The surgeon's role in the management of anal cancer

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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%

Immunosuppressive disorders and risk of anal squamous cell carcinoma: a nationwide cohort study in Denmark, 1978–2005

- 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.

Sunesen et al. International Journal of Cancer 2010;127:675

Immunosuppressive disorders and risk of anal squamous cell carcinoma: a nationwide cohort study in Denmark, 1978–2005

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

Disease	No. patients	Person-years		Obs	Exp	SIR [95% CI][1]
		Mean	Total			
HIV infection	4,448	5.8	25,688	21	0.3	81.1 [51.6; 121.9]
Solid organ transplantation	5,113	8.1	41,554	9	0.6	14.4 [7.0; 26.4]
Haematologic malignancies, all	30,165	5.4	163,548	9	3.9	2.3 [1.1; 4.2]
Psoriasis	24,308 (10.0)	8.6	208,800 (9.8)	14	4.5	3.1 [1.8; 5.1]
Polyarteritis nodosa	1,174 (0.5)	7.8	9,207 (0.4)	2	0.2	8.8 [1.5; 29.0]
Wegener's granulomatosis	992 (0.4)	6.1	6,041 (0.3)	2	0.2	12.4 [2.1; 40.8]
Crohn's disease	12,609 (5.2)	10.0	126,369 (5.9)	6	2.0	3.1 [1.2; 6.4]

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

Chemoradiotherapy of Anal Carcinoma: Survival and Recurrence in an Unselected National Cohort

- Population based retrospective cohort study from Norway
- Included all patients with SCC of the anus treated with chemoradiation and curative intent 2000-2007

Bentzen et al. Int J Radiat Oncol Biol Phys 2012;83:e173

Chemoradiotherapy of Anal Carcinoma: Survival and Recurrence in an Unselected National Cohort

- 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

Bentzen et al. Int J Radiat Oncol Biol Phys 2012;83:e173

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

Eeson et al. American Journal of Surgery 2011;201:628

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

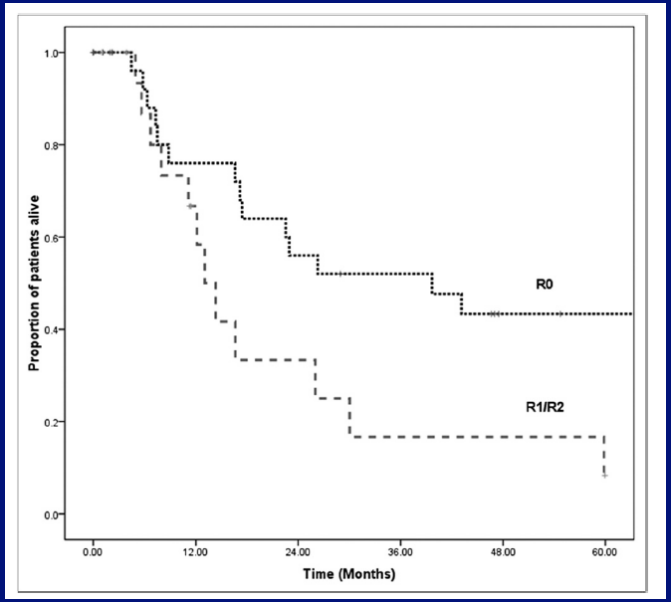
- 5-year overall survival was 29%
- 5-year cancer free survival was 25%

Eeson et al. American Journal of Surgery 2011;201:628

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



Eeson et al. American Journal of Surgery 2011;201:628

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

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

- 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

Lefevre et al. Annals of Surgical Oncology 2012;epub

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

- 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

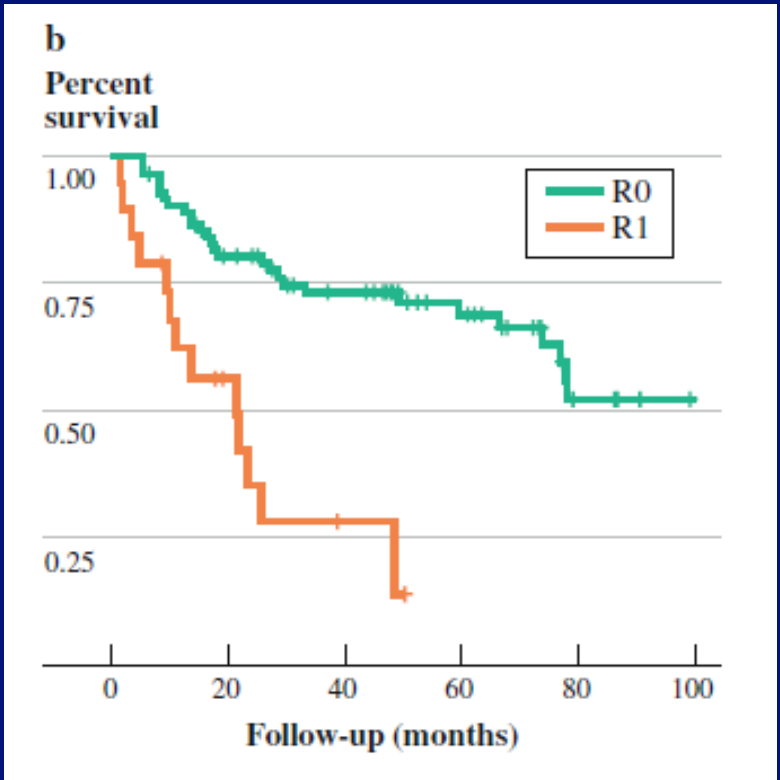
Lefevre et al. Annals of Surgical Oncology 2012;epub

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

- 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

Lefevre et al. Annals of Surgical Oncology 2012;epub

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



Lefevre et al. Annals of Surgical Oncology 2012;epub

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 with 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%