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The Role of Uterine Artery Pulsatility and Resistance Index in Detection of Pre-invasive Cervical Lesions

Preinvaziv Servikal Lezyonların Saptanmasında Uterus Arter Pulsatilite ve Rezistans İndeksinin Rolü

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ABSTRACT

Aim: Our aim was to evaluate the diagnostic strength of uterine arteries (UA) pulsatility index (PI) and resistance index (RI) in the detection of pre-invasive cervical lesions.

Materials and Methods: Data were prospectively collected from a total of 225 patients who were diagnosed with cervical ıntraepithelial neoplasia (CIN) 1 (Group 1) (n=75) and CIN-2/3 (Group 2) (n=75) by colposcopy-guided cervical biopsy previously and from patients with normal cytology assigned as control (Group 3) (n=75). PI and RI of UA were determined by Doppler sonography and the results were compared among the groups.

Results: The mean UA-PI values were found to be 2.52±0.9, 2.51±0.9, and 2.53±0.3 in Group 1, 2, and 3, respectively. The mean UA-RI values were observed as 0.83±0.7, 0.81±0.25, and 0.84±0.1 in Group 1, 2, and 3, respectively. However, UA-PI and UA-RI values were not significantly different among the groups (p>0.05).

Conclusion: PI and RI values are decreased with CIN lesions. Nevertheless, the difference is not large enough to implement these values in current cervical cancer screening program.

Keywords: Cervical intraepithelial neoplasia, Doppler ultrasonography, pulsatility index, uterine artery

ÖZ

Amaç: Preinvaziv servikal lezyonların saptanmasında uterus arter (UA) pulsatilite indeksi (PI) ve direnç indeksinin (RI) tanısal gücünün incelenmesidir.

Gereç ve Yöntem: Kolposkopi eşliğinde servikal biyopsi ile servikal intraepitelyal neoplazi (CIN) 1 (Grup 1) (n=75), CIN-2/3 (Grup 2) (n=75) tanısı alan toplam 225 hastadan prospektif olarak veriler toplandı. Sitolojisi normal olan hastalar kontrol (Grup 3) (n=75) olarak çalışmaya dahil edildi. UA'ların PI ve RI değerleri Doppler sonografi ile ölçüldü ve sonuçlar gruplar arasında karşılaştırıldı.

Bulgular: UA-PI ortalama değerleri Grup 1, 2 ve 3'te sırasıyla 2,52±0,9, 2,51±0,9 ve 2,53±0,3 olarak bulundu. UA-RI ortalama değerleri ise Grup 1, 2 ve 3'te sırasıyla 0,83±0,7, 0,81±0,25, 0,84±0,1 olarak gözlendi. Ancak UA-PI ve UA-RI değerleri gruplar arasında anlamlı farklılık göstermedi (p>0,05).

Sonuç: PI ve RI değerlerinin CIN lezyonlarında daha düşük olduğu gözlendi. Bununla birlikte, bu fark mevcut rahim ağzı kanseri tarama programında bu değerleri uygulayacak kadar istatistiksel açıdan büyük değildir.

Anahtar Kelimeler: Servikal intraepitelyal neoplazi, Doppler ultrason, pulsatilite indeks, uterus arter

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INTRODUCTION

Cervical cancer is the fourth most common cancer in women worldwide[1]. Latterly, the exquisite steps in diminution cervical cancer mortality have been observed with the onset and implementation of screening programs. Paramount approaches have also occurred in the diagnosis and treatment of cervical cancer[2]. Screening for cervical cancer has assuredly gave rise to a drop in cervical cancer incidence and mortality in many countries[3].

Cervical intraepithelial neoplasia (CIN), also known as cervical dysplasia, is the abnormal growth of cells on the surface of the cervix which can likely advance to cervical cancer[4]. An abnormal Pap smear result can necessitate an endorsement for colposcopy of the cervix. A biopsy is employed of any ominous regions and CIN can be detected subsequently. According to patients age, human papillomavirus (HPV) positivity or lesion type, it may be followed or treated by various surgical methods such as LEEP and cold knife conization afterwards[5].

Doppler ultrasonography of the fetoplacental circulation is highly used in daily practice of obstetricians[6]. The use of Doppler ultrasound as an appliance for screening/prediction of preeclampsia is recommended[7]. It was demonstrated that Doppler ultrasound is a valuable and decent predictor of ovarian malignancies[8]. In addition, using Doppler ultrasound for the pre-treatment evaluation of cervical cancer is increasing eventually[9].

In the present study, our aim was to evaluate the discriminative role of uterine artery (UA) Doppler in the detection of cervical intraepithelial lesions.

MATERIALS AND METHODS

This prospective study was conducted at the Gynecologic Oncology Outpatient Clinic at Tekirdağ City Hospital. The study was approved by the Tekirdağ Dr. İsmail Fehmi Cumalıoğlu State Hospital of Local Institutional Ethics Committee (protocol no: 2022/002, date: 04.11.2022). A total of 225 patients were divided into 3 groups. Group 1 represented patients with CIN 1 (n=75), Group 2 included patients with CIN 2-3 (n=75) and Group 3 consisted of patients without cervical pathology as control (n=75). Our exclusion criteria were non-Caucasian ethnics, age <21 and >50 years, body mass index (BMI) <18 or >28 kg/m^2, previous preeclampsia history, hysterectomized patients, history of any vaginal medical application or oral contraceptive use, cervical conization, embolization of the UAs and previous administration of chemo-radiotherapy. Postmenopausal patients or the ones in the menstrual and gestational period were also excluded from the study. Data were prospectively collected including age, parity and BMI.

All measurements were acquired by the same sonographer (C.Y.) with experience in Doppler ultrasound to avoid inter-observer variability. In all cases, Hitachi ARIETTA 60 (Aloka Medical, Ltd. Tokyo, Japan) transvaginal probe (4-9 MHz) with Doppler capability was utilized. For the assessment of UA, patient was placed in the lithotomy position, with her bladder empty in mid-luteal phase. The probe was moved laterally until the paracervical vascular plexus was seen, and the UA was identified at the level of the internal cervical os. The pulsatility index (PI) and resistance index (RI) was calculated when at least three identical waveforms were acquired (Figure 1).

Statistical Analysis

Statistical Package for Social Sciences (SPSS) 25 (SPSS, Chicago, II, USA) Windows package program was applied for statistical analysis. Descriptive statistical methods (mean, standard deviation) were used when evaluating study data. The Mann-Whitney U test was employed to compare differences between two independent groups when the dependent variable was either ordinal or continuous, but not normally distributed. The Kolmogorov-Smirnov test and the Shapiro-Wilk test were used to investigate the conformity of the variables to the normal distribution. Differences were defined as significant for $p<0.05$.

RESULTS

In the present study, there was no statistically significant difference between Groups 1, 2 and controls in terms of age, BMI, and parity (Table 1).

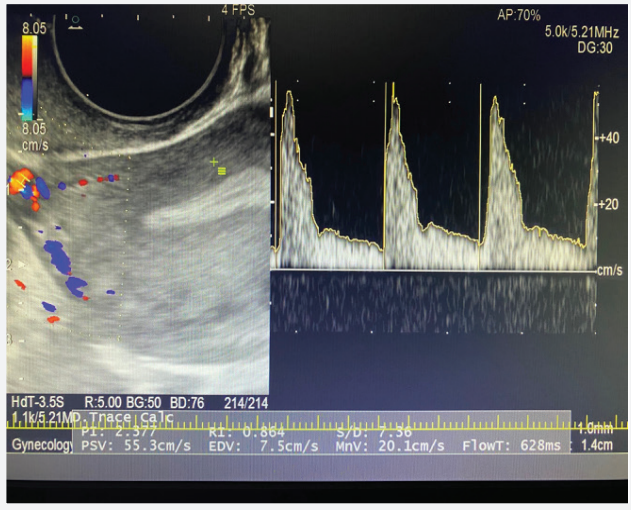

Figure 1. Transvaginal Doppler ultrasound examination of uterine artery is depicted. The uterine artery loop is located in a paracervical section, and at least three identical waveforms are recorded

Table 1. Characteristics of the patients			
	Group 1 and 2 (n=150)	Group 3 (n=75)	p
Age (year)	36.4±91	35.8±82	0.758
BMI (kg/m^2)	25.94±12	26.45±34	0.676
Parity	2 (0-6)	3 (1-7)	0.240
n: Number, BMI: Body mass index			

Table 2. Comparison of Doppler indices of Group 1 and Group 2			
	Group 1 (n=75)	Group 2 (n=75)	p
UA-PI	2.52±0.9	2.51±0.9	0.778
UA-RI	0.83±0.7	0.81±0.25	0.686
n: Number, UA-PI: Uterine artery pulsatility index, UA-RI: Uterine artery resistance index			

Table 3. Comparison of Doppler indices of Group 1 and Group 3			
	Group 1 (n=75)	Group 3 (n=75)	p
UA-PI	2.52±0.9	2.53±0.3	0.869
UA-RI	0.83±0.7	0.84±0.1	0.810
n: Number, UA-PI: Uterine artery pulsatility index, UA-RI: Uterine artery resistance index			

Table 4. Comparison of Doppler indices of Group 2 and Group 3			
	Group 2 (n=75)	Group 3 (n=75)	p
UA-PI	2.51±0.9	2.53±0.3	0.450
UA-RI	0.81±0.25	0.84±0.1	0.388
n: Number, UA-PI: Uterine artery pulsatility index, UA-RI: Uterine artery resistance index			

The mean UA-PI values were found to be 2.52±0.9, 2.51±0.9, and 2.53±0.3 in Group1, 2, and 3, respectively. The mean UA-RI values were observed as 0.83±0.7, 0.81±0.25, and 0.84±0.1 in Group 1, 2, and 3, respectively. There was no statistically significant difference among the groups in terms of UA-PI (p>0.05).

Regarding to UA-PI, we did not detect considerable differences among the groups (p>0.05) (Table 2-4).

DISCUSSION

In our study, UA-PI values were compared among the groups that were similar in terms of age, BMI and parity and no statistically significant difference was found. As the grade of CIN increased, UA-PI and UA-RI was observed to be lower due to increasing vascularization, but this was not statistically significant.

This is the second study to our knowledge investigating the use of Doppler ultrasound indices in CIN lesions. Doğan et al.[10] investigated the diagnostic strength of UA and cervical vascularity by itself or in association with HPV DNA testing and with cytology. They found that using the Doppler indices of UA and cervical arteries was indecisive in discerning CIN-I or above lesions in the early phases, which is compatible with our study.

Transvaginal and transrectal ultrasound is commonly applied to ascertain the characteristics of the cervical tumor[11]. Adding advanced techniques in ultrasound has increased the implementation of ultrasound for cervical cancer in clinical settings. If performed by well-trained gynecologists, ultrasound may give substantially precise information especially on tumor detection and local tumor extension[9]. Finally, ultrasound, besides being faster, radiation-free and non-invasive, is a broadly available imaging technique with lower cost compared to others. High-frequency ultrasound may provide comprehensive delineation of any cervical tumor, particularly when the probe is placed proximal to the tumor transvaginally and transrectally[12]. Even though, sensitivity was low when combined with other screening methods, evaluating the PI and RI of UA and cervical arteries may still stimulate experts given the fact that increased vascularization and thus lower RI and PI is attributed to cervical cancer and they may serve as a prognostic factor[13]. Lower PI and RI levels should alert the clinicians and meticulous investigation should be warranted.

Putting the vascularity index of cervical preinvasive and invasive lesions in the diagnostic algorithm to evaluate the diagnostic efficiency of a 3-step screening approach (cytology, HPV based testing and vascularity index) has recently been investigated. It is shown that to combine 3D vascular findings of a tumor with

cytology and HPV-testing essentially enhances the precision of screening for cervical cancer[14]. The characteristics of the cervical blood flow in healthy controls and in the ones with precancerous lesions or invasive cancers were studied by employing 3D power Doppler ultrasound findings, including the intensity of flow at the time of volume acquisition, the number of vessels within the volume of interest (VI), and both blood flow and vascularization[15]. All of these indices were quite higher in the group with cervical lesions, compared to the controls. The VI was also higher in advanced staged cervical cancer patients compared to less advanced ones. Cervical cancer screening could evolve by adding vascular indices obtained by ultrasound to the algorithm, especially in women of reproductive age, to refrain overdo use of LEEP or conization procedures and this approach may be apparently beneficial.

The strength of our study is that all ultrasonographic measurements were performed by the same gynecologist, a factor that may have an impact on inter-observer reproducibility and the patient number compared to the previous study.

Study Limitations

The most important limitation of our study is that it was conducted in a single center and with a relatively small number of patients.

CONCLUSION

In our research, we noticed that PI and RI values were decreased with CIN lesions. Nevertheless, the difference is not large enough to implement these values in current cervical cancer screening program. Hence, future studies with larger number of participants are needed to improve cervical cancer screening with ultrasound, and further studies are indispensable to provide reference values for Doppler ultrasound indices in cervical lesions and utilization of the tool to determine the vascularity of cervical lesions.

Ethics

Ethics Committee Approval: The study was approved by the Tekirdağ Dr. İsmail Fehmi Cumalıoğlu State Hospital of Local Institutional Ethics Committee (protocol no: 2022/002, date: 04.11.2022).

Informed Consent: Consent form was filled out by all participants.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: M.D., Concept: M.D., Design: C.Y., Data Collection or Processing: C.Y., Analysis or Interpretation: M.D., C.Y., Literature Search: M.D., C.Y., Writing: M.D.

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