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## Ultrasound and Doppler Diagnostic Capabilities of Lymph Nodes in Thyroid Cancer

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*Abstract: nodular lesions, autoimmune thyroiditis and neoplastic processes are the leading diseases of the thyroid gland (TG), when it is characterized by the cervical lymph nodes (LN) enlargement. They can undergo macro- and microscopic changes due to inflammatory processes of bacterial or viral origin, benign and malignant lesions of the neck, head and mediastinum. Doppler ultrasonography (US) plays a significant role among the new methods of screening for altered LN and differential diagnosis of pathological processes. The aim of this work is to determine the prospects for the use of LN lesions' ultrasound diagnostics in inflammatory and oncological processes of the TG. Ultrasound diagnostics was performed to determine Doppler signs (EDV, PSV, RI) and changes in neck LN in 175 patients with and without TG pathologies. According to the results of histopathology, the patients were divided into 4 groups: 46 healthy patients without any thyroid pathology, 44 patients with inflammatory thyroid diseases, 42 patients with thyroid cancer but without metastatic LN involvement, 43 patients with metastatic LN involvement – Thyroid cancer. B-mode ultrasound diagnostic data demonstrated positive complementation with echostructural signs and changes in vascularization. It manifested in a wide range of velocities and atypical angioarchitectonics. 13 (31%) patients had increased vascularization with PSV – 23-45 cm/s, EDV – 14- 8 cm/s, RI – 0.32-0.46. It shows the progression of proliferative processes without necrotic changes in the hilus and its periphery. In 18 (43%) patients dynamic Doppler observation indicated the appearance of accelerated blood flow and an atypical vascular concentration outside nodular capsules. It is an indicator of the cancer spread. Color Doppler mapping and energy Doppler coding of cervical metastases are important diagnostic techniques, that qualitatively and quantitatively complements and details B-mode ultrasound diagnosis.*

**Keywords:** [thyroid neoplasms](#), [thyroiditis](#), [lymph nodes](#), [doppler ultrasonography](#), [metastase](#).

## Introduction

Thyroid diseases have become very common in recent years. Nodular malformations, autoimmune thyroiditis and benign or malignant tumours are the leading ones. According to WHO in 2020 the worldwide incidence of thyroid cancer was 10.1 per 100,000 women and 3.1 per 100,000 men (Pizzato, M. et al., 2022). From data of the cancer registry of Ukraine, 2,900 new cases of thyroid cancer were diagnosed in 2021, which is 13.1% more than in 2020. Primary pathologies were detected in 2361 women (81.4%) and in 539 men (18.6%) (Fedorenko Z. et al., 2023). Papillary (75-80%), follicular (10-20%), medullary (3-5%) and anaplastic (1-2%) forms are the most common among malignant thyroid tumours (Riccardo A. A. et al., 2023).

A rational combination of instrumental methods, cytological diagnostics, studies of tumor markers and radioisotope methods allow us to increase the diagnostic efficiency of thyroid pathologies and to provide a detailed examination with the main focus on all adjacent anatomical structures.

In TG disorders, the lymphatic system of the neck can respond by LN enlargement, changing their morphology and in the processes of interacting with adjacent anatomical structures. It is important, that the LN can undergo macro- and microscopic changes due to any inflammatory processes of bacterial or viral origin, benign and malignant lesions of the neck, head, mediastinum, including the TG (Li F. et al., 2020; Bourcier, S. et al., 2023). Screening of pathologically changed nodes is performed by a combination of clinical, ultrasound, morphological, cytological methods, a fine-needle biopsy with ultrasound control, lymph scanning, and computer tomography (Huang, J. et al., 2023). Their verification frequency is from 72 to 98%.

The paratracheal and vascular (jugular) collectors of LN are the most often firstly affected ones with metastases. It is VI, II, III and IV levels according to the classification developed by the Academy's Committee for Head and Neck Surgery and Oncology (1991) (Robbins K. T. et al., 1991). The localization, size, shape, level of echogenicity, the presence of micro- or macrocalcifications in LN, the ability to accumulate iodine 131 are the leading factors in a differential diagnosis (Sande, C. M. et al., 2023). Ultrasound of neck

anatomical structures is a new common method for the qualitative diagnosis (Seifert, P. Et al., 2023; Spaletta, G. Et al., 2023). The quality of primary information depends on the diagnostic capability of an ultrasound equipment, therefore, methods of colour flow mapping, colour doppler velocity, and colour doppler energy additionally examine small vessels in portal of LN and their parenchymal branches, invisible to Ultrasound examination in B-mode. The use of virtual three-dimensional EDK 3D PowerAngio angiography and pulsed Doppler US provide angioarchitectonics data of the lymphatic system and supplement it with quantitative indicators of blood rapid movement in vessels and vessel resistivity.

## Aim

To determine the prospects of LN lesions' ultrasound diagnostics in inflammatory and oncological processes of the TG.

## Materials and methods

The study was conducted in 175 patients, who were examined or treated at the Department of Endocrine Surgery of Kyiv City Clinical Hospital №3 and at the Surgical Department of Kyivmiskbud Hospital during 2017-2022. Patients aged 18-75 with suspected thyroid pathology were the main selection criterium for the study.

Primary scanning in B-modes using 12.5 MHz linear sensors in longitudinal, oblique and transverse projections was performed for all patients [7]. The structure, size, echogenicity of the tissue, contours, the presence or absence of formations, the nature of the location of vessels in the parenchyma were evaluated [8], [9]. The state of blood flow of regional LN, carotid collector along the vascular bundle, paratracheal, submandibular and periclavicular groups of LN were evaluated in pathological areas, in particular, in the centre and on the periphery.

The following regular examinations on ultrasound scanners HDI 5000 and HDI 3000 (ATL-Philips, USA) with linear broadband sensors L12-5 MHz and Aloka 1700 made it possible to obtain echograms of the LN with the display of color flow mapping, color doppler energy, echograms of three-dimensional virtual angiography. The blood flow spectrogram determined peak systolic velocity (PSV), end-diastolic velocity (EDV), and resistance index (RI).

All patients were divided into 4 groups for further data analysis according to the ultrasound and Doppler diagnostics, fine-needle biopsy and postoperative pathohistological findings:

1) «Control» (healthy patients without pathology of the thyroid gland, ENT organs) – 46;

2) «Experimental 1» (patients with inflammatory diseases of the thyroid gland) – 44;

3) «Experimental 2» (patients with thyroid cancer without metastases to regional lymph nodes) – 42;

4) «Experimental 3» (patients with thyroid cancer and metastases to regional lymph nodes) – 43.

The size of LN, their localization, EDV, PSV, RI were compared to identify LN lesions in inflammatory thyroid diseases and thyroid cancer metastases patterns. Statistical analysis was performed with IBM SPSS Statistics Base (version 22). Parametric and non-parametric methods were used.

### Results

The initial examination of the control group (46 patients) on the ultrasound image showed unchanged multiple oval formations of 4-5 mm diameters. They had smooth clear contours, reduced echogenicity with differentiation of the cortical and central parts of the node. Blood circulation was weakly expressed and limited to the area of the node's hilus or was not determined at all. The average values of indicators in this group were: peak systolic velocity (PSV) – 20-65 cm/s (the norm is 20-65 cm/s), end-diastolic velocity (EDV) –  $8 \pm 3.7$  cm/s (the norm is 5-35 cm/s) and the resistance index (RI) is 0.38-0.85 (the norm is 0.38-0.85).

Ultrasound Doppler examination in the group of patients with inflammatory processes of TG (experimental group №1) revealed numerous signs in LN. In 25 (57%) patients LN had shapes ranging from round one 7 mm in diameter to ovoid – 8-9 mm. Their number and location varied: in 21 (48%) patients the submaxillary area was the most common localization; in 14 (32%) cases the location of some single 2-3 LN was determined along the carotid vascular bundle; 9 (20%) patients had single or aggregated LN in all parts of the neck. According to Doppler characteristics active blood flow in the hilus of nodes was established in 35 (80%) of the examined with peak systolic

velocity (PSV) of 15,1-25,1 cm/s, end-diastolic velocity (EDV) of 5,7-11,7 cm/s and resistance index (RI) – 0.43-0.53. In 9 (20%) patients with lymphadenopathy, it was not possible to establish the quantitative characteristics of the blood flow, only monochromatic pixels of the blood flow were recorded. The average values for indicators in this group were: peak systolic velocity (PSV) –  $20 \pm 5.1$  cm/s, end-diastolic velocity (EDV) –  $8 \pm 3.7$  cm/s and resistance index (RI) –  $0.48 \pm 0.05$ .

42 patients were clinically diagnosed with thyroid cancer with enlarged LN in research group №2. In 23 (55%) patients the B-mode ultrasound picture of the initial metastatic impression of LN is represented by a single or clearly separated formations paratracheally or along the vascular bundle. They are increased in size up to 2 cm in diameter, have a clear equal contour, hyper- and hypoechoic structure. In 9 (21%) the lymphatic collector consists of LN of different sizes. It is located on the back surface of the vascular carotid bundle and spreads behind the sternum and trachea. LN lose the sharpness of their edges. The echostructure may contain small liquid hydrophilic inclusions or microcalcifications with an indistinct ultrasound shadow. The high-risk group includes 4 (10%) patients with metastatic LN. They have signs of invasion or incomplete tumour removal and completed treatment course with radioactive iodine 131. In these cases, LN lose ultrasound and Doppler architecture, while Doppler characteristics don't have a quantitative limit of values, so they become uninformative. The average values for indicators in this group were: peak systolic velocity (PSV) –  $22 \pm 4.8$  cm/s, end-diastolic velocity (EDV) –  $10 \pm 3.6$  cm/s and resistance index (RI) –  $0.43 \pm 0.04$ .

The Doppler image of metastatically affected LN in patients of study group №3 complements the B-mode with echostructural signs and changes in vascularization with a wide range of speeds and atypical angioarchitectonics. The average values for indicators in this group were: PSV –  $26 \pm 6.3$  cm/s, EDV –  $14 \pm 4.2$  cm/s and RI –  $0.32 \pm 0.06$ . Increased vascularization indicates the progression of proliferative processes without necrotic changes in the hilus and periphery of the capsule. The drop in RI values to 0.30 and

less in the absence of tissue decay occurs due to increased blood circulation and the appearance of arteriovenous shunts. Only in 2 (5%) patients it became possible to determine RI in the region of the hilus. This indicator was  $0.51 \pm 0.05$ . Dynamic observation of 18 (42%) patients shows the appearance of accelerated blood flow and atypical concentration of vessels outside the nodular capsule which indicate the spread of cancer. In LN and their conglomerates 9 (21%) persons have no qualitative and quantitative characteristics of blood flow. This is a sign of destructive changes and calcinosis.

According to the results of the statistical analysis it was established, that a statistically significant difference between the changes in the size of LN compared to the control group was only in the «Experimental № 3» group (patients with thyroid cancer and metastasis to LN) ( $P < 0.05$ ). The round or ovoid shape of nodes was associated with inflammatory diseases of the TG. Nodes with a wavy contour prevailed in the group with thyroid cancer without signs of metastasis.

LN took the form of conglomerates in the group of patients with thyroid cancer and metastatic lesions.

For the group of patients with inflammatory diseases of the TG, the predominant location of the affected nodes was the carotid vascular bundle. In patients with thyroid cancer without lesions of the TG, the predominant localization was the vascular carotid and paratracheal nodes. In patients with metastasis to the TG, parathyroid fatty tissue was added.

During the analysis of PSV, it was established, that there was no statistically significant difference in the first and second experimental groups compared to the control group ( $P = 0.612$  and  $P = 0.221$ ), and the changes in PSV in the third experimental group acquired a statistically significant difference and amounted to  $26 \pm 6, 3$  cm/s ( $P < 0.05$ ).

EDV analysis showed no statistically significant difference in the first and second experimental groups compared to the control one ( $P = 0.819$  and  $P = 0.183$ ), but the changes in the EDV of the third experimental group acquired a statistically

**Tab. 1.** Characteristics of lymphadenopathy

Group	Control group	Experimental 1	Experimental 2	Experimental 3
Number of people in the group	46	44	42	43
Size of lymph nodes*	$5 \pm 1,3$ mm	$8 \pm 1,5$ mm $P = 0,568^*$	$8 \pm 1,6$ mm $P = 0,127^*$	$19 \pm 5,8$ mm $P < 0,058^*$
Form*	Round	Round/oval	Oval	Oval/Conglomerate
Contour	Equal	Equal	Equal	Wavy
Localization	Single nodes	Submandibular nodes/ Carotid bundle	Submandibular nodes/ Carotid bundle	Vascular carotid bundle + paratracheal + parathyroid
The presence of micro- and macrocalcifications	–	–	–	+
The nature of the echo	Hypo- and isoechoic	Hypo- and isoechoic	Hypo- and hyperechoic	Hyperechoic
PSV	20-65 cm/s	$20 \pm 5,1$ cm/s $P = 0,612^*$	$22 \pm 4,8$ cm/s $P = 0,221^*$	$26 \pm 6,3$ cm/s $P < 0,05^*$
EDV	$8 \pm 3,7$ cm/s	$8 \pm 3,7$ cm/s $P = 0,819^*$	$10 \pm 3,6$ cm/s $P = 0,183^*$	$14 \pm 4,2$ cm/s $P < 0,05^*$
RI	0,38-0,85	$0,48 \pm 0,05$ $P = 0,438^*$	$0,43 \pm 0,04$ $P = 0,177^*$	$0,32 \pm 0,06$ $P = 0,05^*$

\* comparison with the control group



significant difference and amounted to  $14 \pm 4$ , 2 cm/s ( $P < 0.05$ ).

When analyzing RI, it was established, that there was no statistically significant difference in the first and second experimental groups compared to the control one ( $P = 0.438$  and  $P = 0.177$ ). In the third experimental group RI changes acquired a statistically significant difference and amounted to  $0.32 \pm 0.06$  ( $P = 0.05$ ).

### Discussion

According to the obtained results, the diagnostic value of ultrasound diagnostics and dopplerometric examination of LN lesions in TG inflammatory diseases does not have a statistically significant difference in comparison with healthy patients. This may be due to the absence of reactive changes in LN during inflammatory diseases.

Echographic and dopplerometric symptoms of oncological thyroid processes occurred only in the group of patients with metastases in the cervical LN. In the group of patients without metastases, there was no statistically significant difference in the size, PSV, EDV, RI compared to healthy patients. There is a tendency to changes in shape and localization of LN during oncological processes in the TG. In the group of patients with metastases of thyroid cancer in the LN of the neck, a statistically significant difference in size, PSV, EDV, RI was noted ( $P < 0.05$ ) in comparison with the control group. There is a tendency to changes in contour to a wavy one, the appearance of accumulations of LN in the form of a conglomerate chain. It was established that the paratracheal, parathyroid group and nodes located along the vascular carotid bundle were more often exposed to the pathological process.

The additional presence of hyperechoic foci of calcification within the nodule significantly increases the likelihood of cancer by nearly threefold for microcalcifications and twofold for gross calcifications. Microcalcifications have a specificity ranging from 44% to 95% for thyroid cancer, especially associated with papillary thyroid cancer. However, the sensitivity of microcalcifications is low (from 26% to 59%). Gross macrocalcifications are not specific for

a malignant tumour – they more often occur in multinodular goitre.

### Conclusions

Color Doppler mapping and energy Doppler coding of metastatic LN in the neck is an important diagnostic technique, that qualitatively and quantitatively complements and details B-mode ultrasound diagnosis.

The dynamics of ultrasound Doppler allows to assess the degree of spread and the effectiveness of previous treatment. The topographical and anatomical comparison of the metastatic focus and adjacent anatomical structures contributes to the development of correct tactics in further referrals for surgical treatment.

Ultrasound Doppler is a highly specific and sensitive method for non-invasive diagnosis of pathological conditions of the lymphatic system, including metastatic lesions, which should be implemented during dispensary examination at the early stages of thyroid cancer.

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This study did not receive external funding.

### Conflict of interests

There are no conflicts of interest.

### Consent to publication

The authors certify that they have obtained all appropriate patient consent forms.

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## Ультразвукові та доплерографічні можливості діагностики лімфатичних вузлів при раку щитоподібної залози

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**Анотація:** вузлові ураження, аутоімунний тиреоїдит та пухлинні процеси є провідними серед захворювань щитоподібної залози (ЩЗ), які характеризуються збільшенням шийних лімфатичних вузлів (ЛВ). Лімфатичні вузли можуть зазнавати макро- і мікроскопічних змін внаслідок запальних процесів бактеріального або вірусного походження, доброякісних і злоякісних уражень шийї, голови та середостіння. Серед нових методів скринінгу змінених ЛВ та диференціальної діагностики патологічних процесів значну роль відіграє доплерографія (УЗД). Метою роботи є визначення перспектив використання ультразвукової діагностики уражень ЛН при запальних та онкологічних процесах ЩЗ. Проведено ультразвукову діагностику з визначенням доплерівських ознак (EDV, PSV, RI) та змін ЛШ шийї у 175 пацієнтів з патологією ЩЗ та без неї. За результатами патогістологічного заключення пацієнтів було розподілено на 4 групи: 46 здорових пацієнтів без патології ЩЗ, 44 пацієнти із запальними захворюваннями ЩЗ, 42 пацієнти з раком ЩЗ без метастатичного ураження ЛН, 43 пацієнти з метастатичним ураженням ЛВ – рак ЩЗ. Дані ультразвукової діагностики в режимі В продемонстрували позитивну комплементарність з ехоструктурними ознаками та змінами васкуляризації. Проявляється у широкому діапазоні швидкостей і атипій ангіоархітектоніці. У 13 (31%) хворих була підвищена васкуляризація з PSV – 23-45 см/с, EDV – 14-8 см/с, RI – 0,32-0,46. Показано прогресування проліферативних процесів без некротичних змін у воротах та їх периферії. У 18 (43%) хворих при динамічному доплерометрії спостерігалася поява прискореного кровотоку та атипової судинної концентрації поза капсулами вузликів. Це показник поширення раку. Кольорове доплерівське картування та енергетичне доплерівське кодування метастазів шийки матки є важливими діагностичними методами, які якісно та кількісно доповнюють і деталізують ультразвукову діагностику в В-режимі.

**Ключові слова:** пухлини щитовидної залози, тиреоїдит, лімфатичні вузли, доплерографія, метастаз.



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