A Surgeon's Role in Preventing Anal Squamous Cell Carcinoma

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Introduction

Anal squamous cell carcinoma (ASCC) is a rare malignancy that accounts for just 1–2% of digestive tract tumours. However, its incidence has increased in recent years, particularly among certain high-risk groups [1–3]. In Europe, anal cancer is diagnosed in approximately 2000 men and 2300 women each year, and mortality has risen steadily over the past few decades as well. The 3.1% annual increase recorded from 2001 to 2016 reflects an upsurge in both new cases and patients with more advanced disease at presentation [4]. Five-year survival rates have varied regionally, ranging from 66% in Central Europe to 44% in Eastern Europe.

Following Goldstone's earlier editorial, "*Anal Cancer Prevention: Solving the Puzzle Piece by Piece*" [5], new evidence may guide us toward a viable strategy for prevention, early diagnosis, and treatment of ASCC to help curb current incidence and mortality trends going forward. The surgeon's role is pivotal in this regard, spanning the entire diagnostic and therapeutic spectrum, including follow-up initiatives. Although the treatment of choice for ASCC is chemoradiation (CRT), there is still a possibility of surgery for a number of reasons. Local excision is indicated for Stage I tumours (<2 cm, no lymph node or distant metastases), whereas abdominoperineal resection is the primary treatment option for CRT-ineligible patients [2]. The latter also serves as a salvage procedure following failed CRT or in cases of persistent or recurrent disease. Furthermore, obstructive symptoms, incontinence, pain, or bleeding before or during CRT may call for a diverting stoma. Despite these efforts, ASCC carries a poor prognosis. Therefore, the present discussion is principally focused on the surgeon's role in prevention and early diagnosis.

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Recent guidelines issued by the International Anal Neoplasia Society (IANS) [6] offer a robust preventive framework, specifying screening protocols and therapeutic directives for precancerous anal lesions and identifying two relevant population categories. Category A includes individuals at the highest risk of developing ASCC, such as anyone living with human immunodeficiency virus (HIV)—especially men having sex with men, transgender women, and men having sex with women—women with histories of high-grade squamous intraepithelial lesions (HSILs) or vulvar cancers, and solid-organ transplant recipients, all of whom stand to benefit significantly from strategies for early intervention (between the ages of 35 and 45 years). Category B pertains to others afflicted with persistent human papillomavirus (HPV 16), cervical or vaginal HSILs, autoimmune diseases, or perianal warts. Given their comparatively lower collective risk for ASCC, screening may be achieved through shared patient and doctor decision-making.

Screening and Early Detection

Early detection of HSIL is crucial for ASCC prevention. Biopsy under high-resolution anoscopy (HRA) is now considered the gold standard for diagnosing anal intraepithelial neoplasia (AIN), which encompasses HSIL [6]. The HRA benchmark offers enhanced visualisation, using high magnification level and acetic acid or Lugol's iodine to pinpoint tissue abnormalities. Surgeons can thus observe more subtle lesions that may evade detection (Fig. 1) by standard anoscopy or cytology. HRA improves diagnostic accuracy and promotes timely HSIL detection as a result [6]. Unfortunately, its use outside larger hospitals and research facilities duly engaged in such activities is greatly hindered by the need for specialized equipment and proficiency training [6,7].

Targeted Treatments for HSIL

Once HSIL is confirmed, the timing of surgical intervention is critical to prevent progression to ASCC [8]. The Anal Cancer HSIL Outcomes Research (ANCHOR) trial [8] has shown that in individuals living with HIV, a program of regular screening for HSIL, that is coupled with targeted

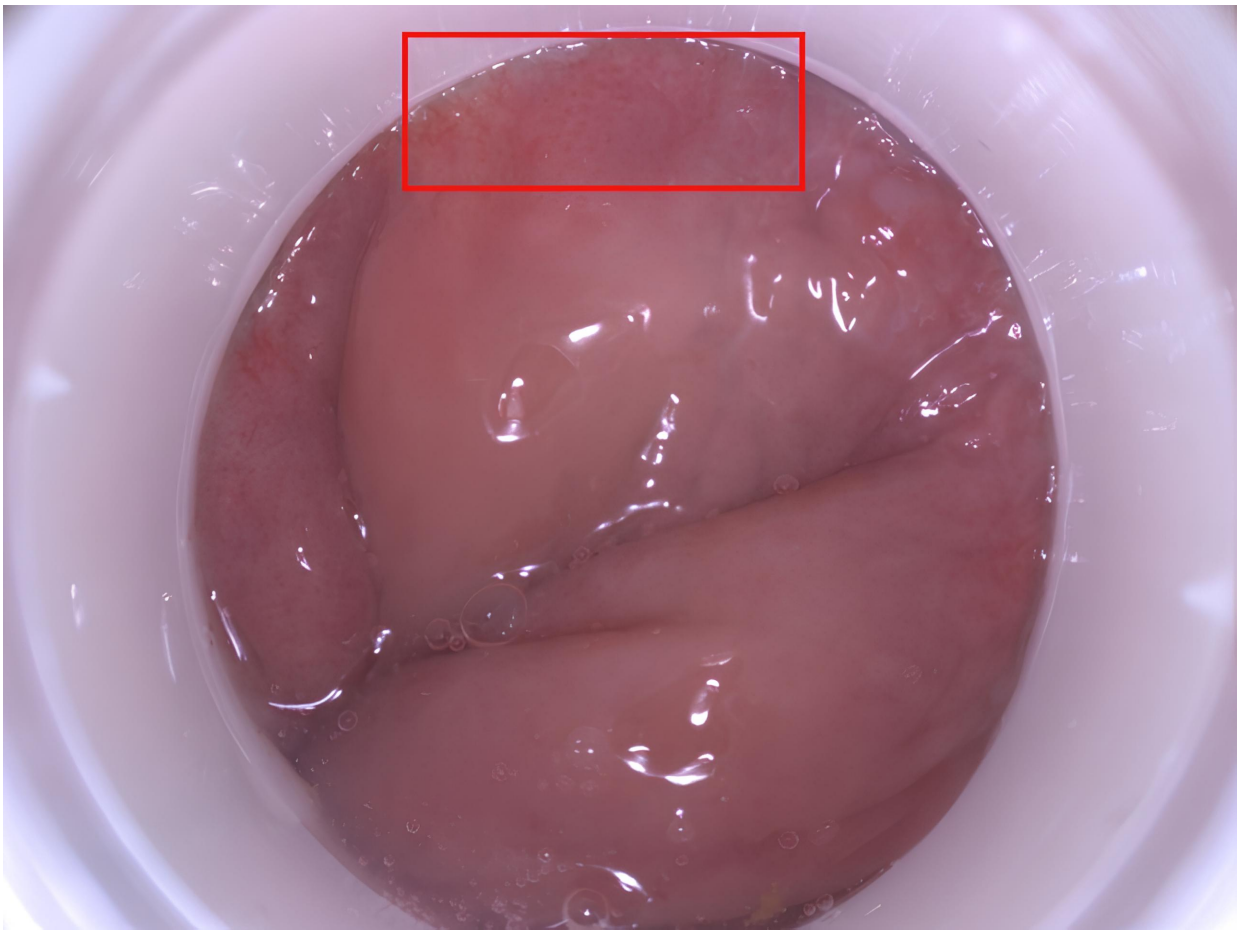

Fig. 1. View during high-resolution anoscopy (inset) showing highlighted area (red box) histologically confirmed as high-grade squamous intraepithelial lesion. The picture was taken at Luigi Sacco Hospital and the patient's consent was obtained for its use.

treatment reduces the chance of progression to invasive carcinoma by 57%. Electrocautery, radiofrequency ablation (RFA), and laser therapy are some of the measures commonly applied by surgeons to remove or obliterate HSIL [9]. Techniques of this sort are minimally invasive and are known to limit morbidity while effectively eradicating precancerous lesions.

Electrocautery, for example, has proven effective in treating HSIL, although recurrence rates remain a concern [10]. Similarly, RFA has emerged as a promising alternative, with reportedly high eradication rates (up to 58.3%) in immunocompromised patients and even greater success achieved through treatment combinations [11,12]. Study outcomes suggest that circumferential RFA may reduce the risk of metachronous occurrences by eliminating occult dysplasia or lesions missed during HRA. Based on available data, the CO_2 laser is another tool for effectively ablating precancerous lesions [13]. The concentrated beam of light emitted vaporises targeted HSILs, leaving surrounding healthy tissue largely intact. This type of laser treatment is particularly favoured for its precision and control over depth of tissue penetration, rendering it quite useful in sensitive areas like anal canal.

Post-treatment recurrences of HSIL are problematic in this setting and require ongoing surveillance [11]. The rates depend on treatment modality and patient population. Surgeons not only perform initial ablation procedures, but also play key roles in follow-up care, conducting repeat HRA exams and biopsies as warranted to document and treat recurrent or metachronous lesions.

Multidisciplinary Care

The complexity of ASCC prevention often requires multidisciplinary support, seeking out infectious disease experts, surgeons, oncologists, and gynaecologists for consultations. High-risk patients no doubt benefit from the coordinated acts of surgical and infectious disease specialists that ensure timely screenings and interventions. This collaborative model of care is paramount in reducing ASCC-related morbidity/mortality, incorporating specific skills and insights of contributors across various fields.

In summary, the surgeon's role in managing ASCC broadly includes surgical procedures and collaborations with other healthcare providers, so that screenings, interventions, and follow-up events are properly timed and executed. By adopting new diagnostic and therapeutic modalities for

high-risk sectors, surgeons are better equipped to treat precancerous anal lesions effectively, ultimately easing the burden of ASCC. A comprehensive and multidisciplinary approach may afford the best means to substantially curtail this challenging malignancy and improve at-risk patient outcomes.

Availability of Data and Materials

All experimental data included in this study can be obtained by contacting the corresponding author if needed.

Author Contributions

AM, GZ and AB contributed to the design of the manuscript. AM and GZ contributed to the drafting of the manuscript. AB supervised and reviewed the work. All authors contributed to important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest. Anna Maffioli and Andrea Bondurri are serving as the Editorial Board of this journal. We declare that Anna Maffioli and Andrea Bondurri had no involvement in the peer review of this article and have no access to information regarding its peer review.

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