ACTA FAC. MED. NAISS.

UDC 616.316-006-07

Original article

ACTA FAC. MED. NAISS. 2004; 21 (4): 205-213

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POTENTIALS OF COLOR DOPPLER SONOGRAPHY IN DIAGNOSIS OF PLEOMORPHIC ADENOMAS

SUMMARY

Aim of this study is to determine color Doppler characteristics of pleomorphic adenomas and possibilities of their differentiation from other salivary gland tumors.

This prospective study enrolled 52 patients with salivary gland tumors, who have been exemined by color Doppler sonography before surgical treatment. Examinations were made with 7.5 MHz linear probe with Doppler imaging. Intratumor vascularity was graded on a four step analog scale, and patterns of vascular distribution were characterized as peripheral (basket-like) or hilar (branching).

After surgical treatment and histopathologic verification, it was established that 28 patients (53.84%) had had pleomorphic adenomas. Fifteen patients (53.57%) had pleomorphic adenomas with the first grade, and 10 (35.71%) with the second grade of vascularity. Three patients (10.71%) did not have any presence of color Doppler signals, while there were no cases of third grade vascularity. As for the pattern of vascularity, pleomorphic adenoma demonstrated peripheral pattern of vascularity in 21 cases (75%).

A statistically significant difference ($p < 0.01$) was found in the patterns of vascularity between the pleomorphic adenoma and other histological types of salivary gland tumors. All pleomorphic adenomas had low or medium grade of vascularity.

Our experience suggests that color Doppler sonography is a sensitive method in diagnosis of pleomorphic adenoma. On the basis of the grade and pattern of vascularity, it is possible to distinguish, with great certainty, pleomorphic adenomas from other salivary gland tumors.

Key words: **color Doppler, pleomorphic adenoma, salivary gland tumor**

INTRODUCTION

The incidence of salivary gland tumors ranges from 0.2 to 0.6% of all tumors in human pathology, ie. 3% od all tumors of the head and neck region, skin tumors being excluded.

The most common tumor of the salivary glands is pleomorphic adenoma (mixed benign tumor) and in relation to all salivary gland tumors it occurs in about 46% of the cases. In over 80% of the cases it occurs in the parotid gland (1). It may occur in all age groups, but it is the most frequent in the 5 decade (2). It has slow evolution, sometimes lasting for several years.

Except for its tendency toward relapsing in up to 10% of the cases, pleomorphic adenoma is the only benign tumor of the salivary glands showing the tendency toward malignant alteration in about 55% of the cases. Different authors reported it from 2% to 10% (3–6).

Malignant alteration is noticed in tumors with long evolution and in older age. Hereby carcinoma occurs in pleomorphic adenoma.

AIM

Aim of this study is to determine color Doppler characteristics of pleomorphic adenoma and the possibility of their differentiation from other tumors of the salivary glands using color Doppler sonography.

PATIENTS

The study enrolled 52 patients with the tumors of big salivary glands. It was performed in the period of 6 years at the Institute of radiology, Clinical Center Nis. Color Doppler examination was performed before surgical treatment and after that histopathologic verification of the removed tumors was done. The average age of the patients was 57 (18–89). The largest number of the patients was in the group of 52 to 59 years (figure 1).

Out of the total number of the patients there were 39 men and 13 women. Thirty four men and 10 women had tumors of the parotid glans, whereas 5 men and 3 women had submandibular tumors (figure 2).

Out of the total number of the tumors there were 42 benign (80.77%) and 10 malignant tumors (19.23%). Out of benign tumors 37 were present in the parotid and 5 in submandibular gland, while out of the malignat tumors, 7 were present in the parotid and 3 in submandibular gland (table 1). Histopathologically, it was determined that out of the total number of the tumors there were 28 pleomorphic adenomas or 53.84% (table 2).

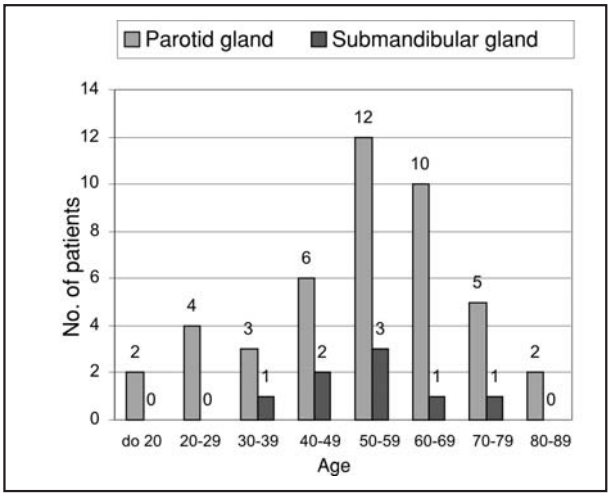

Figure 1. Age distribution of the patients with salivary gland tumors

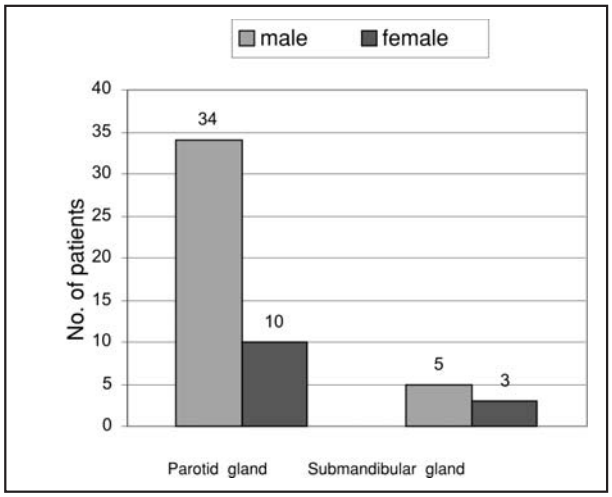

Figure 2. Sex distribution of the patients with salivary gland tumours

Table 1. Distribution of benign and malignant salivary gland tumors per each gland separately

Tumor type	Parotid gland	Submandibular gland	Total
Benign	37	5	42 (80.77%)
Malignant	7	3	10 (19.23%)
Total	44 (84.62%)	8 (15.38%)	52 (100.00%)

Table 2. Distribution of histologic types of salivary gland tumors by patient numbers

Tumor histology	Number of patients	%
Pleomorphic adenoma	28	53.84
Adenolimphoma	11	21.15
Oncocytoma	2	3.84
Lipoma	1	1.92
Non-Hodgkin lymphoma	3	5.76
Adenocarcinoma	2	3.84
Mucoepidermoid carcinoma	1	1.92
Non-differentiated carcinoma	1	1.92
Acinic-cell carcinoma	1	1.92
Metastases	2	3.84
Total	52	100.00

METHOD

All the examinations were performed with Acuson 128 xp10 linear probe of high resolution (7,5 MHz) with Doppler imaging.

Doppler parameters were chosen to enable detection of weak signals in small blood vessels, with low velocity flows, which may occur in and around tumors.

Color gain was different and dynamic during examination in order to enhance color signals or to avoid overexcessive noise.

Intratumor vascularization seen on color Doppler sonograms was graded on the 4 grade analog scale (7) :

0 – without color Doppler signals
+ – occasional color signals, trensiently present in tumor tissue, and/or one feeding blood vessel visible in the hilus
++ – multiple color Doppler signals or feeding blood vessels present in tumor mass
+++ – big feeding blood vessels and large number of blood vessels easily detectable in tumor tissue.

Pattern, form or type of vascular distribution in the nodes were characterized as either peripheral (ring-like or basket-like) or hilar (branchy or punctative), depending on the appearance of tumor vascularization.

Doppler wave forms were estimated in salivary nodes by calculating the resistive index (RI) and systolic peak velocity of arterial flow (PSV).

Doppler sample of the volume is always adapted to the size of the blood vessel and it was 2 to 5 mm.

Doppler scale was adjusted to the flow velocity so that it gave no artefacts.

Statistical processing of the data was performed by means of Pearson-P2 for dependent frequencies (formation of zero and working hypothesis for the examination of the significance of the difference between the observed and empirical incidence). The differences between the middle values of the examined features were tested by t-test for small samples.

RESULTS

After operative treatment and histopathologic verification, it was determined that out of the total number of tumors there were 28 (53.84%) pleomorphic adenomas. The second most frequent tumor of the salivary glands was adenolymphoma (11 patients – 21.15%), table 3.

Out of the total number of pleomorphic adenomas, 3 (10.71%) were without the presence of color Doppler signals; 15 (53.57%) with the first (figure 3) and 10 (35.71%) with the second degree of vascularization (figure 4, table 3).

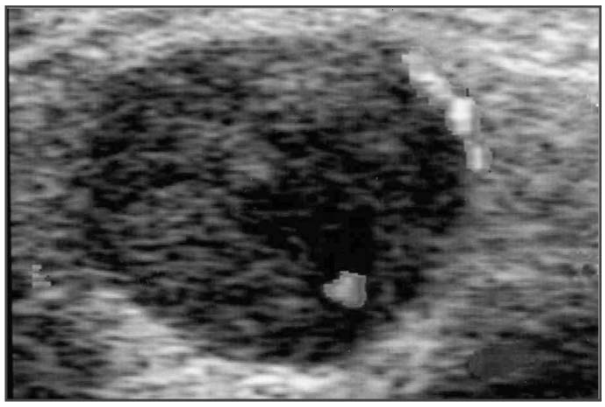

Figure 3. Pleomorphic adenoma with first degree and peripheral vascularisation

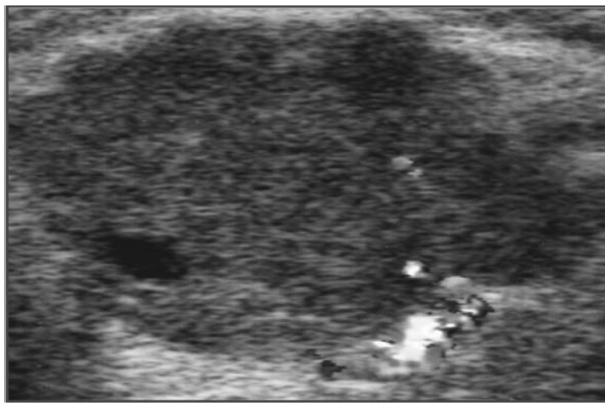

Figure 4. Pleomorphic adenoma with second degree and peripheral vascularisation pattern

Among adenolymphomas, which were in the second place according to the frequency, there were 2 (18.18%) without vascularization; 5 (5.45%) with first (figure 5); 3 (27.27%) with the second (figure 6) and 1 (9.09%) with third degree of vascularization (table 3).

As opposed to this, most malignant tumors had the domination of the first and third degree of vascularization (figure 7, 8; table 3). By application of P2 test it was found that benign and malignant tumors of the salivary glands had statistically significant difference, $p<0.001$.

In relation to the type of vascularization, statistical significance for $p<0.05$ between the group of benign and malignant tumors was determined. Peripheral type of vascularization was dominant in benign tumors and hilar type in malignant tumors (table 5).

In 21 (75%) cases, pleomorphic adenoma had peripheral (Fig. 3,4), and in 4 (14.28%) cases hilar type of vascularization. In 3 (10.71%) tumors there was no vascularization (table 6).

In contrast to this, adenolymphomas, which were on the second place according to the frequency of benign tumors, had hilar type of vascularization in 7 (63.63%) cases (figure 5, 6), and peripheral type in 2 (18.18%) cases (table 6). In 2 cases (18.18%), they were without vascularization.

Table 3. Distribution of the degree of vascularisation of particular histologic types of salivary gland tumors

Tumor histology	Number of patients	Vascularisation degree			
		0	+	++	+++
Pleomorphic adenoma	28(53.84%)	3(10.71%)	15(53.57%)	10(35.71%)	0
Adenolymphoma	11(21.15%)	2(18.18%)	5(45.45%)	3(27.27%)	1(9,09%)
Oncocytoma	2(3.84%)	1(50.00%)	1(50.00%)	0	0
Lipoma	1(1.92%)	1(100%)	0	0	0
Non-Hodgkin lymphoma	3(5.76%)	0	1(33.33%)	0	2(66.66%)
Adenocarcinoma	2(3.84%)	0	0	1(50.00%)	1(50.00%)
Mucoepider-moid Ca	1(1.92%)	0	0	0	1(100%)
Non-differentiated Ca	1(1.92%)	0	0	1(100%)	0
Acinic cell Ca	1(1.92%)	0	0	0	2(100%)
Metastases	2(3.84%)	0	0	0	2(100%)
Total	52	7(13.46%)	22(42.31%)	15(28.85%)	8(15.38%)

Table 4. Distribution of the vascularisation degree related to the type od salivary gland tumors

Tumor type	Number of patients	Vascularisation degree			
		0	+	++	+++
Benign	42(80.76%)	7(16.60%)	21(50.00%)	13(30.85%)	1(2.38%)
Malignant	10(19.24%)	0	1(10.00%)	2(20.00%)	7(70.00%)
Total	52	7(13.46%)	22(42.30%)	15(28.84%)	8(15.38%)

$x^2=28,97 \quad df=3 \quad p<0,001$

Table 5. Distribution of vascularisation type according to the type of salivary gland tumor

Tumor type	Number of patients	Vascularisation type	
		Peripheral	Hilar
Benign	35 (80.76%)	24 (57.14%)	11 (26.10%)
Malignant	10 (19.24%)	1 (10%)	9 (90.00%)
Total	45	25 (55.55%)	20 (44.44%)

$x^2=10,782 \quad df=3 \quad p<0,05$

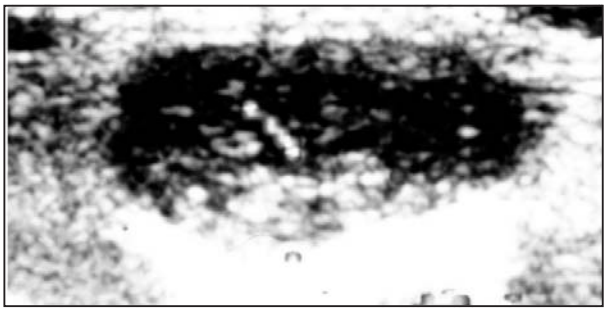

Figure 5. Adenolymphoma with first degree and hilar vascularisation pattern

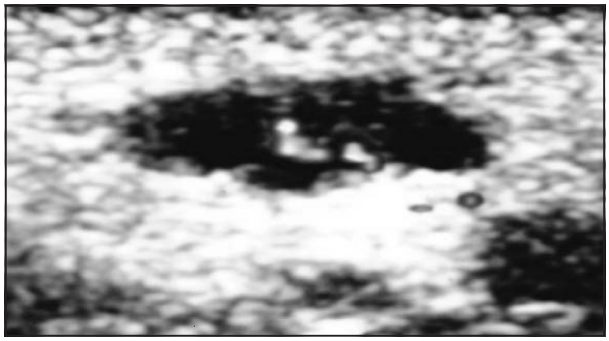

Figure 6. Adenolymphoma with second degree and hilar vascularisation pattern

By application of x^2 test it was found that pleomorphic adenoma and adenolymphoma had statistically significant difference $p<0.01$, which means that one can differentiate between pleomorphic adenoma and adenolymphoma on the basis of the type of vascularization (table 6).

The type of vascularization of pleomorphic adenoma in relation to other histological types of salivary gland tumors also gave statistically significant difference ($p<0.0l$), so that peripheral type of vascularization of pleomorphic adenoma may be considered pathognomonic (table 6).

On the basis of echosonographic appearance on gray sonographic scale, all the tumors are classified into 4 groups:

A – changes of solid appearance, round

B – changes of solid appearance, lobular

C – changes of solid appearance, poorly defined, infiltrant

D – changes of mixed, solid-cystic appearance.

It has been shown that pleomorphic adenoma is a change of solid, round appearance in 85.72% (figure 3), and in 14.28% a change of solid, lobular appearance (figure 4, table 7).

In 54,54% adenolymphoma was a change of solid, round appearance (figure 5, 6); in 27.27% change of solid, lobular appearance and in 18,18% change of mixed solid-cystic appearance (table 7).

By the application of x^2 statistical significance was not found in ultrasound appearance of A and B pleomorphic adenomas and adenolymphomas. This means that it is impossible to differentiate between these two types of tumors on the basis of ultrasound appearance (table 7).

Correlation of ultrasound appearance of the tumor and the degree of vascularization by the application of x^2 showed no statistical significance ($p>0.05$). This means that the degree of vascularization was not dependent on ultrasound appearance of the tumor (table 8).

According to the size, all salivary gland tumors were classified into 3 groups:

I – smaller than 2 cm

II – from 2 to 4 cm

III – larger than 4 cm.

It was established that 53.57% of pleomorphic adenomas were smaller than 2 cm; 35.71% were from 2 to 4 cm and 10.7l% were larger than 4 cm (table 9).

Comparing the size of pleomorphic adenoma and degree of vascularization, it was determined that the tumor size did not correlate with the degree of vascularization (table 10).

The correlation of the size of the pleomorphic adenoma and the type of vascularization also gave no statistical significance, ie. the type of vascularization did not depend on the size of pleomorphic adenoma.

Systolic peak velocity of arterial flow of pleomorphic adenoma ranged from 7 to 45 cm/sec; middle systolic peak velocity was about 15 cm/sec. The resistive index was from 0.45 to 0.75. There was no

Table 6. Distribution of vascularisation type of salivary gland tumors by histology

Tumor histology	Number of patients	Vascularisation type	
		Peripheral	Hilar
Pleomorphic adenoma	28	21(75.00%)	4(14.28%)
Adenolymphoma	11	2(18.18%)	7(63.63%)
Oncocytoma	2	1(50.00%)	0
Lipoma	1	0	0
Non-Hodgkin lymphoma	3	0	3(100%)
Adenocarcinoma	2	0	2(100%)
Mucoepidermoid Ca	1	0	1(100%)
Non-differentiated Ca	1	0	1(100%)
Acinic cell Ca	1	1(100%)	0
Metastases	2	0	2(100%)
Total	52	25(48.08%)	20(38.46%)

$\chi^2=11.17$ df=3 $p<0.01$ between pleomorphic adenomas and adenolymphomas

$\chi^2=16.2$ df=1 $p<0.01$ for pleomorphic adenoma compared to other histologic types

Table 7. Distribution of sonographic patterns of salivary gland tumors related to tumor histology

Tumor histology	Number of patients	Sonographic tumor pattern			
		A	B	C	D
Pleomorphic adenoma	28	24(85.72%)	4(14.28%)	0	0
Adeno-lymphoma	11	6(54.54%)	3(27.27%)	0	2(18.18%)
Oncocytoma	2	2(100%)	0	0	0
Lipoma	1	1(100%)	0	0	0
Non-Hodgkin lymphoma	3	1(33.33%)	2(66.66%)	0	0
Adenocarcinoma	2	0	0	2(100%)	0
Mucoepidermoid Ca	1	0	0	1(100%)	0
Non-differentiated Ca	1	0	0	1(100%)	0
Acinic cell Ca	1	0	0	1(100%)	0
Metastases	2	1(50.00%)	0	1(50.00%)	0
Total	52	35(67.31%)	9(17.31%)	6(11.54%)	2(3.85%)

χ^2=0.61 df=1 p>0.05 for A and B of pleomorphic adenomas and adenolymphomas

Table 8. Distribution of vascularisation degree of salivary gland tumors related to sonographic tumor pattern

Sonographic tumor pattern	Number of patients	Vascularisation type			
		0	+	++	+++
A	35 (67.30%)	6 (17.14%)	16 (45.71%)	11 (31.42%)	2 (5.71%)
B	9 (17.30%)	1 (11.11%)	4 (44.44%)	3 (33.33%)	1 (11.11%)
C	6 (11.53%)	0	0	1 (16.66%)	5 (83.33%)
D	2 (3.84%)	0	2 (100%)	0	0
Ukupno	52	7 (13.46%)	22 (42.30%)	15 (28.84%)	8 (15.38%)

χ^2=8,13 df=5 p>0.05 between A and B

Table 9. Distribution of sizes of salivary gland tumors by their histology

Tumor histology	Number of patients	Tumor size		
		I < 2cm	II 2-4cm	II > 4cm
Pleomorphic adenoma	28	15(53.57%)	10(35.71%)	3(10.71%)
Adenolymphoma	11	5(45.45%)	4(36.36%)	2(18.18%)
Oncocytoma	2	1(50.00%)	1(50.00%)	0
Lipoma	1	0	0	1(100%)
Non-Hodgkin lymphoma	3	0	2(66.66%)	1(33.33%)
Adenocarcinoma	2	2(100%)	0	0
Mucoepidermoid Ca	1	0	1(100%)	0
Non-differentiated Ca	1	1(100%)	0	0
Acinic cell Ca	1	0	1(100%)	0
Metastases	2	1(50.00%)	1(50.00%)	0
Total	52	25(48.07%)	20(38.46%)	7(13.46%)

Table 10. Distribution of vascularisation degree related to the size of pleomorphic adenoma

Size of pleomorphic adenoma	Number of patients	Vascularisation degree			
		0	+	++	+++
I <2cm	15 (53.57%)	2 (13.33%)	5 (33.33%)	8 (53.33%)	0
II 2-4cm	10 (35.71%)	1 (10.00%)	9 (90.00%)	0	0
III >4cm	3 (10.71%)	0	1 (33.33%)	2 (66.66%)	0
Total	28	3	15	10	0

statistical significance regarding the height of systolic peak and value of resistive index between pleomorphic adenoma and other tumors of salivary glands. However, t-test showed statistical significance ($p<0.01$) in medium values of systolic peaks between benign and malignant tumors. It turned out that malignant tumors have arterial flow of higher velocity than benign tumors (table 11).

There was no statistical significance between middle RI values of benign and malignant tumors ($p>0.05$), table 11. This also applied to middle RI values of pleomorphic adenoma in relation to other tumors.

DISCUSSION

Gray sonographic scale may determine the type of tumor (benign-malignant) with the accuracy of 83% (8,9). The best echosonographic indication of malignant tumors is the absence of clearly defined margins (9). Malignant tumors of salivary glands present as solid, poorly defined, infiltrative changes. However 27% of all malignant tumors have sharp margins (9,10).

In our study there were 20% of malignant tumors with well delineated margins. This is confirmed by the fact that various tumors have similar characteristics and it is very difficult to differentiate between benign and low-grade malignant tumors. Therefore, some carcinomas at their early stage may present as well encapsulated and homogenous.

The impossibility of gray sonographic scale to diagnosticise some carcinomas of salivary glands enhanced the application of color Doppler sonography in tumor differentiation.

In this series (11) the largest number of benign tumors (50%) had the first degree of vascularization; 13 tumors (30.85%) had the second degree of vascularization while only one tumor (2.38%) had the highest degree of vascularization. Vascularization was not present in 7 tumors (13.46%).

Out of 28 pleomorphic adenomas, 25 (89.28%) were with the middle (the first and the second) degree of vascularisation. Italian authors report in their series 80% pleomorphic adenoma with middle degree of vascularization (7).

In contrast to this, there were no malignant tumors without vascularization, whereas 70% had the highest degree of vascularization, and 20% had the second degree of vascularization. Only one node (10%) had the first degree of vascularization. These characteristics may refer to more intense vascularity of malignant tumors, due to the presence of arterial-venous shunt.

This study showed the presence of statistical significance of the vascularization type of pleomorphic adenomas in relation to other histological types of salivary gland tumors. In 75% they had peripheral and in 14.28% hilar type of vascularization. Italian authors (7) also found statistical significance of the vascularization type of pleomorphic adenomas, which in 77.41% had peripheral and in 9.67% hilar type of vascularization. Therefore, "peripheral type of vascularization (basket-like) consisting of fine nodular net around nodes could be considered specific for pleomorphic adenoma" (7). However, some authors (12) report that localization

Table 11. Mean values of systolic peak velocity of arterial flow and resistance index related to tumor type

Tumor type	Mean value of systolic peak velocity PSV	Mean value of resistance index RI
Benign	20.4 cm/s ± 5.6	0.55 ± 0.08
Malignant	39.2 cm/s ± 8.1	0.65 ± 0.11

t=7.2 df=28 p<0.01 for mean PSV values of benign and malignant tumors
t=0.02 df=28 p>0.05 for mean RI values of benign and malignant tumors

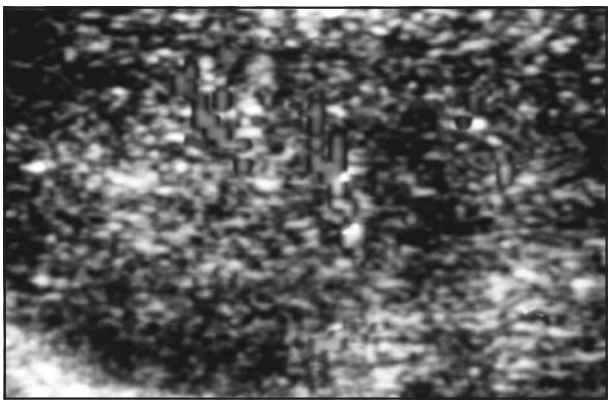

Figure 7. Non-Hodgkin lymphoma with third degree and hilar vascularisation pattern

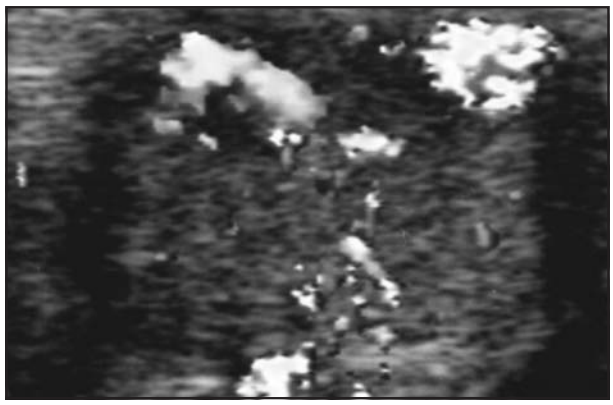

Figure 8. Mucoepidermoid carcinoma with third degree and hilar vascularisation pattern

and texture of intranodular blood vessels provide no information about the nature of neoplasms.

Statistically significant difference of the vascularization type was also found between the group of pleomorphic adenomas and adenolymphomas, most common salivary gland tumors. Adenolymphomas had in 63.63% hilar type of vascularization (in contrast to pleomorphic adenomas), and only in 18.18% peripheral type of vascularization.

The correlation of the size of pleomorphic adenoma and the degree of vascularization gave no statistical significance. This means that the degree of vascularization did not depend on the size of tumors. Also, there was no statistical significance between the size and the vascularization type of pleomorphic adenoma, so that the vascularization type also did not depend on the tumor size.

Detection of low flow velocities did not help in tumor differentiation, because those velocities were found in pleomorphic adenomas as well as in other benign and malignant tumors. Italian authors (7) report that systolic peak velocity higher than 60 cm/sec has never been detected in benign tumors, but was present in 44% of malignant salivary gland tumors. Therefore, they suggest that systolic peak velocity higher than 60 cm/sec should be border value between benign and malignant salivary gland tumors.

RI correlation of pleomorphic adenoma and other salivary gland tumors provided no statistical significance, so that it was impossible to make difference between pleomorphic adenoma and other benign and malignant salivary gland tumors on the basis of RI.

CONCLUSION

Statistically significant difference was found for $p<0.01$ of the vascularization type of pleomorphic adenomas in relation to other histological types of salivary gland tumors. There was also statistically significant difference for $p<0.01$ of the vascularization type of pleomorphic adenomas and adenolymphomas. Peripheral type of vascularization is dominant in pleomorphic adenoma, whereas hilar type is dominant in adenolymphomas.

Low degree of vascularization as well as peripheral type of vascularization suggests the possibility of differentiation of pleomorphic adenomas from other salivary gland tumors.

Color Doppler sonography demonstrated great potentials in determination of vascularization of salivary gland tumors and qualification of pathological changes. Differentiation of pleomorphic adenoma from other salivary gland tumors will be useful for the adequate choice of operative treatment and careful postoperative follow-up. Prevention of relapse and malignant alterations is enabled by frequent and careful clinical and ultrasound control. It has been shown that color Doppler sonography represents a powerful technique in diagnostics of pleomorphic adenomas as well as in differentiation of benign and malignant neoplasms of salivary glands. Further clinical application will clarify the ultimate potentials of this method.

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MOGUĆNOSTI KOLOR DOPPLER ULTRAZVUKA U DIJAGNOSTICI PLEOMORFNIH ADENOMA

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SAŽETAK

Cilj studije je da se utvrde kolor Doppler karakteristike pleomorfnih adenoma i mogućnosti njihove diferencijacije od drugih tumora pljuvačnih žlezda.

Ova prospektivna studija obuhvatila je 52 pacijenta sa tumorima pljuvačnih žlezda ispitivanih kolor Doppler sonografijom pre hirurškog tretmana. Pretrage su učinjene linearnom sondom od 7.5 MHz sa Doppler imidingom. Za definisanje gradusa intratumorske vaskularnosti korišćena je četvorostepena analogna skala, a oblici vaskularne distribucije karakterisani su kao periferni (nalik na korpu) ili hilarni (granajući).

Nakon hirurškog tretmana i patohistološke verifikacije ustanovljeno je da je 28 pacijenata (53.84%) imalo pleomorfne adenome. Petnaest pacijenata (53.57%) imalo je pleomorfne adenome prvog gradusa, a 10 (35.71%) drugog gradusa vaskularnosti. Tri pacijenta (10.71%) nisu imala prisutne kolor Doppler signale; slučajeva trećeg gradusa vaskularnosti nije bilo. U pogledu obrasca vaskularnosti, pleomorfni adenom je pokazivao periferni oblik vaskularnosti u 21 slučaju (75%).

Statistički značajna razlika ($p<0.01$) utvrđena je u oblicima vaskularnosti između pleomorfnog adenoma i drugih histoloških tipova tumora pljuvačnih žlezda. Svi su pleomorfni adenomi imali nizak ili srednji gradus vaskularnosti.

Naša iskustva pokazuju da je kolor Doppler sonografija senzitivna metoda u dijagnostici pleomorfnog adenoma. Na osnovu gradusa i oblika vaskularnosti sa velikom je izvesnošću moguće razlikovati pleomorfne adenome od drugih tumora pljuvačnih žlezda.

Ključne reči: **kolor Dopler, plemorfni adenom, tumor pljuvačnih žlezda**