USEFULNESS OF TRANSCUTANEOUS ULTRASOUNOGRAPY VERSUS COMPUTED TOMOGRAPHY IN THE ASSESSMENT OF CANCER LARYNX

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ABSTRACT:

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Received: 12/5/2019 Accepted: 9/6/2019 Background: The use of ultrasonography as a complementary diagnostic tool to CT in the assessment of cancer larynx has always been underestimated due to the anatomical obstacles in the form of thyroid cartilage calcification yet specific anatomic sites with proper technique implementation raised the sensitivity and specificity of the sonographic results and presented it as a trustable screening tool taking advantage of its additional dynamic criteria.

Aim of work: To evaluate the usefulness of ultrasonography versus Computed Tomography in assessing cancer larynx.

Patients and Methods: 46 patients with histopathologically proven laryngeal carcinoma were enrolled after exclusion of 5 patients from surgery. A comparative assessment was made between the detection rate of localization and sensitivity, specificity, PPV, NPV and accuracy of pre-therapeutic ultrasonography compared to CT with post operative pathology as a standard reference.

Results: Most of the patents were males [47(92.2%)/51] and aged > 60 years [25(49%)/51]. The detection rate was highest in glottic lesions being the same in both ultrasonography and CT [32 (96.9%)/33] with a sensitivity and specificity of 90.9% and 84.6% versus 93.9% and 92.3% in each modality respectively. (p=0.000). The specificity, sensitivity, PPV, NPV and accuracy results of invasion of the intra-laryngeal structures were comparable for both modalities: U/S and CT in detection of thyroid cartilage invasion being 88.8%, 89.3%, 84.2%, 92.5% and 89.1% for U/S versus 88.8%, 96.4%, 94.1%, 93.1 and 93.4% for CT, paraglottic fat infiltration being 90.3%, 86.7%, 93.3%, 81.2% and 89.1% for U/S versus 93.5%, 93.3%, 96.7%, 87.5% and 94.4% for CT and anterior commissure infiltration being 88.5%, 90%, 92%, 85.7% and 89.1% for U/S versus 96.2%, 100%, 100%, 95.2% and 97.8% for CT.

Conclusion: Ultrasonography could be used as a valuable supplementary imaging method to CT and laryngoscopy in the assessment of laryngeal carcinoma, even in male adults with some calcifications of the thyroid cartilage.

Keywords: Cancer larynx, Glottic lesions, paraglottic fat infiltration, anterior commissure infiltration, thyroid cartilage infiltration, transglottic infiltration.

INTRODUCTION:

Laryngeal cancer accounts for approximately one quarter of the head and

neck malignancies worldwide, and the overall survival, disease free survival and laryngeal reservation are largely determined by the initial tumor stage at the time of the diagnosis¹.

A vast majority of these cancers are squamous cell carcinoma (SCC). Tobacco smoking and alcohol consumption are important risk factors for laryngeal SCC, those patients have a higher risk for synchronous malignancies arising from the lung and aerodigestive tract².

Early identification of malignant laryngeal neoplasms results in improved prognosis and functional outcomes. Imaging plays an integral role in the diagnosis, staging and long term follow up of cancer larynx³.

Cross sectional imaging with contrast enhanced CT allows excellent depiction of the detailed anatomy of the larynx and the characteristic pattern of submucosal tumor extension. It also provides vital information about the status of cervical nodal disease, systemic metastasis and any synchronous malignancies as well as post therapeutic recurrence tumor in these patients. Additionally, certain image based narameters like tumor volume and cartilaginous abnormalities have been used of predict the success primary radiotherapy or surgery in these patients².

High frequency ultrasonography is routinely used as an imaging method to evaluate the involvement of cervical lymph nodes, soft tissues and thyroid gland in patients with laryngeal carcinoma, but rarely to evaluate the tumor itself and its invasion of the intralaryngeal structures, mainly because of the calcified thyroid cartilage in adults and the interference of air within the laryngeal cavity. Nevertheless, attempts have been made to use ultrasonography in this area to take advantage of its non invasive and real time imaging features¹.

Our study aims at demonstrating that ultrasonography, which has been used scarcely in the larynx, could supply useful information the detection, localisation, intra and extralaryngeal invasion of laryngeal carcinoma³.

Generally tumours are hypoechoic sonographically and can easily be differentiated from the surrounding tissue especially in the hyperechoic supraglottic structures. Thyroid cartilage infiltration can be easily detected by the interruption of the hyperechoic inner perichondrium⁴.

Assessment of the para glottic space involvement and vocal cord fixation can be fairly detected by ultrasonography³.

Whether ultrasonography has similar ability to evaluate laryngeal carcinoma is worth studying as a supplementary imaging method to laryngoscope or CT^I .

AIM OF THE WORK:

To evaluate the usefulness of ultrasonography versus Computed Tomo-graphy in assessing cancer larynx.

PATIENTS AND METHODS:

A comparative study of two diagnostic tests: CT and ultrasonography, was done by clinical trial selecting 51 patients with pathologically proven cancer larynx from Ain Shams University Hospitals 47 are males and 4 females aged between 30 and 67 years along a period of about 2 years for data collection starting in August 2017 using convenient sampling method.

The pre-therapeutic U/S and CT were retrospectively evaluated including the tumor detection, localization and invasion of intra and extralaryngeal structures. All cases underwent direct laryngoscope and biopsy taking about 10 days prior to ultrasonographic assessment and CT of the neck was performed at the time period between laryngoscope and ultrasonography.

Laryngectomy was performed eventually to 46 patients and histopathological results were documented.

The study population was selected according to the selected criteria as follow:

Inclusion Criteria:

- Patients histopathologically proven, newly diagnosed cancer larynx by direct laryngoscopy (10 days after the performance of the direct laryngoscopy), non operated and didn't receive any type of treatment except methods of securing the airway if needed as tracheostomy tube.
- No age predilection.
- Both sexes are included.

Exclusion criteria:

- Patients diagnosed to have cancer larynx and received any type of medical or surgical treatment whether curative or palliative
- Patients with contraindication for CT exposure, e.g. Pregnant females.
- Patients with contraindications to intravenous contrast administration, e.g. Patients allergic to the intravenous contrast administration, patients with toxic goiter, patients planned for radioiodine treatment of thyroid cancer.
- Patients refusing the intravenous contrast administration.
- Patients with respiratory of hemodynamic instability and inconvenience for the scan.

Patient's preparations:

Patients were subjected to:

- 1. Full history taking including drug history of allergic reaction to IV contrast.
- 2. Detailed explanation of the imaging procedure.
- 3. Consent taking for undergoing the study including contrast administration.
- 4. Recent serum creatinine level (within one week duration).

- 5. 4-6 hours fasting state.
- 6. Administration of 1 ante-cubital intravenous catheter
- 7. CT scan with IV contrast of the neck.
- 8. Transcutaneous ultrasonography of the larynx whether in the same setting or during a different hospital visit about 10 days after the laryngoscopic biopsy taking.
- 9. No interventional procedures were done.

Study tools used along the research course were high-lightened as follow:

The ultrasound machines (Linear probe 7 MHz, Samsung ACCUVIX XG 275-K-B003A).

Acoustic windows that were suitable for the penetration of ultrasound beams were located at the thyrohyoid membrane, cricothyroid membrane and thyroid cartilage lamina, where the structure had less calcification. During scanning, the patient was instructed to hold and relax their breath or talk softly to evaluate the mobility of vocal cords and arytenoid cartilages. These maneuvers were also used to observe the relative movement of the paraglottic fat to the adjacent internal perichondrium of the thyroid cartilage.

Each study took about 3-4 minutes for laryngeal U/S.

The CT study was performed on CT machine (GE Bright Speed, 1023 CT 04), an 8 slices machine x 5 mm detector collimator with a field of view of 16 cm and slice thickness of 5 mm using 120 kV, 220 mAs, 1.5 seconds rotation time, 1 mm interspace were obtained parallel to the plane of the true vocal cords from the skull base to the sternum and examination time of about 1 minute for CT of the neck with IV contrast injection bolus injection of 60–85 ml of ultravist (300 mgI ml⁻¹) by injector or by manual injection at a flow rate of 3 ml

s⁻¹ with a 50 seconds delay, a dose of 1-2 ml/10 kg patient body weight with maximum dose 100 ml. During scanning, patients were instructed to breathe quietly and to avoid swallowing or moving.

Images were reconstructed to axial, coronal and sagittal sections, with both the slice thickness and interspace being 5 mm.

The patient is positioned supine on both CT and U/S with the neck extended slightly, each patient was scanned from the hyoid bone down to the inferior border of the cricoid cartilage in transverse, longitudinal and oblique planes.

The staging of laryngeal cancer was evaluated according to the guidelines of the American Joint Committee of Cancer (AJCC).

Imaging analysis:

Radiographic points assessed by U/S and CT:

- 1. Infiltration of the paraglottic space.
- 2. Subglottic infiltration.
- 3. Pre-glottic infiltration (anterior commissure).
- 4. Invasion of laryngeal cartilage.
- 5. Extra-laryngeal infiltration (tracheal rings and esophagus).
- 6. Ipsilateral lymph node affection (and size)
- 7. Contralateral lymph node affection (and size).

Additional radiographic points assessed by U/S only included:

1. Vocal cord mobility with phonation.

2. Vascularity (on Doppler imaging).

Thyroid cartilage, pre-epiglottic space, paraglottic space, thyroid and cervical soft tissues, lying in the larynx anteriorly or superficially, are easy to be imaged with a high-frequency probe. Commonly, these structures are isoechoic or hyperechoic, which provide a contrast with a hypoechoic invading tumour(*Loveday et al, 1994*)⁵.

Moreover, the paraglottic space normally manifests as a thin layer of fatty tissue that has some mobility during respiration in contrast to the immobility of adjacent inner perichondrium of thyroid cartilage (*Chevallieret al*,2002 ⁶.

When the relative movement decreased or ceased or the fat is obliterated, it was helpful to diagnose the neoplastic spread to the paraglottic space.

We evaluated the mobility of the larynx by having the patients talk softly or relax after breath-holding. Asymmetrical movement or impaired mobility of the vocal cords and on real-time ultrasonography images was almost always associated with thyroid cartilage invasion with or without recurrent laryngeal nerve invasion upgrading the tumor to stage T4 (*Loveday et al, 1994*)⁵.

reference standard:

 The results of histopathological examination of the excised laryngeal tissue and draining lymph nodes were compared to the results obtained by CT and U/S examination performed prior to surgery and were used as a reference standard

RESULTS:

Most of the randomly sampled patients

were males representing 92.2 % (47/51) compared to 7.8 % (4/51) female patients.

		No.	%
Age	30-40 years	2	3.9%
	40-50 years	7	13.7%
	50-60 years	17	33.3%
	>60 years	25	49.0%
Gender	Females	4	7.8%
	Males	47	92.2%

The patients had mostly multiple presenting symptoms yet the main complaint was hoarsness of voice seen in 84.3% (43/51), less frequent complaints either solely or combined were persistent dry cough in 45 % (23/51), dyspnea in 19.6 %

(10/51), otalgia in 13.7 % (7/51), dysphagia in 11.7 % (6/51), life threatening stridor necessitating urgent tracheostomy insertion and ICU admission in 9.8 % (5/51), weight loss in 7.8 % (4/51), halitosis 5.9 % (3/51) and hemoptysis in 3.9 % (2/51).

Presenting complaint	No.	%	
Hoarseness of voice	No	8	15.7%
	Yes	43	84.3%
Dysphagia	No	45	88.2%
	Yes	6	11.8%
Weight loss	No	47	92.2%
	Yes	4	7.8%
Dyspnea	No	41	80.4%
	Yes	10	19.6%
Otalgia	No	45	88.2%
	Yes	6	11.8%
Halitosis	No	48	94.1%
	Yes	3	5.9%
Stridor	No	46	90.2%
	Yes	5	9.8%
Persistent dry cough	No	28	54.9%
	Yes	23	45.1%
Hemoptysis	No	49	96.1%
	Yes	2	3.9%

On clinical examination, signs of locally advanced condition whether single or combined were detected in 23.5% (12/51) patients mainly in the form of cervical palpable lesions in 23.5 % (12/51),

diminished breath sounds due to airway compromise and/or precipitated pneumonia in 21.5 % (11/51) and loss of laryngeal crepitus in 15.6 % (8/51).

Signs of advanced condition	No.	%				
Loss of laryngeal crepitus	of laryngeal crepitus No					
	Yes	8	15.7%			
Diminished breath sound	No	40	78.4%			
	Yes	11	21.6%			
Parotid, thyroid and cervical palpable lesions	No	39	76.5%			
	Yes	12	23.5%			

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Multiple risk factors were identified such as heavy smoking (20 cigarettes/day or more) in 94.1 % (48/51), water pipe in 78.4 % (40/51) and hashish in 41.2 % (21/51) yet combined cigarettes with water pipe in 72.5 % (37/51) and cigarettes with hashish in 35.3 % (18/51) of the patients.

Prolonged smoke inhalation either residential or occupational was seen separate in 68.6 % (35/51) and 35.3 % (18/51) patients respectively and combined in 15.7 % (8/51) patients.

Alcohol consumption (> 8 units (45 ml)/week) was seen in 15.7 % (8/51) patients all combined with only cigarettes or cigarettes with water pipe and/or hashish smoking.

GERD is seen in most of the patients 78.4 % (40/51) being presented as sequel of

the other risk factors as smoking rather than weak additional risk factor to worrisome chronic laryngeal irritation.

Unbalanced diet in the form of deficient fibrous diet (vegetables and fruits) was seen in 70.6 % (36/51) regarded as a common.

Most of the patients were presented with immune compromised state due to one or combined pathological conditions such as HCV infection which was detected in 47 % (24/51) while 13.7 % (7/51) were on regular steroid inhaler for associated asthma and 86.3 % (44/51) had other co-morbidities such as diabetes and/or cardiac condition one of which necessitating regular treatment for more than 5 years.

Positive family history of malignancies was revealed in 29.4 % (15/51)

Risk factors	No.	%	
Cigarettes (>20/day for > 1 year)	No	3	5.9%
	Yes	48	94.1%
Water pipe	No	11	21.6%
	Yes	40	78.4%
Hashish	No	30	58.8%
	Yes	21	41.2%
Alcohol intake	No	43	84.3%
	Yes	8	15.7%
Balanced diet	No	36	70.6%
	Yes	15	29.4%
HCV +ve	No	27	52.9%
	Yes	24	47.1%
Steroid ttt	No	44	86.3%
	Yes	7	13.7%
Other immune compromising co-morbidities	No	7	13.7%
	Yes	44	86.3%
Occupational exposure	No	34	66.7%
•	Yes	17	33.3%
Residential exposure	No	16	31.4%
-	Yes	35	68.6%
GERD	No	11	21.6%
	Yes	40	78.4%
Family history of Head and Neck malignancy	No	48	94.1%
	Yes	3	5.9%
Family history of other malignancies	No	39	76.5%
· ·	Yes	12	23.5%

Laryngectomy was performed eventually to 46 patients out of 51 patients. 5 patients didn't undergo the surgery: two had complicated uncontrolled co-morbidities forbidding the general anesthetic measures and three refused to perform the surgery and preferred conservative medical management as chemotherapy and radiotherapy in private clinics.

The results of histological examination of the excised laryngeal tissue and draining lymph nodes were compared to the results obtained by CT and U/S examination performed prior to surgery.

It was obvious that the lesions were mainly glottic in position seen in 71.7 % (33/46) versus 36.9 % (17/46) supraglottic and 8.6 % (4/46) subglottic.

Tumor location	No.	%
glottic	33	71.7
supraglottic	17	36.9 %
subglottic	4	8.6 %

Detection results of invasion of intra and extra-laryngeal structures by CT and U/S were compared as follow:

	TP	FP	TN	FN	Sensitivity	Specificity	PPV	NPV	Accuracy
Glottic lesions									
CT	17	1	28	0	100.0%	96.6%	94.4%	100.0%	97.83%
US	13	2	27	4	76.5%	93.1%	86.7%	87.1%	86.95%
Supraglottic lesions									
CT	17	1	28	0	100.0%	93.4%	96.6%	0.0%	97.83%
US	13	2	27	4	76.5%	93.1%	86.7%	87.1%	86.95%
Subglottic lesions									
CT	4	1	41	0	100.0%	97.6%	80.0%	100.0%	97.83%
US	3	5	37	1	75.0%	88.1%	37.5%	97.4%	86.96%
Anterior commissur	al infi	ltratio	n						
CT	25	0	20	1	96.2%	100.0%	100.0%	95.24%	97.83%
US	23	2	18	3	88.5%	90.0%	92.0%	85.71%	89.13%
Paraglottic fat infiltr	ation								
CT	29	1	14	2	93.5%	93.3%	96.7%	87.5%	93.48%
US	28	2	13	3	90.3%	86.7%	93.33%	81.25%	89.13%
Thyroid cartilage in	vasion	1							
CT	16	1	27	2	88.9%	96.4%	94.12%	93.1%	93.48%
US	16	3	25	2	88.9%	89.3%	84.21%	92.59%	89.13%
Transglottic infiltrat	ion								
CT	9	1	36	0	100.0%	97.3%	90.0%	100.0%	97.83%
US	7	5	32	2	77.8%	86.5%	58.33%	94.12%	84.78%
Extralaryngeal infilt	ration								
CT	9	1	36	0	100.0%	97.3%	90.0%	100.0%	97.83%
US	7	5	32	2	77.8%	86.5%	58.33%	94.12%	84.78%
Regional lymph nodes assessment									
CT	11	3	28	4	73.3%	90.3%	78.57%	87.5%	84.78%
US	14	2	29	1	93.3%	93.5%	87.5%	96.7%	93.48%
Recurrent laryngeal nerve invasion									
CT	13	1	31	1	92.9%	96.9%	92.86%	96.9%	95.65%
US	10	5	27	4	71.4%	84.4%	66.7%	87.1%	80.44%

None of the lesions showed vascularity on Doppler imaging

Free vocal cords mobility with phonation at the same side of the lesion was seen in the dynamic U/S examination only in (30/46) 65.2% of the patients.

DISCUSSION:

In our study, ultrasonography is proved to be a valuable supplementary method to CT and laryngoscopy in the assessment of laryngeal carcinoma even in male adults with some calcifications of the thyroid cartilage. Nevertheless, attempts have been made to use it in this area, largely to take advantage of its non invasive and real time imaging features.

It can be used as a screening tool⁷.

In this study, we provide evidence that ultrasonography could supply valuable information on the diagnosis of laryngeal carcinoma. It was found that ultrasonography was able to detect most of the laryngeal tumors. Once the tumor was detectable with ultrasonography, its primary could be correctly localized. site both the sensitivity and Furthermore. specificity were high in the evaluation of invasion to intraand extralaryngeal structures.

The uncalcified areas of the larynx usually exist in the superior and middle parts of the bilateral lamina and enable effective ultrasound penetration. Some other anatomical sites are also suitable for the transmission of the ultrasound beam, e.g. the thyrohyoid and cricothyroid membranes. By choosing these acoustic windows, most of the tumors were detected in our study, in which male patients accounted for 92.1 % (47/51) in total. In addition, the laryngeal and hypopharyngeal regions could be visualized much better.

When the landmarks, *i.e.* ventricular bands and vocal cords, were clearly shown for localization, the glottic laryngeal tumor could be correctly located by ultrasonography with a rate [30 (90.9%)/33], which was close to CT detection rate [31 (93.9%)/33] (p=0.001).

In another study of 30 glottic carcinomas, high ultrasonography a detection rate (96.7%) was shown, probably relating to fewer T1 cancers (n=5) in subjects. These results suggest ultrasonography has a satisfying detection rate for laryngeal cancer mainly the glottis lesions even in male adults with thyroid cartilage calcification, excepting some of the early glottic carcinoma 7.

Supraglottic carcinoma had a remarkably lower detection rate by ultrasonography of about [13 (76.4%)/17) compared to [17 (100%)/17] by CT, yet least detection rate was seen in subglottic cancers with [3 (75%)/4] by ultrasonography compared to [4 (100%)/4) by CT. This is mostly attributed to masking effect of air seen in rima vestibuli and infraglottisand the refractive shadowing as well as and accompanying orthopnea patient's intolerance to supine position shortening the examination time which represented the main complaint in supra and infraglottic lesions.

A previous research of 14 advanced laryngeal carcinomas at a stage of T2 or above also showed a high accuracy [11 (100.0%)/11] in localizing the primary site of ultrasonography-visible lesions⁵.

However, some lesions were still not located correctly because of thyroid cartilage calcification or large tumor volumes. One primary glottic tumor with subglottic invasion was mistaken as a subglottic lesion on ultrasonography images because part of the lesion in the glottis was not delineated clearly with the calcification of thyroid cartilage. The remaining three cases with advanced stages (T4, n=2 and T3, n=1) were not localized correctly because the bulky mass itself (transverse diameters, 3- 4 cm and postero-anterior dimensions, 1.9–3.7 cm) made it difficult to confirm the location of the primary site and two of them were not localized correctly by CT, either⁵.

The evaluation of involvement of the related structures is critical because it supplies direct proof for tumour staging and determines the therapy plan⁸

The lower specificity of U/S and CT in the detection of neoplastic spread to the paraglottic space of was related to the overestimation of tumor spread attributed to the peritumoral inflammatory reaction mostly due to biopsy taking or surrounding mild inflammatory process. (Zbären et al, 1997) 9

We evaluated the mobility of the larynx by having the patients talk softly or relax after breath-holding. Asymmetrical movement or impaired mobility of the vocal cords and on real-time ultrasonography images was almost always associated with thyroid cartilage invasion with or without recurrent laryngeal nerve invasion upgrading the tumor to stage T4 with a sensitivity of 88.9% and a specificity of 89.3%.

There are some limitations to the present study, some larynx subsites were not clearly evaluated by ultrasonography, such arvepiglottic folds and posterior commissure. Another limitation was that only one examiner scanned the larynx, leading to the impossibility of determination reproducibility and inter-observer reliability; however, this might be acceptable anyway, considering that it is not difficult for an examiner to perform ultrasonography examination of the laryngeal area after training.

In summary, most of the laryngeal tumors could be detected by sonography, even in male adults with some calcifications of the thyroid cartilage. Once the tumor is detected by ultrasonography, the localization of the primary focus and the assessment of tumor extension inside and outside the larynx are feasible, the results of which could be comparable to those of CT. Noticeably, comparable sensitivity between ultrasonography and CT was mainly noticed

as regard the detection of thyroid cartilage invasion (88.9% each), paraglottic fat infiltration (90.3 % and 93.5 %) and anterior commissure infiltration (88.5% and 96.2 %) respectively, also a real-time feature of ultrasonography could be used to view the mobility of the vocal cords.

Conclusion:

Ultrasonography could be used as a valuable supplementary imaging method to CT and laryngoscopy in the assessment of laryngeal carcinoma, even in male adults with some calcifications of the thyroid cartilage.

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الملخص العربي

المقدمة: طالما لم تستخدم الموجات الصوتية في تشخيص اورام الحنجرة بالشكل الأمثل بسبب وجود صعوبات تشريحيا مثل تكلس غضاريف الحنجرة و لكن انتقاء اماكن و تقنية معينة رفع من نسب الدقة و الحساسية لنتائجها و جعل منها اداة موثوقة النتيجة خصوصا مع التفرد بخاصية الديناميكية.

الهدف من البحث: هو دراسة امكانيات استخدام الموجات الصوتية لتشخيص و تخطيط أورام الحنجرة الخبيثة بالمقارنة بالأشعة المقطعية

المرضى و الطرق المستخدمة: تم البحث على ٤٦ مريض بعد اقصاء ٥ مرضى الذين لم يخوضوا الجراحة لظروف صحية مصاحبة تتعارض معها. تم عمل مقارنة بين نتائج الموجات الصوتية و الاشعة المقطعية من حيث لدقة و حساسية الفحص و القيمة التنبؤية القيمة التنبؤية السلبية بالمقارنة بنتائج الباثولوجي لعينة ما بعد استئصال الحنجرة.

ألنتائج: معظم المرضى كانوا من الذكور (97.1° (97.1° (97.1°))) و اعمار هم تتجاوز الستون عاما (97.1° (93.0°)). معدل التشخيص لحالات اورام الاحبال الصوتية متماثل بالنسبة للموجات الصوتية و الاشعة المقطعية (97.1° (97.1°)) مع معدل حساسية الفحص و دقته يساوى 99.9° (97.1°) هي مقابل 97.9° (97.1°) و 97.9° (97.1°) بالترتيب.

الخلاصة: تمثل الموجات الصوتية أداة تشخيص مكملة للأشعة المقطعية و منظار الحنجرة في حالات.