Accuracy of visual inspection, cytology and colposcopy in the diagnosis of high-grade cervical intraepithelial neoplasia

Acurácia da inspeção visual, citologia e colposcopia no diagnóstico da neoplasia intraepitelial cervical de alto grau

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ABSTRACT

Introduction: Cervical cancer is still one of the leading causes of cancer and mortality in women, especially in low- and middle-income countries. Normally, the prevention of its occurrence is done through efficient screening and treatment programs for high-grade epithelial lesions, which are pre-malignant lesions. Cheaper diagnostic techniques ensure greater access to women, which can prevent a large number of cancer cases worldwide. **Objective:** The aim of the study was to evaluate the accuracy of visual inspection either with acetic acid or with Lugol's iodine, cervical cytology and colposcopy in the diagnosis of cervical intraepithelial neoplasia 2 and 3. **Methods**: This is a study of diagnostic accuracy. We evaluated 115 women with high-grade squamous intraepithelial lesion confirmed by biopsy, 54 with cervical intraepithelial neoplasia 2 and 61 with cervical intraepithelial neoplasia 3, from January 2016 to December 2018 at the Lower Genital Tract Pathology and Colposcopy Service of the Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil. A comparative analysis of the visual inspection, Pap smear and colposcopy diagnostic methods was performed. **Results:** The average age was 33.1 years (standard deviation=9.83) for cervical intraepithelial neoplasia 2 cases and 35.2 years (standard deviation=7.97) for cervical intraepithelial neoplasia 3. In the cervical intraepithelial neoplasia 2 group, visual inspection tests were positive for high-grade squamous intraepithelial lesion in 98.1% of the cases with acetic acid and 94.4% with Lugol's iodine. Colposcopy identified a probable high-grade squamous intraepithelial lesion in 94.4% of the cases, while cytology only in 42.6%. In the cervical intraepithelial neoplasia 3 group, the visual inspection tests were positive for high-grade squamous intraepithelial lesion in 91.8% of the cases with acetic acid and 95.1% with Lugol's iodine. Colposcopy identified a probable high-grade squamous intraepithelial lesion in 93.5% of the cases, while cytology in 65.6%. **Conclusion:** Visual inspection with acetic acid and Lugol's iodine, and colposcopy test were more accurate for the diagnosis of cervical intraepithelial neoplasia 2 and 3 than through cytopathology.

Keywords: Cervical intraepithelial neoplasia. Colposcopy. Papanicolaou test. Diagnostic techniques and procedures. Early detection of cancer.

RESUMO

Introdução: O câncer do colo de útero ainda é uma das principais causas de câncer e mortalidade em mulheres, especialmente em países de baixa e média renda. Normalmente, a prevenção de sua ocorrência é feita por meio de programas eficientes de triagem e tratamento de lesões epiteliais de alto grau, que são as lesões pré-malignas. Técnicas diagnósticas mais baratas garantem maior acesso às mulheres, podendo evitar um grande número de casos de câncer no mundo inteiro. **Objetivo:** O objetivo deste estudo foi avaliar a acurácia da inspeção visual (com ácido acético e com solução de lugol), da citologia cervical e da colposcopia no diagnóstico de neoplasias intraepiteliais cervicais 2/3. **Métodos:** Trata-se de um estudo de acurácia diagnóstica. Foram avaliadas 115 mulheres com lesão intraepitelial escamosa de alto grau confirmada por biópsia, 54 com neoplasias intraepiteliais cervicais 2 e 61 com neoplasias intraepiteliais cervicais 3, no período de janeiro de 2016 a dezembro de 2018 no Serviço de Patologia e Colposcopia do Trato Genital Inferior do Hospital de Clínicas de Porto Alegre, em Porto Alegre, Brasil. Foi realizada análise comparativa dos métodos de diagnóstico Inspeção visual com ácido acético, Inspeção visual com Solução de Lugol, colpocitologia oncótica e colposcopia. **Resultados:** A média de idade foi de 33,11 anos (DP 9,83) para os casos de neoplasias intraepiteliais cervicais 2 e de 35,28 anos (DP 7,97) para neoplasias intraepiteliais cervicais 3. No grupo de neoplasias intraepiteliais cervicais 2, os testes de inspeção visual foram positivos para tratamento de lesões epiteliais de alto grau em 98,1% dos casos com Inspeção visual com ácido acético e em 94,4% daqueles com Inspeção visual com Solução de Lugol. A colposcopia identificou provável tratamento de lesões epiteliais de alto grau em 94,4% dos casos, enquanto a citologia apenas 42,6%. No grupo neoplasias intraepiteliais cervicais 3, os testes de inspeção visual foram positivos para tratamento de lesões epiteliais de alto grau em 91,8% dos casos com Inspeção visual com ácido acético e em 95,1% daqueles com Inspeção visual com Solução de Lugol. A colposcopia identificou provável tratamento de lesões epiteliais de alto grau em 93,5% dos casos, enquanto a citologia em 65,6%. **Conclusão:** A inspeção visual (com ácido acético e com Solução de Lugol) e a colposcopia foram mais precisas para o diagnóstico de neoplasias intraepiteliais cervicais 2/3 do que a citopatologia.

Palavras-chave: Neoplasia intraepitelial cervical. Colposcopia. Teste de Papanicolaou. Técnicas e procedimentos diagnósticos. Detecção precoce de câncer.

INTRODUCTION

High-grade cervical intraepithelial lesions (HSIL) are the actual precursor lesions of cervical cancer, the second leading cause of death and the second most common cancer in the female population in low- and middle-income countries[1], being responsible for around 311,000 deaths per year worldwide[2,3]. This type of cancer is entirely preventable through the detection and treatment of these lesions[4]. However, it is still a great challenge to carry out organized screenings and adequate treatments of all these lesions in the world, given the different economic situations and infrastructure[5].

At the end of the 20th century, there was a considerable reduction in the incidence of cervical cancer and its related mortality in developed countries. This episode occurred due to the systematic implementation of a screening program for cervical cancer, mainly with the Papanicolaou (Pap smear) test. These programs depend on cytological screenings repeated with a certain frequency due to the low

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sensitivity of the method[6]. Low- and middle-income countries cannot implement a model similar to the developed countries because of it is logistically complex, including the lack of laboratory infrastructure and human resources. For these reasons, 86.5% of deaths from cervical cancer worldwide are found in underdeveloped nations[3,6].

The Pap smear test has an approximate 98% specificity for precancerous lesions of the cervix, but low sensitivity, approximately 55 to 80%, depending on the service evaluated[7,8], therefore requiring constant screening to increase sensitivity. In countries where this screening is provided, mainly in those that are developed, there was a reduction in the incidence and mortality of cervical cancer by more than 70%[7,9].

Colposcopy is a diagnostic method of visual inspection that is often used in cases of abnormal cervical cytology[10]. In experienced hands, it is an excellent test for diagnosing cervical lesions. About 93% of women with high-grade intraepithelial neoplasia (CIN 2 and 3) present an acetowhite area on colposcopy. Although this finding is important for the diagnosis of a CIN, acetowhite staining alone is a common and nonspecific finding, and evaluation depends on the subjectivity of the person conducting the exam[11].

Due to the limitations of cervical cytology and the high cost of colposcopy, visual inspection methods have gained support as alternative screening methods for low-income countries. Visual inspection (naked eye) with acetic acid (visual inspection with acetic acid – VIA) and Lugol's solution (visual inspection with Lugol's iodine – VILI) have been proven to be cost-effective and highly sensitive methods (approximately 80% accuracy), even though with less specificity[12]. The advantage of VIA and VILI is that they do not use any sophisticated equipment or laboratory, in addition to being low-cost, easy to perform, safe and easily applicable due to their simplicity[13]. As a disadvantage, the methods have limitations in populations with high cervicitis rates, which can lead to false-positive results and unnecessary treatments[14,15]. Even so, these are very effective screening methods in underdeveloped countries, as observed in studies carried out on the African continent[12].

The aim of this study was to evaluate the accuracy of visual inspection (VIA and VILI), cervical cytology, and colposcopy in the diagnosis of high-grade cervical intraepithelial neoplasia (CIN 2 and 3) before and after treatment with the ablative method of thermocoagulation with the Semm device, with follow-up of 12 months.

OBJECTIVE

The aim of this study was to evaluate the accuracy of visual inspection (VIA and VILI), cervical cytology, and colposcopy in the diagnosis of high-grade cervical intraepithelial neoplasia (CIN 2 and 3) before and after treatment with the ablative method of thermocoagulation with the Semm device, with follow-up of 12 months.

METHODS

Study design and participants

This is a study of diagnostic accuracy. It was approved by the Ethics Committee of the Hospital de Clínicas de Porto Alegre, associated to the Federal University of Rio Grande do Sul (IRB00000921 – Project 10-0126). The sample evaluated consisted of 115 women aged between 25 and 59 years with a histological diagnosis of CIN 2 and 3 attended at the Lower Genital Tract Pathology and Colposcopy Service of the Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil. All study participants signed the Informed Consent Form. Of these 115 women, 54 had CIN 2 and 61 had CIN 3. Biopsy was considered the gold standard in diagnostic criteria and was performed at the time the participants entered the study. All women aged 25 to 59 years who needed treatment for a histologically proven high-grade cervical lesion (CIN 2 and 3) were included in the study (inclusion criteria). All women who had any evidence of infection or vaginal bleeding were excluded from the study (exclusion criteria).

Procedures

Upon being referred to the Lower Genital Tract Pathology and Colposcopy Service of the Hospital de Clínicas de Porto Alegre for the treatment of CIN 2 and 3, all women underwent a new diagnostic evaluation with visual inspection (VIA and VILI), cervical cytology, colposcopy, and biopsy. All studied participants underwent thermocoagulation treatment and were re-evaluated with these diagnostic methods after 12 months for the diagnosis of residual lesion of CIN 2 and 3.

In the first stage, a new collection of Pap smears were performed with care not to interfere with the following exams. The nomenclature used was The Bethesda System (TBS, 2014), classifying major cytological alterations as high-grade squamous intraepithelial lesions (HSIL)[16].

In the second stage, visual inspection was performed according to the technique and nomenclature used by Sankaranarayanan[17]. Firstly, VIA, with the application of 5% acetic acid in the cervix and vaginal fornices, and then inspection of the cervix and vagina with the "naked eye" performed one minute after application. The test was considered positive when opaque and well-defined acetowhite areas were observed. Secondly, VILI, with the application of 2% Lugol's solution following the same technique as before. Positive results were considered when areas of mustard or saffron yellow color were well defined, dense, bright and close to the squamous-columnar junction.

In the third stage, colposcopy was performed with a Microem® brand device with four magnifications (6, 10, 25 and 40) and a green filter, according to standard techniques[18]. Biopsy was performed when any area of major abnormality was observed on colposcopic examination, which included dense acetowhite epithelium, coarse mosaic, coarse punctuation, atypical vascular changes, thickened glandular orifices, and iodine-negative areas. Colposcopy was described according to the 2011 International Federation for Cervical Pathology and Colposcopy (IFCPC) nomenclature[19].

Quality control of the diagnostic tests was carried out by evaluating false negative and positive rates with guided biopsy as a reference (gold standard), compared to colposcopy, cervical cytology, and visual inspection (VIA and VILI).

Outcomes

All studied participants were monitored and reassessed after 12 months of treatment by cervical cytology examination, visual

inspection (VIA and VILI), and colposcopy to evaluate the recurrence of CIN 2 and 3 or even the progression of the disease.

Statistical analysis

The initial sample of this study was 128 women, of which 13 (11.1%) were excluded for not completing the follow-up, leaving a final sample for analysis of 115 women, 54 with a diagnosis of CIN 2 and 61 of CIN 3.

To describe the qualitative variables, absolute and relative frequencies were used, while to describe the quantitative variables, mean and standard deviation (SD) were used. The analyzes were structured by separating the variables related to the CIN 2 and CIN 3 groups. To measure the accuracy in the diagnosis of VIA, VILI, colposcopy, and cytopathology, the biopsy result was used as a gold standard. To describe the accuracy of the tests, exact 95% confidence intervals (95% CI) were constructed for binomial distributions. Also, to compare the accuracy of diagnosis between CIN 2 and CIN 3, Fisher's exact test was used. To verify if the adjusted model was adequate Pseudo R2, Hosmer-Lemeshow test, and accuracy parameters (AUC - Area under the ROC curve, Sensitivity, and Specificity) were conducted. The software used in the analyzes was R (version 3.5.0).

RESULTS

All women referred to the Lower Genital Tract Pathology and Colposcopy Service of the Hospital de Clínicas de Porto Alegre, with CIN 2 and 3 underwent an assessment of socio-demographic characteristics and a new analysis with cervical cytology, visual inspection (VIA and VILI), colposcopy, and biopsy. The participants were divided into separate groups, those with CIN 2 and those with CIN 3.

In the CIN 2 group, the average age was 33.1 years (SD=9.83), 35.2% were married, 55.6% had an education level of 5 to 10 years, and 64.8% had an income of 1 to 3 minimum wages. Visual inspection tests were positive for HSIL in 98.1% of the cases with VIA and 94.4% with VILI. Colposcopy identified a probable HSIL in 94.4% of the cases, while cervical cytology only in 42.6%. The new biopsy result, considered the gold standard, indicated CIN 2 for all 54 women (**Table 1**).

At the 12-month follow-up after treatment, VIA was negative for HSIL in 81.4%, VILI in 75.9%, cervical cytology in 79.6% and colposcopy in 88.9% of the cases. Residual lesion on biopsy was observed in only 5 women (9.3%), all CIN 1, better diagnosed through colposcopy (**Table 2**).

In group CIN 3, the average age was 35.2 years (SD=7.97), 54.1% were married, 49.2% had an education level of 5 to 10 years, and 52.5% had an income of 1 to 3 minimum wages. Visual inspection tests were positive for HSIL in 91.8% of the cases with VIA and 95.1% with VILI. Colposcopy identified a probable HSIL in 93.5% of the cases, while cervical cytology, in 65.6%. The new biopsy result indicated CIN 3 for all 61 women (**Table 3**).

At the 12-month follow-up after treatment, VIA was negative for HSIL in 90.2%, VILI in 96.7%, cervical cytology in 70.5%, and colposcopy in 91.8% of the cases. Residual lesion on biopsy was observed in 7 women (11.4%), two of which were CIN 2/3 (3.2%). Visual inspection and colposcopy methods were similar to each other and better than cervical cytology for this diagnosis (**Table 4**). The flow diagram of patients before and after treatment of CIN 2 and 3 can be seen in **Figures 1A and 1B**, respectively.

When we evaluated the accuracy of the methods, compared with biopsy (gold standard for the diagnosis of these lesions), we observed that for the diagnosis of CIN 2, the accuracy of cervical cytology was significantly lower (42.6%) than that of the other tests, which were higher than 90%. VIA was the most accurate, with 98.1%, but with no statistical difference with the other methods. For the

Table 1. Descriptive analysis of the cervical intraepithelial neoplasia grade 2 group variables before treatment.

		n	%
Sociodemographic variables			
Age (years)	(Mean/SD)	(33,1)	(±9,83)
Marital status	Single	17	31.5
	Married	19	35.2
	Stable union	12	22.1
	Divorced	3	5.6
	Widow	3	5.6
Years of schooling	1–5 years	7	13.0
	5–10 years	30	55.6
	>10 years	17	31.4
Income (minimal wages)	<1	15	27.8
	1–3	35	64.8
	3–5	2	3.7
	>5	2	3.7
Visual inspection tests			
VIA	Negative	1	1.9
	Positive	53	98.1
VILI	Negative	3	5.6
	Positive	51	94.4
Colposcopy			
Colposcopy findings	Negative	1	1.9
	Possible LSIL	2	3.7
	Possible HSIL	51	94.4
Cytopathology			
Results	Negative	4	7.4
	ASC-US	13	24.1
	LSIL	14	25.9
	HSIL	23	42.6
Biopsy			
Results	CIN 2	54	100

SD: standard deviation; VIA: visual inspection with acetic acid; VILI: visual inspection with Lugol's iodine; LSIL: low-grade squamous intraepithelial lesion; HSIL: high-grade squamous intraepithelial lesion; ASC-US: atypical squamous cells of undetermined significance; CIN 2: cervical intraepithelial neoplasia grade 2.

Table 2. Descriptive analysis of variables related to the cervical intraepithelial neoplasia grade 2 group 12 months after treatment.

Results	n	%
Cytopathology		
Negative	43	79.6
ASC-US	9	16.6
LSIL	1	1.9
HSIL	1	1.9
VIA		
Negative	44	81.5
Positive	10	18.5
VILI		
Negative	41	75.9
Positive	13	24.1
Colposcopy		
Negative	48	88.9
Positive	6	11.1
Biopsy		
Not performed	45	83.3
Negative	4	7.5
CIN 1	5	9.2
General Status		
No lesion	49	90.7
Residual lesion	5	9.3
Long term complications		
None	51	94.4
PID	3	5.6

ASC-US: atypical squamous cells of undetermined significance; LSIL: low-grade squamous intraepithelial lesion; HSIL: high-grade squamous intraepithelial lesion; VIA: visual inspection with acetic acid; VILI: visual inspection with Lugol's iodine; CIN 1: cervical intraepithelial neoplasia grade 1; PID: pelvic inflammatory disease.

Table 3. Descriptive analysis of cervical intraepithelial neoplasia grade 3 group variables before treatment.

		n	%
Socio-demographic variables			
Age (years)	(Mean/SD)	(35.2)	(±7,97)
Marital status	Single	14	23.0
	Married	33	54.1
	Stable union	11	18.0
	Divorced	2	3.3
	Widow	1	1.6
Years of schooling	1–5 years	12	19.7
	5–10 years	30	49.2
	>10 years	19	31.1
Income (minimal wages)	<1	24	39.3
	1–3	32	52.5
	3–5	4	6.6
	>5	1	1.6
Visual inspection tests			
VIA	Negative	5	8.2
	Positive	56	91.8
VILI	Negative	3	4.9
	Positive	58	95.1
Colposcopy			
Colposcopy findings	Probable LSIL	4	6.5
	Probable HSIL	57	93.5
Cytopathology			
Result	Negative	3	4.9
	ASC-US	10	16.4
	LSIL	8	13.1
	HSIL	40	65.6
Biopsy			
Result	CIN 3	61	100

SD: standard deviation; VIA: visual inspection with acetic acid; VILI: visual inspection with Lugol's iodine; LSIL: low-grade squamous intraepithelial lesion; HSIL: high-grade squamous intraepithelial lesion; ASC-US: atypical squamous cells of undetermined significance; CIN 3: cervical intraepithelial neoplasia grade 3.

diagnosis of CIN 3, the accuracy of cytopathology was also significantly lower (65.6%) than that of the other tests, higher than 90% as well. Although there is no statistical difference among the other methods, VILI was the one with the highest efficacy, with 95.1%. For the VIA, VILI and colposcopy tests there was no significant difference in the accuracy for the diagnosis of CIN 2 and CIN 3 ($p>0.050$). There was a significant difference ($p=0.016$) in the diagnostic accuracy between CIN 2 and CIN 3 for cytopathology, with better performance for the diagnosis of CIN 3 (65.6% vs 42.6%), as seen in **Table 5**.

DISCUSSION

When we evaluated the diagnostic methods for CIN 2 and 3 used in the study, we observed that visual inspection was the one with the highest diagnostic accuracy. Both VIA and VILI presented diagnostic accuracy of more than 90%, compared to biopsy. However, it is important to point out that all these women had previously diagnosed high-grade lesions and, depending on their age, practically all lesions could be evidenced in the ectocervix. When we extrapolate the visual inspection to the general population, whose positive result ranges from 4 to 8% on average[13-15,20-22], we will have many false-positive cases mainly due to the reparative processes of the cervix, such as immature squamous metaplasia, with much lower specificity. This is what was observed in a study in Africa, which involved 2,203 women screened for precancerous lesion of the cervix with both VIA and cytology; results indicated that VIA was more sensitive than cytology (76.7% vs 44.3%), but with a lower specificity (64.1 vs 90.6%)[21]. The same was observed by Nessa et al, in a study with 104,098 women in Bangladesh who underwent

Table 4. Descriptive analysis of variables for the cervical intraepithelial neoplasia grade 3 group 12 months after treatment.

Results	n	%
Cytopathology		
Negative	43	70.5
ASC-US	13	21.3
LSIL	3	4.9
HSIL	2	3.3
VIA		
Negative	55	90.2
Positive	6	9.8
VILI		
Negative	59	96,7
Positive	2	8.2
Colposcopy		
Negative	56	91.8
Positive	5	8.2
Biopsy		
Not performed	54	88.5
Negative	2	3.3
LSIL	3	4.9
HSIL	2	3.3
General Status		
No lesion	56	91.8
Residual lesion	5	8.2
Long term complications		
None	52	85.2
Pain	6	9.8
PID	3	4.9

ASC-US: atypical squamous cells of undetermined significance; LSIL: low-grade squamous intraepithelial lesion; HSIL: high-grade squamous intraepithelial lesion; VIA: visual inspection with acetic acid; VILI: visual inspection with Lugol's iodine; PID: pelvic inflammatory disease.

screening for cervical cancer using VIA. The sensitivity to detect CIN 2 and 3 was 93.6% and the specificity, 58.3%[18]. The high sensitivity detects more damage, however, the low specificity due to the high number of false positives may lead to unnecessary overtreatment. Nevertheless, this is a diagnostic method that should be thought of in very poor countries or regions. In general, they do not have access to traditional and more specific screening methods to prevent many women from developing cancer, who are, thus, usually diagnosed only in advanced stages.

The reproducibility of cytopathology is low, both inter- and intra-observer, especially in smaller lesions of the cervix. This tends to improve as injuries worsen. Cross-sectional studies carried out in Brazil show a prevalence of CIN 2 or more severe lesions after a cytopathological examination of low-grade squamous intraepithelial lesion (LSIL) between 7.2 and 21.6%[9]. Our results were very similar: CIN 2 lesions had a cytological diagnosis of LSIL in 26% and CIN 3 in 13%. Major cytological changes are more evident and have greater consensus among observers. CIN 2 lesions are intermediate between low- and high-grade lesions, and often confuse the cytopathologist, as we observed in our study, in which cytological diagnosis of HSIL for CIN 2 cases (diagnosed in histopathology) was very low (42.6%). When cytological alterations were greater, as in cases of CIN 3, this percentage increased to 65.6%. Undoubtedly, this is a worrying situation and reaffirms the need for periodic repetition of the Pap smear to reduce these false negatives[9]. When extrapolated to the general population, the sensitivity of cytology for diagnosing a cervical lesion is 47 to 62% in most studies, but specificity is greater among all methods of screening for cervical cancer[23].

Colposcopy has always been considered an excellent method to identify a lesion diagnosed in cytology, as we observed for the diagnosis of CIN 3, with more than 93% confirmation on biopsy. Mitchell et al., in their meta-analysis, demonstrated that the sensitivity and specificity of colposcopy to differentiate a normal from an abnormal cervix (LSIL, HSIL, and cancer) is 96% (87–99%) and 48% (23–87%), respectively, and for a diagnosis of HSIL and cancer is 85% (64–99%) and 69% (30–93%)[24]. This variability is associated with the great subjectivity of the examination, which in skilled hands with great experience, surpasses 90% of diagnostic accuracy, as observed in this study.

Our study had some limitations. All women had already been referred with a histological diagnosis of CIN 2 and 3. Thus, visual methods, both visual inspection (VIA and VILI) and colposcopy, which present a very high degree of subjectivity, may have increased the diagnosis of a larger lesion owing to these previous results. The sensitivity of cytology depends on the observer and the laboratory, therefore results may differ in other diagnostic centers.

Screening and treatment of precancerous cervical lesions, currently associated with HPV vaccination, are the most effective ways of preventing cervical cancer. Visual inspection methods with VIA or VILI, feasible in the poorest places, combined with treatment in a single visit, are likely to prevent a large number of cases of cervical cancer worldwide[17,25].

Strengths

With this study, we can demonstrate that visual inspection and colposcopy is more accurate for the diagnosis of CIN 2 and 3 than cytopathology. This is important for underdeveloped countries, since they can use a very inexpensive technique, such as visual inspection, for the diagnosis of precancerous lesions of the cervix, and combined with treatment in a single visit, will likely prevent a large number of cases of cervical cancer worldwide. However, it is necessary to clarify that team training is necessary so that minor injuries are not overtreated.

CONCLUSION

Visual inspection (VIA and VILI) and colposcopy were more accurate for the diagnosis of CIN 2 and 3 than cytopathology. There was no difference between the methods of visual inspection and colposcopy to differentiate a CIN 2 from a CIN 3, however, there was a significant difference in cytology, with better performance for the diagnosis of a CIN 3.

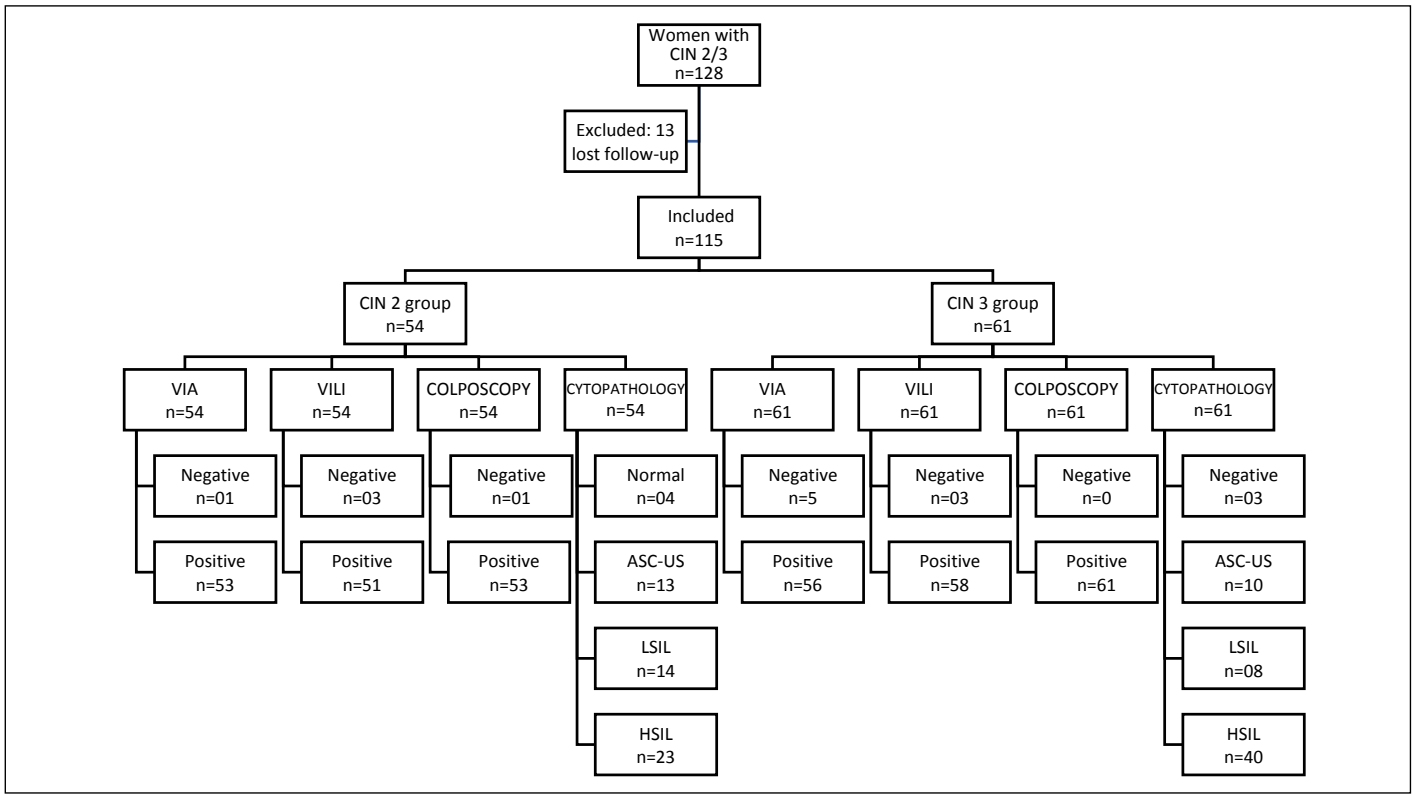

Figure 1A. Flow diagram before treatment of cervical intraepithelial neoplasia grade 2 and 3.

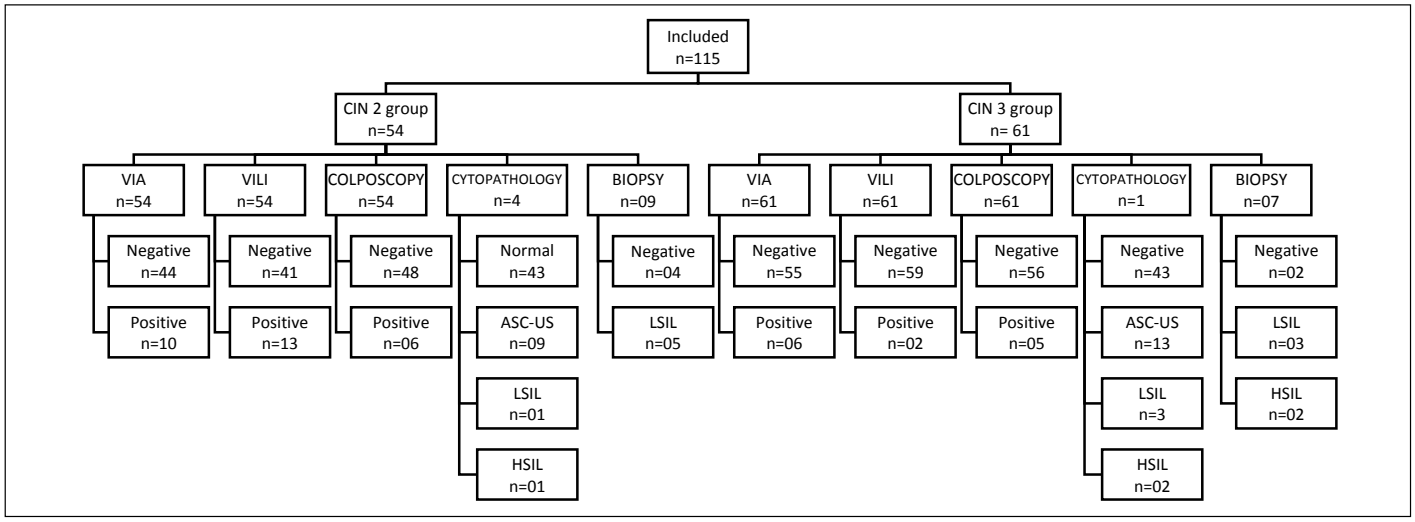

Figure 1B. Flow diagram after treatment of cervical intraepithelial neoplasia grade 2 and 3.

Table 5. Analysis of accuracy in the diagnosis of cervical intraepithelial neoplasia grade 2 and 3.

Diagnosis	CIN 2 (n=54)			CIN 3 (n=61)			p-value[b]
	n	%	95%CI[a]	n	%	95%CI[a]	
VIA	53	98.1	90.1–100.0	56	91.8	81.9–97.3	0.212
VILI	51	94.4	84.6–98.8	58	95,1	86.3–99.0	1.000
Colposcopy	51	94.4	84.6–98.8	57	93.5	84.1–98.2	1.000
Cytopathology	23	42.6	29.2–56.8	40	65.6	52.3–77.3	0.016

CIN: cervical intraepithelial neoplasia; VIA: visual inspection with acetic acid; VILI: visual inspection with Lugol's iodine.
[a]Confidence interval for binomial distributions; [b]χ^2 test.

Approval by the Human Research Ethics Committee

This study was approved by the Ethics Committee of the Hospital de Clínicas de Porto Alegre, associated with Federal University of Rio Grande do Sul (IRB00000921 - Project 10-0126).

Participation of each author

BMK: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. Sak: Formal analysis, Writing – review & editing. Enf: Conceptualization, Data curation, Formal analysis, Methodology, Project administration, Validation, Visualization, Writing – original draft, Writing – review & editing.

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Conflict of interest

The authors declare no potential conflicts of interest.

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