Localization of ectopic and supernumerary parathyroid glands in patients with secondary and tertiary hyperparathyroidism: surgical description and correlation with preoperative ultrasonography and Tc99m-Sestamibi scintigraphy

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Received 22 June, 2013; accepted 12 October, 2013

KEYWORDS
Hyperparathyroidism; Parathyroid glands; Parathyroidectomy; Chronic renal insufficiency; Ultrasonography; Scintigraphy

Abstract
Introduction: Hyperparathyroidism is an expected metabolic consequence of chronic kidney disease (CKD). Ectopic and/or supernumerary parathyroid glands (PT) may be the cause of surgical failure in patients undergoing total parathyroidectomy (PTX).
Aim: To define the locations of ectopic and supernumerary PT in patients with renal hyperparathyroidism and to correlate intraoperative findings with preoperative tests.
Materials and methods: A retrospective study was conducted with 166 patients submitted to PTX. The location of PT during surgery was recorded and classified as eutopic or ectopic. The preoperative localizations of PT found by ultrasonography (USG) and Tc99m-Sestamibi scintigraphy (MIBI) were subsequently compared with intraoperative findings.
Results: In the 166 patients studied, 664 PT were found. Five-hundred-seventy-seven (86.4%) glands were classified as eutopic and 91(13.6%) as ectopic. Eight supernumerary PT were found. The most common sites of ectopic PT were in the retroesophageal and thymic regions. Taken together, USG and MIBI did not identify 56 (61.5%) ectopic glands. MIBI was positive for 69.7% of all ectopic glands located in the mediastinal and thymic regions.
Conclusion: The presence of ectopic and supernumerary PT in patients with renal hyperparathyroidism is significant. Although preoperative imaging tests did not locate most of ectopic glands, MIBI may be important for identifying ectopic PT in the mediastinal and thymic regions.

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DOI: 10.5935/1808-8694.20140008
Introduction

Hyperparathyroidism is a physiological response to metabolic changes that occurs in patients with chronic kidney disease (CKD). In spite of advances in the clinical treatment of these patients, a significant number develops parathyroid (PT) hyperfunction and autonomy, with consequent elevation of parathyroid hormone (PTH). When the harmful effects of hyperparathyroidism are identified, such as severe bone disease, surgical treatment becomes necessary.1

Thus, total parathyroidectomy (PTx) in CKD has been indicated in symptomatic patients with marked and non-suppressible elevations of PTH.1 The goal of surgery is to correctly identify and resect all PTs. Although the hyperplastic glands are much larger than normal due to kidney disease, their identification is not always simple.2,3 Moreover, although the finding of four glands is expected in most patients, there is significant variability in the number of PTs. Supernumerary glands are present in 2.5% to 30% of patients,4,5 and may be the reason for surgical treatment failure, if not properly identified.2,6

There is also considerable variation regarding the location of the PTs, which are often not found in their usual location. The identification of all glands may require a thorough exploration of the superior mediastinum regions, thyroid gland, carotid sheath, and retroesophageal area.5,7

As a result, imaging studies have been performed to quantify and locate the PTs before surgery. However, although widely used in patients with CKD-associated hyperparathyroidism, it is not yet known whether ultrasonography (USG) and 99mTc-sestamibi (MIBI) scintigraphy can affect surgical outcomes, complication rates, and long-term therapeutic success.8-10

This study aimed to evaluate the main locations of the PTs in patients with secondary (SHPT) and tertiary (THPT) hyperparathyroidism, based on intraoperative findings, and to correlate these findings with the preoperative examinations.

Materials and methods

A cross-sectional study including patients with CKD treated at a tertiary referral hospital was performed. Between February of 2011 and October of 2012, 166 patients (44 diagnosed with SHPT and 122 diagnosed with THPT) underwent PTx with preternal parathyroid autotransplantation. All patients were examined by a nephrologist specialized in renal osteodystrophy; surgical indication followed the criteria of clinical treatment failure: hypercalcemia and/or persistent hyperphosphatemia; pruritus; bone pain; fractures or high risk of fractures; skeletal deformities and/or calcifications; calciphylaxis; and radiographic evidence of renal osteodystrophy. Patients who had previously undergone PT surgery were excluded from the analysis.

Patients were referred for surgical evaluation after preoperative imaging examinations had been performed at the service of origin or at the hospital in which the surgery was performed. USG and MIBI images reports from each patient were analyzed, the number of PTs observed, and their locations were quantified for each test. In cases where the MIBI image was not available for analysis by the surgeon, the examination report was considered. Preoperative imaging assessments were not performed by the same radiologist, nor in the same radiology department.
All patients were submitted to surgery by the same surgical team. The surgical technique consisted of conventional parathyroidectomy with bilateral neck exploration and heterotopic prestrernal intramuscular autotransplantation, as previously described. During the procedure, the location of the PT was recorded; it was considered normal when the lower glands were related to the lower pole of the thyroid gland, and when the upper glands were found near the upper pole of the thyroid, by the entry point of the inferior laryngeal nerve in the cricothyroid muscle.

When the PT was not identified in its usual position, a systematic exploration of the following areas was performed: retroesophageal, carotid sheath, thymic tongue, and upper mediastinum. If even then the PT was not identified, an ipsilateral total lobectomy of the thyroid gland was performed.

For those patients in whom the PT was not identified intraoperatively, but with persistence or recurrence of disease in the postoperative follow-up, the gland was classified as ectopic and the case was considered a “surgical failure”. PT fragments were sent for cryopreservation in most cases. Intraoperative frozen pathology was not performed in any case. Although the collection of intraoperative PTH (IOPTH) was performed in all cases (two blood samples, one at anesthetic induction, and another 20 minutes after removal of all glands), the result did not affect the surgical decision in any situation, due to the delay in obtaining these results.

Only patients with a minimum postoperative follow-up period of 6 months were included in the study.

Finally, the data provided by radiological preoperative imaging were compared with the intraoperative findings for each patient. The present study was approved by the research ethics committee of the institution under protocol No. 886/00.

**Results**

Of the 166 patients studied, 44 had a diagnosis of SHPT and 122 of THPT. Regarding gender, 82 were males and 84 were females. The mean age among patients with SHPT and THPT was 46.3 years (range: 23-77 years) and 48.1 years (range: 21-72 years), respectively. The mean duration of dialysis in patients with SHPT was 10.2 years (range: 2-25 years) and in patients with THPT, 6.1 years (range: 0.5 to 17 years).

A total of 664 PTs were found in 166 patients undergoing surgery. Four PTs were identified in 150 patients; five PTs were identified in eight patients (4.8%), and only three PTs in eight other patients (4.8%).

Of the eight patients with only three glands identified intraoperatively, four (2.4%) did not present clinical and laboratory evidence of disease recurrence. The other four patients (2.4%) had evidence of persistent or recurrent hyperparathyroidism in the postoperative follow-up, and their missing glands were considered ectopic. Surgical failure was, therefore, 2.4%.

Regarding the location of PTs, 577 (86.4%) glands were classified as eutopic, and 91 (13.6%) as ectopic (87 located in non-usual position, and four that were not found intraoperatively).

Considering a total number of 668 PTs (ectopic and eutopic), 664 glands (99.4%) were located. The surgical location of PTs is shown in Table 1.

Regarding the 87 ectopic glands, the upper-right PT (URPT) and lower-left PT (LLPT) were the most commonly found in non-usual positions, representing, 36.3% and 28.6% of total ectopic findings, respectively.

Regarding the URPT, it was considered ectopic in 24.6% of cases, and the retroesophageal position was the most frequent (71.8%). The LLPT, in turn, was classified as ectopic in 17% of cases, and the thymic region was the most common location (76%).

Of the eight supernumerary PTs that were identified, seven were located in eutopic positions. Only one was ectopic. Fig. 1 shows the location of ectopic PTs.

During the preoperative assessment, 153 patients (92.1%) underwent USG. The number of glands located is shown in Table 2. As for MIBI, 159 patients (95.7%) underwent the examination. The number of glands located is shown in Table 3. The mean number of glands identified by USG was 1.58 glands/exam. MIBI identified a mean of 2.41 glands/exam.

The association between ectopic PTs and imaging tests was as follows:

- Of the three PTs found in the carotid sheath, only one was located by the USG and MIBI. In the other two cases, both the USG and the MIBI were negative.

<table>
<thead>
<tr>
<th>Table 1 Location of parathyroids, according to intraoperative findings.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Location</strong></td>
</tr>
<tr>
<td>Eutopic</td>
</tr>
<tr>
<td>Retroesophageal</td>
</tr>
<tr>
<td>Intrathyroid</td>
</tr>
<tr>
<td>Subcapsular</td>
</tr>
<tr>
<td>Thymic tongue</td>
</tr>
<tr>
<td>Mediastinum</td>
</tr>
<tr>
<td>Carotid sheath</td>
</tr>
<tr>
<td>Not identified</td>
</tr>
<tr>
<td><strong>Total</strong></td>
</tr>
</tbody>
</table>

URPT, upper right parathyroid; LRPT, lower right parathyroid; ULPT, upper left parathyroid; LLPT, lower left parathyroid; 5th PT, 5th parathyroid (supernumerary).
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Figure 1 Intraoperative identification of ectopic parathyroids. The parathyroid glands that were not identified intraoperatively were also included. URPT, upper right parathyroid; LRPT, lower right parathyroid; ULPT, upper left parathyroid; LLPT, lower left parathyroid; 5th PT, 5th parathyroid (supernumerary).

• Of the five intrathyroid PTs, only two were suggested by USG, and three were not identified either by USG or by MIBI.
• Of the three mediastinal PTs, all were visualized by MIBI.

Regarding the 30 ectopic PTs located in the thymic tongue, five were not identified in any of the examinations, ten were identified only by MIBI, five were identified only by USG, and ten were identified by USG and MIBI.

No ectopic PT located in the subcapsular or retroesophageal region was identified by USG or MIBI before surgery. When considering only the regions of the upper mediastinum and thymus, the USG was able to identify 45.5% of ectopic PTs, all located in the thymic tongue. MIBI identified 69.7% of the glands in these regions.

Preoperatively, the USG and MIBI correctly identified 18 (19.8%) and 24 (26.4%) of ectopic PTs, respectively. Regarding ectopic PTs, 31 (34.1%) were identified by USG and/or MIBI; 60 ectopic glands (65.9%) were not identified by any of the preoperative examinations used in this study.

Discussion

Although IOPTH and frozen pathology were not used to confirm the removal of all glands intraoperatively, 99.4% of PTs were correctly located in the sample presented. Furthermore, only 2.4% of patients had surgical failure in the postoperative follow-up.

The main causes of failure in the surgical treatment of patients with hyperparathyroidism associated with CKD are failure to identify the PTs or presence of supernumerary

Table 2 Number of glands located by preoperative ultrasonography.

<table>
<thead>
<tr>
<th>Number of glands identified</th>
<th>Number of examinations</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>31</td>
<td>20.3%</td>
</tr>
<tr>
<td>1</td>
<td>47</td>
<td>30.7%</td>
</tr>
<tr>
<td>2</td>
<td>45</td>
<td>29.4%</td>
</tr>
<tr>
<td>3</td>
<td>18</td>
<td>11.8%</td>
</tr>
<tr>
<td>4</td>
<td>12</td>
<td>7.8%</td>
</tr>
<tr>
<td>Total</td>
<td>153</td>
<td>100%</td>
</tr>
</tbody>
</table>

Table 3 Number of glands located by preoperative MIBI.

<table>
<thead>
<tr>
<th>Number of glands identified</th>
<th>Number of examinations</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>14</td>
<td>8.8%</td>
</tr>
<tr>
<td>1</td>
<td>32</td>
<td>20.1%</td>
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<tr>
<td>2</td>
<td>30</td>
<td>18.9%</td>
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<td>3</td>
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<tr>
<td>4</td>
<td>45</td>
<td>28.3%</td>
</tr>
<tr>
<td>Total</td>
<td>159</td>
<td>100%</td>
</tr>
</tbody>
</table>
Localization of ectopic and supernumerary parathyroid glands in patients with secondary and tertiary hyperparathyroidism

Objective: The aim of this study was to evaluate the preoperative diagnostic and surgical outcomes of patients with secondary and tertiary hyperparathyroidism associated with CKD submitted to PTx. The low accuracy of USG and MIBI in identifying ectopic glands is explained by the limitations inherent to the methods. In the case of retroesophageal PTs, for instance, USG suffers interference from the trachea, and MIBI, from the thyroid.8,9,18 In this series, no retroesophageal gland was suggested by imaging studies.

Methods: In 114 patients with secondary and tertiary hyperparathyroidism associated with CKD, 25% of whom were operated by surgeons with less experience, a combined use of USG and MIBI was proposed. In this study were the retroesophageal and thymic regions.

Conclusions: This study was conducted in a public hospital with limited resources. Any technology that helps in the treatment of these patients is always well accepted. However, their unavailability should not prevent or contraindicate the surgery. In this study, IOPTH and pathological anatomy were not considered in the intraoperative decisions, which also did not compromise the surgical outcome.

Conclusion

The presence of supernumerary and ectopic parathyroid glands in patients undergoing PTx for CKD-associated hyperparathyroidism is significant and justifies a careful intraoperative search. An exploration routine for the most common sites of ectopic gland location is necessary, which in this study were the retroesophageal and thymic regions for the upper and lower parathyroids, respectively. Although preoperative imaging exams did not identify the majority of ec-
topic glands, MIBI may have an important role as a surgical planning method, in the identification of ectopic PT located in the upper mediastinal and thymic regions.

**Conflicts of interest**

The authors declare no conflicts of interest.

**References**


