The importance of sonographic landmarks by transcutaneous laryngeal ultrasonography in post-thyroidectomy vocal cord assessment

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ABSTRACT

Introduction:

During examination of the vocal cords (VC) using the transcutaneous laryngeal ultrasonography (TLUSG), 3 sonographic landmarks (namely, false VC (FC), true VC (TC) and arytenoids (AR)) are often seen. However, it remains unclear which landmark provide a more reliable assessment and whether seeing more landmarks improves the diagnostic accuracy and reliability.

Methods:

We prospectively evaluated 245 patients from two centers. One assessor from each center performed all TLUSG examinations and their findings were validated by direct laryngoscopy. All 3 sonographic landmarks were routinely visualized whenever possible. Rate of visualization and diagnostic accuracy between three landmarks were compared.

Results:

Eighteen patients suffered postoperative VC palsy (VCP). Both centers had comparable visualization or assessability rate of at least one sonographic landmark (94.9% and 95.3%, $p=1.000$) and 100% sensitivity on postoperative TLUSG. The rate of FC, TC and AR visualization were 92.7%, 36.7% and 89.8% respectively. The sensitivity, specificity and diagnostic accuracy and the proportion of true-positives, false-positives and true-negatives between using 1, 2 landmarks and 3 landmarks were comparable ($p>0.05$).

Conclusion:

Each sonographic landmark had similar reliability and diagnostic accuracy. Identifying all 3 sonographic landmarks was not mandatory and visualizing normal movement in one of the sonographic landmarks would be sufficient to exclude VCP.

INTRODUCTION

Laryngoscopic examination (LE) using a flexible naso-laryngoscope has remained the gold standard in assessing the function of the vocal cords (VC) and recurrent laryngeal nerve (RLN) before and after elective thyroidectomy. However, its routine application in the perioperative period remains controversial.(1-4) One argument against its routine use is that because of the low incidence of vocal cord palsy (VCP), it may cause unnecessary patient discomfort and increase medical cost.(5-7) Although tools such as voice questionnaires or CT scan may reduce the number of unnecessary examinations by selecting out higher risk patients for LE, their sensitivities only ranged from 25% to 74%.(8, 9) Transcutaneous laryngeal ultrasound (TLUSG) has been a good non-invasive selective tool for LE.(10, 11) Our recent study found the overall accuracy of diagnosing VCP using TLUSG in the preoperative and postoperative settings were up to 100.0% and 94.6%, respectively (12) and therefore TLUSG was recommended to be a screening tool for VCP in the preoperative and post-operative assessments.(10-12)

However, TLUSG remains a relative new and evoluting imaging technique in VC assessment. Its diagnostic accuracy and reliability rely on clear visualization of the real-time movements of several sonographic landmarks during examination. The 3 most commonly-described sonographic landmarks are the false cords (FC), true cords (TC) and arytenoids (AR).(13, 14) However, it remains unclear what their relative importance are in VC assessment. Furthermore, it is unknown whether identifying more landmarks during TLUSG would improve the diagnostic sensitivity, specificity and accuracy during VC assessment. We postulated that perhaps identifying all 3 landmarks on TLUSG would give a more accurate and reliable assessment than fewer landmarks. Since its implementation, we have been routinely visualizing the movements of all 3 sonographic landmarks whenever possible, although the supporting evidence for this practice remains scarce. Our study aimed to prospectively evaluate the relative importance of the 3 landmarks in postoperative VC assessment and also to compare visualization rate and diagnostic accuracy between examinations with all three landmarks visualized and those with fewer than three landmarks visualized.

PATIENTS AND METHODS:

Patients

In order to increase the power of the study, after ethics approval, two institutions participated in the patient recruitment. This was a joint international effort between two institutions, namely the University of Hong Kong (center 1) and Seoul National University (center 2). From June to October 2013, all consecutive patients who underwent elective thyroidectomy with or without concomitant neck procedure at either center were recruited for the study. After obtaining consent, all patients underwent a TLUSG followed immediately by a confirmatory direct laryngoscopy (DL) in the same setting one day before and 7 – 10 days after thyroidectomy. Patients with pre-operative VCP were excluded from final analysis.

Standardization before the start of the study

To minimize inter-observer variability, a half-day workshop was organized shortly before the start of the study between the two centers. This basically involved having one of the co-authors (WJW) from center 2 spending a half day learning the technique of TLUSG from center 1. WJW had no prior experience in either USG or TLUSG. At the workshop, steps in performing a proper TLUSG and identification of the FC, TC and AR of the larynx on TLUSG were taught (Figure 1 and 2). WJW was given the opportunity to perform TLUSG on 7 preoperative and 10 postoperative patients. The first 5 examinations were done initially under the supervision of an experienced assessor (KPW) with the rest done independently by WJW. The latter was later cross-checked by KPW. All 3 sonographic landmarks were carefully sought before it was deemed a complete and satisfactory TLUSG examination. At the end of the workshop, both assessors designed a standardized proforma for data collection of this study.

Perioperative TLUSG and DL examinations during study period

During the study period, one assessor from each center was responsible for performing all TLUSG examinations in that center. Similar to the workshop, all 3 sonographic landmarks were carefully sought before it was deemed a complete TLUSG examination. For center 1, KPW carried out all the examinations using portable ultrasound machine (iLook 25 Ultrasound system, Sonosite, Sonosite Inc., Bothell, WA) and a 5- to 10- MHz linear transducer. While for center 2, WJW carried out all the examinations using Philips HD6 Ultrasound system, Philips, Royal Philips, Amsterdam, The Netherlands and 3- to 12- MHz linear transducer at around 9 MHz. To reduce possible assessment biases, both assessors were unaware of the patient's voice status before examination and their findings were validated by a DL immediately afterwards. The details of this set-up had been described previously.(12)

TLUSG technique

Patient was positioned flat with the neck slightly extended and arms on the side during TLUSG. After applying ample amount of gel, an USG transducer was placed transversely over the middle portion of the thyroid cartilage and scanned caudo-cranially until both VCs were visualized. Each assessor was required to carefully identify all three ultrasonic landmarks, FC, TC and AR whenever possible. These findings were prospectively recorded in a previously-agreed proforma. Figure 1 showed a sonographic view of normal symmetrical VC. Figure 2 showed a endoscopic view of normal symmtrical VC. On TLUSG, FCs appeared hyperechoic and TCs were seen as hypoechoic structure with hyperechoic cover (vocal ligament). Arytenoid cartilages were seen as a paired oval hyperechoic strucure underneath the true and false cord.(13, 14) Both passive (i.e. quiet spontaneous breathing) and active (phonation with a sustained vowel "aa") movement of the VCs were assessed. After TLUSG, DL was performed by an separated endoscopist who was also unaware of the patient's voice quality and the TLUSG findings. Visualization and assessment on movement of each sonographic landmark was documented.

Definitions

The TLUSG examination was defined as "assessable" if ≥1 sonographic landmarks were clearly visualized while it was defined as "unassessable" if none of the landmarks were clearly visualized. If there was decreased or no movement in any of the 3 landmarks on passive or active movements during TLUSG, it was defined as VCP. If there was discrepancy between two landmarks on

TLUSG (i.e. one landmark had normal movement while the other had reduced or no movement), it was defined as a VCP. The reason for this definition was because TLUSG had been advocated as a screening or selecting tool for DL rather than a substitute of laryngoscopy.(10,12) Similarly to TLUSG, if there was reduced or no VC movement on DL, it was a VCP. All TLUSG findings were correlated with the DL findings afterwards. If both the DL and TLUSG showed VCP, this was defined as a “true positive” (TP) result whereas if both the TLUSG and DL showed normal VC movements, this was defined as a “true negative” (TN) result. However, if TLUSG showed VCP while DL showed normal VC movement, this was defined as a “false positive” (FP) result. Alternatively, if TLUSG showed normal VC movements while DL showed VCP, this was defined as a “false negative” (FN) result.

Statistics

The statistical analysis was performed using the SPSS (version 18.0, SPSS, Inc., Chicago, IL, USA) software package. For demographic, Chi-square test and the Fisher’s exact test were used for comparison of dichotomous variables and the Mann-Whitney U test was used for comparison of continuous variables between center 1 and center 2. Pair-T test was used for comparison of assessability between sonographic landmarks.. P values <0.05 was considered statistically significant.

RESULTS

Table 1 compares the baseline characteristics between the two centers. Age at operation in center 1 was significantly older than center 2 (53 vs. 48, *p*=0.008) while sex ratio and body mass index were similar. Since suspicious of malignancy / malignancy was the more common surgical indication in center 2 (*p*<0.001), total thyroidectomy was significantly more likely performed in center 2 (49.2% vs. 79.5%, *p*=0.001). In terms of surgical approach, extra-cervical approach was significantly more likely to be performed in center 2 (1.7% vs. 16.5%, *p*=0.001). Based on total number of nerves-at-risk, the rate of postoperative VCP was similar between center 1 and 2 (4.8% vs. 3.9%, p=0.658). There were no recurrent laryngeal nerves being accidentally cut or intentionally sacrificed at the time of operation.

Table 2 shows the correlation between postoperative TLUSG and DL findings stratified by center. Six patients from each center had unassessable VC. Both center 1 and 2 had markedly similar assessability rate (i.e. visualizing at least one sonographic landmarks on TLUSG) (94.9% and 95.3% respectively (*p*=1.000)). Sensitivity of TLUSG was both 100% in both centers in VC assessable patients. While two centers had comparable proportions of TP (7.1% vs 7.4%, *p*=1.00), FP (9.8% vs 6.6%, *p*=0.474), TN (83.0% vs 86.0%, *p*=0.589) and FN (0% vs 0%).

Table 3 shows a comparison of visualization rates and diagnostic accuracies between using one, two and three sonographic landmarks in determining postoperative vocal cord function. All were validated by DL examination afterwards. In view of the similar results between the two centers, data from both centers were pooled together for this analysis. The rate of visualization for FC alone, TC alone and AR alone were 92.7%, 36.7% and 89.8%, respectively. However, both FC and AR had significantly higher visualization rates than TC (*p*<0.05). Using 2 ultrasonic landmarks to determine vocal cord function, the visualization rate for FC & AR together (87.3%) was significantly higher than FC & TC (36.3%) and TC & AR (36.7%) (*p*<0.05). This was because the visualization rate of TC was the lowest (36.7%) among the three landmarks during postoperative TLUSG examinations. Similarly, only 36.3% of patients can visualize all 3 sonographic landmarks.

Since there were no FNs in our cohort, the test sensitivity was 0.0% regardless of the number of landmarks used for determining VC function. Concerning the specificity, there were no difference between one or two sonographic landmarks to determine vocal cord function (p>0.05).

Table 4 shows a comparison of TPs, FPs, TNs and FNs between visualizing only 1, 2 and all 3 sonographic landmarks in determining postoperative vocal cord function. Most patients (92.3%) had two or three landmarks identified on postoperative TLUSG. No differences were found across the three groups. There were two correctly identified VCP which were identified with one single landmark and that single landmark was FC. Although not statistically significant, FC seemed to be the landmark most readily identified (92.7% vs 89.8%, p> 0.05) with comparable accuracy.

DISCUSSION

This was the first bi-institutional study that addressed two seemingly unrelated issues in VC assessment by TLUSG. The first issue was whether the TLUSG technique could be easily learned and reproduced by an individual with no prior experience in USG or TLUSG. The other issue was to assess the relative importance of the 3 sonographic landmarks in VC assessment by TLUSG. We hypothesized that perhaps identifying all 3 sonographic landmarks would improve the diagnostic accuracy and reliability of TLUSG when compared to identifying fewer than 3 landmarks.

Regarding to the first issue, although our study was not specifically designed to assess the learning curve of this technique, our data demonstrated that with appropriate supervised training, this technique was easily acquired and learned by an individual without prior experience in USG. Our data showed that center 2 had very comparable results in terms of assessability / visualization rate of VC landmarks and diagnostic accuracy to center 1. This was despite the fact that there were significant differences in patient baseline characteristics such as patient age, surgical indication, extent of thyroidectomy and surgical approach between the two centers. Both centers achieved an assessability rate of more than 94% which appeared higher than other series.(10, 11, 15, 16) Furthermore, neither center had a FN (i.e. a missed postoperative VCP) on TLUSG. This finding concurred to our previous study that found TLUSG to be an excellent a screening tool for DL in the postoperative setting.(12) Based on these results, hypothetically, if both centers were to proceed post-operative DL only for those with unassessable VC or suspected VCP on TLUSG and to withhold DL for those with normal assessable VC movements on TLUSG, TLUSG would have missed no VCP (i.e. no FN) while reduced the total number of DL in center 1 and 2 by 93 (78.8%) and 104 (81.9%), respectively. These results were also consistent with previous studies. (11, 12)

Regarding to the relative importance of sonographic landmarks during TLUSG, when only one landmark was evaluated, each of the three landmarks was equally important. This was supported by the fact that each landmark had similar diagnostic sensitivity, specificity and accuracy in VC assessment when used alone. However, since TC was the least frequently visualized sonographic landmark during TLUSG, either FC or AR might be clinically more useful and relevant landmarks. In fact, either FC or AR as a stand-alone landmark were almost 3 times more likely to be identified or visualized on TLUSG than TC alone on passive or active movements.

Regarding to the issue of the number of landmarks seen on TLUSG, our data showed that the number of landmarks visualized in VC assessment did not necessarily improve the diagnostic sensitivity, specificity and accuracy of TLUSG. In contrast to our initial hypothesis, visualizing all 3 landmarks on TLUSG did not necessarily make the TLUSG examination more accurate or more reliable than seeing visualizing less. The proportion of TPs, FPs and TNs were not significantly different in the group when all 3 sonographic landmarks were identified and used for VC assessment ($p>0.05$). In fact, although not statistically significant, the proportion of FPs tended to be lower when only one landmark was visualized than when two or three landmarks were visualized (0.0% vs. 7.9% and 10.1%). This implied that liberally visualizing more than one landmark on postoperative TLUSG may increase FPs leading to unnecessary DL.

Clinical implications

The first implication is the technique of using TLUSG in VC assessment is relatively easy to learn and reproduce. With a short-course of appropriate training and supervision, an individual with no prior experience in USG or TLUSG could essentially repeat similar results as an experienced assessor. The second implication is that since only a third of post-thyroidectomy patients would have all 3 sonographic landmarks identified during TLUSG, we would recommend that identifying only one landmark would suffice for future TLUSG examinations. Our data showed that identifying all 3 landmarks did not necessarily improve the diagnostic sensitivity, specificity and accuracy than identifying less number of landmarks.

Despite our data, there were several shortcomings with our study. Similar to our previous study, incidence of preoperative and postoperative VCP was low; sensitivity of TLUSG studied was still considered underpowered. In view of low rate of post thyroidectomy RLN palsy (about 5%), a larger patient sample is necessary to achieve sufficient statistical power. Though both centers can achieve a high satisfactory result after a half-day workshop, the number of patient required to achieve the learning curve has yet to be defined. Last but not least, this cohort recruited normal body build Asian patient with median BMI of 23.1. It remains uncertain to what extent our results could be reproduced in patients with a different body build or ethnicity. Perhaps, future international multi-center studies are required to address some of these unresolved issues.

CONCLUSION

TLUSG is a reproducible, non-invasive tool with high assessability (>90%) on evaluating VCP before and after thyroidectomy. Regardless of which of the 3 landmarks, assessment on passive or active VC movement, it appeared to have similar diagnostic accuracy. Finding all 3 landmarks did not necessarily improve the diagnostic accuracy. Assessing the movement of either FC or AR on TLUSG was clinically most relevant in VC assessment.

Table 1. A comparison of patient baseline characteristics between the two centers

	Center 1 (n=118)	**Center 2 (n=127)**	***p*-value**	**Overall (n=245)**
Median age at operation (years)	53 (24-84)	48 (20-82)	**0.008**	50.5 (20-84)
Sex				
- Male	23 (19.5%)	23 (18.1%)	0.782	46 (18.8%)
- Female	95 (80.5%)	104 (81.9%)		199 (81.2%)
Body mass index (kg/m2)	22.9 (17.0-30.6)	23.3 (17.2-34.0)	0.191	23.1 (17.0-34.0)
Surgical indication for thyroidectomy				
- Benign nodular goiter	60 (50.8%)	7 (5.5%)	**<0.001**	67 (27.3%)
- Thyrotoxicosis	17 (14.4%)	1 (0.8%)		18 (7.3%)
- Suspicious of malignancy/malignancy	41 (34.8%)	119 (93.7%)		160 (65.3%)
Type of operation				
- Hemithyroidectomy	44 (37.3%)	20 (15.8%)	**<0.001**	64 (26.1%)
- Total thyroidectomy	58 (49.2%)	101 (79.5%)		159 (64.9%)
- Reoperative hemithyroidectomy	6 (5.1%)	6 (4.7%)		12 (4.9%)
- Reoperative total thyroidectomy	4 (3.4%)	0 (0.0%)		4 (1.6%)
- Total thyroidectomy with neck dissection	2 (2.7%)	0 (0.0%)		2 (0.8%)
- Total thyroidectomy with total parathyroidectomy	3 (2.5%)	0 (0.0%)		3 (1.2%)
- Total thyroidectomy with Sistrunk's procedure	1 (0.8%)	0 (0.0%)		1 (0.4%)

Surgical approach - Cervical - Extra-cervical	 116 (98.3%) 2 (1.7%)	 106 (83.5%) 21 (16.5%)	 **0.001**	 222 (90.6%) 23 (9.4%)
Total number of recurrent laryngeal nerve-at-risk	186	228		414
Postoperative vocal cord palsy*	9 (4.8%)	9 (3.9%)	0.658	18 (4.3%)

* Data was present as number of nerve at risk & patient with pre-operative vocal cord palsy was excluded.

Table 2. Correlation between transcutaneous laryngeal ultrasonographic (TLUSG) and postoperative direct laryngoscopic (DL) findings in center 1 and 2

			DL findings		Total
			Normal mobile cords	VCP	
Center 1	**TLUSG findings**	Normal mobile cords	93 (TN)	0 (FN)	93
		VCP	11 (FP)	8 (TP)	19
		Not assessable	5	1	6
	Total		109	9	118
			DL findings		Total
			Normal mobile cords	VCP	
Center 2	**TLUSG findings**	Normal mobile cords	104 (TN)	0 (FN)	104
		VCP	8 (FP)	9 (TP)	17
		Not assessable	6	0	6
	Total		118	9	127

Abbreviations: VCP = vocal cord palsy; TP = true positive; TN = true negative; FP = false positive; FN = false negative

* No patient suffered bilateral vocal cord palsy after thyroidectomy

Table 3. A comparison of visualization rates and diagnostic accuracies between using one, two and three sonographic landmarks in determining postoperative vocal cord function. All were validated by direct laryngoscopic examination afterwards.

	Visualization rate	**Sensitivity**	**Specificity**	**Accuracy**
Using one sonographic landmark to determine vocal cord function				
FC alone	92.7% (227/245)	100%	91.9%	92.5%
TC alone	36.7% (90/245)*	100%	89.3%	90.0%
AR alone	89.8% (220/245)	100%	92.7%	93.2%
Using two sonographic landmarks to determine vocal cord function				
FC & TC	36.3% (89/245)	100%	89.2%	89.9%
FC & AR	87.3% (214/245)#	100%	90.5%	91.1%
TC & AR	36.7% (90/245)	100%	89.3%	90.0%
Using all three sonographic landmarks to determine vocal cord function				
FC, TC & AR	36.3% (89/245)	100%	89.2%	89.9%

Abbreviations: FC = false cords; TC = true cords; AR = arytenoids

*$p<0.05$ - between FC alone and TC alone, and also between TC alone and AR alone

#$p< 0.05$ - between FC & TC and FC & AR, and also between FC & AR and TC & AR

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Table 4. A comparison of true positives, false positives, true negatives and false negatives between visualizing 1, 2 and all 3 sonographic landmarks in determining postoperative vocal cord function.

	Visualizing one sonographic landmark (n=18)	**Visualizing two sonographic landmarks (n=126)**	**Visualizing all 3 sonographic landmarks (n=89)**	**p-value**
True positive (n=18)	2 (11.1%)	9 (7.2%)	6 (7.1%)	0.806
False positive (n=19)	0 (0.0%)	10 (7.9%)	9 (10.1%)	0.357
True negative (n=197)	16 (88.9%)	107 (84.9%)	74 (83.1%)	0.816
False negative (n=0)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-

Abbreviations: FC = false cords; TC = true cords; AR =arytenoids; TLUSG = transcutaneous laryngeal ultrasound.

Legends

Figure 1. A sonographic view of normal symmetrical vocal cords. Abbreviations: FC - false cord, TC - true cord, AR - arytenoid

Figure 2. A endoscopic view of normal symmetrical vocal cords. Abbreviations: FC - false cord, TC - true cord, AR - arytenoid

Figure 1. A sonographic view of normal symmetrical vocal cords. Abbreviations: FC - false cord, TC - true cord, AR - arytenoid

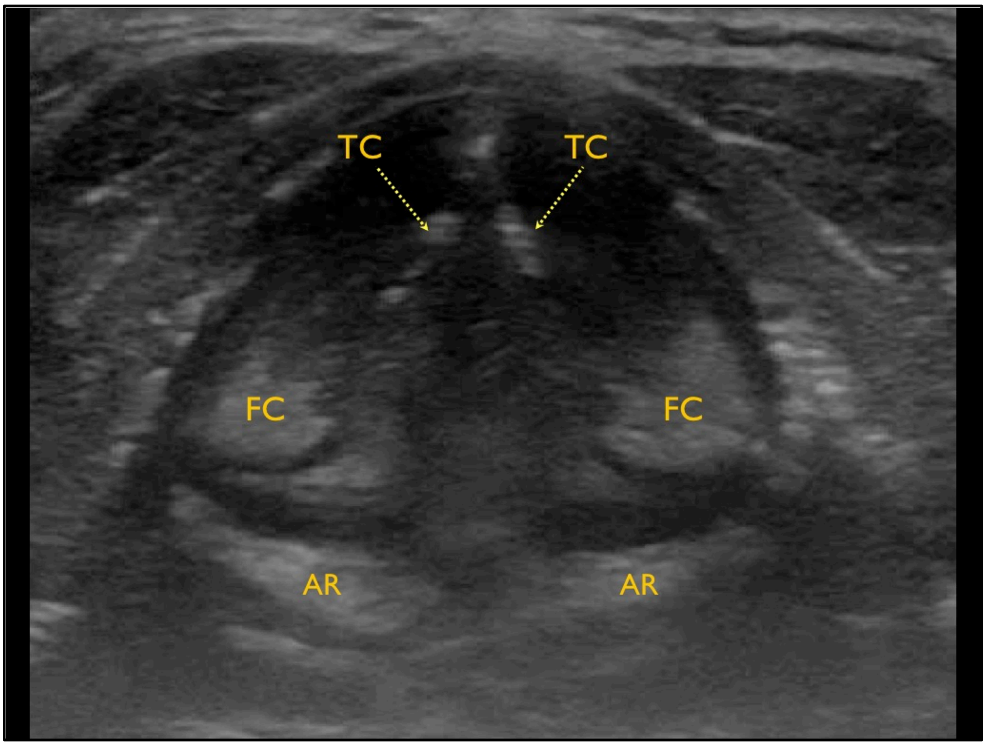
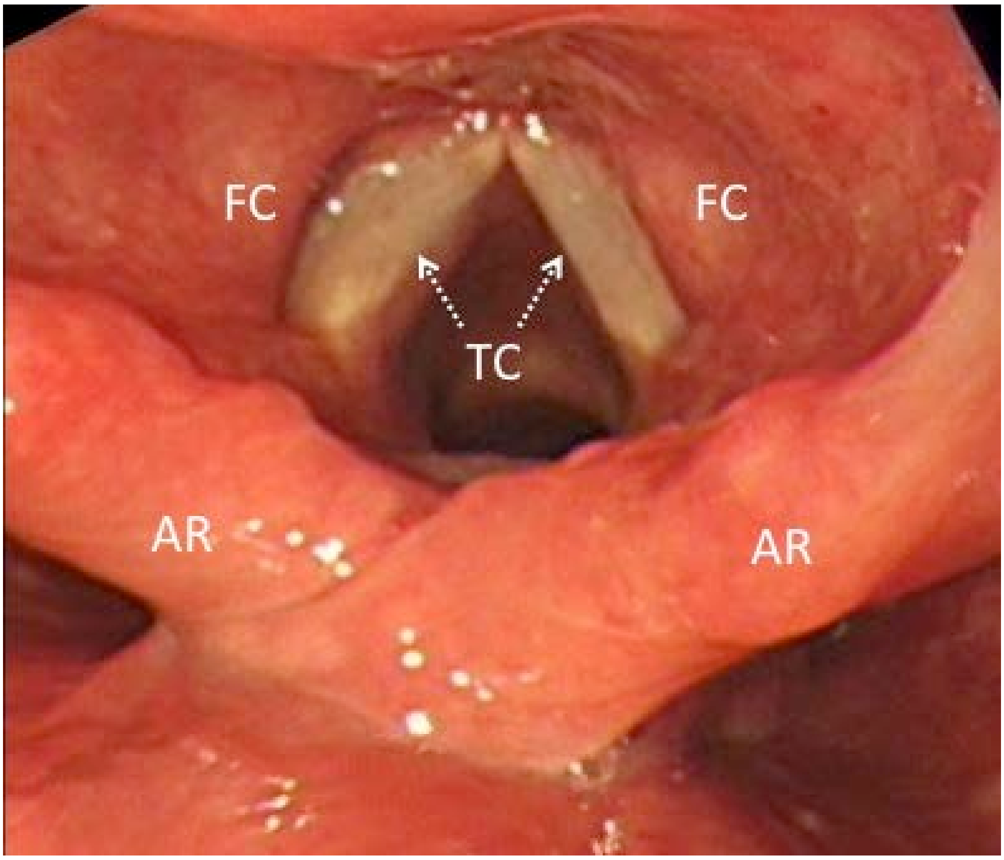


Figure 2. A endoscopic view of normal symmetrical vocal cords. Abbreviation: FC - false cord, TC - true cord, AR - arytenoid



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