

Surgical salvage therapy of anal canal cancer

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Abstract

AIM: To evaluate the results of salvage resection in the management of persistent or locally recurrent anal canal cancer.

METHODS: Details of all patients with anal canal cancer treated from 1978 to 1994 at Cancer Hospital of Chinese Academy of Medical Sciences (CAMS) were reviewed retrospectively. Sixteen patients who presented with persistent or locally recurrent anal canal cancer received salvage surgery. Before surgery all of the patients had received radiotherapy alone as their primary treatments.

RESULTS: Of the 16 patients, 14 received salvage abdominoperineal resection (APR) and two had transanal local excision. There were no deaths attributable to operation. Delayed healing of the perineal wound occurred in eight patients. Complications unrelated to the perineal wound were found in five patients. The median follow-up time was 120 (range 5-245) months after salvage surgery. Nine patients died of disease progression, with a median survival time of 16 (range 5-27) months. Six patients had a long-term survival.

CONCLUSION: Salvage resection after radiotherapy can yield a long-time survival in selected patients with anal canal cancer. However it offers little hope to patients with T₄ and/or N₂₋₃ tumors.

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INTRODUCTION

Anal canal cancer is rare and only accounts for 2% to 4% of all anorectal neoplasms^[1,2]. Radiotherapy alone or concomitant chemoradiotherapy currently is considered as a standard treatment for most of the patients^[3,4]. Although disease control was reported to be excellent, as many as 33% of patients would develop locoregional disease progression^[3-5]. Because this disease is uncommon, there has been no randomized study that compares different salvage approaches^[6]. The aim of this

study was to review our experience in salvage surgery for patients who developed local disease recurrence after radiotherapy.

MATERIALS AND METHODS

Materials

From 1978 to 1994, 83 patients with biopsy-proven anal canal cancer were treated with curative intent at Cancer Hospital of Chinese Academy of Medical Sciences (CAMS). Primary radiotherapy failed to produce any regression of the primary tumor in 16 patients. These 16 patients, including eleven who presented with a persistent disease and five patients who had a recurrent disease, were treated with salvage surgery. Primary tumors were staged in accordance with the criteria of the American Joint Committee on Cancer (AJCC)^[7]. Diagnosis of lymph node metastasis was made clinically, with radiological investigations such as computerized tomography scanning, and confirmed histologically. Pretreatment characteristics of these patients are listed in Table 1.

Table 1 Pretreatment characteristics (n=16)

Characteristics	No. of patients (n)
Demographics	
Median age(y)(range)	56(45-70)
Males/females	9/7
Histology	
Squamous	15
Basaloid	1
Clinical stage (UICC TNM)	
T ₁	1
T ₂	15
T ₃	2
T ₄	1
N ₀	7
N ₂	6
N ₃	3
Stage II	7
Stage IIIB	9

Treatment

Of the 16 patients, 15 received external beam radiation therapy (EBRT) alone. The mean dose of EBRT was 40 Gy(range 30-75 Gy). One patient was implanted with ¹⁹²Ir sources after EBRT. The brachytherapy dose was 14 Gy. No patients received adjuvant or concomitant chemotherapy. After completion of primary treatment, the patients were followed up according to a standard protocol^[8].

RESULTS

Surgical results

Among the 16 patients who failed initial therapy, 14 underwent salvage abdominoperineal resection (APR) and two had transanal local excision. Partial prostatic resection was performed on two males. There were no deaths attributable to operation. Fourteen patients had their perineal wounds packed open for hip bath. Healing time of the perineal wound

exceeding 3 months was considered to be delayed, which occurred in eight patients. In four patients the healing time of perineal wound exceeded six months and in one patient the healing was not achieved within two years. Other complications unrelated to perineal wound were recorded in five patients. These included one small bowel obstruction treated conservatively, one perineourethra fistula after prostatic resection, one abdominal wound infection and two neurocystitis.

Oncological results

All the patients were followed up. The median follow-up time was 120 (range 5-245) months after salvage surgery. At the time of the last follow-up nine patients died of disease progression, with a mean survival time of 16(range 5-27) months. In these patients, eight presented with a persistent disease and one had a recurrent disease. The median follow-up time among survivors was 173 (range 98-245) months. Six patients survived for more than 10 years. According to the initial tumor stage, one of seven patients with T₂N₀M₀ died 18 months after resection whereas eight of nine patients with T₁₋₄N₂₋₃M₀ disease were not controlled. Of the 16 patients, only one patient presented with a second locoregional disease recurrence and was salvaged with radiotherapy.

DISCUSSION

Despite progresses in chemoradiotherapy of anal epidermoid cancer^[3,4,9,10], a substantial percentage of patients, particularly those with more advanced disease, still developed a local failure and demand salvage therapy^[11,12]. Surgical resection was often recommended as the most appropriate salvage method^[13-15]. The overall survival rate for surgical salvage at 5 years was about 30-60%^[16,17]. Some investigators reported disappointingly low success rates^[18] and alternative approaches have been suggested, such as low dose radiotherapy or combined chemoradiotherapy^[19]. In the present study, six of the 16 patients who underwent appropriate surgical treatment survived for more than 10 years. These results are similar to those of Longo *et al*^[20], who reported a survival rate of 53% among 17 patients and Ellenhorn *et al*^[21], who noted that 44% of 38 patients survived for 5 years after salvage resection.

It is well known that delayed healing of perineal wounds is a common complication for patients after radiotherapy. Earlier investigators reported the perineal wound complication rate was up to 30%^[16,17,21]. In the study by Nilsson *et al*^[22], the rate of delayed healing was 66 % (22 of 35). No difference was detected in the radiation dose delivered between patients with delayed healing and those in whom healing was achieved within 3 months. Also in rectal cancer, preoperative radiotherapy whether given in 5.0-Gy fractions or using conventional 1.8-2.0-Gy fractions, always made the healing of perineal wounds delay^[23]. In 14 patients who received salvage APR, eight presented with a delayed perineal wound healing and one did not have a wound healing within two years. It might help the healing of large defects created in an irradiated field by using an omentoplasty or musculo-cutaneous flap^[24,25].

Of the five patients who presented with local recurrence after having achieved complete disease remission, three survived for more than 10 years. In contrast, among the 11 patients who presented with persistent diseases, eight died of the diseases within 3 years. There was a better 10-year survival among patients with recurrences compared with that in patients with a persistent disease. These findings are consistent with those of Nilssio *et al*^[22], who reported a significantly better 5-year survival among patients with recurrences (82% *versus* 33%) and Allal *et al*^[17](56% *versus* 23%), but contradicted with those of Pocard *et al*^[16], who reported that patients with a persistent disease had a longer survival time (74 *versus* 25

months). The difference may be related to the tumors' stage and nodal status at initial presentation, or, alternatively, may reflect more aggressive biologic phenotypes of tumors that are different in response to radiotherapy.

The effect of salvage surgery appeared to correlate with the initial disease stage^[26-28]. In the study by Allal *et al*^[17], 41% of patients who failed local treatment of T₂₋₃N₀M₀ anal canal cancer were successfully salvaged, compared with 17% of patients with T₁₋₄N₂₋₃M₀ anal canal cancer. The effects of initial lymph node involvement and tumor extent on patients' outcome after surgical salvage therapy also were stressed by Ellenhorn *et al*^[21]. In the present study, eight of 9 patients who died of the disease presented with T₁₋₄N₂₋₃M₀ anal canal cancer, whereas most of the survivors had a T₂N₀M₀ anal canal cancer.

In summary, salvage APR after radiotherapy has a high complication rate, but can bring a long-time survival in selected patients with anal canal cancer. Since patients with T₄ and/or N₂₋₃ tumors could not obtain much benefit from salvage surgery, salvage chemoradiotherapy needs to be further investigated.

REFERENCES

- 1 **Whiteford MH**, Stevens KR Jr, Oh S, Deveney KE. The evolving treatment of anal cancer: How are we doing? *Arch Surg* 2001; **136**: 886-891
- 2 **Lai MD**, Luo MJ, Yao JE, Chen PH. Anal cancer in Chinese: human papillomavirus infection and altered expression of p53. *World J Gastroenterol* 1998; **4**: 298-302
- 3 **Anonymous**. Epidermoid anal cancer: results from the UKCCCR randomised trial of radiotherapy alone versus radiotherapy, 5-fluorouracil, and mitomycin. UKCCCR Anal Cancer Trial Working Party. UK Co-ordinating Committee on Cancer Research. *Lancet* 1996; **348**: 1049-1054
- 4 **Bartelink H**, Roelofs F, Eschwege F, Rougier P, Bosset JF, Gonzalez DG, Peiffert D, van Glabbeke M, Pierart M. Concomitant radiotherapy and chemotherapy is superior to radiotherapy alone in the treatment of locally advanced anal cancer: results of a phase III randomized trial of the European Organization for Research and Treatment of Cancer Radiotherapy and Gastrointestinal Cooperative Groups. *J Clin Oncol* 1997; **15**: 2040-2049
- 5 **Cummings BJ**. Concomitant radiotherapy and chemotherapy for anal cancer. *Semin Oncol* 1992; **19**(4 Suppl 11): 102-108
- 6 **Esiashvili N**, Landry J, Matthews RH. Carcinoma of the anus: strategies in management. *Oncologist* 2002; **7**: 188-199
- 7 **Minsky BD**, Hoffman JP, Kelsen DP. Cancer: principles and Practice of Oncology. 6thd. Philadelphia: Lippincott Williams Wilkins 2001: 1319-1342
- 8 **Cummings BJ**, Keane TJ, O' Sullivan B, Wong CS, Catton CN. Epidermoid anal cancer: treatment by radiation alone or by radiation and 5-fluorouracil with and without mitomycin C. *Int J Radiat Oncol Biol Phys* 1991; **21**: 1115-1125
- 9 **Weber DC**, Kurtz JM, Allal AS. The impact of gap duration on local control in anal canal carcinoma treated by split-course radiotherapy and concomitant chemotherapy. *Int J Radiat Oncol Biol Phys* 2001; **50**: 675-680
- 10 **Beck DE**, Karulf RE. Combination therapy for epidermoid carcinoma of the anal canal. *Dis Colon Rectum* 1994; **37**: 1118-1125
- 11 **Spratt JS**. Cancer of the anus. *J Surg Oncol* 2000; **74**: 173-174
- 12 **Faynsod M**, Vargas HI, Tolmos J, Udani VM, Dave S, Arnell T, Stabile BE, Stamos MJ. Patterns of recurrence in anal canal carcinoma. *Arch Surg* 2000; **135**: 1090-1093
- 13 **Ryan DP**, Compton CC, Mayer RJ. Carcinoma of the anal canal. *N Engl J Med* 2000; **342**: 792-800
- 14 **Gao JD**, Shao YF, Bi JJ, Shi SS, Liang J, Hu YH. Local excision carcinoma in early stage. *World J Gastroenterol* 2003; **9**: 871-873
- 15 **Grabenbauer GG**, Matzel KE, Schneider IH, Meyer M, Wittekind C, Matsche B, Hohenberger W, Sauer R. Sphincter preservation with chemoradiation in anal canal carcinoma: abdominoperineal resection in selected cases? *Dis Colon Rectum* 1998; **41**: 441-450
- 16 **Pocard M**, Tiret E, Nugent K, Dehni N, Parc R. Results of salvage abdominoperineal resection for anal cancer after radiotherapy. *Dis Colon Rectum* 1998; **41**: 1488-1493

- 17 **Allal AS**, Laurencet FM, Reymond MA, Kurtz JM, Marti MC. Effectiveness of surgical salvage therapy for patients with locally uncontrolled anal carcinoma after sphincter-conserving treatment. *Cancer* 1999; **86**: 405-409
- 18 **Zelnick RS**, Haas PA, Ajlouni M, Szilagyi E, Fox TA Jr. Results of abdominoperineal resections for failures after combination chemotherapy and radiation therapy for anal canal cancers. *Dis Colon Rectum* 1992; **35**: 574-577
- 19 **Flam M**, John M, Pajak TF, Petrelli N, Myerson R, Doggett S, Quivey J, Rotman M, Kerman H, Coia L, Murray K. Role of mitomycin in combination with fluorouracil and radiotherapy, and of salvage chemoradiation in the definitive nonsurgical treatment of epidermoid carcinoma of the anal canal: results of a phase III randomized intergroup study. *J Clin Oncol* 1996; **14**: 2527-2539
- 20 **Longo WE**, Vernava AM 3rd, Wade TP, Coplin MA, Virgo KS, Johnson FE. Recurrent squamous cell carcinoma of the anal canal. Predictors of initial treatment failure and results of salvage therapy. *Ann Surg* 1994; **220**: 40-49
- 21 **Ellenhorn JD**, Enker WE, Quan SH. Salvage abdominoperineal resection following combined chemotherapy and radiotherapy for epidermoid carcinoma of the anus. *Ann Surg Oncol* 1994; **1**: 105-110
- 22 **Nilsson PJ**, Svensson C, Goldman S, Glimelius B. Salvage abdominoperineal resection in anal epidermoid cancer. *Br J Surg* 2002; **89**: 1425-1429
- 23 **Glimelius B**, Isacsson U. Preoperative radiotherapy for rectal cancer—is 5 x 5 Gy a good or a bad schedule? *Acta Oncol* 2001; **40**: 958-967
- 24 **de Haas WG**, Miller MJ, Temple WJ, Kroll SS, Schusterman MA, Reece GP, Skibber JM. Perineal wound closure with the rectus abdominis musculocutaneous flap after tumor ablation. *Ann Surg Oncol* 1995; **2**: 400-406
- 25 **Giampapa V**, Keller A, Shaw WW, Colen SR. Pelvic floor reconstruction using the rectus abdominis muscle flap. *Ann Plast Surg* 1984; **13**: 56-59
- 26 **Myerson RJ**, Kong F, Birnbaum EH, Fleshman JW, Kodner IJ, Picus J, Ratkin GA, Read TE, Walz BJ. Radiation therapy for epidermoid carcinoma of the anal canal, clinical and treatment factors associated with outcome. *Radiother Oncol* 2001; **61**: 15-22
- 27 **Gerard JP**, Chapet O, Samiei F, Morignat E, Isaac S, Paulin C, Romestaing P, Favrel V, Mornex F, Bobin JY. Management of inguinal lymph node metastases in patients with carcinoma of the anal canal: experience in a series of 270 patients treated in Lyon and review of the literature. *Cancer* 2001; **92**: 77-84
- 28 **Smith AJ**, Whelan P, Cummings BJ, Stern HS. Management of persistent or locally recurrent epidermoid cancer of the anal canal with abdominoperineal resection. *Acta Oncol* 2001; **40**: 34-36

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