

Radiotherapy for Anal Canal Cancer in Japan: A Retrospective Multi-Institutional Study

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Abstract

Purpose/Objective:

Recent studies show concurrent chemoradiotherapy is the standard of care for patients with anal canal cancer, because of their high local control rate and organ preservation concept. But in Japan, abdominal perineal resection has still been considered the standard treatment. However, for squamous cell carcinoma, the number of patients treated with chemo-radiotherapy is increasing recently. Therefore, we investigated the present status of radiation therapy for anal canal cancer.

Materials/Methods:

We analyzed the medical records of patients with anal canal cancer treated with radiotherapy with curative intent from 1995 to 2004 in 32 major institutions throughout Japan. Sixty-one patients were available for analysis. Patient and tumor characteristics were as follows: median age 68 (range 32-92), male/female = 13/48, Performance Status 0/1/2/3/unknown = 23/25/7/1/5, AJCC clinical stage I/II/III/IV = 3/33/9/16, squamous cell carcinoma / adenocarcinoma / baseloid cell carcinoma / transitional cell carcinoma / unknown = 51/5/3/1/1. Median total dose of radiation was 59.6Gy (range 40-76Gy). Brachytherapy was performed in 5 cases. 44 patients were received chemotherapy concurrently. The regimen of chemotherapy were 5-FU+MMC / 5-FU+CDDP / 5-FU alone / others = 20/16/6/2. Median follow up period of alive patients was 42.5 months (range 8.6-108 months).

Results:

After treatment completion, 41 patients had CR and 19 patients had PR. The overall survival rate at 2 and 5 years were 90% and 76% for overall patients, 100% and 100% for clinical stage I, 95% and 75% for stage II, 88% and 88% for stage IIIA, and 80% and 68% for stage IIIB, respectively. Local recurrence occurred in 12 patients. Lymph node and distant metastasis occurred in 6 and 6 patients, respectively. Local control rate of overall patients at 2 and 5 years were 81% and 72%, respectively. There was no significant relationship between radiation dose and local control. 12 patients underwent permanent colostomy from persistent or recurrent disease. Colostomy free survival rate at 2 and 5 years were 78% and 68%, respectively. Grade II toxicity was observed in 41 patients (dermatitis and mucositis (n=24), diarrhea (n=5), nausea (n=5), leukopenia (n=4), anemia (n=2), appetite loss (n=1)). Grade III toxicity was in 26 patients (dermatitis/mucositis (n=17), diarrhea (n=3), leukopenia (n=3), appetite loss (n=3)). Grade IV dermatitis and fistula were observed in one patient each.

Conclusions: Even though treatment methods varied among each institution, our results were comparable to those reported in the literature with satisfactory survival and local control rates. Prospective nationwide trials are warranted

Objectives

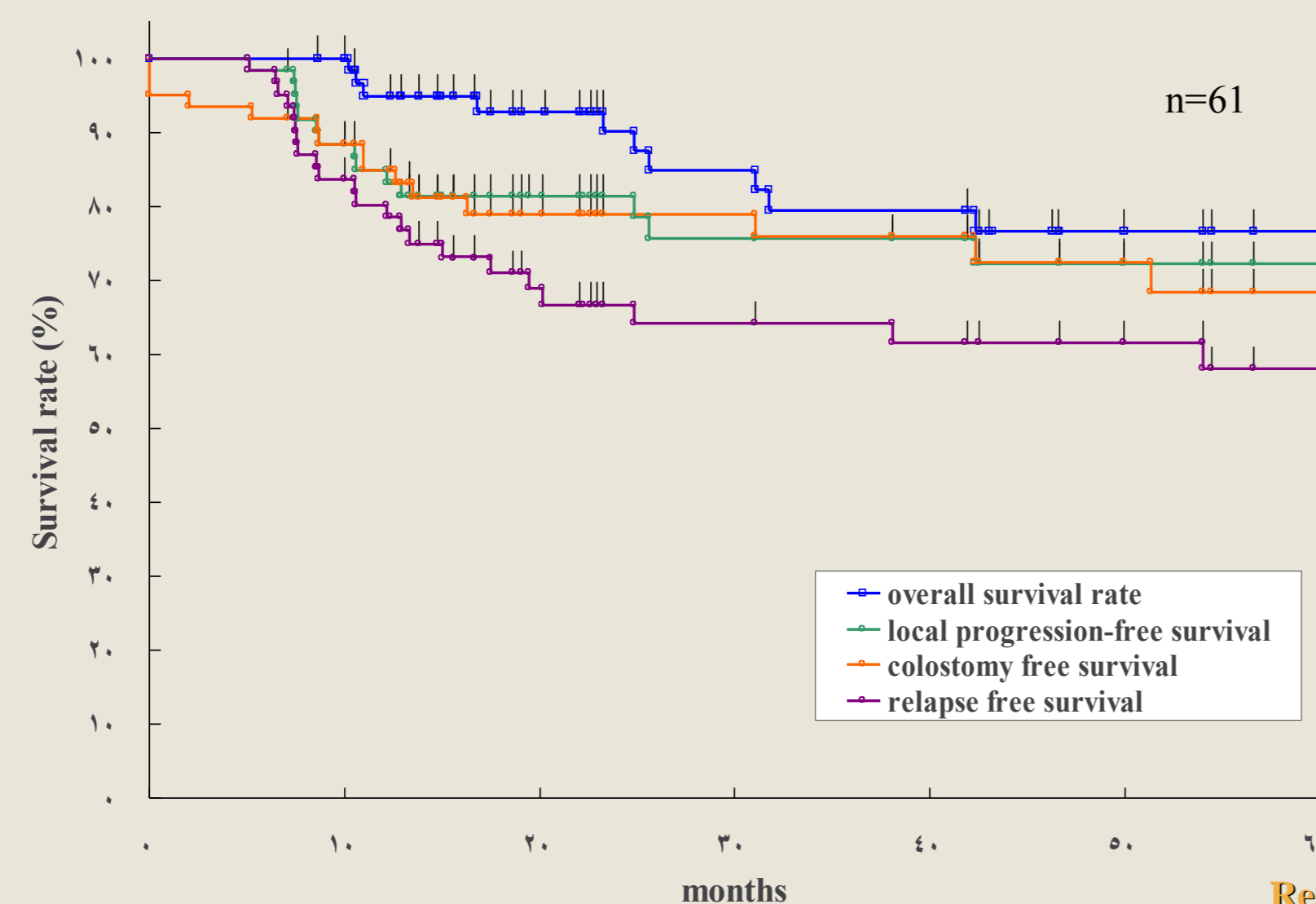
Cancers of the anal canal are uncommon, and have good response to radiation therapy. Recent studies showed multi-modality consisting of radiation therapy and chemotherapy have curability. And their organ preservation concept, the combined chemo-radiotherapy, reserving surgery for salvage, became the standard way of treatment. In Japan, abdominal perineal resection has still been performed as the standard treatment. But the number of patients treated with chemo-radiotherapy is increasing recently. Therefore, we investigated the present status of radiation therapy for anal canal cancer.

Methods

We retrospectively investigated the medical records of patients with anal canal cancer treated with radiotherapy from 1995 to 2004 in 32 major institutions throughout Japan. Records were reviewed for sex, age, staging, histological diagnosis, treatment and outcome.

147 cases were assembled and 61 cases were treated with curative intent. We analyzed the sixty-one patients in detail.

Survival Curve



	1yr	3yr	5yr
overall survival	95%	79%	76%
local progression-free survival	84%	75%	72%
colostomy free survival	84%	75%	68%
relapse free survival	80%	64%	58%

Patient Characteristics of All Cases

No. of Cases	148
Age	79 (27-92)
Gender (M:F)	60 : 88
Histology	Squamous CC 91 Adenocarcinoma 43 Adenosquamous 2 Baseloid CC 4 Transitional CC 2 unknown 6
Stage	I 6 II 51 IIIA 20 IIIB 37 IV 7 relapse 21 unknown 6
treatment method	curative 69 symptomatic 16 pre-operative 26 post-operative 16 relapse 21

Adverse effect

grade 2	dermatitis, mucositis	24 (39%)
	diarrhea	5 (8%)
	nausea	5 (8%)
	leukocytopenia	4 (7%)
	anemia	2 (3%)
	appetite loss	1 (2%)
grade 3	dermatitis, mucositis	17 (29%)
	diarrhea	3 (5%)
	leukocytopenia	3 (5%)
	appetite loss	3 (5%)
grade 4	dermatitis	1 (2%)
	form of fistula	1 (2%)

Results of Chemo-Radiotherapy in Literatures

study	local control	overall survival
RTOG/ECOG ¹⁾	84% (4yr)	76% (4yr)
EORTC 22861 ²⁾	68% (3yr)	70% (3yr)
UKCCCR ³⁾	61% (3yr)	65% (3yr)
EORTC 22953 ⁴⁾	88% (3yr)	81% (3yr)

1) Flam M et al. J Clin Oncol 14:2527-2539, 1996
2) Bartelink H et al. J Clin Oncol 15:2040-2049, 1997
3) Lancet 1996;348:1049-1054.
4) Bosset JF et al. Eur J Cancer. 2003 Jan;39(1):45-51

Patient Characteristics

No. of Cases	61
Age	68 (32-92)
Gender (M:F)	13:48
PS(WHO)	0-1 48 2 7 3 1 unknown 5
Histology	Squamous CC 28 Adenocarcinoma 9 Baseloid CC 1 Transitional CC 2 unknown 1
Stage	I 3 II 33 IIIA 9 IIIB 16

Results

72% of patients were received chemotherapy concurrently.

Median irradiated dose were 59.6Gy. Although we had 9 adenocarcinoma, and 28% of tumor were treated with radiotherapy alone, 41 patients had Complete Response and 19 patients had Partial Response.

Local recurrence were observed in 12 patients. The local progression-free survival rate at 3 years was seventy-five percent. It was no less than those reported. And overall survival rate was the same as those in literatures.

There were 26 grade3 toxicity, and grade 4 dermatitis and fistula were observed in one patient each. They would be acceptable.

Conclusion

Because of the little experience of radiation therapy against anal cancer, there is no standardized irradiating methods in Japan. The treatment dose, irradiating technique differed among each institution. Nevertheless, our results were comparable to those had been reported in the literature with satisfactory survival and local control rates.

In order to confirm the efficacy of multi-modality therapy, and establish the standard way of treatment, prospective nationwide trials are warranted and under consideration.

Treatment Characteristics

Total Radiation Dose (include brachytherapy)	59.6Gy (40-76Gy)
Treatment Extent	Whole Pelvis 21 Small Pelvis 23 Local + pararectal LNs 10 Local only 7
Inguinal Irradiation	30
Use of Brachytherapy	5
Use of Concurrent ChTx	44
5-FU+MMC	20
5-FU+CDDP	16
5-FU alone	6
others	2

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