




Original Article

Anal cancer screening in a high-risk behavior group: A local picture

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ABSTRACT

Study objectives: To perform anal lesion and anal cancer screening in men living with HIV/AIDS.

Methods: This is a descriptive, observational, cross-sectional study. Data were obtained from the Specialized Assistance Service (SAE) in Divinópolis, Minas Gerais. A sociodemographic, epidemiological, and sexual behavior questionnaire was applied; material was collected for cytology, high-resolution anoscopy (AAR) was performed, and an acceptability questionnaire applied.

Main results: Of the 50 men living with HIV/AIDS invited to participate in this study, 6% were excluded because they were illiterate, 40% refused to participate, and 54% participated in the survey. Among these, all answered the self-administered questionnaire. However, ten (37.0%) underwent proctological examination and anal cytology. Of these, two did not respond to the acceptability questionnaire. No anal lesions were identified during AAR and no biopsy was required. A 10% change in anal cytology was found.

Conclusions: Through the study it was possible to construct a flow of referrals from the SAE to the UFSJ Coloproctology outpatient clinic. Moreover, the existence of internal stigmas on the part of the participants regarding the proctological examination and the lack of information about anal cancer screening are challenges to be overcome.

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R E S U M O

Palavras-chave:

Câncer anal
 HIV, vírus da imunodeficiência humana
 HPV, papiloma vírus humano
 Rastreamento

Objetivos do estudo: Realizar o rastreamento de lesões anais e câncer anal em homens vivendo com HIV/AIDS.

Métodos: Trata-se de estudo descritivo observacional transversal, cujos dados foram obtidos no Serviço de Assistência Especializada (SAE) em Divinópolis, Minas Gerais. Foi aplicado questionário sociodemográfico, epidemiológico e de comportamento sexual; realizada coleta de material para citologia, Anuscopia de Alta Resolução (AAR) e aplicado questionário de aceitabilidade do exame.

Principais resultados: Dos 50 homens vivendo com HIV/AIDS convidados a participar do presente estudo, 6% foram excluídos por serem analfabetos, 40% se recusaram a participar e 54% participaram da pesquisa. Entre estes, todos responderam o questionário autoaplicado. Entretanto, 10 (37.0%) realizaram o exame proctológico e a citologia anal. Desses, dois não responderam ao questionário de aceitabilidade. Não foram identificadas lesões anais durante a AAR, não sendo necessária a realização de biópsia. Foi encontrado 10% de alteração à citologia anal.

Conclusões: Por meio do estudo foi possível construir um fluxo de encaminhamentos do SAE para o ambulatório de Coloproctologia da UFSJ. Ademais, a existência de estigmas internos por parte dos participantes no que concerne à realização do exame proctológico e a falta de informação a respeito do rastreamento do câncer anal são desafios a serem vencidos.

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Introduction

In the general population, anal cancer is relatively rare, accounting for 0.43% of all neoplasias and only 2% of malignant tumors of the digestive tract.^{1,2} The most prevalent type is anal squamous cell carcinoma (ASCC), which accounts for 85% of cases, followed by adenocarcinoma (10%) and other rarer types (5%).²

However, its incidence has increased by approximately 50% over the past 25 years,³ now estimated at 1.9:100,000 people/year in the general population.⁴ In Brazil, there are no specific data on the estimated incidence of anal cancer in the population⁵; however, 460 deaths due to this cancer were registered in 2017 in the country, a rate approximately six times higher than that of 1990 (74 deaths).⁶

When compared with at-risk groups, such as men living with human immunodeficiency virus (HIV) and men who have sex with men (MSM), this incidence is disproportionately higher.^{7,8} Studies from Europe and the United States demonstrated an increased incidence of anal cancer, with rates ranging from 75 to 137:100,000 people/year for MSM living with HIV/AIDS after the introduction of antiretroviral therapy (ART).^{8,9}

Historically, anal cancer was believed to develop as a result of chronic irritation of benign conditions such as hemorrhoids, fissures, and inflammatory bowel disease. However, as with cervical cancer, the association between the onset of ASCC and its precursor lesion (anal intraepithelial neoplasia [AIN]), and human papilloma virus (HPV) infection is well established in the literature.^{10–13} In these cases, the prevalence of HPV is 88.3% worldwide, with high-risk HPV-16 being the most common subtype.¹⁴

In addition to HPV infection, receptive anal intercourse is among the major risk factors for the development of AINs and consequently ASCC in individuals living with HIV/AIDS.¹⁵ Other factors include: lifelong sexual practice, smoking, CD4+ T lymphocyte count between 200 and 500 cells/mm³ or less than 200 cells/mm³, and presence of high-risk anal HPV.¹⁶

Some guidelines advocate anal cancer screening for high-risk populations such as MSM living with HIV/AIDS.¹⁷ However, the effectiveness of this screening is still questioned, and there are no formal recommendations to do so. A study comparing the cost-effectiveness of different forms of AIN screening reported that in MSM living with HIV/AIDS, direct use of high-resolution anoscopy (HRA) is a more cost-effective strategy when compared with anal cytology,¹⁸ which is not recommended as the single method of screening.¹⁹ Another study suggests the use of HRA combined with anal cytology, as these exams complement each other in the detection of anal cancer-related lesions.²⁰

Therefore, the present study aimed to analyze the prevalence and factors associated with anal cancer and its precursor lesions in men living with HIV/AIDS followed-up at a specialized public assistance service in the state of Minas Gerais, Brazil. A secondary goal was to provide routine diagnosis and prevention strategies to the service, in order to reduce the mortality and morbidity of this population.

Methods

This was a descriptive observational cross-sectional study conducted at the Specialized Assistance Service (SAE) of the city of Divinópolis, Minas Gerais, Brazil, from January 2018 to

January 2019. The target population consisted of male individuals living with HIV/AIDS followed-up at the SAE. Participants were selected from a convenience sample and recruited at the service's waiting room.

The inclusion criteria were men older than 18 years, known to be HIV-positive, using ART, followed-up at the SAE, who wished to participate in the study and signed an informed consent. The exclusion criteria were individuals with cognitive impairment who did not have the minimum autonomy required to participate in the research without the need for a companion, those who were illiterate, and those incarcerated.

For sample calculation, an estimated prevalence of 23.1% of anal lesions in men living with HIV/AIDS was considered.¹⁶ Considering the population of 823 men over 18 years of age followed-up at the SAE (information provided by the service in April 2017), a margin of error of 5%, a confidence interval of 95%, and considering possible losses, the ideal final sample was calculated at 313 participants.

Procedures

After participants were recruited, the informed consent was read and signed, and the following research steps were carried out: self-administered questionnaire, proctological examination, and application of a questionnaire regarding exam acceptability. The proctological examination consisted of the following steps: anal region inspection, anal cytology, digital rectal exam, 3% acetic acid test, HRA, and biopsy (when lesions were detected). All collected materials were sent for cytological and/or pathological analysis in a specific laboratory. Participants with anal alterations were referred for treatment at the UFSJ Coloproctology Outpatient Clinic, located at the Medical Specialties Center in partnership with the Municipal Health Department of Divinópolis.

Self-applied questionnaire

In a private environment, all participants answered the questionnaire on sociodemographics (*e.g.*, age, marital status, race, education, and income), sexual behavior (*e.g.*, sexual practices with men and women, age at first intercourse, condom use during anal intercourse, number of sexual partners, and whether they had a stable partner), and lifestyle data (*e.g.*, injecting drug use, current smoking or alcohol use, use of illicit drugs, use of sexual stimulants, and history of any sexually transmitted infection [STI]).

Proctological examination

Anal inspection: static and dynamic evaluation for assessment of anal border and/or perianal region lesions. Anal cytology: obtained through a cytobrush, inserted at least 3 cm into the anal canal, and removed by exerting slight pressure against the walls of the canal in a 360° rotation movement; three complete rotations were performed, so as to maximize the collection of cells representative of the entire circumference. The collected material was placed on a standard glass slide identified with the participant code and fixated. After lubricating the anal canal with 2% xylocaine gel and performing the digital rectal exam, a disposable plastic lubricated

anoscope was inserted to allow the insertion of a gauze soaked in 3% acetic acid solution. The anoscope was then removed and the gauze was left in the anal canal for 40 seconds to allow absorption of acetic acid by the anal mucosa. After removal of the gauze, the anoscope was reinserted and the HRA examination was performed.

HRA is a type of anoscopy performed with a colposcope, a device that magnifies images by six to 40 times, which allows the identification of perianal, anal, and rectal lesions with greater precision.²¹ Areas of the anal canal epithelium stained with 3% acetic acid (acetowhite areas) and with an appearance that raised the suspicion of dysplasia could be identified, such as the presence of vascular changes that may give a visual appearance of "fine stipples" or "rough dots" or "mosaic." These lesions were then biopsied and referred for anatomopathological examination.

Cytological evaluation was performed in a specialized laboratory and classified using the Bethesda criteria²² for cervical cytology as: (1) normal squamous, (2) atypical squamous cells of undetermined significance (ASCUS), (3) atypical squamous cells, (4) low-grade anal intraepithelial injury (LGAI), (5) high-grade anal intraepithelial injury (HGAI), or (6) insufficient material.

Local examination results

The researcher/examiner reported the presence or absence of complications, such as bleeding throughout the procedure, as well as the results obtained, on a specific form.

Acceptance questionnaire

Applied after the proctological examination, it consisted of a form intended for the participant to report possible discomfort, pain, or embarrassment associated with the examination.

Statistical analysis

Statistical analysis was performed using IBM SPSS v. 20.0 software. Categorical variables were described as absolute frequencies and percentages. When normally distributed, quantitative variables were described as mean \pm SD. When the variables were not normally distributed (verified by the Shapiro-Wilk test), they were described as medians (Q1; Q3). The significance level was set at 5%.

This study was approved by the Human Research Ethics Committee of the Universidade Federal de São João Del-Rei, Campus Centro Oeste Dona Lindu CEPES/CCO in November 2017, under CAAE: 78739717.5.0000.5545 and Opinion No. 2,403,969.

Results

Of the 50 men living with HIV/AIDS invited to participate in this study, three (6.0%) were excluded because they were illiterate and 27 (54.0%) agreed to participate. Among these, all answered the self-administered questionnaire, ten (37.0%) underwent the proctological examination and anal cytology, and eight (29.6%) answered the acceptance questionnaire. No

Table 1 – Selection of the main descriptive characteristics of the participants' sexual history.

Variables	n (%)
1. Sexual intercourse with women	
Yes	23 (85.2)
No	4 (14.8)
Total	27 (100.0)
2. Sexual intercourse with men	
Yes	17 (63.0)
No	10 (37.0)
Total	27 (100.0)
2.1 Number of steady male partners in the last year	
0	10 (58.8)
1 to 10	7 (41.2)
Total	17 (100.0)
2.2 Number of casual male partners in the last year	
0	8 (47.1)
1 to 10	8 (47.1)
21 to 30	1 (5.9)
Total	17 (100.0)
2.3 Number of hired male partners in the past year	
0	16 (94.1)
21 to 30	1 (5.9)
Total	17 (100.0)
2.4 Number of male partners throughout life	
1 to 10	7 (41.2)
11 to 20	3 (17.6)
21 to 30	1 (5.9)
More than 30	6 (35.3)
Total	17 (100.0)
2.5 Insertive anal intercourse in the last year	
Yes	10 (58.8)
No	7 (41.2)
Total	17 (100.0)
2.5.1 Condom use during insertive anal intercourse in the last year	
Most of the time	3 (30.0)
Rarely	1 (10.0)
Always	6 (60.0)
Total	10 (100.0)
2.6 Receptive anal intercourse in the last year	
Yes	8 (47.1)
No	9 (52.9)
Total	17 (100.0)
2.6.1 Condom use in receptive anal intercourse in the last year	
Most of the time	3 (37.5)
Rarely	1 (12.5)
Always	4 (50.0)
Total	8 (100.0)

anal lesions were identified during HRA and no biopsies were required.

The mean age of the research participants was 46 years. The 27 participants who answered the self-administered questionnaire were from cities in the state of Minas Gerais, and most of them were residents of Divinópolis (47.1%). Regarding marital status, 63% were single, 18.5% married, and 11.1% divorced; 3.7% of the participants were widowers and

Table 2 – History of sexually transmitted infection (STI).

Variables	n (%)
Has had an STI	
Yes	20 (74.1)
No	7 (25.9)
Ulcer or genital lesion	
Yes	10 (37.0)
No	15 (55.6)
I don't know	2 (7.4)
Ulcer or anal lesion	
Yes	4 (14.8)
No	22 (81.5)
I don't know	1 (3.7)
Genital warts	
Yes	3 (11.1)
No	20 (74.1)
I don't know	4 (14.8)
Anal warts	
Yes	7 (25.9)
No	17 (63.0)
I don't know	3 (11.1)
Genital herpes	
Yes	2 (7.4)
No	2 (7.4)
I don't know	23 (85.2)
Syphilis	
Yes	11 (40.7)
No	16 (59.3)
I don't know	0 (0.0)
Chancroid	
Yes	2 (7.4)
No	24 (88.9)
I don't know	1 (3.7)
Gonorrhea	
Yes	6 (22.2)
No	1 (3.7)
I don't know	20 (74.1)
Lymphogranuloma	
Yes	1 (3.7)
No	25 (92.6)
I don't know	1 (3.7)
Genital condyloma	
Yes	1 (3.7)
No	25 (92.6)
I don't know	1 (3.7)
Anal condyloma	
Yes	2 (7.4)
No	22 (81.5)
I don't know	3 (11.1)

3.7% were in a common-law marriage. Regarding education, most participants had completed elementary school.

Regarding sexual history (Table 1), most participants had had sexual intercourse with women (85.2%), and over 50% reported condom use as “most of the time or always” in both vaginal and anal intercourse. The mean age of first sexual intercourse with women was 16 years. Regarding the number of male partners, 58.8% reported having steady partners. A total of 47.1% of the participants reported receptive anal sex in the last 12 months. Condom use in both insertive and receptive anal intercourse was reported as “most of the time” by 30% and 37% of the participants, respectively.

Regarding the pathological history of STIs (Table 2), excluding HIV infection, most (74.1%) have had some infection

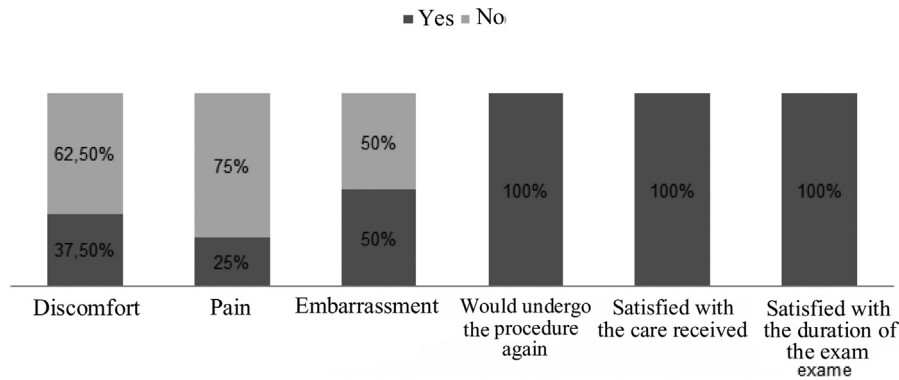


Fig. 1 – Acceptance of proctological examination.

throughout life; syphilis was the most prevalent. Regarding the participant's recognition of conditions affecting the anogenital region, 11% had "genital warts" and 14.8% were unable to report; in turn, 25.9% had "anal warts" and 11.1% were unable to report. Regarding the medical diagnosis of such conditions, 7.4% already had a diagnosis of anal condyloma, while 11.1% were unable to report.

Regarding the history of drug use, 22.2% smoked commercial cigarettes and 44.4% reported current use of alcohol. As for illicit drugs, the use of marijuana in the last 12 months (18.5%) and at some point (37.0%) was noteworthy.

Regarding the history of HIV infection, 35.5% of participants acquired the virus during sexual intercourse with men. Other reported forms were sexual intercourse with women (35.5%), injection drug use (9.7%), blood transfusion (3.2%), occupational accident (3.2%), and oral sex (3.2%); 9.7% were unable to report. Regarding the year of diagnosis of HIV/AIDS, 40.7% had been diagnosed for over ten years.

As for HPV vaccination, 85.2% reported not being vaccinated. The main reason given by the participants was the lack of knowledge about the existence of this vaccine and its importance for patients living with HIV/AIDS.

A total of 81.5% of participants had never consulted a coloproctologist. Of the 14.8% who had consulted, 33.3% reported the presence of an HPV lesion as the reason.

During the proctological examination there was no bleeding, no biopsies were necessary, and no changes suggestive of HPV infection were observed. One participant (10.0%) presented alterations in anal cytology classified as ASCUS.

Regarding the acceptance questionnaire (Fig. 1), all participants reported that they would perform the proctological exam again if necessary.

Discussion

Most participants were single, sexually active middle-aged men who reported condom use in most cases of intercourse. Regarding the pathological history, a predominance of syphilis as the main STI was observed, as well as a significant percentage of reported anal warts. Most participants had not been vaccinated against HPV and were unaware of the vaccine.

The fact that some participants did not know whether they already had anal condyloma reflects the lack of health educa-

tion and information on the subject, which negatively impacts prevention strategies. The lack of knowledge about the HPV vaccine may also be a reflection of this failure, since most participants were unaware of its existence and had never been advised about its importance. Currently, the indication of HPV vaccine for boys and men living with HIV/AIDS aged 9 to 26 years old, provided their CD4+ T lymphocyte count is >200 cells/mm³, is well-established in the literature for primary prevention of anal cancer, penile cancer, and other HPV-related conditions.^{23,24}

Most participants had never consulted a coloproctologist, which may indicate a difficulty in access to these professionals and a prejudice regarding proctological examination. Moreover, this prejudice also appears to have influenced the high rate of refusal to participate in the present study. This internalized stigma among participants is also indicated as a barrier in studies that followed the same methodology.^{25,26}

The acceptability questionnaire indicated that 62.5% of the participants did not feel discomfort during the exam, which corroborates data found in the literature describing high tolerability between MSM and men living with HIV/AIDS, especially at the time of performing HRA.²⁷⁻²⁹

All participants reported that they would undergo the proctological examination again if necessary. One study obtained similar results: 100% of patients who completed their survey stated that they would return for a follow-up HRA if recommended.²⁷ These factors are important considerations for the caregivers of these patients, particularly during pre-procedure counseling.²⁷⁻³⁰

According to the present data, HIV transmission occurred mainly through sexual intercourse, and 40.7% had more than ten years of infection. The natural history of anal dysplasia in the HIV-positive population is known to present a faster progression from LGAI to HGAI in these patients when compared with the general population; the rate of progression from HGAI to ASCC at five years is also higher.³¹

In the collected cytological samples, one alteration was observed and classified as ASCUS. This finding in anal cytology should serve as a warning sign for better follow-up of these patients, as it presents a 46% to 56% risk of HGAI on biopsy.³² As a result, this participant was referred for correct propaedeutic and therapeutic follow-up.

The lack of a multidisciplinary care of patients living with HIV/AIDS, together with the need for participants to travel to the reference center in the Midwestern macroregion of Minas Gerais, where the research was conducted, limited the execution of the research steps.

The study reached only 16% of the ideal sample, which made it impossible to analyze the prevalence and factors associated with anal cancer and its precursor lesions in men living with HIV/AIDS. Nevertheless, it was possible to create a flow of referrals from the Specialized Assistance Service to the UFSJ Coloproctology Outpatient Clinic, offering appropriate support to this group with high-risk behavior, as well as fostering the beginning of a multidisciplinary awareness of the subject and its importance as a prevention strategy.

Conclusion

This study raised important considerations on the current panorama of anal cancer prevention. The high percentage of refusals to participate can be explained by the lack of information about the relevance of this pathology in the study population, as well as the existence of internal stigmas regarding the proctological examination. Public health management must focus on social groups that exhibit high-risk behaviors in order to meet their specific demands.

Conflicts of interest

The authors declare to have no conflicts of interest.

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