



Transoral 980-nm/1470-nm dual-wavelength fiber laser microsurgery for early-stage glottic carcinoma

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ARTICLE INFO

Keywords:

Dual-wavelength fiber laser
Glottic carcinoma
Transoral laser microsurgery

ABSTRACT

Objectives: To investigate the effective and safety of transoral 980-nm/1470-nm dual-wavelength fiber laser microsurgery for early-stage glottic carcinoma by compared with CO₂ laser surgery.

Materials and Methods: From September 2015 to July 2018, 44 patients with early glottic carcinoma underwent transoral microsurgery were divided into 980-nm/1470-nm dual-wavelength fiber laser surgery (Dual-wavelength fiber laser group) and CO₂ laser surgery (CO₂ laser group). The operative time, number of other hemostatic devices used, postoperative blood loss, surgical complications and postoperative length of hospital stay. The time of mucosal epithelialization and Voice Handicap Index-10(VHI-10) in pre-operation, 1-month post-operation and 6-month postoperation in both two groups were retrospectively analyzed.

Results: All the patients underwent successful operation and all the tumors received en-bloc resection with negative margins. The median operative time in Dual-wavelength laser group was faster than CO₂ laser group (32.00 min vs 37.50 min, $p = 0.014$). There was no statistically significant difference between the two groups in the median postoperative hospital stay and the median time of mucosal epithelialization. No patient needed feeding tubes placed temporarily or permanently in both two groups. Tongue numbness, tear of the palatal arch, postoperative vocal cord adhesion, VHI-10 score in Pre-operation, 1-month postoperation and 6-month postoperation were similar in both two groups. No recurrence was reported in both groups during follow-up.

Conclusion: Compared to the CO₂ laser surgery, transoral 980-nm/1470-nm dual-wavelength fiber laser microsurgery is a safe and feasible procedure for early-stage glottic carcinoma. It can provide clearer surgical field without hemorrhage and make the operation simpler, smoother and faster.

Introduction

Laryngeal carcinoma is one of the most common malignant tumors of the head and neck, among which glottic carcinoma is the most common type [1]. The treatment methods include open surgery, transoral laser microsurgery (TLM), radiotherapy and chemotherapy [2]. TLM with CO₂ laser has the same therapeutic effect on early-stage glottic carcinoma as radiotherapy, with a 5-year survival rate of 85–100%. The advantages of CO₂ laser treatment, including minimal trauma, good vocal quality and quick recovery after surgery, have made

it the first choice for early treatment of early stage laryngeal carcinoma [3,4].

Transoral CO₂ laser microsurgery has certain limitations in exposing the anterior commissure [5]. In some cases, it is difficult to reach alignment of the laryngoscope and lesion. Therefore, it is necessary to assess whether the patient is suitable for laser surgery before surgery, which limit the indication of TLM [6]. The emerging fiber CO₂ lasers are flexible and can provide superiority to the treatment of lesions in the anterior commissure if combined with endoscopic or robotic systems [7,8]. However, CO₂ lasers are characterized by strong cutting but

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<https://doi.org/10.1016/j.oraloncology.2019.07.007>

Received 29 March 2019; Received in revised form 31 May 2019; Accepted 5 July 2019

Available online 11 July 2019

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poor hemostatic ability for small artery. Therefore, it is difficult to control intraoperative vascular hemorrhage and easy to cause contamination of the operative field, and it is often necessary to perform hemostasis using monopolar electrocoagulation, followed by continuation of the procedure. To this end, some researchers have explored the application of KTP laser and low-temperature plasma in minimally invasive surgery for the treatment of laryngeal carcinoma [9–11].

The novel 980-nm/1470-nm dual-wavelength fiber laser can be used for simultaneous cutting and hemostasis to achieve fine operation in a small space [12]. However, its use has not been reported in laryngeal carcinoma surgery. This study was aimed to investigate the application value of the 980-nm/1470-nm dual-wavelength fiber laser in early-stage glottic carcinoma by compared with CO₂ lasers.

Materials and methods

Patients

From September 2015 to July 2018, 44 patients with early glottic carcinoma who underwent transoral microsurgery, CO₂ laser or 980-nm/1470-nm dual-wavelength fiber laser surgery were included, and their data were retrospectively analyzed. The inclusion criteria included the following: 1. patients with cT1N0M0 or cT2N0M0 glottic carcinoma; 2. preoperative laryngoscopy biopsy showing moderately differentiated or well-differentiated squamous cell carcinoma; 3. preoperative MR showing no signs of primary tumor invasion in the paraglottic space or thyroid cartilage and no signs of cervical lymph node metastasis. The exclusion criteria were as follows: 1. patients with a history of severe cervical spondylosis or cervical surgery; 2. patients accompanied by other serious organ dysfunction; 3. patients with lateral neck lymph node metastasis or distant metastasis. The study was approved by the ethics committee. The conditions of all patients were discussed in multidisciplinary discussions. And they were informed of the advantages and disadvantages of different treatment methods, included surgery and radiotherapy. All patients in this study were willing to receive TLM with CO₂ laser or 980-nm/1470-nm dual-wavelength fiber laser and informed consent was obtained.

Among them, 22 patients were subjected to CO₂ laser surgery (CO₂ laser group) from September 2015 to September 2017, and they had a median age of 58.00 years (43.00–71.00 years). According to the seventh edition of the American Joint Committee on Cancer (AJCC) Cancer Staging Manual, there were 14 patients were staged at T1aN0M0, 6 at T1bN0M0, and 2 at T2N0M0. 22 patients were subjected to the 980-nm/1470-nm dual-wavelength fiber laser surgery (Dual-wavelength laser group) from October 2017 to July 2018, and they had a median age of 59.00 years (41.00–74.00 years). According to the seventh edition of the AJCC Cancer Staging Manual, there were 15 patients were staged at T1aN0M0, 4 at T1bN0M0, and 3 at T2N0M0.

Surgical equipment and instruments

OPMI® Vario/S88 microscope (Carl-Zeiss co., Oberkochen, Germany); intraoperative 3D imaging system (KestrelView II; Mitaka Kohki Co., Tokyo, Japan); suspension laryngoscope and laryngeal microsurgical instruments (KARL STORZ co., Tuttlingen, Germany); CO₂ laser (Lumenis AcuPulse 40 CO₂ laser, wavelength 10.6 μm, Lumenis Ltd., Yokneam, Israel); 980 nm/1470 nm dual-wavelength fiber laser (CeramOptec GmbH of Biolitec AG, Bonn, Germany); Storz Professional Image Enhancement System (SPIES) (KARL STORZ co., Tuttlingen, Germany).

Surgical procedure

All procedures of Dual-wavelength laser group were performed by the same surgeon (Faya Liang). General anesthesia was administered by transoral intubation. The inner diameter of endotracheal tube was

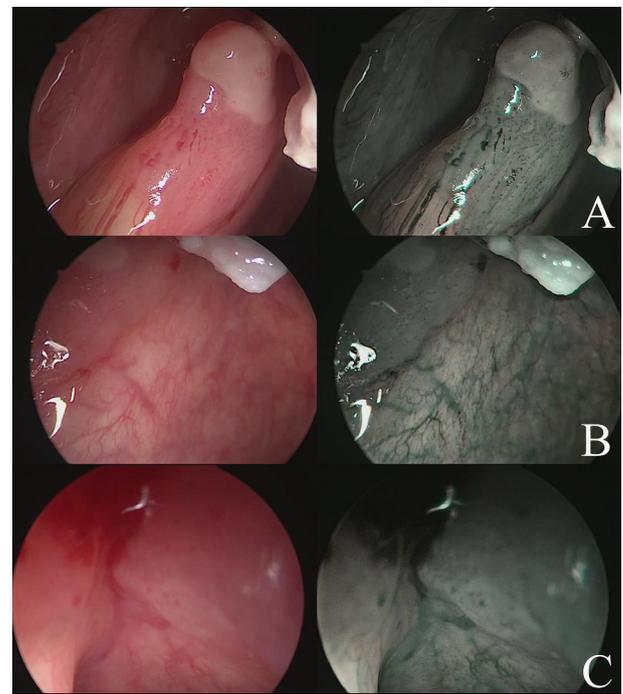


Fig. 1. The morphology of the mucosal vessels at the edge of the tumor was evaluated using the Spectra A mode in the SPIES system. (A) upper and posterior boundaries of tumor in left vocal cord; (B) lower boundary of tumor in left vocal cord; (C) lower boundary of tumor in anterior commissure.

5.0–6.0 mm, and mechanical ventilation was performed using air inhalation or the hypoxia mode (oxygen concentration < 30%). A self-retaining laryngoscope was used to fully expose the glottis and tumor boundary. If the anterior commissure of the larynx was poorly exposed, the assistant could compress the throat, adjust the compressing direction and change the upper tooth supporting point to improve visualization of this site. The relationship between the tumor and surrounding structure was first observed using a 30° or 70° endoscope, and the morphology of the mucosal vessels at the edge of the tumor was evaluated using the Spectra A mode in the SPIES system, which was similar to the narrow band imaging and can provide more clear tumor boundaries [13,14]. If there was more tumor invasion under Spectra A mode than white light mode, the extent of surgical resection should be extended (Fig. 1). The surgical procedure of Dual-wavelength laser group was performed under a 30° endoscope or microscope or intraoperative 3D imaging system (Fig. 2). The balloon of endotracheal tube was covered by wet pledget for protection. The dual-wavelength



Fig. 2. Transoral 1470 nm/980 nm dual-wavelength fiber laser microsurgery for early-stage glottic carcinoma under the intraoperative 3D imaging system.

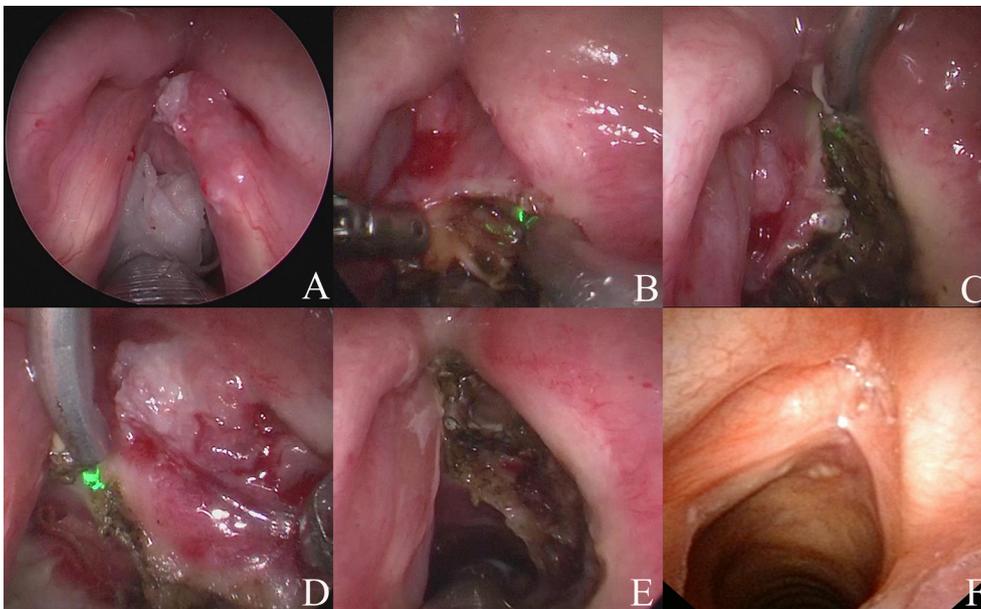


Fig. 3. Operative procedure of Transoral 1470 nm/980 nm dual-wavelength fiber laser microsurgery for early-stage glottic carcinoma and postoperative outcome. (A) endoscopy examination showed tumor was located in right vocal cord and near the anterior commissure; (B) posterior margin was marked by laser; (C) superior margin was marked by laser; (D) inferior margin was marked by laser; (E) en-bloc resection of the tumor and no bleeding during operation; F: 1-year follow-up show no recurrence in the larynx.

fiber laser was mounted in a flexible laser handpiece. The fibers with a diameter of 595 μm were connected to the laser machine. The power was set at 3 w for the 980-nm wavelength laser and 5 w for the 1470-nm wavelength laser (continuous mode). If the ventricular folds were on the way to expose the tumor, the ventricular folds or its anterior commissure could be removed first to determine the tumor boundary before performing the procedure. The excision margin to the tumor was approximately 3 mm. The tumor was completely removed using the contact cutting mode (Fig. 3). If the endotracheal tube blocked the tumor in the posterior portion of vocal cord, the anterior portion of vocal cord could be managed first and then the laryngoscope was adjusted appropriately and endotracheal tube was placed above the laryngoscope before the procedure was continued.

All the procedures of CO₂ laser group were also performed by the same surgeon (Faya Liang), and the surgical procedure was similar to the Dual-wavelength laser group. The power of CO₂ laser was set around 5–8 w with continuous mode.

The frozen pathological examination of the excision margin was performed in both groups. A positive margin indicated that the scope of resection would be extended, while a negative margin indicated that the procedure would be considered completed. No preventive tracheotomy was performed before or during surgery. At the completion of the procedure, dexamethasone (10–20 mg) was administered intravenously and antibiotics were administered for 24–48 h, and Pulmicort respules inhalation was given to prevent postoperative laryngeal edema. Proton pump inhibitor was given upon discharge to prevent granulation.

Observation parameters

The operative time, number of other hemostatic devices used, postoperative blood loss, surgical complications and postoperative length of hospital stay were documented. All patients underwent monthly fiberoptic laryngoscopy to observe granulation and mucosal epithelialization in the outpatient department. The time of mucosal epithelialization in the surgical sites, presence of adhesion in the anterior commissure and tumor recurrence were recorded. All patients were assessed with Voice Handicap Index-10 (VHI-10) in pre-operation, 1-month postoperation and 6-month postoperation.

Statistical methods

Data were analyzed with IBM SPSS (version 24.0). Normal distribution variables were presented as mean \pm standard deviation and non-normal distribution variables were presented as median (P25; P75). The differences of normally distributed variables were determined by the *t* test and the non-normally distributed data were determined by Mann-Whitney rank sum test. The comparison among groups of enumeration data are tested by chi-square. P Value < 0.05 was considered significant (see Table 1).

Results

All the patients underwent successful operation and all tumors received en-bloc resection with negative margins. There was no conversion to open surgery and no patient need tracheotomy or gastrogavage after operation in both groups. According to the classification of the European Laryngological Society in 2000 and supplementary classification in 2007 [3], the type II procedure was performed in 3 patients, type III in 9 patients, type IV in 6 patients, and type V in 4 patients in Dual-wavelength laser group, while the type II procedure was performed in 2 patients, type III in 8 patients, type IV in 6 patients, and type V in 6 patients in CO₂ laser group, respectively. and there was no statistically significant difference between the two groups ($p > 0.05$).

The median operative time in Dual-wavelength laser group and CO₂ laser group were 32.00 min and 37.50 min, respectively, and there was a statistically significant difference between the two groups ($p = 0.014$). The median postoperative hospital stay in both two group were 2 days, and the median time of mucosal epithelialization in both two group were 4 months.

In Dual-wavelength laser group, balloon rupture of endotracheal tube occurred in 2 patients in the early stage, but these accidents did not cause any tracheal burns. No postoperative bleeding was reported in both two groups. Tongue numbness in Dual-wavelength laser group and CO₂ laser group were 1 case and 2 cases, respectively, and there was no statistically significant difference between the two groups. Tear of the palatal arch in Dual-wavelength laser group and CO₂ laser group were 4 cases and 6 cases, respectively, and there was no statistically significant difference between the two groups. Postoperative vocal cord adhesion Dual-wavelength laser group and CO₂ laser group were 7 cases and 8 cases, respectively, and there was no statistically significant difference between the two groups. No patient need feeding tubes place

Table 1
Patient characteristic.

| Parameter | Dual-wavelength laser group | CO ₂ laser group | Z(χ^2) | p Value |
|---|-----------------------------|-----------------------------|---------------|---------|
| Sex | | | – | – |
| Male | 22 | 22 | | |
| Female | 0 | 0 | | |
| Age | 59.00(50.25;68.50) | 58.00(52.00;67.00) | –0.294 | 0.769 |
| T stage | | | 0.635 | 0.728 |
| T1a | 15 | 14 | | |
| T1b | 4 | 6 | | |
| T2 | 3 | 2 | | |
| European Laryngological Society (ELS) endoscopic cordectomy classification | | | 0.659 | 0.883 |
| Type II | 3 | 2 | | |
| Type III | 9 | 8 | | |
| Type IV | 6 | 6 | | |
| Type V | 4 | 6 | | |
| Operative time (min) | 32.00(25.00–36.25) | 37.50(34.75–45.00) | –2.458 | 0.014 |
| Number of other hemostatic devices used | 0(0,0) | 0(0,0) | –3.531 | < 0.001 |
| Postoperative hospital stay(d) | 2 (1;3) | 2 (1;2) | –0.764 | 0.445 |
| Mucosal epithelialization time (months) | 4 (3;5) | 4 (3;5) | –0.676 | 0.499 |
| Complications | | | | |
| Rupture of the tracheal tube balloon | 2 | 0 | 2.095 | 0.147 |
| tongue numbness | 1 | 2 | 0.357 | 0.549 |
| Tear of the palatal arch | 4 | 6 | 0.516 | 0.471 |
| Postoperative bleeding | 0 | 0 | – | – |
| Vocal cord adhesion | 7 | 8 | 0.101 | 0.750 |
| VHI-10 | | | | |
| Preoperation | 25.50(22.00,28.00) | 28.00(24.50,32.25) | –1.888 | 0.059 |
| 1 month-postoperation | 31.00(25.75,33.00) | 28.50(25.00,33.00) | –0.637 | 0.524 |
| 6 month-postoperation | 18.00(15.75,22.25) | 21.00(18.00,23.50) | –1.320 | 0.187 |
| Tracheotomy | 0 | 0 | – | – |
| Gastrogavage | 0 | 0 | – | – |
| Follow-up time(months) | 12.00(9.00–13.00) | 33.00(21.75–36.00) | –5.699 | < 0.001 |
| Local recurrence | 0 | 0 | – | – |
| Regional recurrence | 0 | 0 | – | – |
| Distant metastasis | 0 | 0 | – | – |

temporarily or permanently in both two groups. VHI-10 score in Pre-operation, 1-month postoperation and 6-month postoperation were similar in both two group.

The median follow-up in Dual-wavelength laser group and CO₂ laser group was 12 months and 33 months, respectively, and no recurrence was reported in both two groups.

Discussion

The main treatment options of early-stage laryngeal carcinoma often include surgery and radiotherapy [2]. Radiotherapy can achieve the desired effect in the treatment of early-stage laryngeal carcinoma but has disadvantages, including a longer treatment course, damaged surrounding tissue, and long-term discomfort in the neck after radiotherapy [15]. Failure of radiotherapy requires open salvage surgery that may be associated with more complications. With the development of laser equipment, TLM with CO₂ laser provided another choice for the treatment of patients with early-stage laryngeal carcinoma. According to the previous studies, the rate of the 5-year disease-free survival (DFS) rate and 5-year overall survival (OS) rate in patients with early-stage laryngeal carcinoma after TLM were 80–90% and 95–100%, respectively [4]. Laser surgery can balance disease control and laryngeal function preservation to enable patients to maintain normal breathing and vocal speech function under the premise of same disease control to reduce pain and shorten the hospitalization time [16,17]. Laser surgery can significantly improve the quality of life of patients, with the advantages of minimal trauma, quick recovery, and good vocal quality, which are unmatched by open surgery and radiotherapy [18].

The indications of TLM is closely related to the exposure of laryngeal tumor under the self-retaining laryngoscope. In theory, the tumor can be treated by laser if it can be completely exposed. However, the actual surgical operation is restricted by objective factors, such as intraoperative bleeding and exposure of glottis, as well as surgical

equipment, operative experience and skills, and philosophy of surgeons [5,6]. In general, glottic carcinoma with T1 or T2 without vocal cord immobility are better TLM indications. During tumor resection, the principle of tumor surgery should be followed. Excision should be performed on the normal tissue surrounding the tumor. The surgical excision margin should be more than 3 mm in the glottic carcinoma, and the depth of resection should be as deep as possible to the muscular layer. However, in special sites, such as T1 tumor with anterior commissure mucosal invasion without thyroid cartilage invasion, the use of a microscope and the arm transmitting CO₂ laser is limited due to the difficult anterior commissure exposure. Thus, this is the common area of recurrence in some patients 1 year after laser surgery [19]. A flexible fiber CO₂ laser combined with an angled endoscope or robotic system can solve this problem [7,8].

In type IV or V cordectomy during TLM, hemorrhage of small arteries can often be encountered, which may influence the fluency of operation. It is difficult to stop bleeding by the CO₂ laser. Other hemostatic methods such as monopolar electrocoagulation generally needed. This step may increase the complexity of surgery require surgeons have higher operational skills. The 980-nm/1470-nm dual-wavelength fiber laser is different from CO₂ laser, which can provide the 1470-nm and 980-nm lasers synchronously with different powers [12]. The amplitude of the 980-nm laser is at the golden section point of water and hemoglobin absorption curve and has good hemostatic effect with a certain cutting function, while the water absorption rate of the 1470-nm laser is 40 times larger than that of the 980-nm laser and has a stronger tissue absorption rate and a shallower penetration depth, which can cause extreme rapid cutting effect. Thus, combining the functions of the two lasers can achieve spontaneous cutting and coagulation with contact or noncontact cutting mode during surgery [20]. Compared with CO₂ laser, we found that 980-nm/1470-nm dual-wavelength fiber laser can provide more clear surgical field without hemorrhage, which make the operation more simpler, smoother and

faster.

In Dual-wavelength laser group, en-bloc resection of the tumors were achieved. The boundary of the tumor under the microscope and angled endoscope could be more clearly assessed, especially with the SPIES system. Due to the bendability of the fiber laser, the lesion located in the anterior commissure can still be handled. The slender fiber tip (0.6 mm in diameter) facilitated the accurate determination of the excision margin. The excision margins were negative in all cases in Dual-wavelength laser group. In terms of the short-term effectiveness, all the patients achieved epithelialization of the operative site, especially in the anterior commissure. The degree of carbonization in the operative field was not severe, and the epithelialization time of the operative field after surgery was similar to that after CO₂ laser surgery. Thus far, no signs of tumor recurrence have been detected in the patients. However, due to the short follow-up period, long-term follow up is needed to observe the tumor control.

Seven patients in Dual-wavelength laser group and 8 patients in CO₂ group had partial adhesion in the anterior commissure, which was associated with scar hyperplasia of the bilateral vocal cords and anterior commissure after surgery. Staggering surgery, such as a single sided surgery followed by contralateral surgery in several weeks may help to avoid this complication. But in China, most of the patients tend to complete the treatment in one time. However, the scarring did not affect the patient's respiration and no patient need tracheotomy. Thus, these patients are currently under observation. In the future, we may consider implanting a separation membrane concurrently to prevent scarring after tumor removed.

During fiber laser surgery, the choice of self-retaining laryngoscope is particularly important. In our experience, we preferred the Parsons laryngoscope with lateral opening, which can provide more space for fiber laser operation and reduced the incidence of chopstick effect between instruments during endoscopic surgery. Additionally, similar to CO₂ laser surgery, it is necessary to pay attention to the endotracheal tube balloon rupture caused by the laser, which may lead endotracheal membrane burned. In early stage of Dual-wavelength laser group, endotracheal tube balloon was ruptured in 2 cases during managing the posterior portion of vocal cord, but no tracheal burns occurred. We found that One of the reasons was accidental contact between laser fibers and balloon caused by the limited moving space. Then we try to place more wet pledgets to protect endotracheal tube balloon, and used the Parsons laryngoscope with lateral opening as much as possible. After that, this complication didn't happen again.

Most patients were discharged 1–2 days after operation, but some patients with complication such as tongue numbness and tear of the palatal arch may extent the postoperative hospital stay. These complications may be related to excessive force of self-retaining laryngoscope and long operation time. In our study, the incidence of these complication in Dual-wavelength laser group was lower than CO₂ laser group, but there was no statistically significant difference between the two groups. In the future, we will increase the sample size to explore whether 980-nm/1470-nm dual-wavelength fiber laser can reduce the incidence of these complications.

Conclusion

Compared to the CO₂ laser surgery, transoral 980-nm/1470-nm dual-wavelength fiber laser microsurgery is a safe and feasible procedure for early-stage glottic carcinoma. It can provide clearer surgical field without hemorrhage and make the operation simpler, smoother and faster.

Declaration of Competing Interest

None declared

This study was supported by Natural Science Foundation of Guangdong Province, China (2018A030313691).

Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.oraloncology.2019.07.007>.

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