Original Article

Survivals of Laryngeal Cancer Patients in Thai Military Hospital

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Background: Laryngeal carcinoma is the second most common cancer of head and neck in Thailand. However, the recent information regarding survival of laryngeal carcinoma in Thailand is limited.

Objective: To describe the survival probability among patients diagnosed with laryngeal carcinoma and to evaluate the factors affecting the survival rate in the Thai Military hospital.

Materials and Methods: Patients diagnosed with laryngeal carcinoma, e.g., supraglottic, glottic, and subglottic subsited, in Phramongkutklao Hospital were collected between 2002 and 2012. The study design was retrospective cohort study.

Results: One hundred fifty patients enrolled in the present study. The 5-year overall survival rate of laryngeal carcinoma was 51%. The 5-year survival rate by stages of the disease were stage I 67%, stage II 76%, stage III 59%, and stage IV 36%. The 5-year disease-free survival in laryngeal carcinoma was 64%. According to the treatment, the overall survival and the disease-free survival of laryngeal carcinoma in the early stage patients between primary surgery and primary radiation was similar. In the advanced stage patients, the overall survival with surgery and radiation was higher than the chemoradiation group. Proportional hazards models showed the decreased survival in poorly differentiated cell type, nodal metastasis, and advanced stage patients without operation.

Conclusion: The study revealed 5-year (overall) survival rate of laryngeal carcinoma was 51%. In the early stage of disease, the survival rate was the same in both operative and non-operative group, whereas the surgical option had increased the survival rate significantly in the advanced disease. Furthermore, the factors affecting survival rate were cell type and nodal metastasis.

Keywords: Early stage, Advanced stage, Laryngeal carcinoma, Overall survival, Disease-free survival, Chemoradition

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Laryngeal carcinoma is a common cancer of the head and neck area. The incidence of laryngeal cancer is the eleventh of all cancer in male and is the second most common cancer of the head and neck in USA[1]. In Thailand, Sumitsawan et al[2] reported the incidence of laryngeal cancer between 1998 and 2000 to be 2.7/100,000 in male and 0.38/100,000 in female. Men are seven times more likely than women to develop laryngeal cancer[2].

In the past, there was an alternation of laryngeal cancer treatment. In 1990s, the organ preservation strategy was applied to the patients. According to National Cancer Database [NCDB], Hoffman et al[3] reviewed the data and found that the survival rate of laryngeal cancer patients decreased between 1985 and 2001. He hypothesized that the organ preservation tendency, such as chemotherapy and endoscopic resection, might cause the decreased survival of the patients[3].

The current treatments in our institution for laryngeal carcinoma consist of surgery, radiation, chemotherapy, or combined option. The preference of treatment depends on the patient status, the stage of disease, the accessible treatment, and the doctor-patient agreement. According to Organ Preservation Strategy, the trend of surgery has been diminishing to maintain maximal function of the larynx, especially respiration and vocalization; but some studies found the reduction of survival instead. Therefore, the different treatment on laryngeal carcinoma may affect the survival. Nowadays, there were a small number of survival studies on laryngeal carcinoma for Thai. Dechaphunkul[4] revealed the treatment of glottic cancer, merely surgery, and radiation had the same survival rate. In contrast, surgery with radiation had higher survival rate than only radiation in supraglottic

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cancer[4].

The present study aimed to define the survival of laryngeal carcinoma patients and evaluate the factors affecting survival rate in Phramongkutklao Hospital between 2002 and 2012.

Materials and Methods

Patient and enrollment, the medical records of all patients diagnosed with laryngeal cancer, in Phramongkutklao Hospital between January 1, 2002 and December 31, 2012 were reviewed. The patients who had laryngeal cancer as the second primary, incomplete treatment, or without pathologic report of their lesions were excluded. The demographic data, staging, treatment option, and the clinical outcomes after treatment were abstracted. In addition, the vital status, causes of death, and the date of death among the deceased patients were evaluated starting January 1, 2002 from the database of the National Health Security Office, Ministry of Public Health and the Civil Registration.

Statistical analysis

To estimate time to death from all causes, the primary endpoint in this analysis was death. Those who were reported to be alive were right-censored on December 31, 2012. Survival analysis was evaluated using the Kaplan-Meier method. Overall survival estimates and 95% confidence intervals [CIs] were calculated. Then, we calculated the factors related to the survival by Cox proportional hazard ratio model. The prognostic index [PI] equation was established based on the Cox regression analyses. A *p*-value smaller than 0.05 indicated the statistical significance. Statistically analyses were performed using the Stata/MP 13.

Results

The study population consisted of 150 laryngeal cancer patients. The majority of the enrolled patients were males (137 or 91.3% males and 13 or 8.7% females). The mean age was 62 years old (range 23 to 87, SD 11.9). Glottic cancer was the most common type of cancer (57.3%) found in the present study. The histopathology of the lesions included moderately differentiated squamous cell carcinoma (44%), well differentiated squamous cell carcinoma (24%), poorly differentiated squamous cell carcinoma (11.3%), unclassified (18.7%), and malignant fibrous histiocytosis, liposarcoma, or adenoid cystic cancer for the other 2%.

According to TNM staging by the American Joint Committee on Cancer [AJCC] (Cancer Staging Manual 7th edition), 149 patients were able to be classified by TNM staging (except one patient with malignant fibrous histiocytosis) and grouped as stage I-II for the early stage and stage III-IV for the advanced stage. From our data, the percentage of the early stage of laryngeal cancer was 42.3% (stage I and II as 28.2% and 14.1%, respectively). The advanced stage accounted for 57.7% of the patients and included 16.8% stage III and 40.9% stage IV.

One hundred twenty-five laryngeal cancer patients received tumor specific treatment in Phramongkutklao Hospital. Twenty-four patients received treatment in other institutes. The most common treatment offered was combined therapy (54.4%), following by radiation alone and surgery alone 33.6% and 12%, respectively.

In the early stage group (n = 52), 75% of patients were treated by radiation alone, 15.4% underwent surgery alone, and 9.6% received combined therapy (surgery and radiation). In the advanced stage group (n = 73), 86% of patients received combined therapy, e.g., chemoradiation 34.3%, surgery and postoperative radiation 52%. Twenty-eight patients (38.4%) with positive surgical margin and pathological nodal involvement, who received surgery and postoperative radiation, also received adjuvant chemotherapy.

The median survival time to all causes of death of our study population (n = 149) was 63 months (95% CI 47 to 98), and the 5-year overall survival was 51.2% (95% CI 40 to 61). Overall, 125 patients with laryngeal cancer had complete information for calculation of the disease-free survival, 75 patients (60%) achieved remission, and 5-year disease-free survival presented at 64.5% (95% CI 50 to 76), as shown in Figure 1.

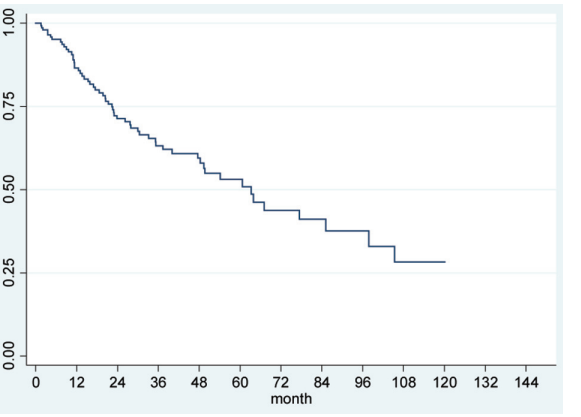

Figure 1. Overall survival of laryngeal carcinoma patients.

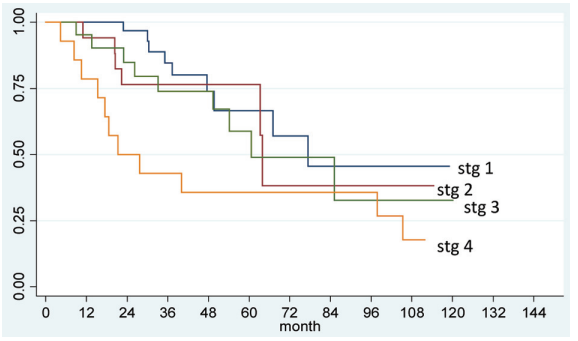

Figure 2. Overall survival of laryngeal cancer patients divided by stage (stg = stage).

The 5-year survival of the early stage was 71.1% (95% CI 52 to 83), and 49.7% (95% CI 31 to 66) for advanced stage patients. In addition, the 5-year survival probabilities by staging classification was 66.6% (95% CI 40 to 83) for stage I, 76.5% (95% CI 49 to 91) for stage II, 59% (95 CI 31 to 79) for stage III, and 35.7% (95% CI 13 to 59) for stage IV, as shown in Figure 2.

According to the treatment in the early stage, 5-year survival from all causes of death of the surgical group was 85.7% (95% CI 33 to 97), and 69.1% for radiation group (95% CI 43 to 85). Nevertheless, there was no statistical difference (hazard ratio [HR] 0.34, *p*-value 0.31) between the two groups. After treatment in the early stage, surgical group and radiation group accomplished the remission rate at 75% and 83.3%, respectively. In terms of 5-year disease-free survival after treatment, the surgical group was 100% (entirely survived, n = 8), and 65% for radiation group (95% CI 33 to 84). The comparison between surgical and radiation group, the disease-free survival could not be performed because of the small number of the samples in surgical group.

In regard to the treatment for the advance stage, the combination of therapies, surgery and postoperative radiation or chemoradiation, would be selected. Due to the severity of diseases in the group of surgery and postoperative radiation, 3 and 5-year overall survival were 73% (95% CI 54 to 85) and 55.5% (95% CI 35 to 72), respectively. In chemoradiation groups, only 3-year overall survival could be obtained and it was 22.4% (95% CI 7 to 43). Moreover, the chemoradiation group had significant shorter survival than the surgery with postoperative radiation group (HR 4.56, *p*-value <0.001). Furthermore, the surgery with postoperative radiation group was 3.7 times shorter survival from all causes of death (HR 3.7, *p*-value 0.04) if receiving adjuvant chemotherapy.

In the aspect of the advanced stage, surgery with postoperative radiation group and chemoradiation group provided the remission rates of 85% and 32.1%, respectively. In addition, the disease-free survival of the surgery and postoperative radiation had 3 and 5-year disease-free survival of 79.6% (95% CI 60 to 90) and 63.7% (95% CI 41 to 79), respectively. However, in chemoradiation group only 3-year disease-free survival could be analyzed of 28.6% (95% CI 4 to 61) and was 3.3 times risk (HR 3.28, *p*-value 0.04) higher than surgery with postoperative radiation group.

Cox proportional hazard model was employed to analyze the factors affecting the overall survival and the disease-free survival. Univariate Analysis model was used to analyze the variable and found that the significant risk factors (*p*-value <0.05) influencing to the overall survival were subsite, cell type, T-stage, node status, and stage of disease. Moreover, the times risk for supraglottic subsite was 3.6 (95% CI 2.12 to 6.11), poorly differentiated squamous cell carcinoma was 2.59 (95% CI 1.09 to 6.15), T4 tumor was 2.88 (95% CI 1.34 to 6.17), stage IV of disease was 3.6 (95% CI 1.42 to 9.09), and all positive nodal status was at the range between 4.9 to 10.05.

Besides, the factors influencing on significant risk to disease-free survival were subglottic subsite (HR 9.32, 95% CI 1.16 to 74.68) and nodal stage II and III (HR 2.98, 95% CI 1.24 to 7.2 and HR 9.19, 95% CI 1.16 to 73.17, respectively) as shown in Table 1.

Multivariate Cox proportional hazards model was used to reanalyze poorly differentiated squamous cell carcinoma, and positive lymph node involvements for identification the powerful factors influencing to the overall survival, as shown Table 2.

Discussion

The present findings revealed 5-year survival rates of patients with laryngeal cancer was 51.2% comparable to Hoffman et al (5-years survival rates was 51.3%)[3]. However, it was lower than some studies such as Piccirillo et al[5], Coleman et al[6], and Jemal et al[7] (in the range of 62% to 66%). In consideration, the study indicated that stage IV patients (40.9%), the major population, might affect 5-year overall survival, which differed from the previous studies above. According to Gourin et al, the study catergorized the overall survival in each stage of disease[8], which our pattern of survival curve paralleled, as shown in Figure 2. Nevertheless, we found that the number of 5-year overall survival in stage I (42 patients, 66.6%) was less than stage II (21 patients, 76.5%). This may

Table 1. The factor affecting overall survival and disease-free survival by univariate Cox proportional hazards analysis

	Overall survival HR (95% CI)	Disease-free survival HR (95% CI)
Age (year)		
>50	1.01 (0.99 to 1.04)	1.01 (0.98 to 1.04)
Gender		
Male	1	1
Female	1.97 (0.89 to 4.38)	0.51 (0.07 to 3.78)
Subsite		
Glottic	1	1
Supraglottic	3.60 (2.12 to 6.11)*	1.89 (0.88 to 4.05)
Subglottic	1.45 (0.19 to 10.78)	9.32 (1.16 to 74.68)*
Cell type		
Well differentiated	1	1
Moderately	1.12 (0.57 to 2.19)	0.90 (0.38 to 2.10)
Poorly	2.59 (1.09 to 6.15)*	0.95 (0.12 to 7.62)
Unclassified SCCA	0.94 (0.41 to 2.14)	1.03 (0.37 to 2.91)
Other	0.75 (0.10 to 5.81)	x
Tumor status		
I	1	1
II	2.06 (0.89 to 4.76)	2.52 (0.90 to 7.10)
III	2.16 (0.98 to 4.77)	1.01 (0.31 to 3.33)
IV	2.88 (1.34 to 6.17)*	1.85 (0.65 to 5.26)
Node status		
0	1	1
I	5.51 (2.22 to 13.69)*	3.46 (0.78 to 15.31)
II	4.90 (2.67 to 9.00)*	2.98 (1.24 to 7.20)*
III	10.05 (3.92 to 25.78)*	9.19 (1.16 to 73.17)*
Metastasis	2.65 (0.95 to 7.43)	x
TNM staging		
I	1	1
II	1.49 (0.52 to 4.31)	1.83 (0.56 to 6.04)
III	1.85 (0.71 to 4.801)	0.94 (0.26 to 3.36)
IV	3.60 (1.42 to 9.09)*	2.25 (0.71 to 7.11)

HR = hazard ratio; SCCA = squamous cell carcinoma antigen; x = no disease-free survival

* *p*-value <0.05

Table 2. The factors affecting survival of laryngeal carcinoma by multivariate Cox proportional hazards analysis

	HR	95% CI	*p*-value
Subsite			
Glottic	1		
Supraglottic	1.713	0.809 to 3.630	0.160
Subglottic	2.227	0.244 to 20.355	0.478
Cell type			
Well difffentiated	1		
Moderately	0.826	0.400 to 1.707	0.606
Poorly	3.971*	1.330 to 11.852	0.013*
Unclassified SCCA	1.517	0.619 to 3.717	0.363
Other	0.000	0.000	1.000
Tumor status			
I	1		
II	1.220	0.442 to 3.369	0.701
III	1.049	0.380 to 2.896	0.927
IV	1.484	0.511 to 4.306	0.468
Node status			
0	1		
I	5.000*	1.477 to 16.932	0.010*
II	4.100*	1.785 to 9.414	0.001*
III	10.935*	2.924 to 40.901	<0.001*
Metastasis	0.528	0.131 to 2.121	0.368

HR = hazard ratio; SCCA = squamous cell carcinoma antigen

* *p*-value <0.05

be because the stage I had two times more population than stage II, which could have affected the statistic calculations. Notwithstanding, there was no statistical difference in the survival compared between stage I and II; HR 1.49, *p*-value 0.46.

The patients were divided into two groups, the early stage (stage I and II) and the advanced stage (stage III and IV), to define the survival of each treatment modalities, single and combination treatment. In the early stage, there was no statistical significant result (HR 0.34, *p*-value 0.31) in comparison between radiotherapy and surgery. This finding was consistent with Mendenhall et al, particularly for patients in stage I[9].

In the advanced stage group, chemoradiation had significant higher 4.56 times risk than surgery with radiation. Patients with both surgery and radiation modalities had higher 3.7 times risk if they achieved adjuvant chemotherapy because of specific indication, such as positive surgical margins resulted in poor survival outcome.

Regarding to the disease-free survival rate, there was no statistical difference between radiation and surgery in the early stage. But in the advanced stage, chemoradiation group had higher risk than surgery combined radiation group. Therefore, with each treatment modalities, the disease-free survival was in correlation with the overall survival.

In the early stage, patients with each treatment options, surgery and radiation, had no different result of disease-free survival and overall survival. However, there might be various quality of life, especially postoperative voice quality and swallowing function. On the other hand, the disease-free survival rate in surgery with radiation therapy for the advanced stage patients was higher than other modalities.

The most powerful factor affecting overall survival rates, when the confounder factors were limited, were poorly differentiated squamous cell carcinoma and nodal involvement. In comparison, the result from Papadas et al[10] with Jose et al[11] found similar correlation.

The nodal involvement and subglottic subsites were found to be strong factors affecting disease-free

survival, as in the study of Dahm et al. The subglottic cancer was lower disease-free survival than other subsites of laryngeal cancer because of the frequently delayed detection[12].

Conclusion

In the early stage of laryngeal cancer, overall survival and disease-free survival did not differ between surgery and radiation. Nevertheless, in the advanced stage, the therapy combined surgery with radiation increased the survival. Moreover, the poorly differentiated squamous cell carcinoma and nodal involvement were the fetal effect for survival.

What is already known on this topic?

The study of the survivals of laryngeal cancer patients in Pramongkutklao Hospital as presented above is finally concluded as similar to those from both Europe and America articles in terms of modalities of treatment and factor affecting survival rates.

What this study adds?

Most cases of laryngeal cancer in this study were more advance stage, so overall result of survival was slightly lower than the reference articles.

Potential conflicts of interest

The authors declare no conflict of interest.

References

1. American Cancer Society. Cancer facts and figures, 2007. Atlanta: American Cancer Society; 2007.
2. Sumitsawan Y, Srisukho S. Larynx ICD 10 C32. In: Khuhaprema T, Srivatanakul P, Sriplung H, Wiangnon S, Sumitsawan Y, Attasara P, editors. Cancer in Thailand, Vol. IV, 1998-2000. Bangkok: Ministry of Public Health; 2007:39-40.
3. Hoffman HT, Porter K, Karnell LH, Cooper JS, Weber RS, Langer CJ, et al. Laryngeal cancer in the United States: changes in demographics, patterns of care, and survival. Laryngoscope 2006; 116(9 Pt 2 Suppl 111):1-13.
4. Dechaphunkul T. Epidemiology, risk factors, and overall survival rate of laryngeal cancer in Songklanagarind Hospital. J Med Assoc Thai 2011;94:355-60.
5. Piccirillo JF, Wells CK, Sasaki CT, Feinstein AR. New clinical severity staging system for cancer of the larynx. Five-year survival rates. Ann Otol Rhinol Laryngol 1994;103:83-92.
6. Coleman MP, Babb P, Damiecki P, Grosclaude P, Honjo S, Jones J, et al. Cancer survival trends in England and Wales 1971-1995: deprivation and NHS region. London: The Stationery Office; 1999.
7. Jemal A, Siegel R, Ward E, Hao Y, Xu J, Thun MJ. Cancer statistics, 2009. CA Cancer J Clin 2009; 59:225-49.
8. Gourin CG, Conger BT, Sheils WC, Bilodeau PA, Coleman TA, Porubsky ES. The effect of treatment on survival in patients with advanced laryngeal carcinoma. Laryngoscope 2009;119:1312-7.
9. Mendenhall WM, Parsons JT, Stringer SP, Cassisi NJ, Million RR. T1-T2 vocal cord carcinoma: a basis for comparing the results of radiotherapy and surgery. Head Neck Surg 1988;10:373-7.
10. Papadas TA, Alexopoulos EC, Mallis A, Jelastopulu E, Mastronikolis NS, Goumas P. Survival after laryngectomy: a review of 133 patients with laryngeal carcinoma. Eur Arch Otorhinolaryngol 2010;267:1095-101.
11. Jose J, Coatesworth AP, Johnston C, MacLennan K. Cervical node metastases in squamous cell carcinoma of the upper aerodigestive tract: the significance of extracapsular spread and soft tissue deposits. Head Neck 2003;25:451-6.
12. Dahm JD, Sessions DG, Paniello RC, Harvey J. Primary subglottic cancer. Laryngoscope 1998; 108:741-6.