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Assessment of parotid gland masses with B-mode ultrasonography and strain elastography findings

Parotis bezi kitlelerinin B-mod ultrasonografi ve strain elastografi bulguları ile değerlendirilmesi

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Abstract

Aim: Ultrasound elastography (USE) has been found useful in differentiation between malignant and benign lesions of various tissues, such as the thyroid, breast, lymph node and prostate, however, there is limited data on the parotid gland. The aim of this study is to assess the diagnostic performance of B-mode ultrasonography (US) and USE findings in differentiating between benign and malignant parotid gland masses. A secondary goal is to evaluate results for the most frequent benign lesions.

Methods: In this cross-sectional study, 57 masses in 48 patients were evaluated. 2 radiologists examined each patient. B-mode US (size, contour, skin depth, internal structures, calcification, cystic component) and USE (a semiquantitative value strain index (SI)) findings were noted. We considered each feature individually. All patients underwent fine needle aspiration cytology (FNAC) and surgical resection.

Results: 50 masses were benign and 7 were malignant. Among B-mode US results, contour irregularity was found to have the highest accuracy (85.7%) in differentiating malignant lesions. When USE findings were considered, intra-observer agreement was moderate to fair and interobserver agreement was moderate. Malignant masses had mildly high SI scores. There was a wide range overlap between malignant and benign lesions. There was no statistically significant difference (P=0.422) and we could not attain a reliable SI cut-off value.

Conclusion: Despite the promising results of USE in breast and thyroid lesions, conventional US findings and FNAC are still the primary diagnostic tool to evaluate parotid lesions.

Keywords: Ultrasound elastography, Strain elastography, Strain index, Parotid gland

Öz

Amaç: Ultrason elastografi (USE) tiroid, meme lenf nodu ve prostat dokularının benign ve malign lezyonlarının ayrımında kullanışlı bulunmuştur. Bununla birlikte parotis bezindeki kullanımında sınırlı data mevcuttur. Biz bu çalışmada parotis bezi lezyonlarında benign malign ayrımında B-mod ultrasonografi (US) ve USE bulgularının tanısal performansını değerlendirmeyi amaçladık. İkincil hedef olarak da en sık rastlanan benign parotis bezi lezyonlarını kendi içerisinde değerlendirmeyi hedefledik.

Yöntemler: Bu kesitsel çalışmada 48 hastada 57 lezyon değerlendirilmeye alındı. Her hasta iki radyolog tarafından muayene edildi. B-mod US (boyut, kontur, ciltten derinlik, içyapı, kalsifikasyon, kistik komponent) ve USE (gerinim oranı olarak belirtilen yarı nicel değer) bulguları not edildi. Her bulgu ayrı ayrı değerlendirildi. Her hastaya ince iğne aspirasyon biyopsisi ve sonrasında cerrahi rezeksiyon uygulandı.

Bulgular: Lezyonların 50'si benign, 7'si malign olarak patolojik tanı aldı. B-mod ultrason bulguları dikkate alındığında düzensiz kontur özelliğinin malign lezyonların ayrımında en yüksek doğruluk oranına (%85,7) sahip olduğu görüldü. USE bulguları değerlendirildiğinde gözlemciler içi uyum orta-ortanın altında; gözlemciler arası uyum ise orta olarak saptandı. Malign kitleler benign olanlar ile kıyaslandığında hafif daha yüksek gerinim oranı değerlerine sahip olmakla birlikte istatistiksel olarak anlamlı fark tespit edilmedi (P=0,422) ve güvenilir bir eşik değer saptanamadı.

Sonuç: USE ile meme ve tiroid lezyonlarındaki umut verici sonuçlar elde edilmesine rağmen parotis kitlelerinin değerlendirilmesinde konvansiyonel US bulguları ve ince iğne aspirasyon biyopsisi hala temel tanı aracı olarak geçerliliğini sürdürmektedir.

Anahtar kelimeler: Ultrason elastografi, Strain elastografi, Gerinim oranı, Parotis bezi

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Introduction

Malignant or benign type of histology, superficial or deep localization of the tumor and differentiation between Warthin tumor and pleomorphic adenoma in benign tumors defines the type of the surgical approach [1]. Although FNAC is considered the gold standard in diagnosis, its sensitivity and specificity varies within a wide range, between 57-98% and 56-100% respectively, with an accuracy of 78-98% [2,3]. Ultrasonography (US) and magnetic resonance imaging (MRI) are the main non-invasive imaging techniques for the evaluation of parotid gland masses. Despite the fact that US and MRI characteristics of parotid lesions are already known, there is notable overlap in imaging findings [4,5]. Therefore, additional methods are needed. USE is an imaging technique based on the evaluation of the differences in tissue stiffness [6,7]. The method was found especially useful in differentiation of malignant and benign breast masses and thyroid nodules [8-12]. The current data regarding the use of this method in the parotid gland is limited. Our aim in this study is to compare strain elastography and B-mode US findings in differentiating between malignant and benign lesions of the parotid gland, and our secondary aim is to evaluate our results for differentiating between pleomorphic adenoma and Warthin tumor, which are the most frequently encountered benign tumors.

Materials and methods

Study design and patient selection

Patients who were diagnosed with intraparotid masses following clinical examination and radiological imaging for the first time, who were between the ages of 18-80 and had no previous surgical intervention were included in this study. Patients with recurring symptoms, extraparotid masses and those younger than 18 or older than 80 years were excluded. Our study was approved by the ethics review committee in accordance with the Declaration of Helsinki. All patients signed an informed consent.

Technique

Two experienced radiologists performed sonographic examinations in a dimly lit room. Patients were evaluated for both parotid glands while lying in supine position with their necks hyperextended. US and USE were performed with the same equipment, using a 17.5 MHz linear probe with elastography software (IU22 digital ultrasonography Philips, Bothell, Washington, USA). B-mode US and sonoelastography images of all cases were obtained. B-mode examination was performed first and size, contour, skin depth, internal structures, calcification, cystic component features of the masses were noted. USE examination followed, using the same transducer in elastographic mode for obtaining real time elastography images. Transducer was held perpendicular to the skin. Minimal compression was applied by the aid of pressure indicator located to the right side of the screen to improve intra and interobserver agreement. Elastograms were located to the right side of the screen and corresponding B-mode images were on the left. Examination frame including the whole mass and surrounding normal parotid tissue was adjusted. Depending on the degree of their stiffness, tissues were color-coded in red and blue with corresponding soft and hard areas with a colorimetric scale. A region of interest (ROI) circle was placed in the area thought to be the stiffest part of the mass while avoiding cystic parts and calcifications. Another ROI with the same diameter was placed at the same depth in the normal parotid tissue. The software assessed a semiquantitative value for SI within the ROI. Both radiologists reviewed two USE images of each mass. A total of four measurements were recorded for each lesion. The highest SI value was defined as SI_{max} after evaluation by each observer both individually and together (Figures 1-3).

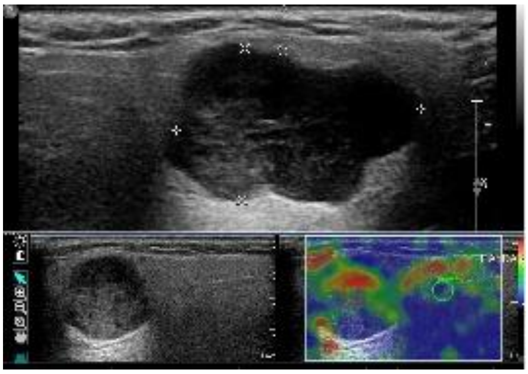

Figure 1: Hypoechogenic solid lesion with lobulated contours and posterior enhancement (SI value: 5.34. Mass is diagnosed as Pleomorphic Adenoma with FNAC.)

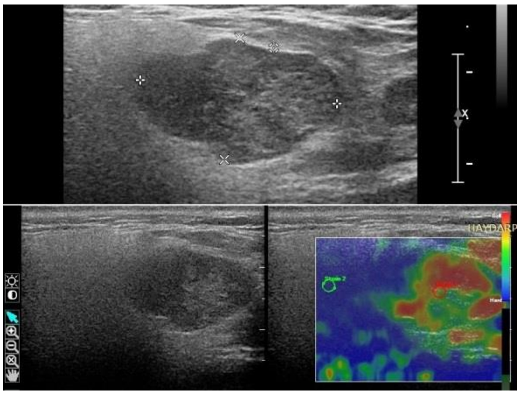

Figure 2: Well-defined hypoechoic lesion with internal microcystic spaces (SI value: 7.86, diagnosed as Warthin Tumor with FNAC.)

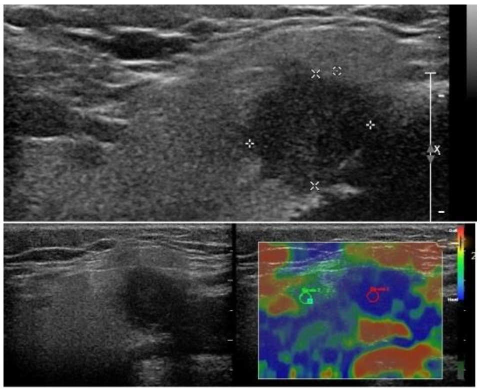

Figure 3: Ill-defined heterogeneous mass lesion with irregular contours (SI value: 2.58, diagnosed with mucoepidermoid carcinoma by FNAC.)

Histopathological diagnosis

The cytopathologist blinded to radiological findings evaluated FNAC. Each patient diagnosed on basis of pathologic examination underwent surgical resection.

Statistical analysis

Descriptive statistics were used to define the characteristics of the continuous variables (mean (standard deviation (SD)) and minimum-median-maximum). Independent and normally distributed two continuous variables were compared with the Student's t-test, while independent and non-normally distributed variables were compared using the Mann

Whitney U test. Chi-square or Fisher's Exact test were used to summarize the relations between categorical variables. To determine intraobserver and interobserver agreement degree, weighted kappa statistics were used. Interpretation was as follows: <0.00 poor agreement, 0.00–0.20: slight agreement, 0.21–0.40: fair agreement, 0.41–0.60: moderate agreement, 0.61–0.80: substantial agreement, and 0.81–1.00: excellent agreement [13]. P<0.05 was considered statistically significant. Analyses were performed with MedCalc Statistical Software version 12.7.7 (MedCalc Software bvba, Ostend, Belgium; http://www.medcalc.org 2013) program.

Power analysis was performed with G*Power 3.1.9.4 software. The power of this data was calculated as $1-\beta=0.82$ with $n1=50$, $n2=7$, $\alpha=0.05$ and an effect size of $d=1.05$.

Results

Forty-eight patients (24 females, 24 male) were included in the study. Age range was between 15-87 years (53 (15.5)). Two patients were excluded from the study due to the lack of a reliable elastographic measurement: The first case had a mass located 15mm deep from the skin surface with half of the lesion extending behind the mandible. The second case had a 4x4 cm mass protruding from skin surface, both of which prevented accurate elastographic examination.

Among 57 masses, 50 masses (87.7%) were benign and 7 masses (12.3%) were malignant. Histological subtypes included 2 lymphomas (3.5%), 5 basal cell adenomas (7.1%), 1 oncocytoma (1.7%), 1 large cell undifferentiated carcinoma (1.7%), 1 granuloma (1.7%), 1 hemangioma (1.7%), 1 metastasis (1.7%), 2 mucoepidermoid carcinomas (3.5%), 1 high grade acinic cell carcinoma (1.7%), 17 pleomorphic adenomas (29.8%), and 25 Warthin tumors (43.8%). FNAC results were confirmed after examination of the whole resection specimen.

Short axes of masses ranged from 4 mm to 37 mm (: 15 (6.8) mm) while long axes ranged from 8 to 45mm (: 15 (6.8) mm). Skin depth of the lesions ranged between 2 mm and 9 mm (: 3 (1.5) mm).

46 (95%) patients had unilateral, and 2 (5%) patients had bilateral (one basal cell adenoma, one Warthin tumor) masses. 39 patients (81.9%) had single, and 9 patients (18.1%) had multiple masses (8 Warthin tumors, 1 lymphoma).

During B-mode ultrasonography, contour, tumor size, internal structure, cystic component, calcification features were noted for each mass (Table 1).

Contour irregularity was the most useful parameter among all B-mode sonography findings (sensitivity 28.5%, specificity 93.8%, accuracy 85.7%) in differentiating between benign and malign masses (Table 2). Heterogeneity of internal structure wasn't found useful in differenting malignant masses (sensitivity 57.1%, specificity 44.1%, accuracy 46%) from benign ones. We observed calcification in both malignant (one high grade acinic cell carcinoma, one metastasis) and benign (two Warthin tumor) masses.

In differential diagnosis of the most frequent benign masses, contour lobulation of the pleomorphic adenoma and the presence of the cystic component in the Warthin tumor were evaluated (Table 3).

Following the B-mode examination, two radiologists recorded two sonoelastography measurements from each lesion. Upon consideration of SI_{max} values, intraoberserver agreement was moderate for the first (0.532) and fair for the second observer (0.375), and interobserver agreement was moderate (0.481).

The SI_{max} data from the elastography measurements were evaluated individually and together for each observer. Malignant masses showed mildly higher elastography scores than benign masses, which were statistically insignificant (Table 4).

Among malignant masses, large cell undifferentiated carcinomas showed the highest SI value (6.91), followed by lymphomas (4.6 (0.8)), mucoepidermoid carcinomas (3.97 (2,1)), metastases (3.9), and high grade acinic cell carcinoma (2.11).

Pleomorphic adenoma and Warthin tumor were the most common benign masses evaluated by USE. No reliable cut-off value could be demonstrated (P=0.990).

Table 1: B-mode US features of the masses

Feature	Benign n=50 Pleomorphic adenoma n=17	Warthin tumor n=25	Others n=8	Malignant n=7
Contour				
Regular	6	22	5	5
Lobulated	8	2	0	0
Irregular	1	1	1	2
Internal structure				
Homogenous	9	10	0	3
Heterogeneous	5	13	6	4
Cystic component				
Present	2	23	5	5
Absent	13	2	1	2
Calcification				
Present	0	2	0	2
Absent	17	23	8	5

Table 2: Diagnostic performances of irregular contour and heterogeneous internal structure (PPV: positive predictive value, NPV: negative predictive value, CI: confidence interval)

Feature	Sensitivity % (CI)	Specificity % (CI)	PPV % (CI)	NPV % (CI)	Accuracy %
Irregular contour	28.5 (3.67-70.96)	93.8 (83.16-98.72)	40 (11.82-76.83)	90.2 (85.14-93.66)	85.7
Heterogeneous internal structure	44.1 (29.08-60.12)	57.1 (18.41-90.10)	86.3 (71.64-94.07)	14.2 (7.68-25.03)	46

Table 3: Diagnostic performances of lobulated contour and cystic component in benign masses (PPV: positive predictive value, NPV: negative predictive value, CI: confidence interval)

Feature	Sensitivity % (CI)	Specifity % (CI)	PPV % (CI)	NPV % (CI)	Accuracy %
Lobulated contour	47 (22.98-72.19)	95 (83.08-99.39)	80 (48.61-94.42)	80 (72.84-86.92)	80.7
Cystic component	92 (73.97-99.02)	55.1 (35.69-73.55)	63.8 (53.76-72.92)	88.8 (67.04-96.92)	72.2

Table 4: USE SI_{max} score of benign – malignant lesions

	Biopsy	Mean (SD)	Range	*P*-value
Observer 1 SI_{max}	Malignant	5.5 (1.9)	2.4- 8.1	0.961
	Benign	5.5 (2.3)	1.1-11.1	
Observer 2 SI_{max}	Malignant	6.2 (2.6)	2.4-9.3	0.645
	Benign	5.8 (2.6)	2.1-13.2	
SI_{max} within two observers	Malignant	7.3 (1.6)	5.6-9.3	0.422
	Benign	6.6 (2.5)	2.1-13.2	

Discussion

A non-invasive, easily applicable, cost-effective, and repeatable method with high sensitivity, ultrasonography is the first step imaging method in the examination of the parotid gland pathologies [14,15]. However it has a low accuracy in differentiating between benign and malignant lesions [16]. Therefore, new diagnostic methods are under investigation. USE is a newly developed qualitative - quantitative reflective imaging method evaluating tissue stiffness. Theoretically malignant tissues are stiffer than the benign tissues. USE has been found useful for differentiating between malignant and benign nodules for breast, thyroid, prostate tissues. There are also a limited number of studies evaluating lymph nodes and pancreas by USE [17-21].

There are studies using different methods of USE to measure tissue stiffness of parotid gland masses [8,22-25]. Bathia et al. used shear wave elastography as a quantitative method of USE to assess parotid masses. They found that SWE values of benign masses (18.3 (6) kPa) significantly overlap with malignant masses (13.5 (4.6) kPa), and that pleomorphic adenomas (22.5 (12.4) kPa) have higher SWE values than Warthin tumors (16.9 (4.8) kPa). In conclusion, they stated that according to the pathologic subtypes, parotid masses have wide range of overlap in the SWE values, which limits SWE use in routine practice to exclude malignancy [24].

Another study conducted on 65 salivary gland masses classified tissue stiffness with elastography score (ES) points between 1 – 4 relative to adjacent normal salivary gland parenchyma. They found that pleomorphic adenomas are stiffer than Warthin tumors and all primary malignant masses had 4 points, while noting the presence of many ES 4 lesions among benign ones. In conclusion, they emphasize that USE is an adjunctive technique in differential diagnosis between benign and malignant masses, but not a primary tool [8].

Yerli et al. examined 36 patients and assessed masses with a 4-point modified Itoh scoring system. They reported that benign masses (n:28) had a score between 1 and 4 and malignant masses (n:8), between 2 and 4. They considered masses scoring between 1 and 2 points as benign, and 3 and 4 as malignant, and found that 64.2% of benign masses were correctly identified. In their study, 10 patients had false positive malignant results [26].

Another study by Celebi et al. [27] included 81 masses in 75 patients, and correctly identified 30 of 49 benign masses and 19 of 32 malign masses using the 4-point scoring system. They determined that pleomorphic adenoma, Warthin tumor, adenoid cystic carcinoma and high-grade tumors had lower scores while low grade tumors (like mucoepidermoid carcinoma), acinic cell cancer, metastasis and basal cell adenocarcinoma had higher scores.

Cantisani et al. [22] evaluated 63 masses prospectively by B-mode US, colored Doppler US (CDUS) and USE. The noted findings for B-mode sonography were contour, echogenicity, and the presence of a capsule, for CDUS, central or peripheral vascularization and for USE, elasticity contrast index (a semiquantitative stiffness evaluation method). The evaluation of B-mode and CDUS results together yielded an accuracy of 61.8%, while the evaluation of ECI results alone with a 3.5 cut-off value yielded an accuracy of 90.3%. There was no statistically significant difference when conventional and USE finding criteria were compared.

Recently a meta-analysis published by Zhang et al. [28] evaluated the role of USE in the assessment of parotid masses, in which ten studies consisting of 711 patients with 725 parotid masses were included. They reported a pooled sensitivity and specificity of 67% and 64%, respectively. Heterogeneity was observed due to assessment method. Quantitative and semiquantitative methods showed higher pooled results compared to qualitative methods. Finally, they concluded that USE has limited and unsatisfactory value in the differential diagnosis between benign and malignant parotid masses.

In our study we evaluated 57 masses (benign: 50, malignant: 7). 17 of the benign masses were pleomorphic adenomas and 25 were Warthin tumors. 4 were primary and 3 were secondary salivary gland masses. The distribution of the malignant masses was consistent with the literature, but the rate of Warthin tumor was higher in our study compared to previous studies [14,29-31].

A well-defined contour on B-mode can be used with high accuracy as a benignity criterion, however, the homogenous inner structure can be observed in malignant lesions as well as benign lesions. Malignant masses also showed calcification that is normally expected in benign masses like hemangioma or vascular malformations. Strain elastography by means of SI was used as a semiquantitative USE method in assessment of parotid masses. We considered each observer's results both individually and together yet could not find a reliable threshold value for differentiating between benign and malignant masses.

The inner structure of malignant breast and thyroid lesions are relatively homogenous. The four-point semiquantitative scoring system was found useful in these tissues. On the contrary, parotid gland neoplasms show marked heterogeneity when histologic subtypes are analyzed. In adenoid cystic carcinoma and mucoepidermoid carcinoma (the most commonly encountered malignant tumors) soft and hard tissues coexist. So higher points (3 – 4) were rarely observed in malignant lesions of the parotid gland. For the above stated reasons, adapting this semiquantitative scoring system to parotid gland lesions was not considered suitable [18,20,32].

Technical aspects that can lead to difficulties and limitations are important in elastography imaging. Parotid gland is superficially located under the skin. Large, protruding lesions may be problematic to examine and get reliable elastography measurements because it's hard to adopt the transducer. Freehand compression, which was used to generate elastograms, presumably creates some subtle tissue displacement. We excluded one patient from our study with a mass located 15mm deep to the skin extending posterior to the mandible because no reliable measurement could be obtained. These controversies may explain why intra-observer agreement is fair-moderate and interobserver agreement is moderate in our study, unlike previous breast and thyroid studies.

Limitations

Our study has limitations. The prevalence of malignant lesions was consistent with the literature, but the number of primary parotid gland malignancy cases were limited. We considered each B-mode and USE features independently while assessing the lesions and did not include CDUS features. Combination of these features may improve diagnostic accuracy. Strain elastography is a semi-quantitative and operator-dependent method that influences intra/interobserver agreement.

Conclusion

Parotid gland lesions are suitable for elastography studies due to their superficial location. Differentiating between benign and malign cases is the key point to decide the choice of treatment. In our study we conclude that strain elastography is not a reliable tool to differentiate benign from malignant masses since there is a wide range overlap. While pleomorphic adenomas containing rigid fibrous tissue are expected to have high SI values, upon evaluation of histological subtypes, no significant association between pleomorphic adenomas and malignant lesions or Warthin tumors were observed. We conclude that in daily practice and algorithm, conventional US findings along with FNAC remain the diagnostic tool to assess parotid gland lesions.

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