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● *Original Contribution*

APPLICATION OF TRANSCUTANEOUS LARYNGEAL ULTRASONOGRAPHY IN THE DIAGNOSIS OF VOCAL FOLD POLYPS

Hua Wang,* Xiaoxue Yang,* Jin Hou,† Xiaopeng Li,* Lei Sun,* Jue Jiang,* and Qi Zhou*

* Department of Ultrasound, The Second Affiliated Hospital of Xi'an Jiaotong University, Xi'an, Shaanxi Province, China; and
† Department of Otolaryngology Head and Neck Surgery, The Second Affiliated Hospital of Xi'an Jiaotong University, Xi'an, Shaanxi Province, China

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Abstract—The aim of this study was to explore the value of transcutaneous laryngeal ultrasonography in the diagnosis of vocal fold polyps. From December 2016 to June 2019, 87 patients with vocal fold polyps diagnosed pathologically in the Otolaryngology Head and Neck Surgery Department of the Second Affiliated Hospital of Xi'an Jiaotong University were enrolled and examined by electronic laryngoscopy and percutaneous laryngeal ultrasound on the same day before operation. To observe the effect of calcification length as a percentage of thyroid cartilage at the glottic level on vocal fold display, the characteristics of ultrasound images of vocal fold polyps and the value of transcutaneous laryngeal ultrasonography in the diagnosis of vocal fold polyps were assessed. Among 87 patients, the calcification rate of thyroid cartilage at the glottic level was 33.3%. The differences in calcification rate and percentage of calcification length between males and females were statistically significant. The rate of detection of vocal folds decreased gradually with an increase in calcification length percentage. Imaging features of vocal fold polyps were hypo-echoic with a clear boundary and regular shape. The detection rates for circular and non-circular polyps were 92.0% and 70.6%. Ultrasound was more likely to detect circular than non-circular polyps; however, the difference was not significant. Transcutaneous laryngeal ultrasonography can identify the morphology and location of vocal fold polyps and is non-invasive and highly accurate. Therefore, it has the potential to be an effective supplement to laryngoscopy for initial screening and post-operative review of vocal fold polyps. (E-mail: zhouqiwh1@163.com)

Key Words: **Transcutaneous laryngeal ultrasonography, Vocal fold polyps.**

INTRODUCTION

Vocal fold polyps are a benign proliferative disease of the superficial lamina propria of the vocal folds, with hoarseness as the main symptom. They are the most common benign vocal fold lesions in clinical practice (Nunes et al. 2013; You et al. 2016; Ogawa and Inohara 2018). At present, laryngoscopy is the main method used to diagnose the disease, although the method is not suitable for some adult patients and children (Zou and Ge 2016). Ultrasound imaging has gradually become a very convenient and powerful tool in examining the head and neck regions because of its low cost, non-ionizing radiation, non-invasiveness and real-time capability (Tsui et al. 2011). High-frequency ultrasound is effective for visualizing the structure of the larynx (Lin and Hua 2018). Prasad et al. (2011) reported that transcutaneous laryngeal ultrasonography can clearly reveal the soft tissues around the upper airways of adults and, thus, has several potential clinical applications. Although high-frequency ultrasound has been used primarily in the diagnosis of vocal fold paralysis and vocal fold nodules in children (Bisetti et al. 2009; Ongkasuwan et al. 2017a and to assess vocal fold function before and after thyroidectomy in adults (Kandil et al. 2016), it has not been widely used for other laryngeal lesions (Wu et al. 2017). Tamura et al. (2001), using intralaryngeal ultrasonography to diagnose vocal fold lesions, summarized the imaging features of vocal polyps, cysts and cancers and reported that laryngeal lesions can be diagnosed by intralaryngeal ultrasonography. However, this method is invasive and requires general anesthesia. Many otolaryngology head and neck surgeons are concerned about the non-invasive diagnosis of vocal fold lesions. However,

Address correspondence to: Qi Zhou, No. 157, Xiwu Road, Xi'an 710004, Shaanxi Province, China. E-mail: zhouqiwh1@163.com

few studies have involved the application of transcutaneous laryngeal ultrasonography in the diagnosis of vocal fold lesions (Bisetti et al. 2009; Tsui et al. 2011; Kandil et al. 2016; Ongkasuwan et al. 2017b; Fukuhara et al. 2018; Dacosta et al. 2019; Derlatka-Kochel et al. 2019; Dubey et al. 2019), and there are few reports on the characteristics of ultrasound images of vocal fold polyps. The purposes of this study were to explore how to clearly visualize vocal folds by transcutaneous laryngeal ultrasonography, to summarize the ultrasonic image characteristics of vocal fold polyps and to explore the value of transcutaneous laryngeal ultrasonography in the diagnosis of vocal fold polyps.

METHODS

General information

We recruited 87 patients who were diagnosed with vocal fold polyps by post-operative pathology in the Otolaryngology Head and Neck Surgery Department of the Second Affiliated Hospital of Xi'an Jiaotong University from December 2016 to June 2019. Participants included 38 males and 49 females, and patient age ranged from 20−73 y, with an average age of 37.3 y. On the same day before operation, the patients were examined by electronic laryngoscopy first and then by transcutaneous laryngeal ultrasonography, which was performed using the blind method. All patients signed informed consent forms, and approval was obtained from the ethics committee of the hospital.

Instruments

We used a laryngeal ultrasound machine (Totem, Hitachi, Tokyo, Japan) with a probe (5−18 MHz; L7-3, Tokyo, Japan). We also used an electronic laryngoscope with host, light source and mirror (otv-s7, enf-vt2 and otv-s45; Olympus, Tokyo, Japan).

Ultrasound examination

During the examination, patients were placed in the supine position. With a small pillow to support the shoulders, the neck was slightly bent back and stretched. The ultrasound probe was slowly moved from the level of the hyoid bone to the level of the front cricoid cartilage. The posterolateral lamina of the thyroid cartilage or anterior border of the sternocleidomastoid muscle came within the scanning range on both sides. When the bilateral vocal folds were observed, the ultrasound operator held the probe, kept it fixed and visualized the vocal fold structure, with the thyroid cartilage as the acoustic window.

For the median section of the neck, patients were asked to inhale, breathe, hold their breath and make a short 'E' sound to hear the amplitude and symmetry of vocal fold movement (Fig. 1). The vocal fold layers could not be clearly displayed in this section.

To examine the side of the neck, the operator shifted the probe from the median section of the neck laterally along the body's surface. Imaging of the right and left side sections revealed the right and left vocal fold structures, respectively, and allowed examination of the vocal fold epithelial layer, lamina propria and muscle layer. The position, size, blood flow and shape of the vocal fold polyps were observed in this section. Because the thyroid cartilage was locally calcified, the probe was adjusted by tilting it up and down so that the sound beam could be used to display the vocal fold layers clearly (Fig. 1).

Method for calculating the length ratio of thyroid cartilage calcification

We placed the ultrasound probe at the level of the glottis of the thyroid cartilage and asked the patient to hold his or her breath, resulting in closure of the vocal folds, and took this section as the measurement standard, calculating the ratio of the length of calcification lesion to the length of the bilateral thyroid cartilage. Participants were divided into three groups according to the ratio: 0, <33%, 34%−66% and >67% (Fig. 2).

Statistical processing

The gender difference in thyroid cartilage calcification at the glottic level, the influence of thyroid cartilage calcification length on vocal cord appearance and the difference in laryngeal ultrasonography of vocal cord polyps of different shapes were all tested using Fisher's exact test. A p value <0.05 was considered to indicate significance. Statistical analysis was performed using the standard software, SPSS Version 20.0 for Windows (IBM, Armonk, NY, USA).

RESULTS

In this study, we found that images of the side sections of the neck revealed the vocal fold layers and vocal folds more clearly than images of the median section (Fig. 1), so all data in this study were collected from side sections

Calcification of thyroid cartilage

Of the 87 patients, 58 had no calcification and 29 had calcification. The calcification rate of thyroid cartilage at the glottic level was 33.3%.

The sex distribution of the groups was as follows: no calcification group (58 cases): 42 female cases, 16 male cases; calcification length <33% group (11 cases): 4 female cases, 7 male cases; calcification length 34%−66% group (10 cases): 1 female case, 9 male cases; and calcification length >67% group (8 cases): 2 female cases, 6 male cases. At the glottic level, probability of calcification and percentage calcification length in the thyroid cartilage were significantly higher in males than in females ($p = 0.000077$) (Fig. 3).

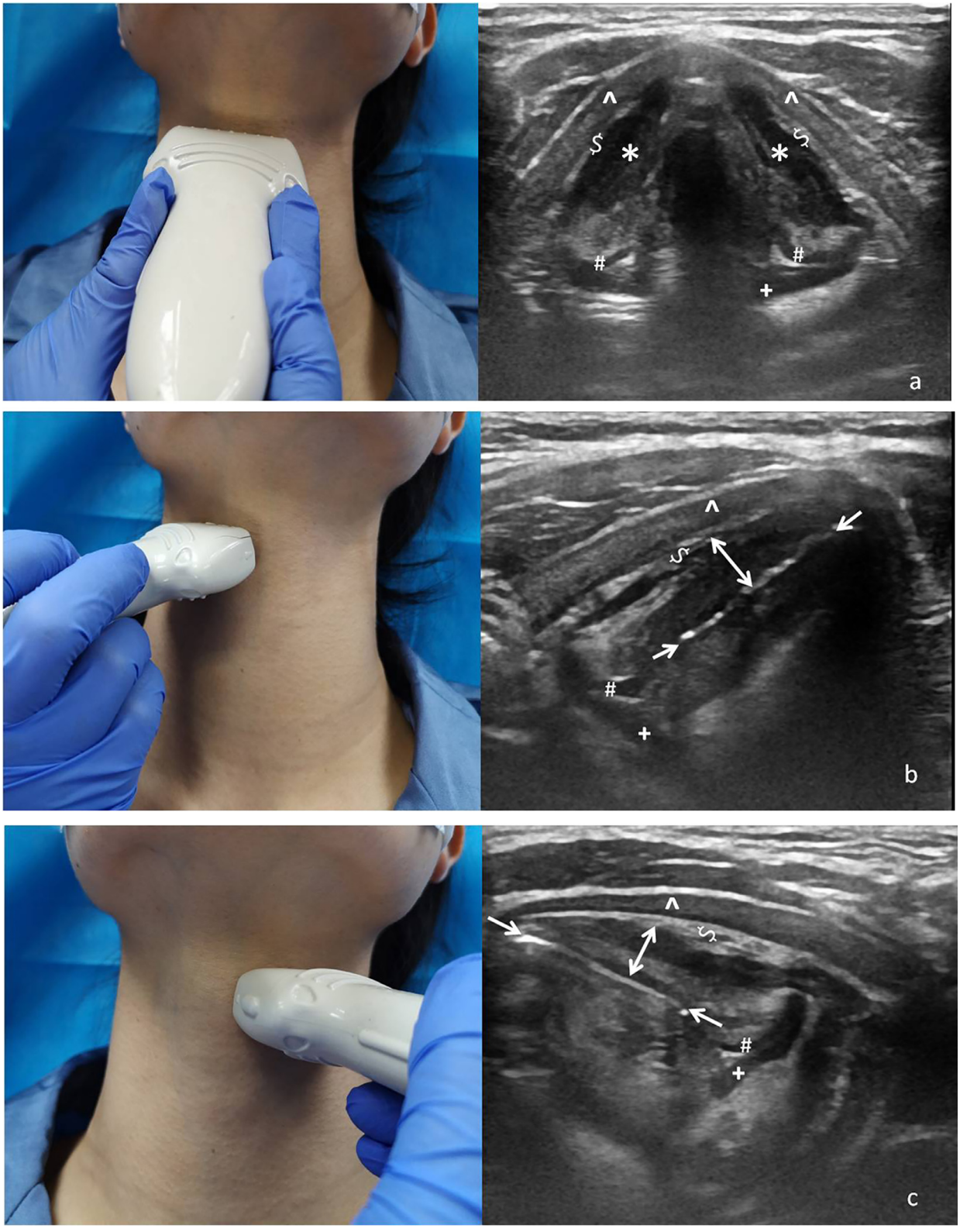
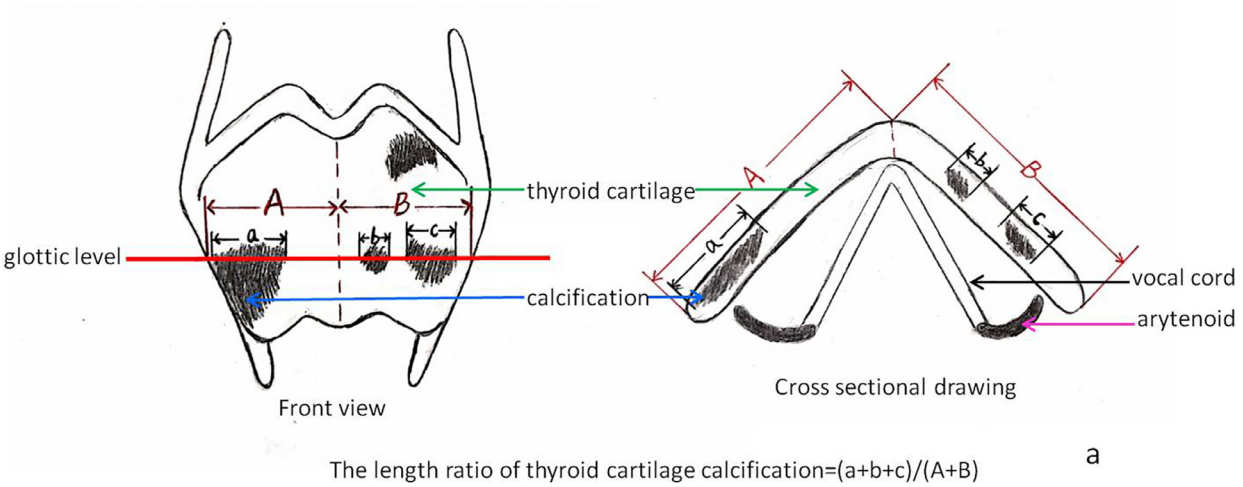


Fig. 1. Structure of glottic region and inspection method. (a) Medial section of the neck. (b, c) Side sections of the neck. *Vocal folds. [#]Arytenoid cartilage. [+]Arytenoid. ^Thyroid cartilage. [†]Epithelium and lamina propria, [‡]muscle layer. [$]Paraglottic space.



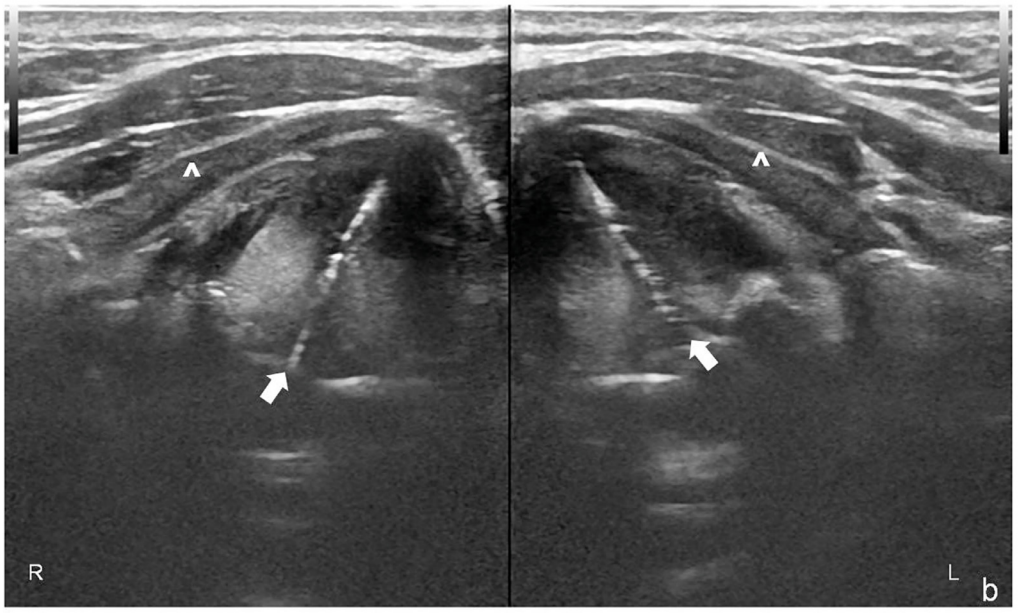


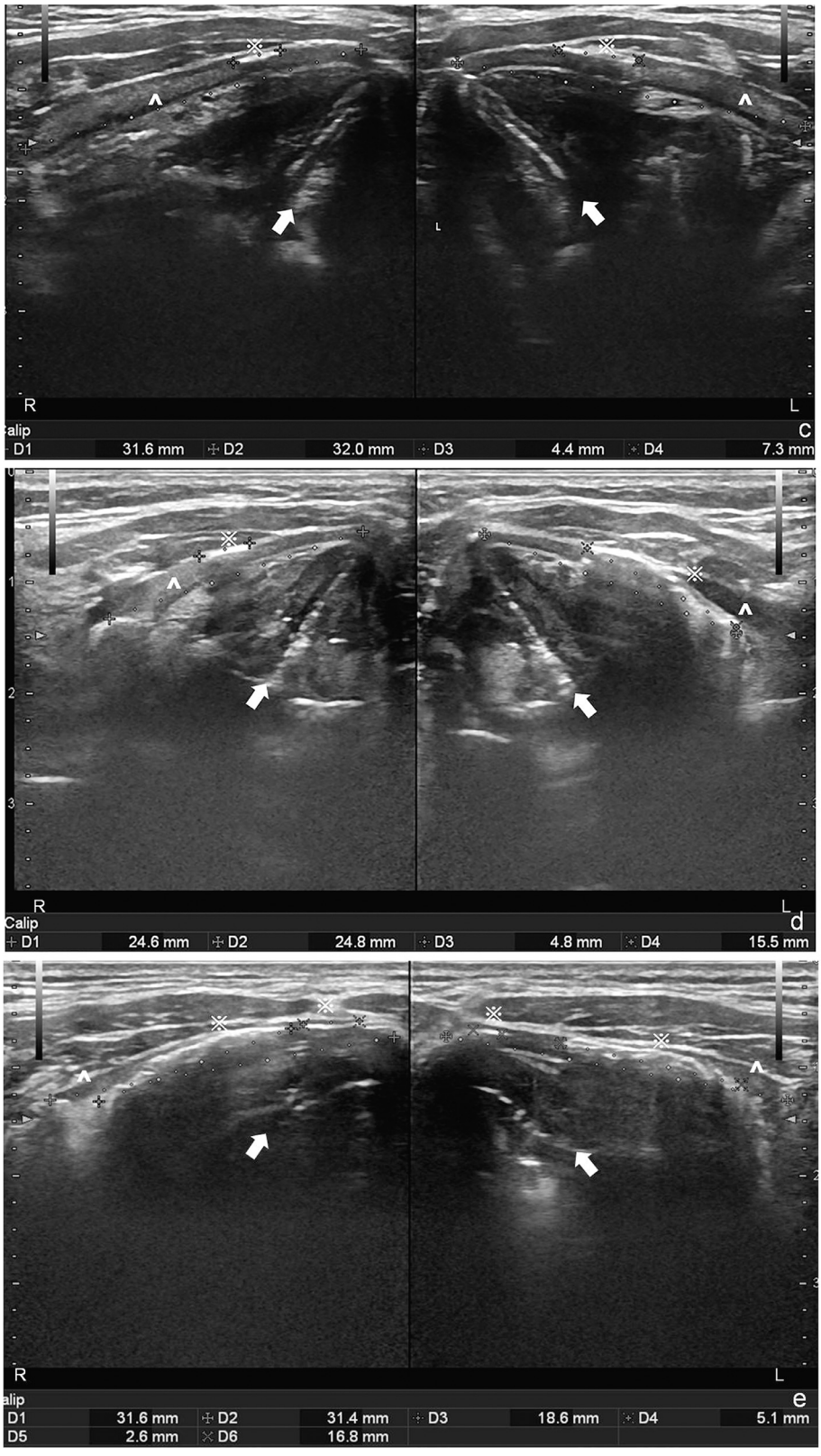
Fig. 2. Measurement of calcification length percentage of thyroid cartilage at the glottic level. (a) Schematic of method used to calculate percentage of thyroid cartilage calcification at the glottic level. (b) No calcification of thyroid cartilage. (c) Thyroid cartilage calcification length percentage 18.3% (<33% group). (d) Thyroid cartilage calcification length percentage: 41.1% (34%−66% group). (e) Thyroid cartilage calcification length percentage 72.6% (>67% group). ^Thyroid cartilage. ↑Glottal closure. ※Calcification.

Effect of percentage calcification length of thyroid cartilage at the glottic level on vocal fold detection rate

For thyroid cartilage without calcification, the vocal fold detection rate was 100.0%. For cases with a calcification length <33%, the vocal fold detection rate was 100.0%; for cases with a calcification length of 34%−66%, the vocal fold detection rate was 90.0%; and for cases with a calcification length >67%, the vocal fold detection rate was 37.5%. As the calcification length percentage increased, the vocal fold detection rate gradually decreased ($p = 0.000024$) (Fig. 4).

Ultrasound manifestations of vocal folds

From shallow to deep, the layers of the vocal folds are the epithelium, lamina propria and muscle layer. Ultrasound reveals that the epithelium is hyper-echoic, the lamina propria is both hypo-echoic and hyper-echoic and the muscular layer is hypo-echoic. We found that



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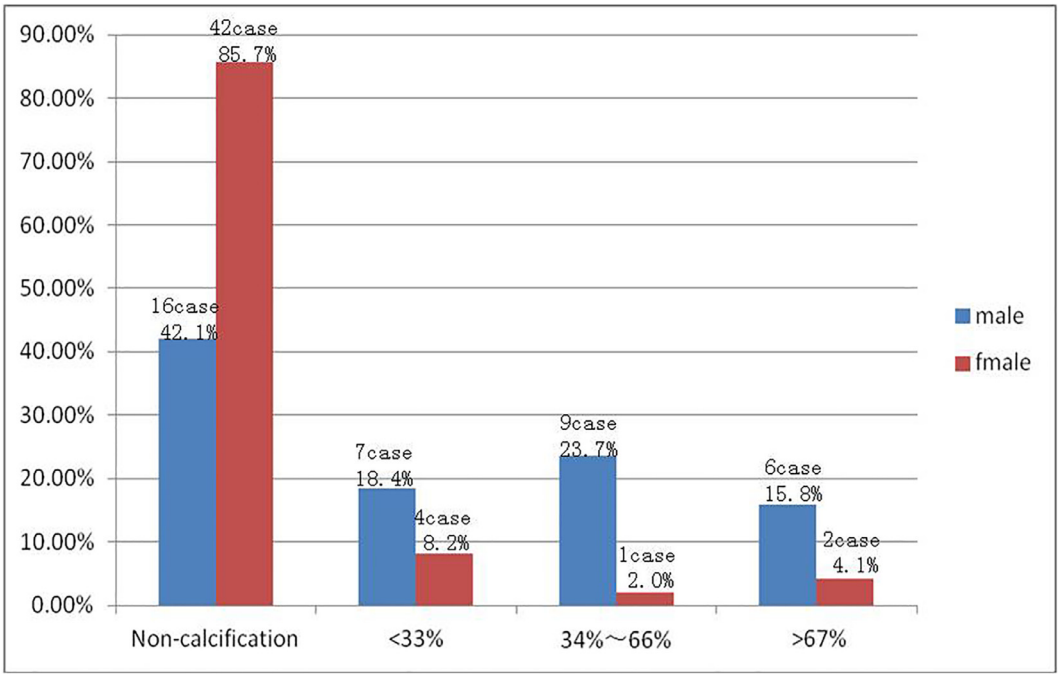

Fig. 3. Comparison of calcification of thyroid cartilage between men and women at the glottic level. The incidence of thyroid cartilage calcification and calcification length percentage were higher in men than in women, $p = 0.000077$

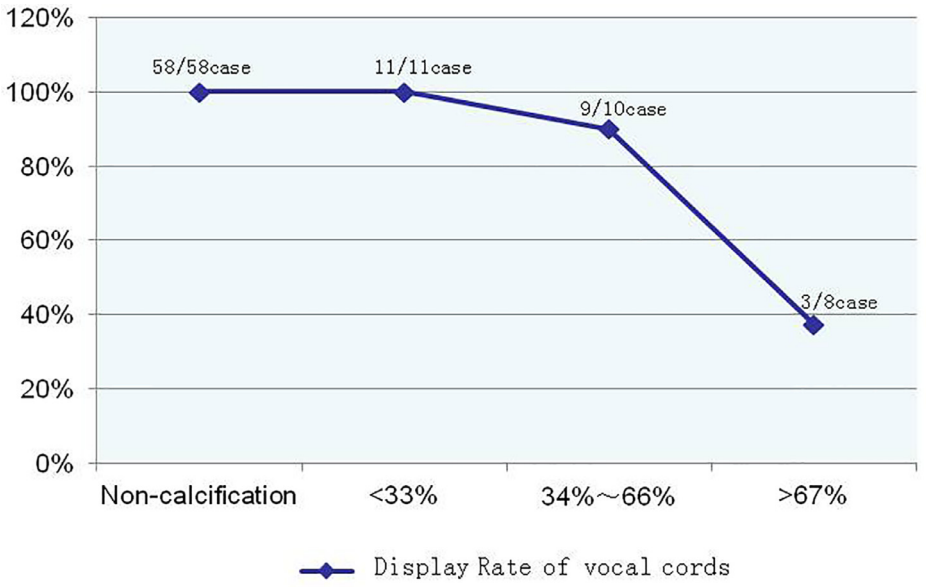

Fig. 4. Effect of calcification length percentage of thyroid cartilage at the glottic level on vocal fold detection rate. As the calcification length percentage increases, the vocal fold detection rate gradually decreases, $p = 0.000024$.

transcutaneous laryngeal ultrasonography could obtain the same image as intralaryngeal ultrasonography (Tamura et al. 2001).

Ultrasound manifestations of vocal fold polyps

High-frequency ultrasound images of vocal fold polyps revealed a limited uniform hypo-echoic region between two hyper-echoic regions (superficial lamina propria). The boundary was clear, and the shape was regular. The capsule had a linear hyper-echoic area, with an apparent free-edge linear hyper-echoic area. Color Doppler flow imaging (CDFI) revealed that blood flow signals could not be detected in most vocal fold polyps (Fig. 5).

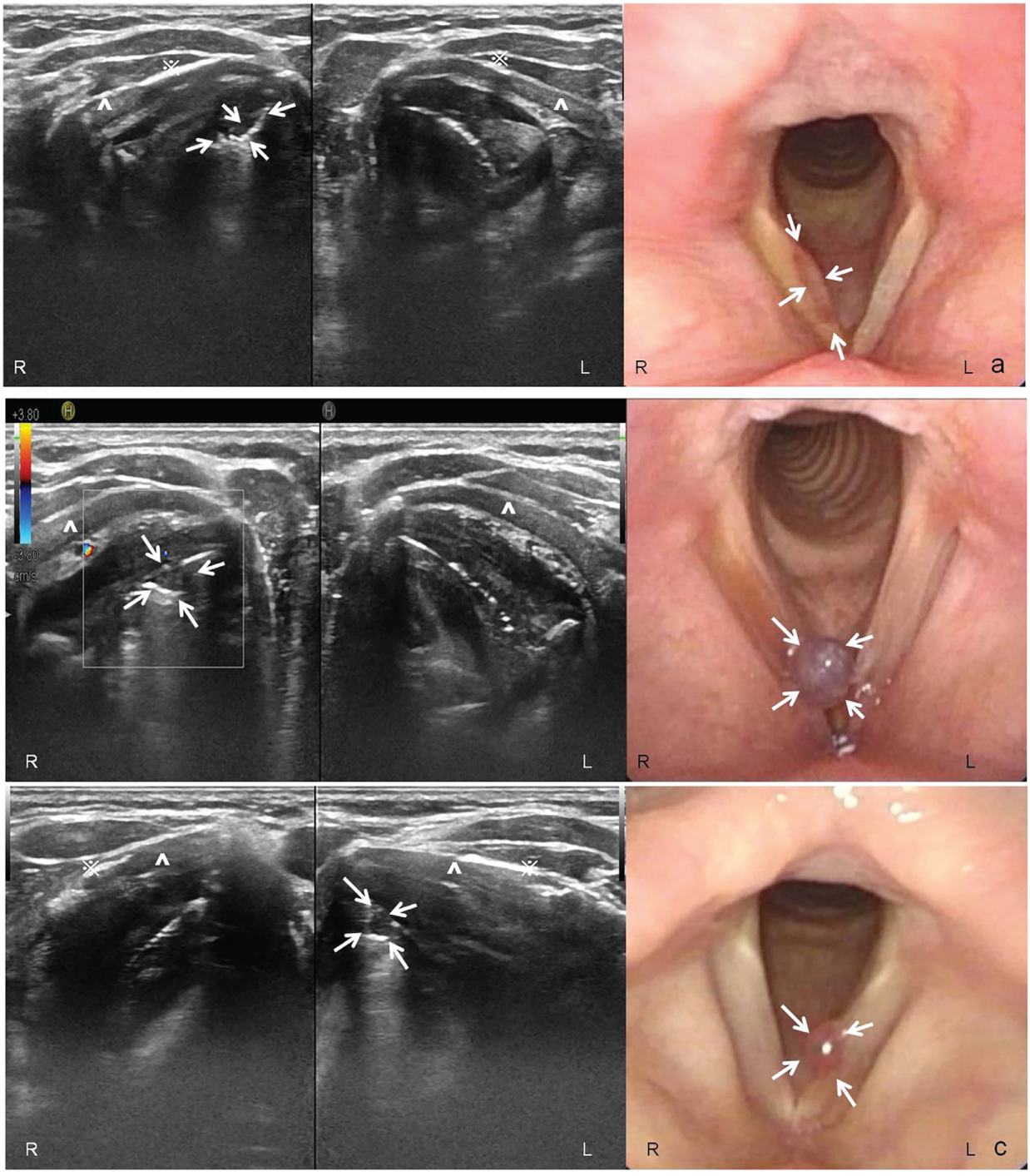

Fig. 5. Ultrasonic manifestations of vocal polyps. (a) Non-circular polyps in the middle third of the right vocal fold. (b) Circular polyps in the first third of the right vocal fold. (c) Circular polyps in the first third of the left vocal fold. ^Thyroid cartilage. ※Calcification. ↑Polyp of vocal fold.

In 87 patients, No,92 vocal fold polyps detected by laryngoscopy, 81 cases with unilateral polyps were modified as 82 cases with unilateral polyps. Eighty-one polyps were detected by ultrasound: 71 cases with unilateral polyps, 5 cases with bilateral polyps.

With respect to location of the 92 vocal fold polyps detected by laryngoscopy, 85 were located in the top third of the vocal folds, 6 were located in the middle third and 1 was located in the lower third. Of the 81 vocal fold polyps detected by ultrasound, 75 were

Table 1. Location characteristics of vocal fold polyps as assessed with laryngoscopy and ultrasound

	Top third	Middle third	Lower third	Total
Laryngoscopy	85	6	1	92
Ultrasound	75	5	1	81

located in the top third of the vocal folds, 5 in the middle third and 1 in the lower third (Table 1).

Of the 92 vocal fold polyps detected by laryngoscopy, 75 were circular and 17 were non-circular. Of the 81 vocal fold polyps detected by ultrasound, 69 were circular and 12 were non-circular.

The rate of detection of vocal fold polyps by transcutaneous laryngeal ultrasonography was 88.0%: 92.0% for circular polyps and 70.6% for non-circular polyps. Ultrasound was more likely to detect circular polyps; however, no significant difference was observed between circular and non-circular polyps (Table 2).

DISCUSSION

Vocal fold polyps are a benign proliferative disease of the superficial lamina propria of the vocal fold. They are the most common benign vocal fold lesions in clinical practice (Nunes et al. 2013; Ogawa and Inohara 2018). Laryngoscopy is currently the primary means of diagnosing the disease; however, in both adults and infants, flexible nasolaryngoscopy, with or without a strobe, can be uncomfortable, causing statistically significant changes in heart rate, blood pressure and oxygen saturation (Ongkasuwan et al. 2012, 2017a).

Numerous studies on adults have reported that compared with laryngoscopy, laryngeal ultrasound is inexpensive, tolerable and reliable in assessing the function of the true vocal folds (Wong et al. 2013; Carneiro-Pla et al. 2014). Laryngeal ultrasound has undergone development over the last 40 y, and several researchers have assessed its utility. Some studies (Klem 2012; Wang et al. 2012) have reported on the anatomic structures revealed by laryngeal ultrasound. Prasad et al. (2011) found that laryngeal ultrasound can clearly visualize the soft tissues around the upper airways of adults and therefore has many potential clinical applications. Although relevant scholars believe that laryngeal ultrasound has certain clinical applications, the application of laryngeal ultrasound in adults is not widespread. It is rarely used in the diagnosis of benign diseases of the vocal fold, such as polyps, mainly because the thyroid cartilage calcification obstructs the penetration of sound beams and gas artifacts in the larynx cause difficulty in the ultrasound display (Bozzato et al. 2007; Kandil et al. 2016). What effect does thyroid cartilage calcification have on visualization of the vocal fold? Can transcutaneous laryngeal ultrasonography visualize the vocal fold layers? What are the characteristics of ultrasound images of vocal fold polyps? Eighty-seven patients were enrolled in this study to answer these questions.

Thyroid cartilage calcification is related to age, sex and other factors. It is characterized by multifocal calcifications (Garvin 2008; Wenaas et al. 2016), and it is difficult to accurately evaluate the calcification range of thyroid cartilage by ultrasound. We found that thyroid cartilage calcification at the level of the glottis was the real influence on the vocal fold visualization. Therefore, we placed the ultrasound probe at the level of the glottis of the thyroid cartilage and asked the patient to hold his or her breath, causing closure of the vocal folds, and took this section as the measurement standard, calculating the percentage of the length of calcification to the length of the bilateral thyroid cartilage. Participants were divided into four groups based on this ratio to evaluate the effect of the percentage of glottic thyroid cartilage calcification on the vocal fold detection rate. The results indicated that a calcification length of the thyroid cartilage $<33\%$ did not affect the vocal fold detection rate, and the vocal fold structure could be fully observed. With a gradual increase in calcification length percentage, the rate of vocal fold display gradually decreased. At a calcification length percentage $>67\%$, the rate of detection of the vocal folds was significantly reduced. In addition, the incidence and length of thyroid cartilage calcification at the glottic level were higher in men than in women.

From shallow to deep, the layers of the vocal folds are the epithelium, lamina propria and muscle. The lamina propria can be divided into three parts: superficial layer, middle layer and deep layer. Polyps, nodules, Reinke's edema and pseudocysts all occur in the lamina

Table 2. Comparison of transcutaneous laryngeal ultrasonography and electronic laryngoscopy results

Polyps	Calcification of thyroid cartilage by ultrasound/laryngoscopy				Total rate of detection*
	None	<33%	34%–66%	>67%	
Circular	47/47 (100%)	10/10 (100%)	9/10 (90%)	3/8 (37.5%)	92.0%
Non-circular	8/12 (66.7%)	4/5 (80.0%)	0/0	0/0	70.6%

* Compared with electronic laryngoscopy, the rates of detection by ultrasound were 92.0% for circular polyps and 70.6% for non-circular polyps, $p = 0.5846$.

propria (Bohlender 2013). Identification of the lamina propria by ultrasound is helpful in the diagnosis of disease. We found that, in the middle section of the neck, we could only see the vocal folds, but we could not clearly distinguish the vocal fold layers. This problem can be solved by imaging the side section of the neck (Wang et al. 2019), where we can see the vocal folds from shallow to deep to hyper-echoic (epithelium), hypo-echoic (superficial layer of lamina propria,), hyper-echoic (middle and deep layers of the lamina propria) and hypo-echoic (muscular layer), which is consistent with the image of intralaryngeal ultrasonography (Tamura et al. 2001) .

In this group of 87 patients, 92 vocal fold polyps were detected by laryngoscopy, of which 75 were circular and 17 were non-circular, and 81 vocal fold polyps were detected by ultrasound, of which 69 were circular and 12 were non-circular. High-frequency ultrasound had a 92.0% rate of detection of circular polyps and 70.6% rate of detection of non-circular polyps. Ultrasound was more likely to detect circular polyps; however, no significant difference was observed between circular and non-circular polyps.

From a histologic point of view, vocal fold polyps are classified as telangiectatic or gelatinous polyps (Malik et al. 2019; Hassan 2020). It has been reported that (Carmel-Neiderman et al. 2018) vocal fold polyps may result from glottic damage, leading to the formation of hematomas in the Reinke layer, followed by local inflammation and eventually the formation of polyps. Vocal fold nodules, polyps and edema have been classified in one category of vocal fold masses, also known as exudation lesions of Reinke's space (Friedrich et al. 2007; Hantzakos et al. 2009). In this group of vocal fold polyps, regardless of the morphology, ultrasound revealed a clear boundary and regular shape. The capsule had a linear hyper-echoic area with an apparent free-edge linear hyper-echoic area. CDFI revealed that blood flow signals could not be detected in most vocal fold polyps. These ultrasonic image features are consistent with the pathologic basis of vocal fold polyps.

Looking forward, we seek to expand our sample size and analyze and summarize the performance of various imaging techniques for vocal fold polyps. We aim to find ways to improve the diagnostic accuracy of ultrasound for non-circular vocal fold polyps, develop ultrasound for the diagnosis of various benign and malignant lesions of vocal folds and provide supportive data for voice and other related research.

CONCLUSIONS

The thyroid cartilage side section clearly reveals the structure of the larynx, allowing identification of the morphology, location and size of vocal fold polyps. This is particularly beneficial for patients with thyroid cartilage without calcification and a calcification length percentage <33%. In this patient group, ultrasound can yield an accurate diagnosis, be non-invasive and safe and be an effective supplement to laryngoscopy for the initial screening of vocal fold polyps and post-operative review.

Conflict of interest disclosure—All the authors declare that they have no conflicts of interest.

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