# Local Control of Piriform Sinus Cancer Treated by Radiation Therapy Alone

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Local control rate by radical radiation therapy was analyzed in 33 patients with a piriform sinus cancer. Twenty-five patients (76%) were in stage T3 + T4. Local recurrence-free survival at 3 years was 49% in T1 + T2 and 25% in T3 + T4 ($p = 0.01$). In T1 + T2 lesions, a biologically effective dose for an acute reaction over 80 Gy and total treatment time less than 70 days appeared to improve local control. In T3 + T4 lesions, good radiation response assessed by the regaining of laryngeal mobility affected local control favorably. An esophageal involvement and destruction of the laryngeal cartilage as well as soft tissue extension precluded the possibility of local control by radiation therapy alone. In addition to the T-stage, other tumor factors should also be considered for predicting local control with radiation therapy.

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The prognosis of the piriform sinus cancer is known to be bleak, because most of the patients have locoregionally advanced disease already at presentation. Although a trend is now shifting to multimodality treatment employing surgery and perioperative irradiation (1–6), some authors emphasize the beneficial effect of radical radiation therapy in controlling the disease (7–9). The reported series of piriform sinus cancers treated solely with radiation therapy have shown that a local recurrence is the most frequently encountered regrowth (7, 9, 10). In contrast, patients given multimodality treatment usually succumb to neck node and/or distant metastases (1, 3–5, 11). In order to improve the treatment results of radical radiation therapy, clarification of the prognostic factors for local control by radiation therapy is imperative. In this institution, all patients with piriform sinus cancers have been treated with radical radiation therapy with surgery reserved only for radiation failures. In the current retrospective study, factors influencing local control in the piriform sinus cancer treated with radiation therapy were investigated.

## MATERIAL AND METHODS

From 1973 through 1993, the treatment policy for piriform sinus cancer has been primarily radical irradiation with surgery reserved for radiation failures in the Department of Radiation Therapy and Oncology, International Medical Center of Japan. Thirty-four patients without distant metastase were consecutively treated with radical radiation during this time period. One patient was excluded because less than 50 Gy was delivered owing to deterioration of general status during the radiation therapy. The remaining 33 patients without distant metastases underwent radical radiation therapy of more than 50 Gy and are the subject of the current study. The mean age was 67 years (range 46 to 84 years) with 25 males and 8 females. Staging was performed retrospectively according to the TNM classification (UICC, 1987) (12). The TN distribution of the 33 patients is presented in Table 1. Fifty-eight percent (19/33) of the patients had cervical lymph node metastasis at presentation.

Radiation therapy was performed using 6 MV x-rays from a linear accelerator with a supplemental electron irradiation if necessary. Total dose ranged from 52 Gy to 76 Gy with a mean of 67 Gy. In general, prophylactic upper and middle jugular chain irradiation was performed up to 40 Gy and was following by shrinking fields encompassing the primary tumor. Involved lymph nodes were further irradiated to the same dose with the primary lesion. Supplemental AP/PA fields were used to irradiate the lower neck, if this was involved. In 25 patients, a fractional dose of 1.8 Gy to 2.25 Gy with 4 or 5 fractions a week was employed, while 6 patients were treated with 3 Gy 3 times a week. Hyperfractionated radiation with a fractional dose

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of 1.2 Gy twice daily was used in 2 patients. In order to compare different fractionation regimens, a biologically effective dose (BED) was calculated with an assumption that the $\alpha/\beta$ equals 10 Gy in an acute reaction and 3 Gy in a late reaction (13). Correction for the total treatment time was not done. The mean BED for an acute reaction was 80 Gy with a range from 63 to 91 Gy, and 114 Gy with a range from 89 to 138 Gy for a late reaction.

Chemotherapy with oral 5-fluorouracil and its derivatives was administered to 15 patients after completion of radiation therapy as an adjuvant. Because no statistical difference in the local recurrence-free survivals could be seen between the patients treated with and without chemotherapy, the groups were considered together.

All survival curves were constructed using the Kaplan-Meier method (14) from the 1st day of radiation therapy. For calculation of the local recurrence-free survival, all local recurrences were considered as an event, even if they occurred secondarily after regional and/or distant regrowth. If complete remission was not obtained in 2 months after the completion of radiation therapy, the patient was considered to have a recurrence at day 0. Laryngectomized patients without local recurrence were censored on the day of the operation. The difference between survival curves was tested by the log-rank test. Mean follow-up of surviving patients was 53 months with a range of 38 to 67 months. No patients were lost to follow-up.

## RESULTS

Of the 33 patients, 5 remained recurrence-free with a 5-year recurrence-free survival of 12%. Fig. 1 demonstrates the first site of recurrence in the 28 patients. Local recurrence was seen in 20 patients, and regional lymph node recurrence in 16. Distant metastasis as an initial event was found in 5 patients.

Local recurrence-free survivals are shown in Fig. 2 according to T stage. Stages T1 + T2 together showed 3-year local recurrence-free survival of 49%, while it was 25% in T3 + T4 with a statistically significant difference ($p = 0.01$). The presence of neck lymph node metastasis also had a statistically significant impact upon local recurrence-free survival. Three-year local recurrence-free survival was 57% in node-negative patients and 20% in node-positive ($p = 0.04$).

**Table 1**

*TN distribution of 33 patients with the piriform sinus cancer*

| | N0 | N1 | N2a | N2b | N2c | N3 | Total |
|---|---|---|---|---|---|---|---|
| T1 | 1 | 0 | 0 | 0 | 0 | 1 | 2 |
| T2 | 2 | 1 | 2 | 0 | 0 | 1 | 6 |
| T3 | 2 | 1 | 2 | 1 | 0 | 1 | 7 |
| T4 | 9 | 4 | 1 | 1 | 2 | 1 | 18 |
| Total | 14 | 6 | 5 | 2 | 2 | 4 | 33 |

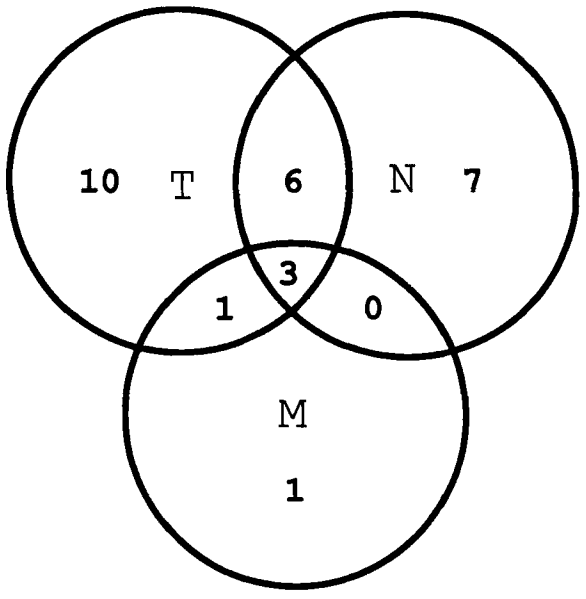


*Fig. 1.* Initial site of recurrence.

In T1 and T2 patients, the dose response relationship was studied using a scattergram (see Fig. 3). All the patients with local control were observed for more than 12 months. BED for an acute reaction of less than 80 Gy and a total treatment time of over 70 days seems to weaken local control rate. The patient who was irradiated with a high BED for a late reaction of 126 Gy succumbed to a complication necessitating laryngectomy. Of the 8 patients with T1 and T2 primaries, 2 patients had an apical involvement, and 4 had an involvement of the lateral wall of the piriform sinus. Both patients with an apical involvement recurred locally, while a local recurrence was seen in one of the 4 patients with lateral wall involvement. Two of the 4 patients with involvement of the anteromedial wall of the piriform sinus recurred locally.

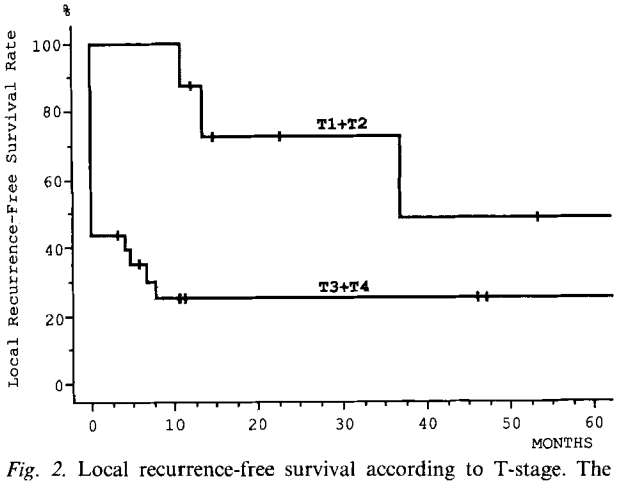


*Fig. 2.* Local recurrence-free survival according to T-stage. The difference reached a statistical significance between T1 + T2 and T3 + T4 ($p = 0.01$)

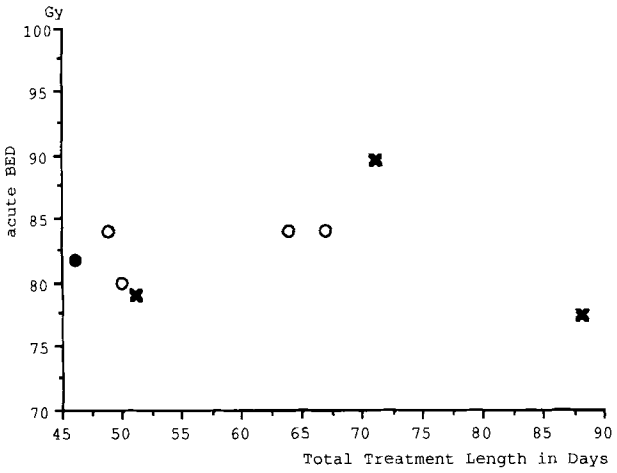


*Fig. 3.* Scattergram showing the relationship between biologically effective dose (BED) for an acute reaction, total treatment length, and local control in T1 + T2. ○ = Local control; × = local recurrence; ● = complication.

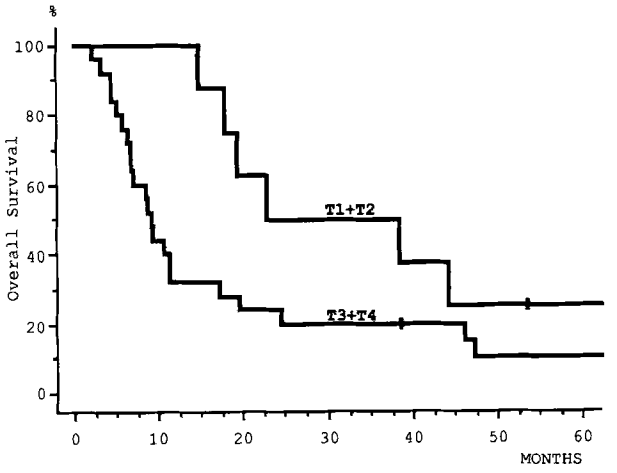


*Fig. 4.* Actuarial survival according to T-stage. The difference reached a statistical significance between T1 + T2 and T3 + T4 (p = 0.05).

In T3 primaries, 4/4 patients with an extensive involvement of larynx with tumorous swelling or destruction of the false vocal cord recurred locally, while in patients with a slight tumor extension over the aryepiglottic fold, a local recurrence was seen in 1/3 patients (Table 2). Recovery from the laryngeal fixation was observed in 2 patients at the completion of the radiation therapy, with one patient locally controlled. Laryngeal fixation remained in 5 patients, one of whom was locally controlled. In T4 primaries, tumor extension to the esophagus and destruction of the laryngeal cartilaginous framework as well as soft tissue extension precluded the possibility of cure by radiation therapy alone (Table 2).

After the local recurrences, laryngopharyngectomy with a neck dissection was performed in 5 patients, of whom only 2 remained disease-free with follow-up length of 40 and 73 months, respectively. The remaining patients with a local recurrence were treated with repeated radiation, or by best supportive care when a poor general status did not allow any interventions. All patients managed by conservative therapy finally died of disease.

**Table 2**

*Site of involvement and local control in T3 and T4 piriform sinus cancers (local control/total number)*

| | |
|---|---|
| T3 (n = 7) | |
| Swelling or tumor at false vocal cord | 0/4 |
| Superficially intact false vocal cord and tumor slightly overcomes aryepiglottic fold | 2/3 |
| Recovery of fixation at completion of RT | 1/2 |
| No recovery of fixation at completion of RT | 1/5 |
| T4 (n = 16)* | |
| Esophageal involvement | 0/6 |
| No Esophageal involvement | 2/10 |
| Cartilage destruction and/or soft tissue extension | 0/7 |
| No cartilage destruction and/or soft tissue extension | 2/9 |
| Recovery of fixation at the completion of RT | 1/2 |
| Non-recovery of fixation at the completion of RT | 1/9 |

* Excluding 2 cases with laryngectomy for complication. RT: radiation therapy.

Concerning complications of radiation therapy, dyspnoe by laryngeal edema mandating surgery was seen in 3 patients, of whom 2 had stage T4. Two of them required a laryngectomy and the remaining patient underwent tracheostomy. Two patients succumbed to bleeding and pneumonia, and the remaining patient suffered from neck metastasis, all with fatal outcomes.

Secondary malignancy was seen in 9 patients, of whom one had a tertiary malignancy. Esophageal cancer was seen in 3 patients. Lung cancer, gastric cancer and colorectal cancer occurred each in 2 patients. Oral cavity cancer was found in one.

Actuarial survival is shown in Fig. 4. For all patients, 3- and 5-year actuarial survivals were 27% and 14%, respectively. The difference between T1 + T2 and T3 + T4 tumors was statistically significant (p = 0.05).

## DISCUSSION

While some authors report a fairly good local control rate in T3 and T4 piriform sinus cancers treated with radiation therapy alone (3, 7), the combined modality treatment with surgery and perioperative radiation is generally accepted in these stages (8, 15). The current study also demonstrated that local control rate was low in T3 and T4 primaries by radiation therapy alone. In T3 and T4 cancers, recovery from a laryngeal fixation appears to be the most readily recognizable sign of radiation effect. In some institutions, locally advanced laryngeal and hypopharyngeal cancers are irradiated with a curative intent, if laryngeal fixation recovers after 50 Gy (16). Our study showed that at the completion of radiation therapy, recovery from the laryngeal fixation was observed in 22% (4/18) of the T3

and T4 patients, while 2 of them remained locally controlled. Both patients regained laryngeal mobility already at 40 Gy. In contrast, local control was obtained in only 2 of the 14 patients whose laryngeal fixation did not change. It would thus appear that recovery from a laryngeal fixation at 40–50 Gy and at the completion of radiation therapy might be useful in predicting local control. In contrast, large tumor volume at presentation appears to have a negative impact upon local control by radiation therapy alone. Unfavorable signs included an extensive involvement of the larynx in T3, and esophageal as well as extralaryngeal soft tissue extension and cartilage destruction in T4. In these patients, radiation therapy alone failed to control the local lesions and the combined modality approach with surgery and perioperative radiation seems mandatory.

There remain some controversies in the treatment policy of T1 and T2 piriform sinus cancers. While some authors reported good local control in T1 and T2 piriform sinus cancers by means of an exclusive radiation (7, 8), others performed combined therapy with surgery and perioperative radiation therapy (1, 2). Mendenhall et al. showed an excellent local control rate of 79% in T1 and T2 piriform sinus cancers by radiation therapy alone (8). In the current study, local rate in T1 + T2 primaries was far from satisfactory. Although the data presented in Fig. 3 suggest that an improvement of local control could be obtained by a dose increment as well as by shortening the total treatment time, the small number of patients precludes any statistically significant conclusions. In the piriform sinus cancers, a partial pharyngolaryngectomy is not indicated for the patients with an apical involvement (17). However, Mendenhall et al. denied the prognostic significance of an apical involvement in attaining local control by radiation therapy alone (8). Although both of the patients with an apical involvement recurred locally in our study, statistically significant relationships could not be demonstrated between involved region and local control in T1 + T2 because of the small number of patients.

The present study suggests that initial tumor volume or T-stage is an important prognostic factor in local control by the radical radiation therapy in piriform sinus cancer. The response to radiation therapy represented by recovery from the laryngeal fixation might also be a useful predictor for local control. In selected patients with a low tumor volume and good radiation response, radical radiation therapy in order to preserve the voice is a rational option combined with a neck dissection to treat neck node metastasis (18).

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