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Concordance of glandular extension between cytology and histopathology in the analysis of high-grade lesions of the uterine cervix

Concordância da extensão glandular entre citologia e histopatologia na análise das lesões de alto grau da cérvice uterina

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ABSTRACT

Introduction: High-grade cervical lesions with glandular extension pose diagnostic challenges that affect clinical management. Glandular occupancy can mimic other lesions, impacting therapeutic decisions. In this context, analyzing the concordance between cytology and histopathology is crucial to optimize diagnostic protocols and individualized treatment.

Objective: To evaluate the efficacy of cytology (cervicovaginal examination) in detecting high-grade intraepithelial lesions with glandular occupancy, comparing its results with histopathology of samples obtained by conization (LEEP) to determine diagnostic accuracy.

Method: This is a cross-sectional, retrospective study based on the analysis of medical records of patients with high-grade lesions of the cervix. Data were collected from cytological and histopathological reports, including information on the presence of glandular occupancy.

Result: Of the 266 patients with these lesions who underwent LEEP, 42 were included due to follow-up. Ages ranged from 20 to 68 years (mean, 40). Glandular occupation was observed in 15 (35%). Cytological criteria for glandular occupation were met in 3, with histological confirmation in only 1. The agreement between cytological and histopathological findings revealed a sensitivity of 33.3%, a specificity of 80%, a positive predictive value of 33.3%, a negative predictive value of 80%, and an efficacy of 69.3%. Post-LEEP recurrence occurred in 30.9% of cases with histological glandular occupation.

Conclusion: The efficacy of cytology in detecting glandular occupation was less than 70%, suggesting the need for additional diagnostic methods, such as colposcopy or imaging, to ensure a more accurate diagnosis and improve prognosis.

KEYWORDS: Cytology. Glandular occupation. High-grade lesion. Gynecology. HSIL. Uterine cervix.

RESUMO

Introdução: Lesões cervicais de alto grau com extensão glandular representam desafios diagnósticos que afetam o manejo clínico. A ocupação glandular pode mimetizar outras lesões, impactando as decisões terapêuticas. Nesse contexto, a análise da concordância entre citologia e histopatologia é crucial para otimizar protocolos diagnósticos e o tratamento individualizado.

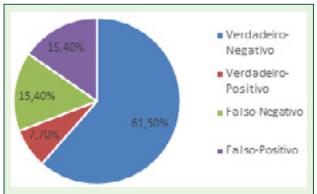
Objetivo: Avaliar a eficácia da citologia (exame cérvico-vaginal) na detecção de lesões intraepiteliais de alto grau com ocupação glandular, comparando seus resultados com a histopatologia de amostras obtidas por conização (CAF), a fim de identificar a precisão diagnóstica.

Método: Trata-se de estudo transversal e retrospectivo, realizado a partir da análise de prontuários de pacientes com lesões de alto grau da cérvix uterina. Foram coletados dados de laudos citológicos e histopatológicos, incluindo informações sobre a presença de ocupação glandular.

Resultado: Das 266 pacientes com essas lesões submetidas à CAF, 42 foram incluídas devido ao seguimento. A idade variou de 20 a 68 anos (média de 40). Ocupação glandular foi observada em 15 (35%). Critérios citológicos para ocupação glandular foram encontrados em 3, com confirmação histológica em 1 apenas. A concordância entre os achados citológicos e histopatológicos revelou sensibilidade de 33,3%, especificidade de 80%, valor preditivo positivo de 33,3%, valor preditivo negativo de 80% e eficácia de 69,3%. Recidiva pós-CAF ocorreu em 30,9% com ocupação glandular histológica.

Conclusão: A eficácia da citologia na detecção de ocupação glandular foi inferior a 70%, sugerindo a necessidade de métodos diagnósticos adicionais, como colposcopia ou exames de imagem, para garantir diagnóstico mais preciso e melhorar o prognóstico.

PALAVRAS-CHAVE: Citologia. Ocupação glandular. Lesão de alto grau. Ginecologia. HSIL. Cérvice uterino.



Confirmed cytological diagnoses of glandular occupation by histopathology (n = 42)

Central Message

The evaluation of the agreement between cytology and histopathology in the detection of glandular extension in high-grade lesions of the uterine cervix is crucial since glandular occupation can impact clinical management and increase the risk of recurrence. Accurate identification of these lesions is essential to optimize therapeutic decisions and improve patients' prognosis.

Perspective

The limited efficacy of cytology in detecting glandular occupancy in high-grade lesions suggests the need for complementary diagnostic methods, such as colposcopy and imaging, to refine diagnostic accuracy. Incorporating new approaches can lead to more individualized treatment and reduction in recurrence rates, thereby improving clinical outcomes for patients with high-grade cervical injuries.

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INTRODUCTION

Squamous cell carcinoma of the uterine cervix, in addition to being the third most prevalent neoplasm in the female population in Brazil, is also the fourth leading cause of deaths of women from cancer in the country and in the world.[1,2] In most cases, the disease is caused by persistent infection by oncogenic strains of the Human Papilloma Virus (HPV), evolving slowly and gradually.[3]

Precursor lesions can be cytologically classified as low-grade intraepithelial lesions (LSIL), corresponding to cervical intraepithelial neoplasia (CIN) grade I, or high-grade intraepithelial lesions (HSIL), corresponding to CIN grades II and III.[3]

Cervical cancer screening can be done quickly and inexpensively by Pap smear testing and, once diagnosed, these precursor lesions are curable in almost all cases.[4] In the planning of treatment for those diagnosed with HSIL, it is essential to consider the presence of glandular occupation because it is associated with a higher rate of postoperative recurrence, often requiring deeper resections.[5]

There are cytological criteria that can be used to detect glandular occupation; however, there are not many studies that evaluate its sensitivity and specificity.[5] The objective of this study is to evaluate the efficacy of the criteria listed for the detection of glandular occupation in cytology by means of the Pap smear, relating it to the histopathological results of the follow-up of patients undergoing treatment by high-frequency surgery (LEEP).

METHOD

This research is in compliance with ethical aspects and was approved by the Institutional Ethics Committee, with the Certificate of Presentation of Ethical Appreciation (CAAE) 99859718.9.0000.0103 and the approval opinion number 2.952.834. This is a retrospective observational study between January 2014 and December 2018, involving patients who underwent high-frequency surgery (LEEP) with a diagnosis of HSIL at the Mackenzie Evangelical University Hospital, Curitiba, PR, Brazil.

Data were obtained from the electronic medical records, and the age of the leveraged patients, the cytological diagnosis (Pap smear) and the anatomopathological reports related to LEEP were analyzed. The cytological slides were reviewed to identify glandular occupation criteria defined by the literature, such as atypical epithelial cells with HSIL characteristics, three-dimensional clusters of atypical squamous epithelial cells with adhered benign endocervical epithelium, digitiform three-dimensional clusters of atypical squamous epithelial cells from borders covered by intact epithelium, and absence of cytological findings of adenocarcinoma in situ of the uterine endocervix. Subsequently, follow-up cytology was also reviewed to determine, whether or not, the lesions regressed.

In the histopathological reports, the presence or absence of glandular occupation was verified. Patients whose CAFs were negative for HSIL and patients who did not have previous cytology at the service were excluded from the study.

After reviewing the slides, the cytology results were compared to the histopathological results to determine epidemiological indices such as efficacy, positive predictive value, negative predictive value, sensitivity, and specificity. The following were considered: 1) true positives (PV), when they had glandular occupation both in cytology and anatomopathology; 2) true negative (VN) regarding glandular occupation in cytology and also in anatomopathological analysis; 3) false positives (PF) when there was glandular occupation in the cytology and negative in the anatomopathological examination; 4) false negatives (FN) when negative for glandular occupation in cytology and positive in anatomopathological analysis.

Sensitivity was defined as PV/VP + FN; specificity by VN/VN + FP; and diagnostic accuracy by PV+VN/(PV +FP + VN +FN).

RESULT

Initially, 266 patients who underwent conization using the LEEP technique were analyzed, but only 42 were included in the sample, as they had follow-up cytology. In this group, the women's ages ranged from 20 to 68 with a mean of 40 years (Figure 1). All cases were diagnosed with HSIL and there was a total of 15 occurrences of glandular occupation diagnosed on histopathology, corresponding to approximately 35% of the sample.

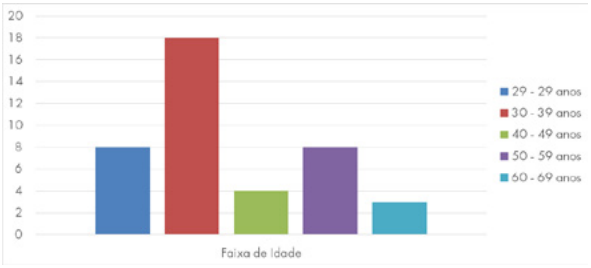

FIGURE 1 — Age group of the patients (n = 42)

Only 13 patients submitted to LEEP had previous cytology. Of these, 3 had cytological criteria for glandular occupation, but only 1 had histological confirmation in LEEP.

Among the 10 patients who did not meet the criteria for glandular occupation in cytology, 8 had their negativity confirmed by LEEP. Thus, in the cytohistological comparison, true-negative cases predominated (61.5%, Figure 2).

A total of 13 recurrences were recorded in the follow-up cytopathology, representing 31% of the sample. Among these recurrences, only 4 occurred in patients with diagnosed glandular occupation.

Statistical analysis

After statistical calculations of the data obtained, it was found that the criteria used for cytological evaluation of occupation in this study had a sensitivity

of 33.3%, specificity of 80%, positive predictive value of 33.3%, negative predictive value of 80% and efficacy of 69.3%.

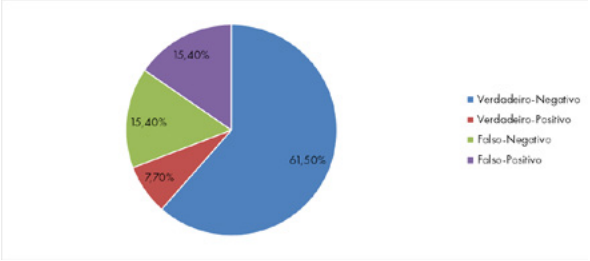

FIGURE 2 — Comparative results of cytological diagnoses of glandular occupation confirmed by histopathology (n = 42)

DISCUSSION

In the current literature, it is stated that glandular occupation is the most important risk factor for recurrence after LEEP, being present in 35% of cases of HSIL recurrence.[6] The data of this study corroborate the literature, since the extension of the lesions to the endocervical glands was present in 30.7% of the cases with proven recurrence.

Among the patients evaluated, only 15 of the 42 (35.7%) had glandular occupation. This is in slight disparity with published data since the average reported is 68.9% of those with HSIL.[7]

Regarding age, there is a peak of CAFs between 30 and 39 years of age, justified by the fact that the incidence of intraepithelial lesions of the uterine cervix reaches its maximum point around 30 years of age.[3] There was a 30.9% recurrence rate among the patients after the initial LEEP, indicating a rate higher than that observed in other studies, which indicate recurrences ranging from 5 to 13% of the cases.[8,9] This, however, may be due to the restricted sample size of this study, in addition to the fact that other characteristics associated with recurrences were not included, such as neoplasm-free margins in the CAFs, relationship with HPV subtype, risk factors such as smoking, and immunodeficiency.[10]

As can be inferred from Figure 2, the cytological criteria for glandular occupation showed a high rate of negative results when compared to the false-negative rate, thus indicating good specificity and low sensitivity for the sample studied, in which the slides were reviewed by a cytopathologist experienced in cervical-vaginal smears.

Regarding the difficulties of the research, it should be noted that those treated in 2012 and 2013 at the hospital could not be included in this study because their records were incomplete. Also, from the initial estimate, 197 were excluded from the study because their CAFs were reported negative for HSIL. In addition, 27 patients were excluded because they had been referred from another service and did not have cervicovaginal cytology at the institution.

The criteria listed have been shown to be effective for the detection of glandular occupation in cytology. Although their positive predictive value and sensitivity are low, they have shown promise in the exclusion of glandular occupation due to their high specificity and negative predictive value. At follow-up, a high rate of recurrence was observed, indicating the need for further investigations regarding the group evaluated. The conclusions drawn from this study are subject to the bias generated by the small sample. This, together with the lack of established parameters regarding cytological criteria for diagnosing glandular occupation, makes it necessary to conduct research with larger populations in the future.

CONCLUSION

In the present study, the efficacy of cytology in detecting glandular occupation in high-grade squamous lesions of the uterine cervix was 69.3%, which is relevant data to be described in the cervical-vaginal examination reports, because among the patients with glandular occupation proven in histopathology followed after LEEP, 30.9% had recurrence.

Authors' contributions
Samya Hamad Mehanna: Formal analysis, supervision, writing.
Gabriela Helena Mota Golçalves: Project administration, supervision
Bruno Granja Marcos: Methodology, formal analysis.
Luiz Martins Collaço: Conceptualization, writing, revision and editing.
Julia Wansaucheki: Writing, proofreading and editing.

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