PREOPERATIVE DIAGNOSIS OF PATHOLOGY OF THE PARATHYROID GLANDS BY RADIODIAGNOSIS METHODS

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ANNOTATION. Recently, surgeons have been using minimally invasive methods to treat parathyroid pathology. More selective surgical approaches are based on the accuracy of preoperative diagnostic techniques. Various radiation diagnostic methods are used to visualize the pathology of the parathyroid glands. Along with long-known techniques, new modalities are entering clinical practice. When choosing a diagnostic algorithm, the attending physician should be guided by the most clinically effective and economically feasible scheme.

Purpose of the study: to find the optimal diagnostic protocol for preoperative diagnosis of parathyroid gland pathology based on the available available data.

Conclusion. Preoperative imaging of the parathyroid glands continues to evolve with changes in old techniques and the emergence of new ones, although no one modality has a clear advantage. The choice of imaging algorithm is largely based on the availability of methods and the experience of specific diagnostic centers. Ultrasound diagnostics and planar scintigraphy have proven themselves and are most widely used. The combination of these methods remains the first line of diagnosis in preoperative imaging. However, there is no consensus on the choice between planar scintigraphy techniques: washout method or subtraction method. Replacing planar scintigraphy with SPECT/CT improves the detection of pathological formations and clarifies their topographic location. Computed tomography and magnetic resonance imaging are used as a second line and are advantageous for small-sized pancreatic adenomas, multiple lesions, ectopia, during repeated operations, as well as in the case of ambiguous ultrasound and scintigraphy data. The value of PET/CT in the diagnosis of PTG pathology has not yet been determined, data is still limited, and published results are very heterogeneous, but due to its excellent diagnostic characteristics, the method seems very promising, especially in patients with persistent disease.

Key words: PTG, PHPT, ultrasound, MRI, CT, SPECT/CT, PET/CT, washout method, subtraction method

Introduction. Primary hyperparathyroidism (PHPT) is a common disease and ranks third among endocrine system pathologies after diabetes mellitus and thyroid pathology [1, p. 3195]. According to published data, the prevalence of PHPT in the world varies widely - from 0.5 to 34 per 1000 people [2, p. 112; 3, p. 485; 4, p. 4]. This scatter is due to the lack of large multicenter studies, standardized assessment criteria and definition of the form of PHPT. According to N.G. Mokrysheva et al. as of December 2017, the detection of PHPT per 100 thousand population is 1.3 cases in the Russian Federation, 7.6 cases in Moscow, 6.1 cases in the Moscow region [5, p. 300]. According to global data, women aged 50 to 60 years are most often affected, which correlates with data from the online registry of the Russian Federation, in which the bulk of all patients with PHPT in Russia are women (72%) in menopause (average age 59±8.2 years) [5, p. 305]. In the USA according to 2008–2009 data. the prevalence of the disease was 0.86% of the general population [6, p. 2], in Brazil - 0.78% [7, p. 70]. In Russia, the number of patients is 1% of the total population [5, p. 7]. The cause of most cases of PHPT is a solitary adenoma (88–90%), hyperplasia of the parathyroid glands is less common (5–7%), multiple adenomas occur with a frequency of 4 to 14%, parathyroid carcinoma is detected in less than 1% of cases [6, With. 2]. In primary hyperparathyroidism (PHPT), increased production of parathyroid hormone (PTH) occurs as a result of the development of a space-occupying lesion or hyperplasia of one or more parathyroid glands (PTG). The main link in the pathogenesis is a defect in calcium-sensitive receptors of tumor and hyperplastic cells of the parathyroid glands, the threshold of sensitivity to calcium is reduced or completely absent compared to the norm. Most cases of PHPT (95%) occur sporadically, but about 5% are part of hereditary syndromes such as multiple endocrine neoplasia (MEN1 and MEN2A) [7, p. 69; 8, p. 36; 9, p. 23; 10 s. 2]. Currently, the main radical treatment for patients with PHPT is surgery. This type of treatment is recommended for all patients with symptomatic disease [9, p. 28; 11, p. 9]. Parathyroidectomy with bilateral neck exploration has historically been the traditional standard for surgical management. However, recently, minimally invasive video-assisted parathyroidectomy is more often used as a standard treatment method [12, p. 1071]. For preoperative planning, various methods of topical radiation diagnostics are used: - ultrasound examination of the neck; — computed tomography (CT) with contrast multiphase enhancement; — magnetic resonance imaging (MRI) with contrast enhancement; — scintigraphy of the parathyroid glands (STG): — washout method; — subtraction method; — single-photon emission computed tomography (SPECT) and SPECT combined with computed tomography (SPECT/CT); — positron emission tomography combined with CT (PET/CT). When choosing an appropriate method or combination of methods, the attending physician must be aware of the main features of the method: sensitivity and specificity, radiation exposure, cost and availability.

Ultrasound examination (US) of the neck is a highly sensitive, widespread, inexpensive and accessible diagnostic method. The literature contains various data on the informativeness of ultrasound for the localization of parathyroid adenomas. The results of the study depend on the qualifications of the specialist conducting it, the class of equipment and sensor used, and the variant of topographic anatomy of the PTG [13, p. 40; 14, p. 34; 15, p. eleven; 16, p. 455; 17, p. 74; 18, p. 273; 19, p. 273]. The sensitivity range of the method varies from 51 to 90%, specificity - from 76 to 90% for solitary adenoma [19, p. 120; 20, p. 269; 21, p. 960; 22, p. 59; 23, p. 121; 24, p. 14]. The sensitivity of ultrasound sharply decreases with multiple hyperplasia and multiple adenomas, as well as with ectopic parathyroid gland. Ultrasound examination is carried out using a linear probe (5–15 MHz), the patient is positioned on his back with his head tilted back. The parathyroid gland has a higher echogenicity compared to unchanged thyroid tissue (thyroid gland). They are best determined by longitudinal scanning, in the form of homogeneous formations of regular oval or round shape, with increased or normal echogenicity. Their contours are clear, even, about 6–8 mm long, about 5 mm wide and about 4 mm thick [18, p. 273; 24, p. 104; 25, p. 50; 26, p. 50]. Ultrasound in gray scale mode shows hyperplastic and adenomatized parathyroid glands in 80–85% of cases as hypoechoic round or oval homogeneous formations larger than 1 cm in size with clear contours and a hyperechoic capsule [21, p. 976; 22, p. 60; 26, p. 8; 27, p. 1707]. The advantages of the method include the absence of radiation exposure, the absence of the need to administer contrast agents (CM), the low cost of the service, and the ability to assess the structure of the thyroid gland. The disadvantages of the technique include the inability to distinguish thyroid nodules from intrathyroidal thyroid gland [28, p. 2169; 29, p. 254], decreased sensitivity in the case of multiple hyperplasia of the pancreas, in the case of ectopia and in previously operated patients [28, p. 2170; 29, p. 261; 30, p. 3562; 31, p. 360].

Computed tomography with contrast multiphase enhancement. Multiphase contrast-enhanced computed tomography is a relatively new method for preoperative imaging of the parathyroid glands. According to the literature, the accuracy of this method varies widely - from 46 to 95% [15, p. 5], specificity - from 82 to 96% [38, p. 470; 39 p. 776]. Rodgers Se was the first to publish the results of using CT in the diagnosis of PHPT . et al. [40, p. 933]. The use of CT is especially relevant due to the possibility of assessing the mediastinum and determining the relationship of the pathological formation with surrounding tissues and organs. On native images, an adenoma usually looks like a hypodense formation of a round and oval shape, with clear, even contours. The densitometric density of the adenoma is slightly lower than the density of unchanged thyroid parenchyma, which contains a significant amount of iodine [31, p. 370; 41, p. 16; 42, p. 152]. The optimal number of phases for a contrast multiphase study has not been established, but most often they use 3 (native, arterial and venous) or 4 (a delayed phase is added). During the arterial phase, the adenoma actively accumulates contrast agent (CM), while during the venous phase, the contrast is washed away. This classic washout pattern is observed in only 20% of cases [43; With. 455]. Recently, a quantitative visual scale has been developed and used to assess the PTC, which makes it possible to determine the likelihood of its involvement. This scale uses differences in the type of CV washout and additional anatomical features [43, p. 460].

Magnetic resonance imaging (MRI) without and with contrast enhancement. The use of MRI for visualization of the prostate gland is limited in modern practice . According to the literature, the sensitivity of MRI varies widely from 43 to 94% [44, p. 960; 45, p. 427; 46, p. 113; 47, p. 665], specificity from 90% to 97% [48, p. 4902; 49, p. 2148] depending on the magnetic field strength (1.5 or 3 Tesla) of the tomograph used. In one study, the sensitivity of MRI without contrast enhancement was 80%; when contrast enhancement was used, it increased to 92% [50; With. 447]. The basic imaging protocol includes: T1- and T2-weighted images, fast spin-echo sequences. Pthyroid adenoma and hyperplasia usually have a high signal intensity on T2. On T1, the parathyroid glands have a low or intermediate signal intensity. With contrast enhancement, the signal from the parathyroid glands is enhanced on T1-weighted images compared to thyroid tissue. The advantages of this method include the absence of ionizing radiation and high resolution. Limitations of the technique: low scanning speed, contraindications in the presence of incompatible devices in the MRI body. MRI is used in the second line when ultrasound and scintigraphy results are questionable (or when scintigraphy is not available). The method has an advantage when used in children and pregnant women due to the lack of radiation exposure. MRI is an effective method for the topical diagnosis of pathological PTC and, like CT, can be useful for patients who require reoperation. In addition, it is an alternative to computed tomography in patients with a severe allergic reaction to iodine-containing CVs.

Scintigraphy of the parathyroid glands (SCG PTG). For parathyroid scintigraphy, different radiopharmaceuticals are used in different imaging protocols. The first radiotracer used for visualization of the prostate gland was thallium-201 in the 80s of the twentieth century. The drug that has been used in recent history for PTG scintigraphy is a complex of technetium-99m with 2-methoxyisobutyl isonitrile (MIBI). This complex, after intravenous administration, is absorbed by pancreatic adenoma cells, which are rich in mitochondria. Normal parathyroid glands are not visible on 99mTc-MIBI scintigraphy, unlike pathologically altered ones. It should be remembered that the thyroid gland, thymus, heart, liver and salivary glands physiologically accumulate 99mTc-MIBI, which may complicate imaging. Another problem for this radiopharmaceutical is that accumulation depends on the phase of the cell cycle, the blood supply to the pancreas, the calcium content in the blood serum, and the expression of P-glycoprotein [51, p. 1442]. Scintigraphy of the parathyroid glands is divided into two techniques: the washout method and the subtraction method. In this case, the subtraction method, in turn, is divided into single-isotopic and dual-isotopic. No consensus has yet been reached regarding the superiority of one of the methods [52, p. 112], but the radiation exposure in a two-isotope study is significantly higher. Nevertheless, there are works that show the advantage of subtraction over the washout method [53, p. 1567]. The washout method is based on the difference in the rate of washout of 99mTc-MIBI from the thyroid gland and parathyroid glands. Images are obtained at the early stage (after 10–15 minutes) and at the late stage (after 2–3 hours). Different washout times from the parenchyma of the thyroid gland and parathyroid glands lead to the fact that only pathological parathyroid glands are visualized on later images. The accuracy of this method is higher when identifying solitary adenomas with a predominance of oxyphilic cells. False-negative results are possible with glandular hyperplasia, with cystic degeneration of the pancreas, with a high body mass index, and small size [48, p. 4907]. The sensitivity of planar scintigraphy using the washout method ranges from 58% to 87% [54, p. 1444; 55, p. 1071], specificity from 65 to 93% [55, p. 1075; 56, p. 44]. One of the recent meta-analyses noted that scintigraphy with 99mTc-MIBI (washout method) and ultrasound of the neck have comparable sensitivity, but the specificity of scintigraphy is higher [1, p. 3198]. For certain types of adenomas with a low content of oxyphilic cells, the washout method does not work [57, p. 780]. There are also several formations that mimic the parathyroid glands when visualized using 99mTc-MIBI: parathyroid carcinoma, thyroid nodules, malignant neoplasms of the thyroid gland, ectopic thyroid tissue, lymphadenopathy - all are potential causes of false-positive conclusions [58, p. 718; 59, p. 823; 60, p. 581; 61, p. 1102].

Positron emission tomography combined with CT (PET/CT). 18F-deoxyglucose PET-CT has proven its value in staging, restaging, and postoperative evaluation of various malignancies. The use of PET/CT with radiopharmaceutical 18F-deoxyglucose for diagnosing PTG pathology has not become widespread due to the physiological accumulation of 18F-deoxyglucose in the thyroid gland [77, p. 336]. Several indicators are used to visualize hyperfunctional parathyroid glands: 11C-methionine, 11C-choline and 18F-fluorocholine. The sensitivity of 11C-methionine PET/CT for lesion detection ranges from 77 to 81% [78, p. 79; 79, p. 925]. The mechanism of absorption of this radiopharmaceutical is not fully understood, but it is assumed that it is involved in the synthesis of PTH precursors [78, p. 78]. The main disadvantage is the short half-life of radiopharmaceuticals. In the past few years, research on 11Scholine and 18F-fluorocholine has shown promising results. Choline is a precursor for the biosynthesis of phospholipids, which are important components of the cell membrane. In cells with a high proliferation rate, such as tumor cells, the need for choline increases due to increased phospholipid synthesis. After choline is taken up by the cell, it is phosphorylated by the enzyme choline kinase and retained in the cell. For imaging, choline can be radiolabeled with positron emitters such as 11C or 18F. In one recent meta-analysis, the sensitivity of choline PET/CT for lesion detection ranged from 88 to 96% [80, p. 102]. The advantages of PET/CT include the high sensitivity of the method, high resolution, and a combination of functional and anatomical methods. Disadvantages include high radiation exposure, low availability of radiopharmaceuticals, and high cost. Currently, PET/CT is used in cases where other techniques have given ambiguous results. Conclusion. 1. Preoperative imaging of the parathyroid glands continues to evolve with changes in old techniques and the emergence of new ones, although no one modality has a clear advantage. The choice of imaging algorithm is largely based on the availability of methods and the experience of specific diagnostic centers. 2. Ultrasound diagnostics and planar scintigraphy have proven themselves and are most widely used. The combination of these methods remains the first line of diagnosis in preoperative imaging. However, there is no consensus on the choice between planar scintigraphy techniques: washout method or subtraction method. 3. Replacing planar scintigraphy with SPECT/CT improves the detection of pathological formations and clarifies their topographic location. 4. CT and MRI are used as a second line and are advantageous for small-sized PTC adenomas, multiple lesions, ectopia, during repeated operations, as well as in the case of ambiguous ultrasound and scintigraphy data. 5. The value of PET/CT in the diagnosis of PTG pathology has not yet been determined, data is still limited, and published studies are very heterogeneous, but due to its excellent diagnostic characteristics, the method seems very promising, especially in patients with persistent disease.

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