

ORIGINAL PAPERS

Intraoperative Post-parathyroidectomy Correlation of PTH Hormone Values with Preoperative Scintigraphy

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Abstract

Preoperative parathyroid evaluation through nuclear medicine and intraoperative hormone monitoring has significantly increased the success of the surgical intervention. **Material and method:** Our study is descriptive, the database is retrospective but it is maintained prospectively. The preoperative protocol included single photon emission computed tomography (SPECT) with the use of technetium-99 sestamibi tracer. We preferred this approach as it allowed 3-D localization of the adenomas. PTH values were obtained from blood drawn from the ipsilateral jugular vein at the regular intervals of 5, 10 and 15 minutes post excision. **Results:** We had 6 cases with false negative which led to necessary dissection of the contralateral neck. Two had previous surgery and 4 had tumors in other locations which were observed after the surgical intervention through methodical investigations. We encountered 3 patients with false positive results. 2 had intrathyroidal adenomas and 1 was diagnosed with thyroid papillary carcinoma. Causes of a misinterpretation are related to: thyroid disease in association with hyperparathyroidism, a history of parathyroid surgery or multiple locations of hyperproductive parathyroid glands.

Keywords: hyperparathyroidism, sestaimibi, surgery

Rezumat

Evaluarea paratiroidiană preoperatorie prin medicina nucleară și monitorizarea hormonală intraoperatorie au sporit semnificativ succesul intervenției chirurgicale. **Materiale și metodă:** Studiul nostru este descriptiv, baza de date este retrospectivă, dar este menținută în maniera prospectivă. Protocolul preoperator a inclus tomografie computerizată cu emisie de fotoni (SPECT) și utilizarea traserului tehneciu-99 sestamibi. Am preferat această abordare deoarece a permis localizarea 3-D a formațiunilor tumorale. Valorile PTH au fost obținute din sângele recoltat din vena jugulară ipsilaterală la intervale regulate de 5, 10 și 15 minute după excizie. **Rezultate:** Am identificat 6 cazuri cu rezultate fals negative - ceea ce a condus la disecție cervicală contralaterală. Dintre aceste cazuri, 2 pacienți au suferit o intervenție chirurgicală anterioară și 4 au fost diagnosticați cu tumori în alte locații care au fost observate după intervenția chirurgicală, prin investigații metodice. Am întâlnit 3 pacienți cu rezultate fals pozitive. 2 au fost diagnosticați cu adenoame intratiroidiene și 1 pacient a fost diagnosticat cu carcinom papilar tiroidian. Cauzele unor rezultate eronate sunt legate de: boală tiroidiană în asociere cu hiperparatiroidism, antecedente de intervenție chirurgicală în regiune cervicală anterioară sau localizări multiple ale glandelor paratiroidiene hiperproductive.

Cuvinte cheie: diverticuloză, diverticulită, colită.

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INTRODUCTION

The parathyroid hormone (PTH) is a hormone secreted by the parathyroid glands, which are located in the anterior neck region posterior to the thyroid gland¹. The hormone plays a critical role in maintaining calcium and phosphate levels in the body. The primary function of PTH is to increase the concentration of calcium in the blood. It does this by stimulating the release of calcium from bones, increasing the absorption of calcium from the intestines, and reducing the excretion of calcium by the kidneys². PTH also regulates the concentration of phosphate in the blood by promoting excretion through the kidneys². PTH secretion is regulated by a negative feedback mechanism. When calcium levels in the blood drop, the parathyroid glands are stimulated to secrete PTH³. PTH then acts on the bones, intestines, and kidneys to increase calcium levels. Abnormalities in PTH levels can have significant health consequences such as hypercalcemia which can result in symptoms such as kidney stones, muscle weakness, and bone pain⁴. Primary hyperparathyroidism is a medical condition characterized by the excessive secretion of parathyroid hormone (PTH) from one or more of the parathyroid glands, resulting in an elevated level of calcium in the blood. The most common cause of primary hyperparathyroidism is a benign tumor of the parathyroid gland, known as a parathyroid adenoma⁴. In some cases, hyperparathyroidism can be caused by hyperplasia, which is an enlargement of one or more of the parathyroid glands. Rarely, primary hyperparathyroidism can be caused by a malignant tumor of the parathyroid gland⁵. Treatment of primary hyperparathyroidism depends on the severity of the disease, the presence of symptoms, and patient overall health. There are several treatment options. Observation: if the patient has a mild disease with no symptoms - watchful waiting⁶. Surgery: the most common treatment for primary hyperparathyroidism is surgery to remove the parathyroid gland that is overactive⁶. This procedure is highly effective and most patients experience a complete remission of symptoms. Medication: in rare cases, surgery is not an option, medications can be prescribed such as bisphosphonates, calcimimetics, and estrogen therapy⁶. The treatment should be individualized based on each patient's unique condition. The surgery is usually performed under general anesthesia and can be done through a small incision in the neck or using minimally invasive techniques. Most patients can go

home on the same day. The arsenal to diagnose primary hyperparathyroidism is vast. Blood tests are usually the first step. These tests will measure the levels of calcium or PTH⁷. Urine test: a 24 - hour urine collection test may be performed to measure the amount of calcium and other minerals that are being excreted in the urine⁷. Imaging: ultrasound, CT scan or MRI may be done to locate any abnormal growths in the parathyroid glands. Genetic tests can be recommended to search for genetic mutations that cause primary hyperparathyroidism⁸. Nuclear medicine tests using sestamibi (^{99m}Tc) tracer can be performed to identify abnormal hyperparathyroidism. The goal of the study was to observe if the intraoperative PTH hormone values decreased after the parathyroid gland was removed by comparing them to the preoperative values. Each parathyroid gland extracted conformed with the sestamibi preoperative evaluation. If the PTH values were maintained at high levels then also the preoperative nuclear medicine evaluation failed. This was another endpoint of the study to observe what is the rate of false positive sestamibi investigation into parathyroid adenoma.

INCLUSION CRITERIA

Diagnosis of primary hyperparathyroidism through sestamibi evaluation with surgical intervention for primary hyperparathyroidism.

MATERIAL AND METHOD

The study is descriptive, and the database is retrospective but it is maintained prospective. The selected variables were: the preoperative diagnosis, PTH values both preoperative and intraoperative, the results of the sestamibi evaluation, and the location of the parathyroid adenoma. Data was gathered from the Surgery Clinic – Agrippa Ionescu, Emergency Hospital, Romania. Inclusion criteria required preoperative Sestamibi evaluation for all the patients and valid preoperative and intraoperative PTH values determined using the same protocol. The protocol included single photon emission computed tomography (SPECT) with the use of a technetium-99 sestamibi tracer. We preferred this approach as it allowed 3-D localization of the adenomas. PTH values were obtained from blood drawn from the ipsilateral jugular vein at the regular intervals of 5, 10, and 15 minutes post excision. The patients were operated on through a small incision in the anterior cervi-

cal region which corresponded with the location of the toxic adenoma confirmed through scintigraphy.

RESULTS

We identified a number of 52 patients. Of these 22 were women and 30 were men. The median age of the group was 53 years. From all of these, 45 had unilocular hyperparathyroidism, and 7 had multilocular hyperparathyroidism. There were no cases of recurrent laryngeal nerve lesions. All of the 52 patients underwent preoperative ^{99m}Tc scanning with Sestambi tracer in the same laboratory using the same protocol. The scan identified correctly the true location in 87% of the cases.

Table 1. The correlation between the scintigraphy results and intraoperative findings

False Negative			False Positive			True positive
Cause	No.	Total	Cause	No.	Total	Total
Previous surgery	2	6	Intrathyroid Adenoma	2	3	43
Other location	4		Thyroid papillary carcinoma	1		

We had 6 cases with false negative-which led to the necessary dissection of the contralateral neck (we did not observe a reduction in PTH values after extraction although the gland indicated by the scintigraphy was extracted). Of these, 2 had previous surgery and 4 had tumors in other locations which were observed after the surgical intervention through methodical investigations. We encountered 3 patients with false positives. 2 had intrathyroid adenomas and 1 was diagnosed with thyroid papillary carcinoma. The average length of hospital stay was 2.4 days.

In the majority, patients who had unilocular parathyroid adenomas were diagnosed correctly through scintigraphy as “true positive”.

DISCUSSION

The amplitude of blind (without preoperative imagistic evaluation) bilateral exploration of the neck for primary hyperparathyroidism is not mentioned in the literature but if it is done correctly it can lead to a high success rate above 90% (9). All of this comes at a cost which

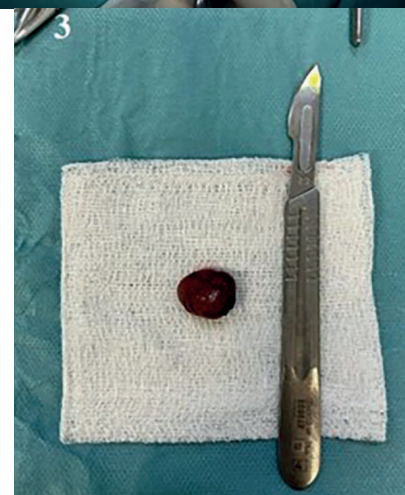
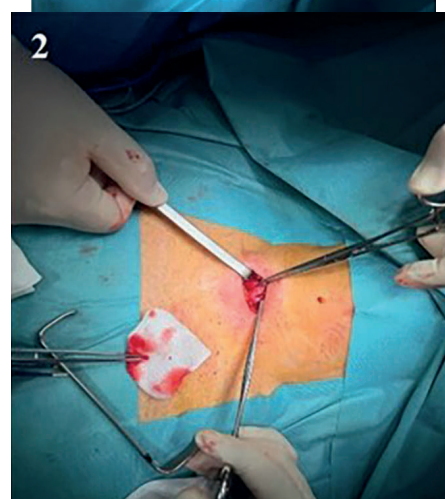


Figure 1. In our institution we adopt the minimally invasive technique which allows for small incisions targeted on the hyperproductive gland identified through preoperative scintigraphy and confirmed through interoperative PTH assay after removal. Figure 1 demonstrates the incision line for the inferior right parathyroid adenoma. Figure 2 demonstrates the size of the minimal surgical site due to precision information. Figure 3 demonstrates the final extracted adenoma.

is manifested in high rates of lesions of the recurrent laryngeal nerve and hypoparathyroidism¹⁰.

Life without the parathyroid glands in theory can exist but the external hormone supplementation is deficient and can lead to a decreased quality of life and severe complications. Reimplantation in the sternocleidomastoidian muscle can have a variable degree of success so it is best to preserve whenever possible the healthy parathyroid glands¹⁰. In the case of primary hyperparathyroidism, it is ideal to identify before the surgical intervention which gland is affected and extract only that one. To increase the rate of success various methods of investigation can aid the surgical team, both imagistic and blood markers.

Currently, the gold standard is the preoperative evaluation using sestamibi tracer which is administered intravenously and the radiation emitted by the tracer can be detected¹¹. The investigation is best used in combination with computed tomography (CT) or magnetic nuclear resonance (MRI) to obtain more detailed images of the parathyroid glands known as Spect CT or Spect MRI¹¹. The advantages are numerous: outpatient basis, a high degree of accuracy in identifying the abnormal parathyroid tissue. Causes that can lead to erroneous sestamibi evaluation are preoperative thyroid surgery, multilocation disease, or concomitant thyroid disease¹¹.

Surgical treatment of primary hyperparathyroidism (HPT) classically requires the identification of the entire parathyroid tissue and the removal of morphologically enlarged tissue¹². In experienced hands, this approach results in a cure rate greater than 95%, with reduced morbidity. Because HPT is caused by a solitary adenoma in 90% of cases, the concept of unilateral parathyroidectomy was introduced¹². A focused or targeted parathyroid exploration decreases the duration of the surgical intervention and complication rates while preserving tissue planes around the normal parathyroid glands¹³. Advances in preoperative imaging such as sestamibi scintigraphy and high-resolution ultrasonography and intraoperative parathyroid hormone assay (iPTH) have allowed a wider application of focused parathyroidectomy techniques¹⁴. The uptake of methoxy isobutyl isonitrile (MIBI) is directly related to the number and activity of mitochondria in parathyroid cells, so can be considered an indicator of the metabolic activity of parathyroid cells¹⁴.

Hyperfunctional parathyroid glands contain a greater number of mitochondria than normal parathy-

roid glands, so MIBI will be stored only by hyperactive parathyroid glands. Sestamibi scintigraphy has a greater than 90% specificity but false negative results can be observed in up to 20% of cases. The problems arise when the PTH values do not decrease after the parathyroid gland with hyperactivity as indicated by the sestamibi evaluation is removed.

Causes of a misinterpretation are related to thyroid disease in association with hyperparathyroidism, a history of parathyroid surgery, or multiple locations of hyperproductive parathyroid glands¹⁵.

If such context is encountered in the preoperative evaluation of the patients, mandatory intraoperative PTH evaluation of the ipsilateral jugular venous blood should be tested and further exploration of the neck should be considered if these are negative. A mention needs to be made about PTH values and attention needs to be awarded to false negative results in cases where multiple glands are hyperproductive. In these situations, one can observe a rapid decrease after excision but the values will increase in the postoperative evaluations.

The guard from these mishaps should terminate the surgical intervention only after there is a drop of above 50% in PTH values at 10 minutes or increase the time to 20 minutes when we should observe a drop of more than 60% in values¹⁶. In our series as mentioned the true positive rate of the scan was 87%. A result can be considered false negative if, after 30min of the excision, the PTH values do not drop. In our institution, the rapid PTH allowed rapid results which were ready in 10 minutes after the blood sample was obtained. A decrease of more than 50% in PTH values 10 minutes after excision in the ipsilateral jugular venous blood is indicative of postoperative normocalcemia. Keep in mind that values of PTH values can rise to values above preoperative in the first minutes due to manipulation of the gland.

In conclusion, this study comes to reinforce data regarding the utility of preoperative investigations such as sestamibi imagistic evaluation. Although false positive results are possible, they are rare and should not by any means contradict this type of evaluation for hyperparathyroidism. There should be a continuous and direct discussion between the surgeon and nuclear physicist regarding the intensity of the uptake in specific locations. Also as mentioned the patient's medical history needs to be known to reduce intraoperative errors due to the extraction of a healthy parathyroid gland.

Another cause of false negative results we can mention although we did not encounter is simply the small size of the adenoma which does not absorb enough tracer to be identified on scintigraphy

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