The surgeon’s role in the management of anal cancer

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• No disclosures
Outline

• Risk factors

• Presentation

• Role of surgery
  – Surgery as the primary treatment modality
  – Salvage surgery after failed chemoradiation

• Surveillance
Introduction

• Squamous cell cancer of the anal canal is relatively rare
  – Accounts for ~2% of all colorectal malignancies
  – Incidence is increasing
Risk factors

- Human papillomavirus infection (strains 16, 18)
- Anal intra-epithelial neoplasia (AIN)*
- HIV seropositivity
- Smoking
- Anoreceptive intercourse
- History of HPV malignancy
  - Cervical cancer, vulvar cancer, CIN, VIN
- Immunosuppression*
Risk factors

- Anal intra-epithelial neoplasia (AIN)
  - Previously referred to as carcinoma *in situ*, Bowen’s disease
  - AIN categorized as grade I, II, III reflecting progressive dysplastic changes and risk of malignant progression
  - Recently terms LGAIN (AIN I & II) and HGAIN (AIN III) have been proposed
Risk factors

• Natural history of AIN not completely understood

• Spontaneous regression has been described
  – AIN I
  – Anal margin vs. anal canal

• Progression of AIN III to invasive cancer 5-13%
Evaluated the Danish population from 1978-2005 using linked administrative data bases

Compared observed and expected cases of anal SCC among immunosuppressed patients
- HIV
- Solid organ transplantation
- Hematologic malignancy
- Autoimmune disorders GI/Neuro/ Connective tissue etc.
Table 2. Standardised incidence ratios (SIRs) of anal squamous cell carcinoma in patients with a first-time hospital contact with HIV infection, solid organ transplantation or autoimmune disease or first-time record of haematologic malignancy in the Danish Cancer Registry, 1978–2005

<table>
<thead>
<tr>
<th>Disease</th>
<th>No. patients</th>
<th>Person-years</th>
<th>SIR [95% CI]³</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV infection</td>
<td>4,448</td>
<td>5.8</td>
<td>81.1 [51.6; 121.9]</td>
</tr>
<tr>
<td>Solid organ transplantation</td>
<td>5,113</td>
<td>8.1</td>
<td>14.4 [7.0; 26.4]</td>
</tr>
<tr>
<td>Haematologic malignancies, all</td>
<td>30,165</td>
<td>5.4</td>
<td>2.3 [1.1; 4.2]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Condition</th>
<th>No. patients</th>
<th>Person-years</th>
<th>SIR [95% CI]³</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psoriasis</td>
<td>24,308 (10.0)</td>
<td>8.6</td>
<td>3.1 [1.8; 5.1]</td>
</tr>
<tr>
<td>Polyarteritis nodosa</td>
<td>1,174 (0.5)</td>
<td>7.8</td>
<td>8.8 [1.5; 29.0]</td>
</tr>
<tr>
<td>Wegener's granulomatosis</td>
<td>992 (0.4)</td>
<td>6.1</td>
<td>12.4 [2.1; 40.8]</td>
</tr>
<tr>
<td>Crohn's disease</td>
<td>12,609 (5.2)</td>
<td>10.0</td>
<td>3.1 [1.2; 6.4]</td>
</tr>
</tbody>
</table>
Diagnosis

- High potential for missed or delayed diagnosis
  - Relatively uncommon cancers
  - Symptoms are similar to common benign ano-rectal conditions

- Having a high index of suspicion is critical
Presentation

- Symptoms
  - Perianal/rectal pain
  - Rectal bleeding
  - Pruritis
  - Presence of a growth or mass
Presentation

• Clinical findings are variable

• Hard ulcerated mass is typical of SCC

• AIN
  – Rash (erythematous, white plaque, lichenification)
  – Discrete raised lesion
  – Irregular skin tag

• Fistula opening that looks unusual/doesn’t heal as expected
Diagnosis

• Critical to have a very low threshold to biopsy any abnormalities in the anorectal area, particularly in high risk patients

• Anoscopy

• Examination under anesthesia
  – Biopsy extensively
Treatment

• Chemoradiation is the primary treatment of choice for patients with SCC of the anus
  – Surgery may be required for a number of reasons

• APR is appropriate primary treatment for patients who cannot tolerate chemoradiation
  – Accounts for <10% of patients who undergo surgery

• APR is most commonly utilized for the management of persistent and recurrent disease

• A diverting stoma may be required
  – Obstruction, poor bowel function/ incontinence
Treatment

• Persistent disease
  – Malignancy within 6 months of completing chemoradiation
  – Consider persistence if there is a mass or ulcer present 12 weeks after completion of treatment

• Recurrent disease
  – Malignancy presenting more 6 months after completing chemoradiation
Population based retrospective cohort study from Norway

Included all patients with SCC of the anus treated with chemoradiation and curative intent 2000-2007
328 patients were identified
- Median follow-up 49 months

43/328 (13%) had persistent disease
- 24 (55%) of these patients were eligible for salvage surgery

73/328 (24%) had recurrent disease
- 48 (66%) had locoregional recurrence
- 19 (26%) had distant recurrence
- 6 (8%) had both
- Overall 33 patients (45%) with recurrence underwent salvage surgery

Outcomes of salvage surgery for epidermoid carcinoma of the anus following failed combined modality treatment

- Retrospective study of patients identified from the BC cancer agency database who underwent APR 1998-2006

- 51 patients met study inclusion criteria
  - 12% HIV+
  - 60% of surgery was done for recurrence, 40% for persistence
5-year overall survival was 29%

5-year cancer free survival was 25%
Outcomes of salvage surgery for epidermoid carcinoma of the anus following failed combined modality treatment

- Surgical margins
  - R0 resection in 63%
  - R1 resection in 22%
  - R2 resection in 8%

Margin status was the only factor associated with overall survival on multiple regression

Abdominoperineal Resection for Squamous Cell Anal Carcinoma: Survival and Risk Factors for Recurrence

- Retrospective cohort study of 105 patients who underwent APR for SCC of the anus 1996-2009

- Indications for surgery
  - Recurrence 52%
  - Persistence 40%
  - Contraindication to chemo/rads 8%

- Median follow-up 33 months

Lefevre et al. Annals of Surgical Oncology 2012;epub
• Margin status
  – R0 resection was achieved in 82%
  – R1 resection was achieved in 18%

• 48% of patients underwent a VRAM reconstruction of the perineum

• Median hospital stay was 19 days
• Peri-operative mortality rate was 2.1%

• 35 patients (33%) had at least 1 complication
  – 20 patients required re-operation
  – 50% of take-back procedures were due to perineal wound problems
• 5-year overall survival was 61%

• 5-year disease free survival was 48%

• On multivariate analysis large tumor size (T3/T4) and positive margin status were associated with poor prognosis
Abdominoperineal Resection for Squamous Cell Anal Carcinoma: Survival and Risk Factors for Recurrence

![Survival curve for R0 and R1 patients](image)

- **Percent survival**
- **Follow-up (months)**
- **Green line** represents R0 patients
- **Orange line** represents R1 patients
Technical considerations

• Plan surgery carefully
  – Liberal use of pre-operative imaging
  – CT, MRI, PET
  – Determine extent of local disease and exclude distant disease

• R0 resection is critical
  – May require extended multi-visceral resection
Technical considerations

• The combination of pelvic radiation and extended surgery is associated with considerable morbidity
  – Urinary and sexual dysfunction are common

• High potential for pelvic sepsis & perineal healing problems
  – 1° closure associated with perineal breakdown ~60%

• Flap reconstruction should be considered in all patients
  – VRAM flap is associated with good outcomes
Surveillance

• Approximately 80% of recurrences will occur within 3 years.

• Patient assessment with inspection, DRE, inguinal palpation ± anoscopy
  – Should begin ~6-12 weeks after treatment
  – Every 3 months for 2 years
  – Every 6 months for 3 years

• Annual imaging of chest, abdomen and pelvis
  – Typically achieved with CT scan
  – Some controversy regarding the role EAUS for assessment of LR
Conclusions

• Squamous cell cancer is a relatively rare

• There are well-defined risk factors
  – High potential for missed or delayed diagnosis

• There clear role for surgery in this patient population
  – Approximately 20-25% of patients will require surgery
  – Appropriately selected patients who undergo an R0 resection can realize 5-year DSS of ~50%