Transvaginal Sonoelastography on Benign Masses of Cervix

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Review Article

ABSTRACT

Cervix is the lowermost portion of the uterus. Benign pathologies of the uterus mostly occur in women falling under the conceptive age profile. Frequently exhibited symptoms are excessive bleeding, menorrhagia and pain during menstruation or coitus. Sonoelastography in comparison to the sonography alone is a rather recent development and is easily affordable and available. This makes it ideal for use as a first – look diagnostic tool to determine the nature of the cervical mass without unnecessary invasive or expensive examinations. There is an urgent need for early differentiation of benign masses from malignant ones as it impacts the type of treatment administered, its efficacy, prognosis, and lifestyle post-treatment. This review aims to evaluate the accuracy of transvaginal sonography in correctly diagnosing benign masses of cervix from malignancy, and thus gives an overview of the evolution of its application in routine clinical practice. As seen in the review, only studies performing strain elastography have been taken into consideration with strain ratio being a focal point as this is a quantifiable unit, used for measurement of tissue elasticity. This gives us comparable results regarding the diagnostic precision of transvaginal elastography in cervical masses. Gold standard is used is histopathological diagnosis.

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1. INTRODUCTION

The female uterus has been divided into the following anatomical regions: "fundus", "body" and "cervix". All three regions are then consequently made up of the stratified tissue, each with its own component and function The inner layer is called the endometrium which is followed by a layer of smooth muscles called the myometrium and an outer surface called the serosa [1].

Benign uterine lesions are particularly common in the reproductive age group and usually restricted to the endometrial and myometrial layers of the uterus. Endometrial polyps distinctly arise from the endometrium and are made of other components like endometrial glands, fibrotic stroma, thick – walled central vessels which jut out into the endometrial cavity. When the polyp arises from the endometrium lining restricted to the cervix, it is called a cervical polyp. Likewise, a cervical leiomyoma is a mass formed by the replication of a single smooth muscle cell fused with changeable bulk of fibrous tissue.

The women usually present with abnormal uterine bleeding, menorrhagia, dysmenorrhea or dyspareunia. Although recent studies do mention the absence of any symptoms in the early stages or incidentally detecting the benign cervical lesion [2].

Although MRI has a significant part to play in staging of any lesion preoperatively or even tissue characterisation [3], the role of first line imaging is still ultrasound, be it transabdominal or transvaginal [1].

US imaging is being used in clinical settings which is far less expensive, require less time, and may have detection ability comparable to MRI. Ultrasonography performed via the vagina (TVUS) using a high-frequency probe in conjunction can impart a better understanding of the lower uterine segment comprising of the cervix and adjoining adnexa [4].

Elastography is a more recent method of determining soft tissue stiffness. Numerous studies have indicated diagnostic benefits in comparing the loss of elasticity of the affected region to the neighboring normal tissue when diagnosing localised lesions in diverse tissues such as the mammary and hepatic tissue as well as in the thyroid gland. Cervical elastography is frequently used to assess both normal and pathological results, such as cervical cancer and questionable histopathologic findings [5].

The distinction between benign and malignant masses is vital since the latter is still a major socioeconomic problem because it primarily affects women of reproductive age. Because the extent of the disease at diagnosis has a significant impact on prognosis, accurate staging is critical for optimal management [6].

Collagen fibres and a small amount of muscle fibres make up the majority of cervical tissue. Cervical tissue elasticity, according to research, is not impacted by age, although it can be altered under specific physiological situations. The inherent elasticity of the cervix is changed when it is inflamed or neoplastic [7].

The stiffness of the tissue can be assessed by analyzing the strain in the tissue under stress, or by measuring the stiffness of the tissue. A compression is administered to the tissue using the quasi-static technique elastography to create a map with a pre-determined color-scheme to assess the strain and observe the studied regions' stiffness [8].

Varying colours symbolise different amounts of tissue firmness: "blue" is firm, "red" is soft, and "green" is in the centre. The "strain ratio (SR)" was estimated by division of the average "strain" in the lesion to the average "strain" in nearby tissue of equivalent extent, size, and structure [9].

2. EMPIRICAL REVIEW

Testa, Antonia Carla, et al. (2009) in one of the earlier studies first attempted to prove the effectiveness of the transvaginal sonography against an already established high end modality; the MRI. So, a prospective assessment was done and transvaginal ultrasonography and magnetic resonance imaging (MRI) diagnostic performance were assessed prospectively in terms of the presence, size, and extent of invasive malignancies of the cervix, as well as the identification of metastatic lymph nodes, using biopsy outcomes as the gold standard. An aggressive cervical cancer tumour was identified in one of the 33 patients who were initially

planned for resection. In 77% of patients who had surgery after adjuvant chemotherapy, a residual tumor tissue was identified with no residual malignancy observed in eight participants (23%). In 56/60 cases (93%) and 53/60 (88%) instances, respectively, transvaginal ultrasonography and MRI scans confirmed the presence of a tumour mass. The depth of stromal invasion was identified by ultrasound and MRI with sensitivity of 100 percent (16/16) and 94 percent (15/16) (P = 1), respectively, and a FPV of 25 percent (13/52) and 15 percent (8/52) (P = 0.58). Both ultrasonography and MRI had low sensitivity (3/5, 60% and 2/5, 40%, respectively, P=1) and the same false-positive rate (7/63, 11%) in the presence of parametrial infiltration. Ultrasound correctly detected a patient from the 11 patients with metastatic lymph nodal spread (sensitivity at 9 percent) with no falsely-positive cases, however MRI correctly identified three positive cases (sensitivity at 27 percent, 3/11) with two false-positive cases (false positive rate 4 percent, 2/55) [10].

Sun, Li-tao, et al. (2012) later published a study upon the medical relevance of transvaginal elastography (TVES) in identifying changes in tissue stiffness of lesions behaving like cervical malignancies on a totality of 109 patients with cervical lesions. Pathological results was used as the ultimate gold standard. Changes in cervical tissue stiffness were detected using TVES. They estimated and compared the strain ratios of benign and malignant lesions. The strain ratio of malignant lesions is significantly greater than that of benign lesions (8.19 and 5.66 vs. 2.81 and 2.24 respectively, P=0.01). The area under ROC curve was 0.905, with a 95 percent confidence interval (0.835–0.976). The optimum strain ratio cut-off point was 4.53. The optimal cut-off point has specificity and sensitivity of 0.788 and 0.897, respectively. The average height of the 56 cancerous tumours was also assessed by transvaginal sono elastography, which had been estimated at 17.8 7.4 mm (range 5.4–43.1 mm), whereas pathological samples revealed 11.5 8.8 mm (range 3.7–38.4 mm). For the two observers, the ICC of the two techniques was 0.87 (95% CI 0.863–0.947) and 0.931 (95% CI 0.902–0.952). This is one of the earlier studies to have specifically identified a strain ratio to identify the difference between benign and malignant lesions. This study also proves in a way that the unit of strain ratio was a reproducible measurement and suggested that the technique can be easily standardized and used to further research and literature [11].

Lu, Rong, et al. (2014) performed transvaginal gray scale sonography and sono - elastography on cervical masses (40 benign and 44 malignant) in 84 persons as part of a study. Across the differential diagnosis of cervical lesions, the elasticity score had sensitivity, specificity of 81.8 percent, 85.0 percent and accuracy, PPV and NPV 83.3 percent, 85.7 percent, and 81.0 percent, meanwhile the same attributes of the strain ratio had 90.9 percent, 90.0 percent, 90.5 percent, 90.9 percent, and 90.0 percent respectively. From the acquired results, the cut-off value of strain ratio at 4.525 was determined as a reference to identify benign lesions from those of malignant strain. Malignant lesions had substantially greater strain ratio values due to loss of elasticity, that is a range of 4.85–8.91 vs 0.62–4.50 for benign lesions The differences were statistically significant (P lesser than .01). This study was similar to the previous study done by Sun, Li-tao, et al. Their results are rather comparable.Their optimum upper limit cut-off for strain ratio to identify benign lesions was 4.53 and 4.52 respectively [9].

Shady, Magda, et al. (2015) discovered that the mean SR varied significantly between normal and abnormal cervixes, as well as in their work, they distinguished malignant from non-malignant masses arising from the cervix (p - value highly significant at 0.0001 for both). An strain ratio of 3.4 resulted in 100% sensitivity, specificity and accuracy in discerning between normal and pathological cervix. With the ability to discriminate between malignant and benign cervical lesions an SR of 8.7 was deduced with sensitivity, specificity, and accuracy were 93.8 percent, 100 percent, and 95 percent, respectively. As a consequence, a conclusion on the strain ratio range in which benign cervical lesions fall may be established. This was a landmark study as it was the first to outline a cut-off for normal cervical tissue from benign pathologies arising from cervix and gave an in depth understanding of the disease process behind benign cervical lesions. The cut-off for differentiating between benign and malignant was raised to 8.7 from the previous 4.52 of the older studies and had a statistically higher significance with a specificity of 100% [4].

Metin, M. R., et al. (2016) executed a research to see how well transvaginal sonoelastography (TSE) differentiated between endometrial hyperplasia and it's malignancy. The research included 61 women with postmenopausal haemorrhage and/or normal TSE. Endometrial

hyperplasia had a mean SI of 0.80 (range: 0.30–1.30), endometrial cancer had a mean SI of 1.80 (range: 0.80–3.20), and control had a mean SI of 1.00 (range: 0.50–4.00). Hardly any statistically noteworthy variation was established between the groups with and without endometrial hyperplasia. However, there were variances between the endometrial carcinoma and hyperplasia groups, as well as the endometrial cancer and control groups (P = 0.0001). In discriminating endometrial cancer from endometrial hyperplasia, TSE exhibited a SN of 81.3 percent, a SP of 100%, a PPV of 100%, and a NPV of 70%. With a threshold SI value of 1.05., AUC to differentiate between malignancy and benign hyperplasia of the endometrium was 0.933 (95 percent CI, 0.853–1.000). Using a threshold SI value of 1.15, the AUC to distinguish between endometrial cancer and control was 0.881 (95 percent CI, 0.735–1.000). The investigation contributed to the clear conclusion that TVES can aid in the differentiation of endometrial hyperplasia from cancer [12].

Ma, X. et al. (2017) conducted a research to correlate the diagnostic accuracy of transvaginal elastography (TVES) when used with high-resolution vaginal ultrasonography (TVS) against MRI in identifying adnexal local encroachment in cervical cancer. Across a two-year period, 52 patients already suffering from histopathologically proven cervical malignancy were given staging in accordance to the "Fédération Internationale de Gynécologie et d'Obstétrique "(FIGO) criteria. MRI and strain elastography combined with TVS were performed by following a standardised methodology before treatment. While a close investigation was conduted to assess adjacent soft tissue involvement in the parametrium with TVS alone, MRI, and a combination of transvaginal strain elastography and TVS in early-stage illness (upto IIa stage). The following results were documented and analyzed with their respective histological results following surgery. Per the traditional FIGO staging, 39 of the 52 patients exhibited initial stage of malignancy (upto stage II a) and 13 had developed advanced-stage disease (from stage II b). The diagnostic sensitivity of MRI and the combination of TVS modalities for detecting parametrial infiltration in earlier stages of cervical cancer was significantly higher than TVS alone (P = 0.03 0.05). Both MRI and the application of TVS and TVES combined revealed 72.73 percent sensitivity; 82.14 percent specificity for MRI with 78.57 percent specificity for the adjunct transvaginal sonography modalities; and observed a diagnostic accuracy rate of 79.49 percent for MRI and 76.92 percent for the TVES and TVS conjunction. As a result, they concluded that TVES in tandem with TVS executed by a gynecologically trained radiologist was a competent and feasible procedure for work-up before surgery in cases suspected of cervical malignancy [13]. This work maybe slightly comparable to the previously mentioned study of Testa, Antonia Carla, et al., however the addition of a combination of transvaginal strain elastography makes this updated study more relevant as it also points to the diagnostic prowess of TV strain elastography with transvaginal sonography and suggests that it is almost as good as MRI which if studied more upon, can give us the same results with lesser investment of money and effort.

Che, Dehong, et al. (2019) 217 participants underwent standard B-mode sonography as well as elastography in this research undertaking. For qualitative analysis, endometrial lesions were classified into three categories, and the "strain ratio" (SR) was calculated for quantification of the data. Histopathological investigations were also performed in order to reach a conclusive diagnosis. 104 instances of endometrial malignancy and 113 cases of benign lesions had been taken into account. All of the type I endometrial lesions were reported to be benign, but 95.8 percent of type III lesions had been discovered as cancerous. The AUC for SR for quantitative elastography results was 0.904, with a 95% CI of 0.866 to 0.942. When utilizing a ROC curve, the desired cut-off value for SR was 3.02, with an 81.7 percent sensitivity. a specificity of 85 percent, a PPV of 83.3 percent, and a NPV of 83.5 percent. In this study, the cut-off for distinguishing benign from malignant had yet again been determined at 3.02, however the study since the specificity was found to be 85% which has a statistically lower significance than the previously established cut-off of SR 8.7 by Shady, Magda, et al. [8].

In of the first systematic study conducted for evaluating strain elastography, Zhu, Yi, et al. (2020) did a meta-analysis of six relevant papers with a comprehensive sampling of 615 cervical lesions (415 malignancies, 200 non malignant lesions). They had derived an aggregated diagnostic odds ratio for TVSE, which was 21.42 (95 percent CI 13.65-33.61), with sensitivity at 0.87 (95 percent CI 0.84-0.90), the specificity at 0.79 (95 percent CI 0.72-0.84), and the AUC was

0.892 (Q* = 0.822). Meta-regression analysis report found that imaging approach as well as the method of evaluation and QUADAS score were not significant (all having P > 0.05), ultimately having no impact on research variability [14]. This study was pioneered by an effort to increase literature material on TV strain elastography material in cases presenting with masses of cervix.

A systematic review conducted by Dudea – Simon, Marina et al. (2021) shortlisted 23 articles in an attempt to review the existing evidence on the use of sonoelastography via transvaginal examination in cases of cervical masses [15]. Beginning with technique and technological restrictions and progressing through diagnosis, staging, and the capacity to predict response to oncologic curative treatment therapy, this paper discussed the efficacy of sonoelastography in cervical malignancy and non invasive cervical intraepithelial neoplasia. Eleven of these studies pertained to strain elastography, which is the subject of our review. Even with the inclusion of the other types of elastography, they still found the literature somewhat lacking. They, therefore decided that there was insufficient material for ultrasound elastography to be used as a diagnostic criterion in any uniform therapeutic or staging categorization. As a result, additional study is needed to bridge this gap and examine this modality as an alternative to existing high-end and invasive procedures. Evidences from other relevant studies were reported [16-20].

3. CONCLUSION

After careful review of the selected articles, one can come to a reasonable verdict that transvaginal strain elastosonography has a high diagnostic precision in distinguishing benign from cancerous tumor tissues of the cervix. It can be a powerful tool for screening and planning further management, as its power lies in the widespread availability, affordability and reproducibility of results from an objective point of view. However, this is still not in effect, only due to the paucity in research material suggesting a need for increase in interest in this field.

CONSENT AND ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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