ANALYSIS OF 3-YEAR SURVIVORS OF ESOPHAGEAL CANCER PATIENTS TREATED WITH HIGH-DOSE-RATE INTRALUMINAL BRACHYTHERAPY AFTER EXTERNAL RADIOThERAPY

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Abstract Between May 1980 and June 1987, 100 patients with thoracic esophageal cancer were treated with high-dose-rate intraluminal brachytherapy (HDRIBT) after external radiotherapy (ERT). The standard treatment protocol was 60 Gy/6 weeks of ERT and 12 Gy/week of HDRIBT. Follow-up time was 3 to 9 years (median 5 years). The 100 patients were classified into two groups according to 3-year survival after the initiation of radiotherapy. Fourteen patients survived for 3 or more years; the other 86 patients died within 3 years. The data of all patients were examined, and the following factors correlated with 3-year survival: female sex, shorter tumor length, superficial or tumorous-type x-ray appearance before treatment, earlier stage, and better local response to treatment. In 3-year survivors, intercurrent death was the main cause of death, whereas uncontrolled cancer was the main cause among patients who died within 3 years.

Key words: Radiotherapy, Intraluminal brachytherapy, Esophageal cancer, Staging

INTRODUCTION

Esophageal cancer is a disease that still has a poor prognosis despite recent medical advances. The disease is advanced in most patients at the time of presentation, which is one reason for its poor prognosis. Another reason is that the local tumor has not been easily controlled with external radiotherapy (ERT) alone. Recently developed adjuvant radiotherapy using intraluminal brachytherapy after ERT has proven to be effective treatment for localized lesions of esophageal cancer. In our hospital, high-dose-rate intraluminal brachytherapy after ERT (ERT+HDRIBT) has been administered since May 1980. This is an analysis of the data of 3-year survivors among the patients treated with ERT+HDRIBT.

PATIENTS AND METHODS

Between May 1980 and July 1987, 100 patients with thoracic esophageal cancer were treated with ERT+HDRIBT in our department. The patients were classified into two groups according to 3-year survival from the start of radiotherapy.

For each group the following data were recorded: age, sex, tumor site, tumor length, radiological findings of tumor, stage, other diseases present prior to treatment, presence of other primary cancer, and local response to treatment. The disease stage was classified as limited disease (LD) or extensive disease (ED): LD included disease of stages I and II according to the clinical diagnostic classification of AJCC classification of 1983, and ED included stages III and IV (Table 1). For staging, all patients were examined by barium esophagography, endoscopy, computed tomo-
graphy, chest X-ray, and most also underwent liver scanning. Biopsy via endoscopy showed squamous cell carcinoma in all cases.

ERT was performed with either 10 MV X-rays (LMR-15, Toshiba, Tokyo) or a cobalt-60 beam (Theratron 80, Atomic Energy of Canada, Ottawa). Opposed anteroposterior/posteroanterior fields were used up to 40 Gy, followed by the rotation technique. The field was 6 cm in width, and extended 3 cm beyond the superior and inferior margins of the tumor. HDRIBT was performed using a high-dose-rate, remote afterloader (RAL-303, Toshiba, Tokyo). The source was $^{60}$Co (2.2 Ci in May 1980 and in March 1987). Its dose rate was 680 R per min ($17.5 \times 10^{-2}$ C/kg) in May 1980 and in March 1987, and 270 R per min ($6.9 \times 10^{-2}$ C/kg) in February 1987, at a point 1 cm from the source. The delivered dose was calculated using a computerized radiotherapy planning system (RO-7, Varian Associates, Palo Alto, Calif.). Radiation was administered to a level 5 mm below the surface of the mucosa, 1 cm from the source. Details on the technique and dosimetry of HDRIBT have been reported previously. On the basis of our earlier studies of survival and local control, complications, and autopsy results, the following standard treatment regimen has been developed: ERT (60 Gy in 30 fractions over 6 weeks), followed by no treatment for one week, followed by HDRIBT (12 Gy in 2 fractions during one week).

The local response was evaluated by barium esophagography, or endoscopy, or both one month after completion of the radiotherapy. The clinical efficacy was judged by the following criteria: complete response (CR) 100% regression, partial response (PR) greater than 50% reduction in tumor bulk but less than 100% regression. When endoscopic biopsy showed cancer in a clinically CR or PR patient, the response was classified as neither CR nor PR. During the first 6 months of follow-up, examination was performed every month, and thereafter every 2 or 3 months. Endoscopic biopsy was performed in all patients in whom tumor recurrence was suspected. Survival time calculated from the beginning of radiotherapy to death, or to June 30 1990. No patients were lost to follow-up. The follow-up time was 3 to 9 years (median 5 years). Statistical analysis was performed using Student's t-test or the chi-square test.

### RESULTS

Out of 100 patients, 14 survived for 3 years or longer. Comparisons between 3-year survi-
Table 3. Prognosis after radiotherapy

<table>
<thead>
<tr>
<th>Survivors</th>
<th>3-Year</th>
<th>less than 3-Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alive</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Death from</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancer</td>
<td>2</td>
<td>66</td>
</tr>
<tr>
<td>Intercurrent disease</td>
<td>5</td>
<td>17</td>
</tr>
<tr>
<td>Unknown</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

vors and non-survivors are shown in Table 2. Sex, tumor length, radiological appearance of tumor, stage, and local response after treatment were found to be significant prognostic factors of 3-year survival. In the 3-year survivors, the female/male ratio was higher, and the mean tumor length was shorter. Superficial and tumorous-type tumor were found in 8 of the 14 3-year survivors, but in only 19 of the 86 non-survivors. All 3-year survivors were LD, but 52 of the 86 non-survivors were ED. CR rate was 71% (10/14) of the 3-year survivors and 23% (20/86) of the non-survivors.

Of the 14 3-year survivors, 7 are still 3–9 years alive at the time of this writing. The causes of death of the 86 non-survivors are shown in Table 3. The main cause of death among the patients who survived for more than 3 years has been intercurrent disease.

DISCUSSION

Staging of cancer prior to treatment is a most important procedure. TNM classification of AJCC of 1987 for esophageal cancer has two main differences from the previous AJCC classification of 1983: (1) the separate classifications for clinical and pathological staging have been merged in a new edition; (2) the staging classification based upon wall penetration and lymph node status.

The new classification is based on the examination of esophagectomy specimens, in which wall penetration and spread to regional lymph nodes are important independent prognostic factors. The AJCC classification of 1987 is simplified and very useful for the surgically treated patients in whom precise staging can be performed. However, it is very difficult to use this staging for patients treated by radiotherapy since the diagnosis may be incorrect, and a shorter time is available for staging. Prior to radiotherapy, wall penetration and lymph node spread are difficult to diagnose accurately in all patients using diagnostic imaging devices, even with CT, MRI, and echography. If staging of the patient prior to treatment is not accurate, the outcome of the following treatment cannot be exactly determined. In patients treated surgically, the exact pathological classification may be determined before their recovery from the surgery, and after recovery, adjuvant chemotherapy or postoperative radiotherapy can be performed according to the stage. However, in patients treated by radiotherapy, the disease stage must be determined as soon as possible so radiotherapy can commenced as soon as possible. At present, a simple classification is used in our department. The disease stages are classified as LD or ED, based on the clinical staging of AJCC of 1983. Stages I and II are collectively known as LD, and stages III and IV as ED. If the patient is fit for surgery, LD signifies operable disease, and ED signifies inoperable disease. Most candidates for surgery are patients with LD, and those for radiotherapy are patients with ED or inoperable LD. Compared with pathological staging after surgery, clinical staging performed prior to radiotherapy is inaccurate, so we use the simple, rough staging system of LD and ED for patients with esophageal cancer undergoing radiotherapy.

Several factors affect the long-term survival of patients with esophageal cancer treated by radiotherapy. Beatty et al. reported that sex, tumor size, and stage correlated with patient survival, and in our series, the same results were found. Smaller tumor size and earlier stage are the most important factors for better prognosis after radiotherapy in patients with esophageal cancer. Thus, earlier diagnosis results in a better prognosis after radiotherapy. The clinical effect of radiation differs in patients with different types of tumor. Radiotherapy is more effective in superficial or tumorous-types than in other types. Eight of the 14 3-year survivors of our series had superficial or tumorous-types of tumor. Prior to
radiotherapy, we will now be able to predict a higher likelihood of local response in patients with superficial or tumorous-type tumors than in patients with other types.

Informed consent of the patient is necessary before treatment, and patients with esophageal cancer should be informed of the possibility of cure after radiotherapy. In this study, we found that factors associated with a better prognosis were female sex, smaller tumor size, earlier stage, and radio-sensitive tumor-type. In surgical candidates with these factors and high surgical risk, we should treat with ERT+HDRIBT rather than with surgery.

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REFERENCES


要旨：1980年5月から1987年6月の間に外照射後高線量率腔内照射で治療した胸部食道癌症例は100例であった。治療方法は、外照射60Gy/6週の後、高線量率腔内照射12Gy/1週を行うのを基準とした。経過観察は3年から9年であった。100症例を3年以上生存者と3年未満死亡者に分け分析した。3年以上生存者は14例で他の86例は3年未満死亡であった。3年以上生存に関係した因子は性、腫瘍長径，型，病期，局所治療効果であった。3年以上生存者の死因は，他病死が主であったのに，3年未満死亡者では，癌死が主であった。

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