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Chinese expert consensus on diagnosis and treatment of anal intraepithelial neoplasia

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INTRODUCTION

Anal high-grade squamous intraepithelial lesion (HSIL) refers to the precancerous lesions of anal squamous cell carcinoma (ASCC). Anal cancer is often asymptomatic in its early stage, and most of the disease is found in advanced stage with poor prognosis. In recent years, the incidence of anal cancer has been increasing worldwide,[1–3] drawing more attention to the precancerous condition of anal intraepithelial neoplasia (AIN). Screening methods for anal cancer include digital anorectal examination (DARE), anal cytology, high-risk human papillomavirus (HPV) testing and high-resolution anoscopy (HRA). HRA, in particular, has significantly improved the detection rate of high-grade AIN, enhancing the ability of trained physicians to identify the disease.

Unlike the well-established screening system for cervical cancer, relevant research and clinical practice regarding anal precancerous lesions only witness a relatively short time on a global scale, and there is no unified diagnostic and treatment standard for anal precancerous lesions domestically and internationally. In recent years, guidelines for the diagnosis and treatment of HPV-related anogenital lesions have been introduced in the USA, Europe and other regions,[4–6] and the International Anal Neoplasia Society (IANS) has also released the first HRA screening consensus.[7] However, China has not issued any relevant guidelines and consensus. In clinical practice, many physicians, including gastroenterologists, surgeons and gynaecologists, still have misconceptions about the diagnosis and treatment of AIN, and there is a lack of consensus on the screening of anal cancer and its precancerous lesions. Additionally, many patients are asymptomatic or only exhibit non-specific symptoms, leading to clinical oversights, missed diagnoses and misdiagnoses. Therefore, it is urgent to further understand and standardise the diagnosis, treatment and comprehensive management of AIN to achieve early detection and treatment, thus reducing the incidence of anal cancer.[8–11]

ANAL ANATOMY AND AIN NOMENCLATURE

The anus consists of the anal canal and the perianal region. The anal canal can be defined from the perspectives of embryology and functional morphology as the anatomical anal canal and the surgical anal canal, with the latter being defined according to the widely accepted definition proposed by the American Joint Committee on Cancer. The surgical anal canal begins at the distal end of the rectum, corresponding to the apex of the anal sphincter complex, where the squamous epithelium of the anal canal merges with the perianal skin. The length of the anal canal is approximately 3.5–5 cm in males, which is slightly shorter in females. The perianal region starts from the anal verge, which is the junction between the anal canal epithelium and the skin covered with hair, and extends outward to a circumferential area of 5 cm. The proximal part of the anal canal is lined with columnar epithelium of the rectal mucosa, while the perianal region is covered by stratified squamous epithelium. The area between the original squamocolumnar junction beginning from the dentate line and the physiological squamocolumnar junction where columnar epithelium transformed into squamous epithelium is known as the anal transformation zone (AnTZ).[12]

In 1981, Fenger and Nielsen first proposed the term 'anal dysplasia'. In 1986, Fenger and Nielsen recommended adopting the term

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'AIN' parallel to cervical intraepithelial neoplasm (CIN), with AIN1, AIN2 and AIN3 representing the progression of the disease from mild intraepithelial lesions to severe lesions. In 2012, the American Society for Colposcopy and Cervical Pathology recommended a unified naming system for anogenital lesions, replacing AIN1 with 'low-grade squamous intraepithelial lesions' and AIN2 and AIN3 with 'HSILs'.[13] However, currently, both naming methods are still used concurrently in clinical practice worldwide.

EPIDEMIOLOGY OF AIN

In the general population, the incidence of anal cancer is relatively low. Among them, the most common type is ASCC, accounting for approximately 85% of anal cancer cases. Over the past decade, there has been a significant increase in the incidence and mortality rates of anal cancer. According to the Global Cancer Statistics Report 2018, there are over 35 000 new ASCC cases worldwide each year, with an annual increase in incidence rates of 2–3%,[1 7] and an average annual increase in mortality rates of about 3%. Reports from China indicate that the mortality rate of anal cancer increased by 5.51% from 1990 to 1992 to 2004–2005.[1–3] The estimated incidence rate of AIN in the general population is less than 0.1%. However, there is evidence that the incidence of AIN is increasing due to changes in lifestyle and behaviour. Anal cancer peaks in individuals over the age of 70 years, while the incidence of AIN is higher among those under the age of 60 years. Several studies conducted abroad have shown that the incidence rate among female patients is approximately 1.5–2 times higher than that among male patients,[14–17] while recent reports from the Chinese population suggest a slightly higher proportion of male patients compared with female patients.[13 17]

AETIOLOGY OF AIN

AIN, CIN and vulvar intraepithelial neoplasm (VIN) share significant similarities in terms of aetiology. However, compared with CIN and VIN, there is currently limited understanding of the natural course of AIN, and the prospective data are scarce. Recent studies have shown that approximately 90% of anal cancer cases are associated with HPV infection, especially HPV types 16 and 18.[1 2] However, the probability of developing anal cancer is lower than that of developing cervical cancer for individuals with HPV infection, and the exact reasons for this are not fully understood. It may be due to the lower susceptibility of the anal region to malignant transformation based on persistent HPV infection compared with the cervix. Research indicates that concurrent CIN can be found in 0.2–10.5% of female patients with AIN, and 7~20% of female patients with CIN3 may have concomitant AIN. More than half of women with multisite intraepithelial neoplasia in the genital tract may have associated anal lesions.[18]

HPV infection in the low genital tract is believed to spread directly to adjacent areas, which can extend from the external genitalia to the perianal and anal regions. Anal intercourse is a common mode of transmission, but it is not the only form of transmission. Sexual activities other than anal intercourse and HPV shed from other surfaces of the genital organs can also cause autoinoculation. Other high-risk factors for AIN include men who have sex with men (MSM), HIV infection, HPV-related lower anogenital tract lesions, solid organ transplantation (especially kidney transplantation), autoimmune diseases (such as systemic lupus erythematosus), immunosuppressive states or undergoing immunosuppressive therapy, smoking, etc. In the aforementioned high-risk populations, the incidence of AIN is significantly higher than in the general population. For example, the incidence rate of anal cancer in MSM populations can reach 40/100 000, and the incidence rate of AIN in HIV-positive MSM can range from 26% to 89%.[1] Other risk factors include chronic irritation, such as haemorrhoids, fissures and anal fistulas.[2 3]

CLINICAL PRESENTATION

Medical history

When the presence of AIN is suspected, relevant risk factors must be considered when collecting the medical history. These factors include sexual behaviour and orientation, smoking history, history of genital warts, history of solid organ transplantation, history of autoimmune diseases, history of immunosuppression or undergoing immunosuppressive therapy, etc. For individuals with HIV infection, the severity of the disease, such as CD4 count, should also be assessed. Additionally, attention should be paid to the possibility of concomitant HPV-associated lower genital tract lesions, including vulvar, vaginal or cervical precancerous lesions with suspected anal involvement (especially in cases of extensive vulvar lesions), which should alert clinicians to the possibility of concomitant anal disease.[8 14–17]

Symptoms and signs

AIN can be asymptomatic or present with mild symptoms. A study on female AIN in China showed that the majority of patients (85.9%) were diagnosed with anal abnormalities during gynaecological examinations or routine physical examinations. Symptomatic patients may present as anal itching, anal secretions, burning sensation, anal irritation, anal bleeding, etc.[10] For patients with suspected AIN, a comprehensive examination of the perianal region, anal canal and perineum is necessary. The lesions are often multifocal. Perianal lesions may resemble vulvar lesions, while anal canal lesions often require HRA for examination. The following signs indicate the presence of AIN: raised or white hyperkeratotic plaques, eczema, fissures, hyperpigmentation or erythema, ulcers, anal excrescences, hypopigmentation of the anus, etc. In the case of anal genital warts, the lesions can range from

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scattered small papules to large cauliflower-like lesions. It should be noted that before any AIN examination, DARE must be performed to rule out the possibility of anal cancer or pelvic masses.

SCREENING AND DIAGNOSIS OF AIN

Screening for anal cancer is currently in its early stages. However, with the increasing incidence of anal cancer and AIN among high-risk populations, the necessity for screening for anal cancer has been highlighted, with the aim of preventing invasive anal cancer and reducing its incidence and mortality. Current research data are insufficient to support routine screening for anal cancer in HIV-negative populations with normal sexual behaviour and immunity, but screening for anal cancer is considered necessary for high-risk populations such as HIV-infected individuals and MSM.[4] High-risk populations for anal cancer screening include: (1) HIV-infected individuals; (2) long history of anal sex, such as MSM; (3) extensive precancerous lesions of the lower genital tract (including the vulva, cervix, vagina, etc); (4) organ transplant recipients; (5) autoimmune diseases (such as systemic lupus erythematosus, etc); (6) patients in the immunosuppressive state or receiving immunosuppressive therapy.[7]

Screening methods for AIN include DARE, anal cytology, anal HPV testing, etc. The diagnosis of AIN is based on a high index of suspicion for symptomatic high-risk patients, such as those with a history of anal intercourse or itching, as well as on histological examination of suspicious areas through biopsy. Among them, histological examination of biopsy specimens under HRA guidance is considered the gold standard for diagnosis.

Digital anorectal examination

DARE is an important component of anal cancer screening and is often performed after anal cytology collection and before HRA. All patients with suspected AIN should undergo DARE, especially those suspected of having invasive cancer. The goal of DARE is to evaluate palpable abnormalities, including suspicious masses, ulcers, warts, nodules, and areas of discomfort or pain. Starting from the rectum, the entire anal canal, internal anal sphincter and distal anal canal mucosa are comprehensively palpated, followed by a comprehensive examination of the perianal area, which is correlated with a visual inspection. DARE can be used in combination with other screening methods or as a standalone test, particularly in regions where anal cytology or HRA is not available. It may discover early invasive cancers without clinical symptoms and is a cost-effective and resource-saving screening tool.

Anal cytology

The purpose of anal cytology is to obtain epithelial cells from the entire surface of the anal canal, including epithelial cells from the distal end of the rectum to the anal margin, the keratinised and non-keratinised parts of the AnTZ and the anal canal, and the cells hidden in folds and crevices of the anal epithelium. Anal cytology collection requires the insertion of a swab into the anal canal about 5–7 cm, rotating the swab 360° in a circular motion, and the collection process usually takes 10–20 s. Due to the inability to directly visualise the anal canal during sample collection, there may be greater sampling errors compared with cervical cytology, which limits its effectiveness as a screening method for AIN. Therefore, according to the IANS quality control standards, a sufficient anal cytology examination should contain at least 2000–3000 cells, or 1–2 nucleated squamous epithelial cells visible per high-power field (HPF) in thinpreps, or 3–6 nucleated squamous epithelial cells visible per HPF in SurePath preparations; technically, unsatisfactory anal cytology samples should be less than 5% in high-risk populations (such as HIV-positive MSM) and less than 15% in low-risk populations (such as HIV-negative women).[4 10]

Anal HPV testing

HPV infection is the most important risk factor for AIN, especially HPV types 16 and 18. Therefore, similar to cervical cancer screening, the role of HPV testing in the early detection of anal precancerous lesions is relatively certain. The sample collection method is similar to the above anal cytology collection method, and the testing method is consistent with cervical HPV testing. However, due to the high infection rate of HPV in high-risk populations, there is some uncertainty for HPV testing in screening for anal cytology and triaging mild dysplastic cells, and more evidence-based studies are needed to further confirm its effectiveness in AIN screening.

High-resolution anoscopy

HRA is a specialised endoscopic technique for examining the anal canal and the surrounding area of the anus. It uses a high-resolution double-lens colposcope to magnify tissue under the lens by 25–40 times and uses reagents such as acetic acid and iodine to aid in the examination. It observes subtle changes in the anal mucosa and blood vessels to detect AIN and ASCC at an early stage. Currently, HRA is recognised as the gold standard for AIN diagnosis.[12]

Indications for HRA examination

Indications for HRA examination include: (1) anal cytology abnormalities (atypical squamous cells of undetermined significance or above); (2) anal high-risk HPV positivity (such as HPV types 16 and 18); (3) suspected precancerous lesions of ASCC, including those that involve the anus and are suspected to be related to vulvar, vaginal or cervical precancerous lesions, especially in cases of extensive vulvar lesions; patients with significant clinical symptoms such as anal itching, erosion, condyloma, mass, anal bleeding, obvious internal and external anal growths, history of anal and rectal malignancy, as well as other symptoms that cannot be explained by routine anal examination; (4) other special reasons, such

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as when forensic evidence is required, especially in cases of suspected child sexual abuse.[7]

Referring physicians for HRA are not limited to gynaecologists, but can also include dermatologists, proctologists, venereologists and other specialists.

HRA examination method

1. Patient position: any position can be used, such as left or right lateral position, prone position or lithotomy position. Most patients and examiners prefer the left lateral position.
2. Anaesthesia method: depending on the patient's condition, anaesthesia may not be necessary, and local anaesthesia may be administered to sensitive patients. Anorectal biopsy above the dentate line does not require anaesthesia; local anaesthesia with lidocaine gel, spray or injection of 1~2% lidocaine is required for distal rectal and perianal biopsies.
3. Examination equipment: HRA requires a higher magnification than a vaginal speculum and should be magnified at least 25 times. Therefore, a vaginal speculum magnified only to 10 times cannot be used for HRA. Since a direct-view vaginal speculum is not ergonomically designed and is difficult to use for HRA, a vaginal speculum with an angled eyepiece is required. Disposable or non-disposable anoscope can be used. Small biopsy forceps with a mouth opening of ≤3 mm, such as infant Tischler or otolaryngology throat forceps, can be used for biopsies. Other instruments are similar to vaginal speculum examination.
4. Examination steps: after lubricating the anus, insert the anoscope into the anus, remove the anoscope obturator and insert a cotton swab previously soaked in 3–5% acetic acid and wrapped in gauze. Remove the anoscope, leaving the cotton ball or gauze wrapped in place. Allow the acetic acid to soak into the anal epithelium for 1–2 min. Remove the cotton swab or gauze and reinsert the anoscope obturator; remove the obturator again for examination. For perianal acetic acid testing, a gauze block soaked or a large cotton swab coated with acetic acid can be used for at least 1 min. Keratinised epithelial cells require longer to absorb acetic acid. Lugol's solution can be used to help differentiate high-grade and low-grade lesions, but it can mask the edges of lesions previously identified with acetic acid.[7 12] Throughout the HRA examination, the examiner should continuously move the vaginal speculum to maintain a fixed focus. The recommended duration for HRA operation is 5–15 min; the proportion of patients feeling pain should be ≤10%, and those with significant bleeding should be ≤10%.[7]

HRA terminology

Satisfactory HRA examination includes visualisation of the entire anus, including the entire anal canal from the squamocolumnar junction (SCJ) at the distal edge of the rectum, the AnTZ, the distal end of the anal canal, the anal verge and the perianal region. SCJ refers to the area where the anal squamous epithelium and rectal columnar epithelium meet, and AnTZ is the area where different stages of squamous metaplasia can be observed.

Location description can be done using the 'eight-quadrant method' or the 'clock method' with the posterior aspect of the anus being 12 o'clock, following the convention used in colorectal surgery, but the patient's position must also be documented. In addition, the relationship between the lesion and the SCJ, mid-anal canal, distal anal canal and perianal region must be recorded to describe its location in the anal canal.

Lesion terminology should be described as adequate or inadequate (and the reason for this), and SCJ visibility as complete, partial or absent, to provide an overall assessment. For abnormal HRA findings, the site of the lesion, lesion size (number of quadrants involved, percentage of the anal canal affected), lesion colour and lesion-specific description should be recorded.[7] The lesion-specific description should include colour, contour, surface morphology, edge, vascular pattern, iodine staining and some unique HRA terms such as epithelial honeycomb and tortuous vessels.[7]

HRA-guided biopsy

All patients with visibly abnormal lesions under microscopy should undergo a biopsy. For small or homogeneous lesions, a single-point biopsy can be performed, while for multifocal or extensive lesions, multiple biopsies are recommended. For rectal biopsies, small biopsy forceps should be used to minimise the risk of bleeding and infection. Most post-biopsy bleeding can be stopped by applying pressure for 3 min or using Monsel's solution or silver nitrate. Electrocoagulation hemostasis can be considered for patients with large amounts of continuous bleeding. Minor bleeding and a sense of defecation are common after the procedure, and anal intercourse should be avoided for at least 1 week.[7]

Requirements for HRA operators

Experienced senior colposcopists (specialised in colposcopy for more than 5 years) should form the basis of HRA operators. They should receive professional HRA training (>1 year) and obtain qualifications. Based on the IANS standards, a proficient HRA operator should independently perform HRA on at least 50 cases annually (recommended number: ≥100 cases) and diagnose at least 20 cases of HSIL per year (recommended number: ≥50 cases).[7]

Quality control requirements for HRA

The proportion of the entire SCJ, AnTZ, distal rectum and perianal area that can be fully observed should exceed 90%; the insufficient biopsy rate (including reasons such as insufficient depth, biopsy samples from the colon or absence of tissue in the sample, making it impossible for the pathologist to identify the grade of squamous epithelial lesions) should less than 10%; for cases whose cytological results indicate HSIL but HSIL is not found

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histologically, more than 90% of patients should undergo a repeat HRA examination within 6 months.[7]

Differential diagnosis of AIN

Perianal AIN needs to be differentiated from lichen sclerosis, simple lichen, flat lichen, faded keratosis, genital warts, skin vegetations, flat condyloma (secondary syphilis), infectious soft warts, common warts, molluscum contagiosum, etc. Anal canal AIN often requires examination under HRA to be detected and differentiated from anal squamous cell hyperplasia, leukoplakia, condyloma, physiological papillae, rectal polyps, rectal stenosis (congenital developmental anomalies or post-treatment changes), erosion, ulceration, early infiltrating carcinoma of the anus, etc.

The appearance of low-grade and high-grade AIN in immature AnTZ under HRA is often difficult to distinguish. The thickness of the acetic acid-white epithelium, and vascular changes including punctuation, mosaic and characteristic striate vessels, all aid in the detection of AIN. Lugol's iodine staining helps to determine the boundaries of the lesions. Brittle and elevated or ulcerative lesions combined with atypical vascular changes are suggestive of early infiltrating carcinoma of the anus, and large or multiple biopsies are indicated at the site of the lesion.[7]

TREATMENT AND MANAGEMENT OF AIN

The primary objectives in treating AIN are to reduce symptoms and prevent progression to anal cancer. Currently, there is no unified consensus on the treatment of AIN, both domestically and internationally. Due to the rare rapid progression of AIN1 and AIN2 to AIN3 or invasive cancer, conservative approaches are often recommended, similar to the management of low-grade cervical and vulvar lesions.[19] AIN3 carries a significant risk of progression to invasive cancer; thus, active management of AIN3 is recommended. However, for individuals with HIV infection and MSM, the principles of management may differ due to their higher risk of progression and recurrence.[20–25]

Treatment principles

For individuals with AIN1 or AIN2 diagnosed through HRA-guided biopsy, a follow-up examination is recommended after 6 months. The follow-up assessment may include anal cytology, anal HPV testing, DARE, HRA and other evaluations to comprehensively assess the condition of anal and perianal lesions. If persistent AIN is present, ablative surgery or medical treatment can be considered.[4–6 20–23]

For individuals with AIN3 diagnosed through biopsy, a multidisciplinary consultation and pathology review are recommended to confirm the diagnosis. For HIV-negative individuals or those not engaged in male–male sexual behaviour, if the lesion is localised and involves less than 30% of the perianal skin/anal canal, local excision with the marking of the boundaries is recommended. If the lesion is multifocal and involves more than 30% (circumference), marking the boundaries and excising the most severe area are suggested. Ablative therapy can also be considered for individuals with good compliance during follow-up. If invasive cancer is suspected, surgical excision should be the preferred option.[4–6 20–23]

For individuals engaged in male–male sexual behaviour, HIV testing should be conducted. For HIV-positive individuals with localised symptomatic lesions, excision and a 6-month follow-up are recommended. If the lesion is multifocal and involves more than 30%, the use of imiquimod with a 6-month follow-up should be considered.[4–6 20–23] A recent multicentre prospective randomised controlled phase III trial conducted in 4459 HIV-infected individuals with anal HSIL confirmed a 57% reduction in the risk of progression to anal cancer in those treated with ablation, excision or local use of fluorouracil or imiquimod compared with the observation group.[26] Therefore, treatment for individuals with HIV infection and anal HSIL is necessary.

Choice of treatment methods

Observation

Evidence suggests that the likelihood of AIN progressing to cancer is very low in immunocompetent males and females. Overly aggressive surgical treatment for AIN can result in high recurrence rates. Therefore, cautious 6-month follow-up observation is recommended when a biopsy confirms AIN1/2.[4 6 20–23]

Ablative therapy

Prior to ablative therapy, an HRA-guided biopsy must be performed to rule out the presence of invasive cancer. Ablative methods that can be used for treating AIN include CO_2 laser vaporisation, cryotherapy, electrocautery and infrared coagulation.[4–6 20–23] CO_2 laser vaporisation is an effective method for removing localised lesions. Similar to the treatment of vulvar lesions, it is advisable to leave epithelial bridges between laser-treated areas to facilitate skin regeneration when treating anal lesions. Recurrence often stems from persistent HPV infection, and in some cases, ablative therapy may not completely eliminate the lesions due to the deep involvement of perianal skin and appendages by AIN. During treatment, it is important to preserve the submucosal layer to avoid the risk of scar contraction or anal stenosis. In cases of circumferential lesions in the anal canal, a sufficient number of 'epithelial islands' should be preserved, or a two-stage segmented treatment approach can be considered. Care should be taken to avoid tissue damage around the rectal glandular ducts. Both cryotherapy and electrocautery treatments may be partially effective, but both methods can be associated with high recurrence and incidence rates. In addition, the depth of penetration in cryotherapy is often difficult to control. Infrared coagulation therapy has been used since the 1990s. However, this technique is associated with a high rate of persistent

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disease and significant postoperative pain, often requiring multiple treatments. Further long-term trials are needed to determine its role in the ablative treatment of AIN.[27]

Pharmacological treatment

Due to the potential of severe adverse reactions and the high risk of recurrence, pharmacological treatment is generally considered as an alternative treatment option for certain cases of AIN.[4–6 20–23] Imiquimod has potent antitumour and antiviral activity and promotes an inflammatory response through various subcellular pathways. However, it is not suitable for lesions in the anal canal, the side effects are obvious and the recurrence rate is high. For warts, 0.5% podophyllotoxin solution or gel, 15% tea polyphenol ointment and other topical agents can be tried. Currently, there are no approved topical medications for the anal mucosa, and it is challenging for patients to self-administer various topical formulations (creams, ointments, solutions).

Photodynamic therapy

Photodynamic therapy is a painful and multiple-session treatment method and is an alternative option for AIN treatment. It is contraindicated in persons allergic to photosensitisers.[4–6 20–23] There is a lack of large-scale and long-term clinical evidence to prove its effectiveness. The high cost of photodynamic therapy partly limits its application.

Surgery

Management mode: the patients were referred to the anorectal surgery department, and the multidisciplinary comprehensive management mode was adopted in combination with the surgery department.

Local surgical excision: local excision can be used for AIN3 lesions involving less than 30% of the perianal skin or the anus. The defect can be closed primarily or left for secondary healing. It is recommended marking the surgical boundaries before the procedure, and written or image documentation of the biopsy site is required. Extensive local excision can also be performed for extensive AIN3 lesions to facilitate observation of residual lesions. Surgical techniques can use a surgical knife, fine diathermy needle, CO_2 laser excision or a combination thereof.[4–6 20–23] Extensive surgical excision: multifocal epithelial neoplasia involving the perineum and anus requires extensive surgery, including definitive vulvar and perineal excision combined with skin grafting and local flaps for vulvar reconstruction. This often requires staged surgeries to achieve the goals of disease elimination, symptom alleviation, functional preservation and attempted restoration of normal anatomy. This procedure is associated with significant trauma, and there is a lack of evidence regarding its definitive efficacy. However, it allows for an ample amount of lesion tissue for pathological analysis to exclude invasive cancer. Attention should be paid to preserving the skin during surgery to avoid anal stenosis. The use of flaps is an optional approach for skin defect reconstruction but not mandatory.[4–6 20–23]

Follow-up

Patients with AIN have a lifelong risk of recurrence or progression, and long-term close follow-up is needed to prevent the occurrence of invasive cancer. In particular, for AIN2/3, subsequent follow-up is mandatory as the natural course of the disease is still unclear.[4–6 20–23]

In terms of low-grade AIN1, if there is a good response to treatment and no new lesions occur, follow-up visits should be scheduled at 6 and 12 months after the initial treatment, followed by annual regular follow-up visits. For recurrent cases, follow-up every 3–6 months is recommended for at least 12 months, followed by annual regular follow-up visits. For patients with immunodeficiency or HIV-positive status, due to the increased risk of recurrence and HPV-related cancer, follow-up visits every 3–6 months are advised, and lifelong follow-up is recommended. For high-grade lesions AIN2/3, in the absence of recurrence, follow-up visits every 6 months are recommended for at least 5 years. In patients with immunodeficiency and HIV-positive status, follow-up visits every 3–6 months (intervals depending on individual symptoms) are advised, and lifelong follow-up is recommended.[4–6 20–23]

PREVENTION OF AIN

Currently, there is a lack of early screening methods for anal lesions and treatment strategies for anal HSIL. Therefore, primary prevention through HPV vaccination becomes even more important.[4–6] The existing bivalent, quadrivalent and nonavalent HPV vaccines can prevent AIN and anal HPV infection. Therefore, vaccination is recommended for eligible females and males. At present, the indicated population of HPV vaccine does not include males in China, but clinical trials of domestic and imported vaccines in males have been carried out.

Early screening is also crucial due to the rare rapid progression of AIN1 and AIN2 to AIN3 or invasive cancer. The existing research data are insufficient to support routine anal cancer screening in HIV-negative individuals with normal sexual behaviour. However, anal cancer screening is considered necessary for high-risk populations such as HIV-infected individuals and MSM.

SPECIALTY POSITIONING AND CLINIC SETTING RECOMMENDATIONS

Specialty positioning and clinic setting

It is recommended performing HRA procedures in the gynaecology clinic, preferably within the colposcopy examination room. The HRA examination should be conducted by experienced colposcopists who have received HRA training, and they should undertake the HRA examination and make a diagnosis and treatment. Integration with cervical cancer prevention and control is advised.

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Specialty management model

The specialty positioning should be under the jurisdiction of departments such as gynaecology, cervical disease specialty (colposcopy), dermatology, colorectal surgery, gastroenterology, pathology and sexually transmitted disease. A multidisciplinary comprehensive management model should be adopted. For example, patients with indications of HRA are referred to the colposcopy room. Patients with surgical indications are referred to the department of surgery. Patients with indications for ablation treatment are referred to the gynaecological or cervical disease centre.

Clinical referral directions

Referrals can be made to gynaecologists, dermatologists, colorectal surgeons, gastroenterologists and specialists in sexually transmitted diseases. Patients with indications for HRA examination should be uniformly referred to colposcopy physicians for HRA.[7]

CONCLUSIONS

Currently, the overall duration of AIN-related research and clinical practice worldwide is still relatively short, and clinical practices in most countries and regions are still in the early stages. According to statistics, there are less than 50% of HRA practitioners worldwide. Particularly in China, due to economic constraints and limited promotion efforts, there are not many medical institutions and clinical doctors capable of conducting HRA examinations. Many misconceptions still exist in the diagnosis and treatment of anal AIN in clinical practice. This consensus aims to standardise the diagnosis, treatment and comprehensive management of AIN in China, enhance the unified understanding of AIN and ultimately reduce the incidence of anal cancer.

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