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Diagnostic Accuracy of Triplex Ultrasound in Malignant Parotid Tumors

Background/Objective: The gray scale sonography (GSS) in initial studies and color Doppler sonography in more recent studies have been used for evaluation of parotid tumors. The objective of this study is to evaluate the validity of triplex sonography, *i.e.*, GSS, color Doppler mapping (CDM) and spectral Doppler sonography (SDS) to differentiate the malignant from benign parotid tumors.

Patients and Methods: Fifty parotid tumors were evaluated. On GSS the tumor margin was evaluated and divided into "well-defined" and "ill-defined." On CDM, tumors vascularity was divided into two groups of "hypovascular" ($\leq$2 arteries) and "hypervascular" (>2 arteries). On SDS, the peak systolic velocity (PSV) of tumor arterial blood flow was measured. The diagnostic indices (sensitivity, specificity, positive predictive value and negative predictive value) of GSS, CDM and SDS findings alone and in combination were calculated, considering the histopathology results as the gold standard. For PSV, we used the receiver operating characteristic (ROC) curve analysis and calculated the area under the ROC curve.

Results: After excisional biopsy and histopathologic examination, 18 out of 50 tumors were malignant and 32 were benign. The sensitivity and specificity of the GSS was 77.8% and 90.6%, respectively. These diagnostic indices for CDM were 83.3% and 87.5%, respectively. The mean$\pm$SD PSV was significantly higher in malignant tumors than in benign ones (40.1$\pm$9.9 *vs* 19.1$\pm$4.9 cm/s) ($p<0.0001$). For PSV, the area under the ROC curve was 0.98; with a cut-off point of $\geq$24 cm/s; the sensitivity was 100% and the specificity was 81.2%. With a cut-off point of $\geq$29 cm/s for PSV, the sensitivity was 83.3% and the specificity was 100%. Using a cut-off value of 27.5 cm/s for PSV, the sensitivity and specificity of this modality for differentiation of malignant tumors were 88.9% and 96.9%, respectively. Combining the results of triplex sonography in a scoring system showed a little improvement in the diagnostic indices.

Conclusion: The PSV alone and combination of the GSS, CDM and SDS findings are sensitive and specific methods in differentiation of malignant parotid tumors from benign diseases.

Keywords: parotid neoplasms, ultrasonography, doppler, color, diagnostic tests.

Introduction

Eighty percent of the salivary gland tumors originate in parotid glands. The pathologic nature and diagnosis of these tumors are made by histopathologic examination, after fine needle aspiration (FNA), biopsy or resection of the tumor.

Since more than a decade, sonography has been recognized as a reliable imaging modality for evaluation of neck tumors including those of the salivary glands.[1-12] Some authors suggest that sonography could be the first-line imaging modality for evaluation of salivary gland pathologic processes.[7,10,11] In some studies, the accuracy of the gray scale sonography (GSS) has been reported 100% for detection of parotid tumor.[7-9,11,12]

To avoid invasive and painful diagnostic procedures, many researchers have evaluated the ability of sonography to differentiate the malignant from benign parotid tumors.

In initial studies, differentiation of malignant from benign parotid tumors was

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based on the evaluation of tumor size, echo texture, posterior enhancement and margin on GSS.[1-13] For these findings, an accuracy of 76% has been reported.[10] Among the mentioned GSS characteristics of tumors, the margin has been reported to be more sensitive than the other factors. In fact, the most malignant tumors were reported to have ill-defined margins.[7]

In more recent studies, researchers have evaluated the value of color Doppler sonography (CDS) for this purpose.[14-17] In these studies the tumor vascularity was evaluated by color Doppler mapping (CDM), the peak systolic velocity (PSV) and resistance index (RI) were evaluated by spectral Doppler sonography (SDS). In comparison to GSS alone, the specificity reported to be increased, but the sensitivity has not been improved.[15]

The objectives of this study are evaluation of the diagnostic efficacy of the GSS, CDM and SDS (in terms of PSV) alone and also to verify whether the combination of these modalities (GSS, CDM and SDS that are known as "triplex Ultrasound") could increase the ability of sonography to differentiate the malignant from benign parotid tumors.

Patients and Methods

This cross-sectional study was performed from November 2003 to November 2005, in the Departments of Otolaryngology and Radiology of Amir Aalam Hospital, Tehran, Iran.

All patients presented with parotid mass were considered to enter the study. Among these patients, those with signs and symptoms of inflammatory process (e.g., tenderness, warmness, redness and fluctuation) were excluded from the study. Therefore, all patients with parotid mass without the clinical findings of inflammatory process were included. Some of patients were also excluded from the study for the following reasons:

-Patients who refused to be investigated.

-Those with masses which had previous definite histopathologic diagnosis and that the radiologist was not blind to the nature of the mass.

- Inappropriate angle of Doppler interrogation due to tumor arterial tortuousity

Triplex Ultrasound consisted of gray scale sonography (GSS), color Doppler mapping (CDM) and spectral Doppler sonography (SDS) was performed for all the included patients by a radiologist experienced in neck Ultrasonography, using an Alloka SSD 1700 system (Japan) with a 7.5-MHz linear transducer. Angle of Doppler interrogation was between 55 and 65 degrees.The radiologist was blind about the clinical and probable histological results of the patients achieved by needle aspiration.

On GSS, the parotid tumor margin, as the most sensitive gray scale finding,[7] was evaluated; based on the margin, the tumors were classified as "well-defined" and "ill-defined." A well-defined tumor was defined as tumor that its margin can entirely and precisely be differentiated all around from the peripheral sonographic normal parotid tissue. All masses without this feature were considered ill-defined.

On CDM, the parotid tumor vascularity was considered as the main factor. The degree of vascularity in a single field of view (FOV) = 2×2 cm and a sampling gate of 3 mm were classified as hypovascular (≤2 arteries) or hypervascular (>2 arteries).

On SDS, the PSV value of the artery or arteries detected within the parotid tumor was measured. Among the tumors with more than one artery, the highest PSV value was considered.

All cases underwent surgery and the definite tissue diagnosis determined after the excisional biopsy was considered as the gold standard.

For each element of triplex Ultrasound, we calculated the diagnostic indices, i.e., sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of the test in differentiating the malignant from benign parotid tumors. Also for the PSV, we used the receiver operating characteristic (ROC) curve analysis. Then, we selected the best cut-off point of PSV in this ROC curve. For better differentiation of malignant from benign tumors, we considered a new scoring system consisting of all the gathered data of the three said elements of the triplex Ultrasound, i.e., GSS in terms of tumor margin, CDM in terms of vascularity and SDS in terms of selected PSV cut-off point. For GSS, the well-defined tumors were assigned as score 1 and the ill-defined tumors as score 2. Furthermore, in CDM, the hypervascular tumors were assigned as score 2 and hypovascular ones as score 1. According to this assumption, the

PSV values of equal or greater than the selected cut-off value were assigned as score 2 and the values lower than this cut-off value as score 1. Then, we add the scores of GSS, CDM and SDS for each patient and the total score calculated in all of them. Accordingly, the total score varied in range of 3 to 6. For assessment of this scoring system in differentiating the malignant from benign tumors, we had to categorize scores into two groups. This categorization was done in three methods:

A) The score of 3 representing benign tumors and scores of 4–6 representing malignant tumors.

B) The scores of 3 and 4 representing benign tumors and scores of 5–6 representing malignant tumors.

C) The scores of 3–5 representing benign tumors and score of 6 representing malignant tumors.

The results were then analyzed by SPSS software version 11. A $p<0.05$ was considered as statistically significant.

Results

A total of 88 patients were initially considered as having non-inflammatory parotid masses. Of these patients, 38 were excluded for the above-mentioned criteria leaving 50 patients in the study. Of these patients, 30 (60%) were male and 20 (40%) were female. The mean±SD age of the patients was 44.0±17.8 (range: 3-71) years.

Totally, we had 32 (64%) patients with benign parotid tumors; 23 (46%) of them had pleomorphic adenoma, six (12%) had warthin's tumor, one (2%) had hemangioma, one (2%) histiocytoma and another one (2%) had schwanoma.

We had also 18 (36%) patients with malignant parotid tumors; 11 (22%) had mucoepidermoid carcinoma, four (8%) pleomorphic carcinoma, one (2%) adenoid cystic carcinoma, one (2%) metastatic melanoma and another one (2%) had metastatic adenocarcinoma with unknown origin.

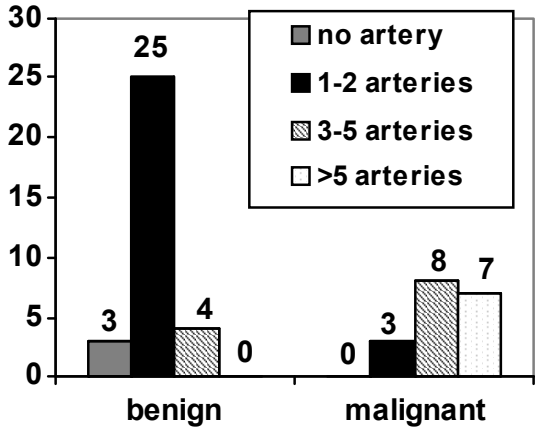

Fig. 1. Number of detected arteries in a single field of view in benign and malignan tumors.

While three (9%) patients of those with benign tumors had ill-defined margins, 14 (78%) of those with malignant tumors did so in GSS ($p<0.0001$). Therefore, the sensitivity and specificity of GSS for detection of malignant parotid tumors were 78% (95% Confidence Interval (CI)=52%-93%) and 91% (95% CI=75%-98%), respectively (Table 1). All four patients with malignant tumors and well-defined mar-

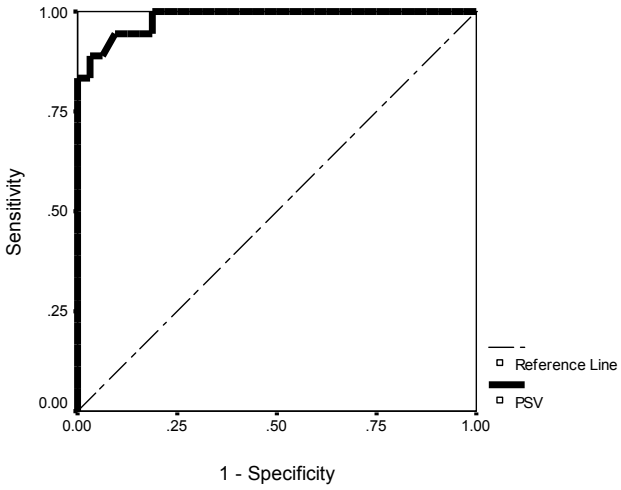

Fig. 2. ROC curve of PSV in differentiation of malignant from benign parotid tumors.

Table 1. Results of different elements of triplex sonography in differentiation of malignant from benign parotid tumors

	Sensitivity (95% CI)	Specificity(95% CI)	PPV(95% CI)	NPV(95% CI)
GSS*	0.78 (0.52-0.93)	0.91 (0.75- 0.98)	0.82 (0.57- 0.96)	0.88 (0.72- 0.97)
CDM**	0.83 (0.59- 0.96)	0.88 (0.71- 0.96)	0.79(0.54- 0.94)	0.90 (0.74- 0.98)
SDS(PSV)†	0.89 (0.65- 0.99)	0.97 (0.84- 0.99)	0.94 (0.71- 0.99)	0.94 (0.71- 0.99)

* According to tumor margin
** According to tumor vascularity
† Cut-ff value 27.5 cm/s

Table 2. Results of ROC curve assuming different cut-off values of PSV in detection of parotid malignant from benign tumors

Cut-off value cm/s	Sensitivity(95% CI)	Specificity(95% CI)	PPV(95% CI)	NPV(95% CI)
24	1 (0.81- 1)	0.81 (0.64- 0.93)	0.75 (0.53- 0.90)	1 (0.87- 1)
24.5	0.94 (0.72- 0.99)	0.81 (0.64- 0.93)	0.74 (0.52- 0.90)	0.96 (0.81- 0.99)
26	0.94 (0.72- 0.99)	0.91 (0.75- 0.98)	0.85 (0.62- 0.97)	0.97 (0.82- 0.99)
27. 5	0.89 (0.65- 0.97)	0.97 (0.84- 0.99)	0.94 (0.71- 0.99)	0.94 (0.80- 0.99)
29	0.83 (0.59- 0.96)	1 (0.89- 1)	1 (0.78- 1)	0.91 (0.77- 0.98)

Table 3. Calculated diagnostic indices for each categorization of the scoring system

Scoring System	Sensitivity(95% CI)	Specificity(95% CI)	PPV(95% CI)	NPV(95% CI)
Score[3/(4-6)]	1 (0.81-1)	0.84 (0.67- 0.95)	0.78 (0.56- 0.93)	1 (0.87- 1)
Score[(3,4)/(5,6)]	0.94 (0.73- 0.99)	0.94 (0.79- 0.99)	0.89(0.67- 0.99)	0.97 (0.83- 0.99)
Score[(3-5)/6]	0.56 (0.30- 0.78)	0.97 (0.84- 0.99)	0.91 (0.59- 0.99)	0.79 (0.64- 0.91)

gins had mucoepidermoid carcinoma.

Hypervascularity was seen in four (13%) patients with benign tumors, while it was seen in 15 (83%) of those with malignant tumors ($p<0.0001$). Therefore, the sensitivity and specificity of CDM for detection of malignant parotid tumors were 83% (95% CI=59%-96%) and 88%(95% CI=71%-96%), respectively (Table 1). Details of the tumor vascularity based on the number of detected arteries are shown in Figure 1.

The mean±SD PSV in benign tumors was 19.1±4.9 (range: 11.2–28.2) cm/s while it was 40.1±9.9 (range: 24.3–56.2) cm/s in malignant tumors ($p<0.0001$).

For evaluation of the PSV in detection of the malignant parotid tumors, we drew the ROC curve (Fig. 2). The area under the curve was 0.98 ($p=0.014$; 95% CI: 0.96–1.01). The diagnostic indices of different PSV cut-off values are presented in Table 2.

Considering a cut-off value of 24 cm/s for PSV for differentiating malignant from benign parotid tumors, we had a sensitivity of 100% and a specificity of 81.2%; considering a cut-off value of 29 cm/s yielded a sensitivity of 83.3% and a specificity of 100% (Table 2). Using a cut-off value of 27.5 cm/s, one (3%) patients with benign tumor had a PSV >27.5 cm/s while 16 (89%) patients with malignant tumors had a PSV ≥27.5 cm/s ($p<0.0001$). Therefore, the sensitivity and specificity of PSV ≥27.5 cm/s for differentiating of malignant from benign parotid tumors were 89% and 97%, respectively (Table 2).

Based on the scoring system described earlier, the calculated diagnostic indices for each of these three categorizations are shown in Table 3.

Discussion

In this study, we conducted several sonographic diagnostic modalities to evaluate the diagnostic accuracy of them individually and compare these methods together to select the best method for differentiation of malignant from benign parotid tumors. As it was shown, GSS was a moderately efficient method for this purpose. Of course, the sensitivity of GSS in terms of tumor margin was not acceptable for screening of parotid masses. In fact, GSS misses about one-quarter of the parotid malignant masses which is clearly not acceptable. Shimizu, et al, in their study considered the boundaries of tumor in gray scale sonography for the differentiation of malignant parotid tumors.[18] They categorized the boundary of tumor into three classes of "very clear," "relatively clear" and "partially unclear." If the lesion had either a thin hyperechoic line on the anterior side or a capsule-like structure, it was considered as very clear. If a lesion showed no distinct thin hyperechoic line on the anterior side or showed no capsule-like structure, but no interruption of the contour, it was categorized as relatively clear and if the contour showed any interruptions, it was classified as partially unclear. According to this categorization, they found 12 out of 14 malignant tumors which did not have clear boundaries, if we consider the relatively clear and partially unclear as ill-defined tumors, their sensitivity of GSS for malignant tumors would be 71.2% that is relatively similar to the sensitivity of 77.8% found in our study.

Similarly, the CDM could not show an acceptable sensitivity and specificity in these patients (because of

a little higher sensitivity and lower specificity in comparison to GSS). Although the sonographic findings of GSS and CDM could help us in diagnosing malignant from benign tumors, their precisions are not so good.

By considering diagnostic indices of SDS in terms of PSV, we could see different results; in the PSV ROC curve, the area under the curve of 0.98 of PSV was excellent. Reviewing the indices at different cut-off values, could obviously show good discrimination ability of the PSV as a diagnostic test in malignant cases. In the case of PSV cut-off point of 24 cm/s, the sensitivity is 100%; this means that none of the malignant masses is missed in Doppler sonography and that if the highest arterial PSV of the mass is <24 cm/s, that mass would be benign (NPV=100%). With this cut-off value, the specificity is 80% that is fairly acceptable. Moving to upper cut-off points, the specificity increases and the sensitivity decreases, so that at a cut-off value of 29 cm/s the specificity reached to 100% and sensitivity reach to 91%. This means that if the PSV is >29 cm/s, the tumor should be considered malignant (PPV=100%).

Between these two cut-off values, we could see the cut-off value of 27.5 cm/s that showed an acceptable sensitivity and specificity of 89% and 97%, respectively.

These findings make the PSV as a highly-acceptable way of differentiating malignant from benign parotid tumors. Bradely, et al, studied seven malignant and 49 benign salivary gland tumors.[11] They found that the PSV was not different between malignant and benign tumors. This discrepancy could be due to some reasons: they assessed all salivary gland tumors; the mean age of their patients was about one decade greater than that of our patients and the number patients with malignant diseases in their series was low (7 vs 18 patients in our study) that might decrease their study power.

Combining the results of these three findings (GSS, CDM and SDS) in the scoring system as described in patients and methods section could yield a little better diagnostic ability, i.e., in the case of sensitivity equal to 100% for PSV (corresponding to a cut-off value of 24 cm/s) and the scoring system (scores in two categories of 3 and 4–6, PSV cut-off value of 27.5 cm/s), we could see 3% increase in specificity for the scoring system (81% vs 84%). This means that the scoring system could be better than the PSV alone in differentiation of malignant from benign parotid tumors. Considering that three elements of triplex ultrasound (GSS, CDM and SDS) in a single session are feasible, applying triplex ultrasound in the form of mentioned scoring system for parotid tumor evaluation could be recommended. To the best of our knowledge, we could not find any similar studies to combine results of triplex ultrasound in a scoring system. Some recent articles have reported that applying of sonographic contrast media could be promising and improve the accuracy of sonography to differentiate the malignant from benign parotid tumors by better appreciation of tumor vascularity.[19,20]

Performing studies with greater sample size would be of benefit to assess the results of this study.

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