina cavity	114
Stage III	Lump, stripe infiltrating around the pelvic cavity or the uterine	48
Stage IV	Pelvic lymphadenopathy with effusion after an obvious infiltration of the rectum, bladder, or abdominal cavity	45

Table IV. Imaging findings of 200 patients with cervical carcinoma by vagina contrast-enhanced ultrasonography.

Staging	Imaging Findings of Contrast-enhanced Ultrasonography	Number of Cases
Stage Ib	The abnormal perfusion area was confined to the cervix	13
Stage II	The boundary between the lesions and tissues and organs around para-uterine was unclear or adhesive	103
Stage III	The lesions were immersed in the lower margin of the vagina, and the boundary between the lesions and tissues and organs Around para-uterine was unclear or adhesive	39
	Lymphadenopathy was seen on the right or left side of para-uterine	4
Stage IV	Lump infiltrating bladder mucosa	40
	Adhesion of the rectal mucosa with lump	1

cervical carcinoma was 60.00% (21/35), 69.80% (141/202), 78.69% (48/61), 94.00% (45/50), respectively. The total accuracy of contrast-enhanced ultrasonography in cervical carcinoma staging was 57.47% (200/348), and the diagnostic accuracy of contrast-enhanced ultrasonography in stage IB, stage II, stage III and stage IV of cervical carcinoma was 37.14% (13/35), 50.99% (103/202), 70.49% (43/61), 82.00% (41/50), respectively. The accuracy of MRI in the diagnosis of stage IB and stage II of cervical carcinoma was higher than that of contrast-enhanced ultrasonography and CT (p<0.05), and the accuracy of CT in the diagnosis of stage IB and stage II of cervical carcinoma was higher than that of contrast-enhanced ultrasonography (p<0.05). The differences among the three methods were statistically significant. However, there was no statistically significant difference among the accuracy of MRI, CT and contrast-enhanced ultrasonography in the diagnosis of stage III and stage IV of cervical carcinoma (p>0.05). The details were shown in Table V.

Contrast of the Sensitivity and Specificity of MRI, CT and Contrast-enhanced Ultrasonography in the Diagnosis of Different Stages of Cervical Carcinoma

According to the results of pathological sections, it was judged by MRI that in stage IB of cervical carcinoma, 4 cases were false-negative, 1 case was false-positive, the sensitivity was 86.67% and the specificity was 90.00%; in stage II of cervical carcinoma, 7 cases were false-negative, 2 cases were false-positive, the sensitivity was 95.62% and the specificity was 96.08%; in stage III of cervical carcinoma, 3 cases were false-negative, 1 case was false-positive, the sensitivity was 94.55% and the specificity was 90.00%; in stage IV of cervical carcinoma, 9 cases were false-negative, 1 case was false-positive, the sensitivity was 83.93% and the specificity was 75.00%.

According to the results of pathological sections, it was judged by CT that in stage IB of cervical carcinoma, 5 cases were false-negative, 2 cases were false-positive, the sensitivity was 80.77% and the specificity was 87.50%; in stage II of cervical carcinoma, 27 cases were false-negative, 3 cases were false-positive, the sensitivity was 83.93% and the specificity was 95.31%; in stage III of cervical carcinoma, 5 cases were false-negative, 2 cases were false-positive, the sensitivity was 90.57% and the specificity was 86.67%; in stage IV of cervical carcinoma, 21 cases were false-negative, 1 case was false-positive, the sensitivity was 73.77% and the specificity was 83.33%.

According to the results of pathological sections, it was judged by contrast-enhanced ultrasonography that in stage IB of cervical carcinoma, 3 cases were false-negative, 4 cases were false-positive, the sensitivity was 81.25% and the specificity was 84.62%; in stage II of cervical carcinoma, 23 cases were false-negative, 14 cases were false-positive, the sensitivity was 81.75% and the specificity was 87.61%; in stage III of cervical carcinoma, 6 cases were false-negative, 3 cases were false-positive, the sensitivity was 87.76% and the specificity was 85.71%; in stage IV of cervical carcinoma, 11 cases were false-negative, 2 cases were false-positive, the sensitivity was 78.85% and the specificity was 81.82%.

There were statistically significant differences in sensitivity and specificity among the three methods in stage IB and stage II, but there was no statistically significant difference among the three methods in stage III and stage IV. The details were shown in Table VI.

Discussion

At present, most stages of cervical carcinoma are confirmed by gynecological examination[12]. The judgment of pelvic wall, uterine body, and

Table V. The diagnostic accuracy (%) of MRI, CT and contrast-enhanced ultrasonography in the diagnosis of different stages of cervical carcinoma.

Staging	MRI	CT	Contrast-enhanced Ultrasonography	χ^2	p
Stage Ib	74.29	60.00*	37.14*#	3.06	0.01
Stage II	75.74	69.80*	50.99*#	2.68	0.03
Stage III	85.25	78.69	70.49	2.56	0.05
Stage IV	94	90	82	2.73	0.06

*Note: represents a comparison with MRI, p<0.05. #represents a comparison with CT, p<0.05.

Table VI. Comparison of the sensitivity and specificity of MRI, CT and contrast-enhanced ultrasonography (%).

Staging	MRI		CT		Contrast-enhanced Ultrasonography		*p*
	Sensitivity	Specificity	Sensitivity	Specificity	Sensitivity	Specificity	
Stage Ib	86.67	90	80.77*	87.5*	81.25*#	84.62*#	0.02
Stage II	95.62	96.08	83.93*	95.31*	81.75*#	87.61*#	0.02
Stage III	94.55	90	90.57	86.67	87.76	85.71	0.05
Stage IV	83.93	75	73.77	83.33	78.85	81.82	0.06

*Note: represents a comparison with MRI, $p<0.05$. #represents a comparison with CT, $p<0.05$.

para-uterine infiltration is subjective, the accuracy is low and it is impossible to understand whether lymph nodes have metastasized to the peripheral aorta or pelvic cavity[13]. Therefore, the current diagnosis of cervical carcinoma clinical staging is not cautious enough and it needs to be further improved. Matsuo et al[14] reported that the accuracy of clinical staging of cervical carcinoma was 64%-69%. With the development of modern medical treatment and the accumulation of clinical experience, people had a deeper understanding of tumor, and the method of the diagnosis of cervical carcinoma staging was continuously improved and corrected. So this technique could be applied to clinical practice. However, there was a lack of a method that could be combined with imaging staging, pathological staging and clinical staging to judge tumor invasion and metastasis[15,16].

The key of imaging diagnosis of cervical carcinoma staging is whether the pelvic tissue and structure can be displayed, and whether the difference between tumor and normal tissues can be directly expressed[17]. The main imaging methods of cervical carcinoma are MRI, CT and contrast-enhanced ultrasonography. In this study, it was shown that the diagnostic accuracy of contrast-enhanced ultrasonography in the diagnosis of stage IB and stage II of cervical carcinoma was only 37.14% (13/35) and 50.99% (103/202), respectively. According to the study of Rowe et al[18], the accuracy of contrast-enhanced ultrasonography in the diagnosis of stage IB of cervical carcinoma was 39.43% and the diagnostic accuracy of stage II was 51.47%. Likewise to our data, it was shown that contrast-enhanced ultrasonography could provide some information for the diagnosis of cervical carcinoma, but it was of limited values to clinical staging. In our work, it was found that the diagnostic accuracy of CT in stage IB and stage II of cervical carcinoma was only 60.00% (21/35) and 69.80% (141/202), respectively. In the study of Hicks et al[19], it was shown that the diagnostic accuracy of CT in stage IB of cervical carcinoma was 58.96% and that of stage II was 70.48%. Similar to our findings, it was observed that CT could not judge the extent of tumor invasion in the cervix due to the lack of tissue specificity, and it could not distinguish the inflammation, blood vessel and lymphoid tissue around the cervix, which resulted in the decrease of sensitivity to the para-uterine infiltration[20]. This study showed that the diagnostic accuracy of MRI in stage IB and stage II of cervical carcinoma was 74.29% (26/35) and 75.74% (153/202), respectively. Compared with the research of Bilfeld et al[21], which showed that the accuracy of MRI in the diagnosis of stage IB of cervical carcinoma was 70.45% and that of stage II was 72.42%, our research data were relatively high. The difference might be caused by the differences between machine and diagnostics, but both studies showed that MRI had high diagnostic values and significances. Because of the characteristics of multi-sequence imaging and signal difference of MRI, there were distinct levels of images in the pelvic cavity and in various organs and tissues[22]. In this report, MRI was used to detect the patients, and the tissue signals of cervical carcinoma could be clearly observed, which was helpful to cervical carcinoma staging. At the same time, the radiation before and after radiotherapy and the observation of organs and tissues in the field could also be compared[23]. Therefore, MRI had high diagnostic significances in the diagnosis of stage IB and stage II of cervical carcinoma. Thus, we performed pelvic MRI examination and clinical examination in order to select the appropriate treatment for the preoperative staging of cervical carcinoma. Because of the limitation of CT imaging, the fusion technique of pelvic MRI and pelvic CT was used to accurately locate the target area in radiotherapy of the tumor

of pelvis[24]. In this work, due to the limited medical resources in our hospital, there were only 348 cases selected. This number of cases could not be counted as a big data study, and there might be some contingency in the results of the paper. Besides, the imaging diagnostic instrument used was not the most advanced instrument at present, so the results of analysis might be different from that of other reports, but we have avoided the errors caused by all human factors as far as possible.

Conclusions

We found that because of the characteristics of multi-sequence imaging and signal difference of MRI, there were distinct levels of images in the pelvic cavity and in various organs and tissues. In cervical carcinoma staging, compared with contrast-enhanced ultrasonography and CT, MRI had obvious advantages and had higher values in the diagnosis of cervical carcinoma, which was worthy of promotion in clinical practice.

Ethics Approval and Consent to Participate

The study was approved by the Ethics Committee of People's Hospital of Dongying. Signed written informed consents were obtained from the patients.

Conflict of Interest

The authors declare that they have no conflict of interests.

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