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The importance of atypical squamous cells in cervical PAP smear in patients aged 65 years and older and their association with HPV

65 yaş ve üzeri hastalarda servikal PAP smearde atipik skuamöz hücrelerin önemi ve HPV ile ilişkisi

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ABSTRACT

Aim: This study aims to determine the significance of atypical squamous cells (ASC) in women 65 years of age and older, and the high-risk HPV (hrHPV) status of patients diagnosed with ASCs.

Materials and Methods: Data base of the Department of Pathology between February 2019 and December 2020 were screened and patients over the age of 65 who had 'ASC of undetermined significance' (ASC-US) and 'ASC-cannot exclude high-grade squamous intraepithelial lesion' (ASC-H) diagnosis on cervical PAP smear (CPS) were identified. hrHPV positive and negative patients were also examined.

Results: 164 patients (151 (92.1%) ASCUS and 13 (7.9%) ASC-H were included in the study. Follow-up information of 95 cases showed 16.8% low grade squamous intraepithelial lesion (LSIL), 5.3% high grade squamous intraepithelial lesion (HSIL), 1.1% endocervical adenocarcinoma following ASC diagnosis. 19.6% patients were hrHPV positive. In the follow-up of HrHPV positive patients, 38.9% LSIL, 22.2% HSIL, 5.6% cervical adenocarcinoma developed. Intraepithelial lesions (LSIL + HSIL) and high-grade cervical lesions (HSIL + invasive cervical carcinoma) were more common in hrHPV positive ASC-US cases compared to hrHPV negative ASC-US cases. Patients with ASC-H were more likely to have LSIL and intraepithelial lesions at follow-up compared to patients with ASC-US.

Conclusion : In patients aged 65 years and older, hrHPV positive ASC cases carry a high risk for LSIL, HSIL and high grade cervical lesions. Further studies on absolute referral to hrHPV test screening in these patients would significantly contribute to the management of these patients.

Keywords: Atypical squamous cells, cervical cancer, PAP smear, HPV, age over 65

ÖZ

Amaç: Bu çalışmanın amacı 65 yaş ve üzeri kadınlarda atipik skuamöz hücrelerin (ASH) önemini ve ASH tanısı alan hastaların yüksek riskli HPV (hrHPV) durumunu belirlemektir.

Gereçler ve Yöntem: Şubat 2019 ve Aralık 2020 tarihleri arasında Patoloji Anabilim Dalı veri tabanı taranmış ve servikal PAP smear (CPS) incelemesinde 'önemi belirsiz ASH' (ASCUS) ve 'yüksek dereceli skuamöz intraepitelyal lezyonu dışlayamayan ASH' (ASC-H) tanısı olan 65 yaş üstü hastalar belirlenmiştir. hrHPV pozitif ve negatif hastalar da incelenmiştir.

Bulgular: 164 hasta (151 (%92,1) ASCUS ve 13 (%7,9) ASC-H çalışmaya dahil edilmiştir. Takip bilgileri olan ASH tanılı 95 olguda %16,8 düşük dereceli skuamöz intraepitelyal lezyon (LSIL), %5,3 yüksek dereceli skuamöz intraepitelyal lezyon (HSIL), %1,1 endoservikal adenokarsinom saptandı. Hastaların %19,6'sında hrHPV pozitifti. HrHPV pozitif hastaların takibinde %38,9 LSIL, %22,2 HSIL, %5,6 servikal adenokarsinom gelişti. İntraepitelyal lezyonlar (LSIL + HSIL) ve yüksek dereceli servikal lezyonlar (HSIL + invaziv servikal karsinom) hrHPV pozitif ASC-US olgularında, hrHPV negatif ASC-US olgularına kıyasla daha yaygındı. ASC-H hastalarında takip sırasında LSIL ve intraepitelyal lezyonların görülme olasılığı ASC-US hastalarına kıyasla daha yüksekti.

Sonuç: Yaşları 65 ve üzeri olan hrHPV pozitif ASH vakaları LSIL, HSIL ve yüksek dereceli servikal lezyonlar için yüksek risk taşımaktadır. Bu hastalarda hrHPV testi taramasına mutlak yönlendirmeye ilişkin daha fazla çalışma yapılması, bu hastaların yönetimine önemli katkı sağlayacaktır.

Anahtar Kelimeler: Atipik skuamöz hücre, serviks kanseri, PAP smear, HPV, 65 yaş üstü

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INTRODUCTION

Despite the invention of the cervical PAP smear (CPS) by George Papanicolaou in 1928, which resulted in a notable reduction in cervical intraepithelial neoplasms and malignancies, cervical cancer continues to pose a substantial health challenge today (1). The CPS is the most effective cancer screening test ever developed to identify cervical precancerous lesions, with a well-established reporting system called the Bethesda system (2).

In the Bethesda system, "Epithelial cell abnormality: Squamous" encompasses the squamous intraepithelial lesion (SIL) category, which includes a range of squamous cell lesions starting from the precancerous lesions of low-grade SIL (LSIL) to high-grade SIL (HSIL), and ultimately invasive squamous cell carcinoma (1).

Nonetheless, due to the qualitative and quantitative constraints of the specimen, certain ambiguous morphological characteristics indicative of squamous cell abnormalities may be classified as "Atypical Squamous Cells" (ASCs), which are further divided into two categories: "Atypical Squamous Cells of Undetermined Significance" (ASC-US) and "Atypical Squamous Cells, HSIL cannot be excluded"(ASC-H), based on the suspected underlying lesion of LSIL versus HSIL, respectively (2).

The United States Preventive Services Task Force (USPSTF) and the American Cancer Society (ASC) advise women over 65 who have not had a CIN2 or more advanced lesion within the previous 25 years and have been properly screened in the past to stop screening for cervical cancer (3,4). The ASC considers three consecutive negative cytologies during the last 10 years, with the last screening conducted within the last 5 years, or the presence of two negative cotests or primary HPV tests as sufficient screening criteria. However, in the United States, 20% of cervical cancer cases are discovered in people over 65 (5). In cancers diagnosed at an older age, the prognosis is worse and mortality rates increase (6). Despite this, since 2012, screening for cervical cancer in women 65 and older has been ceased (7).

Numerous studies have evaluated the role of CPS in recognizing cervical intraepithelial lesions in the young population (1). However, studies on the importance of CPS in patients over 65 years of age are limited due to the cessation of screening under appropriate conditions (5,6). Today, women are living longer, and patients 65 and older are expected to have a longer life. As it is well known, the mortality rate decreases when cervical cancer is detected early.

In this study, in order to determine the significance of ASCs in women 65 years of age and older, we aimed to investigate the clinical and histopathologic follow-up of patients diagnosed with ASCs in CPS. We also aimed to determine the high-risk HPV (hrHPV) status of patients diagnosed with ASCs.

MATERIALS AND METHODS

The study was approved by the Ethics Committee of Ankara Bilkent City Hospital on date 26.03.25 and TABED1-25-1190 numbered board. In this study, data base of the Department of Pathology of Ankara Bilkent City Hospital between February 2019 and December 2020 were screened and patients over the age of 65 who had CPS were identified. Among the CPS samples, patients diagnosed with ASC-US and ASC-H were identified and included in the study.

The presence of hrHPV examination was also investigated, and hrHPV positive and negative patients were identified in the study group. The follow-up information of the patients with biopsy and/or CPS within 3 years after the initial CPS was analyzed. In cases with follow-up information, the results were categorized as follows:

- LSIL
- HSIL
- high-grade cervical lesion (HSIL + invasive cervical carcinoma)
- invasive cervical carcinoma (squamous cell carcinoma and/or endocervical adenocarcinoma)
- invasive gynecologic malignancy (including cervical and/or endometrial and/or ovarian carcinomas)
- benign (cases with benign histopathologic diagnosis and/or CPS diagnosis of 'negative for malignancy and intraepithelial lesions' (NMIL) within 3 years)

Statistical Analysis

The SPSS 22.0 for Windows software (SPSS, Inc.; Chicago, IL. USA) was conducted to analyse the obtained data. The normal distribution of data was assessed using histogram, q-q plot, and Shapiro-Wilk's test. Descriptive statistics were reported as number (n), percentage (%), mean ± standard deviation, and median [min-max] values. The Fisher's exact test and Pearson chi-square were employed to evaluate the categorical variables. A value of $p<0.05$ was considered statistically significant.

RESULTS

A total of 7653 were examined in the study period and among these 164 (2.1%) cases with diagnosis of ASC-US and ASC-H were

included in the study. The mean age of the patients was 70.9 (65-94).

Of the 164 patients, 151 (92.1%) were diagnosed with ASCUS and 13 (7.9%) with ASC-H (Table 1). The distribution of these diagnoses in total CPS samples in patients aged 65 years and older was as follows: ASC-US 1.97% and ASC-H 0.17%.

Table 1. General characteristics of the patients

		n (%)
CPS diagnosis		
	ASC-US	151 (92.1)
	ASC-H	13 (7.9)
hrHPV*		
	Positive	21 (19.6)
	Negative	86 (80.4)
Follow-up		
	Present	95 (57.9)
	NA	69 (42.1)
Total		164 (100)

CPS: cervical PAP smear, ASC-US: Atypical Squamous Cells of Undetermined Significance, ASC-H: Atypical Squamous Cells - HSIL cannot be excluded, NA: not-available
*hrHPV was not available in 57 patients.

Histopathologic follow-up and hrHPV status of all CPSs diagnosed as atypical:

Follow-up information was available for 95 of 164 patients. 63 (66.3%) were benign, 16 (16.8%) LSIL, 5 (5.3%) HSIL, 1 (1.1%) endocervical adenocarcinoma, 8 (8.4%) endometrial adenocarcinoma, 2 (2.1%) ovarian serous carcinoma. Follow-up data for each diagnostic group and total patient population are detailed in Table 2.

In 107 patients, hrHPV was evaluated, 21 of them were found to be hrHPV positive (19.6%), while 86 were found to be hrHPV negative (80.4%) (Table 3).

Of the 21 hrHPV-positive patients, 18 had follow-up and diagnosed as benign in 6 (33.3%), LSIL in 7 (38.9%), HSIL in 4 (22.2%), and cervical adenocarcinoma in 1 (5.6%) (total 11 intraepithelial lesions, 5 high-grade cervical lesions, 1 invasive cervix) (Table 3).

Of the 86 hrHPV-negative patients, 49 had follow-up and 40 (81.6%) were benign, 4 (8.2%) LSIL, 1 (2%) HSIL, and 4 (8.2%) endometrial carcinoma (total 5 intraepithelial lesions, 1 high-grade cervical lesion, 0 invasive cervical carcinoma, and 4 invasive gynecologic carcinoma) (Table 3)

hrHPV positive patients had a higher rate of intraepithelial lesions and high-grade cervical lesions at follow-up compared to hrHPV negative patients ($p<0.001$) (Table 3).

Follow-up information and hrHPV status of ASC-US cases:

86 of 151 ASC-US cases had follow-up, of which 60 (69.8%) were benign, 12 (13.9%) LSIL, 4 (4.7%) HSIL, 8 (9.3%) endometrial adenocarcinoma, 2 (2. 3%) were diagnosed as ovarian serous carcinoma (total 16 intraepithelial lesions, 4 high-grade cervical lesions, 0 invasive cervical carcinoma and 10 invasive gynecologic carcinomas) (Table 2).

Table 2. Follow-up results for patients with ASC in each group and in total

FOLLOW-UP	ASC-US n (%)	ASC-H n (%)	TOTAL n (%)	p values
Benign	60 (69.8)	3 (33)	63 (66.3)	
LSIL	12 (13.9)	4 (44.5)	16 (16.8)	0.028*
HSIL	4 (4.7)	1 (11.1)	5 (5.3)	0.402**
İnvasive cervical carcinoma	-	1 (11.1)	1 (10.1)	
Intraepithelial lesion (LSIL +HSIL)	16 (18.6)	5 (55.5)	21 (22.1)	0.021***
High grade cervical lesion (HSIL + invasive cervical cancer)	4 (4.7)	2 (22.2)	6 (6.3)	0.057****
Invasive gynecologic cancer (invasive cervical and/or endometrial and/or ovarian cancer)	10 (11.6)	1 (11.1)	11 (11.6)	1.000*****
Total	86/151 (57)	9/13 (69.2)	95/164	

P values according to follow-ups between ASC-US and ASC-H: Follow-ups: *Benign and LSIL, **Benign+LSIL and HSIL, ***Benign and LSIL+HSIL, ****Benign+LSIL and HSIL+invasive cervical carcinoma *****Benign and invasive gynecologic
Abbreviations: LSIL: low-grade squamous intraepithelial lesion, HSIL: high-grade squamous intraepithelial lesion, ASC-US: Atypical Squamous Cells of Undetermined Significance, ASC-H: Atypical Squamous Cells - HSIL cannot be excluded

Table 3. Follow-up information for patients with ASC in each group and in total according to hrHPV status

	hrHPV	ASC-US n/total (%)	ASC-H n/total (%)	TOTAL n/total (%)
	hrHPV positive	17 *	4 **	21/107 (19.6)
1	Benign	5 (35.7)	1 (25)	6/18 (33.3)
2	Intraepithelial lesion (LSIL +HSIL)	9 (64.3)	2 (50)	11/18 (61.1)
3	High grade cervical lesion (HSIL + invasive cervical cancer)	3 (21.4)	2 (50)	5/18 (27.8)
	hrHPV negative	**84*** **	**2**** **	**86/107 (80.4)**
1	Benign	39 (81.3)	1 (100)	40/49 (81.6)
2	Intraepithelial lesion (LSIL +HSIL)	5 (10.4)	-	5/49 (10.2)
3	High grade cervical lesion (HSIL + invasive cervical cancer)	1 (2.1)	-	1/49 (2)
	p^1	0.001	1.000	<0.001
	p^2	0.033	1.000	<0.001

*14 of 17 patients, **all the patients, ***48 of 84 patients, ****1 of 2 patients have follow-ups
p^1:comparisons of follow-ups as benign or intraepithelial lesion between hrHPV positive and hrHPV negative cases
p^2: p value for comparing the benign+LSIL and high grade cervical lesion follow-usps between hrHPV positive and hrHPV negative cases
Abbreviations: LSIL: low-grade squamous intraepithelial lesion, HSIL: high-grade squamous intraepithelial lesion, ASC-US: Atypical Squamous Cells of Undetermined Significance, ASC-H: Atypical Squamous Cells-HSIL cannot be excluded

HPV was examined in 101 (66.9%) of 151 ASCUS patients and hrHPV was found to be positive in 17 (16.8%) of these patients. 14 of the 17 hrHPV positive cases had follow-up information, of which 5 (35.7%) were diagnosed as benign, 6 (42.9%) as LSIL and 3 (21.4%) as HSIL (9 intraepithelial lesions, 3 high-grade cervical lesions, 0 invasive cervical carcinoma and 0 invasive gynecologic carcinoma). 3 cases had no follow-up information (Table 3).

Of 151 patients with ASCUS, 84 (83.2%) were found to be hrHPV negative. Of these, 48 had follow-up information, of which 39 (81.3%) were diagnosed as benign, 4 (8.3%) as LSIL, 1 (2.1%) as HSIL, and 4 (8.3%) as endometrial adenocarcinoma. (5 intraepithelial lesions, 1 high-grade cervical lesion, 0 invasive cervical carcinoma and 4 invasive gynecologic carcinoma) (Table 3). 36 patients had no follow-up information

In cases with ASC-US diagnosis, intraepithelial lesions (LSIL + HSIL) and high-grade cervical lesions (HSIL + invasive cervical carcinoma) were more common in hrHPV positive patients compared to hrHPV negative patients (p=0.001 for intraepithelial lesions and p=0.033 for high-grade cervical lesions).

Follow-up information and hrHPV status of ASC-H patients:

9 of 13 ASC-H patients had follow-up information, of which 3 (33.3%) were diagnosed as benign, 4 (44.5%) as LSIL, 1 (11.1%) as HSIL, and 1 (11.1%) as endocervical adenocarcinoma (5 intraepithelial lesions, 2 high-grade cervical lesions, 1 invasive cervical carcinoma and 1 invasive gynecologic carcinoma) (Table 2).

Of the patients diagnosed with ASC-H, 4 were hrHPV positive and 2 were hrHPV negative. In 7 cases, hrHPV was not evaluated.

Of the 4 hrHPV positive cases, 1 (25%) was diagnosed as benign, 1 (25%) as LSIL, 1 (25%) as HSIL, 1 (25%) as endocervical adenocarcinoma (2 intraepithelial lesions, 2 high-grade cervical lesions, 1 invasive cervical carcinoma and 1 invasive gynecologic carcinoma) (Table 3).

One of the 2 hrHPV-negative cases (50%) was diagnosed as benign, while no follow-up was observed in 1 case.

There was no statistically significant difference between hrHPV positive and hrHPV negative patients with intraepithelial lesions (LSIL + HSIL), high-grade cervical lesions (HSIL + invasive cervical carcinoma) in cases diagnosed with ASC-H (p>0.05).

Comparison of follow-up data of patients with ASC-US and ASC-H:

Patients with ASC-H were more likely to have LSIL and intraepithelial lesions at follow-up compared to patients with ASC-US (p=0.028 for LSIL and p=0.021 for intraepithelial lesions). However, there

Table 4. Previous diagnosis, current diagnosis, follow-up information and hrHPV status in patients with an abnormal previous smear

Previous CPS diagnosis	Current CPS diagnosis	Follow-up	hrHPV	Total number of the cases
ASC-US	ASC-US	2 BENİGN 2 LSIL 2 HSIL 4 NA	3 Positive 6 Negative 1 NA	10
ASC-H	ASC-US	1 LSIL 1 NA	1 Positive 1 Negative	2
AGC	ASC-US	2 BENİGN	2 Negative	2
LSIL	ASC-US	NA	Negative	1
HPV 16 Positive	ASC-H	BENİGN	Negative	1
				16

CPS: cervical PAP smear, NA: not-available, hrHPV: high risk-Human Papilloma Virus
ASC-US: atypical squamous cells of undermined significance, ASC-H: atypical squamous cells-HSIL cannot be exluded, AGC: atypical glandular cells LSIL: low grade squamous intraepitehlial lesion, HSIL: high grade squamous intraepithelial lesion

was no statistically significant difference between patients with ASC-US and ASC-H in terms of the detection of HSIL, high-grade cervical lesion or invasive gynecologic cancer during follow-up (p>0.05). (Table 2)

Previous CPS screening:

16 (9.5%) of 169 patients had a previous abnormal CPS diagnosis, while 153 (90.5%) did not have sufficient follow-up and negative smear results to decide to discontinue screening. Table 4 shows the previous abnormal smear diagnosis, hrHPV status and follow-up information in these patients.

DISCUSSION

The present study examined the role of ASCs in CPS test among the patients over their 65 years of age. In cases with follow-up information, 16.8% LSIL, 5.3% HSIL, 1.1% endocervical adenocarcinoma were detected following ASC diagnosis. 19.6% of 107 patients were hrHPV positive. It was observed that 38.9% LSIL, 22.2% HSIL, 5.6% cervical adenocarcinoma developed in the follow-up of hrHPV positive patients. hrHPV positive patients had a higher rate of intraepithelial lesions and high-grade cervical lesions at follow-up compared to hrHPV negative patients.

Cervical PAP testing is an effective and organized population-based screening program that has been used for decades and has significantly reduced the risk of cervical cancer (8). In our country, cervical cancer is observed as 4.7/100,000 according to the 2020 Turkey Unified Database and ranks 8th in women's cancers in Turkey (9). In the world, it ranks 4th in women according to the 2022 GLOBAN database (10).

The American Society for Colposcopy and Cervical Pathology (ASCCP) and the USPSTF advise starting cervical cancer screening at age 25 and recommends stopping screening in women over 65 years of age (11,12). There are publications showing the benefits of continuing screening beyond age 65, for women who have not been adequately screened between the ages 50-64 years (13,14). Therefore, in patients with abnormal screening results, and in whom adequate screening results cannot be documented, screening should be continued until the necessary conditions for discontinuation of screening are obtained (12). There are also results suggesting that it may be inadvisable to discontinue cervical cancer screening at 65 years of age and older, even if there are sufficient negative results (15,16). According to the United Kingdom National Health Service (NHS) cervical cancer screening data, 40% of cervical cancer cases diagnosed at the age of 65 years and older are patients in whom screening was stopped at age 65 years with adequate normal cytology results (17).

According to another UK study, women who have not been screened since the age of 50 had nearly six times the risk of developing cervical cancer at age 65 and beyond compared to those who have been adequately screened (14). As life expectancy rises and hysterectomy rates decline [5,6], it is possible that the incidence of cervical cancer in women aged 65 and older might be expected to rise even more than already seen (5). In our study, 9.8% of the patients were continued screening due to abnormal CPS results and 90.2% were continued screening due to insufficient negative screening before. There were no patients who continued screening despite adequate negative results.

ASC is used to describe cytologic alterations that are suggestive of SIL but that are not sufficiently qualitative or quantitative to be definitively interpreted as such (1). The differential diagnosis is

complicated by the fact that many nonneoplastic conditions can cause cytologic changes that warrant an ASC designation, such as inflammation, reactive/reparative or degenerative changes, air-drying with artifactual enlargerment, atrophy patterns, hormonal effects, and other artifacts. Even after a diagnostic workup, the process that led to the ASC interpretation is frequently still unclear (1). In order to use CPS as an effective screening test in laboratories, it is recommended to keep ASC rates low in the Bethesda classification and not to use this intermediate diagnostic category as a wastebasket. In this context, the diagnosis of ASC-US in a cytopathology laboratory should not be more than 5% of all CPSs and this is an important criterion for the quality control of a laboratory (18).

In different studies, the ASC accounts for about 4% of CPSs (2). In studies conducted in different centers in our country, these ratios vary between 0.8% to 3% (19-22). In our study, the total ASC rate among all CPSs was 2.1% (ASC-US 1.97%, ASC-H 0.17%). This rate is similar to both international and national studies and are consistent with the recommendations of the Bethesda system.

The last ten years have seen a shift in cervical cancer preventive strategies from primary cytology testing to HPV analysis due to the discovery that HPV is a precondition for cervical cancer (23). According to screening programs that are representative of the US population, between 40-50% of women with ASC had high-risk/oncogenic HPV infections (1). In the current study, hrHPV positivity rate was 19.6% in patients diagnosed with ASC.

Changes that are suggestive of LSIL but not sufficient for a conclusive determination as such are referred to as ASC-US. About 90% of ASC interpretations in the majority of laboratories are anticipated to be ASC-US (1,19-22). Consistent with this result, ASC-US cases constituted 92.1% of all ASC cases in our study. The qualifier "undetermined significance" is favored since roughly 10–20% of women with ASC-US turn out to have an underlying HSIL (CIN 2 or CIN 3), even though the majority of ASC-US interpretations are suggestive of LSIL (1). In studies conducted in Turkey, it was reported that 11-23% of ASC-US cases developed HSIL during follow-up (21,22,24). In our study, HSIL was detected in 4.7% of ASC-US cases, which is lower than other studies. However, this rate increases in hrHPV positive ASC-US cases and the rate of high-grade cervical lesion was found to be 21.4% in this population. High grade cervical lesion rate decreases to 2.1% in hrHPV negative ASC-US cases. The difference between these two groups is statistically significant. This finding proves the association of hrHPV-positive ASC-US cases with high-grade cervical lesions and suggests that the follow-up and treatment of hrHPV-positive ASC-US cases should be more closely.

The ASC-H category is designed for situations where cytologic alterations are indicative of HSIL but not sufficient for a conclusive diagnosis. ASC-H have a higher positive predictive value for identifying an underlying HSIL (CIN 2 or CIN 3) than ASC-US (1). Studies from Turkey reported that 8-67% of ASC-H cases developed HSIL during follow-up (21,22,24). In the current study, the rate of HSIL was 11.1% in ASC-H patients. The rate of HSIL detection in ASC-H cases was higher than in ASC-US cases, but no statistically significant difference was observed. It was thought that the lack of statistically significant difference may be due to the significantly lower number of ASC-H cases. On the other hand, in all ASC cases evaluated for hrHPV (ASC-US+ASC-H), there was a significant difference in the detection of intraepithelial lesions and high-grade cervical lesions between hrHPV positive and negative patients, with a higher rate in hrHPV positive patients. Since mimetic lesions including changes caused by atrophy are frequently observed in patients aged 65 years and older, interobserver agreement in both intermediate diagnostic categories may be low. Therefore, hrHPV evaluation after ASC diagnosis in this age group may contribute more to the detection of high-grade lesions and patient management than ASC-US or ASC-H differentiation.

Studies in the literature have reported that high-grade cervical lesions are less common in postmenopausal patients compared to premenopausal patients (25). Since our study included only patients aged 65 years and older, this comparison could not be made. Izadimood et al. found significant anomalies in 74.2% of patients over 50 years of age with ASC, when they considered 'LSIL, HSIL, adenocarcinoma insitu, squamous cell carcinoma, adenocarcinoma, endometrial hyperplasia and endometrial adenocarcinoma' as significant anomalies (26). In the current study, the rate of high-grade cervical lesions was 6.3% and the rate of 'significant anomalies' was 33.7%.

Women over 60 years of age are more likely to have uterine and ovarian cancers (27). Although the PAP smear is a screening test developed for detection of intraepithelial lesions and the early detection of cervical cancer, it can occasionally contribute to the early detection of endometrial pathologies and rarely even ovarian cancers due to the collection of shed cells. In our study, the rate of invasive gynecologic cancers, most of which were endometrial cancers, was 11.6% in the follow-up of ASC patients. The rate of endometrial cancer was higher than cervical cancer. This is due to the fact that the study population consisted of elderly patients.

The current study is a single-center study evaluating the importance of ASC diagnosis and its association with hrHPV in patients aged 65 years and older. This is a single-center study and that patients under 65 years of age were not included. These were the limiting factors in our study.

The level of knowledge and awareness of the impact of hrHPV infection on cervical cancer and the importance of CPS in screening for cervical cancer and precursor lesions is generally lower in older patients compared to younger patients. This is an important reason why these patients are not adequately screened until the age of 65. Also discomfort and pain during gynecological examination in this age group should be other common barriers toward cervical cancer secreening (28). In our study, most of the patients did not have sufficient screening that could lead to a decision to terminate screening. This suggests that in order to terminate screening in patients aged 65 years and older, there is a need for national plans to increase the participation of these patients in screening in earlier years.

CONCLUSION

Considering the efficacy of hrHPV test screening, further studies on absolute referral to hrHPV test screening in patients aged 65 years and older, would significantly contribute to the management of these patients. The planning of multicenter national studies including larger case series will help us to answer more clearly the questions of how to intervene when ASC is diagnosed in this age group, and whether to terminate or continue screening when appropriate conditions are met.

Author Contributions

AAA, TDKÖ, ŞB: methodology, data collection, analysis, writing, editing, KK, DÖT, MNÇ, EŞ, MMK, ÖBA, ZRH, OA: technical assistance, data collection, analysis, NS,FE: methodology, design, correction

Conflict of Interest

No conflict of interest was declared by the authors.

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