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Review of Transvaginal Sonoelastography Effectiveness in Differentiation between Cervical Cancer and Intraepithelial Neoplasia

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ABSTRACT

Cancer cervix is a critical disease with high morbidity and mortality rates .Current imaging modalities used for the assessment of uterine cervical cancer include magnetic resonance imaging (MRI), computed tomography (CT), and ultrasound.In comparison, CT has a low contrast resolution of soft-tissue, while MRI is the ideal modality for the evaluation of the cervix. However, MRI is not usually performed immediately in regard to convenience and the limitations of intra-uterine contraceptive devices. On the other side, ultrasound is gaining clinical importance because it is cheaper, less time consuming and could have similar diagnostic accuracy as MRISonoelastography is rapid non expensive test so it can be used as a screening test .The aim of this study to review the transvaginalsonoelastography effectiveness in differentiation between cervical cancer and intraepithelial neoplasia in cervix.

Keywords: Sonoelastography;Cervical Cancer; Intraepithelial Neoplasia

INTRODUCTION

The cervix is a fibromuscular organ that links the uterine cavity to the vagina. Although it is described as being cylindrical in shape, the anterior and posterior walls are more often ordinarily apposed. The cervix is approximately 4 cm in length and 3 cm in diameter. The cervix of a parous woman is considerably larger than that of a nulliparous woman, and the cervix of a woman of reproductive age is considerably larger than that of a postmenopausal woman. The cervix occupies both an internal and an external position. Its lower half, or intravaginal part, lies at the upper end of the vagina, and its upper half lies above the vagina, in the pelvic/abdominal cavity **(1).**

Sonography Anatomy of normal Cervix

Representing the lower cylindrical portion of the uterus, the normal cervix measures 2.5–3 cm in length and 2.5 cm in width in women .Unlike the uterine myometrium, which is composed of approximately 65%–70% smooth muscle tissue , the cervical stroma is primarily collagenous tissue and is only approximately 15% smooth muscle. The cervix is considered to be composed of two portions, an upper or supravaginal portion and a lower portion that protrudes into the upper vaginal canal and is termed the *ectocervix* . The ectocervix is palpable during gynecologic pelvic examination, and its surface and opening into the vaginal canal (the external os) are readily visible at speculum examination, whereas the supravaginal cervix cannot be

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assessed with these techniques. The superior aspect of the vagina encircles the ectocervix and extends slightly higher posteriorly and laterally than anteriorly, forming the vaginal recesses or fornices (**2).**

The junction of the supravaginal cervix with the uterine body is referred to as the isthmus, and often there is a slight external tapering of the outer contour of the uterus at this level. The canal at the isthmus narrows, measuring 1–12 mm in width over a length of 1 cm. This corresponds to the location of the internal cervical os, which is the opening of the endocervical canal that connects with the endometrial cavity (**1).**Although sometimes visible at US and MR imaging, the plicaepalmatae are best visualized on a hysterosalpingogram, and their appearance ranges from closely spaced and thin with numerous folds to thicker and sparse with widely separated folds. The mucosa in the most superior aspect of the endocervical canal may undergo cyclical menstrual changes, although to a lesser degree than does the endometrium (**3).**In contrast to the endocervix, the mucosa of the ectocervix is composed of stratified squamous epithelium similar to the vaginal epithelium. The *transformation zone* is the region of the mucosa where the glandular tissue (columnar epithelium) is replaced by squamous epithelium. The location of this transformation zone, or squamocolumnar junction, varies with age. It is located in the ectocervix in 94% of women younger than 25 years but in only 2% of women older than 65years . The transformation (or transition) zone is not discernible at imaging. The proximal migration of the transition zone results in decreased accessibility for tissue sampling as women age, which has important clinical implications because most carcinomas of the cervix arise in this transformation zone **(4).**

Cervical Intraepithelial Neoplasia (CIN):

Cervical intraepithelial neoplasia (CIN) is a premalignant cervical disease that is also called cervical dysplasia or cervical interstitial neoplasia or cervical squamous intraepithelial lesions (CSIL). The nomenclature in use in the past was mild, moderate, and severe dysplasia, these were the terms used to describe premalignant squamous cervical cellular changes. Although still in use by some, it has generally been replaced by the term Cervical IntraepitheliaNeoplasia(CIN), which is used to describe histologic changes on the uterine cervix. The trend is now tending towards the use of Squamous IntraepitheliaLesions(SIL) (**5).**

The main clinical reference to this is basically in the epithelia changes between pre pubertal and post pubertal period.The epithelia lining of the cervical canal (endocervix) is the columnar epithelium while that of external cervix (endocervix) is squamous epithelium. The squamo-columnar junction is located at the point where the squamous epithelium and the columnar epithelium meet. The location varies throughout a woman's life due to the process of metaplastic changes in the cervical epithelium which occur after puberty and in pregnancy (**6).**

Cervical Cancer

Cervical cancer is the major cause of cancer deaths in women worldwide (. The global estimate for 2000 was 470,600 new cases of cervical cancer and 233,400

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deaths **(7).** Of the half million new cases of cervical cancer reported yearly, nearly one-fifth are detected in India alone. Removal of the primary cancer by surgery and the immunological response to the metastatic cancer cells remaining after surgery play a major role in the morbidity and mortality of patients with cervical cancer **(8).**

Obviously Infection of the genital tract with HPV 16 is relatively common whereas invasive cancer is rare; and integration has been detected in some cases of genital warts and CIN lesions. A number of associated-factors have been proposed such as impaired immune response, persistence of virus, smoking and administration of steroid hormones (as oral contraceptives). Other genetic events such as loss of tumour suppressor genes and the activation of oncogenes may also play a role . Mutations in ras ,fos and other oncogenes have been detected in cervical cancer cell lines but their role in vivo is still to be determined. The knowledge of HPV infection has made a remarkable improvement in the screening,diagnosis,treatment,prevention and prognosis of cancer of the cervix **(9)**.

According to the International Federation of Gynecology and Obstetrics – FIGO 2009 staging of cervical cancer, stage IA includes the preclinical cancer that is diagnosed only by microscopic findings. This stage is divided into IA1 (microinvasive cancer), where the invasion does not exceed 3 mm in depth and 7 mm in width, and in stage IA2 (microcarcinoma), where the stromal invasion depth is between 3 and 5 mm and the width is less than 7 mm. Even though, in the latest FIGO staging, the importance of damaged volume is identified for the first time, other investigators report that the evaluation of the damaged volume by the use of three dimensions is a complicated procedure and not enough practical to be applied routinely **(10).**

TransvaginalSonoelastography

Transvaginal ultrasonography (TVUS) arranged with a high resolution probe, may give a clearer image of the uterine cervix and parametrial tissue. It is well-known that the malignant tissues are generally harder than adjacent normal tissues, and this could distinguish benignly from malignant tissues based on their elasticity. Real-time ultrasound elastography is a rising technique, now readily available on conventional ultrasound systems with modified software(**11).**

The basic principle in ultrasound elastography, is non-invasive imaging and estimation of tissue elasticity by measuring local tissue displacements from returning ultrasonic signals before and after application of a compressive force. Under compression, stiff tissues show less deformation or strain than soft tissues. Applying the property that malignant tissues have higher stiffness than benign tissues, ultrasound elastography has been shown to differentiate malignant from benign lesions in the prostate, breast, liver, pancreas, lymph nodes, and gastrointestinal tract. In addition, there are promising results showing that ultrasound elastography has a high accuracy for predicting malignant thyroid nodules. However, little effort was done on the detection and diagnosis of cervical cancer until now(**12).**

Despite extensive screening for the known precursors of cervical carcinoma, this lesion is still the most common malignant uterine neoplasm, causing 30% of all

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gynecologic cancer deaths. The peak incidence of the disease is between the ages of 45 and 55, a decade earlier than endometrial carcinoma. Patients are often asymptomatic, with bleeding or leukorrhea occurring in less than onethird**(11).**

Nevertheless the fact that nowadays approximately one-third of all cervical cancers are found at stage I and about one-third at stage II is due to regular gynecological check-ups including cytology, colposcopy and palpation. The prognosis is largely limited by the volume of the primary tumor and the stage of the disease **(10).**The internationally accepted staging system is the FIG0 classification (classification of the International Federation of Gynecologists and Obstetricians). Treatment of patients with cervical cancer is determined primarily by stage according to the FIG0 classification, which is based on visual inspection, palpatory findings and surgical staging. The literature however indicates a high rate of inaccuracy in clinical evaluation: only 20-30% of stage-I, 44-75% of stage-II and 50-94% of stage-III disease are detected (**13).**

Most errors are linked to the wrong interpretation of parametrial features with understaging of early parametrial involvement and overstaging in cases of peritumoral inflammatory reaction. In order to improve pretreatment staging, new imaging techniques have been employed. Among these techniques transvaginalsonography (TVS) seems to be the most promising method as it is non-invasive and low cost, and allows prompt visualization of the uterine cervix and paracervical tissue **(14).**

Potential clinical applications, like assessing the severity of liver fibrosis and differentiating breast lesions, thyroid nodules and prostate abnormalities, are proposed by the guidelines published by the European Federation for Ultrasound in Medicine and Biology. In obstetrics and gynecology, possible uses of elastography include prediction of preterm delivery and successful labor induction(**15).**

A real-time elastographical study showed high agreement with diagnosis related to magnetic resonance imaging for fibroids and adenomyosis. Considering that cervical cancer might cause changes in tissue elasticity, elastography can provide extra insights into differentiating between cervical malignancies and benign lesions(**14)**

A light displacement force was applied with the transducer in the form of light repetitive compressions. The device's software includes an exam quality indicator box to consider the displacement force as optimal this box must be colored in green(**16).**

A simultaneous view of a gray scale image on the right side of the screen and the elastographic image, with the color-coded stiffness map on the left side of the screen was obtained(**17).**

The allotment of the colors was chosen as follows: red - low stiffness, blue - increased rigidity and green, intermediate stiffness. After obtaining an adequate image, two circular ROIs were traced on the grey scale image, the first on the cervix, which was the tissue to be analyzed (T1) and the second on the ED, which served as a reference material (R)(**18).**

Several studies have proved that real-time elastography is feasible and improves the diagnostic accuracy for tumors of the breast, the prostate and the thyroid gland. Endosonographicelastography has been used in the examination of lymph nodes and

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the pancreas. However, to the best of our knowledge, only few articles have assessed its application in diagnosis and evaluation of the cervical lesions(**19).**

Previous studies investigated tissue elasticity of normal and abnormal cervix and concluded that computer-assisted and subjective evaluation of cervical elastography allows differentiation of malignancy from normal findings and cervical tissue is of medium hardness and does not change with age. Strain ratio was useful in differentiation between normal cervix (control group) and pathological cervix (diseased group) and using the cutoff value of 3.4 resulted in sensitivity, specificity and accuracy of 100% for differentiation between normal and pathological cervix. Using the strain ratio of 8.7 as a cutoff value resulted in 93.8% sensitivity, 100% specificity, 95% accuracy, 100% PPV and 80% NPV for differentiation between malignant (primary and recurrent cancer cervix) and benign (fibroid) lesions**(16).**

In a previous study, when SR of 4.53 was used as a cut-off point, sensitivity and specificity of elastography were 78.8% and 89.7% respectively in differentiating malignant from benign cervical lesions. They concluded that elastography should be used combined with conventional B-mode ultrasound to provide extra information and help confirming the diagnoses. There was no significant difference between strain ratios of primary cervical carcinoma and recurrent cervical carcinoma(**17).**

CONCLUSION

Transvaginalultrasonographyused to assess the cervix are diverse, and none have become universally accepted. For, in the gynecological pathology of the cervix with regard to cervical cancer and cervical intraepithelial neoplasia, elastography is still an ongoing research field.

No Conflict of interest.

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