Cancer National Specialist Advisory Group

Position Statement for Management of Anal Cancer

Summary of recommendations and perspective for Wales

Published 2014
Acknowledgments

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- Andrew Radcliffe (Retired Consultant surgeon and QA Bowel Screening Services)
- Members of Cancer National Specialist Advisory Group and Colorectal MDTs across Wales.
- Louise Hanna (Consultant Oncologist, Velindre NHS Trust and Chair of Cancer NSAG Gynae subgroup).

The drafting and consultation process is described in Appendix 8

Contacts

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Background

The Association of Coloproctology of Great Britain and Ireland (ACPGBI) published a position statement in 2011 for management of anal cancer, which covers staging, pathology, and management of local disease relapse.

This document has been drafted by the colorectal subgroup of the Cancer NSAG in response to the ACPGBI publication. Its purpose is to (i) summarise the recommendations within the position statement for ease of reference by multidisciplinary teams (MDTs) managing anal cancer; (ii) to update the position statement with recent advances (e.g. staging) and (iii) provide recommendations for patient follow up and data collection in Wales, areas not explicit in the ACPGBI statement.

The overarching aim of this document is to improve the quality of care for patients with anal cancer in Wales. It provides MDTs with a summary of the available evidence, and will be of relevance to Local Health Boards (HBs) and Service Commissioners in planning delivery of services for this rare malignancy.

Executive Summary

Management of Anal Intraepithelial Neoplasia (AIN) is hampered by a lack of understanding of its natural history. It is recommended that an all-Wales database is established. A suggested minimum dataset for AIN is included (appendix 2). All cases of AIN III should be discussed at network MDT (2 D).

A clinical dataset for anal cancer was recommended by the 2006 Wales anal cancer audit and would facilitate audit and recruitment to clinical trials (3). A minimum dataset for anal cancer is provided for discussion/implementation (appendix 3).

1 The Level of Evidence is given where possible using Oxford Centre for Evidence-based Medicine 2011 classification; see footnote on page 5 for abbreviations.
All patients should be staged by clinical examination, CT thorax/abdomen and pelvis and pelvic MRI (3 D). Endoanal ultrasound may also be appropriate in selected cases (p5).

Combination chemoradiotherapy is the treatment of choice for anal cancer (1 P). Local excision (T1 disease) and primary surgery may be appropriate in certain circumstances (p6).

Patients at high risk of local disease relapse are defined as T4 stage, fistulation, age >75, HIV-positive, immunosuppression and anal adenocarcinoma (3). It may be appropriate for high risk patients (approx 5 new cases per anal MDT per year) to have intensive follow up by central anal cancer MDT providers (2;TB) (p6).

Variation in follow up strategy after definitive treatment was evident following a survey of the 3 anal cancer MDTs in Wales (appendix 5). An evidence based recommendation for follow up is presented for discussion (3 P) (appendix 7).

High rates of salvage surgery after chemoradiotherapy are encouraged and can be delivered through centralised MDT care. Plastic reconstructive surgery at the time of salvage surgery is considered the norm (2 P). A single specialised centre providing salvage surgery per network or region is appropriate (p8).
Introduction

Anal cancer is a rare malignancy representing 2 per cent of all gastrointestinal cancers, although the incidence is thought to be increasing. In 2011 the ACPGBI published a Position Statement for the management of anal cancer to update and expand upon the 2007 ACPGBI guidance\(^2\). The document presented here is a Position Statement for local discussion and interpretation; it does not constitute Guidelines or Practice Parameters. Where “should” or “could” are used, these indicate a declining strength of recommendation. The document summarises the recommendations of the ACPGBI Statement and discusses application of the recommendations on an all-Wales basis. The Level of Evidence is given where possible (Oxford Centre for Evidence-based Medicine 2011 classification; see footnote for abbreviations\(^2\)\(^3\)).

Management of Anal Intraepithelial Neoplasia (AIN)

The prevalence of AIN is unknown and the natural history poorly understood compared with CIN or VIN. The risk of progression of AIN to invasive cancer approximates to 10 per cent at 5 years\(^4\)\(^5\) (3 P).

AIN III should be considered separately to AIN I/II in terms of progression to invasive disease, management and follow up (see appendix 1). Similarly multifocal disease and AIN in the context of HIV and/or immunosuppression require special consideration\(^6\) (3 P).

Cases of AIN III should be discussed at a specialised anal cancer MDT to ensure correct diagnosis and to determine management. These cases benefit from review by more than one histopathologist due to the high interobserver variation of micro-invasive disease\(^7\) (2 D). Each MDT should consider centralisation of AIN III cases to one or two colorectal surgeons per region with an expressed interest in this disease with appropriate support. There is no role for anal cytology, anal colposcopy or screening at the present time.

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\(^2\) Levels of Evidence suffix guide: P=Prognosis; D=Diagnosis; TB=Treatment Benefit; TH=Treatment Harms
Management should be expectant rather than attempting to eradicate disease through radical excision/ ablative therapies\textsuperscript{8} (3 P). A suggested approach for this expectant management is outlined in Appendix 1\textsuperscript{9}.

AIN I and II is managed expectantly with 12 monthly follow up\textsuperscript{10} (4)

AIN III should have disease extent defined through anal mapping biopsies\textsuperscript{11} (3). Exclusion of vulval and cervical disease (VIN/CIN) by a gynaecologist is a minimum standard.

Women with AIN III should have 12 monthly cervical examination (colposcopy rather than smear cytology) as part of follow up\textsuperscript{12} (4 P). This should be done by local arrangement with gynaecology rather than through Cervical Screening Wales.

HIV positive patients should have 6 month follow up as the risk of recurrence and progression is higher than HIV negative cases\textsuperscript{13} (3 P)

Collaboration with local GUM and HIV clinicians is recommended in areas with large AIN practices by local arrangement.

An all-Wales AIN database should be established to determine incidence, prevalence, natural history and practice to inform commissionaires. The database should be populated by new pathological diagnoses of AIN through CANISC. A minimal dataset would be required along similar lines to anal cancer with standardised proforma-based pathological reporting. Suggested fields are shown in Appendix 2\textsuperscript{14}. Dependent on patient numbers, as informed by improved data collection, a centralised or supra-regionalised model of management of AIN III is likely to be required.

Imiquimod is a nucleoside analogue that holds promise in the treatment of AIN, particularly multifocal disease or disease in the context of HIV\textsuperscript{15} (3 P). Due to a lack of definitive evidence for its efficacy it is recommended to be used only within a clinical trial setting. The use of HPV immunotherapy is limited to phase II/III trials presently.
Anal Cancer: Pathology, Staging, Minimum Data Set (clinical and pathological)

The definition of the anal canal for purposes of staging should be standardised. The surgical definition is most widely accepted *ie* anorectal junction to nonkeratinised squamous epithelium \(^{16}\). Distinction between anal canal and margin is important for treatment and outcomes.

The term ‘SCC’ covers all histological variants of SCC of the anal canal\(^{17}\).

Most anal cancers are staged clinically with emphasis on tumour size as opposed to a pathologically oriented TNM system based on depth of invasion. Lymph node status determines prognosis and recurrence\(^{18}(2)\) and is established by clinical examination, biopsy and CT.

Tumour size, persistent disease (positive biopsies <6 months after CRT) and positive lateral margins are adverse prognostic parameters after salvage surgery\(^{19}(2)\).

A clinical dataset for anal cancer is urgently needed to reduce variation in data quality as recommended by the 2006 audit of anal cancer in Wales \(^{20}(3)\). This would require addition of fields to CANISC. A suggested proforma is in appendix 3.

Pathological reporting following salvage surgery is not yet standardised, but development of a minimum dataset for anal cancer is due for publication by the Royal College of Pathologists. This dataset should be used by all pathologists reporting such specimens.

**Anal Cancer MDT**

Both NICE and the ACPBG&I recommend that each cancer network establishes a single specialised anal cancer MDT\(^{21}\). The National Cancer Standards for Colorectal Cancer Services require that this implemented, however these were written at a time when three Cancer Networks were extant in Wales. Decisions regarding the site/s where surgery is performed lies with planners and commissioners who can base their decisions on case volume, audited outcomes and clinical governance.
Each Anal Cancer MDT should be composed of no more than 2 clinical oncology core members and 2 consultant surgical core members performing anal cancer surgery. Additional MDT members are a urologist and a gynaec-oncologist with experience in multivisceral resection, a reconstructive plastic surgeon, a core pathologist experienced in anal cancer, 2 core radiologists with experience in anal cancer and a clinical nurse specialist.

Anal canal cancers should be clinically staged using the 7th edition of AJCC (appendix 4). Anal margin cancers should continue to use the 6th edition of AJCC as the 7th edition categories are not applicable to anal margin SCCs. It is not known whether this distinction is made in Wales anal cancer reporting. Tumour location (canal or margin) should be clearly stated on imaging requests to allow the correct AJCC edition to be used for radiological reporting.

All patients should have local staging in the form of MRI of the pelvis and distant metastases assessed by CT of thorax, abdomen and pelvis.

The use of endoanal ultrasound is appropriate only in early (T1-T2) cancers.

Newly applied staging modalities- update from 2011 ACPGBI Statement

PET-CT may have a role in distinguishing indeterminate lesions on CT/MRI and to exclude distant disease prior to salvage surgery. In line with updated NCCN recommendations PET/CT can be considered in the workup of anal canal cancer (but not anal margin cancer) and should be considered for treatment planning (3 D). PET/CT is not currently recommended for the assessment of local treatment response.

Sentinel lymph node biopsy (SLNB) in anal cancer is technically feasible and may avoid unnecessary groin irradiation in early stage disease. The current literature is limited to small case series. SLNB is currently under evaluation through clinical trials and cannot be recommended at present.
Local excision of T1 anal margin tumours is a treatment option but surgical margins must be free of cancer and nodal disease excluded\textsuperscript{26}. Limitations of this approach may be a higher recurrence rate which should be discussed with the patient.

Pre-treatment colostomy may be indicated for pain, incontinence or fistulation\textsuperscript{27} (2). A low rate of closure of temporary colostomies is observed which reflects its use in advanced disease\textsuperscript{28} (3).

The MDT should be used to recruit patients to suitable trials and permit clinical audit. This has administrative implications and would require a prospective patient database (see appendix 3).

**Staging and Management of Inguinal Lymph Nodes**

All patients should have staging of inguinal lymph nodes by clinical examination and radiology with ultrasound guided biopsy of suspicious nodes\textsuperscript{28} (4).

The best modalities for increasing detection of occult inguinal metastases appear to be PET-CT\textsuperscript{29} and sentinel node biopsy\textsuperscript{30}, although the latter technique is not in routine use (3 D).

Non-involved nodes at presentation can be managed by a watch and wait policy in T1/T2 tumours as an alternative to prophylactic irradiation\textsuperscript{31} (4 P).

Synchronously involved inguinal lymph nodes may receive treatment by RT boost to the groins\textsuperscript{32} (2,TB), however this is a controversial area and a subject for future research.

Residual or recurrent groin nodal disease after RT should be treated by block dissection\textsuperscript{33} (3,TB).

Metachronous nodes can be treated by RT or block dissection depending on the clinical context.
Chemoradiotherapy in anal cancer

Chemoradiotherapy in accordance to the ACT-II protocol (5-FU and mitomycin C in combination with 50.4cGy radiotherapy) is considered to be the current standard of care (2,TB). It is recognised that patients with reduced performance status and medical co-morbidities may not tolerate this regime and dose reduction or radiotherapy alone may be more appropriate at the discretion of the responsible oncologist (4, TB).

Whilst combination chemoradiotherapy will be the treatment of choice for the majority of patients it is recognised that primary surgery may be necessary in certain circumstances eg history of prior pelvic irradiation, sepsis, fistulating disease, etc.

Renal function and performance status should be assessed before treatment with mitomycin C or cisplatin (4,TH)

A minimum dose of 50.4cGy in 28 fractions over 5.5 weeks is recommended for local control. There is no evidence for dose escalation in T3/4 tumours. Planned gaps in RT treatment should be avoided (2;TB). 30Gy may be used in frail patients with T1/T2 tumours at the expense of higher recurrence rates.

5-FU and mitomycin C is recommended over 5-FU and cisplatin (1,TB). There is no present role for neoadjuvant chemotherapy outside of clinical trials (2,TB).

Patient participation in clinical trials is to be encouraged.

There is an international and national drive towards improved quality radiotherapy planning to reduce acute and late toxicity. This will be implemented through the addition of intensity modulated radiotherapy (IMRT or similar) on a network basis.

Follow up

Regular follow up is necessary to identify patients with locoregional persistent disease or failure in order to offer salvage surgery. Strategy depends of risk of recurrence and treatment intent.
Each MDT should review their follow up protocols in the light of emerging evidence and participate in clinical trials.

Follow up strategy should be intensified in those deemed at high risk for local relapse if medically fit for salvage surgery. Close follow up is necessary in the first 3 years to detect locoregional failure\(^{42}\) (4 P).

‘High risk’ for local disease relapse is defined as: T4 stage, carcinoma with fistula, age \(>75\), HIV-positive and immunosuppressed patients, anal adenocarcinoma\(^ {43}\).\(^ {3}\)

It may be appropriate for high risk patients (approx 5 new cases per anal MDT per year) to be followed up by core members of the anal MDT who provide salvage surgery to permit timely intervention. Serial digital examination by the same individual is to be recommended\(^ {44}\).

The optimum timing of initial assessment of response to chemoradiotherapy is debated, but is widely performed at 6-12 weeks post-treatment in phase III trials\(^ {42}\) (1 D). Too early an assessment may lead to an erroneous diagnosis of treatment failure. Tumour regression can occur up to 6 months following completion of treatment\(^ {38}\) (2;TB).

Core anal cancer MDT members from North, South West and South East Wales were invited as part of this review to detail current follow up strategy. The results are summarised in appendix 5; there is significant variation in frequency of clinical and radiological follow up which reflects the lack of substantial evidence base.

The ACPGBI guidance follows ACT-II recommendations for frequency of clinical follow up. Physical examination in ACT-II was 2-monthly in the first year, 3-monthly in year two and 6-monthly in years three to five, regardless of risk group.

ACT-II recommended a single CT scan at 6 months for all patients. Low risk patients may not need centralised follow up. Such patients should not have further imaging after the 6 month assessment in keeping with ACT-II protocol. High risk patients would benefit from locoregional imaging beyond this single 6 month scan. ACPGBI recommend 6 monthly pelvic MRI for 3 years and CT thorax, abdomen and pelvis at 6 months then annually for the first 3 years in high risk cases (see appendix 7 for follow up recommendation)\(^ {1\,38\,44}\).
Distant metastasis is uncommon. There is no effective treatment for distant metastases from anal cancer at present. It is not clear if imaging beyond 6 months is of clinical benefit in this regard.

Use of PET-CT for follow-up purposes should be restricted to excluding metastatic disease prior to salvage surgery outside of a clinical trial.

Histological proof of local disease failure should be obtained prior to salvage surgery.

No recommendation is made regarding nature of follow up following salvage surgery.

**Management of Local Disease Relapse**

Up to 25% of patients after chemoradiotherapy will have local disease relapse (3 P). Protocol driven follow up at a dedicated anal cancer unit is recommended to permit timely detection of patients requiring salvage surgery (appendix 7).

Centralised MDT care delivers a higher rate of salvage surgery (>70%) than multicentric care (50%, 46 47 2;TB. Hence all patients with local disease relapse should be evaluated through a central anal cancer MDT.

A standardised pathological reporting system should be encouraged

**Delivery of salvage surgery**

Routine use of primary perineal reconstruction using autologous tissue is now considered the norm as part of salvage surgery for anal cancer following radiotherapy because of the high rate of perineal wound failure if plastic reconstructive surgery is not performed (37%, 3,TB).

Radical abdominoperineal excision in this setting should be performed by an experienced anal cancer surgical team which includes tissue reconstruction by a plastic surgeon with an expressed interest as part of the anal cancer MDT (3).

Considering the relatively small numbers of patients requiring salvage surgery (11 patients in 8 years in the Swansea series 51 4,TB) and given the almost universal
need for plastic surgical reconstruction it is logical for this expertise to be
conzentrated in supra-regional referral units. Patients in the North Wales network
who require salvage surgery are currently referred to the Christie Hospital in
Manchester. Similarly a single site in the South Wales Cancer Network is
appropriate, considering population size and the relatively small number of cases
requiring this type of specialised multidisciplinary surgery.

Audit standards

The audit standard for those with local disease relapse being offered salvage
surgery should exceed 60% (IIb).

The audit standard for delayed perineal healing with plastic reconstruction is
<25% (III)

Major (non-wound) morbidity after salvage surgery should be <30% (III)

The audit standard for the proportion of patients achieving local pelvic disease
control after salvage surgery is >50% (IIb)

The audit standard for 5 year post-salvage survival is >40% (IIb)

Periodic evaluation against standards should be undertaken through the anal
cancer MDT.

Actions arising:

Implementation of both AIN and anal cancer minimum data sets is imperative to
establish current practice and provide a basis for audit. A clinical minimum
dataset is suggested as the basis for this and is for discussion. It should be
explored whether CANISC can be utilised to collect this data prospectively.
Completion would require clinician input with coordination by cancer services as
is the current situation with colorectal cancer.

It is timely to re-audit staging, treatment, pathology reporting and outcomes in
anal cancer given the better defined standards of care since the 2006 report
(Karandikar et al). This would be facilitated by prospective data collection.
Similarly salvage surgery outcomes in each MDT should be undertaken given the audit standard recommendations in the ACPGBI position statement.

Agreement for a common follow up protocol following chemoradiotherapy for anal cancer in Wales should be sought.

The arrangement for provision of salvage surgery in South Wales needs to be defined and referral pathways agreed.
List of appendices

**Appendix 1** Suggested protocol for management of AIN

**Appendix 2** Suggested AIN minimum dataset

**Appendix 3** Suggested Clinical dataset for anal cancer

**Appendix 4** AJCC clinical staging systems for anal cancer.

**Appendix 5** Summary of current follow up strategies in Wales 2011

**Appendix 6** MDT pathway for anal cancer in Wales (version 1)

**Appendix 7** Follow up regimes

**Appendix 8** Development process for position statement

Abreviations

References
Appendix 1  Suggested protocol for management of AIN

MSM, men who have sex with men.

Circ= circumferential

Reproduced with kind permission from Wiley.

### Appendix 2. Suggested AIN minimum dataset (modified from Christie Hospital proforma)

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Modified from Comparative Audit of the Centralised Treatment of Anal Cancer with the Non-centralised Treatment of related Benign Precursor Diseases report 2010,


N.b the pathology fields of this suggested dataset are subject to change pending the publication of the RCPPath dataset.

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<td></td>
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Post-mortem Y/N

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<th>Current</th>
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<th>Male No</th>
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<td>(men who have sex with men)</td>
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Tumour details

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<table>
<thead>
<tr>
<th>Date of receipt of referral</th>
<th>Date of first hospital visit</th>
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Was this first referral to a member of the MDT Y/N

Was this first appointment offered Y/N

USC Y/N | NUSC Y/N

Date referred to colorectal specialist nurse
Date seen by colorectal specialist nurse

Tumour site (ICD-10)

C21Malignant neoplasm of anus and anal canal
  ▶ C21.0 Malignant neoplasm of anus, unspecified
  ▶ C21.1 Malignant neoplasm of anal canal
  ▶ C21.2 Malignant neoplasm of cloacogenic zone
  ▶ C21.8 Malignant neoplasm of overlapping sites of rectum, anus and anal canal

Site* - anal canal/ anal margin/ both/ uncertain

Biopsy date

Biopsy-differentiation well/mod/poor/ undiff/ n/a/ not stated AIN presence
Y/N

Tumour type - Squamous cell carcinoma Verrucous variant
  Mucinous microcysts variant Nonsquamous carcinoma
  Adenocarcinoma Mucinous adenocarcinoma
  Small cell carcinoma Undifferentiated carcinoma

Size of primary lesion: clinical (cm)___________ MRI (cm)___________

Depth of primary lesion (radiological) (mm) _______________

Palpable inguinal lymph nodes: None Ipsilateral Bilateral

Biopsy of inguinal node (if enlarged): Y/N

Inguinal biopsy result: Malignant Benign Uncertain

CT performed Y/N Date

MRI performed Y/N Date

Endoanal ultrasound performed Y/N Date

Clinical Stage*: T stage N stage M stage

Defunctioning stoma before definitive treatment Y/N

**Primary treatment**

Performance status 0 1 2 3 4 5

Date of start of definitive treatment:

Primary treatment: CRT RT radical surgery local excision
  other treatment no treatment uncertain

If other treatment, specify

Intent: Curative Palliative Uncertain
Cancer NSAG position statement on the management of anal cancer  
*Published July 2014*

<table>
<thead>
<tr>
<th>Date start RT</th>
<th>Date end RT</th>
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<table>
<thead>
<tr>
<th>Planned fractions</th>
<th>Actual fractions</th>
<th>Total dose (cGy)</th>
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<tr>
<td>Groin boost Y/N</td>
<td>Fractions</td>
<td>Boost dose</td>
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<td>Chemotherapy given:</td>
<td>Yes</td>
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<tr>
<td>Start dates</td>
<td>1</td>
<td>2</td>
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<tr>
<td>Regimen</td>
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<td>CIS+MMC</td>
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<td>Toxicity grade 3/4</td>
<td>Y/N</td>
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<tr>
<td>Toxicity</td>
<td>Bowel</td>
<td>Skin</td>
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<tr>
<td>Dose reduction Y/N</td>
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<td></td>
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<tr>
<td>Reason if dose reduction</td>
<td>Toxicity</td>
<td>Patient age</td>
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<td>Trial inclusion</td>
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<td>No</td>
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<tr>
<td>Primary surgery:</td>
<td>Yes</td>
<td>No</td>
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<tr>
<td>Procedure</td>
<td>Local excision</td>
<td>APR</td>
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<tr>
<td></td>
<td>Palliative colostomy (definitive)</td>
<td>Other</td>
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<tr>
<td>Plastic reconstruction</td>
<td>Yes</td>
<td>No</td>
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</table>

**Follow up**

‘High risk’ features: one of T4 tumour, carcinoma with fistula, age >75, HIV-positive/ immunosuppression  Y/N

Date EUA post-treatment:

Findings: Complete response Partial response Persistent disease Uncertain

Biopsy performed at initial EUA  Y/N

Result of biopsy Persistent malignancy No malignancy Uncertain

Date of closure of temporary stoma

Permanent stoma-any stoma not closed within 3 years of definitive treatment Y/N

Local disease relapse Y/N Date of diagnosis

Local disease relapse diagnosed by Clinical Imaging Histology Other

Groin node relapse Y/N Date
Groin node relapse diagnosed by Clinical Imaging Histology Other

Metastatic disease Y/N Date

Referral to palliative care Y/N

Date referred to palliative care

Survival after definitive treatment end:

**Salvage surgery**

No surgery carried out Y/N

Reason no surgery performed Patient unfit Patient refuses treatment

Advanced disease Other, specify

Previous operation related to this tumour Y/N

Previous procedure Stoma Local excision Anorectal excision

Date surgery offered

Curative resection Curative Palliative Uncertain

If palliative, due to Local disease Distant disease Other, specify

Surgeon name

Grade of surgeon Cons Assoc Specialist Staff grade SpR other

Anaesthetist name

Grade of anaesthetist Cons Assoc Specialist Staff grade SpR other

Date of surgery

Start time of surgery

Mode of operation Elective Scheduled Urgent Emergency

Procedure type Closed without procedure Stoma only Excision EUA Other (specify)

Procedure name (OPCS code)

EUA only H44.4

Block dissection groin

Defunctioning stoma
Abdominoperineal excision H33.1

Pelvic exenteration

Other

Method of reconstruction: Direct closure Omentoplasty Closure with implant

Myocutaneous flap Fasciocutaneous flap Other

Local complications Y/N Type

Tumour complications

Date discharged

Postoperative death within 30 days Y/N

Complications Y/N Delayed perineal healing (>3 months) Other

Reoperation within 30 days Y/N

Readmission within 30 days Y/N

**Histopathology details**

To be finalised upon publication of the RCPath dataset.

**Notes**

* The anal canal is defined according to the AJCC 7th ed.: anal canal begins where rectum enters puborectalis sling at apex of anal sphincter complex (palpable as anorectal ring) and ends at squamous mucocutaneous junction with perianal skin; includes 1-2 cm of rectal-type glandular mucosa and possibly transitional mucosa at the dentate line. Anal verge or anal margin: junction between anal canal and anal skin

# TNM staging

T stage:

Tx primary tumour cannot be assessed

T0 no evidence of primary tumour

Tis Carcinoma in situ (Bowen’s disease, AIN II/III)

T1 Tumour 2 cm or less

T2 Tumour more than 2 cm but less than 5 cm in greatest dimension

T3 Tumour more than 5 cm in maximal dimension
T4 Tumour of any size invades adjacent organ(s) eg vagina, urethra, bladder (but not rectal wall, perirectal skin, subcutaneous tissue or sphincter muscle); or for anal margin cancer invades deep extradermal structures (cartilage, skeletal muscle or bone)

Regional lymph nodes

Nx Regional lymph nodes cannot be assessed

NO No regional lymph node metastasis

N1 Metastasis in perirectal lymph node(s)

N2 Metastasis in unilateral internal iliac and/or inguinal lymph node(s)

N3 Metastasis in perirectal and inguinal lymph nodes and/or bilateral internal iliac and/or inguinal lymph nodes

Note: anal margin cancer nodal metastasis is either N0 or N1.

Metastasis

Mo No distant metastasis

M1 Distant metastasis

References


Appendix 4. AJCC clinical staging systems for anal cancer

AJCC 7th edition clinical category definitions for anal canal cancer

Primary tumour (T)
TX Primary tumour cannot be assessed
T0 No evidence of primary tumour
Tis Carcinoma in situ (Bowen’s disease, high-grade squamous intraepithelial neoplasia II-III (AIN II-III)
T1 Tumour 2 cm or less in greatest dimension
T2 Tumour more than 2 cm but not more than 5 cm in greatest dimension
T3 Tumour more than 5 cm in greatest dimension
T4 Tumour of any size invades adjacent organ(s), e.g. vagina, urethra, bladder*

Regional Lymph Nodes (N)
NX Regional lymph nodes cannot be assessed
N0 No regional lymph node metastasis
N1 Metastasis in perirectal lymph node(s)
N2 Metastasis in unilateral internal iliac and/or inguinal lymph node(s)
N3 Metastasis in perirectal and inguinal lymph nodes and/or bilateral internal iliac and/or inguinal lymph nodes

Metastasis
M0 No distant metastasis
M1 Distant metastasis

*Note: direct invasion of the rectal wall, perirectal skin, subcutaneous tissue or the sphincter muscle(s) is not classified as T4.

AJCC 6th edition clinical category definitions for anal margin cancer

Primary tumour (T)
TX Primary tumour cannot be assessed
Tis Carcinoma in situ
T1 Tumour 2 cm or less in greatest dimension
T2 Tumour more than 2 cm but not more than 5 cm in greatest dimension
T3 Tumour more than 5 cm in greatest dimension
T4 Tumour invades deep extradermal structures (i.e. cartilage, skeletal muscle, or bone).

Regional Lymph Nodes (N)
NX Regional lymph nodes cannot be assessed
N0 No regional lymph node metastasis
N1 Regional lymph node metastasis

Metastasis
M0 No distant metastasis
M1 Distant metastasis
Appendix 5. Summary of current follow up strategies in Wales 2011

This summary follows responses from North Wales (N), South East (SE) and South West (SW) Wales Anal Cancer MDTs.

Protocol-driven follow up is currently used in 2 centres and being developed in one.

Two of the three MDTs stratify follow-up protocol into low-risk and high-risk categories.

**Initial evaluation**

The earliest time point for initial evaluation of response to radiotherapy was 4 weeks, although respondents also felt that this was too early in some cases. It was acknowledged that individual response to radiotherapy influences the timing of initial evaluation. In cases of doubt regarding response evaluation was repeated at 3 months post-completion of treatment.

**Clinical follow up**

Further follow up was stated as follows:

SE:  Low risk patients-  3, 6, 9, 12, 18, 24, 30, 36, 48, 54, 60
     High risk patients- 2, 4, 6, 8, 10, 12, 15, 18, 21, 24, 28, 32, 36, 42, 48, 54, 60 months

SW:  Low risk- 2, 4, 6, 8, 10, 12, 15, 18, 21, 24, 30, 36, 42, 48, 54, 60
     High risk- 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 30, 36, 42, 48, 54, 60

N: 3, 6, 9, 12, 15, 18, 21, 24, 28, 32, 36, 42, 48, 54, 60.

**Radiological follow up**

N- MRI at 3 months

SW- CT at 12 and 24 months, low threshold for earlier CT and USS after initial EUA

SE- Low risk-CT/MRI at 3, 12, 24 months; High risk 4, 12, 18, 24 and 36 months
Appendix 6. MDT pathway for anal cancer in Wales (version 1)

1. Biopsy proven anal SCC
2. Staging: Clinical - T stage (size, fistulation) - N stage (inguinal nodes) with FNAC if palpable groin nodes
   Radiological - CT CAP/ MRI pelvis/ endoanal US (where locally available)
3. Specialised Anal cancer MDT with minimum dataset completion
4. Outcomes:
   - Adequate treatment (locally excised with negative margins, T1 stage)
   - Further assessment by clinical core member (EUA etc)
   - Consider temporary colostomy (pain/incontinence/fistulation)
   - Primary chemoradiotherapy (5-FU/MMC/50.4Gy)
   - Radiotherapy alone (elderly/frail/palliation)
   - Primary surgery (unusual:fistulating disease, prior pelvic radiotherapy,etc)
5. Risk stratification (for local recurrence after treatment)
   - Low Risk: T2-3, age <75
     - Standard follow-up
   - High Risk: T4 tumour, carcinoma with fistula, incomplete CRT, age >75, HIV-positive/immunosuppression
     - Intensive follow up by network MDT core members
6. Local recurrence
   - Staging-CT CAP/MRI pelvis/ assess fitness for surgery
   - PET-CT/ biopsy confirmation
   - Multidisciplinary salvage surgery
Appendix 7 Follow up regimes

The aim of follow up is to detect local recurrence at an early stage to permit salvage surgery.

Local disease failure is most common in the first 3 years after treatment.

**Low risk group**

Clinical examination (anal/groins) is the mainstay of follow up

Patients should have response assessed between 6 weeks and 3 months following completion of CRT then 3 monthly assessment for 3 years. Thereafter 6 monthly assessment until 5 years is appropriate.

ie 3, 6, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 42, 48, 54, 60 months.

Patients with suspicion of local disease failure or persistent ulceration need discussion in network MDT

**High risk group**

Examination under anaesthesia with biopsies of suspicious areas should be performed at 6 weeks following completion of CRT then 2 monthly for the first year and 3 monthly until year 3. Six monthly examinations should occur in years 4 and 5. EUA may be substituted by local clinical examination where tolerated and when fibrosis is considered stable.

ie 2, 4, 6, 8, 10, 12, 15, 18, 21, 24, 27, 30, 33, 36, 42, 48, 54, 60 months

It is recommended that digital assessment is performed by the same clinician where possible.

MRI pelvis should be performed 6 monthly for 3 years post-treatment.

CT surveillance is recommended at 6 months and then annually for 3 years in accordance with ACPGBI guidance.

After 5 years patients in both groups can be followed up annually in local colorectal surgical clinics.
Appendix 8 development process for position statement

The Cancer NSAG colorectal sub-group agreed to summarise the Association of Coloproctology Great Britain and Ireland (ACPGBI) position statement on Anal Cancer\(^1\) within a Welsh context, updating subsequent developments where necessary, as part of their work programme.

Professor Dean Harris drafted the document on behalf of the colorectal subgroup undertaking the following steps:

- Review of ACPGBI document
- Additional literature sourcing
- Review of evidence using OCEBM 2011\(^{52}\)
- Iterative drafting of position statement
- Presentation to Cancer NSAG colorectal subgroup for comment.
- Review post comments from NSAG subgroup.
- Editorial sweep by Cancer NSAG Core Team.
- Sign-off for consultation by Cancer NSAG colorectal subgroup
- 1 month consultation to stakeholders including:
  - all colorectal MDT members
  - Cervical and Bowel screening services
  - Cancer NSAG gynaecology subgroup Chair
  - Cancer NSAG colorectal subgroup
  - Welsh Health Specialist Services Commissioner
  - Cancer Networks

  - Editorial group responded to consultation comments and amended doc as necessary
  - Sign off to publish.
### Abbreviations

<table>
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<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tr>
<td>AJCC</td>
<td>American Joint Committee on Cancer</td>
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<tr>
<td>CANISC</td>
<td>Cancer Network Information System Cymru</td>
</tr>
<tr>
<td>CIN</td>
<td>Cervical Intraepithelial Neoplasia</td>
</tr>
<tr>
<td>GUM</td>
<td>Genitourinary Medicine</td>
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<tr>
<td>HIV</td>
<td>Human Immunodeficiency Virus</td>
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<td>HPV</td>
<td>Human Papilloma Virus</td>
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<td>NCCN</td>
<td>National Comprehensive Cancer Network</td>
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<td>PET-CT</td>
<td>Positron Emitting Tomography-Computed Tomography</td>
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<td>SLNB</td>
<td>Sentinel Lymph Node Biopsy</td>
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<td>TNM</td>
<td>Tumour Node Metastasis Classification System</td>
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<tr>
<td>VIN</td>
<td>Vulval Intraepithelial Neoplasia</td>
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</table>
References

1. ACPGBI Position Statement for Management of Anal Cancer. Colorectal Disease 2011; 13(S1)


14. Renehan A, Miles L. A Comparative Audit of the Centralised Treatment of Anal Cancer with the Non-centralised Treatment of related Benign Precursor Diseases...
Cancer NSAG position statement on the management of anal cancer

Published July 2014


James R, Wan S, Glynne-Jones R et al. A randomised trial of chemoradiation using Mitomycin or cisplatin, with or without maintenance cisplatin / 5FU in squamous cell carcinoma of the anus. J Clin Oncol 2009; (Proc ASCO) 27: 18S (part II of II); 797s (abstract LBA-4009)


41 Sun Myint A. Follow up. ACPGBI Position Statement for Management of Anal Cancer. Colorectal Disease 2011; 13(S1); 39-43


44 Christie Hospital NHS Foundation Trust and Central Manchester NHS Trust Follow-Up Guidelines with acknowledgement to Mr Andrew Renehan, Chair of the Regional Anal Cancer MDT

45 Renehan AG, O’Dwyer ST. Management of Local Disease Relapse. ACPGBI Position Statement for Management of Anal Cancer. Colorectal Disease 2011; 13(S1); 44-52.


50 Sunesen KG, Buntzen S, Tei T, Lindegaard JC, Nørgaard M, Laurberg S. Perineal Healing and Survival After Anal Cancer Salvage Surgery: 10-Year
