GYNECOLOGY

How long is too long? Application of acetic acid during colposcopy: a prospective study

Ziad Hilal, MD; Clemens B. Tempfer, MD; Lucie Burgard, MD; Sadia Rehman, MD; Günther A. Rezniczek, PhD

BACKGROUND: Application of acetic acid to the cervix followed by colposcopic assessment with or without colposcopically directed biopsy is the standard test used to detect dysplastic lesions of the cervix. However, there is no evidence-based common standard defining how exactly to perform this test.

OBJECTIVE: To prospectively define the optimal timing for the colposcopic assessment of acetowhite lesions.

MATERIALS AND METHODS: Consecutive women referred to our colposcopy unit were recruited. Using a standardized colposcopy protocol, we recorded the most severe colposcopic lesion 1, 3, and 5 minutes after application of acetic acid (primary study end point). The time to first appearance of the most severe colposcopic lesion, highest staining intensity, and fading of the most severe colposcopic lesion were video documented (secondary study end points, assessed independently by 3 raters). Results were compared using parametric and nonparametric tests.

RESULTS: A total of 300 women were included. After 1 minute, 290 of 300 patients (96.7%) were diagnosed with the most severe colposcopic lesion. This proportion did not improve after 3 minutes (290/300 [96.7%]) or after 5 minutes (233/264 [88.3%]). The proportion of minor and major changes continuously declined over time from 142 in 300 (47.3%; 1 minute) to 107 in 264 (40.5%; 5 minutes) and from 110 in 300 (36.7%) to 91 in 264 (34.5%), respectively. The median time until the first appearance of the most severe colposcopic lesion was 13.5 (interquartile range, 3−27.25) seconds and was significantly lower in high-grade squamous intraepithelial lesion (7 [interquartile range, 1−20] seconds) compared to low-grade squamous intraepithelial lesion (19 [interquartile range, 9−39.5] seconds; $P < .001$). We observed fading of acetowhite lesions in 78% of cases, occurring at a median of 191 (interquartile range, 120−295) seconds after application of acetic acid. Fading started earlier in high-grade squamous intraepithelial lesion compared to low-grade squamous intraepithelial lesion (179.5 [interquartile range, 110−253.25] versus 212.5 [interquartile range, 146.5−300]; $P = .044$). Overall, the net difference between colposcopic assessments at 3 minutes versus at 1 minute was 1 more high-grade squamous intraepithelial lesion and 1 less low-grade squamous intraepithelial lesion.

CONCLUSION: It is reasonable to conclude that the best time to identify lesions is 1 minute after the application of acetic acid. Continued evaluation for up to 3 minutes may be considered reasonable for an optimal high-grade squamous intraepithelial lesion yield. However, fading of acetowhite lesions is common, especially in high-grade squamous intraepithelial lesions, and supports a recommendation of not prolonging colposcopy beyond 3 minutes.

Key words: acetic acid test, acetowhite lesion, colposcopy, HSIL, LSIL

Applying acetic acid (AA) to the cervix followed by colposcopic assessment with or without colposcopically directed biopsy is the standard test used to detect dysplastic lesions of the cervix. The AA test is used worldwide and is an integral part of the management of cervical intraepithelial neoplasia. This test is recommended as standard of care by the International Federation for Cervical Pathology and Colposcopy,[1] as well as national societies such as the American Society for Colposcopy and Cervical Pathology (ASCCP)[2] and the German Society of Colposcopy and Cervical Pathology (AG-CPC).[3]

Surprisingly, recommendations for how exactly to perform AA testing in order to obtain optimal results vary considerably. For example, historical textbooks such as the original description of colposcopy and the AA test by Hinselmann in 1925 recommended applying AA for up to 5 minutes.[4] Recent recommendations include application of 5% AA followed by a delay of 1−2 minutes before colposcopic assessment,[5] 3% AA for 30−60 seconds before assessment,[6] 5% AA for 1 minute followed by immediate assessment,[7] or application of 5% AA for 1 minute followed by another minute of waiting.[8] In a large randomized screening trial with >130,000 participants, 4% AA with assessment 1 minute after AA application was used as a standard,[9] based on the World Health Organization (WHO) International Agency for Research on Cancer's handbook on cervical cancer screening[10] and their own previous trial.[11] In many studies, the specifics of AA testing are not defined at all. It is noteworthy that the ASCCP and other national societies do not delineate the details of the AA test in their colposcopy standards.

Therefore, based on the data in the literature and based on existing practice guidelines, there is no common standard for AA testing during colposcopy. Current practice of this important and commonly used diagnostic tool is not evidence based. This statement is supported by a PubMed literature search (search terms: colposcopy, acetic acid test, acetowhite; search date September 27, 2019), through which we identified no controlled trial defining the optimal point of time for AA testing during colposcopy. Because the AA test is an integral part of the management of women with cervical dysplasia, there is a medical need to properly define the specifics of this test in a prospective study.

Cite this article as: Hilal Z, Tempfer CB, Burgard L, et al. How long is too long? Application of acetic acid during colposcopy: a prospective study. Am J Obstet Gynecol 2020;223:101.e1-8.

0002-9378/$36.00

https://doi.org/10.1016/j.ajog.2020.01.038

AJOG at a Glance

Why was this study conducted?

Although application of acetic acid to the cervix followed by colposcopic assessment is the standard test used to detect dysplastic lesions of the cervix, there is no common standard for performing this test.

Key findings

The optimal timing for the colposcopic assessment of acetowhite lesions is 1 minute after the application of acetic acid. Fading of acetowhite lesions is common, starts after 1 minute, and is more pronounced in high-grade than in low-grade squamous intraepithelial lesions.

What does this add to what is known?

Using a prospective design, this study clearly defines the optimal time frames for colposcopic assessment after application of acetic acid, allowing colposcopists to minimize the examination's duration without compromising reliability.

To address this issue, we designed a prospective study to investigate the AA test in detail in a large patient population. The aim of our study was to properly define the optimal point of time for the colposcopic assessment of acetowhite lesions after AA application. In addition, we wanted to quantify the increases and decreases in acetowhite lesion severity over time, and to specify the proportion and timing of fading of acetowhite staining.

Materials and Methods

We recruited consecutive women referred to the colposcopy outpatient unit of the Department of Obstetrics and Gynecology of the Ruhr-Universität Bochum, Germany, or the doctor's office of the Institute of Cytology and Immune Cytochemistry, Dortmund, Germany, for further assessment of a pathologic Papanicoloaou (Pap) smear result. After giving informed consent, a detailed personal history was taken and documented. We used a standardized protocol for colposcopy and AA testing and in all women as follows: using a binocular colposcope (Model 1D LED, Leisegang, Berlin, Germany), the native impression of the cervix was recorded with ×7.5 and ×15 magnification. Then, acetic acid 5% was applied to the cervix with 3 pushes using a commercially available household spray can (Wilpeg, Großenlüder, Germany), corresponding to a total volume of 3 mL. Next, the colposcopist assessed and classified the most severe colposcopic lesion (MSCL) 1, 3, and 5 minutes after the application of AA. The primary end point of this study was the proportion of MSCL after 1, 3, and 5 minutes using the International Federation for Cervical Pathology and Colposcopy Rio classification criteria.[1] Secondary study endpoints included the time from AA application to the first appearance of the MSCL, the time from AA application to the highest staining intensity of the MSCL, and the time from AA application to the start of fading of acetowhite staining of the MSCL. These were recorded and video documented for every patient. Of these, 85 videos were selected (with an allocation of 1:2:2 to histological outcome: negative for dysplasia, low-grade squamous intraepithelial lesion [LSIL], high-grade squamous intraepithelial lesion [HSIL]/carcinoma) for detailed assessment by 3 colposcopists to further specify the dynamics of acetowhitening. This sample size was calculated based on the experience that acetowhitening of HSIL is faster than that of LSIL lesions (assumed on average to be most intense after 60 seconds) and assuming a fixed standard deviation of ±15 seconds, so that a difference in time needed to reach maximum intensity of 20% could be detected at an α of 0.05 with a power of at least 90%, and allowing for a dropout/error rate of 15% (video not of suitable quality, wrong group assignment due to clerical errors). G*Power 3.1.9.2 was used for this calculation.[12] All 3 colposcopists, who were blinded to patient information and histological outcomes, assessed each video with regard to the exact time (in seconds) until the first and secondary endpoints occurred. Endpoints not occurring before the end of the observation period (300 seconds after application of AA) were censored with a value of 300 seconds. Waterfall plots were used to visualize the time points of fading in low-grade and high-grade lesions as determined by the 3 raters; each bar represents 1 observation. To determine proportions of nonfaded acetowhite lesions, the time points of fading onset determined by the 3 raters were averaged per video.

All colposcopists were certified specialists with more than 300 annual colposcopies performed. The study was approved by the Ethics Committee of the Medical Faculty of Ruhr-Universität Bochum, Bochum, Germany (registration number 18-6370, dated August 24, 2018).

Assuming a continuous outcome measure such as the time until the appearance of the MSCL, a sample size calculation with the confidence level set at 95% and the confidence interval set at 5% resulted in a sample size of 278 patients for a population size of 1000 women (roughly corresponding to the number of women seen by a colposcopists with 300 cases per year over 3 years). Therefore, we aimed to recruit at least 300 patients, allowing for approximately 10% of dropouts/protocol violations.

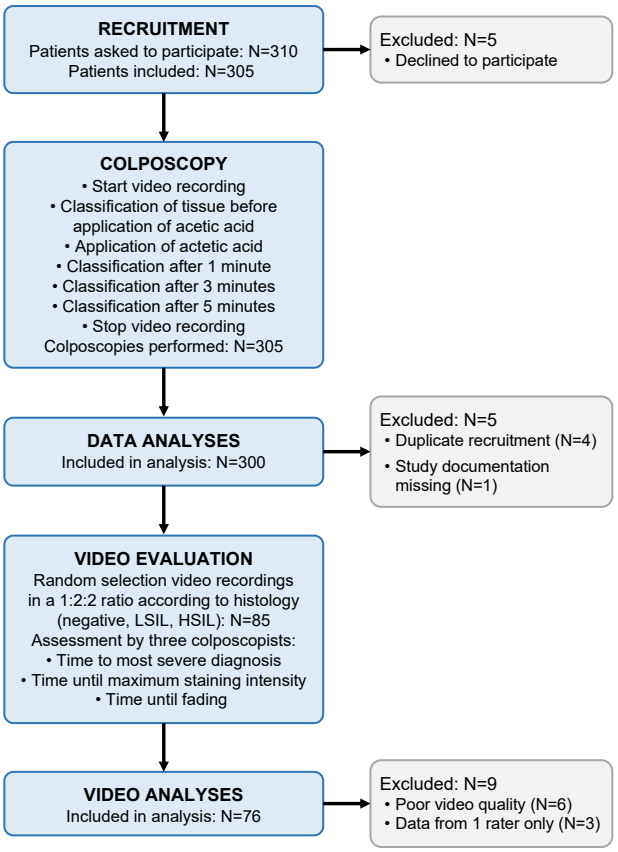
Study data were collected and managed using REDCap (Research Electronic Data Capture), a secure, Web-based application designed to support data capture for research studies.[13] After data collection had been concluded, exported data were further processed in Microsoft Excel (Microsoft Inc,

Redmond, WA) and prepared for statistical analyses using SigmaPlot 14 (Systat Software Inc, San Jose, CA). Descriptive statistics are reported using means and standard deviations for normally distributed data, and medians and interquartile ranges (IQR) for data not meeting this assumption. Accordingly, statistical analysis was performed using parametric (t test) or nonparametric tests (Mann−Whitney U test for pairwise comparison and analysis of variance on ranks for multiple comparisons). All P values are 2-tailed, and $P < .05$ was considered statistically significant.

Results

From September 2018 to May 2019, we prospectively recruited 305 consecutive women from our colposcopy units into this study. Of these, 4 women were excluded because of protocol violation. In 1 case, study documentation was missing. Thus, data from 300 colposcopies were evaluated. Figure 1 gives a detailed account of the patients' flow through the study and the workflow. Patient characteristics are shown in Table 1. All patients underwent a standardized colposcopy and AA test protocol as delineated in the Materials and Methods section. Table 2 lists the Pap smear results, the colposcopic findings before and after AA testing, and the corresponding histopathological results. Specifically, type I, type II, and type III transformation zones were identified in 195 (65.0%), 58 (19.3%), and 47 (15.7%) of cases. At the end of colposcopy, that is, 5 minutes after AA application, colposcopic assessment found a normal cervix in 61 cases (23.1%), minor changes in 107 cases (40.5%), major changes in 91 cases (34.5%), and major changes suspicious for invasion in 1 case (0.4%), respectively. The colposcopic findings changed over time. When comparing the colposcopic assessments 1 minute, 3 minutes, and 5 minutes after AA application, the proportion of minor changes continuously declined from 142 (47.3%) after 1 minute to 137 (45.7%) after 3 minutes and 107 (40.5%) after 5 minutes. The proportion of major change lesions also declined over time, from 110 (36.7%) to 114 (38.0%) and to

FIGURE 1
Flow diagram of the study and analysis



Hilal et al. Acetic acid test in colposcopy. Am J Obstet Gynecol 2020.

TABLE 1
Patient characteristics

Characteristic	Value
No. of patients	300
Age, y	35.2 (29.4−44.3); range 19.8−78.4
Body mass index, kg/m^2	23.7 (21.3−27.3) [44]
Parity	1 (0−2) [44]
Allergy, yes/no	94 (37.2%)/159 [47]
Smoking, yes/no	98 (37.8%)/161 [41]
Alcohol abuse, yes/no	7 (2.4%)/288 [5]
Drug abuse, yes/no	10 (3.5%)/274 [16]
Concomitant disease, yes/no	103 (41.2%)/147 [50]
Prescription drug use, yes/no	118 (48.8%)/124 [58]
Immunosuppressive conditions, yes/no	4 (1.6%)/247 [49]

Values are counts (percentage proportions) or medians (interquartile ranges). Numbers in square brackets indicate the number of missing values.

Hilal et al. Acetic acid test in colposcopy. Am J Obstet Gynecol 2020.

TABLE 2
Colposcopy and histopathology

Item	n (%)			
Type of transformation zone				
Type 1	195 (65.0%)			
Type 2	58 (19.3%)			
Type 3	47 (15.7%)			
Indication for colposcopy (HPV, Pap)				
Persistent HPV	32 (10.7%)			
ASC-US	11 (3.7%)			
ASC-H	21 (7.0%)			
AGC-NOS	2 (0.7%)			
AGC favor neoplasia	10 (3.3%)			
LSIL	69 (23.0%)			
HSIL	146 (48.6%)			
AIS	8 (2.7%)			
Squamous cell carcinoma	1 (0.3%)			
HPV status (positive/negative/unknown)	118 (39.3%)/11 (3.7%)/171 (57.0%)			
Colposcopic findings (before/after acetic acid)	Before	1 min	3 min	5 min [36]
Normal	221 (73.7%)	40 (13.3%)	43 (14.3%)	61 (23.1%)
Minor changes	n/a	142 (47.3%)	137 (45.7%)	107 (40.5%)
Major changes	n/a	110 (36.7%)	114 (38.0%)	91 (34.5%)
Nonspecific	6 (2.0%)	1 (0.3%)	1 (0.3%)	0 (0.0%)
Suspicious for invasion	2 (0.7%)	2 (0.7%)	2 (0.7%)	1 (0.4%)
Miscellaneous findings	29 (9.7%)	1 (0.3%)	1 (0.3%)	3 (1.1%)
Other	42 (14.0%)	3 (1.0%)	2 (0.7%)	1 (0.4%)
Histological results				
Negative for dysplasia	78 (26.0%)			
LSIL	65 (21.6%)			
HSIL	150 (50.0%)			
AIS	2 (0.7%)			
Invasive cancer	5 (1.7%)			

Values are counts (percentage proportions). Numbers in square brackets indicate the number of missing values.

AIS, adenocarcinoma in situ; *AGC,* atypical glandular cells; *AGC-NOS,* AGC not otherwise specified; *ASC,* atypical squamous cells; *ASC-H, ASC,* cannot exclude HSIL; *ASC-US,* ASC of undetermined significance; *HPV,* human papillomavirus; *HSIL,* high-grade squamous intraepithelial lesion; *LSIL,* low-grade squamous intraepithelial lesion; *n/a,* not applicable; *Pap,* Papanicoloau.

Hilal et al. Acetic acid test in colposcopy. Am J Obstet Gynecol 2020.

91 (34.5%), respectively. Of note, this effect was restricted to minor and major changes and was not observed in the categories "nonspecific findings," "miscellaneous findings," and "other findings" (as defined by the Rio classification system[1]).

We were interested in defining the optimal time point for the colposcopic assessment after AA application. Thus, we analyzed the proportion of the MSCL at the time points 1, 3, and 5 minutes after AA application (Table 3). We found that after 1 minute, 290 of 300 patients (96.7%) were diagnosed with the MSCL. This proportion did not improve after 3 minutes (290/300 [96.7%]) or after 5 minutes (233/264 [88.3%]). Therefore, the optimal time point for the colposcopic assessment of acetowhite lesions based on our study is 1 minute after the application of AA. An increase in the severity of acetowhite lesions or a change from no acetowhite lesion to acetowhite lesion from 1 minute and 3 minutes was observed in 8 of 300 cases (2.7%) (Table 3). Of these 8 cases, 5 changed their colposcopic appearance from negative/

unspecific to minor/major change. In other words, a colposcopic assessment at 1 minute would have missed 5 cases because no biopsies would have been performed (1 HSIL, 2 LSIL, 2 with negative histology). A further increase of lesion severity from 3 to 5 minutes was not observed. Conversely, a decrease in lesion severity from 1 minute to 3 minutes was observed in 8 of 300 cases (2.7%; colposcopy: 7 cases from minor change to negative, 1 case from major to minor change; histology: 1 HSIL, 3 LSIL, 4 with negative histology). In other words, a colposcopic assessment at 3 minutes (as compared with 1 minute) would have missed 3 cases of LSIL, because these lesions were no longer visible (the HSIL would still have been biopsied because it changed only from major to minor change). Thus, the net difference between colposcopic assessments at 3 minutes versus at 1 minute was 1 more HSIL and 1 less LSIL in a population of 300 case patients.

The median time from application of AA until the first appearance of the MSCL was found to be 13.5 (interquartile range [IQR], 3−27.25) seconds (Table 4). Interestingly, the median time until the first appearance of the MSCL was significantly lower in HSIL compared to LSIL (7 [IQR, 1−20] versus 19 [IQR, 9−39.5]; $P < .001$). The median time from the application of AA until the maximum staining intensity of the MSCL was 50.5 (IQR, 29−75.75) seconds. Again, the median time until maximum staining intensity was significantly lower in HSIL compared to LSIL (46 [IQR, 32.25−70.75] versus 60 [IQR, 44.75− 81.5] seconds; $P = .039$). Of note, we observed the phenomenon of fading of acetowhite lesions over time in the majority of cases (78.4%). In the video analysis, the median time from application of AA until the start of fading of the MSCL was 191 (IQR, 120−295) seconds. In line with the previous observations, fading started earlier in HSIL compared to LSIL (179.5 [IQR, 110−253.25] versus 212.5 [IQR, 146.5−300] seconds; $P = .044$). Fading was found to be continuously increasing until the end of the recordings, starting around 50 seconds after AA (Figure 2). Although fading started significantly earlier in HSIL compared to LSIL ($P = 0.016$), it affected the majority of HSIL (86.8%) as well as LSIL (72.7%) cases. This finding underscores the necessity of defining the optimal time point for the colposcopic assessment after application of AA to avoid missing lesions because of fading. When we looked at the assessments by the 3 investigators separately, there was a fair congruence with regard to their determinations of when the MSCL became evident, when lesions reached their maximum staining intensity, and when fading started. No statistically significant variability was noted, suggesting an acceptable interobserver variability (Table 4).

TABLE 3
Primary and secondary study outcomes

Outcome	n (%)
Most severe diagnosis found (before/after application of acetic acid)	
Before acetic acid	73/300 (24.3%)
After 1 min	290/300 (96.7%)
After 3 min	290/300 (96.7%)
After 5 min [36]	233/264 (88.3%)
Increase in severity of diagnosis	
Before acetic acid to 1 min	222/300 (74.0%)
1 min to 3 min	8/300 (2.7%)
3 min to 5 min [36]	0/264 (0.0%)
Decrease in severity of diagnosis	
Before acetic acid to 1 min	2/300 (0.7%)
1 min to 3 min	8/300 (2.7%)
3 min to 5 min [36]	22/264 (8.3%)

Values are counts (percentage proportions). Numbers in square brackets indicate the number of missing values.
Hilal et al. Acetic acid test in colposcopy. Am J Obstet Gynecol 2020.

Comment

Principal findings

The optimal timing of the colposcopic AA test is unclear.[1−9] In the present study, we aimed to define the optimal timing of the colposcopic assessment of acetowhite lesions after AA application. We found that 97% of patients were diagnosed with the MSCL 1 minute after AA application. This proportion did not improve after 3 and 5 minutes. Therefore, we conclude that the optimal time point for the colposcopic assessment of acetowhite lesions is 1 minute after the application of AA.

Results and clinical implications

Our study has implications for clinical practice. Identifying the optimal time point for the colposcopic assessment after AA testing is important, and affects how women with cervical dysplasia or abnormal Pap smear results are being managed. An erroneous use of the AA test may lead to the underdiagnoses of cervical dysplasia, with the potential for subsequent progression of such unnoticed lesions. Specifically, performing colposcopic assessment after AA application too early might lead to a reduced sensitivity by overlooking lesions not yet visible. Conversely, waiting for too long may lead to overlooking lesions because of fading of acetowhite staining, a phenomenon that we observed in 78% of cases. In addition, performing unnecessarily lengthy tests is time consuming and causes patient discomfort. Based on our prospective data collected under standardized conditions, it can now be stated that the optimal balance between quick

TABLE 4
Video evaluation

Group	Time after acetic acid application to		
	Most severe diagnosis	Maximum staining intensity	Start of fading
Overall (n = 76 videos)	13.5 (3–27.25)	50 (29–76.75)	191 (120–295)
Grouped by rater			
Rater 1	14.5 (1.25–28.75)	43.5 (28.25–70.0)	210 (120–300)
Rater 2	16 (5.5–30)	67 (47–89.5)	179 (127–246)
Rater 3	10 (1–20)	48 (39–62)	213 (115.5–300)
Grouped by histopathology			
No pathology (n = 15)	15 (3–22)	50 (40–73)	210 (110–300)
LSIL (n = 24)	19 (9–39.5)	60 (44.75–81.5)	212.5 (146.5–300)
HSIL (n = 34)	7 (1–20); $P < .001$ vs LSIL	46 (32.25–70.75); $P = .039$ vs LSIL	179.5 (110–253.25); $P = .044$ vs LSIL
Carcinoma (n =3)	29 (14–30)	72.5 (46.75–87.5)	248 (218.5–296)

Values are medians (interquartile ranges) of times in seconds. Statistics for histopathology groups: analysis of variance on ranks with Dunn pairwise comparison (using data from all raters).

HSIL, high-grade squamous intraepithelial lesion; *LSIL*, low-grade squamous intraepithelial lesions.

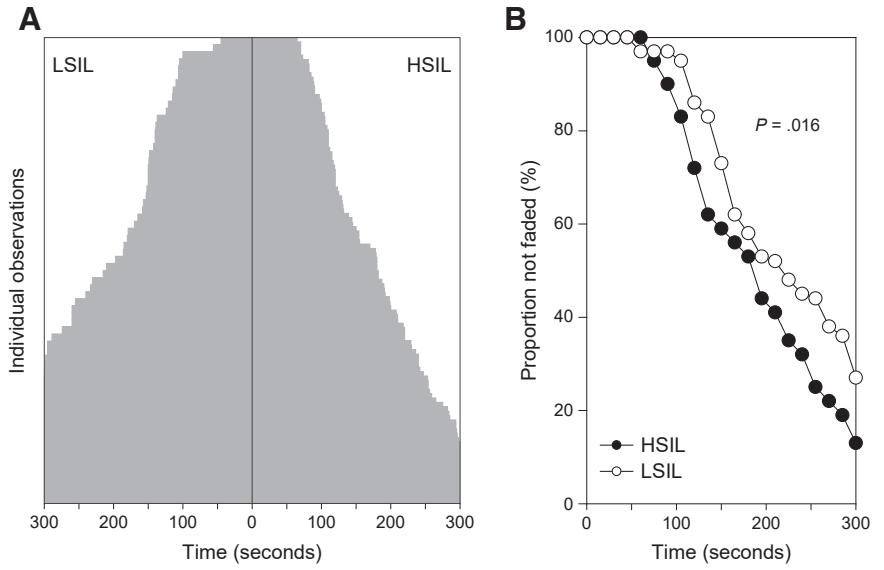
Hilal et al. Acetic acid test in colposcopy. Am J Obstet Gynecol 2020

diagnosis and optimal test yield is 1 minute. This strategy will identify 97% of the MSCL, and this percentage cannot be improved by waiting for a longer time. To the contrary, a continuously increasing number of lesions will go unnoticed from 1 minute on, because of the fading of acetowhite staining, a phenomenon seen in the vast majority of cases.

Interestingly, HSIL and LSIL pick up acetowhite staining very quickly. For example, HSIL became first evident after a median of only 7 seconds and LSIL after a median of only 19 seconds. Although the staining process of HSIL and LSIL progressively intensifies after that until reaching a maximum after 50 seconds, this does not change the fact that the MSCL can already be identified seconds after AA application. However, it is reasonable to wait for 1 minute until colposcopic assessment and colposcopically guided biopsy, because this time is needed to reach the maximum test yield of 97%. This sensitivity maximum plateaus between 1 and 3 minutes and then even declines after that because of the effect of fading. The potential pitfall of waiting too long is underlined by the observation that HSIL fade significantly more quickly than LSIL, thus aggravating the clinical relevance of loss of test sensitivity by waiting too long before colposcopy and biopsy. Some colposcopists argue that a longer waiting time is better, in the mistaken belief that more high-grade lesions will become visible the longer the test lasts. We noted in our study that the contrary is true, because fading is not a threshold phenomenon but a continuous process already starting 50 seconds after AA application and continuously increasing, especially in HSIL, until it ultimately affects the vast majority of lesions.

The results of our study do not imply that colposcopy should be abruptly stopped after 1 minute. They do imply, however, that the best time to identify lesions is 1 minute after the application of AA. Continued evaluation for up to 3 minutes may be

FIGURE 2
Assessment of acetowhite fading in video colposcopy recordings



A, Waterfall plots showing time points of fading in low-grade squamous intraepithelial lesions (LSIL) (left side) and high-grade squamous intraepithelial lesions (HSIL) (right side) as determined by 3 raters. **B**, Plots of the proportions of nonfaded acetowhite LSIL (open circles) and HSIL (filled circles) (fading times averaged over the 3 raters) vs time after acetic acid application at a resolution of 15 seconds. *P* value, Mann–Whitney *U* rank sum test

Hilal et al. Acetic acid test in colposcopy. Am J Obstet Gynecol 2020.

considered reasonable for an optimal HSIL yield. However, fading of acetowhite lesions is common, especially in HSIL, and supports a recommendation of not prolonging colposcopy beyond 3 minutes.

Strengths and limitations

Our study has both strengths and limitations. Strengths are the prospective design, the large number of patients, and the standardized technique, which was defined before the start of the trial. In addition, all study procedures were video documented, thereby ensuring that all patients were treated in the same way. Limitations of our study include selection bias, because we recruited only women referred to a specialized colposcopy unit; therefore, the likelihood of finding LSIL/HSIL is increased compared to that in an unselected group of women in a population-based screening program. An increased likelihood of a positive diagnostic test might inflate the sensitivity of the AA test. However, because procedural aspects of the test and not test accuracy were the primary end point of our study, we believe that the possible selection bias does not affect the validity of our results. Furthermore, all patients were referred to us by a constant group of gynecologic practices, which are being served by our units. Therefore, ascertainment bias is unlikely, as is self-selection of patients. Finally, according to trial design, only 3 investigators performed the study procedures. All of them were experienced colposcopists, thus excluding bias due to learning curve effects.

Conclusion

In summary, our study defines the proper timing of the AA test during colposcopy (ie, to assess acetowhite lesions 1 minute after application of AA). Colposcopy and the AA test are widely used by gynecologists and are clinically important tools in the management of women with cervical dysplasia. Although the results of our study are not practice changing, they may be helpful in using the AA test in a more comprehensive and efficient way, and should therefore be incorporated into clinical practice as well as into guideline recommendations. ■

References

1. Bornstein J, Bentley J, Bösze P, et al. 2011 Colposcopic terminology of the International Federation for Cervical Pathology and Colposcopy. Obstet Gynecol 2012;120:166–72.

2. Waxman AG, Conageski C, Silver MI, et al. ASCCP colposcopy standards: how do we perform colposcopy? Implications for establishing standards. J Low Genit Tract Dis 2017;21:235–41.

3. Kühn W, Gieseking F. Die aktuellen Empfehlung der AG-CPC zur Kolposkopie 2015. Deutsche Gesellschaft für Gynäkologie und Geburtshilfe, Arbeitsgemeinschaft Zervixpathologie und Kolposkopie e.V. Available at: https://www.ag-cpc.de/empfehlungen/. Accessed September 29, 2019.

4. Hinselmann H. Verbesserung der Inspektionsmöglichkeiten von Vulva, Vagina und Portio. Münchener Med Wochenschr 1925;72:1733.

5. Pogue BW, Kaufman HB, Zelenchuk A, et al. Analysis of acetic acid-induced whitening of high-grade squamous intraepithelial lesions. J Biomed Opt 2001;6:397–403.

6. Vahedpoor Z, Behrashi M, Khamehchian T, Abedzadeh-Kalahroudi M, Moravveji A, Mohmadi-Kartalayi M. Comparison of the diagnostic value of the visual inspection with acetic acid (VIA) and Pap smear in cervical cancer screening. Taiwan J Obstet Gynecol 2019;58:345–8.

7. Massad LS, Jeronimo J, Katki HA, Schiffman M. The accuracy of colposcopic grading for detection of high-grade cervical intraepithelial neoplasia. J Low Genit Tract Dis 2009;13:137–44.

8. Li W, Venkataraman S, Gustafsson U, Oyama JC, Ferris DG, Lieberman RW. Using acetowhite opacity index for detecting cervical intraepithelial neoplasia. J Biomed Opt 2009;14:14020.

9. Sankaranarayanan R, Nene BM, Shastri SS, et al. HPV screening for cervical cancer in rural India. N Engl J Med 2009;360:1385–94.

10. IARC. Cervix cancer screening (IARC Handbooks of Cancer Prevention, vol. 10). Lyon: IARC Press; 2005.

11. Sankaranarayanan R, Nene BM, Dinshaw KA, et al. A cluster randomized controlled trial of visual, cytology and human papillomavirus screening for cancer of the cervix in rural India. Int J Cancer 2005;116:617–23.

12. Faul F, Erdfelder E, Lang A-G, Buchner A. G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behav Res Methods 2007;39:175–91.

13. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009;42:377–81.

Author and article information

From the Department of Obstetrics and Gynecology (Drs Hilal, Tempfer, Burgard, Rehman, and Rezniczek), Ruhr-Universität Bochum, Bochum, Germany; ZydoLab (Dr Hilal), Dortmund, Germany.

Received Oct. 4, 2019; revised Jan. 15, 2020; accepted Jan. 15, 2020.

The authors report no conflict of interest.

The authors report no funding for this work.

Corresponding author: Günther A. Rezniczek, PhD guenther.rezniczek@rub.de