Imaging methods of Cervical Cancer

SHANG Linjing, Lydia
Shang.bio.sci.ms@lydiashaw.asia

1. Introduction

Cervical cancer is a frequent cancer concerned by women all around the world. According the cancer report in 2019, China released that the incidence rate of cervical cancer ranked second in female malignant tumors with high mortality rate, which was followed by breast cancer[1]. The incidence rate has been increasing consistently in recent years, let alone the situation is getting worse when an increasing number of young women suffered from this tumor[2].

1.1 Related Tissues

Cervix is the narrow part at the bottom of the uterus connecting vagina[3]. The normal organ of cervix is composed of an inner mucosal layer, a smooth thick mucosal layer, and adventitia. The structure of cervix is more tightly than the rest of the uterus which mostly includes two kinds of cells[4]. The histopathology image demonstrated that the squamocolumnar junction of the cervix,which includes squamous epithelium and columnar epithelium cells. The former is visible on the left and the later is on the right.

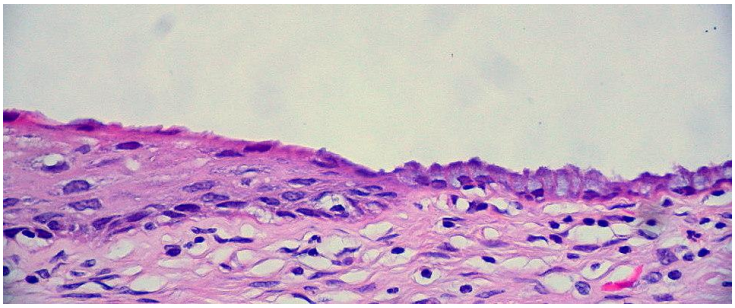

Figure 1. squamous epithelium and columnar epithelium cells[5]

1.2 Clinical Symptoms

When it comes to clinical symptoms, it is undeniable that the judgment criteria for cervical cancer is histopathology which is a traditional gold standard taking an overwhelming role in clinic.

The morphological characteristics of normal cervical cells have long nucleus and

loose cell density[6]. However, when the cervical cells change to the cancer cells, cytoplasm would be fewer. Meanwhile, it would be larger nucleus and darker colour as the hematoxylin eosin staining method shown in the figure above. Finally, after being changed the shape, topology of cells gets higher density.

For its complex processing procedure, a better non invasive imaging method is still supposed to study. These conventional imaging methods including CT, MRI or ultrasound would be illustrated for proposing an optimum solution.

1.3 Staging System

Before illustrating the conventional imaging methods for its diagnosis, FIGO (Federation of Gynecology and Obstetrics), mainly guiding the treatment of cervical cancer, released the staging system in 2018 which is the latest version of staging system[7]. Utilizing the staging system, either histologic pathology results or radiographic imaging examination results could be proposed. The imaging and pathological data obtained in all stages can be used to supplement clinical findings, assess tumor size and extent of spread, and form the final stage. According the staging system, it would be easier to compared these conventional imaging methods.

Characteristics	2014 FIGO system	2018 FIGO system
Stage IB1	Tumor size ≤4 cm	Tumor size <2 cm
Stage IB2	Tumor size >4 cm	Tumor size 2–3.9 cm
Stage IB3	n/a	Tumor size ≥4 cm
Stage IIIC1	n/a	Pelvic lymph node metastasis only[a]
Stage IIIC2	n/a	Para-aortic lymph node metastasis[a]

Figure 2. new staging system[7]

In conclusion, it is the early stage (≤IIa) if the tumor is confined to the cervix; once the tumor infiltrates to the uterus, it belongs to the late stage (≥IIb)[8]. According to the NCCN (National Comprehensive Cancer Network) clinical practice guidelines, advanced cases of stage IIb and above tend to receive chemotherapy and radiotherapy rather than surgery[9].Therefore, it is important to determine whether there is parauterine infiltration before treatment for it determines the procedure of surgical treatment so that the question of evaluating the accuracy of imaging methods turn to the judgment parauterine invasion.

2. Imaging Methods

Currently used in the evaluation of uterine infiltration of imaging techniques are MRI, CT, ultrasound, meanwhile, some extra auxiliary examinations such as colposcopy, biopsy, cervical conization, cystoscopy and rectosigmoidoscopy are also be used[10]. According articles existed, MRI has a higher accuracy of diagnosis of uterine, however, some emerging imaging methods have potential prospect as well,

such as PET/CT or PET/MR, etc.

2.1 Computed Tomography

According some articles of researchers, some comparison of CT and other imaging methods have been came out. The meta-analysis by BipatS et al. showed that the sensitivity of CT for the diagnosis of parauterine infiltration was higher than FIGO staging and the specificity was close to that of MRI[11]. Although the accuracy of CT in evaluating parauterine invasion of cervical cancer is just 55%, the examinations before surgery still enhance the understanding of invasion status. It can supply the morphological information for clinical treatment.

It is undeniable that CT scans are faster and easier to obtain than MRI. The imaging range also larger than MRI, but the healthy problem has to be taken into consideration. Considering the cost is cheaper, at present, CT of cervical cancer patients also accounts for a large part.

Considering the limitations, it is undeniable that the resolution of CT is lower than MRI especially when it comes to the soft tissue, therefore,it is hard to accurately distinguish tumors from normal cervical tissue near the uterus. Besides,the edge of images is rough even there may be shadow which leads to the fat space around the cervix is unclear or completely disappeared, indicating the presence of parauterine tissue infiltration.

2.2 Ultrasound

There are some main signs of ultrasound diagnosis of parauterine invasion. One is that the patient's cervical tumor has abundant blood flow; another is that cervical cancer tissue breaks through the cervical interstitium so that irregular hypoechoic burr infiltration appears in the surrounding tissue. In clinic, three-dimensional ultrasound tend to be used frequently which also be called Transvaginal Ultrasonography(TVUS) allowing the evaluation of any slice of a given anatomical area, and it can accurately estimate the size and volume of the tumor.

A study of 24 patients by Byun et al. showed that the sensitivity and specificity of transvaginal ultrasonography for the diagnosis of parauterine infiltration can reach 75% and 90%, respectively. Results of MRI are 75% and 55.6% compared to TVUS[12]. Subsequently, Arribas et al. also studied a similar work participating a total of 40 patients. The results showed that the two-dimensional ultrasound and MRI had a moderate consistency of 70%, three-dimensional ultrasound and MRI were 80%[13].

In general, reviewing the current articles, although some comparative studies with MRI show that ultrasound is prospective for the uterus, lacking of sufficient studies on the application of ultrasonography in the diagnosis of cervical cancer parauterine invasion based on the research using postoperative pathology as the gold standard is still worthy of further investigation.

2.3 Magnetic Resonance

Infiltration makes low signal loop on the T2 sequence.According FIGO staging report released in 2018, it was significantly revised that MRI was officially included in the system as a non-invasive, radiation-free and reproducible imaging which has became the popular choice for pre-treatment[14,15].

As the comparative studies with ultrasound, MRI has good tissue resolution, therefore as the table shows, it has high accuracy in the diagnosis of parauterine invasion. Meanwhile, MRI can be used for multi-directional imaging,so that it is available for observing the cervical infiltration in multi-directional and multi-angle.

Author	Accuracy	Sensitivity	Specificity
Yang, K	77.2%	53.8%	82.1%
Shweel, M. A	92.2%	100%	85.7%
Thomeer, M. G	98.4%	84%	92%

Table1.MRI comparative study[16-18]

Meanwhile, some articles illustrated some new approaches to enhance MRI imaging. For example, diffusion-weighted imaging (DWI) is the only imaging method that can observe the microscopic activities of water molecules in vivo. Compared normal tissue, water molecule diffusion in tumor cells is limited, and the DWI sequence shows obvious high signal, which forms a good contrast with the surrounding tissues. By selecting the lesion and measuring the corresponding apparent diffusion coefficient, it can assist in the judgment of the nature of the abnormal parauterine lesions.

In conclusion, MRI scanning can be combined with DWI, which is more accurate for clinical staging diagnosis. Therefore, MRI has a high application value and high potential for continuous improvement.

2.4 Positron Emission Tomography

Because of the preference for functional imaging and loss of morphological information, PET tends to used together with CT or MRI. Therefore, there are some studies of PET/CT and PET/MRI in cervical cancer imaging.

Treatment guidelines recommend that patients with first stage of Ib or above ought to undergo whole-body PET/CT examination. Its main function is to evaluate whether the tumor has metastasis, and its effect on lymph node metastasis and distant metastasis. PET combines CT or MRI can provide morphological and functional data. Studies have confirmed that it is very accurate in staging many solid tumors, which is more objective and accurate than traditional staging systems.

Zhuo Yang et al. retrospected approximately 110 patients to get the accuracy is 94.7%[19]. The analysis of solid tumors shows that PET/CT is more accurate in staging tumors than CT or PET alone. Grueneisen et al. utilized medical records of 27 patients assessed the PET/MRI concluding the high potential of prospect.

Leonardo et al. compared PET/CT and PET/MRI in breast cancer, however, lacking of related references, PET/CT or PET/MRI has not determined which is better to detect cervical cancer[21].

3. Discussion

Considering all the imaging methods mentioned above,MR, US, and CT have their own pros and cons. MR has the highest accuracy, but its scanning speed is slow, and the price is more expensive. Ultrasound is cheap and easy to obtain. More importantly, it can be dynamically observed, so that doctors are available to obtain dynamic information. Three-dimensional ultrasound also has considerable accuracy. However, as for the sonographer's operate,the repeatability is poor. CT is the fastest among them and the price is relatively low, but the accuracy is relatively low according the data mentioned above.

In recent years, image fusion has gradually emerged. Since both MRI and ultrasound have high accuracy rates, combining the two is a good choice.Therefore, in my opinion, TVUS/MRI would be a more potential trend in clinic. Using TVUS/MRI, it will have higher accuracy for both static and dynamic information. For these cervical cancer patients, for further detection,PET/TVUS/MRI would be utilized for more functional information. Taking into account the gold standard of pathology,it may be supposed to more research in the future to judge its accuracy.

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