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Main Article

Dr M Faisal takes responsibility for the integrity of the content of the paper

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Abstract

Background. Early laryngeal cancer treated with definitive radiotherapy or surgery has a high cure rate. This study evaluated the patterns of treatment failure and long-term results of early laryngeal cancers treated with definitive radiotherapy.

Method. From January 2002 to December 2014, a total of 242 patients with early-stage laryngeal cancers were treated with radical radiotherapy.

Results. All patients had squamous cell carcinoma of the larynx (92 per cent male and 8 per cent female). Median follow-up was 4.5 years. The majority of patients were smokers (57.4 per cent). Local failure was seen in 12.5 per cent of stage I patients and 22.8 per cent of stage II patients. The 5-year overall survival and disease specific survival were 84 per cent and 91 per cent, respectively.

Conclusion. In summary, radiotherapy is a suitable treatment modality for patients with early-stage laryngeal cancer, with an overall locoregional control rate of 84 per cent. Patients who fail radiotherapy may still undergo salvage laryngectomy.

Introduction

Laryngeal cancer is one of the most common cancers of head and neck, and in 2007 it accounted for one fourth of the approximately 45 000 head and neck cancers diagnosed in the USA.¹ More than 95 per cent of these cancers are squamous cell carcinomas histologically, and 60–65 per cent of them arise from the glottis followed by the supraglottis, whereas only 2 per cent arise from the subglottis.²

Patients with glottis cancer mostly present with hoarseness and are therefore identified in the early stages (T1 or T2).³ Additionally, glottic tumours have sparse lymphatic drainage and rarely metastasise in the early course of the disease. Early-stage laryngeal cancers have good cure rates with radiotherapy and larynx preservation surgical procedures. Because all the evidence consists of non-randomised studies, the treatment of choice remains a controversial issue.⁴ The reported cure rates using radiotherapy for early-stage laryngeal cancers (T1 and T2) range from 75–95 per cent.⁵

There are multiple factors that contribute to the prognosis of laryngeal cancers such as tumour site, age, gender, histological grade, anterior commissure involvement, histology, addictions, performance status, haemoglobin level and duration of primary treatment.⁶ All patients are at highest risk of recurrence in the first two to three years of their follow up. After this, the chances of recurrence are low, and any lesion represents a new primary cancer.⁷

The rationale for this review was to find the predictors of treatment failure in early laryngeal carcinomas (T1 or T2) treated with hypo-fractionated radical radiotherapy in a high-volume, third-world cancer hospital.

Materials and methods

The head and neck oncology department at Shaukat Khanum Memorial Cancer Hospital, Lahore, Pakistan, maintains a prospective database of all cancer patients. A total of 249 patients with early-stage laryngeal cancers were treated from January 2002 to December 2014 at the Department of Head and Neck Oncology.

We excluded seven patients who had histopathology other than squamous cell carcinoma. All cancer patients were assessed with a comprehensive head and neck examination including flexible direct laryngoscopy and imaging (computerised tomography (CT) scans and chest X-rays). Tumour staging was done according to the American Joint Commission on Cancer manual (6th edition). Electronic records were used to extract data variables including demographic data, primary tumour classification (histology, tumour node metastasis, classification, stage and histological grade) and primary treatment-related factors (treatment regimen, start and end of treatment, type of surgery,

Table 1. Characteristics of patients

Characteristics	Value
Median age (years)	62.6
Gender (n (%))	
– Male	223 (92.1)
– Female	19 (7.9)
Smoking (n (%))	
– Yes	139 (57.4)
– No	103 (43.6)
Subsite (n (%))	
– Supraglottis	6 (2.5)
– Glottis	233 (96.3)
– Subglottis	3 (1.2)
Stage (n (%))	
– I	207 (85.5)
– II	35 (14.5)
Grade (n (%))	
– Well	105 (43.4)
– Moderate	96 (39.7)
– Poor	14 (5.8)
– Unknown	27 (11.1)

treatment of neck, radiotherapy doses, duration of treatment, interruptions, follow up and outcomes).

All patients were treated with conventional radiotherapy simulated in a supine position and immobilised in a thermo-plastic shell with two lateral beams at 2.75 Gy per fraction (total dose 55 Gy in 20 fractions) from Monday to Friday. The radiation field was bounded by the upper border of hyoid bone superiorly, the lower border of cricoid cartilage inferiorly, and the posterior limit was defined by vertebral bodies, but keeping the cord off the radiation field.

Assessment of response

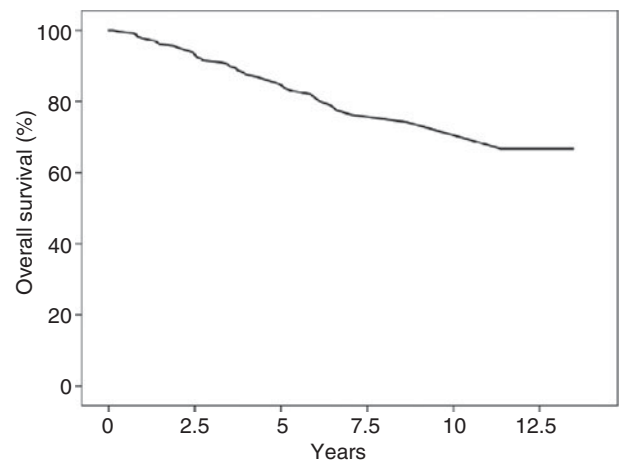
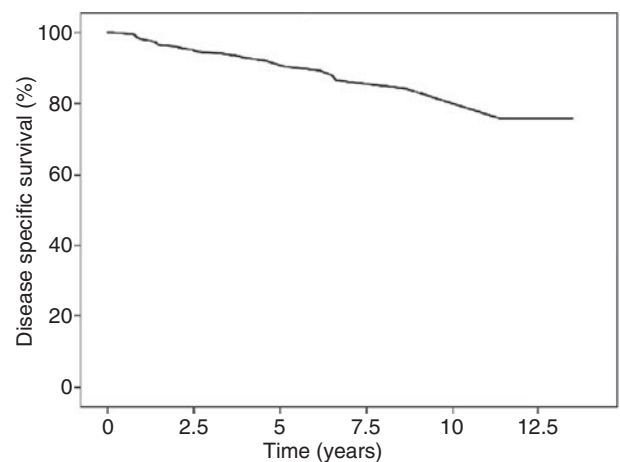
Radiation response was assessed at six weeks after radiotherapy by performing a complete head and neck examination and fiberoptic nasopharyngoscopy. All patients were followed up in the clinic every three months in the first year, every four months in the second year and every six months thereafter.

Table 2. Treatment characteristics

Disease stage	Treatment	Patients (n)	Mean radiation dose (Gy)	Median follow up (years)
I	Radiotherapy	207	55	
II	Radiotherapy	31	65	4.5
II	Chemoradiotherapy	4	65	

Table 3. Pattern of recurrence according to stage

	Local	Regional	Locoregional	Distant	Total failures (n (%))
Stage I	26	2	1	2	31 of 207 (15)
Stage II	8	0	1	0	9 of 35 (26)

**Fig. 1.** Overall survival.**Fig. 2.** Disease specific survival.

Any patient with the suspicion of recurrence was restaged using a CT scan and biopsy.

Statistical analysis

The data were analysed using SPSS® statistical software (version 20). Survival rates were calculated using Kaplan–Meier curves. Overall survival was defined as the time between first presentation in the head and neck clinic and death due to any cause or last follow-up examination. Disease specific survival was defined as the time between first presentation in the

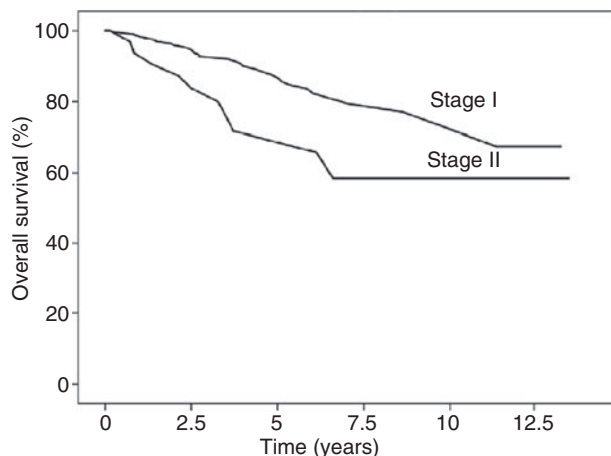


Fig. 3. Overall survival by stage.

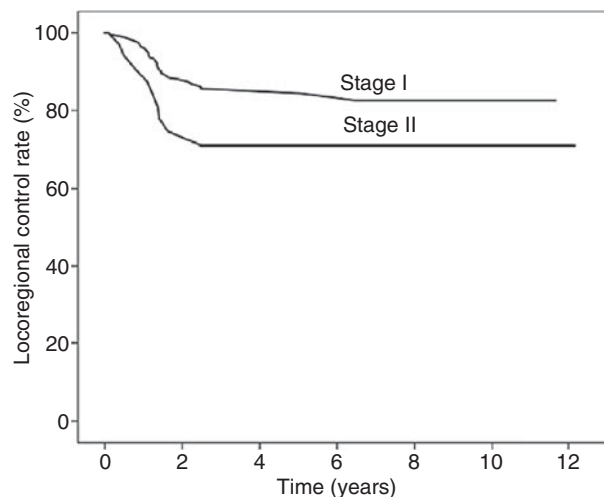


Fig. 6. Rate of locoregional control according to stage.

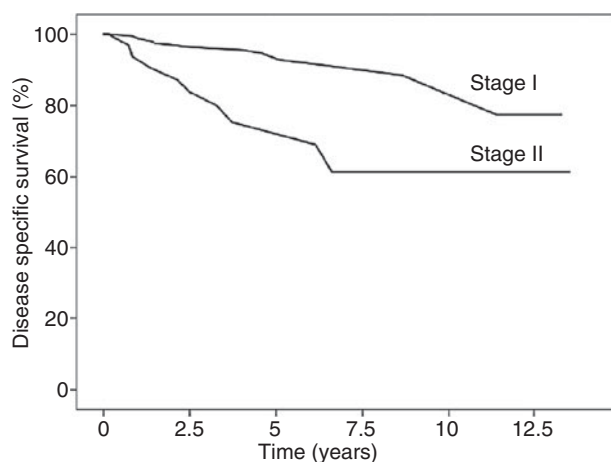


Fig. 4. Disease specific survival by stage.

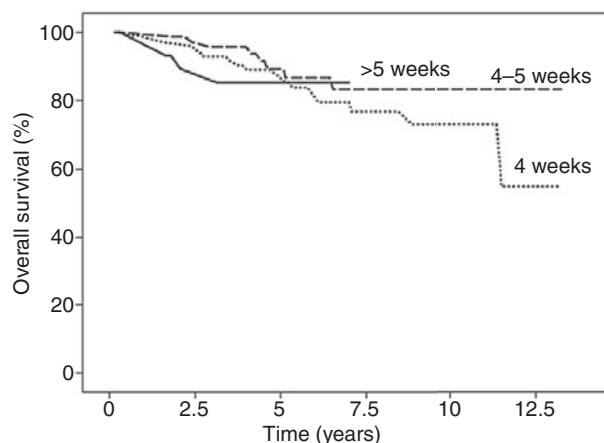


Fig. 7. Impact of treatment duration on overall survival.

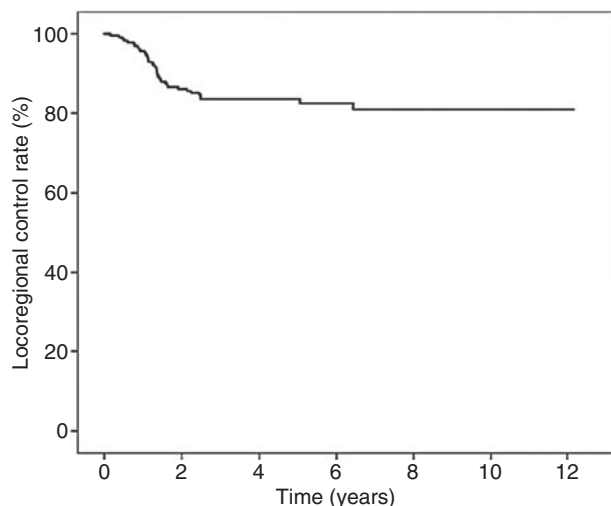


Fig. 5. Rate of locoregional control.

head and neck clinic and death due to disease only or last follow-up examination. Locoregional control was defined as the time interval from the treatment start date until the locoregional failure date, date of death if the patient died from non-cancerous causes but without relapse or date last seen at follow up if alive and relapse free.

Results

Table 1 shows the characteristics of the study population. The majority of our patients were male (92.1 per cent). The glottis was the most common cancer subsite (96.3 per cent), and 85.5 per cent of patients had stage I disease. All stage I patients received an average of 55 Gy of radiotherapy, whereas all stage II patients received 65 Gy of radiotherapy except for two patients who received chemoradiotherapy (Table 2).

Median follow up of our patients was 4.5 years. Locoregional or distant failure was seen in 15 per cent (31 of 207) of stage I patients and 26 per cent (9 of 35) of stage II patients (Table 3). Of all the local failures, 26 patients underwent salvage total laryngectomy, and 8 patients refused surgery. At the last follow up, 14 patients who underwent laryngectomy were alive without disease, 4 were alive with disease and 8 had died. The incidence of second primary malignancy was only 2.5 per cent (6 of 242), and two patients developed distant metastasis.

The 5-year overall survival and disease specific survival rates were 84 per cent and 91 per cent, respectively (Figures 1 and 2). Patients with stage I and II disease had overall survival rates of 87 per cent and 67 per cent, while their disease specific survival rates were 93 per cent and 71 per cent, respectively (Figures 3 and 4). The overall locoregional control at 5 years was 84 per cent, while locoregional control for stage

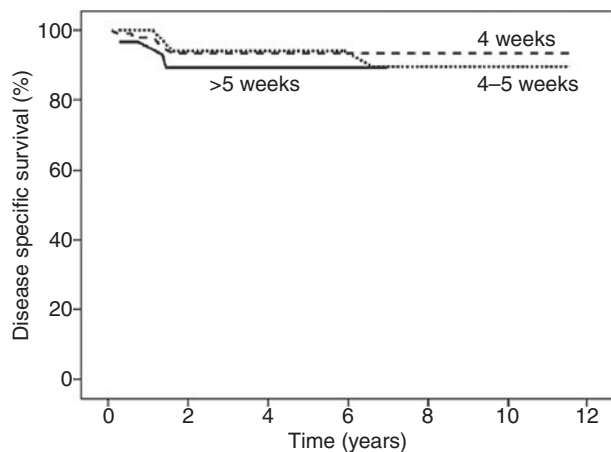


Fig. 8. Impact of treatment duration on disease specific survival.

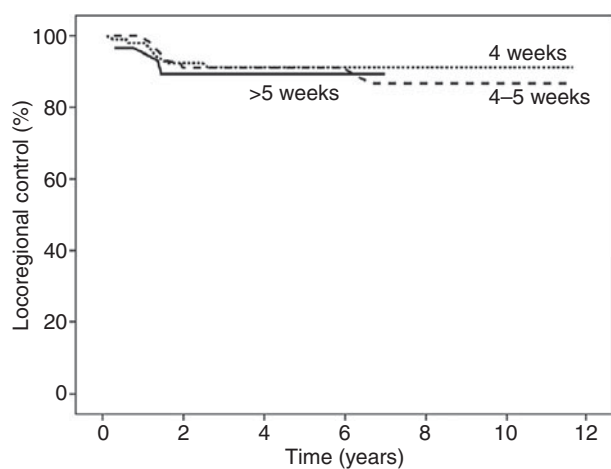


Fig. 9. Impact of treatment duration on locoregional control.

I and II disease was 84 per cent and 71 per cent, respectively (Figures 5 and 6). We also looked at the impact of duration of treatment on overall survival, disease specific survival and locoregional control. It was seen that this variable had no impact on survival (Figures 7, 8 and 9). At the time of analysis, 81.4 per cent of patients were alive, and disease related deaths were seen in 9.5 per cent of cases. Deaths due to reasons other than the tumour were reported in 7 per cent of patients, and 2 per cent of patients were alive with disease.

Discussion

Laryngeal cancers have been treated both by surgery and by radiotherapy with equivalent results. The choice of treatment depends on institutional practice, availability of surgical expertise and selection of the treatment modality by the patient undergoing surgery. The primary aim of treatment is to preserve the organ and its function of speech and swallowing. The current series study is a retrospective review of stage I and II laryngeal cancer patients treated at a single institution. At our institution, primary radiotherapy is the main stay of treatment for early-stage laryngeal cancers.

Smoking contributed as a risk factor in only 57 per cent of our patients compared to the published literature where it was 82 per cent. The possible explanation is a high prevalence of smoking among females in the western population.⁸ During

follow-up, only 6 patients (2.5 per cent) developed second primary malignancy as compared to 22.2 per cent reported by Franchin *et al.*, and this high incidence is probably related to the higher incidence of smoking in that series. A similar pattern has also been shown in other studies.⁹

The prognosis is reported to be better in stage I cancers than stage II cancers. In this study, overall survival at 5 years was 87 per cent and 67 per cent for stage I and II, respectively. Frata *et al.* and Cellai *et al.*^{10,11} reported much lower survival in 1087 patients treated with radiotherapy (77 per cent and 59 per cent, respectively). Locoregional control in our study was 84 per cent and 71 per cent for stage I and stage II, respectively, which is comparable to other published literature.¹²

During treatment, interruption or delay negatively impacted survival. This impact is reinforced by the need for additional fractions of radiation. We did not enforce additional fractions of radiation in cases of treatment delay. In our study, we found that duration of treatment had no significant difference on overall survival, disease specific survival and locoregional control. Johannes *et al.*¹³ reported a drop of 5 years local control from 95 per cent to 79 per cent when the treatment duration was prolonged by 40 days, whereas, in our report, the local control remained around 90 per cent for all 3 groups (1: treatment duration less than 4 weeks; 2: treatment duration of 4–5 weeks; and 3: treatment duration more than 5 weeks). Similarly, in a study by Rudoltz *et al.*,¹⁴ the overall survival and disease specific survival went down from 100 per cent to 80 per cent after a delay of more than 5 weeks, which was contrary to our findings of 87 per cent irrespective of duration of treatment.

Salvage rates after radical radiotherapy were satisfactory because we were able to salvage just above 50 per cent of patients. The majority of our patients use an electrolarynx for their voice, and they find it very helpful in routine communication. These results necessitate regular follow up as surgical salvage is a reasonable and effective option.

- This study was one of the largest series studies from a resource-limited, high-volume cancer centre in a third-world country
- This study uses comprehensive records from an updated database
- Treatment duration was not shown to have an impact on survival outcome

For early laryngeal cancers, besides radical radiotherapy, transoral laser resection and open partial laryngectomy are other acceptable options.^{15,16} With any of these options, the probability of cure and retention of voice is comparable to radical radiotherapy. The drawback of radiotherapy is the long duration of treatment.¹⁶ Transoral laser surgery is best suited for patients with small lesions, specifically those limited to the middle third of one vocal fold.

We acknowledge certain limitations of our study. Since it is a retrospective review, it is therefore susceptible to deficiencies in data collection. For a similar reason, we were not able to assess patients' voices and record after radiotherapy complications. The strength of the study is, however, the completeness of the study population, as our department prospectively maintains a head and neck database; therefore, no patient was excluded because of an inability to retrieve their medical records.

Conclusion

In summary, radiotherapy is a suitable treatment modality for patients with early-stage laryngeal cancer. In fact, radiotherapy achieved an overall locoregional control rate of 84 per cent. Furthermore, treatment duration had no negative impact on survival. Patients who fail radiotherapy may still undergo salvage laryngectomy.

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Competing interests. None declared

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