

5 **Use of transoral Co2 laser microsurgery for treatment of** 6 **cancerous neoplasms of the larynx in Vietnam**

7 **Le Minh Ky¹, Pham Van Huu³, Nguyen Xuan Quang³, Tang Hai⁵, Mai Quang Hoan⁴, Nguyen**
8 **BacHai², Nguyen DinhPhuc^{2*}**
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10 ¹National Otorhinolaryngology Hospital of Vietnam; Vietnam National University, Hanoi (VNU)

11 ²Hanoi Medical University -Vietnam

12 ³National Otorhinolaryngology Hospital of Vietnam

13 ⁴Tay Nguyen University-Daklak-Vietnam

14 ⁵Nghe An Maternity - Pediatric Hospital, Viet Nam
15
16

17 ***Corresponding author:** Phucnguyendinh11@yahoo.com.vn
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19 **Abstract.** Laryngeal cancer remains one of the most common head and neck tumors. In the treatment
20 of this disease, it is important to assess the overall survival when using transoral CO2 laser
21 microsurgery. Aim of the research was to make an evaluation of treatment of patients with laryngeal
22 cancer using CO2 laser transoralmicrosurgery. A number of 50 patients aged 40-82 years (average age
23 58.7 years) with early-stage laryngeal cancer were treated with CO2 laser transoral microsurgery at the
24 National ENT hospital from January 2012 to August 2014. Tumors at the T1aN0M0 stage were detected
25 in 34 people (68%), T1bN0M0 in 7 cases (14%), T2N0M0 in 9 cases (18%). Overall survival was 87.1
26 ± 2.3 months, and 5-year survival was 92%. The survival rate depending on the type of surgical
27 intervention Type III, Type IV, Type Va, Type Vb, Type Vc was 92.3%, 93.8%, 100%,100%, and
28 100%, respectively. The survival rate depending on the stage T1aN0M0 was 91.2%, on the stage
29 T1bN0M0 was 100%, on the stage T2N0M0 was 87.5%. Transoral CO2 laser microsurgery shows
30 excellent results in laryngeal tumors, especially in the T1aN0M0 stage, makes it possible to perform
31 surgery in more comfortable conditions, provides high survival rates, excellent cosmetic and functional
32 results compared to classical open access, without compromising immediate and long-term treatment
33 results.
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35 **Key words:** CO2 transoral laser microsurgery; larynx; carcinoma; T1- T2; survival

36 INTRODUCTION

37
38 Laryngeal cancer remains one of the most common head and neck tumors, and
39 although significant progress has been made over the past few decades, the diagnosis
40 and treatment of laryngeal cancer, given its complexity, is a unique problem (Le et al.,
41 2019). In particular, squamous cell carcinoma of the larynx accounts for 30-50% of all
42 neoplasms in the head and neck: 157,000 new cases were diagnosed worldwide in
43 2012 (Ferlay et al., 2015). As a result of the evolution of diagnostic measures,
44 treatment strategies, and follow-up protocols, early- stage treatment of laryngeal
45 cancer (T1-T2) has transformed from classical methods of open surgical resection into
46 a less aggressive and more functional endoscopic approach over the past 40 years.
47 Today, the efficiency and favorable outcome of transoral resection using a CO2 laser
48 for pharyngeal cancer (T1-T2) are 80-90% (Mendelsohn and Remacle, 2018). The
49 main advantages of transoral laser microsurgery (TLM) are the ability to minimize
50 damage to the larynx, maximize the preservation of healthy tissues, as well as
51 respiratory, chewing, and speech functions (Chiesa-Estomba et al., 2019). In addition,
52 the benefits of this type of treatment include a reduced risk of fistula, abscesses, and
53 osteoradionecrosis, as well as a shorter hospital stay, which significantly reduces
54 treatment costs (Golusiński et al., 2019). A number of large studies published between
55 2000 and 2010 showed that TLM shows excellent results with very high disease-
56 specific survival for all stages of early carcinoma, especially with Tis and T1
57 (Sjögren,2017).

58 However, transoral laser microsurgery has several disadvantages. These include
59 certain difficulties in providing hemostasis, access and tissue manipulation (Howard et
60 al., 2016). Inadequate effects on the larynx, damage to the anterior commissure in the
61 craniocaudal plane, invasion of the preepiglottic space, massive infiltration of the
62 preepiglottic space, and even slight erosion of the thyroid cartilage impose certain
63 restrictions on the use of TLM (Peretti et al., 2016). In connection with the foregoing,
64 the aim of the study was to evaluate the treatment of patients with laryngeal cancer
65 using CO2 laser transoralmicrosurgery.

66 MATERIAL AND METHODS

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69 A number of 50 male patients with diagnosed early-stage laryngeal cancer aged
70 40-82 years (mean age 58.7 years) were operated at the National ENT Hospital during
71 the period from January 2012 to August 2014 (Figure 1). All patients provided written
72 informed consent to participate in the study, as well as to use the data in this article.
73 The study protocol was approved by an independent ethics committee. All procedures
74 were carried out in accordance with the ethical principles of the Helsinki Declaration.

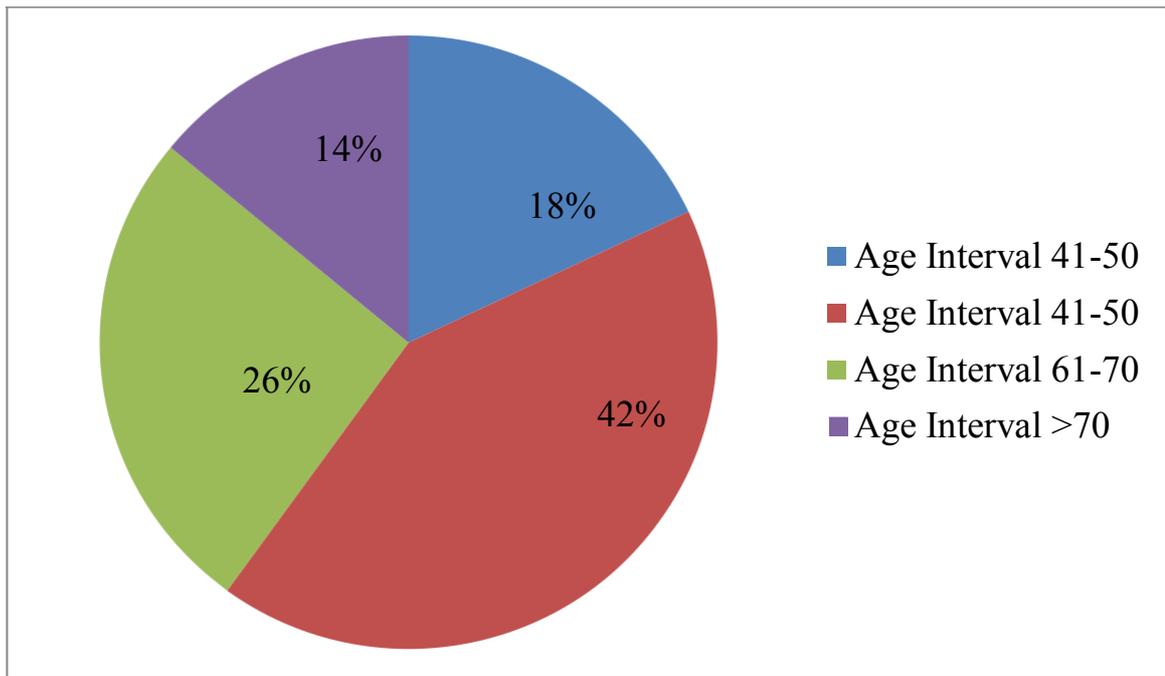


Figure 1. Distribution of study participants by age

72% abused smoking, 36% abused alcohol, and 40% abused smoking and alcohol in this cohort. The types of laryngeal lesions that occurred in our study are presented in Table 1. Tumors at the T1aN0M0 stage were detected in 34 cases (68%), at the T1bN0M0 stage were detected 7 cases (14%), at the T2N0M0 stage were detected 9 cases (18%).

Table 1. Lesions

<i>Lesions</i>	N	%
1CV, Anterior commissure intact	25	50
1Cv, Anterior commissure involve	15	30
2Cv, Anterior commissure involve	10	20

The availability and stage of neoplasm were determined during the preoperative examination using micro laryngoscopy. All patients underwent a biopsy to diagnose tissues, as well as an pan-endoscopy to exclude tumors in the upper digestive tract. Distant metastases were excluded by chest x-ray and abdominal ultrasound.

Statistical processing. The results were recorded prospectively with subsequent recording and storage in the database. Observation data was available to all patients. The total observation interval was 87.1 ± 2.3 months. Survival was calculated by the Kaplan – Meier method. All data were expressed descriptively and compared between subgroups.

RESULTS

Depending on the stage of the tumor, its location and the volume of tissue

removed, a different type of surgical intervention was used in accordance with the classification of cordectomies of the European Laryngological Society (ELS) (Table 2).

Table 2. Types of surgical intervention used in this study

Type	Type III	Type IV	Type Va	Type Vb	Type Vc	Type Vd
N	13	17	17	2	1	0

In some cases, postoperative radiation therapy was used (Figure 2).

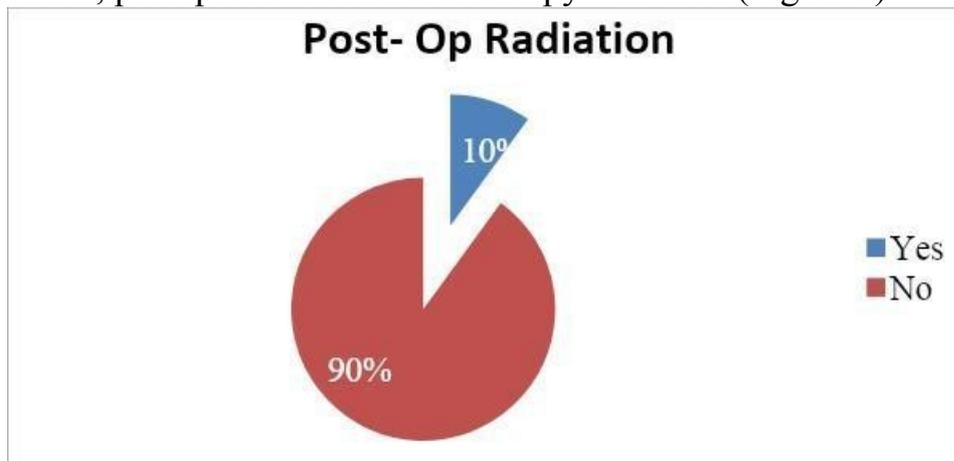


Figure 2. The proportion of postoperative radiation therapy

Survival based on the stage of the tumor process is presented in Table

3. Table 3. Survival based on tumor stage

Stage	Time of survival		mean (months)
	> 5 years		
	n	%	
T1aN0M0	31	91,2	68,87±9,5
T1bN0M0	7	100	65,13±5,2
T2N0M0	8	87,5	64±3,2

Survival depending on the type of surgical intervention is shown in Table 4.

Table 4. Survival according to operative types

OP types	Time of survival		mean (months)
	> 5 years		
	n	%	
Type III	12	92,3	66,7±8,4

Type IV	15	93,8	72,8±10,3
Type Va	17	94,4	63,8±3,3
Type Vb	2	50	61,0±1,3
Type Vc	1	100	64,0±0,8

In our study, relapse was detected in 8 (16%) patients (Table 5).

Table 5. The number of identified relapses during the observation period

Relapse – Metastasis	N=50	
	n	%
Local relapse	2	4
Cervical Lymph node metastasis	0	0

DISCUSSION

In laryngeal cancer, it is important to choose a surgical approach that provides adequate access and visualization (Baskin et al., 2018). The TLM method, especially at stages T1 or T2, shows some of the best results (Mehanna et al., 2016), and application of the CO₂ lasers for laser transoral resection of laryngeal cancer is the gold standard (Strieth et al., 2020). In particular, the transoral laser microsurgical technique offers a beneficial alternative to primary chemotherapy (Lane et al., 2020).

Studies comparing the treatment of laryngeal cancer with TLM and radiation therapy give somewhat conflicting results. For example, one study showed that survival was higher in patients with Tis/T1a laryngeal cancer who underwent TLM compared with radiation therapy (Guimarães et al, 2018). In turn, another study showed that the oncological relapse rate is higher in patients with T1a and T1b treated with TML compared to radiation therapy (Gioacchini et al, 2017). The third study did not reveal differences over a 5-year period in patients with laryngeal cancer in stage T2 (Warner et al., 2017). According to the latest data in this area (2003-2018), the overall five-year survival rate is 90%, the survival rate for concomitant diseases is 100%, and the larynx retention rate is 85% (Forner et al., 2020). In another study, the five-year level of local control was: Tis – 81.5%, T1a – 88%, T1b – 100%, and T2 – 58%; the overall 5-year survival rate is 87%, and the degree of organ preservation is 93% (Shiner et al., 2020). In the work of Lei et al. (2019) the local relapse rate for stages Tis, T1a, T1b, and T2 was 25%, 22.7%, 23.4%, and 22.1%. In our study, a relatively small number of relapses and a high 5-year survival rate are observed, which indicates a significant positive effect of this type of treatment for laryngeal cancer.

Compared with open larynx surgery methods, TLM as a method of treating laryngeal cancer combines high results with a simultaneous reduction in the number of

159 complications, improved voice and swallowing capabilities, and reduced
160 hospitalization (Meulemans et al., 2017). According to the literature, the 5-year
161 survival rate after laser surgery of T1 carcinomas of the vocal folds is 74-100%,
162 according to other sources, the 5-year survival rate after TLM tumors in the T1 / T2
163 stage is 82% (Wiegand, 2016). The results of 27-year-old observations (1979-2006)
164 were published, including 404 cases of T1a carcinoma, which reported a local control
165 rate of 86%, laryngeal preservation of 97% and a survival rate of up to 98% (Canis et
166 al ., 2015). Chiesa-Estomba et al. (2016) reported local control in 79.3%, with one
167 operation including T1a, T1b and T2 tumors reaching 98.3% of the local control.

168 One of the main issues in the treatment of laryngeal cancer is the subsequent
169 quality of life. The work (Vilaseca et al, 2016) showed that
170 94% of 401 patients who underwent CO₂ TLM had a high quality of life 1 year after
171 treatment. Another publication demonstrates that voice and swallowing function after
172 this type of treatment remains unchanged over time and does not worsen (Valls et al.,
173 2016).

174 The involvement of anterior commissure in the cancer process has long been
175 considered a risk factor for relapse. For example, it was found that in patients with
176 Tis-T2 carcinoma of the vocal fold and lesion of the anterior commissure, local
177 control, the degree of larynx preservation, and survival are reduced (Hoffmann et al.,
178 2016). However, it is emphasized that when assessing a tumor in the anterior
179 commissure, it is important to assess the degree of damage in the horizontal and
180 vertical planes affecting different areas of the pharynx, since tumors with apurely
181 horizontal spread are a good indicator for CO₂ TLM (Peretti et al., 2016). Studies in
182 Vietnam indicate that the use of CO₂ TLM for the treatment of patients with cancer of
183 the oropharyngeal zone shows high positive results (Tran and Nguyen, 2018). In
184 another work involving Vietnamese patients, laser surgery gives a very good positive
185 prognosis for pharyngeal cancer in stages T1 and T2 with a low number of
186 complications (Nguyen and Tran, 2017). In our study, in some cases, there was a
187 lesion of the anterior commissure, however, as the results showed, 5-year survival,
188 despite this factor, remained at a fairly highlevel.

189 **CONCLUSION**

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192 The results of the study suggest that the use of CO₂ laser provides thorough
193 hemostasis, makes it possible to carry out the operation in more comfortable
194 conditions, clearly see the border between healthy and tumor tissue and more
195 accurately determine the prevalence of tumor processes. A significantly smaller area
196 of coagulation necrosis allows you to save a significant amount of healthy tissue
197 without the use ofplastics.

198 Transoral laser microsurgery in the treatment of laryngeal cancer (T1-T2)
199 provides high survival rates, excellent cosmetic and functional results compared
200 toclassic open access, without compromising the immediate and long-term results of
201 treatment.

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203

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207 CONFLICTS OF INTEREST

208 The authors declare no conflict of interest.

211 REFERENCES

- 212 Baskin R.M., Boyce B.J., Amdur R., Mendenhall W.M., et al. (2018). Transoral robotic surgery for
213 oropharyngeal cancer: patient selection and special considerations. *Cancer Manag.*
214 *Res.*, 10:839-846.
- 215 Canis M., Ihler F., Martin A., Matthias C., et al. (2015). Transoral laser microsurgery for T1a glottic
216 cancer: review of 404 cases. *Head Neck*, 37(6):889-95.
- 217 Chiesa-Estomba C.M., González-García J.A., Larruscain E., Calvo-Henríquez C., et al. (2019). CO2
218 Transoral Laser Microsurgery in Benign, Premalignant and Malignant (Tis, T1, T2) Lesion of
219 the Glottis. A Literature Review. *Medicines (Basel)*, 6(3):77.
- 220 Chiesa-Estomba C.M., Reinoso F.A., Velasquez A.O., Fernandez J.L., et al. (2016). Transoral CO2
221 Laser Microsurgery Outcomes for Early Glottic Carcinomas T1-T2. *Int. Arch.*
222 *Otorhinolaryngol.*, 20(3):212-217.
- 223 Ferlay J., Soerjomataram I., Dikshit R., Eser S., et al. (2015). Cancer incidence and mortality
224 worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int. J. Cancer*,
225 136(5):359-386.
- 226 Forner D., Rigby M.H., Corsten M., Trites J.R., et al. (2020). Oncological and functional outcomes
227 after repeat transoral laser microsurgery for the treatment of recurrent early glottic cancer. *J.*
228 *Laryngol. Otol.*, 21:1-5.
- 229 Gioacchini F.M., Tulli M., Kaleci S., Bondi S., et al. (2017). Therapeutic modalities and oncologic
230 outcomes in the treatment of T1b glottic squamous cell carcinoma: a systematic review. *Eur.*
231 *Arch. Otorhinolaryngol.*, 274(12):4091-4102.
- 232 Golusinski W. and Golusinska-Kardach E. (2019). Current Role of Surgery in the
233 Management of Oropharyngeal Cancer. *Front. Oncol.*, 24(9):388.
- 234 Guimarães A.V., Dedivitis R.A., Matos L.L., Aires F.T., et al. (2018). Comparison between
235 transoral laser surgery and radiotherapy in the treatment of early glottic cancer: A systematic
236 review and meta-analysis. *Sci. Rep.*, 8(1):11900.
- 237 Hoffmann C., Cornu N., Hans S., Sadoughi B., et al. (2016). Early glottic cancer involving the
238 anterior commissure treated by transoral laser cordectomy. *Laryngoscope*, 126(8):1817-
239 1822.
- 240 Howard J., Masterson L., Dwivedi R.C., Riffat F., et al. (2016). Minimally invasive surgery versus
241 radiotherapy/chemoradiotherapy for small-volume primary oropharyngeal carcinoma.
242 *Cochrane Database Syst. Rev.*, 12:010963.
- 243 Lane C., Rabbani R., Linton J., Taylor S.M., et al. (2020). Systematic review and meta-analysis of
244 transoral laser microsurgery in hypopharyngeal carcinoma. *Laryngoscope Investig. Otolaryngol.*,
245 5(1):66-73.
- 246 Le H.J., Chen S.Y., Li Y., Xu Y., et al. (2019). The progress on diagnosis and treatment of larynx
247 cancer. *Lin Chung Er Bi Yan Hou Tou Jing Wai Ke Za Zhi*, 33(11):1017-1021.
- 248 Lei L., Zhong D., Zou J., Wang H., et al. (2019). Oncological outcomes of early stage glottic
249 squamous cell carcinoma treated with transoral laser microsurgery. *Am. J. Otolaryngol.*,
250 2019:102364.
- 251 Mehanna H., Kong A., and Ahmed S.K. (2016). Recurrent head and neck cancer: United Kingdom
252 National Multidisciplinary Guidelines. *J. Laryngol. Otol.*, 130(S2):181-190.
- 253

- 254 Mendelsohn A.H. and Remacle M.J. (2018). Vocal Fold Cancer Transoral Laser Microsurgery
255 Following European Laryngological Society Laser Cordectomy Classification. *Front. Oncol.*,
256 (8):231.
- 257 Meulemans J., Delaere P., Nuyts S., Clement P.M., et al. (2017). Salvage Transoral Laser
258 Microsurgery for Radiorecurrent Laryngeal Cancer: Indications, Limits, and Outcomes.
259 *Curr. Otorhinolaryngol. Rep.*, 5(1):83-91.
- 260 Nguyen T. and Tran T. (2017). Transoral Laser Microsurgery for Early Glottic Cancer.
261 *Biomed. Res. Ther.*, 2017,4(S):S54.
- 262 Peretti G., Piazza C., Mora F., Garofolo S., et al. (2016). Reasonable limits for transoral laser
263 microsurgery in laryngeal cancer. *Curr. Opin. Otolaryngol. Head Neck Surg.*, 24(2):135-139.
- 264 Shiner Y., Lubianiker B., and Doweck I. (2020). Early laryngeal cancer – treatment outcomes of
265 transoral laser microsurgery. *Harefuah*,159(1):77-82.
- 266 Sjögren E.V. (2017). Transoral Laser Microsurgery in Early Glottic Lesions. *Curr.*
267 *Otorhinolaryngol. Rep.*, 5(1):56-68.
- 268 Strieth S., Hagemann J., and Hess M. (2020). Angiolytic laser applications for the larynx:
269 Phonosurgical concepts for transoral laser microsurgery. *HNO*, 68(1):59-68.
- 270 Tran T. and Nguyen T. (2018). Early Outcomes of Transoral Laser Microsurgery for T1- T2
271 Oropharyngeal Cancer. *Asian J. Pharmaceut. Res. Health Care*, 10(4):104-108.
- 272 Valls-Mateus M., Ortega A., Blanch J.L., Sabater F., et al. (2016). Long-term quality of life after
273 transoral laser microsurgery for laryngeal carcinoma. *Surg. Oncol.*, 114(7):789-795.
- 274 Vilaseca I., Bernal-Sprekelsen M., Him R., Mandry A., et al. (2015). Prognostic factors of quality of life
275 after transoral laser microsurgery for laryngeal cancer. *Eur. Arch. Otorhinolaryngol.*,
276 272(5):1203-1210.
- 277 Warner L., Lee K., and Homer J.J. (2017). Transoral laser microsurgery versus radiotherapy for T2
278 glottic squamous cell carcinoma: a systematic review of local control outcomes. *Clin.*
279 *Otolaryngol.*,42(3):629-636.
- 280 Wiegand S. (2016). Evidence and evidence gaps of laryngeal cancer surgery. *GMS Curr. Top*
281 *Otorhinolaryngol. Surg.*, 15:Doc03.