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ScienceDirect

EJSO 41 (2015) 653–658

EJSO the Journal of Cancer Surgery

www.ejso.com

Review of anal cancer patients at the Ottawa hospital

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Accepted 13 February 2015
Available online 4 March 2015

Abstract

Background: Anal cancer is uncommon. We reviewed the treatment and outcomes of anal cancer patients in a population referred to the Ottawa Hospital Cancer Centre (TOHCC) over a 12-year period.
Methods: A chart review was conducted with patient data collected from hospital records, including: demographic, treatment and outcome information. Outcomes of interest included: overall survival (OS), disease free survival (DFS), and colostomy free survival (CFS).
Results: 180 patients were included in the study population. 72% (n = 130) female and 28% (n = 50) male. 6.7% (n = 12 males) of patients were HIV positive − all were on anti-retroviral therapy. 60% (n = 108) of patients were ever-smokers, mean patient age was 62 [range 35–90] years. The most frequent presenting symptoms were blood per rectum and anal pain. Treatment intent was curative in 87%. Treatment included radiotherapy (94%), brachytherapy (26%), chemotherapy (73%). Among patients treated with curative-intent, 72% had a complete response, 31% had local/regional recurrence, 16% required salvage surgery and 21% had distant recurrence. The colostomy rate was 23%. 5 year overall survival (OS) was not significantly different for patients by HIV status. Survival was superior if MMC-FU was used first vs. CIS-FU; OS HR 0.47 (0.24–0.94), $p < 0.033$.
Conclusions: The outcomes of patients in this large retrospective cohort study are similar to the outcomes of patients in highly selective clinical trials. Five year overall survival and colostomy free survival are encouraging. MMC-FU was found to be superior to CIS-FU.
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Keywords: Anal cancer; HPV; Mitomycin; Cisplatin; Squamous cell carcinoma; Chemoradiotherapy

Introduction

Anal cancer is uncommon, comprising only 2.5% of all digestive system malignancies in the U.S., but with a rising incidence over the last 30 years.[1,2] With some similarities to cervical cancer in its etiology, the risk factors predisposing to anal cancer include female gender, infection with human papillomavirus (HPV), lifetime number of sexual partners, genital warts, cigarette smoking, receptive anal intercourse, and infection with human immunodeficiency virus (HIV).[3]

Anatomically, the anal canal includes 3 types of epithelium. From proximal to distal these are glandular, transitional and squamous. Tumors that arise from the transitional or squamous mucosa are squamous cell cancers and behave similarly. The term "anal cancer" typically refers to squamous cell cancers that are generally 2 cm or less from the dentate line.[4–6]

Anal cancer most often presents with rectal bleeding, anorectal pain, or anal mass sensation. However, approximately 20 percent of patients have no symptoms.[7–9] Clinical (digital rectal) exam including vaginal exam, and proctoscopy (sometimes with examination under anesthesia) facilitate biopsy for histological classification, determination of tumor size and clarification of anatomical relationship to surrounding structures.[10] TNM staging is employed, with local staging by magnetic resonance imaging (MRI) of the pelvis, and computerized tomography (CT) thorax and abdomen to assess distant metastases.[10]

Significant progress has been made in the diagnosis and management of anal cancer. Prior to the 1960s, primary treatment consisted of an abdominoperineal resection,

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http://dx.doi.org/10.1016/j.ejso.2015.02.004
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which resulted in a permanent colostomy. Conventional management with chemo-radiotherapy often preserves anal sphincter function. Abdominoperineal resection can be used as a salvage procedure in refractory or local recurrent disease.[10]

Recent randomized trials have helped to determine the role of specific chemotherapy agents including cisplatin (CIS), 5-fluorouracil (FU), and mitomycin-C (MMC), as well as the optimal timing and duration of chemotherapy with respect to radiotherapy (RT). However these trials involve selected populations and may not reflect outcomes in population based cohorts. Based on the RTOG-9811 trial, combination chemoradiotherapy (CRT) with MMC, FU and RT is the standard of care for localized disease (T1-4N0-3 = stage I–IIIB).[11] An update of this study demonstrated that concurrent MMC-FU/RT was superior to induction plus concurrent CIS-FU/RT for both disease free survival (DFS) and overall survival (OS).[11]

The Ottawa Hospital Cancer Centre is the sole provider of chemotherapy and RT in the Champlain region of Eastern Ontario, which serves a population of 1.4 million. This study was undertaken to evaluate the characteristics and outcome of all patients with anal canal cancer over a 12-year period from 2000 to 2011.

Patients and methods

Study design

Following approval by the research ethics board approval, a retrospective cohort study of patients referred for anal cancer at The Ottawa Hospital Cancer Centre between January 1st, 2000 and December 31st, 2011 was undertaken.

Participants

In order to be included in the study, participants 18 years of age or older needed to have histologically confirmed anal cancer, and be referred to the Ottawa Hospital Cancer Centre between January 1st, 2000 and December 31st, 2011. Patients who received primary treatment at another institution were excluded. Patients with non-invasive carcinoma, or with other non-squamous anal cancer (e.g. melanoma, sarcoma, lymphoma, neuroendocrine or adenocarcinoma) were excluded.

Data collection

Medical records were analyzed to assess baseline demographics, staging, clinical management, chemotherapy, RT, surgery and outcome. OS, DFS, colostomy rates, and colostomy free survival were calculated from the data collected.

Statistical analyses

Statistical analyses were done using IBM® SPSS® Statistics 21.0 software. The Kaplan–Meier approach was used to estimate OS with differences between subgroups assessed using the log-rank test. A Cox proportional-hazards model was used to investigate independent associations between outcome and the various prognostic variables; hazard ratios and 95% confidence intervals were calculated from the model for all prognostic variables. Descriptive statistics were performed with differences between subgroups assessed using the Chi-square test for categorical variables and the t-test or Mann–Whitney test for continuous variables. A multi-variate analysis was performed to control for potentially confounding variables.

OS was defined from date of diagnosis to death. Among curatively treated patients with localized disease, DFS was calculated from date of onset of CRT to date of recurrence or progression. Colostomy free survival was defined from date of onset of CRT to date of colostomy. For time to event variables, patients without events were censored at last follow-up.

Results

In the 12 years under review, 180 patients with anal cancer were identified. Patients were 72% (n = 130) female and 28% (n = 50) male, with 6.7% (n = 12, all male, $p < 0.05$) having known infection with HIV, and 108 having a smoking history (67% of 162 evaluable for smoking history). The median age was 62, with a range between 35 and 90 years. 60% of the population either had smoked, or were current smokers at diagnosis.

Histologic description of the tumor included 78% (n = 140) squamous cell, 15% (n = 27) basaloid, 6.7% (n = 12) cloacogenic, and 1 mixed adenocystic/basaloid. Tumor stage at diagnosis among 175 evaluable patients was 8.3% stage I, 42% stage II, 6.7% stage IIIA, 33% stage IIIB, and 7.2% stage IV.

Treatment

Table 1 summarizes the treatment intent for the population. Among the 122 (79%) patients who were treated for

Table 1
Summary of treatments.

Primary treatment	N (%) total 178; 2 unknown status
Curative intent	
–surgery alone	6/155; 3.9%
–radiation alone	17/155; 11.0%
–chemoradiotherapy	122/155; 79%
Palliative	
–radiation alone	13/23; 56.5%
–chemotherapy alone	1/23; 4.34%
–chemotherapy and radiation	9/23; 39.1%
–palliative care alone	0

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