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The Lymph Node Roundness Index in the Evaluation of Lymph Nodes of the Neck

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A B S T R A C T

The study assessed the validity of the lymph node »roundness index« (RI) in the evaluation of enlarged lymph nodes of the neck. A total of 107 subjects were included in the prospective study, and 135 enlarged lymph nodes were examined. All the subjects were examined clinically and sonographically, the lymph node roundness index was determined, and soon after the nodes was surgically removed and pathohistologically diagnosed. On the basis of pathohistological diagnosis the study subjects were divided into two groups. The first group consisted of patients with benign lymph nodes, and the second one comprised patients with malignant nodes. The second group was further divided into two sub-groups: those with primary malignant nodes and those with secondary lymph nodes (metastases). The study showed that the lymph node RI statistically differs between the groups. In benign lymphadenopathy the RI was 1.66±0.26, in primary malignant lymphadenopathy it was 1.31±0.25 and in secondary malignant lymphadenopathy 1.13±0.11. The analysis demonstrated that 82.9% of subjects randomly chosen from the group with primary malignant lymphadenopathy and 94.6% from the group with the secondary malignant lymphadenopathy have a smaller RI compared to randomly chosen subjects from the group with benign lymphadenopathy. Sensitivity of the method for primary malignant lymphadenopathy was 66.7% and specificity was 92.9%. For secondary malignant lymphadenopathy the sensitivity was 95.5% and specificity 92.9%. Based on this result we can conclude that the lymph node RI is a valid, simple, cost-effective and non-aggressive method which may »increase the suspicion« for a benign or malignant lymphadenopathy. RI≤1.5 is indicative of malignant lymphadenopathy and RI≥1.5 of benign lymphadenopathy.

Key words: *ultrasonography, roundness index, lymphadenopathy*

Introduction

The evaluation of enlarged lymph nodes of the neck, i.e. the differentiation between benign and malignant lymphadenopathies, is of crucial importance in the planning of treatment of patients with suspect malignancy[1–5]. The available data show that the presence of metastatic lymph nodes on one side of the neck reduces a 5-year survival period by 50%, while the presence of metastatic lymph nodes on both sides of the neck reduces the same period by 75%[3,5]. Likewise, lymph nodes on the neck are a frequent location of the appearance of lymphomas which are difficult to differentiate from other lymphadenopathies[6].

Inspection and palpation of the neck are unreliable[7,8], while CT and MR show significant limitations in differentiating benign from malignant lymph nodes[5,9–11]. SPECT and PET have made significant clinical inroads in the past few years, thanks to new, appropriate radiopharmaceuticals, but they are still beyond the reach of smaller health centers[10–12]. Nevertheless, recently available data show large numbers of false positive results PET CT scans[13–15].

Ultrasound (US) has proven to be a valid, simple, non-aggressive and relatively cheap method in detecting enlarged lymph nodes, although the differentiation between benign and malignant lymphadenopathy remains to be a problem. The size of the node, echogenicity and hilus circulation are important diagnostic signs, and must be included on the whole clinical pictures[16–18]. The method heavily depends on the observer. US-guided citopunction is a much more reliable method having high sensitivity and precision but it is still insufficient to replace the extirpation of the node and a pathohistological analysis as a »golden standard« in the diagnostics of lymph nodes[19–21]. US-guided citopunction should be sufficient in most cancer patients for diagnostic method, not for therapy and only in lymphomas, and rare tumors do we need extirpations for diagnostic methods.

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TABLE 1
BREAKDOWN OF PATIENTS BY RI

Group	N	Roundness index			Statistics
		$\overline{X}$±SD	M (5^{th}–95^{th})	Range	
Benign changes	42	1.66±0.26	1.70 (1.09–2.00)	1.00–2.20	One-way ANOVA F=94.90 p<0.001
Primary malignant changes	27	1.31±0.25	1.20 (1.04–1.73)	0.96–2.06	
Secondary malignant changes	66	1.13±0.11	1.10 (1.00–1.30)	1.00–1.53	Kruskal Wallis p<0.001
Total	135	1.33±0.31	1.20 (0.96–2.20)	0.96–2.20	

The aim of this study is to assess the validity of the lymph node »roundness index« (RI) in the differentiation of benign and malignant lymph nodes. The lymph node RI is the relationship of the longitudinal and transversal cross section of the lymph node, i.e. the relationship of the longer and shorter cross section of the lymph node (longitudinal/transverse diameter ratio, L/T)[16,22]. Literature indicates the tendency of malig nantly changed lymph nodes towards a round shape (RI≤2), by contrast to a more oval shape in benign changes (RI≥2)[16,22].

TABLE 2
RESULTS OF POST-HOC ANALYSIS FOR THE RI

Tukey HSD test Approximate Probabilities for Post Hoc Tests Error: Between MSE= 0.3909, DF=132.00			
Group category	(1) 1.6641	(2) 1.3093	(3) 1.1269
1		0.000022	0.000022
2	0.000022		0.000176
3	0.000022	0.000176	

Patients and Methods

The study comprised 107 patients who were sonographically examined between 2002 and 2009 at the Department for ORL of the County Hospital in Livno, BIH and the retrospective study comprised 135 lymph nodes which were enlarged and manifested various diseases. All the nodes were surgically removed from the neck region of sonographically examined patients, and pathohistologically analyzed. Depending on the pathohistological finding, patients were assigned into groups. The first group consisted of patients with benign lymph node changes and the second group consisted of patients with malignant lymph nodes. The second group was further divided into two sub-groups: those with primary malignant lymph nodes and those with secondary malignant lymph nodes (metastases).

Sonographic examination of the neck was done in all patients by the »SIEMENS SONOLINE SI-450« ultrasound system with a 7.5 MHz short focus probe 6 cm long. During the examination longitudinal and transversal cross sections of lymph nodes were measured and documented on the points where the dimensions of the lymph nodes were the greatest, and the RI of every lymph node was determined. All sonographic examinations and measurements were done by the same physician.

Statistical elaboration of data was done by Statistica for Windows, release 8.1 (Stasoft, Inc., Tulsa, OK, USA).

Results

Of the 135 analyzed lymph nodes, 42 were benign: 15 with a diagnosis of reactively changed node, 9 with chronic inflammation, 17 with a diagnosis of lymph node TB and one with purulent inflammation. Of the 27 primary malignant lymph nodes, 5 were diagnosed pathohistologically as chronic lymphatic leukemia, 17 as non-Hodgkin lymphoma and 5 as Hodgkin lymphoma. Of the 66 secondary malignant lymph nodes 38 were metastases of planocellular carcinoma, 10 metastases of adenocarcinoma, 7 metastases of melanoma, 2 metastases of follicular carcinoma of the thyroid, 5 metastases of papillary carcinoma of the thyroid, 1 metastasis of the medullary carcinoma of the thyroid, 1 metastasis of anaplastic thyroid carcinoma, 1 metastasis of epipharyngeal carcinoma and 1 metastasis of the sarcoma.

In Table 1 the lymph node RI by patient groups are shown.

The RI differs significantly between groups (p<0.001). Therefore, a post-hoc analysis was done to determine which of the groups differ significantly (Table 2).

Significant differences between the RI of all groups were determined (all p<0.001). The subjects with benign changes have a significantly greater RI than the subjects with primary malignant changes (p<0.001) or subjects with secondary malignant changes p<0.001). Subjects with primary malignant changes have a significantly greater RI than the subjects with secondary malignant changes (p<0.001).

The potential of the lymph node RI as a parameter in the differentiation of the above groups was evaluated by the »receiver operating characteristic« (ROC) analysis.

ROC analysis for primary malignant changes

Table 3 shows the values obtained by ROC analysis for the RI of primary malignant tumours.

TABLE 3
VALUES OBTAINED BY ROC ANALYSIS FOR THE RI OF PRIMARY MALIGNANT CHANGES

Area under the ROC curve	0.829
Standard Error	0.048
95% Confidence Interval	0.735 to 0.924
Significance level p	0.001

Figure 1 shows the ROC curve for the RI of primary malignant changes.

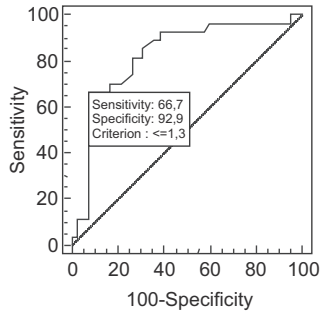

Fig. 1. ROC curve for the RI (full line on the basis of measured values, dashed line on the basis of theoretical values; rectangle describes the sensitivity =66.7%, specificity =92.9% and criterion predictor ≤1.3).

Roundness index is a variable with which it is possible to differentiate, with statistical significance, benign changes from primary malignant changes (p=0.001). By means of the ROC analysis it was determined that 82.9% of patients randomly chosen from the group with malignant changes will have a smaller RI than the randomly chosen patients from the group with benign changes. Because p<0.001, it means that the area below the curve (0.829) is statistically significantly different from 0.5 (the diagonal on the figure) which supports the conclusion that the value of the RI does not statistically significantly differentiate the diagnosis made by US from the diagnosis made on the basis of pathohistological finding.

ROC analysis for secondary malignant changes

Table 4 shows the values obtained by ROC analysis for the RI of secondary malignant changes.

Figure 2 shows the ROC curve for the RI of secondary malignant changes.

RI is a variable with which it is possible to statistically significantly differentiate benign changes from secondary malignant changes (p<0.001). By means of the ROC analysis it was determined that 94.6% of subjects randomly chosen from the group with secondary malignant changes will have a smaller RI from randomly chosen subjects in the group with benign changes. Because p<0.001, it means that the area below the curve (0.946) is

TABLE 4
VALUES OBTAINED BY ROC ANALYSIS FOR THE RI OF SECONDARY MALIGNANT CHANGES

Area under the ROC curve	0.946
Standard Error	0.025
95% Confidence Interval	0.897 to 0.996
Significance level p	<0.001

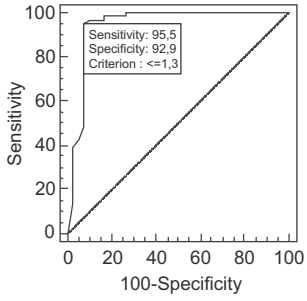

Fig. 2. ROC curve for the RI (full line on the basis of measured values, dashed line on the basis of theoretical values; rectangle describes sensitivity =95.5%, specificity =92.9% and criterion predictor ≤1.3).

statistically significantly different from 0.5 (the diagonal in the figure) which supports the conclusion that the value of RI does not statistically significantly differentiate the diagnosis made by US from the diagnosis made on the basis of pathohistological finding.

ROC analysis between primary and secondary malignant changes

Table 5 shows the values obtained by ROC analysis between primary and secondary malignant changes.

Figure 3 shows the ROC curve for the RI between primary and secondary malignant changes.

The RI is a variable with which it is possible to statistically significantly differentiate primary malignant changes from secondary ones (p<0.001). By means of the ROC analysis it was determined that 75.0% of subjects randomly chosen from the group with secondary malignant changes will have a smaller RI from randomly chosen subjects from the group with primary changes. Because p<0.001, it means that the area below the curve (0.750) statistically significantly differs from 0.5 (diagonal

TABLE 5
VALUES OBTAINED BY ROC ANALYSIS FOR THE RI BETWEEN PRIMARY AND SECONDARY MALIGNANT CHANGES

Area under the ROC curve	0.750
Standard Error	0.0598
95% Confidence Interval	0.633 to 0.868
Significance level p	<0.001

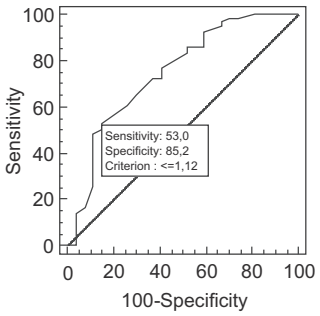

Fig. 3. ROC curve for the RI (full line on the basis of measured values, dashed line on the basis of theoretical values; rectangle describes sensitivity =53.0%, specificity =85.2 and criterion predictor ≤1.12).

on the figure) which supports the conclusion that the value of RI does not statistically significantly differentiate the diagnosis made by US from the diagnosis made on the basis of pathohistological finding.

Discussion

The differentiation of benign and malignant lymphadenopathies is of crucial importance for patients with enlarged lymph nodes of the neck. It is especially important in patients with malignant tumors of head and neck, because it fundamentally affects prognosis and choice of treatment. Likewise, the region of head and neck is a frequent location for the appearance of lymphomas which are often difficult to differentiate from other lymphadenopathies.

With respect to the importance of the evaluation of lymph nodes of the neck and with respect to the more or less uncertain methods of differentiation between benign and malignant lymphadenopaties in current use, all the way to surgical extirpation and a pathohistological analysis as a »golden standard«, the paper assesses the validity of the lymph node roundness index (RI). Literature suggests the inclination of malignantly changed lymph nodes toward the round shape (RI≤2), by contrast to a more oval shape in benign lymph node changes (RI≥2)[22].

In several published studies different values of the RI for malignantly changed lymph nodes appear. Solbiati et al. determined that an average RI of 1.5 is characteristic of malignant lymph nodes, while the RI above 2 is characteristic for benign lymph nodes[18]. Similar results were obtained by other authors[18,20,23–26].

In our study average RI for benign lymph nodes was 1.66±0.26 (range 1.00–2.20). Of the 42 benign lymph nodes, 37 (88%) had a RI greater than 1.5, while for 5 nodes (12%) the RI was smaller than 1.5. For primary malignant lymph nodes the average RI was 1.31±0.25 (range 0.96–2.06); 24 of the lymph nodes (88.9%) had a RI smaller than 1.5. Secondary malignant lymph nodes had a RI of 1.13±0.11 (range 1.00–1.53). Of the 66 secondary malignant lymph nodes, 63 (95.5%) had a RI smaller than 1.5. The results in our study are in agreement with the previously quoted results from literature, in that the RI for malignant lymph nodes was smaller than 1.5 (1.31 and 1.13)[23–26]. Benign lymph nodes had a RI smaller than 2, but greater than 1.5 (1.66) which contradicts with previously published studies according to which the lymph node RI between 1.5 and 2 can indicate both a benign and malignant lymphadenopathy[18].

A post-hoc analysis showed statistically significant differences of the RI between groups, so that the subjects with benign lymphadenopathy have a statistically significantly greater RI than subjects with malignant lymphadenopathy.

The ROC analysis showed that the lymph node RI is a variable by which we can statistically significantly differentiate benign lymphadenopathy from the malignant one. It was proven that 82.9% of subjects randomly chosen from the group of primary malignant lymphadenopathies and 94.6% of subjects from the group with secondary malignant lymphadenopathies will have a smaller RI from randomly chosen subjects from the group with benign lymphadenopathies.

The sensitivity of the method for primary malignant lymphadenopathy was 66.7%, and specificity was 92.9%. For secondary malignant lymphadenopathy the sensitivity was 95.5% and specificity was 92.9%. High values of sensitivity and specificity of the lymph node RI make it a useful modality in the diagnostics of enlarged lymph nodes of the neck. The obtained results lead us to conclude that a certain value of the RI can help a physician in the diagnostics of enlarged lymph nodes of the neck, »increasing the suspicion« that we are dealing with benign or malignant lymphadenopathies. Together with other available methods, in a certain number of cases, it can reduce the need for a surgical intervention for diagnostic purposes, especially in cases of metastases of malignant tumors.

The determination of the RI is very simple and can be done during a sonographic examination which is an easily accessible, cost-effective, easily repeatable and non-aggressive method. Algorithms of the diagnostics of enlarged lymph nodes list the US examination as an initial one, after the clinical examination. The determination of the RI does not require any additional equipment, and is not time-consuming. It is understood that the lymph node RI as a modality in the diagnostic procedure of enlarged lymph nodes cannot be a replacement for cytological puncture controlled by ultrasound or biopsy with a pathohistological diagnosis as a »golden standard«, but it can »increase the suspicion« in benign or malignant lymphadenopathy and in a certain number of cases avoid the need for surgery – the biopsy of the lymph node.

On the basis of results of this study we can conclude that the lymph node RI smaller than 1.5 (RI≤1.5) speaks in favor of malignant lymphadenopathy, whereas the lymph node RI greater than 1.5 (RI≥1.5) speaks in favor of benign lymphadenopathy. Therefore, we feel free to assert that the determination of lymph node RI should be included in the algorithms of diagnostics of enlarged lymph nodes of the neck.

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INDEKS ZAOKRUŽENOSTI LIMFNIH ČVOROVA U EVALUACIJI LIMFNIH ČVOROVA NA VRATU

SAŽETAK

U istraživanju je procijenjena valjanost indeksa zaokruženosti limfnog čvora (engl. Roundness indeks, RI, Solbiati indeks) u evaluaciji uvećanih limfnih čvorova vrata. Istraživanjem je obuhvaćeno 107 pacijenata, a prospektivna studija je uključila 135 uvećanih limfnih čvorova. Svi pacijenti su klinički pregledani, ultrazvučno pregledani te im je određen indeks zaokruženosti limfnih čvorova a potom su u kraćem vremenskom razdoblju čvorovi kirurški odstranjeni i patohistološki dijagnosticirani. Temeljem patohistološke dijagnoze ispitanici su podijeljeni u dvije skupine. Prvu skupinu su činili bolesnici s benignim limfnim čvorovima a drugu skupinu bolesnici s malignim limfnim čvorovima. Druga skupina je podijeljena u dvije podskupine; primarni maligni čvorovi i sekundarni limfni čvorovi (presadnice). Istraživanje je pokazalo da se indeks zaokruženosti limfnog čvora (RI) statistički značajno razlikuje između skupina. RI za benigne limfadenopatije je bio 1,66±0,26, za primarne maligne limfadenopatije 1,31±0,25 te 1,13±0,11 za sekundarne limfadenopatije. Analizom je ustvrđeno da će 82,9% ispitanika slučajno odabranih iz skupine s primarnim malignim limfadenopatijama i 94,6% iz skupine sa sekundarnim malignim limfadenopatijama imati manji RI od slučano odabranih ispitanika iz skupine s benignim limfadenopatijama. Osjetljivost metoda za primarne maligne limfadenopatije bila je 66,7% a specifičnost 92,9%. Za sekundarne maligne limfadenopatije osjetljivost je iznosila 95,5% a specifičnost 92,9%. Temeljem rezultata ovoga istraživanja možemo zaključiti da je indeks zaokruženost limfnog čvora valjana, jednostavna, jeftina i neagresivna metoda koja može »povećati sumnju« u benignu ili malignu limfadenopatiju. RI≤1,5 govori u prilog malignih limfadenopatija a RI≥1,5 za benigne limfadenopatije.