

THE POSSIBILITIES OF QUANTITATIVE ASSESSMENT OF SINGLE-PHOTON EMISSION COMPUTED TOMOGRAPHY IN THE DIAGNOSIS OF THYROID DISEASES

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ABSTRACT

Relevance: The main pathologies of the thyroid gland (TG) include hyperthyroidism, hypothyroidism, nodular goiter, autoimmune diseases (AIT), and cancer. An increase in morbidity from TG pathologies in the Republic of Kazakhstan requires more efficient diagnostic and treatment methods.

The study aimed to determine the diagnostic value of SPECT with sodium pertechnetate (^{99m}Tc) quantitative parameters in TG pathologies.

Methods: The study involved 112 patients. SPECT assessment of the TG was carried out using a Philips Forte gamma camera and a radionuclide drug – ^{99m}Tc. A boxplot diagram was used for statistical analysis of the results, with which the data was visualized, as well as SPSS software ver-sion 21.0 and Microsoft Office Excel.

Results: Of the 112 patients, 96 (85.7%) were women, and 16 (14.3%) were men. The participants were aged from 10 to 89 years, with a mean age of 50.9 years. The median administered activity of the ^{99m}Tc was 160 MBq. The analysis showed that the largest proportion of patients with SPECT studies of the TG were in the age group over 55 years (37.5%). Regarding the distribution of TG nodules, 47 (42%) patients had nodular formations, including 25 (53.2%) "hot," 20 (42.6%) "cold," and 2 (4.3%) "warm." Classification of thyroid diseases in patients with nodular formation showed that 13 (27.7%) suffered from diffuse goiter, 19 (40.4%) had nodular goiter, 12 (25.5%) had AIT, and 3 (6.4%) patients had cancer. Analysis of the distribution of radiopharmaceutical accumulation in the TG depending on the diagnosis showed that the median accumulation of radiopharmaceuticals in cancer was 0.6, in AIT – 1.15, and in diffuse and nodular goiter – approximately 1.5 and 1.7, respectively.

Conclusion: Our study confirms the importance of quantitative SPECT parameters for understanding the various manifestations and pathological processes in the TG. Future research may improve diagnostic and treatment strategies for this disease by further exploring the relationship between these parameters and various forms of TGC.

Keywords: Thyroid gland, node, single-photon emission computed tomography (SPECT), radiopharmaceuticals, radiopharmaceutical accumulation, quantitative assessment.

Introduction: Thyroid gland (TG) disorders are the conditions that impact the TG function, size, and structure. The TG disorders primarily include hyperthyroidism, hypothyroidism, TG nodules, autoimmune diseases, and thyroid cancer. Worldwide, approximately 200 million persons have been diagnosed with TG disorder. The prevalence rate of hyperthyroidism ranges from 0.2% to 1.3%, while the prevalence rate of hypothyroidism ranges from 1% to 2%. And the proportion of palpable TG nodules ranges from 4% to 7% [1]. Besides, there is a constant increase in thyroid cancer, according to the International Agency for Research on Cancer. For example, the number of newly diagnosed thyroid cancer cases increased by 1.4 times (from 586,202 to 821,214) from 2020 to 2022 [2, 3].

In the Republic of Kazakhstan, the incidence of TG disorders has also increased. Kh.I. Kudabayeva et al. report that foci of endemic goiter have been registered in 11 regions [4]. The share of thyroid cancer in the structure of oncological morbidity is 1-3% and is in the 17th place [5].

New diagnostic methods appear with the development of science and technology in medicine. Ultrasonic scanning (Ultrasound) is still the main TG examination method [6]. The ultrasound is sensitive to TG nodules in 19-67% of cases but has a limited capacity to differentiate benign and malignant neoplasms. Fine-needle aspiration puncture biopsy (TAPB) is a mandatory part of the examination to assess nodular neoplasms [7]. High sensitivity and specificity are the strengths of this method. Scintigraphy or single-photon emission computed tomography (SPECT) is used to visualize the TG functional activity. This method allows for assessing the TG function and determining the number, location, and types of foci. Scintigraphy or SPECT before TAPB is recommended to sort out patients with non-functioning "cold" nodules.

The study aimed to determine the diagnostic value of SPECT with sodium pertechnetate (^{99m}Tc) quantitative parameters in TG pathologies.

Materials and methods: The data for this retrospective study were collected from 112 patients who underwent TG examination from 2016 to 2023 in the Department of Radiology and Nuclear Medicine of the Kazakh Research Institute of Oncology and Radiology (Almaty, Kazakhstan). The collected data included the SPECT, US, and TAPB results, data on the therapy performed, and the results of the postoperative histological examination.

The SPECT study was conducted under the recommendations of the European Society of Nuclear Medicine (EANM) for TG scintigraphy and SPECT [8]. The patients who had undergone TG examinations had a referral from a physician. Patients received detailed information about the study while making an appointment and preparing for it. Pregnancy and breastfeeding were contraindications for the study.

The thyroid SPECT was performed using a Philips Forte gamma camera equipped with a high-energy collimator or a pinhole collimator centered on a photopeak with an energy of 140 keV. A radioactive pharmaceutical ^{99m}Tc was used for the study. The activity dose was calculated individually for each patient at 1-1.5 MBq/kg b.w. The syringe with the product was measured on an immersion dosing device and directly with a gamma camera before and after administration to calculate the administered dose. The study was conducted 10-15 minutes after administering ^{99m}Tc in the supine position with the patient's head thrown back. The image was obtained in

3 minutes per the standard gamma camera examination protocol. Parameters such as thyroid size, uniformity of radioactive pharmaceutical (RPh) uptake, and local foci of increased or decreased accumulation of RPh were evaluated as a result of the scanning. Nodules in the thyroid indicate that a focal formation has formed. Nodular formations of the thyroid were classified depending on the degree of RPh accumulation. Nodular formations were classified according to the adopted standard, as: "cold" – not accumulating RPh, "warm" – with the accumulation of RPh equivalent to the thyroid tissues, and "hot" (autonomous) – with the accumulation above the accumulation of thyroid tissues. Two nuclear medicine doctors from the Radiology and Nuclear Medicine Department of the Kazakh Institute of Oncology and Radiology (Almaty, Kazakhstan) interpreted the study results.

Statistical analysis of the results was conducted with the help of a boxplot, and such parameters as median, arithmetic mean, and standard deviation were used. All data obtained during the study were statistically processed. Statistical data processing was conducted using SPSS software version 21.0 and Microsoft Office Excel.

Results: 112 thyroid SPECT studies with ^{99m}Tc were performed in the Department of Radiology and Nuclear Medicine of the Kazakh Research Institute of Oncology and Radiology from 2016 to 2023. Demographic variables such as gender, age, and ethnicity were collected during the study (Table 1).

Table 1 – Demographic characteristics of the study participants

Category	Subgroup	Absolute Parameter	Percentage Parameter
Gender	Men	16	14.3%
	Women	96	85.7%
Age	0-24	5	4.5%
	25-34	17	15.2%
	35-44	23	20.5%
	45-54	25	22.3%
	55<	42	37.5%
Ethnic group	Kazakhs	63	56.25%
	Russians	31	27.69%
	Dungans	2	1.79%
	Ukrainians	1	0.89%
	Koreans	2	1.79%
	Uyghurs	3	2.68%
	Tatars	4	3.57%
	Kurds	1	0.89%
	Azerbaijanis	1	0.89%
	Kirgiz	1	0.89%

As seen from Table 1, most patients were women, 96 out of 112 (85.7%). The ages of the patients ranged from 10 to 89 years. The group over 55 prevailed in the age range of 42 persons (37.5%). The mean age of all patients was 50.9 years, 44.8 years in men and 51.4 years in women. The Kazakhs were the largest among the patients based on ethnic group, accounting for 56.25%.

The median of the introduced RPh activity during the study was 99mT – 160 MBq (60-260 MBq). The distribu-

tion of RPh accumulation in the thyroid, depending on gender, was visualized using boxplot analysis. As a result, the minimum value of RPh accumulation in women and men was the same - 0.1, and the maximum value was 13.8 and 9.1, respectively. The median in the first group, that is, in women, was 1.2; in the second group, it was less by 33.3% (0.8). The lower and upper quartiles in women were 0.6 and 2.3, respectively, and 0.4 and 1.6 in men (Figure 1).

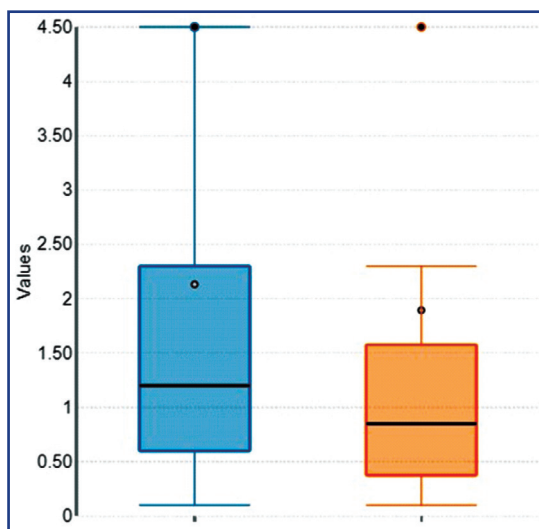


Figure 1 – Accumulation of RPh ^{99m}Tc in the thyroid in men and women

Table 2 – Distribution of TG nodules depending on the accumulation of ^{99m}Tc

Group	Category	Absolute parameter	Percentage Indicator
Presence of nodules	Present	47	41.96%
	Absent	65	58.04%
Classification of Nodules	Hot	25	53.2%
	Warm	2	4.3%
	Cold	20	42.6%
Nodule locations	Left lobe	15	31.9%
	Right lobe	25	53.2%
	Isthmus	3	6.4%
	Left/Right Lobes	4	8.5%

Nodular formations were found during the examination of the thyroid gland. The characteristics of the found TG nodules are presented in Table 2.

Table 2 shows that nodules were found in 47 (42%) patients, of which 25 (53.2%) were “hot,” 2 (4.3%) nodules were “warm,” and 20 (42.6%) nodules were “cold.” More than half of the nodules were located in the right lobe, at 25 (53.2%), and only 15 (31.9%) were in the left lobe. The

nodule’s location in the isthmus was 6.4% and 8.5% in both lobes.

The nodules were categorized by visual qualitative assessment for the RPh accumulation degree (Figure 2).

Patients with nodular formations were classified into 4 groups according to TG disorder: diffuse goiter, nodular goiter, autoimmune thyroiditis (AIT), and thyroid cancer (Table 3).

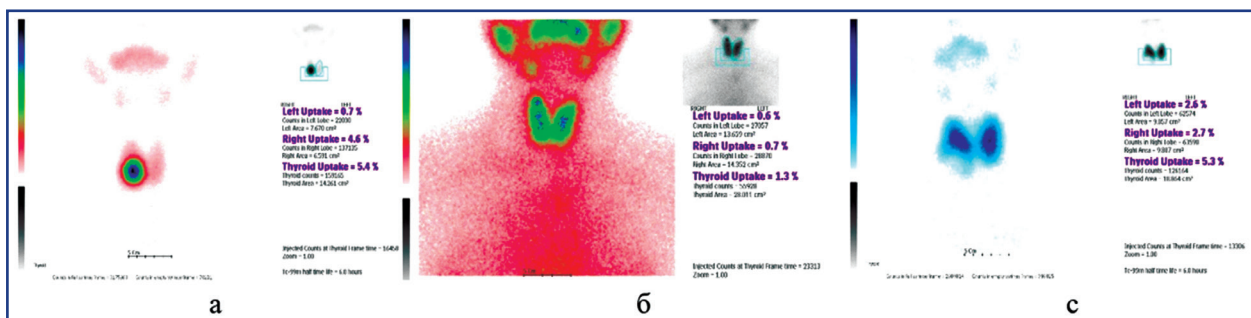


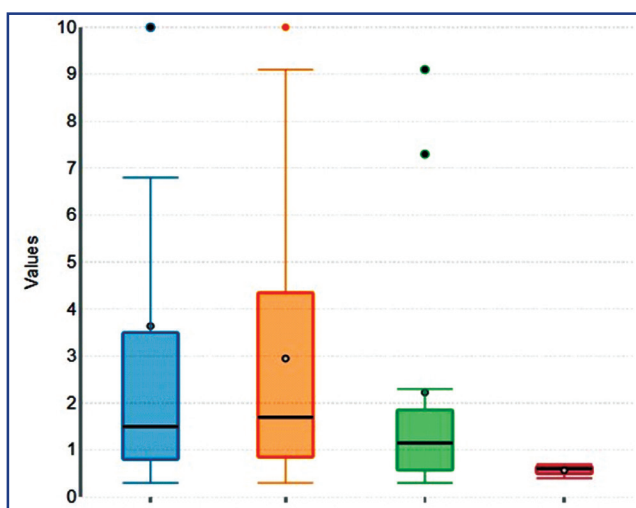
Figure 2 – Images of the thyroid: a) “hot” nodule, b) “warm” nodule, c) “cold” nodule

Table 3 – Classification of TG nodular formations

Group of disorders	Absolute parameter	Percentage parameter
Diffuse goiter	13	27.7%
Nodular goiter	19	40.4%
Autoimmune thyroiditis	12	25.5%
Thyroid cancer	3	6.4%

The number of patients with thyroid cancer was 6.4%, and the number with diffuse goiter and AIT were approximately the same, 27.7% and 25.5%, respectively, and the largest part of patients was with nodular goiter, 40.4% (Table 3).

The distribution of RPh accumulation in the thyroid, depending on the disorder, can be seen in Figure 3 and Table 4.



Note: Y-axis – values; Diagrams (from left to right): diffuse goiter, nodular goiter, autoimmune thyroiditis, thyroid cancer

Figure 3 – RPh accumulation in the thyroid under diagnosis

Table 4 – Summary data

Group	Number	Min.	Q1	Median	Q3	Max.	Medium value	Standard deviation
Diffuse goiter	13	0.3	0.8	1.5	3.5	13.8	3.6385	4.6543
Nodular goiter	19	0.3	0.85	1.7	4.35	10.2	2.9474	2.8899
Autoimmune thyroiditis	12	0.3	0.575	1.15	1.85	9.1	2.225	2.8794
Thyroid cancer	3	0.4	0.5	0.6	0.65	0.7	0.5667	0.1528

Analysis of quantitative SPECT parameters showed that the median RPh accumulation in thyroid cancer was 0.6 (mean value was 0.7). In contrast, this parameter was 2 times higher (1.15) in AIT. And the median RPh accumulations were approximately the same – 1.5 and 1.7, respectively, in diffuse and nodular goiter (Figure 3).

Discussion: We studied thyroid SPECT data from 2016 to 2023 as part of our study performed in the Department of Radiology and Nuclear Medicine of KazRIOR. During 112 thyroid studies, it was found that 85.7% (96) of participants were females, while males accounted for 14.3% (16). In the studies by G.B. Morand et al. [9], N. Bilen et al. [10], and C. Gong et al. [11], an average of 78% of patients were females. According to GLOBOCAN, females are also more affected by breast cancer; i.e., in 2022, the women-to-men ratio was 2.98 [3]. The gender imbalance in our study probably reflects the high incidence of TG disorder in the female population. There are several reasons for the explanation of this difference. The estrogenic environment and the cyclic nature of hormonal changes in women are strong stimulators of thyroid dysfunction in women. The fact that TG disorders are the most common endocrine factors affecting women of reproductive age is of paramount importance [12-15].

Analysis of the age distribution of patients allows us to see that thyroid studies with SPECT were conducted in a wide age range - from 10 to 89 years. In our studies, most patients were aged 35 to 44 years or above 55 years. In the study by N. Kwong et al., nodular TG disorders in patients of the oldest group (>70) increased by 0.7 [16]. Thyroid cancer was found oftener in the age group above 55, accord-

ing to the 2022 GCO observation [3]. It may indicate an increased need for such diagnostics at an older age.

Several key aspects should be discussed regarding the study's results on the distribution of RPh accumulation in thyroid tissue depending on gender. First, it is noticeable that the minimum RPh accumulation in women and men is the same, at 0.1. It indicates a similarity in the initial levels of thyroid activity in both genders. Second, the differences become more pronounced in the maximum value analysis: in women, the maximum value is 13.8 vs. 9.1 in men. This indicates various pathological processes or metabolic characteristics related to thyroid activity in different genders. The third important observation concerns the median. The median value of the RPh accumulation in women is 1.2, while this value in men is lower by 33.3% and is 0.8. It indicates potential differences in the distribution of thyroid activity between the genders.

Thus, the study results highlight potential differences in thyroid activity between men and women. It may have clinical implications in assessing thyroid function and possible pathological processes. Further studies may focus on identifying the causes of these differences and their clinical implications for understanding TG disorders.

The study of the characteristics of TG nodules provides valuable information about the various manifestations of this disease. It is noted that 42% of patients were found to have nodules, and many of them were classified as "hot," which is 53.2% of the nodules found. In previous studies, the proportion of hot TG nodules found during SPECT ranged from 8-72% [17-21]. Many authors in their research papers concluded that the "cold nodules" are mostly ma-

lignant, while the “hot nodules” are benign based on the comparison of the preoperative study results of SPECT and histology [22]. However, several studies show that it is not always the case, and 11.5% of hot nodules turn out to be malignant, while the rate for cold nodules is only 5-8%, and it was 25% in some studies. Radionuclide diagnostics is limited in differentiating benign tumors from malignant ones.

Analysis of the distribution of nodules by thyroid lobes showed a higher frequency of localization in the left lobe (53.2%). However, the location of the nodules, depending on the pole, is more significant, according to the works of other authors [23,24].

Classifying TG disorders among patients with nodular formations helps better understand their clinical manifestations. It was found that nodular goiter (40%) and diffuse goiter (27.7%) were the most common TG disorders in the cohort of patients in our study.

The thyroid gland increases evenly in diffuse goiter, one or more nodular formations are observed in the thyroid in nodular goiter, and their simultaneous combination is noted in diffuse-nodular goiter. Interestingly, the median of the RPh accumulation in these two cases does not differ much. At the same time, the RPh accumulation rate was lower than in diffuse goiter in patients with AIT but twice as high as in thyroid cancer.

US is widely used as a primary examination method for TG disorders. However, the US capabilities may be limited in the differential diagnosis of benign and malignant nodules [25,26]. Usually, TAPB is the “gold standard” for the differential diagnostics of thyroid lesions [27,28], and SPECT is used to diagnose thyroid goiter in certain cases. This method can help determine the goiter’s size, shape, activity, and spread. Their combined use is important for this reason [29]

Quantitative SPECT/CT is considered useful for risk stratification of functional TG disorders. It becomes obvious from the quantitative SPECT data analysis that the RPh accumulation level in thyroid cancer was noticeably lower than in other groups. It may be due to a decrease in the ability of the thyroid gland to concentrate iodine in some types of malignant neoplasms [30]. Due to the similarity of technetium and iodine in terms of physical and chemical properties, technetium uptake is also reduced [28].

This figure doubled with AIT, reaching 1.15. The median indicators of RPh accumulation were approximately equal in diffuse and nodular goiter and amounted to 1.5 and 1.7, respectively.

The work by H. Lee et al. showed that the quantitative parameters of SPECT/CT were the highest in diffuse goiter and lower in the euthyroid state, but this parameter was the lowest in thyroiditis ($p < 0.0001$). The work demonstrated that the quantitative assessment of SPECT/CT is more accurate than the qualitative assessment of the RPh accumulation, so it is considered the main method [31]. In the work of H.J. Kim et al., the percentage of RPh uptake was

also more significant in detecting euthyroidism and made it possible to distinguish destructive thyroiditis from a euthyroid state [32].

Thus, the results of our study showed that the quantitative parameters of SPECT are informative in the differentiation of thyroid cancer from other thyroid pathologies. However, the method has a lower diagnostic accuracy in the differential diagnostics between non-oncological thyroid pathologies. Further studies may deepen the understanding of the relationship between the quantitative parameters of SPECT and various thyroid pathologies. It will help to develop more effective strategies for the diagnostics and treatment of TG disorders.

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АНДАТПА

ҚАЛҚАНША БЕЗІНІҢ АУРУЛАРЫН ДИАГНОСТИКАЛАУДА БІР ФОТОНДЫ ЭМИССИЯЛЫҚ КОМПЬЮТЕРЛІК ТОМОГРАФИЯНЫҢ САНДЫҚ БАҒАЛАУЫҢ МҮМКІНДІКТЕРІ

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Өзектілігі: Қалқанша безінің негізгі патологияларына гипертиреоз, гипотиреоз, түйінді зоб, аутоиммунды аурулар және қатерлі ісік жатады. Қазақстан Республикасында диагностика мен емдеудің неғұрлым тиімді әдістерін талап ететін ҚБ ауруымен ауыратын науқастар санының артуы байқалады.

Зерттеудің мақсаты – ҚБ-нің патологиясын зерттеу кезінде натрий pertechnetатын (^{99m}Tc) қолданып БФЭКТ-ның сандық параметрлерінің диагностикалық мәнін анықтау болып табылады.

Әдістері: Зерттеу барысында 112 науқастың деректері қамтылды. ҚБ-дің сцинтиграфиясы Philips Forte гамма камерасы және радионуклидті препарат – ^{99m}Tc көмегімен жүргізілді. Нәтижелердің статистикалық талдауы кезінде, boxplot диаг-

рамасы көмегімен деректер визуализацияланды және SPSS-тің 21.0 нұсқасы мен Microsoft Office Excel бағдарламалық құралы пайдаланылды.

Нәтижелері: 112 науқастардың 96 (85,7%) әйелдер, 16 (14,3%) ер адамдар болды. Зерттеу жүргізілген науқастардың жасы 10-нан 89 жас аралығында болды, ал орташа жасы 50,9 құрады. Енгізілген радиофармдәрінің (РФД) ^{99m}Tc -дің белсенділігінің медианасы 160 МБк құрады.

Талдау ҚБ-інің БФЭКТ-лық зерттеуінен өткен науқастардың үлкен үлесі 55 жастан асқан (37,5%) жас тобы екенін көрсетті. ҚБ-інің түйіндерінің таралуына келетін болсақ, 47 (42%) науқаста түйінді түзілімдер болды, оның ішінде 25 (53,2%) «ыстық», 20 (42,6%) «суық» және 2 (4,3%) – «жылы» болды.

ҚБ-нің Түйінді формациясы бар науқастардың жіктелуінде: 13 (27,7%) диффузды зобпен, 19 (40,4%) – түйінді зобпен, 12 (25,5%) – аутоиммунды тиреоидитпен (АИТ) және 3 (6,4%) – қатерлі ісікпен ауырғанын көрсетті.

Диагнозға байланысты ҚБ-де РФД-тің жинақталуының таралуын талдау кезінде, препараттың жинақталу медианасы қатерлі ісік кезінде 0,6, АИТ-те – 1,15, ал диффузды және түйінді зобта сәйкесінше 1,5 және 1,7-ні құрайтыны анықталды.

Қорытынды: Біздің зерттеуіміз ҚБ-дегі әртүрлі білінулер мен патологиялық процестерді түсіну үшін БФЭКТ сандық параметрлерінің маңыздылығын растайды.

Түйінді сөздер: қалқанша безі, түйін, бір фотонды эмиссиялық компьютерлік томография (БФЭКТ), радиофармдәрі (РФД), РФД-тің жинақталуының, сандық бағалау.

ABSTRACT

ВОЗМОЖНОСТИ КОЛИЧЕСТВЕННОЙ ОЦЕНКИ ОДНОФОТОННОЙ ЭМИССИОННОЙ КОМПЬЮТЕРНОЙ ТОМОГРАФИИ В ДИАГНОСТИКЕ ЗАБОЛЕВАНИЙ ЩИТОВИДНОЙ ЖЕЛЕЗЫ

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Актуальность: Основные патологии щитовидной железы (ЩЖ) включают гипертиреоз, гипотиреоз, узловой зоб, аутоиммунные заболевания (АИТ) и рак. В Республике Казакхстан наблюдается увеличение заболеваемости ЩЖ, требующее более эффективных методов диагностики и лечения.

Цель исследования – определение диагностической ценности количественных параметров однофотонной эмиссионной компьютерной томографии с натрия пертехнетатом (^{99m}Tc) при патологиях щитовидной железы.

Методы: Материалы для исследования включали данные 112 пациентов. Количественная оценка ОФЭКТ ЩЖ проводилась с использованием гамма-камеры Philips Forte и радионуклидного препарата ^{99m}Tc . Для статистического анализа результатов использовали программное обеспечение SPSS версии 21.0 и Microsoft Office Excel, а также диаграммы boxplot для визуализации данных.

Результаты: В исследование было включено 112 пациентов, в т.ч. 96 (85,7%) женщины и 16 (14,3%) мужчины. Возраст участников находился в диапазоне от 10 до 89 лет, средний возраст составил 50,9 лет. Медиана введенной активности радиофармпрепарата (РФП) ^{99m}Tc составила 160 МБк.

Анализ показал, что большинство пациентов (37,5%) были старше 55 лет. Что касается распределения узлов ЩЖ, то у 47 (42%) пациентов были выявлены узловые образования, среди которых 25 (53,2%) были «горячими», 20 (42,6%) – «холодными» и 2 (4,3%) – «теплыми».

Классификация заболеваний ЩЖ у пациентов с узловым образованием показала, что 13 (27,7%) страдали диффузным зобом, 19 (40,4%) – узловым зобом, 12 (25,5%) – АИТ и 3 (6,4%) – раком ЩЖ.

Анализ распределения накопления РФП в ЩЖ в зависимости от диагноза показал, что медиана накопления РФП при раке составила 0,6, при АИТ – 1,15, а при диффузном и узловом зобе – примерно 1,5 и 1,7, соответственно.

Заключение: Наше исследование подтверждает важность количественных параметров ОФЭКТ для понимания разнообразных проявлений и патологических процессов в ЩЖ. Дальнейшие исследования могут улучшить стратегии диагностики и лечения этого заболевания, глубже изучив связь между этими параметрами и различными формами заболеваний ЩЖ.

Ключевые слова: щитовидная железа (ЩЖ), узел, однофотонная эмиссионная компьютерная томография (ОФЭКТ), радиофармпрепараты (РФП), накопление РФП, количественная оценка.

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