

Results of salvage abdominoperineal resection after failed chemoradiation therapy for epidermoid anal canal carcinoma: Retrospective analysis at a single institution

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Summary

Purpose: The standard therapeutic approach to epidermoid anal canal cancer consists of combined radiation therapy and chemotherapy. Although disease control has been reported to have excellent results, as many as 40% of patients will develop locoregional disease progression. The treatment of choice for patients with persistent (PD) or recurrent disease (RD) is salvage abdominoperineal resection (APR). The purpose of this study was to review our experience with salvage surgery in this group of patients.

Methods: The medical records of all patients with epidermoid anal canal cancer treated from 1997 to 2010 in our department were retrospectively reviewed. Nine patients who presented with persistent or locally recurrent anal canal cancer were subjected to salvage APR. Before surgery, all of the patients had received chemoradiation therapy (CRT).

Results: There were 9 patients (7 women, 2 men) with a median age of 59 years (range 40-79). Six patients underwent radical salvage APR for persistent disease and 3 patients for recurrent disease. There were no deaths attributable to operation. The median follow-up time was 31.75 months (range 3-108) after salvage surgery. Two patients died of disease progression, with a median survival time of 24 months (range 12-36). At the time of last follow-up, 6 patients were alive without evidence of recurrent disease, and one patient was lost to follow-up. The median follow-up time for survivors was 34.3 months (range 3-108).

Conclusion: Long-term survival can be achieved in the majority of patients who undergo radical salvage APR after failed CRT for epidermoid carcinoma of the anal canal.

Key words: abdominoperineal resection; anal canal cancer; combined chemoradiation

Introduction

Epidermoid anal cancer represents a rare clinical entity that requires a multidisciplinary approach in order to achieve optimal results. It accounts for 1.6% of gastrointestinal malignancies and 4% of anorectal malignancies [1].

Since the introduction of the Nigro protocol in 1974, the treatment of anal cancer has radically changed, with combined CRT becoming the mainstay of treatment [2,3]. Despite the overall excellent reported results of CRT as a primary therapy for epidermoid anal carcinoma, treatment failure occurs in up to 33% of patients. Initial treatment failure is experienced in approximately 10-15% of patients, whereas an additional 10-30% of patients develop tumor recurrence after an initial complete

response (CR) to CRT [4-8]. For patients with persistent or locally recurrent disease following CRT, radical salvage APR remains the treatment of choice. Due to the rarity of epidermoid anal cancer, the outcomes reported by several studies range from poor to encouraging with regards to survival among patients undergoing salvage APR [6-13].

The aim of this retrospective study was to present our experience with salvage APR for patients with locoregional failure following CRT treated at a single institution.

Methods

Between January 1997 and December 2010, 31

patients with biopsy-proven epidermoid anal carcinoma were diagnosed and treated in our hospital. Patients were reviewed weekly during treatment. Primary tumors were staged according to American Joint Committee on Cancer (AJCC) criteria. The nodal stage was assigned based on the presence or absence and location of clinically palpable or radiographically enlarged lymph nodes at the time of initial patient presentation, prior to CRT.

Patients with histologically proven epidermoid carcinoma detected within 6 months of completion of CRT were classified as having PD. Those patients who had an initial CR to CRT, but in whom recurrence was diagnosed 6 months or more after treatment were classified as presenting with locally RD.

After completion of treatment, patients were evaluated with history and physical examination every 3 to 6 months. Patients were further assessed with chest X-ray and an abdominopelvic CT scan annually. Only clinically suspicious lesions were biopsied.

Nine patients were identified as having isolated locoregional failure after CRT and all of them underwent radical salvage APR. The medical records of these patients were retrospectively reviewed.

Statistical analysis

Univariate analysis of predictive variables was performed using the log-rank test. Survival curves were calculated from the time of APR and were based on the method of Kaplan and Meier.

Results

Patient characteristics

A total of 9 patients (7 women, 2 men) underwent radical salvage surgery. All patients had anal canal cancer; no cancer of the anal margin was included. The median age of the patients was 59 years (range 40-79). All of the patients had received a combination of 5-fluorouracil and mitomycin C, and they had been treated with an initial dose of radiation ≥ 55 Gy. The initial prescribed CRT regimen was completed by all of the patients. Histology prior to CRT revealed that all of the cancers were squamous cell type. Six patients were classified as having PD, and 3 as having RD.

Operative data and complications

All of the patients underwent APR, including 3 women who underwent APR with a total salpingo-oophorectomy and hysterectomy due to vaginal invasion.

There were no postoperative deaths. Primary closure of the perineal wound alone was performed in all of the patients. Healing time of the perineal wound exceeding 2 months was considered to be delayed, which occurred in 2 (22%) patients. The healing was achieved within 4 months in both of them. Other complications included one small bowel obstruction requiring laparotomy on the 10th postoperative day.

Oncological results

All of the patients except one were followed-up. The median length of follow-up time was 31.75 months (range 3-108) after salvage surgery. At the time of the last follow-up, 2 patients had died as a result of disease progression, with a mean survival time of 24 months (range 12-36) (Figure 1). Of these patients, one presented with PD, whereas the other one developed lung metastases. The median follow-up time among survivors was 34.3 months (range 3-108). One patient survives for 9 years. One female patient presented with a solitary liver metastasis 12 months after salvage APR and underwent a liver segmentectomy. She remains alive with disease 60 months following her last operation.

Discussion

Since the publication of the pioneering work of Nigro et al. [2,3], combination of chemotherapy and radiation therapy has emerged as the primary treatment modality for epidermoid carcinoma of the anal canal, with reported 5-year survival rates ranging from 60-90% [14-

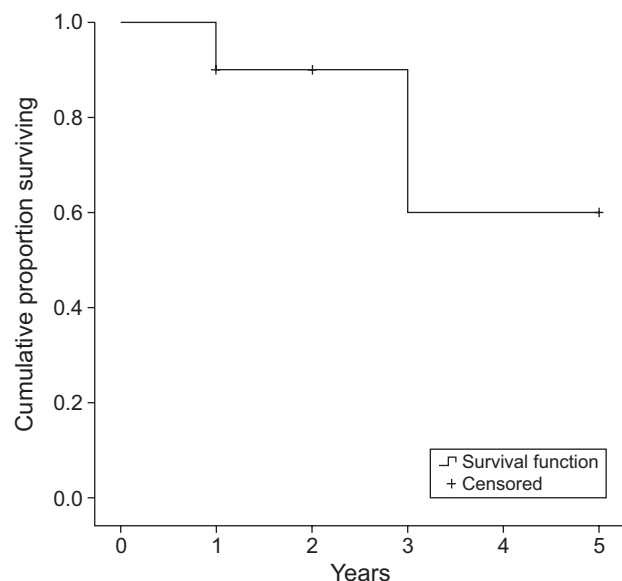


Figure 1. Overall survival after radical salvage surgery.

18]. Despite the undoubted success of CRT, a substantial percentage of patients, especially those with more advanced disease, will eventually develop locoregional failure [19,20]. Salvage CRT with cisplatin-containing regimens has been advocated in some series, reporting 50% survival at 4 years [15], whereas others have reported more disappointing results with salvage CRT [7]. Therefore, radical salvage surgery remains the only possible therapeutic option in patients who fail CRT. Previous investigators have provided information on 5-year survival rates after salvage APR, that range between 24 and 58% [8,21,22]. In a recent study, however, the reported 5-year overall survival reached 64%, which was attributed to careful patient selection, and meticulous surgical technique including total mesorectal and wide perineal resections [23]. In the present study, the median overall survival for all patients undergoing salvage surgery was 31.75 months with a median follow-up of 34.3 months, which is in accordance to previous reports [6,8,21,24].

Patients who fail CRT can be classified in two distinct groups: those with PD and those with RD [8,10,21,25]. In this study, 3 (33%) of 9 patients underwent salvage APR for RD. With regards to difference in survival between the persistent and recurrent anal cancer, several groups report no difference [8,21,23,26]. Other investigators, however, demonstrate a significantly improved overall survival in patients with RD, as opposed to patients presenting with PD [6,10,25,27]. These contradictory findings could be related to the tumor stage and nodal status at initial presentation, or they may reflect a more aggressive phenotype of tumors that respond differently to radiotherapy [12]. Alternatively, the difference may be a result of a rather arbitrary selection of 6 months as the dividing line between the two types of failure, as well as the timing and accuracy of the biopsy [23]. Due to the small sample size in the present study, no statistical analysis could be performed to determine risk factors of survival.

A well documented complication of salvage APR following radiation therapy is the delayed healing of the perineal wounds. The perineal wound complication rate reported by most authors is up to 36% [8,12,21,25]. In this series, among 9 patients who underwent APR, 2 presented with delayed perineal wound healing. Omentoplasty, or musculo-cutaneous flaps [9,28,29] have been reported to show promising results for large defects in an irradiated field.

Up to 50% of patients develop localized disease alone or associated with metastases [9,13,23]. These local recurrences usually involve bladder invasion, hemorrhage, perineal pain, and are often difficult to manage, suggesting that adjuvant chemotherapy in conjunction

with salvage surgery should be warranted for selected cases.

In conclusion, salvage abdominoperineal resection, although associated with a high morbidity, should be considered after CRT for epidermoid carcinoma of the anal canal, as long-term survival can be achieved in a large proportion of patients.

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