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Ultrasound characteristics of early glottic laryngeal cancer: diagnostic value and preoperative T staging

Hua Wang, Lei Sun, Xiang-ru Wang, Xin-xin Lu, Fang-xi Zhao, Si-yuan Zhang, Liang Wu, Xiao-peng Li

Department of Ultrasound, The Second Affiliated Hospital of Xi'an Jiaotong University, Xi'an, Shaanxi Province, China

Abstract

Aim: To analyze the ultrasound characteristics of early glottic laryngeal cancer and evaluate their value in diagnosis and T-stage prediction. **Material and methods:** A total of 154 patients with postoperative diagnosis of early glottic cancer were included. Ultrasonic findings were summarized, and factors influencing diagnosis and T staging were analyzed. **Results:** Key findings included mucosal roughness, reduced echogenicity, vocal cord masses, and Adler grade III blood flow. Ultrasound showed 87.66% sensitivity. Adler grade and vocal cord mass were independent predictors of diagnosis. T-staging concordance was 74.51% for T1a, 72.73% for T1b, and 86.21% for T2, with no significant difference among stages. Adler grade and resistance index differed significantly across T stages, with resistance index and vocal cord mass being independent staging factors. **Conclusion:** Ultrasound can clearly distinguish mucosal layer lesions on the vocal cords, and it has a certain value in the diagnosis and T staging of early glottic laryngeal cancer.

Keywords: Laryngeal cancer; Ultrasonography; T stage

Introduction

Laryngeal cancer is a common malignant tumor of the head and neck region [1], the most common type of which is glottic laryngeal cancer. The cure rate for early-stage T1 and T2 laryngeal cancer can reach as high as 80% to 90%, while the survival rate for patients at stage T4 drops to 40% [2,3]. Early detection and accurate staging have a significant impact on the choice of treatment, prognosis, and overall quality of life for patients, In addition to cure, the treatment goal for early-stage laryngeal cancer is to preserve laryngeal function and maximize the patient's quality of life. Therefore, early detection and accurate staging are particularly crucial for patients with early-stage laryngeal cancer.

Clinical examinations and clear imaging are the foundation for early detection and precise staging [4]. Since laryngeal cancer originates in the mucosal layer, laryngoscopy is currently the preferred examination method, as it is highly effective in detecting mucosal layer lesions and assessing vocal cord movement; however, laryngoscopy cannot evaluate the extent of submucosal infiltration, which may lead to a potential underestimation of tumor stage [5]. CT and MRI can provide information on the extent of local invasion in laryngeal cancer and the presence of cervical lymph node metastasis; however, both methods are limited in their ability to identify superficial mucosal lesions, leading to lower detection rates for T1-stage laryngeal cancer. High-frequency ultrasound (US) can provide clear visualization of tissue structures and has gradually become an effective means of examining the head and neck region in real-time. In recent years, this imaging modality has been applied in the evaluation of vocal cord function [6,7] and has gradually been used for assessing various diseases of the vocal cord and Reinke's

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Corresponding author: Xiao-peng Li
Department of Ultrasound,
The Second Affiliated Hospital of
Xi'an Jiaotong University, 157 Xiwu Road,
Xi'an 710004, Shaanxi Province, China
Email: lixiaopeng123@xjtu.edu.cn

space, such as vocal cord polyps, vocal cord cysts [8,9], and even laryngeal cancer [10]. However, there is limited research on whether US can identify mucosal lesions on the vocal cords or detect early glottic laryngeal cancer through the identification of characteristic US imaging features. Additionally, there is limited research on whether US can accurately stage early laryngeal cancer.

Therefore, the aim of this study is to investigate the US image characteristics of early glottic laryngeal cancer, explore the diagnostic value of high-frequency US in early glottic laryngeal cancer, and analyze the factors affecting US T stage in early glottic laryngeal cancer.

Materials and methods

This study was designed as a retrospective analysis. All US examinations were performed and interpreted by attending physicians specializing in head and neck ultrasonography, each with over five years of experience. To minimize diagnostic bias, the sonographers were blinded to the laryngoscopy findings, histopathological results, and the clinically suspected side of the lesion. Furthermore, all US images were independently evaluated by three senior physicians holding the rank of associate chief physician or higher. Any discrepancies in interpretation were resolved through consensus discussion.

This study received approval from the hospital's Ethics Committee (Ethics Approval No: 2021052; 2023503), and all patients provided informed consent. Inclusion criteria: glottic carcinoma confirmed by laryngoscopy and biopsy. Exclusion criteria: glottic laryngeal carcinoma recurrence; prior chemotherapy or radiotherapy; patients with a vocal cord horizontal thyroid cartilage calcification length percentage greater than 67% [8]. Strictly according to the inclusion and exclusion criteria, data of 154 patients with early glottic laryngeal carcinoma diagnosed in Department of Otolaryngology from February 2017 to September 2023 were collected, including 149 males and 5 females, with ages ranging from 37 to 76 years.

Equipment and methods

Laryngeal US was performed using An HI VISION Ascendus with EUP-L75 probe operating at a frequency range of 5 to 18 MHz.

The patient underwent US examination before biopsy. During the examination, the patient laid in a supine position with a small pillow under the shoulder and neck area. The neck was appropriately extended backward. The US probe slowly scanned the patient from the level of the hyoid bone to the level of the cricoid cartilage arch, moving from top to bottom. The scanning range on both

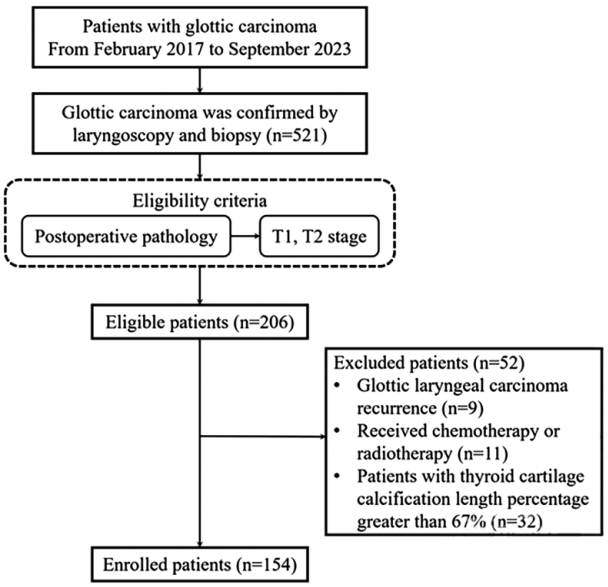

Fig 1. Flowchart of participant selection.

sides extended to the posterior lateral aspect of the thyroid cartilage lamina or he anterior edge of the sternothyroid muscle. Once the vocal cords on both sides were visible, the probe was fixed in place, and the thyroid cartilage itself was used as the acoustic window for observing the vocal cord structures.

Thyroid cartilage midline section: the patient was instructed to perform a breath hold after a deep inhalation, and the amplitude and symmetry of vocal cord motion during breathing was observed.

Thyroid cartilage lateral section: the US probe was moved laterally along the surface from the midline neck section, displaying the structures of the right and left vocal cords separately. Observations were made of the vocal cord mucosal layer, ligament layer, and muscle layer. For patients presenting with localized calcification of the thyroid cartilage, a clearer display of the vocal cord structures could be obtained by tilting the probe up and down and adjusting the beam direction. The patient was instructed to perform a breath hold to observe vocal cord closure in lateral sections of the thyroid cartilage.

US examination is performed by attending physicians with more than 5 years of diagnostic experience in the US head and neck group.

US T-staging criteria

US-based T-staging was conducted in accordance with the American Joint Committee on Cancer (AJCC) Cancer Staging Manual, 8th Edition. The specific sonographic criteria employed for staging were as follows: T1a Stage: tumor confined to a single vocal fold without involvement of the anterior commissure or the contralateral vocal fold, normal vocal fold mobility observed

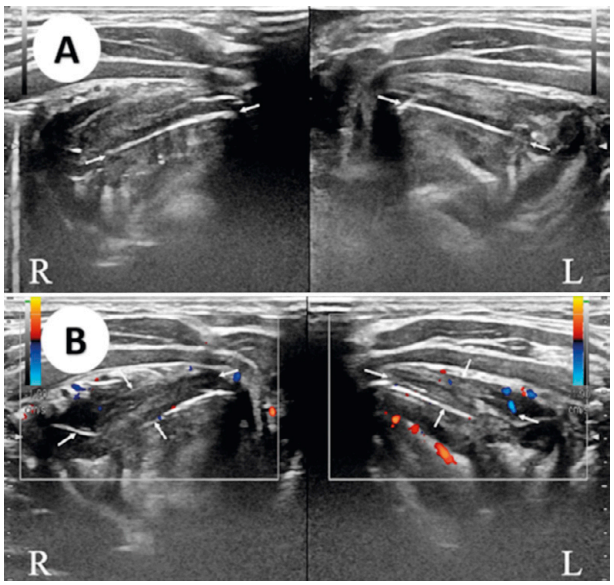

Fig 2. Normal vocal cord ultrasound images: A) The normal mucosal layer of the vocal cords is a continuous and smooth hyperechoic band, while Normal vocal cords exhibit low echogenicity; B) Normal vocal cords only show a few punctate blood flow signals, Alder grade I.

during dynamic assessment; T1b Stage: tumor involving both vocal folds without evidence of invasion into the paraglottic space, normal vocal fold mobility preserved; T2 Stage: tumor extension into the paraglottic space and/or impairment of vocal fold mobility, without fixation.

Vocal cord observations

The following findings were noted: vocal cord mucosa (smooth/rough); vocal cord echogenicity (normal/reduced); vocal cord masses (absent/present), including their location, size, depth of invasion, and whether they invaded the paraglottic space; Adler blood flow grade [11] - Grade 0 (no blood flow signal), Grade I (1-2 punctate or short rod-shaped blood flow signals), Grade II (one blood vessel with clear wall or 3-4 punctate blood flow signals), Grade III (multiple blood flow signals in a grid or patchy shape or two blood vessels with clear walls); resistance index (RI), of two arterial blood vessels in the lesion (the mean value was used).

Statistical analysis

Statistical analysis was performed using SPSS 26.0 software. Continuous variables were compared among multiple groups with analysis of variance and are presented as the means ± standard deviations (SDs). Pearson's χ^2 test was used to compare categorical data (shown as the numbers and percentages (%) of patients) between groups. Binary logistic regression analysis was employed to identify factors influencing the US diagnosis and T stage of laryngeal cancer. All test results were considered statistically significant at $p<0.05$.

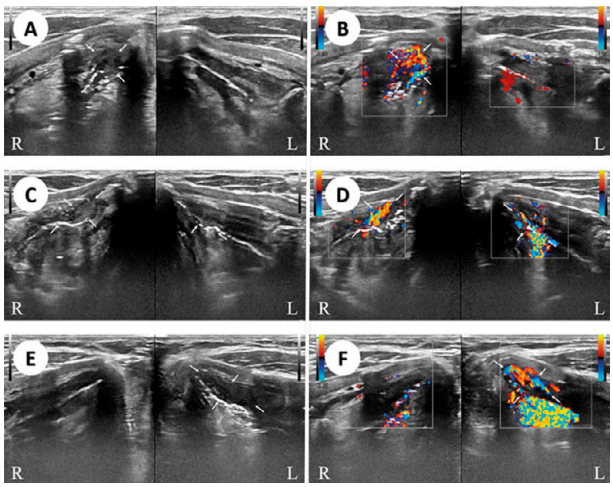

Fig 3. Ultrasound imaging features of T1- and T2-stage laryngeal cancer: A) Male, 49 years, with hoarse voice for 2 months, postoperatively diagnosed with T1a stage cancer. The right vocal cord mucosa (arrow) appears rough with discontinuous echogenicity, and a hypoechoic mass can be seen at the front; B) CDFI evidences a rich and chaotic blood supply within the mass, with visible thickened and tortuous blood vessels (Adler grade III); C) Male, 61 years, with hoarse voice for 7 months, postoperatively diagnosed with T1b stage cancer. Both vocal cord mucosae appear rough with discontinuous echogenicity (arrow), and hypoechoic masses can be seen in the anterior and middle parts of both vocal cords. The mass on the left vocal cord invades the superficial muscle layer; D) CDFI reveals a rich and chaotic blood supply within the mass (arrow), with visibly thickened and tortuous blood vessels (Adler grade III). The rich blood supply area of the left vocal cord appears only in the superficial muscle layer; (E) Male, 57 years, with hoarse voice for 6 months, postoperatively diagnosed with T2 stage cancer. The left vocal cord mucosa appears rough with discontinuous echogenicity (arrow), and a hypoechoic mass is visible throughout the entire length of the vocal cord, extending upward and downward but not in the paraglottic space. The right vocal cord mucosa appears smooth; F) CDFI shows a rich and chaotic blood supply within the mass (arrow), with visible thickened and tortuous blood vessel (Adler grade III).

Results

All 154 patients were diagnosed with squamous cell carcinoma of the larynx. Postoperative T stage: 95 patients had T1 stage cancer, including 51 with T1a and 44 with T1b. The remaining 59 patients had T2 stage cancer.

Glottic laryngeal cancer was identified via US in 135 patients, laryngeal papilloma in 8 patients, and granuloma in 6 patients. The larynxes of the remaining 5 patients were considered to be normal (no cancer detected).

US imaging characteristics of early glottic laryngeal cancer (fig 3, Tabel I)

- Mucosae of the affected vocal cord: a 'rough mucosa' of the vocal cord was defined when the continuous, smooth, linear, hyperechoic band of the vo-

cal cord mucosa layer was interrupted, and the echo itself was uneven. Out of the 154 patients, 142 had rough mucosae of the affected vocal cord, while 12 had smooth mucosae on the affected side.

- Echogenicity on the affected side: normal vocal cords typically exhibit low echogenicity. In 144 patients' echogenicity was reduced on the affected side, while 10 cases had normal echogenicity on the affected side.
- vocal cord masses: 126 patients presented with a mass on the affected side; the other 28 patients did not present with a mass but rather exhibited thickening of the vocal cord on the affected side. For the 44 patients diagnosed with T1b stage tumors, where both vocal folds were involved, the sonographic characteristics were recorded and analyzed based on the more severely affected side to ensure consistency and clinical relevance.
- Adler blood flow grading: grade III 105 patients, grade II in 49 patients, and none with grade 0 or I.
- RI: ranged from 0.50 to 0.55 in 22 patients, from 0.56 to 0.60 in 36 patients, from 0.61 to 0.65 in 79 patients, and from 0.66 to 0.70 in 17 patients.

Factors affecting US diagnosis of early glottic laryngeal cancer

Among the 154 patients with early glottic laryngeal cancer, US diagnosis identified the disease in 135 patients, misdiagnosed 14 patients and missed the diagnosis in 5 patients, resulting in an US sensitivity of 87.66%. Analysis of the five missed diagnoses indicated that the primary causes were likely significant acoustic shadowing from air within the laryngeal ventricle which obscured clear visualization of the vocal cords, and cases where the lesion presented only as minimal focal thickening without a distinct mass formation, making sonographic differentiation from benign conditions such as chronic inflammation challenging.

Table I. Ultrasound imaging characteristics of early glottic laryngeal cancer

Category	Number (%)
Vocal card mucosa rough/smooth	142 (92.21) / 12 (7.79)
Echogenicity reduced/normal	144 (93) / 10 (6.49)
Vocal cord masses yes/no	126 (81.82) / 28 (19.18)
Adler blood flow grading 0/I/II/III	0 / 0 / 49 (31.82) / 102 (68.18)
RI	
0.51~0.55	22 (14.29)
0.56~0.60	36 (23.38)
0.61~0.65	79 (51.29)
0.66~0.68	17 (11.04)

Using laryngeal cancer as the dependent variable and resistance index, Adler blood flow grading, mucosal changes, vocal cord echogenicity, and vocal cord masses as independent variables, binary logistic regression analysis was conducted. The results revealed that Adler blood flow grading and vocal cord mass were independent factors affecting the US diagnosis of early glottic laryngeal cancer (Table II).

US T stage agreement for early glottic laryngeal cancer

In table III the comparison of ultrasound T stage with clinical T stage for early glottic laryngeal cancer is detailed. The US T stage agreement rate for T2-stage laryngeal cancer was higher than that for T1a and T1b stages, but the difference was not statistically significant (p=0.184) (Table III).

Table II. Logistic regression analysis results of factors affecting ultrasound diagnosis of early glottic laryngeal cancer

	B	SE	Wald	p	OR	OR 95%CI
Mucosal changes	0.736	0.865	0.725	0.394	2.089	0.383~11.374
Echogenicity	0.067	0.942	0.005	0.943	1.070	0.169~ 6.781
Vocal cord lump	1.518	0.710	4.575	0.032	4.563	1.135~18.337
Adler grading	2.656	0.836	10.084	0.001	14.237	2.764~73.341
RI	-9.473	13.647	0.482	0.488	0.000	0.000~31774861.668
Constant	5.181	9.014	0.330	0.565	177.828	

Table III. Comparison of ultrasound T stage agreement for early glottic laryngeal cancer

T stage	Number	Ultrasound stage					χ^2	p
		T1a	T1b	T2	Unstaged	Concordance rate		
T1a	51	38	5	0	8	74.51%	3.383	0.184
T1b	44	2	32	4	6	72.73%		
T2	59	0	3	51	5	86.44%		

Table IV. Logistic regression analysis results for factors affecting ultrasound T stage in early glottic laryngeal cancer

Variable	B	SE	Wald	p	OR	OR 95%CI
Mucosal changes	0.052	0.738	0.005	0.944	1.053	0.248~4.477
Echogenicity	-0.511	0.870	0.345	0.557	0.600	0.109~3.298
Vocal cord lump	1.141	0.524	4.736	0.030	3.129	1.120~8.742
Adler grading	0.784	0.492	2.536	0.111	2.191	0.834~5.750
RI	-19.522	8.444	5.345	0.021	0.000	0.000~0.051
Constant	12.700	5.570	5.198	0.023	327587.019	

Factors affecting US T stage in early glottic laryngeal cancer

In binary logistic regression analysis, the RI and presence of vocal cord masses were the independent factors affecting the T stage of laryngeal cancer. Specifically, a higher RI was associated with a lower relative T stage in laryngeal cancer, while patients with vocal cord masses tended to have a higher T stage of laryngeal cancer (Table IV).

Discussion

Given the critical impact of accurate staging on treatment selection and laryngeal preservation in early glottic cancer, this study evaluated the role of high-frequency ultrasonography as a complementary diagnostic tool. While laryngoscopy, CT, and MRI each have established roles [4,5], high-frequency US offers unique advantages in visualizing superficial vocal cord structures. This study aimed to define the characteristic sonographic features of early glottic cancer and assess its value in diagnosis and T-staging. In recent years, with the continuous development of new US equipment, high-frequency US probes have achieved high tissue resolution, allowing clear identification of fine tissue structures, and consequently, the application of US in laryngeal diseases has expanded [13,14]. US has especially provided new possibilities in the diagnosis of diseases of the vocal cords and Reinke's space, particularly laryngeal diseases [8,9]. Therefore, we sought to answer the following questions: Can US detect early glottic laryngeal cancer? Are there characteristic US features of early glottic laryngeal cancer? What factors influence the US-based T staging of early glottic laryngeal cancer?

We found the sensitivity of US in diagnosed early glottic laryngeal cancer to be 87.66%. Adler blood flow grading and the presence of vocal cord masses were identified as independent influencing factors in the US diagnosis of early glottic laryngeal cancer. The sensitivity of US diagnosis in this group of cases is consistent with research by Zou et al [15], which was higher than that of conventional white-light electronic laryngoscopy, CT, and MRI [1,4] but lower than that of narrowband imaging electronic laryngoscopy [16]. This is because high-frequency US offers high-resolution imaging that can clearly distinguish the tissue layers of the vocal cords. US, by virtue of its high-resolution capability for superficial structures, holds the potential advantage of detecting minor mucosal lesions and assessing the depth of superficial muscle invasion more effectively than CT or MRI in certain contexts [13-16]. This potential is supported by studies highlighting the superior spatial resolution of high-frequency US for layered soft-tissue anatomy, though direct intra-patient comparative studies are needed for definitive conclusions. Additionally, US can provide clear information on the distribution of blood flow in the vocal cord mucosa and muscle layers. When compared to conventional white-light laryngoscopy, US provides both morphological and vascular information about the tumor, leading to higher sensitivity. Currently, US has lower sensitivity for glottic laryngeal cancer than narrow-band imaging electronic laryngoscopy. This difference may be attributed to the fact that the vascular morphology and blood flow distribution under US for laryngeal cancer have not been thoroughly documented, and specific US blood flow features that could enhance laryngeal cancer diagnosis have yet to be defined. Further investigation into the US blood flow characteristics associated with laryngeal cancer may provide a breakthrough for improving sensitivity using US. This will be one of the main directions for our future research.

Some studies have suggested that T stage and N stage are independent factors affecting patient prognosis [17]. For T1- and T2-stage glottic laryngeal cancer, minimally invasive surgical approaches can be selected [18,19], as they allow preservation of laryngeal function to a greater extent and improving patient quality of life. Therefore, the T stage for laryngeal cancer holds a similarly important prognostic role as early detection. In this study, the US T stage was compared with the postoperative pathological T stage, resulting in a concordance rate of 74.51% for T1a, 72.73% for T1b, and 86.44% for T2 cancer. US had a higher concordance rate for T2-stage laryngeal cancer than for T1a and T1b stage cancer, but

the difference was not statistically significant. Since US can clearly distinguish the paraglottic space and thyroid cartilage plate [20], none of the 154 patients in this group were overstaged. Our research revealed significant differences in Adler blood flow grade among the different T stages, with no significant difference between T1a and T1b but significant differences between T2 and T1a/T1b; blood flow resistance indices were significantly different among different T stages, with no significant difference between T1a and T1b but a significant decrease in T2. Moreover, the blood flow resistance index and the presence of a vocal cord mass were identified as independent factors affecting the US T stage of early glottic laryngeal cancer. Specifically, a higher blood flow resistance index was associated with a lower T stage in laryngeal cancer, and patients with vocal cord masses had a higher T stage. Angiogenesis is closely related to the biological behavior of tumors and is a prerequisite for tumor invasion and metastasis, and changes in microvascular morphology are characteristic of laryngeal cancer [21,22]. As laryngeal cancer progresses and tumor volume increases, the blood vessels within the tumor become thicker, more numerous, and distorted [23], forming arteriovenous fistulas. Under US, as the T stage increases, vocal cord masses become more pronounced, and blood flow resistance indices decrease.

In summary, the main US features of early glottic laryngeal cancer include roughness of the vocal cord mucosa, reduced echogenicity, vocal cord masses, and Adler grade III blood flow. Among these features, Adler blood flow grade and the presence of vocal cord masses were identified as independent factors for diagnosing early-stage glottic laryngeal cancer, while the RI of blood flow and vocal cord masses were identified as independent factors for the US T staging of laryngeal cancer. US can clearly differentiate vocal cord mucosal lesions and provides value in the diagnosis and staging of early glottic laryngeal cancer. It is expected that US can complement laryngoscopy, CT, and MRI, promoting earlier and more accurate detection of laryngeal cancer.

Limitations

This study has several limitations that should be considered when interpreting the results. First, its retrospective design inherently carries the risk of selection bias. Furthermore, the absence of a control group comprising patients with benign vocal cord lesions or healthy controls limits the assessment of the specificity of the described US features. Second, thyroid cartilage calcification can significantly impair acoustic penetration and vocal cord visualization. While our exclusion criteria specifically addressed this by excluding patients with thyroid cartilage calcification length exceeding 67%, moderate calcification may still have degraded the image quality in some included cases. Finally, despite implementing a blinding protocol, the operators' potential prior awareness of a high clinical suspicion for malignancy in referred patients could have introduced unconscious diagnostic bias.

Conclusion

This study is part of an ongoing series of studies, ranging from assessing vocal cord motion to diagnosing various vocal cord lesions. During this study, we found that vascular morphology, diameter, and distribution, among other blood flow characteristics may be a breakthrough point in improving the sensitivity of laryngeal cancer. We hope that through the joint efforts of numerous researchers, the study of laryngeal US can be further deepened and its results widely applied in clinical practice.

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Conflict of interest: none

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