Assessment of the Diagnostic Precision of Sonoelastography in the Detection of Malignant Major Salivary Gland Lesions

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Abstract:

Background:
Sonoelastography is a novel technology that relies on the elastic properties of soft tissues, with the premise that malignant lesions are stiffer than benign or normal tissue. It may have a promising role in detecting malignant salivary gland lesions, in the same manner as it has been applied to different parts of the body, such as the breast.

Imaging is required to diagnose the salivary gland diseases, which range from mild inflammatory conditions to a group of benign and malignant neoplasms, as physical examinations and laboratory tests alone are insufficient to distinguish between these diseases. Also, conventional imaging modalities are inconclusive in differentiating between benign and malignant lesions because of the significant overlap between their imaging features.

Results: The study included 34 patients with salivary gland lesions. By comparing the sonoelastography features between patients with malignant versus those with benign lesions, we observed that mean shear moduli and strain ratio were significantly higher in malignant lesions than in benign ones [P < 0.05].

Also, the elasticity score was completely blue in malignant lesions, whereas no cases with benign lesions showed a blue color when measuring the elasticity score.

Conclusion: Sonoelastography is reliable in assessing major salivary gland lesions and detecting malignant ones.

Keywords: Parotid; Sub-mandibular salivary glands; Shear wave elastography; Strain elastography.

Introduction:

Imaging of the salivary gland lesions and differentiating between them presents a significant difficulty for radiologists, and it is mandatory to distinguish between benign and malignant lesions.

Currently, CT, MRI, and ultrasonography (grey scale and color Doppler) are the standard imaging techniques for assessing lesions of the major salivary glands. Although extremely sensitive, they are inaccurate in distinguishing between benign and malignant lesions [2].

This study aims to assess the diagnostic accuracy of sonoelastography in detecting malignant major salivary gland lesions.

Methods:

Patient Population:

All patients with parotid or sub-mandibular salivary gland swelling or pain who visited the maxillofacial surgery department of Assiut University Hospital during the study period from January 1st, 2022, to the end of December 2023 were included in the study. The sample size was calculated based on the sensitivity of elastography in detecting salivary gland lesions, which is 100% and the prevalence is 3% [3]. With a confidence level of 95% and a confidence limit of 5%, the minimum sample size is 34 cases.

The inclusion criteria were all patients of any age and any sex who had swelling or pain in the region of the parotid or sub-mandibular salivary glands and who agreed to participate in the study. Exclusion criteria were patients with conditions that may hinder sonoelastography examination, like subcutaneous emphysema and thick skin scarring, or those with a mass with a rough or ulcerated surface, affecting the entire gland, or a history of previous surgery.

The study was conducted after the approval of the Ethical Committee of the Faculty of Medicine (approval number 17101693), and all participants provided written informed consent, and information confidentiality was maintained throughout the study.

1.Personal Data: Detailed history including name, age, sex, telephone number, and address.

2.2. Initial Evaluation: Included relevant information, such as whether the lesion was present at birth, if there is associated pain or fever, a history of trauma, and whether the size of the lesion has changed with time.

3.Sonoelastography Evaluation:

- All participants received comprehensive information regarding the study's objectives and expected benefits. All ethical considerations were taken throughout the whole work.
- Patients were scanned while supine during free breathing, with a slight tilt to the opposite side of the examination, and neck hyperextension.
- The parotid and sub-mandibular salivary glands were examined thoroughly in the transverse and longitudinal orientations by a high-frequency linear probe (3-12 MHz) using a GE Logiq P9 device.
- Sonoelastography was performed. Firstly, strain elastography was performed. The identified elastogram images were assessed using color coding ranging from blue to green and red.
- Using a 4-grade scale, all lesions were graded on the elastogram according to how stiff they were compared to normal parenchyma.
- All of the lesion grading values provided by Dumitriu D. et al.'s strain ratio values
- Secondly, individual calculations were also made for shear wave elastography.

The results of strain ratio calculations, mean shear moduli, and elasticity scores were compared with histopathological diagnosis.

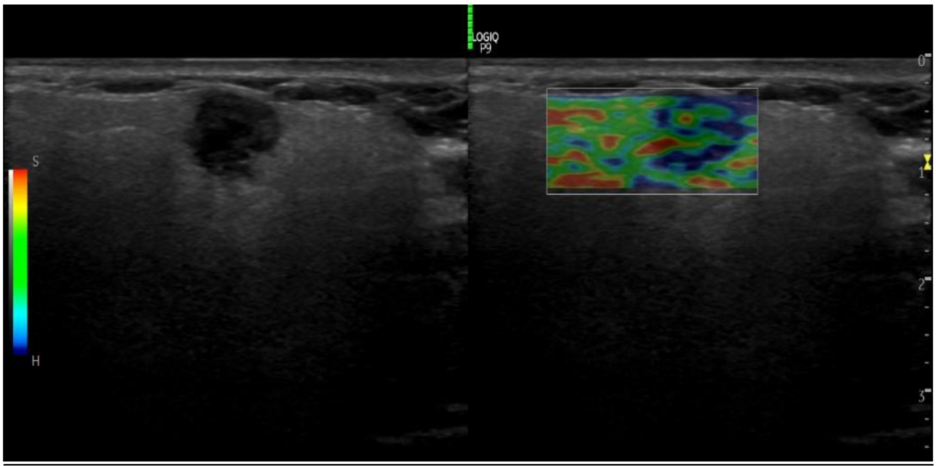

Figure 1: Sonography of parotid gland lesion and corresponding elastogram showing a predominant green elasticity score.

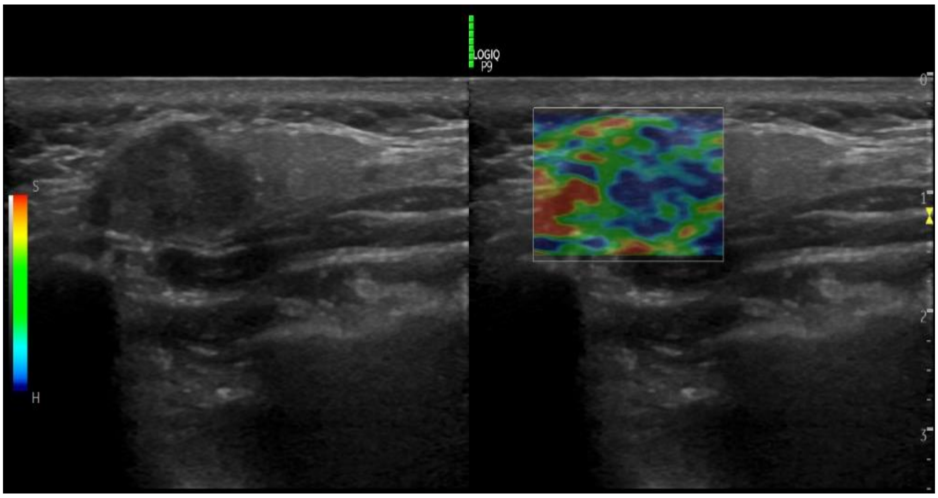

Figure 2: Sonography of parotid gland lesion and corresponding elastogram showing a predominant blue elasticity score.

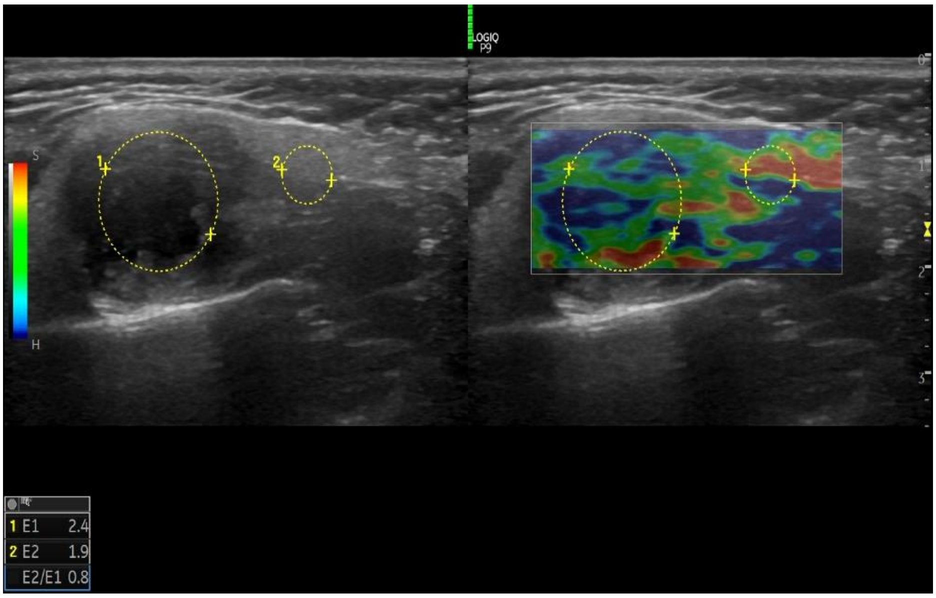

Figure 3: Strain elastography of a parotid gland lesion shows a strain ratio of 0.8.

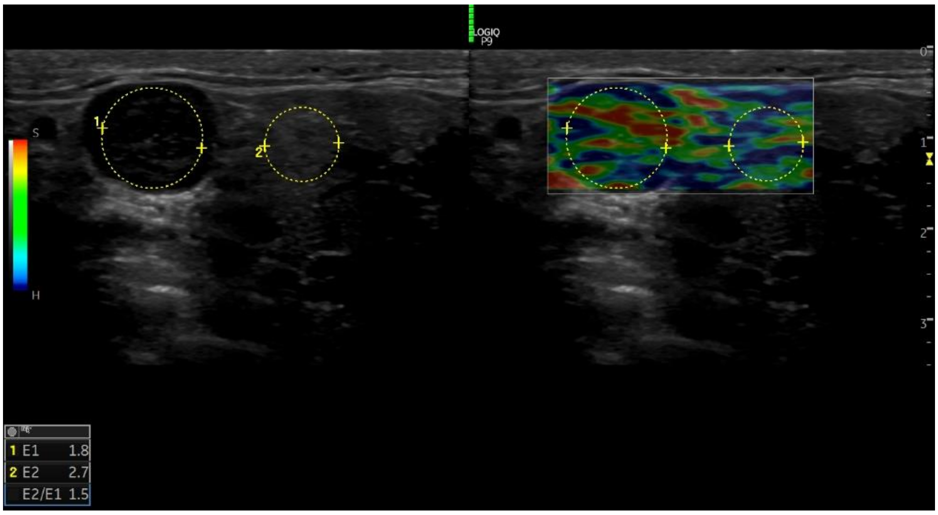

Figure 4: Strain elastography of a sub-mandibular salivary gland lesion shows a strain ratio of 1.5.

Statistical Analysis:

The statistical software SPSS version 22 was used for all calculations. The statistical descriptions of the data were mean ± standard deviation (±SD), frequencies (number of cases), relative frequencies (percentages) when applicable, or median (range) when the data were not normally distributed. Since the data were not normally distributed, the Mann-Whitney U test was used to compare the quantitative variables. Because the anticipated frequency was less than 5, the Fisher Exact test was utilized to compare categorical data rather than the Chi-square ($\chi2$) test. For the studied imaging modalities and the final used scores, using tissue pathology as the gold standard, the sensitivity and specificity of these variables were compared using Open Epi software (Open Epi version 2.3.1 from the Department of Epidemiology, Rollins School of Public Health, Emory University, Atlanta, GA 30322, USA) [4]. The P-value is set to be significant at the 0.05 level.

Results:

The present study was a prospective observational study aiming to assess the diagnostic accuracy of sonoelastography in detecting malignant major salivary gland lesions.

1. Demographic data of the studied participants:

The study included 34 patients with a mean age of 45.74 ± 15.70 years, ranging from 15 to 67 years. The main clinical presentation among the studied cases was neck swelling in 25 cases (73.5%), pain in addition to swelling in seven cases (20.6%), and two cases (5.9%) were diagnosed incidentally.

The lesions were in the parotid gland in most studied cases (88.2%), while only four cases (11.8%) suffered from sub-mandibular salivary gland lesions.

According to the histopathological studies among the studied participants, out of 34 studied cases, seven cases (20.6%) were proved to be malignant, and 27 cases (79.4%) had benign lesions. Both groups were comparable in age, sex, clinical presentation, associated co-morbidities, and lesion site, with no significant difference (P >0.05), as shown in **Table 1**.

Table 1: Demographic data of the studied participants (n =34).

Variable name	Total cases (n=34)	Benign cases (n=27)	Malignant cases (n=7)
Age (years)			
• Mean ±SD	45.74 ± 15.70	48.30 ± 15.24	35.86 ± 14.37
• Median (range)	46 (15 – 67)	55 (15 – 67)	34 (21 – 65)
Clinical presentation, n (%)			
• Swelling	25 (73.5)	19 (70.4)	6 (85.7)
• Pain & swelling	7 (20.6)	6 (22.2)	1 (14.3)
• Incidental finding	2 (5.9)	2 (7.4)	0 (0.0)
Location, n (%)			
• Parotid gland	30 (88.2)	24 (88.9)	6 (85.7)
• Sub-mandibular gland	4 (11.8)	3 (11.1)	1 (14.3)

Quantitative data are presented in mean ±SD and median (range), and qualitative data are presented as numbers (%). Significance is defined by $p < 0.05$.

2. **Sonoelastography Features of Studied Lesions:**

By comparing the sonoelastography features between patients with malignant versus those with benign lesions, we observed that the mean shear moduli were significantly higher in malignant lesions compared to benign lesions [median (range) was 140 (115–178) vs. 54 (5.4–188.0), P = 0.001] in both groups, respectively. Also, the elasticity score was completely blue in malignant lesions, whereas no cases with benign lesions showed a blue color on measuring the elasticity score (P < 0.001).

Furthermore, the strain ratio was significantly higher in malignant lesions compared to benign lesions [median (range) was 2.9 (0.8–3.9) vs. 0.4 (0.1–3.6), P<0.001] in both groups, respectively, as shown in **Table 2**.

Table 2: Sonoelastography Features of Benign and Primary Malignant Tumors

Sonoelastography Features	Total cases (n=34)	Benign cases (n=27)	Malignant cases (n=7)	P value
Stiffness (mean shear moduli)	68 (5.4-188.0)	54 (5.4-188.0)	140 (115-178)	**0.001**
IQR (%)	15.2 (5-28)	16 (5.7-27)	8 (5-28)	0.206
Elasticity score				**<0.001**
• Green is dominant	21 (61.8)	20 (74.1)	1 (14.3)	
• Blue is dominant	9 (26.5)	7 (25.9)	2 (28.6)	
• Completely blue	4 (11.8)	0 (0.0)	4 (57.1)	
Strain ratio	0.8 (0.1 – 3.9)	0.4 (0.1 – 3.6)	2.9 (0.8 – 3.9)	**<0.001**

Quantitative data are presented in the median (range), and qualitative data are presented as a number (%). Significance is defined by $p < 0.05$.

3. Final Diagnosis:

Regarding the malignant lesions (n =7), three cases (42.9%) had acinic cell tumors, two cases (28.6%) had mucoepidermoid carcinoma, one case (14.3%) had cystic mucoepidermoid carcinoma, and another case (14.3%) had squamous cell carcinoma, as shown in **Figure 5**.

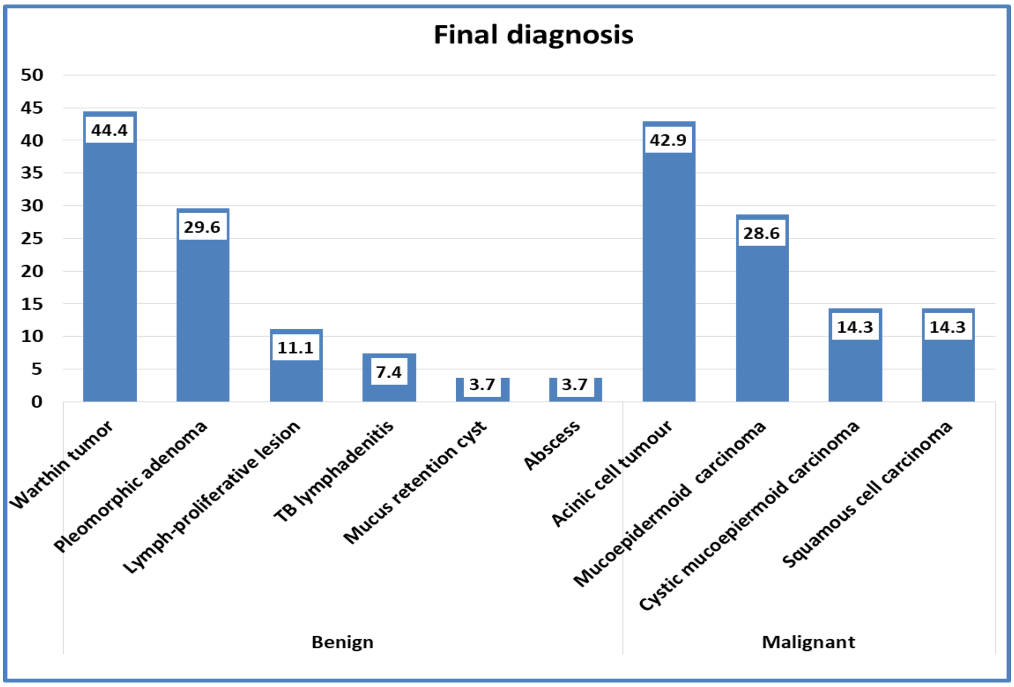

Figure 5: Bar graph showing the distribution of the final diagnosis among benign and malignant lesions.

Regarding the benign lesions (n =27), warthin tumor (44.4%) was the most common benign lesion, followed by pleomorphic adenoma (29.6%), lymph-proliferative lesion in three cases (11.1%), and TB lymphadenitis in two cases (7.4%). One case (3.7%) suffered from a mucus retention cyst, and another (3.7%) suffered from an abscess.

Table 3 and Figure 6 show the predictive ability of sonoelastography for the detection of malignant salivary gland lesions by using the ROC curve analysis:

- For stiffness (mean shear moduli) at a cut-off value of ≥ 115, the areas under the ROC curves were 89.9% (95% CI: 0.794–1.0, P = 0.001) with a sensitivity of 100.0%, a specificity of 85.2%, and an accuracy of 88.2%.
- For strain ratio at a cut-off value of ≥ 2.1, the areas under the ROC curves were 92.1% (95% CI: 0.816–1.0, P = 0.001) with a sensitivity of 85.7%, a specificity of 92.6%, and an accuracy of 91.2%.

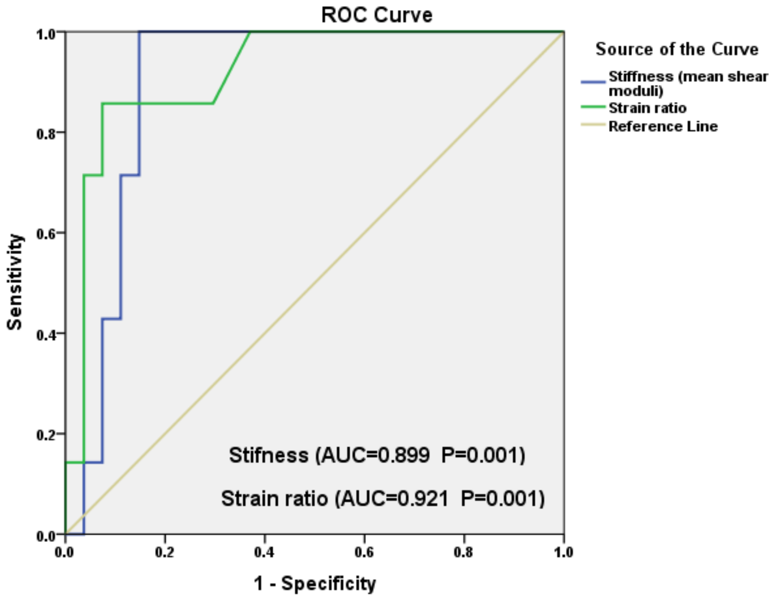

Figure 6: ROC curves for malignant salivary gland detection in studied participants. Stiffness (blue), strain ratio (green), and reference line (brown). AUC = 0.899 (0.794 to 1.0), P value = 0.001 for stiffness, and AUC = 0.921 (0.816 to 1.0), P value = 0.001 for strain ratio.

Table 3: The best cut-off, sensitivity, and specificity for predicting malignant salivary gland lesions by sonoelastography findings (n=34).

Sonoelastography	Cut off	95% CI	Sensit-ivity	Speci-ficity	PPV	NPV	Accuracy	AUC	p-value
Stiffness (mean shear moduli)	≥115	1.0-0.794	100.0%	85.2%	63.6%	100.0%	88.2%	0.899	**0.001**
Strain ratio	≥ 2.1	1.0-0.816	85.7%	92.6%	75.0%	96.2%	91.2%	0.921	**0.001**

PPV: positive predictive value; **NPV:** negative predictive value; **AUC:** Area under the curve; **CI:** confidence interval. Significance defined by $p < 0.05$

Discussion:

Conventional imaging modalities are insufficient for differentiating between benign and malignant salivary gland tumors because of significant overlap between benign and malignant imaging criteria, so the provisional diagnosis, which is based only on conventional imaging criteria, needs to be followed by imaging-guided needle biopsy and histopathological examination for a definite final diagnosis. [3].

However, imaging-guided needle biopsy is an invasive procedure, and when the outcomes are comparable, non-invasive procedures are usually preferred. Also, the course of the facial nerve within the parotid gland and the risk of its injury explain the persistent need for additional non-invasive diagnostic alternatives.

Our study uses sonoelastography for the assessment of salivary gland lesions. Sonoelastography enables both semi-quantitative and real-time qualitative assessment with newer technologies. [1].

The role of elastography in salivary gland disorders has not been extensively studied.

In our study, 30 of 34 patients had a neoplasm, of which only 7 (22%) were malignant.

The results of the recent study demonstrated that there is a statistically significant difference between benign and malignant lesions based on the elastography score ($p < 0.001$), as well as a recent semi-quantitative analysis using strain ratio ($p<0.0001$).

Furthermore, a more recent method, shear wave elastography, allows quantitative analysis and shows a better reflection of tissue elasticity with the ability to differentiate benign and malignant lesions ($p < 0.001$).

According to Dumitriu et al., there was a statistically significant difference between benign and malignant lesions in a research on 74 salivary gland tumors (18 malignant and 56 benign tumors) using a four-point elasticity score, consistent with our findings [5].

Contrarily, BAGRI et al. found that the elastography score alone does not significantly differentiate between benign and malignant conditions ($p = 0.308$ for the score) [2]. Also, Bhatia et al. reported that qualitative elastography scores alone cannot distinguish malignant lesions from benign ones, particularly pleomorphic adenomas [6]. Based on the elasticity score, Wierzbicka et al. observed different degrees of sensitivity and specificity [7]. Fifty-five benign lesions and only five malignancies were enrolled in the cohort of Bhatia et al., making it impossible to compare the two groups [6] statistically. Also, no malignant tumors were enrolled in the cohort of Olgun et al. [8].

In this study, we found that a cut-off value of strain ratio >2.1 predicts malignancy with an accuracy of 91.2%, a sensitivity of 85.7%, and a specificity of 92.6%.

Using this cut-off value, there were 27 benign and seven malignant lesions (p-value <0.0001).

Coman et al. and BAGRI et al. concluded that a strain ratio (SR) of >3 is suspicious for malignancy [9, 2]. In another study, the cut-off value for the elasticity score was higher than 3.5 [10].

This mild difference in the strain ratio values between our study and the other studies could be explained by the fact that our study included many cases with mucoepidermoid cystic neoplasm (which has significant areas of cystic degeneration) that subsequently had lower strain ratio values. For that reason, cystic areas of the tumors must be avoided during strain elastography whenever possible [11].

Theoretically, it would be discovered that every malignant lesion had a high strain ratio and mean shear moduli, indicating their hardness. The increased stiffness is thought to be due to tumor growth within a constrained interstitial matrix, which led to reactive interstitial fibrosis. However, the condition in the parotid gland seems more complex. The reason for this is the great difference in the histoarchitecture of salivary gland tumors, which leads to significant variation in stiffness. For example, pleomorphic adenomas and malignant lesions were found to have a significant overlap in their elastography scores.

In concordance with our results, Bhatia et al. reported that 16 of 23 pleomorphic adenomas were recorded as stiff in addition to true malignant masses [12]. This is because pleomorphic adenomas may have a stiff, fibrous component, which results in a higher elastography score and strain ratio. Additionally, because of the myxochondroid component, the stiffness of this benign lesion can be very high, even exceeding that of malignant tumors [5].

The study's positive and negative predictive values, sensitivity, and specificity are parallel to those of other studies evaluating the usefulness of elastography in assessing salivary gland masses. It is questionable if elastography is useful in diagnosing salivary gland masses because benign lesions might exhibit elastography patterns thought to be malignant. In other words, elastography proved to be more reliable at identifying benign diseases than malignancies.

Also, quantitative and shear wave elastography may have a promising role in differentiating and characterizing salivary gland lesions.

On the contrary, there was no statistically significant difference between the elastography scores of benign and malignant lesions and the strain ratios (p 0.708 for the score and = 0.698 for the ratio) in the study done by Farasat et al. on 27 lesions (2 in the sub-mandibular salivary gland and 25 in the parotid, with 20 benign and seven malignant) [13]. However, this study's small number of malignant lesions could impact the results.

The strain ratio in this study demonstrates a statistically significant difference ($p<0.0001$) between benign and malignant lesions.

In concordance with our results, Ghajarzadeh et al. reported that sonoelastography had a pooled sensitivity of 63% and a pooled specificity of 59% for distinguishing between benign and malignant salivary gland tumors [14]. However, the current study revealed a significantly higher specificity of 85.2% and sensitivity of 100%.

Another recent assessment of the literature by Zhang Y et al. found that sonoelastography had a pooled specificity of 0.64, sensitivity of 0.67, and an AUC of 0.77 after examining 10 studies with a total sample size of 725 salivary gland lesions [15]. On the other hand, the current study demonstrates that the strain ratio of >2.1 has higher diagnostic accuracy than the study by Zhang Y et al., with a specificity of 92.6%, a sensitivity of 85.7%, and an AUC of 0.92 ($p<0.0001$).

Limitations:

Enrolling a limited number of patients from a single recruiting medical center limits this study. Thus, future prospective multicenter trials with a larger sample size are required to verify our results.

Conclusions:

This study concluded that sonoelastography is a non-invasive, available, radiation-free, and cost-effective technique that can detect malignant major salivary gland lesions. However, standard clinical practice still requires imaging-guided needle biopsy and histopathological examination to distinguish benign from malignant salivary gland lesions.

List of abbreviations:

IQR: Interquartile range

SPSS: Statistical Package for the Social Sciences

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