Epidemiology, Risk Factors, and Overall Survival Rate of Laryngeal Cancer in Songklanagarind Hospital

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Objective: *To study epidemiology, risk factors and overall survival rate of patients with laryngeal cancer.*
Material and Method: *A chart review of the patients diagnosed with laryngeal cancer in Songklanagarind Hospital over the past 10 years was performed.*
Results: *Two hundred eighty nine patient cases were reviewed, in which 106 patients were diagnosed with supraglottic cancer, 180 with glottic cancer and three with subglottic cancer. The majority of the patients was male, active smokers, alcohol consumers and had a histology showing squamous cell carcinoma. Disease characteristics indicated that most cases of supraglottic cancer were in a locally advanced stage (84.4%), whereas most patients with glottic cancer were diagnosed with early stage (61.3%). Hoarseness was the most common presenting symptom. Regarding the complete response rate, glottic cancer was superior to supraglottic cancer. For glottic cancer treatments, surgery alone or primary radiation showed good 5-year overall survival rates with no difference in modality results (87.5% versus 83.2%). In supraglottic cancer treatments and contrary to glottic cancer, surgery with postoperative radiation improved the 5-year overall survival rate in comparison with primary radiation alone (52.2% versus 39.2%).*
Conclusion: *Primary radiation or surgery alone is suitable treatments for early stage laryngeal cancer especially in glottic cancer, whereas surgery with postoperative radiation should be the treatment for advanced stage laryngeal cancer.*

Keywords: *Epidemiology, Risk factors, Overall survival rate, Laryngeal cancer*

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Laryngeal cancer is the eleventh most common form of cancer among men worldwide and is the second most common malignancy of the head and neck. In the United States, there were approximately 11,300 new cases of laryngeal cancer in 2007.

In Thailand, head and neck cancer represents about 10% of all cancers with males predominant and laryngeal cancer is the second most frequent cancer of the head and neck. However, concerning the data of Songklanagarind Hospital, in 2005 there were 73 new cases of laryngeal cancer and it was the fifth most common cancer among all head and neck cancers.

Laryngeal cancer patients lose their laryngeal function, which affects speech, swallowing and breathing. Therefore, the normal activities of these patients are impaired[1]. Frequently, these patients manifest with hoarseness, odynophagia, dysphagia, neck mass, referred otalgia, dyspnea, or aspiration[2].

Several risk factors of laryngeal cancer are found today, such as smoking, alcohol consumption, occupation-related carcinogens (asbestos, nickel, etc), HPV infection, and laryngopharyngeal reflux[2-8].

In addition, many treatments for laryngeal cancer have been developing, especially laryngeal preservation protocol. Other studies focus on chemotherapy and molecularly targeted therapy to preserve laryngeal function. Previously, for Songklanagarind Hospital, a report was not available on basic epidemiology, risk factors, response rate and overall survival rate for laryngeal cancer. The purpose of the present study was the clarification of this data for a 10-year period in Songklanagarind Hospital.

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Material and Method

Patients

Cases of patients diagnosed with laryngeal cancer during a 10-year period at Songklanagarind Hospital were retrieved for further review. All patients

had to have complete data and treatment follow-up questionnaires.

Study procedure

Medical record review

All patients were reviewed for their characteristics (age, sex, and risk factors), clinical information (signs and symptoms), pathological data, staging, treatment and outcome, and survival data. The data was obtained from the in- and out-patient charts and follow-up questionnaires dated between January 1, 1999 and December 29, 2008.

Statistical analysis

The mean and standard deviation (SD) were used to describe parametric and non-parametric continuous data, and number and percentages to describe categorical data. The following data was assessed using the Fisher's exact test and estimate survival probability was assessed with Kaplan-Meier methods by the R software package Epicalc. A p-value of less than 0.05 was considered statistically significant.

Results

During the assessment period, there were 625 patients diagnosed with laryngeal cancer. Three hundred thirty six patients were excluded from the present study due to incomplete data, missing diagnoses, or loss to follow-up. The remaining 289 patient cases were analyzed.

The median age of the patients was 64 years with an age range of 29 to 90 years. The majority of the clients were male (92.3%). The risk of laryngeal cancer for those patients with a family history of cancer was 15.4%, who were active smokers was 83.2%, and for alcohol consumers was 58.4%.

More than half of the cancers were carcinoma of the glottis (62.2%), while the less common cancers were the supraglottis (36.7%) and subglottic (1%) carcinoma. Squamous cell carcinoma accounted for all subgroups of laryngeal cancer more than 95%, whereas the spindle cell carcinoma, undifferentiated carcinoma, adenoid cystic carcinoma and muco-epidermoid carcinoma had a small proportion. Disease characteristics indicated that most cases of supraglottic cancer were advanced stage cancer (84.4%). In contrast, most cases of glottic cancer were diagnosed in an early stage (61.3%) (Table 1).

The most common symptom of glottic cancer was hoarseness (97.2%). The three other prevalent complaints were dyspnea (24.4%), odynophagia (13.3%) and neck mass (6.1%), while hoarseness was the most common symptom in supraglottic cancer (56.6%) similarly. However, the other symptoms had more proportions in supraglottic cancer including odynophagia (49.1%), neck mass (42.5%) and dyspnea (34.9%).

The most common treatment modality used in laryngeal cancer was primary radiation, especially in early stage disease (64% of glottic cancer, 82.2% of supraglottic cancer). Surgery alone, surgery with postoperative radiation and chemoradiation were more prevalent in advanced staging however, primary radiation was still the predominant treatment (Table 2).

The outcome data is presented in Table 3. In patients with glottic cancer, a favorable complete response rate was achieved in all treatment modalities (surgery 91.6%, primary radiation 81.4% and surgery with postoperative radiation 82.7%). Compared to glottic cancer, supraglottic cancer patients had a worse complete response rate, 66.7% in surgery, 42% in primary radiation, and 62% in surgery with postoperative radiation.

Regarding survival outcome, 5-year overall survival rate in glottic cancer patients was significantly better than that of supraglottic cancer patients. There was no significant difference in the 5-year overall survival rate between surgery and primary radiation treatment in glottic cancer patients (87.5% versus 83.2%) particularly in the early stage of disease. In addition, surgery with postoperative radiation had

Table 1. Basic clinical characteristics

Characteristics	Supraglottic cancer (n = 106) No. (%)	Glottic cancer (n = 180) No. (%)
Histopathology		
Squamous cell Ca	102 (96.2)	178 (98.9)
Spindle cell Ca	1 (0.9)	-
Undifferentiated Ca	3 (2.8)	-
Adenoid cystic Ca	-	1 (0.6)
Mucoepidermoid Ca	-	1 (0.6)
AJCC* staging		
stage I	7 (3.9)	71 (39.2)
stage II	21 (11.7)	40 (22.1)
stage III	31 (17.3)	52 (28.7)
stage IVa	34 (19.0)	16 (8.8)
stage IVb	10 (5.6)	1 (0.6)
stage IVc	3 (1.7)	-

* American Joint Committee on Cancer

Table 2. Treatment modality in laryngeal carcinoma

	Surgery alone[#] No. (%)	Primary radiation No. (%)	Surgery + post operative radiation* No. (%)	Concurrent chemoradiation No. (%)
Supraglottic cancer (n = 106)				
Early stage (Stage I, II)	2 (7.1)	23 (82.2)	2 (7.1)	1 (3.6)
Locally advanced stage (Stage III, IVa, IVb)	1 (1.3)	43 (57.4)	27 (36.0)	4 (5.3)
Metastasis stage (stage IVc)	-	3 (100)	-	-
Glottic cancer (n = 180)				
Early stage (Stage I, II)	7 (6.3)	71 (64.0)	33 (29.7)	-
Locally advanced stage (Stage III, IVa, IVb)	5 (7.2)	42 (60.9)	19 (27.5)	3 (4.4)

[#] Endoscopic supraglottis laryngectomy, total laryngectomy or laser cordectomy

* Neck dissection, supraglottis laryngectomy, total laryngectomy with neck dissection, total laryngectomy with gastric pull up, or cordectomy and post-operative radiation

Table 3. Outcome data and overall 5-year survival rate for laryngeal cancer

Treatment modality	Complete response rate, No. (%)	5-year overall survival rate (%)
Supraglottic cancer		
Surgery alone	2 (66.7)	X
Primary radiation	29 (42.0)	39.2
Surgery plus post operative radiation	18 (62.0)	52.2
Glottic cancer		
Surgery alone	11 (91.6)	87.5
Primary radiation	92 (81.4)	83.2
Surgery plus post operative radiation	43 (82.7)	61.4

X: Cannot be analyzed because of the small number of patients

a favorable result in the 5-year overall survival rate (61.4%) in glottic cancer patients. As opposed to glottic cancer, surgery with postoperative radiation improved the 5-year overall survival rate in supraglottic cancer over primary radiation alone (52.2% versus 39.2%). (Table 3).

Discussion

The present study reviewed the basic characteristics, presenting symptoms, treatment modality, and outcome data for patients diagnosed with laryngeal cancer during a 10 years period. The epidemiology of laryngeal cancer is of foremost importance for head and neck surgeons in Thailand, since it is the second most common form of head and neck cancer. Moreover, laryngeal cancer patients will have dysfunction of their speech, swallowing and breathing; therefore, their normal daily activities will be unavoidably affected.

Basic characteristics of patients, such as sex and age, are similar to those that were reported previously[9]. Laryngeal cancer is mainly a disease with an older age of onset and a peak incidence in the sixth to eighth decades of life, more common among men, and strongly associated with tobacco smoking and alcohol consumption[1,3-5,9]. The majority of recorded laryngeal cancer occurred in the area of the glottis, followed in prevalence by the supraglottis, with a small proportion in the subglottis[9].

Squamous cell carcinoma is by far the most common histologic finding in laryngeal cancer. It accounts for more than 90% of laryngeal cancer in most studies[1,9,10]. Similar results were found in the present study; the incidence of squamous cell carcinoma was 96.2% of supraglottic cancer, and 98.9% of glottic cancer. However, we found only three cases in subglottic cancer, possibly due to rare form of cancer site so it is difficult to analyze this subset of patients.

Hoarseness is the major symptom of glottic cancer. Supraglottic cancer is a more advanced cancer and may cause a miscellany of symptoms like sore throat, dysphagia, and dyspnea. A neck mass of nodal metastasis may be present also due to greater lymphatic drainage. In the present study, the most common presenting symptoms were hoarseness, dyspnea, odynophagia and neck mass, which was not significantly different from those described in previous literature[1,11].

From the previous literatures, the local control rate of laryngeal cancer with radiation therapy ranges from 61%-94%. Surgery has been reported to have local control rates in the range of 66%-92%. The 5-year survival rate for surgery has been reported to be 86%-98% and for primary radiation 88-96%[11-20]. In this study, the complete response rates of supraglottic cancer were about 66.7% with surgery alone, 42% with primary radiation and 62% with surgery plus postoperative radiation. In glottic cancer, patients with surgery alone achieved a complete response rate of 91.6%, 81.4% with primary radiation and 82.7% with surgery plus postoperative radiation. Regarding the 5-year overall survival rate, glottic cancer treated with surgery alone, primary radiation and surgery and postoperative radiation was 87.5%, 83.2% and 61.4% respectively. In supraglottic cancer, surgery plus postoperative radiation had a better 5-year overall survival rate than primary radiation (52.2% versus 39.2%). This data confirmed that primary radiation or surgery alone in Songklanagarind Hospital has an excellent response and overall survival rates in early stage laryngeal cancer; however, advanced stage laryngeal cancer treated with surgery plus postoperative radiation offered a better outcome. Since there were a small number of subglottic patients due to its rarity, it is difficult to analyze in this study.

On the other hand, chemoradiation has become recently the standard treatment for laryngeal preserving protocol, because it improves laryngectomy-free survival. However, there is no available data to be discussed in the present study due to the limited number of patients and the predominance of surgery for advanced stage cancer. Moreover, chemoradiation has been used as a treatment of laryngeal preservation in Songklanagarind Hospital for just 2-3 years.

In the present study, some patient cases were excluded due to incomplete data and follow-ups and therefore, the outcome of the research may have been affected. Without complete data, a further prospective study is still needed for a better result.

In conclusion, the epidemiology and basic characteristics of laryngeal carcinoma in the present study are not different from those in other countries. Primary radiation and surgery alone are suitable treatments for early stage laryngeal cancer, whereas surgery plus postoperative radiation should be used as a treatment in advanced stage laryngeal cancer.

Potential conflicts of interest

None.

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ระบาดวิทยา ปัจจัยเสี่ยง อัตราการอยู่รอดโดยรวมของมะเร็งกล่องเสียงในโรงพยาบาลสงขลานครินทร์

ธนเดช เดชาพันธุ์กุล

วัตถุประสงค์: *เพื่อศึกษาระบาดวิทยา ปัจจัยเสี่ยง และอัตราการอยู่รอดของผู้ป่วยมะเร็งกล่องเสียง*

วัสดุและวิธีการ: *ทบทวนข้อมูลเวชระเบียนของผู้ป่วยมะเร็งกล่องเสียงที่ได้รับการรักษาในโรงพยาบาลสงขลานครินทร์ ช่วง 10 ปีที่ผ่านมา*

ผลการศึกษา: *ผู้ป่วยทั้งหมด 289 คน แบ่งเป็นผู้ป่วยมะเร็งเหนือเส้นเสียงแท้ 106 คน, มะเร็งเส้นเสียงแท้ 180 คน และมะเร็งใต้เส้นเสียงแท้ 3 คน ผู้ป่วยส่วนใหญ่เป็นเพศชาย สูบบุหรี่ ดื่มสุรา และเนื้อเยื่อวิทยาเป็นชนิด squamous cell carcinoma ลักษณะโรคบ่งแสดงว่า ส่วนมากของมะเร็งเหนือเส้นเสียงแท้เป็นระยะลุกลามร้อยละ 84.4 ในขณะที่มะเร็งเส้นเสียงแท้วินิจฉัยในระยะเริ่มต้นร้อยละ 61.3% อาการเสียงแหบเป็นอาการนำแสดงที่พบบ่อยมากที่สุด สำหรับอัตราการตอบสนองแบบสมบูรณ์มะเร็งเส้นเสียงแท้ได้ผลดีกว่ามะเร็งเหนือเส้นเสียงแท้ สำหรับมะเร็งเส้นเสียงแท้ การผ่าตัดเพียงอย่างเดียวหรือการรักษาแบบปฐมภูมิด้วยรังสีมีอัตราการอยู่รอดโดยรวม 5 ปี ไม่พบความแตกต่างของการรักษา (ร้อยละ 87.5 และร้อยละ 83.2) ในการรักษามะเร็งเหนือเส้นเสียงแท้ ด้วยการผ่าตัดร่วมกับรังสีรักษาหลังการผ่าตัด ทำให้อัตราการอยู่รอดชีวิต 5 ปี เท่ากับร้อยละ 52.2 เปรียบเทียบกับรังสีรักษาเพียงอย่างเดียว เท่ากับร้อยละ 39.2*

สรุป: *การรักษาปฐมภูมิด้วยรังสีรักษาหรือการผ่าตัดเพียงอย่างเดียวเป็นรักษาที่เหมาะสมสำหรับมะเร็งกล่องเสียงในระยะเริ่มต้น โดยเฉพาะมะเร็งเส้นเสียงแท้ ในขณะที่การผ่าตัดร่วมกับรังสีรักษาหลังผ่าตัดควรเป็นการรักษามะเร็งกล่องเสียงระยะลุกลาม*