

The Treatment Outcome of Radical Radiotherapy in Laryngeal Cancer

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Objective: This study reports the treatment outcome of radiotherapy alone for laryngeal cancer.

Material and Method: A retrospective analysis was performed on 138 patients with stage I to IV squamous cell carcinoma of larynx who received radiotherapy alone in Division of Therapeutic Radiology and Oncology, Faculty of Medicine, Chiang Mai University, Thailand between 2003 and 2009.

Results: The 4-year local control (LC) rate in all patients was 44.1%. The 4-year overall survival (OS) was 82.1%. The 4-year LC rates for stage I, II, III, and IV were 75.3%, 69.4%, 57.1%, and 36.9%, respectively ($p = 0.0055$). Finally, the 4-year OS rates for stage I, II, III, and IV were 85%, 78.6%, 91.1%, and 71.5%, respectively. The laryngeal preservation rate of all stages was 73%.

Conclusion: In conclusion, the treatment outcome of radiotherapy alone in all stages of laryngeal cancer in our center was unsatisfactory when compared to other series.

Keywords: Laryngeal cancer, Radiotherapy alone, Outcome

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One thousand two hundred thirteen new cases of laryngeal cancer were diagnosed in Thailand in 2008 (1,068 males, and 145 females). Six hundred forty seven patients died of this disease⁽¹⁾. The data from cancer registry of Chiang Mai University Hospital reported 31 new cases of laryngeal cancer in the year 2008⁽²⁾.

Small lesions without laryngeal fixation or lymph node metastasis can be treated by surgery alone or radiotherapy alone with the similar outcome. For locally advanced stages, a combined modality approach, either surgery plus radiotherapy or chemoradiotherapy alone were the treatment options. Direct comparison of the outcome of radiotherapy versus surgery is difficult since clinical staging in radiotherapy would cause stage migration; some patients would have been under-staged. In surgical studies, outcomes are reported based on pathological staging. Additionally, most of the patients in surgical

series must have a high enough performance status to tolerate surgery. Lower performance status patients get shifted to radiotherapy. This skews the outcomes in favor of surgery. The purpose of study was to retrospectively evaluate the treatment outcome of radical radiotherapy alone in terms of local control and overall survival in patients with laryngeal cancer.

Material and Method

The medical records of all laryngeal cancer patients who were treated with radiotherapy alone at Division of Therapeutic Radiology and Oncology between January 2003 and December 2009 were reviewed.

Eligibility criteria for this retrospective single-institutional study were squamous cell carcinoma of the larynx, no distant metastasis at the time of diagnosis, curative intent by radical radiotherapy. Recurrent laryngeal cancer patients who were previously treated with any modalities and referred to receive radiotherapy were excluded. Patients who received chemotherapy or palliative radiotherapy were also excluded from the present study. Finally, patients who were diagnosed with laryngeal cancer in our center but then referred to

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receive radiotherapy at other radiotherapy cancer centers were excluded. Demographic and radiotherapy treatment details were obtained from the medical records of the hospital. For patients with a clinical follow-up lapse longer than six months, information on their status was obtained via telephone.

Radiotherapy was delivered at 2 to 2.25 Gy per fraction, one fraction per day, five days per week to a total dose of 63 to 66 Gy (Only T1N0M0 glottic cancers received 2.25 Gy per fraction. The remaining patients received 2 Gy per fraction). All patients were treated with parallel opposed lateral fields using a 6 MV linear accelerator or a Cobalt-60 machine. Wedges were used to improve dose homogeneity in most cases. The radiation portals were planned according to the primary site and the stage of disease.

All patients were scheduled for follow-up at six to eight weeks after completing radiotherapy to assess the treatment outcome. Subsequent follow-up were scheduled every three to six months for the first five years and annually thereafter.

Descriptive statistics are used as frequencies, percentages, medians, and ranges cumulative survival rates were estimated by Kaplan-Meier survival analysis and a log-rank test was used to compare between different stages. Kaplan-Meier survival curves were used for treatment outcome analysis of the 5-year local control (LC) and overall survival (OS) rates. The present study was approved by the Institutional Review Board of Faculty of Medicine, Chiang Mai University.

Results

Two hundred seventy four laryngeal cancer patients registered to receive radiotherapy at our center between January 2003 and December 2009. Eleven patients were excluded because they did not undergo radiation therapy at our center and were referred to an outside institution, 15 due to induction chemotherapy, 18 due to concurrent chemo-radiotherapy, 20 due to having recurrent locoregional disease, 58 due to postoperative irradiation, nine due to palliative radiotherapy, and five due to a diagnosis of distant metastasis. Finally, 138 patients fit our inclusion criteria and were eligible for analysis.

The median age was 66 years (range 27-91 years). The male and female ratio was 3:1. The most common primary tumor subsite was supraglottis followed by glottis. Two-thirds of our patients were of a locally advanced stage at the time of diagnosis. Baseline characteristics are shown in Table 1.

The median follow-up was 46.8 months (range 3.7-111.40 months). The 4-year treatment outcomes of all patients were as follows: LC rate of 44.1% and OS rate of 82.1% (Fig. 1, 2). The Kaplan-Meier curves show the estimated 4-year LC was 75.3%, 69.4%, 57.1%, and 36.9% for stage I, II, III, and IV respectively ($p = 0.0055$). The 4-year OS was 85%, 78.6%, 91.1%, and 71.5% for stage I, II, III, and IV respectively ($p = 0.5701$). The LC and OS curves for each stage of laryngeal cancer are shown in Fig. 3, 4. At the time of analysis, June 2012, of the 82 patients surviving, 15 patients had local recurrence at the primary site alone and seven had primary and regional recurrence and eventually required salvage total laryngectomy. None had distant metastasis. The rate of laryngeal preservation for all stages was 73% (60/82 patients).

The most common acute toxicity was RTOG grade 2 pharyngitis that found in 112 patients (81%). No patient required therapeutic naso-gastric tube insertion. No severe late complications were found. Only low grade (RTOG grade 1-2) late radiation toxicities were seen, the two most common being grade 1 skin and subcutaneous tissue toxicity and grade 1 laryngeal toxicity (hoarseness and slight arytenoidal edema). No patient required laryngectomy due to late complications.

Discussion

The median age in the present study was 66 years confirming that laryngeal cancer generally occurs in the older population. It was also most often

Table 1. Baseline characteristics

Characteristics	Number (%)
Total patients	138
Median age (range)	66 (27-90)
Sex	
Male	106 (76.8)
Female	32 (23.2)
Tumor subsite	
Supraglottis	75 (54.3)
Glottis	32 (45.6)
Subglottis	-
Stage	
I	30 (21.8)
II	14 (10.1)
III	41 (29.7)
IV	53 (38.4)

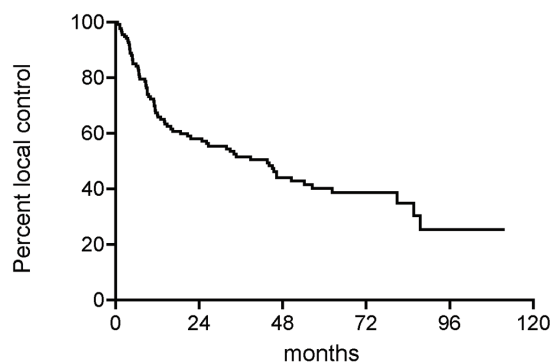


Fig. 1 Local control rate in total group.

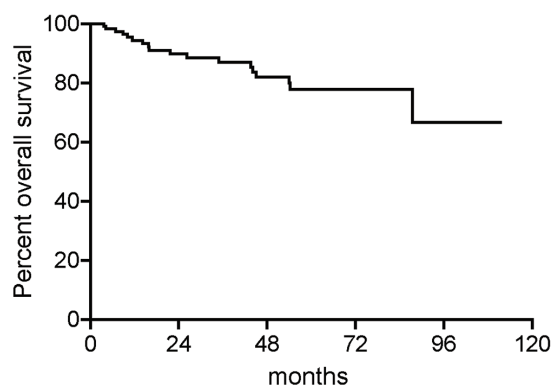


Fig. 2 Overall survival rates in total group.

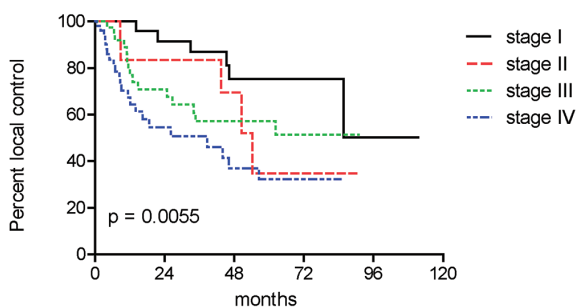


Fig. 3 Local control rates according to stage.

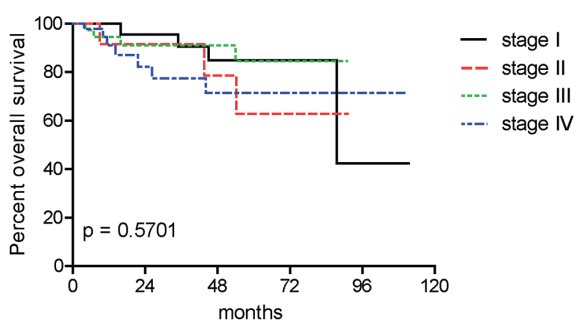


Fig. 4 Overall survival rates according to stage.

in seen in males, which consistent with other squamous cell carcinomas of head and neck.

This retrospective study also reflects the clinical practice in our hospital. The strategy of treatment selection for each patient depends on the clinical stage of tumor, performance status, and patient/doctor preference. Generally, early stage I and II laryngeal cancer in our hospital were treated with single modality surgery or radiotherapy. For locally advanced stage III and IV patients, the first option was combined modality therapy, with surgery plus postoperative radiation with or without chemotherapy selected more than radiotherapy combined with chemotherapy (either induction approach or concurrent approach). The reasons for using radical radiotherapy alone instead of a combined modality approach in locally advanced cases (94 patients) were as follows: old age, poor renal function, refusal of chemotherapy, and co-morbid disease.

The 4-year overall survival rate of all our patients was 82.1%, which was comparable to other studies. The Danish group reported an estimated crude survival after five years among 643 patients with glottic carcinomas treated with curative radiotherapy of 65.3%, and 49.4% for 339 supraglottic cancer patients⁽³⁾.

In the present study, analysis of early stage laryngeal cancer patients (44 patients) treated with radical radiotherapy showed that LC and OS rates at four years were 75.3% and 85% for stage I, 69.4% and 78.6% for stage II, respectively. Upon comparative literature review, this result was much lower than many studies. Tamura et al⁽⁴⁾ reported the 5-year LC rate of approximately 80 to 90% in the same category stage I and II patients treated with conventional radiotherapy (60-66 Gy) or twice-daily hyperfractionated radiotherapy (70-74 Gy). The results of definitive radiotherapy for squamous cell carcinoma of the supraglottic larynx from University of Florida⁽⁵⁾ had an excellent 5 year local control rates of 83% and 100% for T1 and T2 lesions, respectively, which was also not consistent with our result. Looking at our patient characteristics, we found that more than 55% of the patients in stage I-II in our series had a supraglottic primary, and about two thirds of patients had anterior commissure involvement. Anterior commissure involvement may or may not play a role in the poorer treatment outcome of our study. Some authors suggest that anterior commissure involvement should be treated with surgery⁽⁶⁾, but others reported the same recurrence rates, irrespective of the treatment modalities⁽⁷⁾.

For patients with locally advanced (stage III-IV) in the present study, the 4-year LC and OS rates were 57.1% and 91.1% for stage III, and 36.9% and 71.5% for stage IV, respectively. As stated earlier, combined modality therapy is the standard of care for these stages of tumor and we expected lower rates of control for radiotherapy alone (As mentioned above, the reasons for radiotherapy alone in this group of our patients were old age, poor renal function, refusal of chemotherapy, and co-morbid disease). Historical series reported the local control rates of T3 glottic cancer treated with irradiation alone range from 31 to 77%⁽⁸⁻¹⁴⁾ and 26 to 91% for T3 and T4 supraglottic cancer after radiotherapy⁽¹⁵⁻²⁰⁾. The 4-year overall survival of patients with locally advanced cancer in our series was slightly lower than a published data range of 50 to 63%⁽¹⁵⁻²¹⁾. However, the treatment outcome of radiotherapy alone arm in RTOG 91-11⁽²²⁾, which was included only patients with stage III-IV supraglottic and glottic laryngeal cancer showed the 5-year LC rate of 51% and OS rate of 53.5% that was comparable with our result.

The authors did not study any relationship between the treatment outcome and patient or treatment variables such as sex, age, primary subsite, total dose of irradiation, fraction size, or treatment machine. However, it must be noted that it is difficult to allow meaningful analyses in this small of a sample size.

When focused on the 4-year larynx preservation rate, our result also was comparable to other studies. Our laryngeal preservation rate for all stages was 73%, whereas RTOG 91-11 (RT alone arm) had 5-year larynx preservation rate of 66%⁽²²⁾ and Corry J et al reported at 77%⁽²³⁾. However, both studies enrolled only loco-regionally advanced laryngeal cancer, but our study had patients with stage III-IV patients only 69%.

One of the probable reasons that our study had poorer treatment outcomes than other studies of irradiation alone, especially in locally advanced stage III and IV, is that most of our patients had been staged by physical examination only (direct or indirect laryngoscope) and less than 10% received a CT scan for staging, thus resulting in a downward stage migration.

Conclusion

This retrospective study showed an unsatisfactory result of radiotherapy alone in all stages laryngeal cancer in terms of local control, overall survival, and larynx preservation rate, which was lower

than other studies. Stage migration may have played a role in the poorer outcome.

What is already known on this topic?

There are many studies reported on the results of the outcome of radiation therapy in laryngeal carcinomas, which were equal to the treatment outcome of surgery, especially for early stage cancer. By the way, there are a lot of studies of combined modalities treatment such as surgery and postoperative radiotherapy or concurrent chemo-radiotherapy or induction chemotherapy followed by radiotherapy which were recommended for loco-regionally advanced stage.

What this study adds?

This study is the first study in Thailand that reported the outcome of radiotherapy alone in all stages of laryngeal carcinoma.

Potential conflicts of interest

None.

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ผลการรักษามะเร็งกล่องเสียงโดยใช้รังสีรักษาเพียงอย่างเดียว

อิมใจ ชิตาพนารักษ์, เอกสิทธิ์ ธรวิจิตรกุล, สมวิไล จักรพันธ์, พิชญากรณ์ กลั่นกลิ่น, วัชรก อ่อนจันทร์, นันทกา ภูักัณห์พันธุ์, จิรวัดนา ศรีกาวิณ, พิชิต สิทธิไตรย์, รอย วงศ์ธรรม

วัตถุประสงค์: เพื่อศึกษาผลของการฉายรังสีเพียงอย่างเดียวในการรักษาโรคมะเร็งกล่องเสียง

วัสดุและวิธีการ: การศึกษานี้เป็นการศึกษาย้อนหลังในผู้ป่วยมะเร็งกล่องเสียงระยะที่ I-IV ที่มีผลชิ้นเนื้อเป็นมะเร็งชนิดสแควมัสเซลล์ จำนวน 138 ราย ซึ่งได้รับรังสีรักษาเพียงอย่างเดียวเพื่อการควบคุมโรค ณ หน่วยรังสีรักษาและมะเร็งวิทยา ภาควิชารังสีวิทยา คณะแพทยศาสตร์ มหาวิทยาลัยเชียงใหม่ในระหว่างปี พ.ศ. 2546-2552

ผลการศึกษา: จากการศึกษาพบว่าผู้ป่วยมีอัตราการควบคุมโรคที่ 4 ปี เท่ากับ 44% มีอัตราการรอดชีวิตที่ 4 ปี เท่ากับ 82.1% เมื่อแบ่งตามระยะของโรค พบว่าอัตราการควบคุมโรคที่ 4 ปี ในผู้ป่วยระยะที่ I, II, III และ IV เท่ากับ 75.3%, 69.4%, 57.1% และ 36.9% ตามลำดับ ($p = 0.0055$) และมีอัตราการรอดชีวิตที่ 4 ปี ในผู้ป่วยระยะที่ I, II, III, และ IV เท่ากับ 85%, 78.6%, 91.1%, และ 71.5% ตามลำดับโดยที่สามารถรักษากล่องเสียงไว้ได้หลังการรักษาร้อยละ 73 ของผู้ป่วย

สรุป: โดยสรุปแล้วผลของการให้รังสีรักษาเพียงอย่างเดียวในผู้ป่วยมะเร็งกล่องเสียงทุกระยะที่หน่วยรังสีรักษาและมะเร็งวิทยา ภาควิชารังสีวิทยา คณะแพทยศาสตร์ มหาวิทยาลัยเชียงใหม่ นั้นให้ผลไม่เป็นที่น่าพอใจเมื่อเปรียบเทียบกับผลการรักษาจากสถาบันอื่น
