

ROLE OF ULTRASOUND AND DIFFUSION WEIGHTED MRI IN DETECTION OF THYROID CARTILAGE INVASION IN PATIENTS WITH LARYNGEAL CARCINOMA

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ABSTRACT:

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Background: Cartilage invasion is one of the critical determinants of tumour staging for laryngeal cancer and of particular importance in assessing the suitability for partial laryngectomy and/or chemoradiation therapy

Compared to CT, diffusion-weighted magnetic resonance imaging (MRI) has a similar ability to define the interface between fat and tumor, but is superior for assessing muscle and cartilage invasion. Diffusion-weighted MRI may be indicated if there are equivocal findings in the CT, including possible cartilage invasion. ultrasonography has the advantage of its non-invasive and real-time imaging features and it has been used to evaluate laryngeal tumours and it could assist tumour staging in patients with advanced laryngeal cancer.

Aim of the work: To compare between the role of US and diffusion weighted MRI in the detection of thyroid cartilage invasion in patients with laryngeal malignancy by correlating the radiological findings with the postoperative histopathological findings of the total or partial laryngectomy specimen.

Patients and Methods: A prospective study was carried out between December 2018 to September 2021. The study included 36 patients. Thirty five patients underwent total laryngectomy and one patient underwent partial laryngectomy. Histopathology reports of resected specimens and pre-operative staging were blind to the consultant radiologist who reviewed the scans to comment on thyroid cartilage invasion with special emphasis on inner and outer lamina invasion by conventional MRI criteria, and DWI and ultrasound.

Results: our study showed that DWMRI has sensitivity of 81.2%, specificity 50%, PPV of 86.7%, NPV of 40% and accuracy of 75% in detection of inner lamina invasion and it has sensitivity of 84.6 %, specificity of 71.4%, PPV of 84.6%, NPV of 71.4% and accuracy of 80% in detection of outer thyroid lamina invasion. In our study, we found that ultrasound has sensitivity of 78.6%, specificity of 60%, PPV of 84.6%, NPV of 50% and accuracy of 73.7% in detection of inner cortex invasion. & it has sensitivity of 75%, specificity of 66.7%, PPV of 90%, NPV of 66.6% and accuracy of 78.9% in detection of outer thyroid cortex invasion.

Conclusion: Diffusion-weighted MRI and ultrasound showed high validity and precision in detecting inner and outer thyroid lamina invasion. This can have an important impact on the decision making for management of laryngeal carcinoma.

Key Words: *Laryngeal neoplasm, Magnetic resonance imaging, Ultrasound, Thyroid cartilage/pathology*

INTRODUCTION:

The aim of cross-sectional imaging in laryngeal carcinoma is to determine deep extension into laryngeal spaces, muscles and cartilages, including pre-epiglottic space, paraglottic space, thyro-arytenoid muscle and thyroid cartilage. Of particular importance is assessing the suitability for partial laryngectomy and/or chemoradiation therapy in an attempt to preserve voice⁽¹⁾. The cartilaginous invasion determines the T and is one of the most frequent sources of error in tumor staging, it is of big significance when planning any therapeutic options as the majority of authors agree that cartilage invasion contraindicates partial surgical techniques⁽²⁾ radiotherapy⁽³⁾ and it is in addition considered a poor indication of organ preservation treatment with chemo and radiotherapy⁽²⁾. Compared to CT, diffusion-weighted MRI (DW-MRI) has a similar ability to define the interface between fat and tumor, but is superior for assessing muscle and cartilage invasion⁽³⁻⁵⁾, DW-MRI is indicated if there are equivocal findings on multidetector CT, including possible cartilage invasion. DW-MRI has the following advantages: does not require iodinated contrast, has no exposure to ionizing radiation, has no dental amalgam artifact, and has superior soft tissue contrast.

Ultrasonography is one of the few diagnostic techniques that could be done at the bedside and gives a lot of advantages over other techniques. It is willingly available and moveable, and images are seen concurrently. As well, it is cheap and noninvasive than other modalities. Sedation and contrast dye are seldomly required; but, recent studies with contrast are emerging. Most significantly it is a harmless study and, consequently is the initial suggested imaging of choice for pregnant women and children⁽⁶⁾.

The majority of the laryngeal tumors can be identified via sonography, Once the tumor is identified by ultrasonography, the localization of the main focus and the evaluation of tumour extension inside and outside the larynx are possible, the outcome of which can be comparable to those of CT. Obviously, a higher specificity can be obtained by ultrasonography than by CT in the assessment of paraglottic space involvement, and a real-time feature of ultrasonography might be used to examine the mobility of the vocal folds⁽⁷⁾.

AIM OF THE WORK:

This work was designed to compare between the role of US and diffusion weighted MRI in the detection of thyroid cartilage invasion in patients with laryngeal malignancy by correlating the radiological findings with the postoperative histopathological findings of the total or partial laryngectomy specimen.

MATERIAL AND METHODS:

Study population: Thirty -six patients with histological confirmation of laryngeal carcinoma were enrolled in this study. Patients scheduled to have partial or total laryngectomy for newly diagnosed laryngeal carcinoma were included.

Methods: Prior to surgery, all participants had routine laboratory investigations, chest X-ray, contrast-enhanced CT, DW-MRI and ultrasound. Histopathology reports of resected specimens and pre-operative staging were blind to the consultant radiologist, who reviewed the scans to comment on thyroid cartilage invasion; with special emphasis on inner and outer lamina invasion by conventional MRI criteria, DWI and

ultrasound. The criteria used to diagnose thyroid cartilage invasion included one or more of the following: (1) T1WI: low to intermediate signal; (2) T2WI: cartilage signal iso-intense to the tumor signal suggests invasion; (3) proton density fat suppression (PD FS) which is a specific sequence for cartilage evaluation; further evaluate inner versus outer cortex invasion; (4) T1WI + C: cartilage enhancement similar to the tumor suggests cartilage invasion; more likely, however, enhancement more than tumor suggests that cartilage invasion is less likely; (5) DWI: restricted diffusion as high signal in DWI and low signal in (apparent diffusion coefficient) ADC maps; (6) on evaluation of ADC value ranging from 0.6 to 0.8×10^{-3} , the cutoff value was 1.2×10^{-3} . (7) US: interruption of inner and/or outer membranes that normally are hyperechoic lines on ultrasonography images and the replacement of the central medulla by hypoechoic tumors

Radiological findings were then compared with histological findings, and sensitivity, specificity, negative and positive predictive values, and effectiveness of the MRI and ultrasound in detecting inner and outer thyroid lamina invasion were analyzed.

MRI protocol:

The study was held in the MRI unit, at Ain Shams University Hospitals (1.5 T, Philips®, Healthcare). There were two blinded radiologists one for MRI and another for US. Using surface coil coverage from skull base to supra clavicular fossa, the following sequences was obtained: axial and coronal T1WI, axial and coronal T2WI, and axial proton density with fat suppression. DWI 3b values and axial, coronal, and sagittal T1WI post-contrast fat saturation parameters were: FOV, 20–22 cm; slice thickness, 4 mm; interslice gap, 0.5–1 mm, matrix, 192×256 .

Ultrasound protocol:

The ultrasonography examination was performed by a radiologist, who only know

that the patient suffered from a laryngeal neoplasm and was unaware of other clinical or imaging information.

In a supine position 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. Acoustic windows that were suitable for the penetration of ultrasound beams was located at the thyrohyoid membrane, cricothyroid membrane and thyroid cartilage lamina, where the structure have 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 manoeuvres were used to observe the relative movement of the paraglottic fat to the adjacent internal perichondrium of the thyroid cartilage.

An iU22 ultrasound scanner with L9-3 and L17-5 probes (Philips Healthcare, Bothell, WA) and a LOGIQ 9 machine with 7L and M12L probes (GE Healthcare, Milwaukee, WI) were used⁽⁷⁾.

The collected data were coded and entered to a personal computer utilizing Microsoft Office Excel 2007.

- The data was analyzed with the program (SPSS) statistical package for social science to give real information and to demonstrate the relation between particular items and the final result.
- The results were analyzed to detect the significance of DW MRI for evaluation of thyroid cartilage invasion in cases with advanced cancer larynx in comparison to ultrasound findings.
- The following quality indices were calculated: sensitivity, specificity, positive predictive value, and negative predictive value.

Ethical Considerations: Verbal consent was obtained from all patients

before imaging after explaining the aim of the study.

59 years with an interquartile range of 39–74. Thirty-five patients underwent total laryngectomy and one patient underwent partial laryngectomy with block neck dissection when needed (Table 1).

RESULTS

Thirty-six patients were studied, 36 (100 %) male and no female. Their median age was

Table (1): Descriptive for demographic and characteristics of the studied patients.

		No.= 36
Age (years)	Mean ± SD	59.11 ± 8.12
	Range	39 – 74
Sex	Male	36 (100.0%)
Smoking	Negative	No.= 36 0 (0.0%)
	positive	36 (100.0%)
Site	Glottic	7 (19.4%)
	Supraglottic	9 (25.0%)
	Infraglottic	3 (8.3%)
	Transglottic	17(47.2%)
Size (cm)	Mean ± SD	3.12 ± 1.08
	Range	1.5 – 6
Histological type and grade	Moderately differentiated scc	22 (61.1%)
	Poorly differentiated scc	5 (13.9%)
	Well differentiated scc	6 (16.7%)
	Basaloid SCC	3 (8.3%)

Due to the fact that the line of management and the prognosis depend on the degree of thyroid cartilage invasion, we investigated the ability of DW-MRI and ultrasound to detect inner and outer lamina invasion by the tumor.

Inner lamina invasion:

There is non-significant relationship between ultrasound and pathology, DW MRI and pathology in detection of thyroid cartilage inner lamina invasion.

Table (2): Showing statistical relationship between ultrasound pathology DW MRI in detection of thyroid cartilage inner lamina invasion.

		Pathology (inner)		Test value	P-value	Sig.
		Negative	Positive			
US (inner lamina)	Negative	3 (60.0%)	3 (21.4%)	2.537*	0.111	NS
	Positive	2 (40.0%)	11 (78.6%)			
DW MRI (inner lamina)	Negative	2 (50.0%)	3 (18.8%)	1.667*	0.197	NS
	Positive	2 (50.0%)	13 (81.2%)			

Consequently, the sensitivity, specificity, Accuracy, and positive and negative predictive values of MRI for identification of inner lamina involvement in this study were: 81.2%, 81.2%, 75%, 86.7%,

and 40.0%, respectively while ultrasound has a sensitivity of 78.6%, specificity of 60% with accuracy of 73.3% in detection of inner lamina invasion in relation to pathological results .

Table (3) Diagnostic value of MRI and ultrasound for identification of inner lamina invasion

(inner)	TP	TN	F P	F N	Sensitivity	Specificity	PPV	NPV	Accuracy	P-value
US	11	3	2	3	78.6%	60.0%	84.6%	50.0%	0.737	0.624
DW MRI	13	2	2	3	81.2%	81.2%	86.7%	40.0%	0.750	

Outer lamina invasion:

pathology in detection of thyroid cartilage outer lamina invasion.

There is significant relationship between ultrasound and pathology, DW MRI and

Table (1): Showing statistical relationship between ultrasound pathology DW MRI in detection of thyroid cartilage outer lamina invasion.

		Pathology (outer)		Test value	P-value	Sig.
		Negative	Positive			
US (outer lamina)	Negative	6 (85.7%)	3 (25.0%)	6.537*	0.011	S
	Positive	1 (14.3%)	9 (75.0%)			
DW MRI (outer lamina)	Negative	5 (71.4%)	2 (15.4%)	6.282*	0.012	S
	Positive	2 (28.6%)	11 (84.6%)			

Our study showed that the ultrasound has a sensitivity of 75%, specificity of 66.7% with accuracy of 78.9% in detection of outer lamina invasion in relation to pathological results

while the DW MRI has a sensitivity of 84.6%, specificity of 71.4% and accuracy of 80% with no statistically significant difference between both methods with p-value = 0.535

Table (5) Diagnostic value of MRI and US for identification of outer lamina involvement

Outer	TP	TN	FP	FN	Sensitivity	Specificity	PPV	NPV	Accuracy	P-value
US	9	6	1	3	75.0%	66.7%	90.0%	66.7%	0.789	0.535
DW MRI	11	5	2	2	84.6%	71.4%	84.6%	71.4%	0.800	

Fig. 1: Patients whose c: CT scan showed right supraglottic and glottic mass with invasion of both outer and inner lamina of thyroid cartilage in right side(c). The patient has evidence of thyroid cartilage

invasion (both inner and outer cortex) in DWMRI images and US (a, b) This patient was proved to have right sided thyroid cartilage invasion in histopathology.

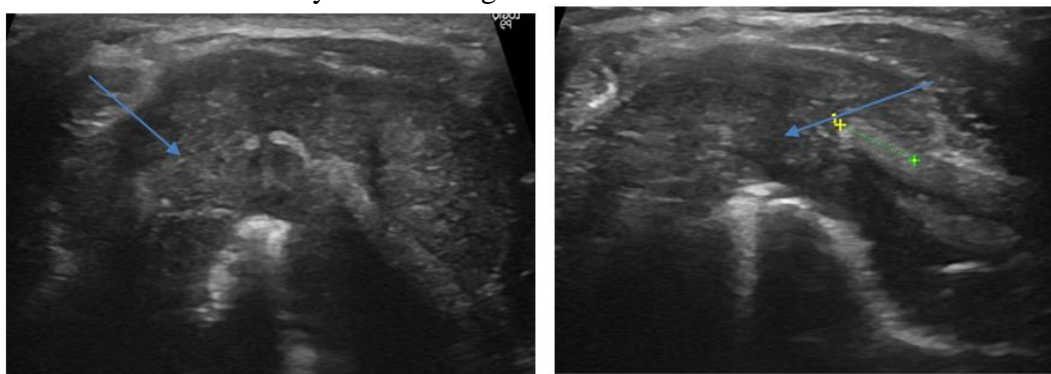


Figure (a): Us shows both invasion of outer and inner lamina of thyroid cartilage

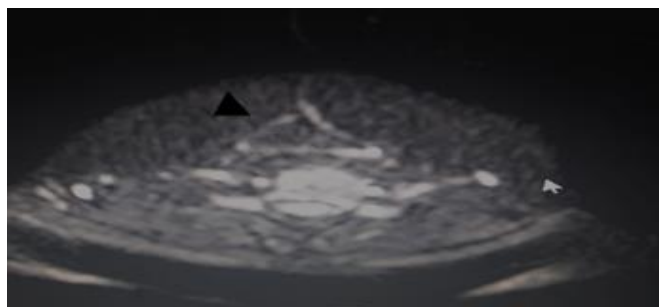


Figure (b): DW MRI shows restricted diffusion

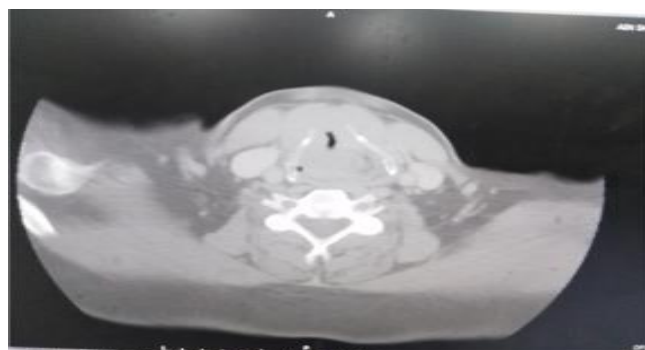


Figure (c): CT shows invasion of both outer and inner lamina of thyroid cartilage in right side

DISCUSSION:

To facilitate therapeutic decision making, the accurate pre-treatment assessment of cartilage invasion is of great significance.

The diagnosis of thyroid cartilage invasion in cases presenting with SCC of the larynx is vital for pre-therapeutic staging of laryngeal carcinoma. Thyroid cartilage invasion is associated with a worse response rate to radiation therapy and a greater risk of tumor recurrence⁽⁸⁾. Cartilage invasion has frequently been recommended as a contraindication to partial laryngectomy

It has been previously documented that both CT and MRI have restrictions in predicting tumor invasion of thyroid cartilage⁽⁹⁾. CT may fail to spot minor or early cartilage invasion, owing to ordinary irregular patterns of calcification and ossification of thyroid cartilage⁽¹⁰⁾, and MRI can show details of non-ossified and ossified cartilage better than CT.^(11& 12), fulfilled that in recurrent laryngeal cancer, CT imaging has

obvious limitations for identification of cartilage invasion or tumor spread. Moreover,⁽⁹⁾ found that pre-operative CT was not efficient in detecting thyroid cartilage invasion in early to mid-stage cancer and overestimating cartilage invasion for anterior commissure lesions.

DW-MRI can make fine abnormality more clear⁽¹³⁾. It gives better description of tissues and their physiological processes because it reflects the haphazard motion of water protons, which is disturbed by the intracellular organelles and macromolecules situated in tissues⁽¹⁴⁾.

Ultrasonography has been posited as a promising method for examination of the larynx since the 1960s⁽¹⁵⁾. By the late 1980s, ultrasound was found to be valuable for real-time assessment, not only of the true vocal folds, but also of the false vocal folds and the vocal fold mobility⁽¹⁶⁾.

Ultrasonography is a noninvasive technique; it is available at nearly all institutions, cheap, simply reproducible

technique for examining the larynx in infants and children, can be used safely throughout pregnancy in contrast to CT scan, is transferable and could be easily transported to patients with trouble in mobilization. As well it is painless and Anaesthesia is not essential during laryngeal ultrasonographic assessment.

Regarding the DWMRI, our study showed that DWMRI has sensitivity of 81.2%, specificity 50%, PPV of 86.7%, NPV of 40% and accuracy of 75% in detection of inner lamina invasion and it has sensitivity of 84.6 %, specificity of 71.4%, PPV of 84.6%, NPV of 71.4% and accuracy of 80% in detection of outer thyroid lamina invasion.

In our study, we found that ultrasound has sensitivity of 78.6%, specificity of 60%, PPV of 84.6%, NPV of 50% and accuracy of 73.7% in detection of inner cortex invasion. & it has sensitivity of 75%, specificity of 66.7%, PPV of 90%, NPV of 66.6% and accuracy of 78.9% in detection of outer thyroid cortex invasion.

Our study showed overall higher sensitivity (81.2% for inner and 84.6% for outer lamina invasion) of DWMRI compared to US (78.6% for inner and 75% for outer lamina invasion). Higher accuracy of DWMRI (75% for inner and 80% for outer lamina invasion) compared to US (73% for inner and 78% for outer lamina invasion), but higher specificity (60% for inner and 71% for outer lamina invasion) of US compared to DW MRI (50% for inner and 71% for outer lamina invasion)

These results were as well similar to the study of *Priya in (2013)*⁽¹⁷⁾, who found that DWMRI had a higher sensitivity in the recognition of neoplastic thyroid cartilage invasion and reported sensitivity of 91.7% DWMRI

Our results regarding ultrasound sensitivity and specificity came in concordance with *(Xia et al., 2013)*⁽⁷⁾, who found a sensitivity of 83% and a specificity of

90% in a prospective study of 72 patients with cancer larynx, who were treated surgically.

Many authors therefore recommend MRI as the primary means of evaluating cartilage invasion in patients with laryngeal carcinomas⁽¹⁸⁻²⁰⁾. Another study concluded that CT may be the primary imaging method in hypopharyngeal and laryngeal carcinomas, but DW-MRI should be reserved for cartilage invasion assessment in candidates for partial laryngectomy. On the contrary, Kinshuck et al. in their study found that the specificity was higher than the sensitivity (71 and 64 %) for detecting thyroid cartilage invasion, so they recommended that surgeons should be aware of the fact that pre-operative MRI will often overpredict thyroid cartilage invasion. Reliance on the findings of pre-operative MRI in these circumstances may easily result in overtreatment. Consequently, treatment judgments should rely on clinical assessment rather than MRI results.

The agreement between MRI scanning and histopathologic examination and ultrasound and histopathologic examination with regard to the identification of inner lamina involvement showed that there was no good agreement between both.

The value of MRI for identification of outer lamina invasion in this study showed that the sensitivity, specificity, accuracy (Correct classification rate), and positive and negative predictive values were: 84.6 %, 71.4%, 80%, 84.6%, 71.4% ,respectively so, there was good agreement between DWI scanning and histopathologic examination as regards the identification of outer lamina involvement.

The value of ultrasound for identification of outer lamina invasion in this study showed that the sensitivity, specificity, accuracy, and positive and negative predictive values were: 75%, 66.7%, 78.9%, 90%, 66.6% ,respectively .so, there was good agreement between ultrasound and

histopathologic examination as regards the identification of outer lamina involvement.

From our results we can conclude that both DWI and ultrasound can play a vital role in decision making for treatment and pre-therapeutic staging of cancer larynx, where DW MRI is more sensitive, while US is more specific in identification of thyroid cartilage invasion. So both methods can be complementary to each other in pre-therapeutic staging of laryngeal carcinoma.

Conclusion

- DW-MRI showed high validity and precision in detecting inner and outer thyroid lamina invasion. This can have an important impact on the decision making for management of laryngeal carcinoma.
- 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
- In our study DWMRI was more sensitive but ultrasound was more specific in assessment of malignant invasion of inner and outer laminae of thyroid cartilage.
- We can conclude that both DWI and ultrasound can play an important role in decision making for management and pre-therapeutic staging of laryngeal carcinoma, so both method can be complementary to each other in pre-therapeutic staging of laryngeal carcinoma.
- DW-MRI showed high validity and precision in detecting inner and outer thyroid lamina invasion. This can have an important impact on the decision making for management of laryngeal carcinoma.

Conflicts of Interest: The authors state that the publishing of this paper is free of any conflicts of interest.

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دور الموجات الصوتية ونشر مرجحه التصوير بالرنين المغناطيسي في الكشف عن غزو الغضروف الدرقي في المرضى الذين يعانون من سرطان الحنجرة

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الخلفية: يعد تشخيص غزو الغضروف الدرقي أمراً حيوياً لتحديد مرحلة ما قبل العلاج لسرطان الحنجرة ويعتبر ذو أهمية كبيرة لتقييم القابلية للاستئصال الجزئي للحنجرة والعلاج الإشعاعي .

مقارنةً بالأشعة المقطعية ، فإن نشر مرجحه التصوير بالرنين المغناطيسي لديه قدرة مماثلة على اكتشاف الحدود بين الدهون والورم ولكنه أفضل لتقييم غزو العضلات والغضاريف. الموجات فوق الصوتية هي تقنية متوفرة في جميع المؤسسات تقريباً ، وهي رخيصة الثمن ، ويمكن استخدامها أكثر من مره لفحص الحنجرة .

الهدف: المقارنة بين الموجات فوق الصوتية و نشر مرجحه التصوير بالرنين المغناطيسي في تشخيص غزو الغضروف الدرقي لسرطان الحنجرة بالمقارنة بين نتائج الأشعة وتحليل الأنسجة بعد الاستئصال الكلي او الجزئي للحنجرة

المرضى والطرق: اجريت الدراسة من ديسمبر ٢٠١٨ الي سبتمبر ٢٠٢١ علي ٣٦ مريض , ٣٥ مريض اجريت له استئصال كلي للحنجرة و مريض اجري له استئصال جزئي للحنجرة وتقارير تحليل الأنسجة للعينات المستئصله كان مخفيا عن استشاري الاشعه الذي يعلق علي غزو الغضروف الدرقي مع التعليق علي غزو الصفيحه الخارجيه والداخليه للغضروف الدرقي بنشر مرجحه التصوير بالرنين المغناطيسيو الموجات فوق الصوتية

النتائج: وقد اظهرت الدراسات نشر مرجحه التصوير بالرنين المغناطيسي لديه حساسيه ٨١,٢٪, نوعيه ٥٠٪ وقيمه تبيؤيه ايجابيه ٨٦,٧٪, وقيمه تبيؤيه سلبيه ٤٠٪ ودقه ٧٥٪ في تحديد غزو الصفيحه الداخليه للغضروف الدرقي و لديه حساسيه ٨٤,٦٪, نوعيه ٧١,٤٪ وقيمه تبيؤيه ايجابيه ٨٤,٦٪, وقيمه تبيؤيه سلبيه ٧١,٤٪ ودقه ٨٠٪ في تحديد غزو الصفيحه الخارجيه للغضروف الدرقي والموجات فوق الصوتية لديها حساسيه ٧٨,٦٪, نوعيه ٦٠٪ وقيمه تبيؤيه ايجابيه ٨٤,٦٪, وقيمه تبيؤيه سلبيه ٥٠٪ ودقه ٧٣,٧٪ في تحديد غزو الصفيحه الداخليه و لديها حساسيه ٧٥٪, نوعيه ٦٦,٧٪ وقيمه تبيؤيه ايجابيه ٩٠٪, وقيمه تبيؤيه سلبيه ٦٦,٦٪ ودقه ٧٨,٩٪ في تحديد غزو الصفيحه الخارجيه للغضروف الدرقي.

الخلاصه: نشر مرجحه التصوير بالرنين المغناطيسي و الموجات فوق الصوتية ليهما صلاحيه ودقه في تحديد غزو الصفيحه الخارجيه والداخليه للغضروف الدرقي مما قد يكون له تأثير هام في اتخاذ القرار لمرضى سرطان الحنجرة.