

Anal Canal Cancer Screening: Integration of Evidence

Anal canal cancer screening has evolved from a controversial hypothesis to a practice focused on high-risk groups in the last decade. The clinical trial Anal Cancer/ High-Grade Squamous Intraepithelial Lesion (HSIL) Outcomes Research Study (the ANCHOR study) demonstrated that treating anal HSIL reduces anal cancer incidence by more than 50%, thereby solidifying the rationale for structured programs.¹ In 2024, the consensus of the International Anal Neoplasia Society (IANS) published the first global guideline with explicit recommendations on who, when, and how to screen for anal cancer.² Subsequently, other clinical guidelines from the American Society for Colposcopy and Cervical Pathology/National Institutes of Health (ASCCP/ NIH) and performance studies supported the inclusion of anal cytology, high-risk human papillomavirus (HPV) DNA genotyping test (specifically HPV 16), and high-resolution anoscopy (HRA) for diagnostic confirmation, in addition to the Digital Anorectal Examination (DARE), as simple and low-cost measures.³⁻⁵

From a biological perspective, the natural history of anal cancer parallels that of cervical cancer: oncogenic HPV integrates into the host cell and promotes the overexpression of oncoproteins E6/E7, favoring cellular transformation and the progression of precursor lesions to squamous cell carcinoma – the predominant subtype (85%) – coexisting with less frequent subtypes, including adenocarcinoma, melanoma, lymphoma, gastrointestinal stromal tumor (GIST) and neuroendocrine tumors.^{6,7}

The global incidence remains lower than 2/100,000 person-years; however, it is on the rise in several countries and age groups.⁸ In Brazil, the actual magnitude is uncertain due to the aggregation of anal cancer with colorectal tumors in the information registries, which suggests an underestimation. A study conducted in Northeastern Brazil observed a 12% anal cancer prevalence in women with cervical neoplasia.⁹ Furthermore, evidence points to an increasing mortality trend and underreporting due to coding issues and unequal access.¹⁰

The primary risk-factors for anal canal cancer, irrespective of the gender, include age over 40 years, smoking, immunosuppression (including HIV infection and organ transplantation), sexual practices with increased mucosal exposure, and anogenital warts. Among women, these include a history persistent high-risk cervical HPV, HSIL, cervical cancer, and vulvar cancer.^{11,12}

The IANS consensus categorizes risk-groups and recommends anal cancer screening for HIV-positive transgender women aged ≥ 35 years; for men who have sex with men (MSM) regardless of HIV status, and HIV-positive women aged ≥ 45 years; for transplant recipients starting 10 years post-transplant; and for those with a history of HSIL/vulvar cancer starting one year after diagnosis.²

The best practices for anal canal cancer screening vary according to the healthcare setting, target population, and available resources. The DARE is useful for the early detection of masses and tumors, although it has low sensitivity for HSIL, but high specificity when performed by trained examiners.¹³ Anal cytology is the most widespread technique, with high sensitivity (70% to 90%) and moderate specificity (40% to 65%) in high-risk populations. Both conventional cytology and liquid-based cytology (LBC) are used for screening anal precursor lesions. However, LBC reduces the rate unsatisfactory of samples and permits the performance of the polymerase chain-reaction (PCR) test for HPV and other biomarkers.⁵

High-risk HPV PCR with genotyping (particularly HPV 16) offers the highest sensitivity and the best risk stratification, and when associated with immunohistochemistry using p16/Ki-67, this combination may increase specificity.¹⁴ It is worth noting that the anal self-collection for HPV emerges as a viable alternative



to expand coverage in people who are reluctant to undergo examinations.¹⁵ The HRA-guided biopsy is considered the diagnostic gold standard for anal HSIL; however, it requires expertise and appropriate outpatient setting structure.²

The prognosis for anal cancer is generally favorable and improves with early detection, with an overall 5-year survival rate of approximately 70%, which is higher for localized disease. However, the stage at diagnosis is the most critical factor, with survival diminishing if the cancer involves regional lymph nodes (58 to 61%) or distant organs (30 to 36%).

In conclusion, in settings with limited HRA availability, a phased protocol is recommended: this involves initially integrating DARE into routine practice; adopting cytology and/or high-risk HPV testing with HPV 16 genotyping, based on laboratory capacity, and establishing referral pathways for HRA. Policy formulation requires acknowledging underreporting, improving surveillance and information recording systems and prioritizing professional training.

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