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Anal cytology screening in men who have sex with men with HIV at a university hospital in Bogotá, Colombia

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Abstract

Background: Risk of anal squamous cell carcinoma (anal cancer) is greater among men who have sex with men (MSM) living with human immunodeficiency virus (HIV). We describe the frequency of and factors associated with abnormal anal cytology results in Colombian MSM living with HIV.

Methods: This retrospective observational cohort study included MSM ≥18 years old living with HIV screened with anal cytology at Hospital Universitario San Ignacio in Bogotá, Colombia between January 2019 and February 2020. A multivariable log-binomial regression model estimated associations with abnormal anal cytology.

Results: A total of 211 patients were included. Mean age was 35.6 years. Sixty-eight (32.3%) had an abnormal anal cytology result: ASC-US 33.8% (n=23); LSIL 60.3% (n=41); and HSIL 5.9% (n=4). MSM with an STI diagnosis in the previous 12 months (RR 1.48, [95% CI 1.03–

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Competing interest
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2.12], p=0.032) or with a $CD4^+$ T cell count <200 (RR 2.08 [95% CI 1.16–3.73], p=0.014) were significantly more likely to have abnormal anal cytology.

Conclusions: These data provide crucial information to guide scale up of anal cancer screening at select centers in Colombia. Our results also suggest STI prevention efforts and improved virological control among MSM living with HIV may have the secondary benefit of reducing the risk of anal cancer.

Keywords

Anus neoplasms; human immunodeficiency virus; men who have sex with men; cancer screening

Background

Risk of anal squamous cell carcinoma (anal cancer) is increased for men who have sex with men (MSM) living with human immunodeficiency virus (HIV)(1). While the global age-standardized incidence of anal cancer in men in the general population was 0.5 per 100,000 Person Years (P-Y) in 2020 (2), MSM living with HIV have an anal cancer incidence as high as 131 per 100,000 P-Y (3,4). This increased risk is due in part to the high prevalence of anal human papillomavirus (HPV) infection among MSM (5,6), which is associated with the development of anal dysplasia and cancer (3).

Anal Papanicolaou cytological testing (anal cytology) has been proposed as a screening tool to identify early-stage anal dysplasia in this high-risk population, before progression to anal cancer (6). Various groups and institutions have adopted anal cancer screening protocols for MSM living with HIV (7). The AIDS Study Group (GeSIDA) and the European AIDS Clinical Society (EACS) recommend anal cytology screening, followed by diagnostic workup and treatment of high-grade dysplasia via high-resolution anoscopy (HRA) for those with abnormal cytology (7). Recent observational data suggested a decreased incidence of cancer in those who were screened and treated (8) and the Anal Cancer/HSIL Outcomes Research (ANCHOR) randomized clinical trial recently found that treating high-grade dysplasia reduced risk of progression to anal cancer (9).

Colombia is an upper-middle-income country in South America, and the capital city of Bogotá has a population of nearly 11 million (10). There were an estimated 123,490 people living with HIV (PLWH) in Colombia in 2020 (11), with the prevalence of HIV in the Colombian MSM population estimated to be as high as 23.7% in some cities (12). The five-year prevalence of anal cancer in Colombia was 2.6 per 100,000 (13) in 2020, but data are not available for MSM living with HIV specifically. In 2014, the Colombian Ministry of Health (MoH) released clinical practice guidelines for the care of PLWH, which recommended consideration of anal cancer screening via anal cytology for MSM or other PLWH who reported multiple sexual partners, condomless anal sex, or a history of anal or genital condyloma (14). In response to these recommendations, the Comprehensive HIV Care Clinic at Hospital Universitario San Ignacio (HUSI) in Bogotá, Colombia implemented a pilot anal cancer screening program for MSM living with HIV beginning in January 2019.

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To date, there remains a lack of data on the burden of anal dysplasia among MSM living with HIV in Colombia and implementation of anal cancer screening in the country has been limited by lack of HRA, referral for which is a key component of international guidelines for anal cancer screening (7). In order to address this data gap and inform further scale up of HUSI's newly established anal cancer screening program, this study utilizes data from the first fourteen months of the pilot screening program to describe the frequency of and factors associated with abnormal anal cytology screening results among MSM living with HIV in Bogotá, Colombia.

Methods

Study Design

We conducted a retrospective cohort study of male patients 18 years or older who were living with HIV, reported any history of sex with other men, and underwent anal cancer screening via anal cytology at the Comprehensive HIV Care Clinic at HUSI in Bogotá, Colombia between January 2019 and February 2020. Of note, this period represented the first fourteen months of the pilot anal cancer screening program before HRA was available at HUSI. Screening with anal cytology was offered to all MSM receiving care at HUSI's HIV clinic. Anal cytology was performed by trained staff by inserting a collection swab into the anus and applying pressure against the walls of the anal canal while removing the swab. Processing of samples was performed by the Department of Pathology at HUSI using the conventional Papanicolaou stain. Follow-up data were collected through July 2020. Data were collected via chart review of HUSI's electronic medical record and were compiled using the online platform REDCap™ hosted at HUSI (15). All records were reviewed by two authors to ensure data quality.

Variables

Social and demographic data—Age was collected and analyzed as a continuous variable. Education levels included high school or less, technical college, and university or higher. No formal education, elementary school, middle school, high school, were combined in the single category of "high school or less," while university undergraduate, graduate, and postgraduate were combined into "university or higher." Sexual partners were classified as only men; men and women; or men, women and, transgender individuals. Smoking status was collected as current, former, or never smoker.

Sexual health and HIV virologic data—Diagnoses with the following sexually transmitted infections (STIs) in the previous 12 months were recorded: condyloma (penile or anal), syphilis, herpes, hepatitis B, hepatitis C, unspecified proctocolitis, and unspecified urethritis. For analysis, STI diagnoses were grouped as "none," "condyloma," or "other STI." Date of original HIV diagnosis was used to calculate "time since HIV diagnosis," measured in months. Current antiretroviral therapy (ART) regimen was recorded, but duration of ART was not. Lastly, we recorded HIV stage at diagnosis according to the 2014 CDC stages 1, 2, and 3 (16). HIV control laboratory data were collected within a time frame of six months prior to or following collection of anal cytology. These data included $CD4^+$ T Lymphocyte (CD4) count (cells/μL), CD4 percentage, nadir CD4 count (cells/μL;

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defined as the lowest CD4 count since diagnosis), and HIV-1 viral load (copies/mL) above the lower limit of the detection.

Outcomes

The primary outcome of interest was abnormal anal cytology. Anal cytology results were presented using Bethesda terminology: normal, atypical squamous cells of undetermined significance (ASC-US), low-grade squamous intraepithelial lesions (LSIL), atypical squamous cells – cannot exclude HSIL (ASC-H), and high-grade squamous intraepithelial lesions (HSIL) (17). ASC-US, LSIL, and HSIL were all considered abnormal. While HUSI did not have HRA available for diagnostic workup of those with abnormal anal cytology results, certain MSM had macroscopically visible anal condyloma amenable to surgical resection without HRA, which is described in more detail separately (18). If a patient with ASC-US or LSIL on anal cytology underwent anal condyloma resection with pathology showing high-grade anal intraepithelial dysplasia (HGAIN), that patient was included in a composite HSIL group (cHSIL) for a secondary analysis. Thus, a second dichotomous outcome was those with cHSIL compared to all others (normal, ASC-US, and LSIL).

Statistical Analysis

Descriptive statistics were used to summarize the sociodemographic and clinical characteristics of the population using central tendency measures. Categorical variables were compared using Pearson's χ^2 statistic, and continuous variables via either student's t-test of means or Wilcoxon rank-sum, depending on the normality of data distribution. For the exploratory analysis of risk factors, those with any abnormal anal cytology result (ASC-US, LSIL, and HSIL) were compared against those with normal anal cytology results using a log-binomial regression model to estimate relative risk (RR) with 95% confidence interval (CI). Variables with a p value of less than 0.05 on univariable analysis were included in the multivariable regression, as well as age, which was included as a confounder. A log-binomial regression was not performed for the cHSIL secondary outcome because of a low number of observations. Data analysis was performed using Stata/SE 14.2.

Ethics

Approval for this study was granted by the HUSI Ethics Committee (FM-CIE-0366–20) and the University of California, Los Angeles (UCLA) institutional review board (IRB#19–002232). Consent was not required for this retrospective study.

Results

A total of 211 MSM were screened for anal dysplasia via cytology between January 2019 and February 2020. The mean age of participants was 35.6 years (standard deviation (SD) 11.0) (Table 1). A majority (80.6%) reported only male sexual partners, and most (56.9%) reported a university- or higher-level education. More than one third (n=81, 38.4%) reported at least one STI in the previous 12 months, with the most common infection being syphilis (n=66, 31.3%). Median time since HIV diagnosis was 21.9 months (Interquartile Range 11.6–56.2). Nearly all (97.6%) had initiated ART by the time of anal cytology screening.

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Only n=81 (38.4%) had a detectable viral load. Mean CD4 count and CD4 nadir were 430.0 (SD 193.7) and 286.4 (SD 171.4), respectively.

There were 68 (32.2%) participants with an abnormal anal cytology result: 23 (33.8%) with ASC-US, 41 (60.3%) with LSIL, and 4 (5.9%) with HSIL (Table 2). There were no results classified as ASC-H or unsatisfactory. Few (n=11, 16.2%) of the MSM with abnormal cytology had subsequent resection of anal condyloma by colorectal surgery (18), of whom 2 received a histopathologic diagnosis of HGAIN and were re-categorized as cHSIL (n=6, 2.8%).

Table 3 compares demographic and sexual health data for those with normal and abnormal anal cytology results. Participants with abnormal results are further stratified between cHSIL and a combined ASC-US/LSIL grouping. There were no significant differences between groups with regards to age, sexual partners, education level, or cigarette smoking. Those with any abnormal anal cytology result were more likely to have a recent STI diagnosis (48.5% versus 33.6%, p=0.037) compared to those with normal results, while history of condyloma was more common specifically in those with cHSIL (p=0.001). There was a non-significant association with shorter time since HIV diagnosis in those with abnormal results, particularly in the cHSIL group. There was a higher percentage of CDC Stage 3 HIV at diagnosis in those with abnormal results, particularly when comparing cHSIL against all others (83.3% v. 33.2%, p=0.011). Participants with any abnormal anal cytology result were more likely to have a detectable viral load compared to those with normal results (50.0% v. 32.9%, p=0.017). CD4 counts were significantly lower in those with abnormal anal cytology results, particularly in the cHSIL group. A larger percentage of those with abnormal results had a CD4 count less than 200 (22.1% v. 6.3%, p=0.001) and a nadir CD4 count less than 200 (38.2% v. 25.2%, p=0.052) when compared to those with normal results.

Results from a multivariable log-binomial regression model estimating associations with abnormal anal cytology results are presented in Table 4. MSM with an STI diagnosis in the previous 12 months (RR 1.48, [95% CI 1.03–2.12], p=0.032) and with a CD4 count less than 200 (RR 2.08 [95% CI 1.16–3.73], p=0.014) had significantly higher risk of having an abnormal anal cytology result when screened for anal cancer.

Discussion

This study is the first to describe results from an anal cancer screening program for MSM living with HIV in Colombia since the MoH made recommendations for screening, and one of few publications to have described anal cytology screening in MSM living with HIV in Latin America (19–22). These data offer important insights into the burden of anal dysplasia among MSM living with HIV in Bogotá, Colombia and will serve to inform future scale up of HUSI's screening program, including implementation of HRA necessary for diagnostic confirmation of anal dysplasia, as well as decisions to implement similar screening programs in a region where few exist.

Approximately one-third of MSM in this study had abnormal screening results, representing the group that would require access to further diagnostic workup via HRA when made

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available at HUSI. A slightly higher percentage of abnormal cytology was previously reported among MSM living with HIV from Colombia in 2006 (19), and other studies from Latin America have reported anal dysplasia prevalences ranging from 25.5% to 45.5% (20–22). Likewise, the proportion of MSM with abnormal cytology in our study coincides with the frequencies reported in other screening programs for anal cancer in MSM living with HIV in high-income countries (23). For instance, Conley et al documented ASC-US in 22%, ASC-H in 4%, LSIL in 22%, and HSIL in 1% of MSM, (23), while Revollo et al diagnosed ASC-US in 12%, LSIL in 37%, and HSIL in 7% of MSM (8).

Our results offer key insights into risk factors for anal dysplasia, which can be used to guide prevention efforts in Bogotá. Nearly 40% of our study cohort had at least one STI in the previous 12 months, which was significantly associated with risk of anal dysplasia on cytology. While our study did not include testing for high-risk anal HPV genotypes, it is likely the associations between STI and anal dysplasia are related to anal HPV infection. It is estimated that more than 80% of MSM living with HIV have anal HPV infection, leading to an increased risk of anal squamous intraepithelial lesions despite adequate virologic suppression (5,6). In fact, anal cancer in PLWH is thought to be related to HPV infection in 98% of cases (29). Co-infection of anal HPV with other STIs in PLWH is related to condomless sex, as STIs may destroy the integrity of anogenital epithelial cells and facilitate infection by another pathogen (for example, co-infection with syphilis and anal HPV) (30). Comprehensive STI control strategies to improve education and reduce condomless sex could then decrease the incidence of both STIs and HPV-associated anal dysplasia. Moreover, future screening strategies in Colombia could consider HPV genotyping as an adjunct to anal cytology, as recommended in Clinical Practice Guidelines for Anal Squamous Cell Cancer of the American Society of Colon and Rectal Surgeons (31).

We also found that patients with abnormal anal cytology were more likely to have a CD4 count lower than 200 cells/ mm^3. The relationship between low CD4 count and anal dysplasia is related to the immune suppression effect on HPV reactivation (32). Large prospective cohorts have demonstrated that sustained virologic suppression by effective ART can decrease the risk of persistent high-risk HPV infection and lead to more rapid clearance of HPV-related lesions (33). Palefsky et al. showed that for HIV-infected men, a CD4 cell count below 200 cells/mm^3 was associated with a more than three-fold increase in the incidence of progression of normal to a high-grade anal dysplasia (based on cytology and/or biopsy) (33). Our data offer further support to efforts currently underway in Colombia to improve virologic control of MSM living with HIV through increasing access to care and ART.

The lack of high quality, evidence-based guidelines has been a limitation for clinicians in screening for anal cancer among MSM living with HIV (24,25), and implementation of screening programs has been limited by lack of training in equipment use, specifically HRA (4). In interviews with 25 healthcare practitioners providing care for MSM living with HIV in the USA, anal cancer screening practices varied widely, with differences in choice of screening test, frequency of screening, and follow-up interval (4). Moreover, practitioners took different approaches to treating those who were diagnosed with high-grade anal

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dysplasia. The inconsistency, however, will likely change as a result of the recent ANCHOR study results suggestive of improved outcomes when high-grade anal dysplasia is treated (9).

A key limitation of this study is that our outcome of anal dysplasia was largely based on anal cytology, rather than HRA-guided exam and biopsy, which is the gold standard for confirmatory diagnosis and treatment of abnormal screening cytology results (7). The sensitivity and specificity of abnormal anal cytology predicting high-grade anal dysplasia varies widely from 47 to 90% and 22 to 60%, respectively (26,27), which is why diagnostic confirmation with HRA-informed exam and biopsy is important. HRA is a magnified exam of the anus after application of acetic acid and/or iodine, which, like colposcopy for cervical cancer screening, allows for identification of dysplastic tissue for biopsy and targeted treatment (28). However, the Colombian MoH recommendation for anal cancer screening was made before HRA was available in the country, and there were no HRA providers in the city of Bogotá during the period of this study. A minority of patients in this study with abnormal cytology underwent resection of condyloma, but the remaining patients with abnormal cytology lacked any diagnostic workup (18). Despite this limitation, we believe our results offer important preliminary data to understand who will require access to HRA when the program at HUSI is further expanded or similar screening programs are implemented in Colombia and Latin America. Since the completion of this study, HUSI's colorectal surgery department has acquired equipment and training to perform both HRA and HPV PCR testing, which will be used to conduct further research on anal dysplasia.

There are several additional limitations to address. As a single-center study from a university-affiliated tertiary care hospital, these results are not necessarily generalizable to other settings. Due to the retrospective nature of the study design, it is not possible to establish causality with the identified associations. Additionally, our small sample size could have led us to miss significant associations with abnormal anal cytology and we did not have enough events to perform a multivariate analysis of the risk factors for cHSIL. Some recorded STI diagnoses in the prior twelve months were self-reported, since not everyone had their confirmatory laboratory testing done at our HIV clinic. While current tobacco smoking status was recorded for all patients, few had information pertaining to pack years smoked or time since quitting. Additionally, we were not able to collect data on specific higher-risk sexual behaviors, given these data were not recorded in clinic visit documentation.

Conclusion

MSM living with HIV are at high-risk of developing anal cancer, and anal cytology screening is recommended in Colombia to identify and treat anal dysplasia prior to progression to cancer. Our data contribute to a limited body of literature describing the frequency of and factors associated with abnormal anal cytology results among MSM living with HIV in Colombia. Abnormal cytology results in this high-risk population were associated with recent STI diagnoses as well as immunologic suppression, assessed via CD4 count, suggesting improved access to HIV care, ART, and counseling regarding safer sexual practices could have an impact on reducing anal dysplasia among MSM living with HIV in Bogotá. These data will be used to inform scale up of anal cancer screening programs

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in Colombia, including the expansion of HUSI's screening program through the addition of HRA.

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Declarations

This study received approval from the ethics committee at Pontificia Universidad Javeriana – Hospital Universitario San Ignacio (FM-CIE-0366–20) and from the Institutional Review Board at the University of California Los Angeles (IRB #19–002232). The Institutional Review Board (IRB) of each institution granted approval to the research project with an informed consent waiver, as no interventions or therapeutic modifications were made.

Availability of data and materials

Data is available in the HUSI's REDcap website repository of the project. It can be consulted in the following link: https://redcap.husi.org.co/redcap_v9.1.18/FileRepository/index.php?pid=343&instance=1

List of abbreviations

MSM	Men who have sex with men
HIV	Human immunodeficiency virus
(P-Y)	Person-years
HPV	Human papillomavirus
Anal	cytology Anal Papanicolaou cytological testing
GESIDA	The AIDS Study Group
HRA	High-resolution anoscopy
ASR	Estimated age standardized incidence rate
PLWH	People living with HIV
STIs	Sexually transmitted infections
CD4	CD4+ T Lymphocyte
ASC-US	Atypical squamous cells of undetermined significance
LSIL	Low-grade squamous intraepithelial lesions
HSIL	High-grade squamous intraepithelial lesions

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cHSIL	Composite HSIL
CI	Confidence interval
RR	Relative risk
SD	Standard deviation
ART	Antiretroviral therapy
PCR	Polymerase chain reaction
HUSI	Hospital Universitario San Ignacio

References

1. Gilbert M, Kwag M, Mei W, Rank C, Kropp R, Severini A, et al. Feasibility of incorporating self-collected rectal swabs into a community venue-based survey to measure the prevalence of HPV infection in men who have sex with men. Sex Transm Dis. 2011;38(10):964–9. [PubMed: 21934574]
2. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021 May;71(3):209–49. [PubMed: 33538338]
3. Silverberg MJ, Lau B, Justice AC, Engels E, Gill MJ, Goedert JJ, et al. Risk of anal cancer in HIV-infected and HIV-uninfected individuals in North America. Clin Infect Dis. 2012;54(7):1026–34. [PubMed: 22291097]
4. Koskan AM, Brennhofer SA, Helitzer DL. Screening for anal cancer precursors among patients living with HIV in the absence of national guidelines: practitioners' perspectives. Cancer Causes Control. 2019;30(9):989–96. [PubMed: 31302838]
5. Goldstone SE, Kawalek AZ, Goldstone RN, Goldstone AB. Hybrid capture II detection of oncogenic human papillomavirus: A useful tool when evaluating men who have sex with men with atypical squamous cells of undetermined significance on anal cytology. Dis Colon Rectum. 2008;51(7):1130–6. [PubMed: 18481150]
6. Wang CJ, Palefsky JM. HIV/AIDS-Associated Viral Oncogenesis [Internet]. Vol. 177. Springer International Publishing; 2019. 183–209 p. Available from: http://link.springer.com/10.1007/978-3-030-03502-0
7. Panel de expertos de GeSIDA. Guía de práctica clínica sobre los tumores no definitorios de SIDA e infecciones por el VIH. (Actualización marzo 2019) [Internet]. 2019. Available from: https://gesida-seimc.org/wp-content/uploads/2019/05/gesida_DC_TumoresNoDefinitorios_Marzo_2019_14_05_19.pdf
8. Revollo B, Videla S, Llibre JM, Paredes R, Piñol M, García-Cuyàs F, et al. Routine screening of anal cytology in persons with human immunodeficiency virus and the impact on invasive anal cancer: A prospective cohort study. Clin Infect Dis. 2020;71(2):390–9. [PubMed: 31504329]
9. The ANCHORstudy.org [Internet]. Treating Anal Cancer Precursor Lesions Reduces Cancer Risk for People with HIV: Groundbreaking National Clinical Trial Halted Due to Therapy's High Success Rates; 2021 Oct 7 [cited 2021 Nov 18]; 2 pages. Available from: https://anchorstudy.org/sites/default/files/newsletters/anchor_press_release_07oct202
10. The world factbook: Colombia [Internet]. [cited 2021 Jan 31]. Available from: https://www.cia.gov/the-world-factbook/countries/colombia/
11. Fondo Colombiano de Enfermedades de Alto Costo, Cuenta de Alto Costo [CAC]. Sitación del VIH/SIDA en Colombia, 2020 [Internet]. 2021 [cited 2021 Jul 3]. Available from: https://cuentadealtocosto.org/site/publicaciones/nueva-publicacion-situacion-del-vih-sida-2020/?1622137761444

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12. Mendoza MLR, Jacobson JO, Morales-Miranda S, Alarcón CÁS, Núñez RL. High HIV burden in men who have sex with men across Colombia's largest cities: Findings from an integrated biological and behavioral surveillance study. PLoS ONE. 2015;10(8):1–15.
13. World health organization, Global cancer observatory. Colombia Globocan 2020 [Internet]. 2021 Mar p. 2. Available from: https://gco.iarc.fr/today/data/factsheets/populations/170-colombia-fact-sheets.pdf
14. Álvarez C, Martínez E. Guía de práctica clínica (GPC) basada en la evidencia científica para la atención de la infección por VIH/Sida en adolescentes (con 13 años de edad o más) y adultos [Internet]. Ministerio de Salud y Protección Social. 2014. 46–47 p. Available from: http://gpc.minsalud.gov.co/gpc_sites/Repositorio/Otros_conv/GPC_VIH_adolescentes/GPC_Comple_VIHADULTOS_web.pdf
15. Harris PA, Taylor R, Minor BL, Elliott V, Fernandez M, O'Neal L, et al. The REDCap consortium: Building an international community of software platform partners. J Biomed Inform. 2019;95(May):103208. [PubMed: 31078660]
16. Centers for Disease Control. Revised Surveillance Case Definition for HIV Infection. Morb Mortal Wkly Rep. 2014;63(3):29–31.
17. Bean SM, Chhieng DC. Anal-rectal cytology: The other pap test. Lab Med. 2010;41(3):168–71.
18. Blair KJ, Martínez-Vernaza S, Ordóñez-Blanco IT, Hernandez W, Quiroga C, Lowenstein E, et al. Screening With Anal Cytology in Colombia: Initial Experience and Need for High-Resolution Anoscopy. J Surg Res. 2021 Nov;267:374–83. [PubMed: 34216798]
19. Cataño J, al E. Prevalencia de cambios en la citología anal de pacientes VIH positivos para y posibles factores de riesgo asociados Prevalence of anal cytology changes in HIV positive patients and possible associated risk factors. Infectio. 2006;10(4):214–9.
20. Boldrini NAT, Volpini LPB, De Freitas LB, Musso C, De Vargas PRM, Spano LC, et al. Anal HPV infection and correlates in HIV-Infected patients attending a sexually transmitted infection clinic in Brazil. PLoS ONE. 2018;13(7):1–14.
21. Gimenez F, da Costa-e-Silva IT, Daumas A, de Araújo J, Medeiros SG, Ferreira L. The value of high-resolution anoscopy in the diagnosis of anal cancer precursor lesions in hiv-positive patients. Arq Gastroenterol. 2011;48(2):136–45. [PubMed: 21709956]
22. Maia LB, Marinho LC, Wanderley Paes Barbosa T, Batalha Filho ES, Ribeiro Velasco LF, Garcia Costa PG, et al. A comparative study between conventional and liquid-based cytology in screening for anal intraepithelial lesions in HIV-positive patients: CONVENTIONAL AND LIQUID BASED CYTOLOGY. Diagn Cytopathol. 2014 Oct;42(10):840–5.
23. Conley L, Bush T, Darragh T, Palefsky J, Unger E, Patel P SM, Group SS. Incidence and Predictors of Abnormal Anal Cytology Findings Among HIV-Infected Adults Receiving Contemporary Antiretroviral Therapy. J Infect Dis. 2016;213(3):351–60. [PubMed: 26268855]
24. Rosa-Cunha I, Cardenas GA, Dickinson G, Metsch LR. Addressing anal health in the HIV primary care setting: A disappointing reality. AIDS Patient Care STDs. 2010;24(9):533–8. [PubMed: 20731611]
25. Apaydin KZ, Fontenot HB, Shtasel DL, Mayer KH, Keuroghlian AS. Primary Care Provider Practices and Perceptions Regarding HPV Vaccination and Anal Cancer Screening at a Boston Community Health Center. J Community Health. 2018;43(4):792–801. [PubMed: 29480339]
26. Siddharthan RV, Lanciault C, Liana V, Siddharthana RV, Lanciault C, Tsikitis VL. Anal intraepithelial neoplasia : diagnosis, screening, and treatment. Ann Gastroenterol. 2019;32(3):257–63. [PubMed: 31040622]
27. Gonçalves JCN, MacEdo ACL, Madeira K, Bavaresco DV, Dondossola ER, Grande AJ, et al. Accuracy of Anal Cytology for Diagnostic of Precursor Lesions of Anal Cancer: Systematic Review and Meta-analysis. Dis Colon Rectum. 2019;62(1):112–20. [PubMed: 30451747]
28. Palefsky JM. Practising high-resolution anoscopy. Sex Health. 2012;9(6):580. [PubMed: 23380236]
29. Daling JR, Madeleine MM, Johnson LG, Schwartz SM, Shera KA, Wurscher MA, et al. Human papillomavirus, smoking, and sexual practices in the etiology of anal cancer. Cancer. 2004;101(2):270–80. [PubMed: 15241823]

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30. Zhang X, Yu J, Li M, Sun X, Han Q, Li M, et al. Prevalence and related risk behaviors of HIV, syphilis, and anal HPV infection among men who have sex with men from Beijing, China. AIDS Behav. 2013;17(3):1129–36. [PubMed: 22076229]

31. Stewart DB, Gaertner WB, Glasgow SC, Herzig DO, Feingold D, Steele SR. The American society of colon and rectal surgeons clinical practice guidelines for anal squamous cell cancers (Revised 2018). Dis Colon Rectum. 2018;61(7):755–74. [PubMed: 29878949]

32. Van Schalkwyk C, Moodley J, Welte A, Johnson LF. Are associations between HIV and human papillomavirus transmission due to behavioural confounding or biological effects? Sex Transm Infect. 2019;95(2):122–8. [PubMed: 30171173]

33. Palefsky JM, Holly EA, J Hogeboom C, Ralston ML, DaCosta MM, Botts R, Berry JM, TMD N Jay. Virologic, Immunologic, and Clinical Parameters in the Incidence and Progression of Anal Squamous Intraepithelial Lesions in HIV-Positive and HIV-Negative Homosexual Men. J Acquir Immune Defic Syndr Hum Retrovirol. 1998;17(4):314–9. [PubMed: 9525431]

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Table 1:

Demographic and sexual health data for MSM with HIV screened with anal cytology

Variable	Overall N=211
Age (years)	
Mean ± SD	35.6 ± 11.0
Sexual Partners, n (%)	
Men	170 (80.6%)
Men & Women	41 (19.4%)
Education, n (%)	
University or Higher	120 (56.9%)
Technical College	54 (25.6%)
High School or Less	37 (17.5%)
Cigarette Smoking, n (%)	
Never	156 (73.9%)
Past	16 (7.6%)
Current	39 (18.5%)
Recent STI Diagnosis, n (%) [a]	
None	114 (54%)
Condyloma (penile or anal)	21 (10.0%)
Other STI [b]	81 (38.4%)
Syphilis	66 (31.3%)
Hepatitis B	8 (3.8%)
Hepatitis C	8 (3.8%)
Herpes	7 (3.3%)
Proctocolitis unspecified	4 (1.9%)
Urethritis unspecified	3 (1.4%)
Other	1 (0.5%)
Months since HIV Diagnosis	
Median [IQR]	21.9 [11.6–56.2]
CDC HIV Stage at Diagnosis, n (%)	
Stage 3	73 (34.6%)
Stage 2	107 (50.7%)
Stage 1	31 (14.7%)
Antiretroviral Therapy, n (%)	206 (97.6%)
HIV Viral Load [c]	
Detectable, n (%) [d]	81 (38.4%)
Median [IQR] [e]	354 [33–48,700]

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Variable	Overall N=211
CD4 Count (cells/μL) [c]	
Mean ± SD	430.0 ± 193.7
< 200 (categorized), n (%)	24 (11.4%)
Percent CD4 [c,f]	
Mean ± SD	25.6 ± 10.4
< 15% (categorized), n (%)	34 (16.3%)
CD4 Nadir (cells/μL)	
Mean ± SD	286.4 ± 171.4
< 200 (categorized), n (%)	62 (29.4%)

[a] Diagnosis in the 12 months prior to collection of anal cytology sample. Individual may have had more than one diagnosis

[b] Includes syphilis, hepatitis B, hepatitis C, herpes, proctocolitis unspecified, urethritis unspecified, other

[c] Laboratory data from six months before or after collection of anal cytology sample

[d] For the n=130 with undetectable viral load, the limit of detection was < 20 copies/ml for n=122, <40 copies/ml for n=1, and unknown for n=7.

[e] Median for those (n=81) with detectable viral load

[f] n=209; missing data from n=2

Abbreviations: MSM (men who have sex with men), SD (standard deviation), STI (sexually transmitted infection), HIV (human immunodeficiency virus), IQR (interquartile range), CD4 ($CD4^+$ T lymphocyte)

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Table 2:

Anal cytology and composite results

Grade [a]	Anal cytology result n (%)	Composite result [c] n (%)
Normal [b]	143 (67.8%)	143 (67.8%)
ASC-US	23 (10.9%)	23 (10.9%)
LSIL / cLSIL [d]	41 (19.4%)	39 (18.5%) [d]
HSIL / cHSIL [d]	4 (1.9%)	6 (2.8%) [d]

[a] Cytologic results follow the Bethesda System: atypical squamous cells of undetermined significance (ASC-US), low-grade squamous intraepithelial lesion (LSIL), and high-grade squamous intraepithelial lesion (HSIL).

[b] Includes those with inflammatory changes without evidence of neoplasia

[c] Composite result considers the highest result between anal cytology and tissue pathology.

[d] n=2 of those who had LSIL on anal cytology had subsequent resection of condyloma, with high-grade anal intraepithelial neoplasia (AIN) on pathologic analysis. These two individuals were thus re-categorized, from the composite LSIL (cLSIL) into the composite HSIL (cHSIL) group.

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Table 3:

Comparison of demographic and sexual health data between those with abnormal and normal anal cytology

Variable	Normal	Abnormal		p value		
	n=143	ASC-US / cLSIL [a] n=62	cHSIL [a] n=6	Overall [b]	Abnormal v. Normal [c]	cHSIL v. Other [d]
Age (years)						
Mean ±SD	36.0 ±11.2	34.8 ±10.9	32.0 ±7.8	-	0.361	0.425
Sexual Partners						
Men, n (%)	113 (79.0%)	52 (83.9%)	5 (83.3%)	0.712	0.410	0.862
Men and Women, n (%)	30 (21.0%)	10 (16.1%)	1 (16.7%)			
Education						
University or Higher, n (%)	76 (53.2%)	41 (66.1%)	3 (50.0%)	0.213	0.113	0.730
Cigarette Smoking						
Past, n (%)	10 (7.0%)	6 (9.7%)	0 (0%)	0.761	0.742	0.535
Current, n (%)	25 (17.5%)	12 (19.3%)	2 (33.3%)			
Recent STI Diagnosis [e]						
Condyloma, n (%)	13 (9.1%)	5 (8.1%)	3 (50.0%)	0.004	0.544	0.001
Other STI, n (%) [f]	48 (33.6%)	30 (48.4%)	3 (50.0%)	0.113	0.037	0.553
Months since HIV Diagnosis						
Mean ±SD	50.1 + 61.8	44.1 ±57.4	8.9 ±6.3	-	0.301	0.113
CDC HIV Stage at Diagnosis						
Stage 3, n (%)	44 (30.8%)	24 (38.7%)	5 (83.3%)	0.021	0.090	0.011
Antiretroviral Therapy						
Currently Taking, n (%)	141 (98.6%)	60 (96.8%)	5 (83.3%)	0.048	0.179	0.019
HIV Viral Load [g]						
Detectable, n (%) [h]	47 (32.9%)	30 (48.4%)	4 (66.7%)	0.039	0.017	0.148
CD4 Count (cells/μL) [g]						
Less than 200, n (%)	9 (6.3%)	11 (17.7%)	4 (66.7%)	<0.001	0.001	<0.001
Percent CD4 [g]						
Less than 15%, n (%)	14 (9.9%)	16 (25.8%)	4 (66.7%)	<0.001	< 0.001	0.001
CD4 Nadir (cells/μL)						
Less than 200, n (%)	36 (25.2%)	21 (33.9%)	5 (83.3%)	0.006	0.052	0.003

[a]Cytologic results follow the Bethesda System: atypical squamous cells of undetermined significance (ASC-US), low-grade squamous intraepithelial lesion (LSIL), and high-grade squamous intraepithelial lesion (HSIL). cLSIL and cHSIL refer to composite results, in which n=2 MSM were moved from the LSIL to the HSIL group after tissue pathology demonstrated high-grade anal intraepithelial neoplasia.

[b]Comparison across three groups: normal, combined ASC-US / cLSIL, and cHSIL

[c] Any abnormal anal Pap result (ASC-US, LSIL, or HSIL) compared against normal.

[d] cHSIL compared against all others (cLSIL, ASC-US and normal anal Pap results)

[e] Diagnosis in the 12 months prior to collection of anal Pap sample

[f] Includes Syphilis, Hepatitis B, Hepatitis C, Herpes, Proctocolitis unspecified, Ureteritis unspecified, Other. None of these individual infections was significant between groups; however, Syphilis (39.7% vs. 27.3%, p=0.069) and Hepatitis C (7.4% vs. 2.1%, p=0.062) tended toward higher rates in those with abnormal anal Pap results (ASC-US, LSIL, or HSIL) compared against those with normal results.

[g] Laboratory data from six months before or after collection of anal Pap sample

[h] Limit of detection was < 20 for n=122, <40 for n=1, and unknown for n=7.

Other Abbreviations: SD (standard deviation), STI (sexually transmitted infection), HIV (human immunodeficiency virus), CD4 ($CD4^+$T lymphocyte)

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Table 4:

Multivariable log-binomial logistic regression predicting abnormal anal cytology

Variable [a]	RR	95% CI	p value
Age [b]	1.00	[0.98–1.02]	0.899
Recent STI Diagnosis			
Other STI [c]	1.48	[1.03–2.12]	0.032
HIV Viral Load [d]			
Detectable [e]	1.37	[0.90– 2.09]	0.145
CD4 Count (cells/μL) [d]			
Less than 200	2.08	[1.16–3.73]	0.014
CD4 Nadir (cells/μL)			
Less than 200	0.93	[0.52–1.67]	0.817

[a] Variables which achieved a p-value of 0.05 or less on univariable analysis comparing abnormal v. normal anal Pap results were included in the model. Percent CD4 was not included given its co-linearity with CD4 count.

[b] Age was included as a confounder.

[c] Includes syphilis, hepatitis B, hepatitis C, herpes, proctocolitis unspecified, urethritis unspecified, Other

[d] Laboratory data from six months before or after collection of anal Pap sample

[e] Limit of detection was < 20 for n=122, <40 for n=1, and unknown for n=7.