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COMPARATIVE ANALYSIS OF MORPHOFUNCTIONAL INDICES OF THE THYROID GLAND IN INDIVIDUALS WHO HAVE HAD CORONAVIRUS

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ABSTRACT

A number of targeted scientific studies are being conducted around the world to study the impact of coronavirus infection on the thyroid gland. World scientists claim that there are ACE2 receptors in the tissues of the hypothalamus and pituitary gland, and it has been established that these glands are damaged by SARS-CoV-2 directly or as a result of the immune process. However, at present, the pathophysiological features and clinical significance of the impact of SARS-CoV-2 on the organs of the endocrine system, as well as the impact of concomitant endocrine dysfunction on the prognosis of patients infected with coronavirus, have not been fully studied and are insufficiently covered in the literature. Given that coronavirus infection can lead to autoimmune thyroiditis or subacute thyroiditis, it is especially important to improve early diagnosis and treatment measures, as well as early assessment of the possibility of disability.

Key words: SARS-Cov-2 pandemic, thyroid gland, autoimmune thyroiditis, ultrasound.

INTRODUCTION

Relevance of the problem. In February 2020, a new type of pneumonia caused by coronavirus was named Novel coronavirus pneumonia (NCP, COVID-19). The World Health Organization assigned an official name to the infection caused by the new coronavirus – COVID-19. The International Committee on Toxonomy of Viruses assigned an official name to the pathogen SARS-CoV-2 [9].

In the early stages of the pathological process, the target cells for SARSCoV-2 are epithelial cells of the respiratory and gastrointestinal tracts, where the pathogen binds to the angiotensin-converting enzyme 2 (ACE2) receptor via the viral structural S protein. Then, the transmembrane serine protease type 2 (TMPRSS2) present in the host cell promotes the uptake of the virus by cleaving the S protein and activating the SARS-CoV-2S complex, which mediates the entry of the coronavirus into the host cell. In addition to epithelial cells, SARS-CoV-2 infects endothelial cells of the pulmonary capillaries, enhancing the inflammatory response and causing an influx of monocytes and neutrophils [8].

Since SARS is a disease known to cause multiple organ damage (lungs being the main target organ), it is assumed that SARS may also have a detrimental effect on the thyroid gland [2]. However, there are only a few publications reporting clinical observations based on blood samples from SARS patients tested for thyroid function. In addition, only a few direct studies of the hypothalamic-pituitary-thyroid (HPT) axis in SARS patients have been published [2, 11]

Several other viruses can also cause thyroid diseases, such as subacute thyroiditis and autoimmune thyroid diseases. Clear evidence for the presence of viruses (or their components) in the thyroid is available for retroviruses and mumps in subacute thyroiditis, for retroviruses in Graves' disease, and for human T-lymphocyte-trophic virus-1, enterovirus, rubella, mumps, herpes simplex virus, Epstein-Barr virus, and parvovirus in Hashimoto's thyroiditis [2]. There is no evidence that patients with autoimmune thyroid disease are more susceptible to viral infection (including SARS-CoV-2), nor that they are at risk of developing more severe COVID-19. However, two reports by Matau-Salat M et al. suggest that SARS-CoV-2 may also cause autoimmune thyroid disease [4]

We know that viruses can cause thyroid disease. Coronaviruses can also affect thyroid activity. We have learned that people who survived SARS and COVID-19 had thyroid abnormalities. Based on the available results from the SARS-CoV-2 pandemic [14], more attention should be paid to both patients with undiagnosed thyroid disease and treated COVID-19 patients. There is no routine monitoring of thyroid function. However, as recommended by the guidelines, we suggest the importance of monitoring thyroid hormones in COVID-19. We know that viruses can cause thyroid disease. Coronaviruses can also affect thyroid activity. We have learned that people who survived SARS and COVID-19 had thyroid abnormalities. Based on the available results of the SARS-CoV-2 pandemic [14], more attention should be paid to both patients with undiagnosed thyroid disease and treated COVID-19 patients. There is no routine monitoring of thyroid function. However, as recommended by the guidelines, we suggest the importance of monitoring thyroid hormones in COVID-19.

Autoimmune diseases of the thyroid gland have been observed even among patients with lungs manifestations of COVID-19. Evidence has been provided of a possible molecular mimicry between COVID-19 viral proteins and human tissue antigens. They demonstrated that antibodies to SARS-CoV-2 react with several various human tissues, including the thyroid gland. By selective epitope mapping they showed similarity and homology between spike, nucleoprotein and many other SARS-CoV-2 proteins and antigen thyroid tissue - thyroid peroxidase [1]. It was noted that subacute thyroiditis was associated with the appearance of newly identified antithyroid antibodies to thyroglobulin [5]. There are reports of the development of chronic autoimmune thyroiditis and hypothyroidism after subacute thyroiditis, which allows suggest that a viral infection may cause abnormal immune response against the thyroid gland in genetically predisposed individuals [7].

These data testify SARS-CoV-2 in triggering or enhancing autoimmune diseases diseases after COVID-19 among susceptible patients or worsening of pre-existing autoimmune disorders, which increases the likelihood of developing autoimmune thyroiditis, as well as autoimmune polyglandular syndromes these in patients [4].

Ultrasound diagnostics is a safe and informative method diagnostics of endocrine diseases. Today, ultrasound is considered the “gold standard” for detecting thyroid nodules both in the world and in Russia [12]. The advantages of this method are recognized throughout the world, despite the existing element of subjectivity [1, 3]. The American Thyroid Association believes that thyroid sonography should be performed on all patients with detected nodes or with a suspected node [6]. Ultrasound can visualize not only a typically located thyroid gland, but also conduct differential diagnostics with a tumor of a different etiology and identify metastases to the lymph nodes [10]. Today, most medical institutions in the world use a gradation of images called The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC), adopted at the 2007 US National Cancer Institute conference [6]. Gradually It is also being implemented in Russia [10]. The implementation of The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC - Bethesda) in the practice of cytology laboratories has created conditions for more efficient work of cytologists [6, 10,12]. Ultrasound doctors and cytologists are important stages of the treatment and diagnostic process, the task of which is to make an informed decision on the choice of treatment for nodes Thyroid gland [3]. But the initial, key and final point of the diagnostic chain are the endocrinologists of the polyclinics [13].

Purpose: to examine the morphofunctional parameters of the thyroid gland in people who have suffered coronavirus.

Material and methods: The research was conducted at the Bukhara State Medical Institute and the Bukhara Regional Endocrinology Dispensary. A total of 186 patients were included in the study, they were studied in the following groups: The main group consisted of 86 Sars-Cov-2 infected patients with thyroid disease, the comparison group consisted of 60 Sars-Cov-2 infected patients without thyroid disease, and the control group consisted of 40 relatively healthy people.

The study was conducted taking into account the results of anamnestic data on a specially developed individual patient card that meets the requirements, an objective examination and study of the thyroid gland status, a conclusion of an ultrasound examination with color Dopplerography (CDG), hormonal and general clinical laboratory examination, and coagulogram indicators.

Results: The shape, contours and dimensions of the thyroid gland were assessed using ultrasound in the patients included in the study. The results of the analysis are presented by measuring the maximum length, width and thickness for each lobe and isthmus.

According to the results of the ultrasound examination conducted to assess the morphometric characteristics of the thyroid gland in the examined groups (Table 1), such indicators as the width, length and thickness of the thyroid gland in patients of the main group were higher than in patients in the comparison and control groups, but these indicators did not acquire statistical significance. (P>0.2; P>0.1).

Table 1.

Comparative characteristics of morphometric parameters of the thyroid gland in the study groups

№	Indicators	Main group (n=86)		Comparison group (n=60)		Control group (n=40)		P
		M	m	M	m	M	m	
1	RIGHT LOBE:							
	Width (mm)	20.86	0.50	19.74	0.77	19.80	0.50	>0.2
	Thickness (mm)	24.09	0.53	23.06	0.82	23.07	0.44	>0.2
	Length (mm)	48.43	0.87	45.21	1.94	48.28	0.63	>0.1
	Volume (cm^3)	13.43	0.65	11.54	0.85	10.54	0.85	<0.05
2	LEFT LOBE:							
	Width (mm)	20.66	0.41	19.75	0.46	18.71	0.32	>0.2
	Thickness (mm)	26,24	2.53	23,21	0.44	22.65	0.43	>0.2
	Length (mm)	51.37	0.79	46,45	1.42	48.28	0.58	>0.1
	Volume (cm^3)	14.98	0.55	12.43	0.65	9.23	0.65	<0.05
3	Isthmus thickness (mm)	7.44	0.42	7.19	0.35	5.90	0.31	<0.01
4	Total volume (cm^3)	28.41	1.06	23.97	1.23	19.77	0.60	<0.05
5	Thyroid volume/body weight ratio	0.38	0.01	0.36	0.03	0.35	0.02	>0.2

Note: P – Significance of differences between compared groups according to Student's t-test.

The analysis results showed that in patients of the main group the average volume of each lobe increased by 1.3 and 1.6 times, respectively, compared to the control group and amounted to 13.43±0.65 cm3 and 14.98 ±0.55 cm3 (P <0.05). This indicator in the comparative group is higher than in the control group and amounts to 11.54 ± 0.85 cm3 and 12.43 ±0.65 cm3 (P <0.05). It was found that the average volume of each lobe was 1.1 and 1.2 times greater in patients of the main group compared to patients of the comparison group, however, these indicators did not reach statistical significance. (P>0.01).

When analyzing the examined groups by the total volume of the gland compared to the control group, it was 1.4 and 1.2 times higher in patients of the main and comparative groups and amounted to 28.41±1.06 cm3 and 23.97±1.23 cm3. When comparing the main group and the comparison group by the total volume of the gland, it was found that the main group exceeded the comparison group by 1.1 times, but did not reach statistical significance (P>0.01).

Moreover, it was found that the isthmus of the thyroid gland in patients of the main and comparative groups, compared to the control group, was 1.3 and 1.2 times larger, respectively, and amounted to 7.44±0.42 cm3 and 7.19±0.35 cm3 (P < 0.05; P <0.01).

Analysis of ultrasound parameters of the thyroid gland was carried out in patients of the main group before and after coronavirus infection (Table 2).

Table 2 .

Morphometric parameters of thyroid ultrasound before and after coronavirus in the main group

№	Indicators	Main group (n=86) Before COVID -19		Main group (n=86) After COVID-19		R
		M	m	M	m	
1	RIGHT LOBE					
	Width (mm)	20.64	0.47	20.86	0.50	>0.5
	Thickness (mm)	23.88	0.52	24.09	0.53	>0.5
	Length (mm)	38.51	0.79	48.43	0.87	>0.5
	Volume (cm3)	11.35	0.67	13.43	0.65	<0.05
2	LEFT LOBE:					
	Width (mm)	20.57	0.45	20.66	0.41	>0.5
	Thickness (mm)	23.64	0.41	26,24	2.53	>0.2
	Length (mm)	41.93	0.74	51.37	0.79	>0.5
	Volume (cm3)	12.96	0.57	14.98	0.55	<0.05
3	Isthmus thickness (mm)	7.03	0.43	7.44	0.42	>0.2
4	Total volume (cm3)	24.31	0.37	28.41	1.06	<0.05
5	Thyroid volume/body weight ratio	0.32	0.02	0.48	0.05	>0.5

Note: P – Significance of differences before and after treatment according to Student's t-test.

According to the results of the analysis, in the main group of patients after coronavirus infection, although a change in the thickness, length and width of the lobes of the thyroid gland was detected, it was not statistically significant (P >0.5).

However, when analyzing the average sizes of the right and left lobes, it was found that in the main group of patients after coronavirus infection, the lobes increased by 1.2 and 1.1 times, respectively, and the figures were 13.43±0.65 cm3 and 14.98±0.55 cm3. When analyzing the total volume of the thyroid gland, it was found that after infection it increased by 1.1 times, the average volume was 24.31±0.37 cm3 before infection and 28.41±1.06 cm3 after infection (<0.05).

Among the examined groups, cases of heterogeneity (uneven echogenicity) of the thyroid gland structure in the main and comparative groups of patients were 6.4 and 6.9 times higher in the right lobe and when analyzing the left lobe it turned out to be 5.0 and 5.4 times higher (Table 3).

Table 3.

Comparative analysis of the echostructure of the thyroid gland in the examined groups

Signs		Main group (n=86), %	Comparison group (n=60), %	Control group (n=40), %	χ2	R
Echostructure of the right lobe	heterogeneous	86.0	92.3	13.3	0.72	<0.05
	homogeneous	14.0	7.7	76.7	0.72	0.398
Echostructure of the left lobe	heterogeneous	84.9	92.3	16.8	0.95	<0.05
	homogeneous	15.1	7.7	73.2	0.95	0.330

Note: χ2, P — reliability of differences in the results of the Pearson test of the compared groups.

Cases with the same homogeneity had a higher percentage in the control group than in both groups. However, the case of heterogeneous echostructure in the main group was 86% and 84.9%, respectively, and 92.3% in the comparison group (P<0.05).

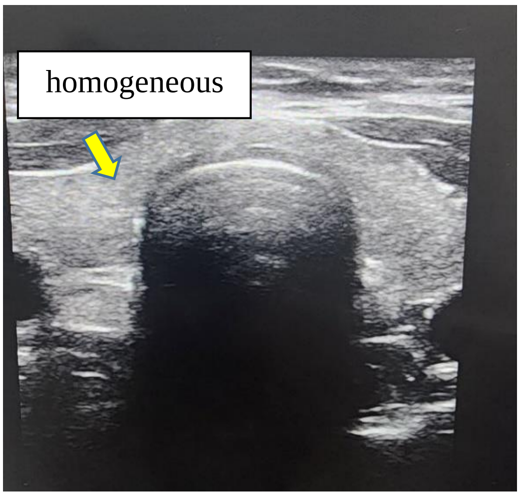

Figure 1. External appearance of the thyroid gland structure during ultrasound examination

A comparative analysis of morphometric parameters of ultrasound examination of the thyroid gland in the study groups was carried out (Table 4).

Table 4.

Comparative characteristics of morphometric parameters of ultrasound examination of thyroid gland echo density in the examined groups

Signs		Main group (n=86), %	Comparison group (n=60), %	Control group (n=40), %	χ2	R
Echo density of the right lobe	Hyperechoic	19.3	26.9	2.7	5.34	<0.05
	Average	69.1	57.7	97.3	4.75	0.029
	Hypoechoic	11.6	15.4	0,0	0.26	<0.05
Echo density of the left lobe	Hyperechoic	18.1	15.4	3.2	1.18	<0.05
	Average	81.4	73.1	96.8	0.85	0.358
	Hypoechoic	10.5	11.5	0,0	0.02	<0.05

Note: χ2, P — reliability of differences in the results of the Pearson test of the compared groups.

When analyzing echogenicity among the study groups, the average echogenicity had a high percentage in all three groups. In the main group of patients, hyperechogenicity of each lobe was 19.3 and 18.1%, hypoechogenicity - 11.6 and 10.5%. In patients in the comparison group, hyperechogenicity by lobes was 26.9% and 15.4%, hypoechogenicity - 15.4% and 11.5%, respectively. When comparing the main group with the control group, compared to the main group, in patients of the comparison group, hyperechogenicity was 1.4 times higher, and hypoechogenicity was 1.3 times higher ($p < 0.05$).

In addition, in the group of patients with altered echogenicity, unevenness and blurring of the contours of the gland in some places (where the inflammation is more pronounced) are noticeable (Fig. 2)

After infection with coronavirus in the main group and the comparison group, it was noted that the contours of the thyroid gland were uneven in 26.7 and 17% of cases, but the boundaries were clear, and the echogenicity was 2.3 and 2.4 times higher than in the control group. ($P < 0.001$).

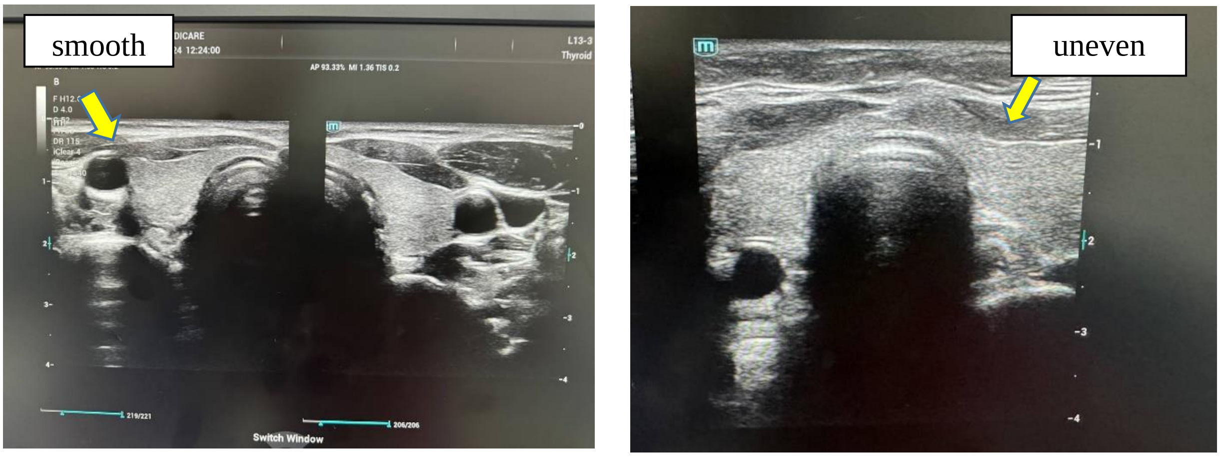

Figure 2. View of the thyroid gland contours during ultrasound examination

During ultrasound examination, the echogenicity of the thyroid gland changed and the blood supply (hypervascularization) increased in the CDC study in 18.6% of patients in the main group and in 19.2% of patients in the comparison group (Fig. 3).

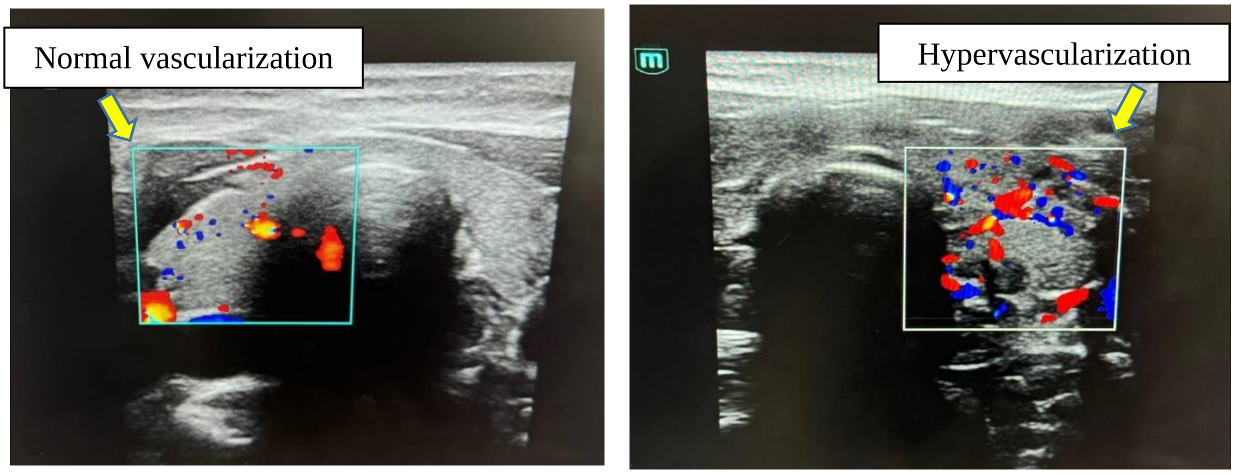

Figure 3. External appearance of the thyroid gland CDC

When studying the results of thyroid analysis according to the TI-RADS classification developed in 2009, during ultrasound examinations in the main group of patients, TI-RADS-1 was 55.8%, TI-RADS-2 was 30.2%, TI-RADS-3 and 4 were 10.5% and 1.2%, respectively. When assessing patients in the comparison group according to the TI-RADS system, it was found that TI-RADS-1 was 42.3%, and TI-RADS-2 and 3 were 53.8% and 3.8%, respectively, but TI-RADS-5 was not detected in both groups (Fig. 4).

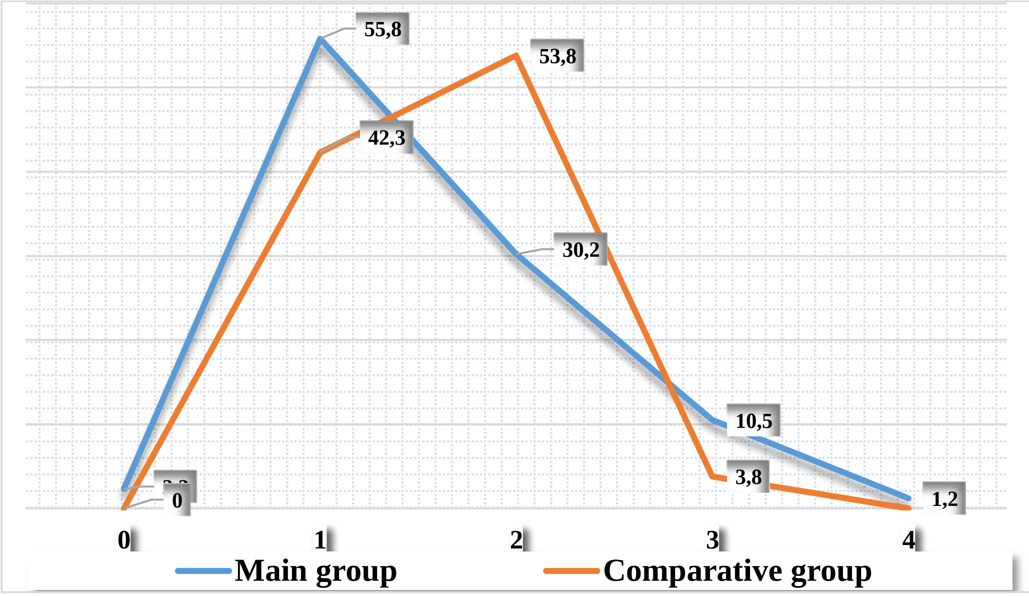

Figure 4. Results of the classification analysis TI-RADS

According to this classification, TI-RADS 1 pathological process in the thyroid gland is safe, which means that it is necessary to undergo UTT examination once a year. However, according to TI-RADS 3 and TI-RADS 4, it was found that in the main group, 1.0 and 1.2 times more were registered than in the comparison group, respectively, and this was considered an indication for a more in-depth examination, i.e., a puncture biopsy.

The results of the analysis showed that the ultrasound signs have a high level of reliability, the most important parameters in assessing the “Graphic Value” were echogenicity, exostructure and border accuracy, the total dispersion of their elementary properties is 53.78%, these indicators are determined according to the TIRADS system.

Conclusion:

1. When analyzing the groups by the total volume of the thyroid gland after infection with Covid-19 compared to the control group, it was found that it was 1.4 and 1.2 times higher in patients of the main group and the comparison group, and the average value was 28.41 ± 1.06 cm3 and 23.97 ± 1.23 cm3, respectively, in the groups. ($P < 0.05$). After infection with coronavirus, the heterogeneity of the echostructure of the thyroid gland averaged 85.45% in patients of the main group and 92.3% in patients of the comparison group ($P < 0.05$). When analyzing the examined groups by thyroid echogenicity, hyperechogenicity in the main group averaged 18.7%, hypoechogenicity - on average 11.05%. In the comparison group, hyperechogenicity averaged 21.15%, hypoechogenicity - 13.45%. When comparing the groups, the hyperechogenicity of the comparison group patients

compared to the main group was 1.4 times higher, and hypoechogenicity was 1.3 times higher ($P<0.05$). In patients of the main and comparison groups, the indicators of unevenness of the gland contours were noted in 26.7% and 17% of cases, respectively.

2. With CDC, hypervascularization was detected in 18.6% of patients in the main group and in 19.2% of patients in the comparison group. In the main group, it was found that 14% of thyroid formations were perinodular, 13% were intranodular, and 2.3% had mixed blood supply. In the comparison group, mixed blood supply to the nodes was not detected, but intranodular blood supply was detected in 12% of cases and perinodular blood supply in 7.7% of cases.

3. When assessing the thyroid parameters using the TI-RADS system in the main group of patients, TI-RADS-1 was 55.8%, TI-RADS-2 was 30.2%, TI-RADS-3 and 4 were 10.5% and 1.2%, respectively. In the control group, TI-RADS-1 was detected in 42.3%, TI-RADS-2 and 3 were detected in 53.8% and 3.8%, respectively, but TI-RADS-5 was not detected in either group.

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