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Anal cytology in women with cervical intraepithelial or invasive cancer: interobserver agreement

Citologia anal em mulheres com neoplasia intraepitelial ou invasiva cervical: concordância interobservadores

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ABSTRACT

Introduction: Incidence rates of anal cancer have been rising worldwide in the last 20 years. Due to embryological, histological and immunohistochemical similarities between the anal canal and the cervix, routine screening with anal cytology for precursor lesions in high-risk groups has been adopted. **Objective:** To determine interobserver agreement for the diagnosis of anal neoplasia by anal cytology. **Material and methods:** A cross-sectional observational study was conducted in 324 women with cervical intraepithelial or invasive cancers, for screening of anal cancer, from December 2008 to June 2009. Three hundred twenty-four cytological samples were analyzed by three cytopathologists. Cytological evaluation was based on the revised Bethesda terminology; samples were also classified into negative and positive for atypical cells. We calculated the kappa statistic with 95% confidence interval (95% CI) to assess agreement among the three cytopathologists. **Results:** Interobserver agreement in the five categories of the Bethesda terminology was moderate (kappa for multiple raters: 0.6). Agreement among cytopathologists 1, 2 and 3 with a consensus diagnosis was strong (kappa: 0.71, 0.85 and 0.82, respectively). **Conclusion:** Interobserver agreement in anal cytology was moderate to strong, indicating that cervical cytomorphological criteria are reproducible also in anal samples.

Key words: early diagnosis; anus neoplasms; uterine cervical neoplasms.

INTRODUCTION

Incidence rates of anal canal cancer have been increasing in the last 20 years worldwide. In the general population, they range from 0.7 to 2 per 100 thousand inhabitants. The incidence of this neoplasia in high-risk groups, namely human immunodeficiency virus (HIV)-positive individuals and homosexual men[(1)], is similar to that of cervical cancer before screening programs[(1)].

Women with history of genital neoplasia present 10.5-fold higher chance of developing anal cancer than those with no report of neoplasia[(2)]. Invasive anal cancer, similarly to what happens with invasive cervical carcinoma, is preceded by a long phase of pre-invasive or precursor disease, called anal intraepithelial lesion (AIL). Researchers demonstrated that high-grade AIL (HGAIL) may develop into invasive neoplasia over a five-year period in immunosuppressed individuals[(3)]. Thus, diagnosis and treatment of AIL could prevent the development of anal cancer.

Due to embryological, histological and immunohistochemical[(4)] similarities, the similar pathogenesis of anal cancer and cervical cancer, the classical triad for screening of precursor cervical lesions (cytology, colposcopy and biopsy) was adopted for the screening of AIL in risk groups[(5, 6)]. Likewise, the Bethesda Consensus (2001) terminology for reporting cervical cytological diagnoses was adapted and proposed for cytology of the anal canal.

Although cytomorphological criteria are well established for the diagnosis of cervical intraepithelial lesions, some authors have suggested that peculiarities of the anal canal, collection technique and experience of professionals may determine high rates of false negatives and slight agreement between cytology and histopathology, although this is controversial in the literature[(7-9)].

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Our study aimed at measuring the degree of identification of cytomorphological criteria for the diagnosis of AIL by means of interobserver agreement and agreement between cytological and histopathological diagnoses.

MATERIAL AND METHODS

An observational cross-sectional study was carried out for screening of anal cancer precursor lesions in women with intraepithelial or invasive cervical neoplasia, at the outpatient department of lower genital tract pathology of Instituto de Medicina Integral Prof. Fernando Figueira (Imip), from December 2008 to December 2009. The sample size was calculated using the function StatCalc of Epi Info 7 software (Centers for Disease Control and Prevention [CDC]), based on a 13% frequency of AIL in women with cervical neoplasia[10]. With a 95% confidence level and a 30% relative precision, 286 women were necessary, number that was increased to 324, foreseeing eventual losses.

Women with histopathological diagnosis of cervical intraepithelial neoplasia or cancer treated at the outpatient department of lower genital tract pathology of Imip were included. Exclusion criteria were: being mentally ill, imprisoned, pregnant, HIV-positive and undergoing radiotherapy or chemotherapy for treatment of genital cancer.

The research was approved by the research ethics committee of Imip, under number 1324. All patients voluntarily agreed to participate, signing the informed consent and filling a standard form.

Anal cytology specimens were collected by the main researcher, from all women, by inserting an endocervical brush with silicone ball at end, humidified with saline, 4 cm into the anal canal (blind collection), rotating it 360º while softly pressing the anus walls. The collected material was arranged longitudinally on the slide, immediately fixed in 96% ethanol and sent to the pathology laboratory, where it was stained by Papanicolaou technique. Results were characterized by the cytomorphological criteria adopted by the Bethesda System (TBS); those classified as unsatisfactory by air-drying artifact or scant cellularity were excluded at the moment of data analysis.

High-resolution anoscopy (HRA) was performed in all women, after specimen collection for anal cytology. A disposable non-slotted anoscope was used, which was inserted in the anal canal after topical application of 2% lidocaine. The mucosa was examined using a colposcope DF Vasconcelos, with objective lens of 25× magnification. Colposcopic images were analyzed after application of 5% acetic acid and 2% lugol's solution. In the presence of abnormal areas suggestive of anal intraepithelial neoplasia (AIN), biopsy was carried out, even without the result of the cytopathological examination. The women who presented HRA suggestive of metaplasia or viral infection were biopsied when anal cytology indicated atypia[11].

Material collection for the deoxyribonucleic acid (DNA) study of human papilloma virus (HPV) was conducted with an endocervical brush humidified with saline. DNA was extracted from 500 µl of vaginal secretion, using Wizard Genomic DNA Purification kit (Promega®). Samples were treated with ribonuclease (RNase), taken to a water bath at 50ºC for denaturation of this protein, and kept at a temperature of -20ºC. The presence of HPV was diagnosed by two sets of consensus primers. For each patient, two reactions were performed, one using primers MY09 and MY11; the other, GP05+ and GP06+. Quality of the extracted DNA was confirmed by the globin primer pair[12].

The slides collected from the 324 women were analyzed by three cytopathology specialists experienced in gynecologic cytology, in a masked fashion, that is, they did not know the clinical data, HRA report of the patient and cytological diagnosis of the other observers. Each cytopathologist received the slide for analysis together with the cytomorphological criteria for lesion classification according to the 2001 Bethesda Consensus[13].

The cytological criteria for alterations of atypical squamous cells of undetermined significance (ASC-US) were the following: nuclear enlargement from 2.5- to 3-fold over the size of a normal intermediate cell nucleus, or nuclear enlargement from 1.5- to 2-fold over the size of a normal metaplastic cell nucleus; finely granular nuclear membrane distributed in a homogeneous manner; finely granular chromatin distributed in a homogeneous manner; absent to mild nuclear hyperchromasia and imperceptible or absent nucleoli; HPV cytopathic effect and/or binucleation; HPV alterations that still do not fit into low-grade AIL (LGAIL).

For the diagnosis of squamous cell alterations, not being possible to exclude high-grade lesion (ASC-H), the following cytological criteria were related: immature cells, generally isolated or in small clusters of fewer than 10 cells; nuclear enlargement from 0.5- to 2.5-fold over the size of a normal nucleus; increased nucleus/cytoplasm (N/C) ratio, with nuclear abnormalities; hyperchromasia, nuclear membrane and chromatin irregularities.

The cytological criteria for LGAIL were the following: cells with distinct cytoplasmic limits, indicating mature epithelium (superficial and intermediate cells), predominantly isolated, or in loose clusters; nucleus enlargement 3- to 4-fold over the size of a normal intermediate cell nucleus; nucleus varying significantly in form and size, with nuclear membrane smooth to irregular, binucleation or multinucleation; chromatin slightly more coarse, but evenly distributed, or degenerated; variable hyperchromasia and well-defined cytoplasmic cavitations – koilocytes (**Figures 1**, **2** and **3**).

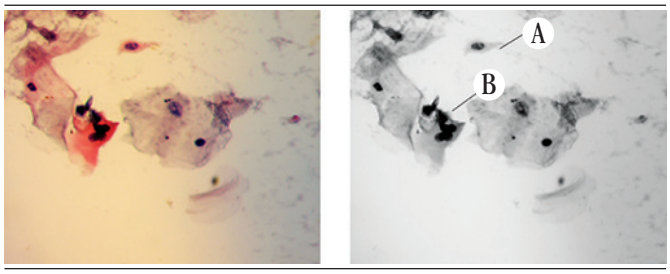

FIGURE 1 – *Low-grade anal lesion (Papanicolaou stain, 40×), granular background*

A) parakeratotic cell with enlarged nucleus, beginning karyolysis; B) cluster of atypical cells with dense orangeophilic cytoplasm; visible cell borders; enlarged nuclei irregular in shape, hyperchromatic and binucleated.

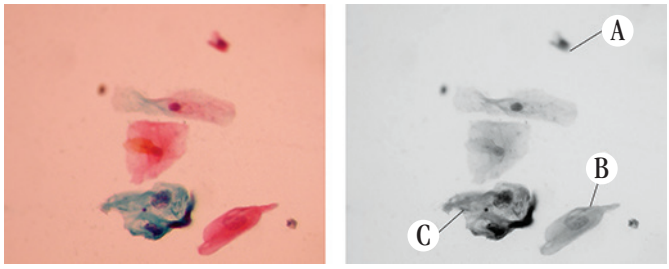

FIGURE 2 – *Low-grade anal lesion (Papanicolaou stain, 40×), clear background*

A) parakeratotic cell with pyknotic nucleus; B) polygonal cell with dense orangeophilic cytoplasm and nucleus beginning karyolysis; C) two polygonal cells, cyanophilic cytoplasm with clear perinuclear halos with thickened cytoplasmic borders; enlarged hyperchromatic nuclei and regular finely granular chromatin.

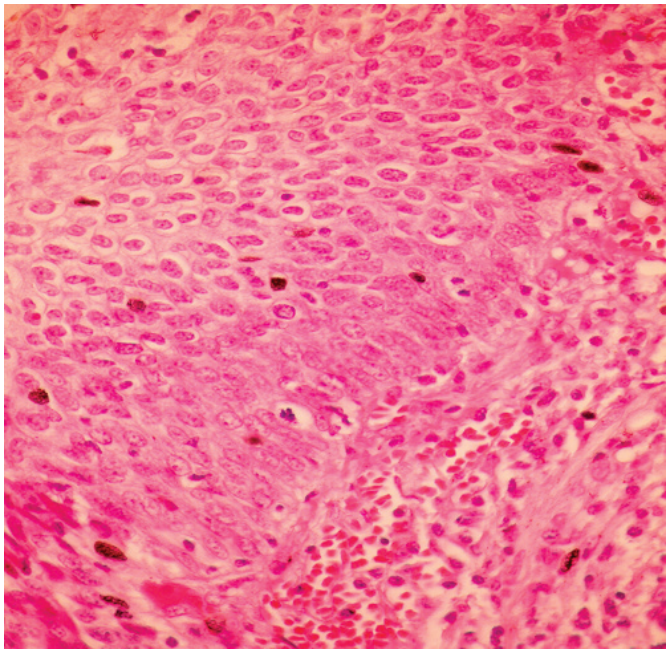

FIGURE 3 – *Low-grade anal lesion (HE stain, 40×)*

Histological section of anal canal with immature cells occupying the lower third of the epithelium, with atypical maturating cells, and koilocytosis in the upper two-thirds.

HE: hematoxylin and eosin.

The cytological criteria for HGAIL were: cytological alterations that affect immature cells with marked increase in N/C ratio; single cells, in sheets, or in syncytial clusters; nuclear hyperchromasia, accompanied by variations in nuclear size and shape; fine to coarsely granular and evenly distributed chromatin; irregular borders of the nuclear membrane, frequently with prominent indentations; generally absent nucleoli, which may be observed occasionally; cytoplasm with immature aspect, lacy and delicate, or densely metaplastic; occasionally mature and densely keratinized cytoplasm (**Figures 4** and **5**).

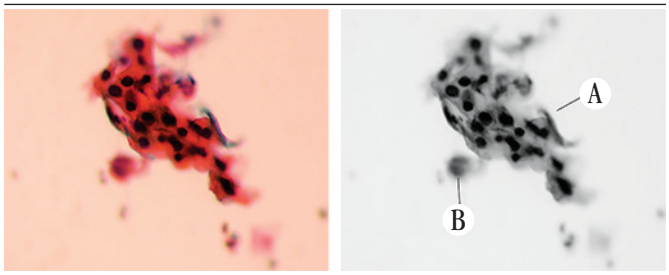

FIGURE 4 – *High-grade anal lesion (Papanicolaou stain, 40×), clear background*

A) cluster of atypical parakeratotic cells; binucleated cell with dense eosinophilic cytoplasm, elongated in shape; B) altered nucleus/cytoplasm ratio, hyperchromatic nuclei with irregular borders, granular chromatin.

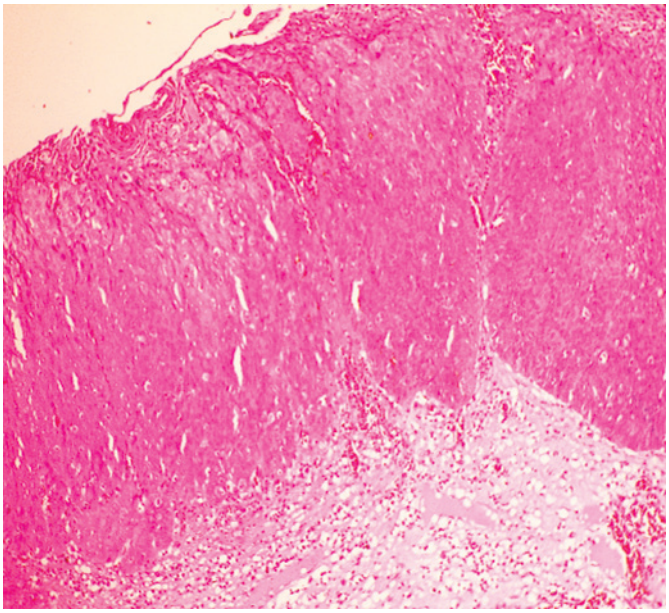

FIGURE 5 – *High-grade anal lesion (HE stain, 40×)*

Histological section of anal canal with immature cells occupying more than the lower two-thirds of the epithelium with a thin layer of atypical maturating cells on the surface.

HE: hematoxylin and eosin.

Smears were considered satisfactory for cellularity when the average number of nucleated squamous cells in the 40× objective lens, in 10 observed fields, was six or more cells per field[14]. Smears that presented cellularity of fewer than six cells per field, or more than 75% obscured by air-drying artifact, or contaminants, were considered unsatisfactory for analysis, and the reason was specified. However, any sample with cell alterations was considered satisfactory for evaluation, regardless of the number of squamous cells. Before report delivery, discordant cases were discussed in group, and a consensus diagnosis was reached.

Data analysis was performed using Stata 12.1 SE (StataCorp 4905 Lakeway Drive College Station, Texas 77845 USA). Initially, frequency distribution tables were created for categorical variables. For quantitative variables, measures of central tendency were calculated, as well as measures of dispersion. In order to assess interobserver agreement, kappa coefficient for multiple raters was quantified; to calculate agreement between cytological and histological diagnoses, the simple kappa coefficient was used, as well as its 95% confidence interval (CI). Values were interpreted as: poor (0), slight (0.01-0.2), fair (0.21-0.4), moderate (0.41-0.6), substantial (0.61-0.8), and almost perfect (0.81-1)[15].

RESULTS

In the current study of 342 women, 8% (n = 26) presented invasive cervical neoplasia; 62% (n = 201), cervical intraepithelial neoplasia grade 2/3; and 29% (n = 97), cervical intraepithelial neoplasia grade 1. Regarding the sample profile, the mean age was 33.6 (standard deviation [SD]: 10.5) years; in 67% (n = 217), the onset of sexual activity was before age 17 years; 55.2% (n = 179) referred anal sex, and 40.4% (n = 131) were smokers. Among the 324 conducted HRA, just 37% (n = 120) were normal.

Among the 324 obtained smears, the consensus diagnosis evidenced that 6.2% (n = 20) were unsatisfactory for the analysis, and 93.8% (n = 304) were satisfactory, out of wich 63% (n = 204) were within normal limits and 30.9% (n = 100) presented squamous cells with some degree of atypia. Among the 104 performed biopsies, 32.7% (n = 34) were positive; 11.5% (n = 12) had findings compatible with HPV infection. There were eight cases (7.7%) of AIN grade 1 (AIN 1); 11 (10.6%) of AIN grade 2 (AIN 2), and three (2.9%) of AIN grade 3 (AIN 3) (**Table 1**).

In order to calculate the kappa index for multiple raters among the three observers, in the five categories, the cytologies with results given by each of the three examiners were considered, that is, 48 cytologies that presented at least one absent diagnosis were excluded. Therefore, in the calculation, 276 subjects with kappa index for multiple raters = 0.6 were involved (**Table 2**).

In the following step, cytopathological diagnoses were classified into two groups: 1) negative for neoplastic cells, which included the diagnoses within the normal limits and reactive/reparative alterations; 2) positive for neoplastic cells with the diagnoses of atypical squamous cells, LGAIL and HGAIL. Diagnostic agreement of each cytopathologist with the consensus diagnosis was evaluated. Cytopathologist 2 had the highest concordance rate on the consensus diagnosis with kappa index = 0.85 (95% CI: 0.73-0.96), $p < 0.0001$ (**Table 3**).

Agreement among the three pathologists was calculated, and the histopathological results were classified into two groups: 1) negative for AIN; and 2) positive for AIN. The three pathologists presented slight agreement with the consensus diagnosis (**Table 4**).

Samples for HPV DNA test were collected from the 324 women. In 6.5% (n = 21) DNA extraction was unsatisfactory, with 303 women remaining for analysis. Among these, 84.2% (n = 255) tested positive for HPV DNA. When we analyzed the frequency of HPV DNA in atypical cytologies, we found 94.9% of HPV DNA-positive samples. All HGAIL tested positive for HPV DNA (**Table 5**).

TABLE 1 – Cytopathological consensus diagnoses and anal histopathological anal diagnoses in women with cervical neoplasia

Cytopathological diagnosis	*n*	%
Squamous cell atypias	30	9.3
HGAIL	9	2.8
LGIEL	61	18.8
Within normal limits	204	63
Unsatisfactory	20	6.2
Total	324	100
Histopathological diagnoses		
HPV	12	11.5
Anal intraepithelial lesion grade 1	8	7.7
Anal intraepithelial lesion grade 2	11	10.6
Anal intraepithelial lesion grade 3	3	2.9
Normal	24	23.1
SHME	24	23.1
SHME with vacuolization	10	9.6
Inflammatory	12	11.5
Total	104	100

HGAIL: high-grade anal intraepithelial lesion; LGAIL: low-grade anal intraepithelial lesion; HPV: human papillomavirus; SHME: simple hyperplasia of the Malpighian epithelium.

TABLE 2 – Absolute agreement among the three cytopathologists' diagnoses and on the consensus diagnosis in anal cytologies of women with cervical neoplasia

	Consensus					
	ASC	WNL	UNS	HGAIL	LGAIL	Total
Cytopathology 1						
ASC	23	19	2	0	15	59
%	39	32.2	3.4	0	25.4	100
WNL	2	166	6	0	7	181
%	1.1	91.7	3.3	0	3.9	100
UNS	1	8	12	0	0	21
%	4.8	38.1	57.1	0	0	100
HGAIL	1	2	0	8	2	13
%	7.7	15.4	0	61.5	15.4	100
LGAIL	3	9	0	1	37	50
%	6	18	0	2	74	100
Cytopathology 2						
ASC	12	2	0	0	4	18
%	66.7	11.1	0	0	22.2	100
WNL	6	189	2	0	7	204
%	2.9	92.6	1	0	3.4	100
UNS	0	9	18	0	1	28
%	0	32.1	64.3	0	3.6	100
HGAIL	2	0	0	6	4	12
%	16.7	0	0	50	33.3	100
LGAIL	10	4	0	3	45	62
%	16.1	6.5	0	4.8	72.6	100
Cytopathology 3						
ASC	15	0	0	1	6	22
%	68.2	0	0	4.5	27.3	100
Carcinoma	1	0	0	0	0	1
%	100	0	0	0	0	100
WNL	9	194	0	1	10	214
%	4.2	90.7	0	0.5	4.7	100
Inflammatory	0	2	0	0	0	2
%	0	100	0	0	0	100
UNS	1	6	20	0	1	28
%	3.6	21.4	71.4	0	3.6	100
HGAIL	2	1	0	7	0	10
%	20	10	0	70	0	100
LGAIL	2	1	0	0	44	47
%	4.3	2.1	0	0	93.6	100
Multi-rater kappa						0.6

ASC: atypical squamous cells of undetermined significance (ASC-US or ASC-H); WNL: within normal limits; UNS: unsatisfactory; HGAIL: high-grade anal intraepithelial lesion; LGAIL: low-grade anal intraepithelial lesion; ASC-US: atypical squamous cells of undetermined significance; ASC-H: high-grade lesion. The underlined values represent the overall agreement.

TABLE 3 – Agreement on positive and negative diagnoses among the three cytopathologists, and on consensus of anal cytologies in women with cervical neoplasia

	Consensus diagnosis						
	Positive		Negative		*Kappa*	95% CI	*p*
	n	%	*n*	%			
Cytopathologist 1							
Positive	90	75	30	25	0.71	0.6-0.83	< 0.0001*
Negative	9	5.1	166	94.9			
Cytopathologist 2							
Positive	86	93.5	6	6.5	0.85	0.73-0.96	< 0.0001*
Negative	13	6.4	189	93.6			
Cytopathologist 3							
Positive	78	97.5	2	2.5	0.82	0.71-0.93	< 0.0001**
Negative	20	9.3	196	90.7			

*CI: confidence interval: *Chi-squared test; **Fisher's exact test.*

TABLE 4 – Agreement on positive and negative diagnoses among the three cytopathologists, and histopathology in women with cervical neoplasia

	Histopathological diagnosis						
	Positive		Negative		*Kappa*	95% CI	*p*
	n	%	*n*	%			
Cytopathologist 1							
Positive	25	37.3	42	62.7	0.17	0.01-0.33	0.14*
Negative	8	22.9	27	77.1			
Cytopathologist 2							
Positive	26	40.6	38	59.4	0.16	0-0.32	0.03*
Negative	7	19.4	29	80.6			
Cytopathologist 3							
Positive	21	38.2	34	61.8	0.14	-0.03-0.31	0.11*
Negative	11	23.4	36	76.6			
Consensus							
Positive	28	38.9	44	61.1	0.16	0.02-0.31	0.02**
Negative	5	16.1	26	83.9			

*CI: confidence interval: *Chi-squared test; **Fisher's exact test.*

TABLE 5 – Result of the cytopathological diagnosis and PCR for anal HPV DNA in women with cervical neoplasia

Cytopathologic diagnosis	Positive PCR		Negative PCR	
	n	%	*n*	%
Atypias of undetermined significance	25	86.2	4	13.8
Low-grade anal intraepithelial lesion	60	98.4	1	1.6
High-grade anal intraepithelial lesion	9	100	0	0

PCR: polymerase chain reaction; DNA: deoxyribonucleic acid; HPV: human papillomavirus.

DISCUSSION

Our study reached substantial interobserver agreement among cytological diagnoses and poor agreement between cytopathologic and histopathologic diagnoses of anal lesions. In the literature, there are few studies involving interobserver agreement on the interpretation of cytological and histological AIN smears.

One of the first studies about interobserver agreement in anal cytology diagnosis was published in 1998[5]. Six cytopathologists with experience in interpreting anal smears received 30 slides with material collected from women with multifocal genital neoplasia, and guidelines for cytological diagnosis, in a masked fashion. Diagnostic concordance was evaluated between two categories: high-grade intraepithelial neoplasia and other cytological conditions. There was concordance among observers in more than 95% of the cases, with kappa ranging from 0.66 to 1. The authors concluded that the existence of previous guidelines for interpretation of anal cytological smears may result in high interobserver agreement on the diagnosis of anal conditions.

Another work analyzed diagnostic agreement among four pathologists experienced in the interpretation of cytopathology and histopathology cervical and anal specimens[8]. The pathologists evaluated 120 anal cytological smears collected from HIV-positive patients. There was substantial agreement in classifying smears as negative (kappa = 0.84), moderate agreement in classifying them as LGAIL or HGAIL (kappa = 0.52 and 0.45, respectively), and just slight agreement in classifying them as ASC-US (kappa = 0.12). The authors concluded that even among experienced pathologists, interobserver agreement was moderate. Moreover, a new gold standard would be desirable for the diagnosis of anal cancer, as well as an investigation into its precursor lesions.

A more recent study, analyzing diagnostic concordance between two cytopathologists on anal cytologies of HIV-positive homosexual men, found overall concordance of 66% (95% CI: 61-71) and kappa = 0.54. Between both cytopathologists there was moderate concordance on cytology interpretation[16].

Our study observed higher overall concordance between the initial diagnosis of each cytopathologist and the consensus diagnosis to define absence of atypias (90.7%-92.6%), and LGAIL or HGAIL (72.6%-93% and 61.5%-70%, respectively). Atypias in ASC-US presented higher degree of difficulty for characterization among participants (39%-68.2%), what was already expected considering the weak reproducibility and the high degree of subjectivity of cytomorphological criteria[17]. When we analyzed interobserver concordance in the five categories, the multi-rater kappa revealed moderate concordance.

When establishing negative and positive (≥ ASC-US) smears as cut-off point, concordance among cytologists was substantial (kappa = 0.71-0.85). When comparing our findings with those of the literature[8, 9], our study verified better concordance to identify negative and positive smears (≥ ASC-US), but lower concordance on the identification of HGAIL[5]. We believe that the good performance of cytopathologists was due to the fact that there was a previous cytomorphological panel, what made observers more attentive to the criteria agreed upon. However, the small number of HGAIL in the study did not allow a better performance when we evaluated diagnosis among observers in this category.

Although the morphological criteria for diagnosis among cytopathologists were well standardized, we came across a slight (kappa = 0.16) concordance between the cytopathological consensus diagnosis and the histopathological results. Up to the moment, the gold standard diagnosis of anal cancer and its precursor lesions is the histopathological study, similarly to what happens to cervical cancer. For the latter, interobserver variability among experienced pathologists ranges from moderate to almost perfect[18, 19]. For anal cancer, on the other hand, there are several studies in the literature showing diagnostic imperfections in histopathological analysis of specimens, even among experienced pathologists[8, 20]. We believe that factors such as the small size of the samples, tangential sections of the lesion, coexistence of reactive and inflammatory processes, and thermal artifacts of processing may have also contributed to this slight concordance[21].

Another aspect that we need to consider is that although there are embryological, histological and immunohistochemical similarities between the cervix and the anal canal, some peculiarities (deeper crypts and greater predisposition of the epithelium towards hyperkeratosis and atypical parakeratosis, for instance) may contribute to increase disagreement among methods[22, 23]. Differently from what happens with the cervix, for which there is a procedure that allows a more accurate analysis between cytological diagnosis and final histopathological diagnosis (the classical conization or excision of the transformation zone by high-frequency surgery), there is no such a kind of procedure for the study of the anal canal.

Mathew *et al.*[24], when estimating the accuracy of anal cytology in the presence of an imperfect reference standard, reached the conclusion that we must consider: a) the commonly available reference test (HRA-guided anal biopsy) is also subject to sampling and measuring errors; b) in recommendations for anal cancer screening in high-risk populations, anal cytology, HRA and biopsy provide valuable but fallible information about the true category of anal neoplasia. In light of the possibility of error in classification of anal neoplasia, recent studies have suggested additional tools for the detection of anal neoplasia, aimed at improving AIN diagnosis. Among these, HPV DNA tests, E6/E7 oncogene ribonucleic acid messenger (RNAm) testing[25], and markers for protein Ki67, protein p16 or the minichromosome maintenance proteins 3, 4, 6, and 7[26]. HPV DNA positive results in the presence of positive anal cytology and negative anal biopsy suggest that cytology is more sensitive to diagnose HPV-induced lesions, due to the factors mentioned in previous paragraphs.

CONCLUSION

Cytomorphological criteria for the classification of cervical cytology according to the Bethesda system are reproducible in anal cytology interpretation, although with slight agreement with histopathological examination. This suggests the necessity of associating other diagnostic techniques to improve sensitivity and specificity of AIN screening.

RESUMO

Introdução: *O número de casos de câncer de canal anal vem aumentando nos últimos 20 anos no mundo. Devido às similaridades embriológicas, histológicas e imuno-histoquímicas do canal anal com o colo uterino, adotou-se a citologia anal para rastreamento das lesões precursoras desse tipo de câncer em grupos de risco.* ***Objetivo:*** *Determinar a concordância interobservadores na citologia anal e a concordância entre os diagnósticos citológico e histopatológico no rastreamento das neoplasias anais.* ***Material e métodos:*** *Foi realizado um estudo observacional do tipo corte transversal para rastreamento de câncer anal em 324 mulheres com neoplasias intraepiteliais ou invasivas cervicais, no período de dezembro de 2008 a junho de 2009. Foram colhidas amostras citológicas anais, as quais foram analisadas por três citopatologistas; a seguir, elas foram classificadas de acordo com o consenso Bethesda 2001, sendo agrupadas em negativas e positivas para células atípicas. Biópsias e reação em cadeia de polimerase (PCR) para papilomavírus humano (HPV) foram realizadas para verificar a concordância interobservadores. Foi aplicado o coeficiente* kappa *múltiplo e simples, bem como o seu intervalo de confiança de 95%.* ***Resultados:*** *A concordância interobservadores, incluindo todas as categorias diagnósticas, foi moderada (coeficiente* kappa *múltiplo: 0,6). A concordância para identificar citologias anormais entre os citopatologistas 1, 2 e 3 com o diagnóstico de consenso foi forte (coeficiente de* kappa *simples: 0,71; 0,85 e 0,82; respectivamente).* ***Conclusão:*** *A concordância interobservadores na citologia anal foi de moderada a forte, indicando que os critérios citomorfológicos são reprodutíveis na interpretação de material anal.*

Unitermos: *detecção precoce de câncer; neoplasias do ânus; neoplasias do colo do útero.*

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