Computed tomography of the parathyroids: The value of density measurements to distinguish between parathyroid adenomas of the lymph nodes and the thyroid parenchyma

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Abstract

Purpose: To compare the densities of parathyroid adenomas, lymph nodes and the thyroid parenchyma during multi-phase cervico-thoracic computed tomography to determine the differentiating threshold values.

Materials and methods: This study comprises 30 patients operated for a parathyroid adenoma after computed tomography without injection and then 45 and 70 seconds after the injection of an iodine based contrast product (350 mgI/mL, 150 mL, 3 mL/s). The density of the adenomas, lymph nodes and thyroid was measured during the three phases (D0, D45, D70). The relative enhancement (RE) at 45 seconds was calculated: \( \text{RE} = \frac{D45 - D0}{D0} \).

Results: A significant difference was found in the spontaneous density of the parathyroid adenomas of the thyroid (\( P < 0.01 \)) with a threshold value of 75 HU. A significant difference is found in the enhancement after injection of the adenomas and lymph nodes (\( P < 0.01 \)). The adenomas present an enhancement peak at 45 seconds while the maximum enhancement of the lymph nodes is at 70 seconds. At 45 seconds, a threshold value of 114 HU and an RE 125% allows them to be distinguished (sensitivity and specificity 0.96).

Conclusion: Measurement of the densities can differentiate between the parathyroid adenomas, lymph nodes and thyroid.

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A parathyroid adenoma is the most common cause of primary hyperparathyroidism. The diagnosis is biological. The classic curative treatment is surgical. Mini-invasive surgery involving resection of the parathyroid adenomas has quickly developed over the last few years [1]. This consists of a small elective approach opposite the adenoma. This technique has been made possible by the exact localisation of parathyroid adenomas by imaging before the intervention [2]. Currently, there is no consensus about the exact order of the imaging examinations required. Nevertheless, compliance between two imaging examinations is usually required before carrying out mini-invasive surgery.

Two examinations are usually requested: sonography for the morphological analysis and scintigraphy for its functional and localising contribution. Classically, computed tomography is used to search for ectopic localisations, disparity between sonography and scintigraphy or after the failure of a surgical treatment [3]. The use of multi-section computed tomography to locate parathyroid adenomas is increasing due to the excellent anatomical visualisation of computed tomography and its good diagnostic efficacy [4]. However, certain inappropriate images such as the lymph nodes or thyroid growths sometimes render the interpretation difficult [4]. Parathyroid adenomas, due to their endocrine nature, are hypervascularised while lymph nodes are usually little vascularised. The density of the thyroid is spontaneously relatively high since its iodine content is high. Therefore, this study compares the densities of the thyroid parenchyma, lymph nodes and parathyroid adenomas spontaneously and then after the injection of iodine based contrast product in order to determine the density criteria to differentiate between these three structures.

Density measurement

By consensus, two senior radiologists measured the density of each parathyroid adenoma, the normal thyroid parenchyma and a lymph node in Hounsfield Units (HU). In the two cases of goitre, the densities of the thyroid were measured in an homogenous zone, away from the nodes. The localisation of each parathyroid adenoma was confirmed by the data from the scintigraphy, sonography and the surgical report. The density was measured by acquisition without injection (D0), acquisition beginning 45 seconds after the beginning of the injection of contrast product (D45) and finally by acquisition carried out 70 seconds after the beginning of the injection (D70). The relative enhancement was calculated as follows: \((D45 - D0) / D0\).

Statistical analysis

The densities of the lymph nodes and thyroid were compared with that of the parathyroid adenomas by means of Fisher’s test and the ROC curves.

Results

The 30 parathyroid adenomas were located by computed tomography. Their major axis ranged from 6 to 29 mm (mean: 14 mm). Their weight, in anatomopathology, ranged from 100 mg to 12 g (mean: 1.7 g). Before injection of contrast product, a significant difference in density gradient was noted \((P < 0.01)\) between the parathyroid adenomas (45 HU) and the thyroid parenchyma (90 HU): a threshold of 75 HU determined on the ROC curves distinguished, with a 96% sensitivity and specificity, the density of a thyroid adenoma from that of the normal thyroid parenchyma (Fig. 1). With this threshold, one case of parathyroid adenoma and one case of thyroid parenchyma were poorly classified. The difference in the spontaneous density of the parathyroid adenoma and that of the lymph node is not significant \((P > 0.05)\).

After injection of contrast product, the parathyroid adenomas and the thyroid parenchyma present a maximum enhancement during the phase acquired 45 seconds after the beginning of the injection. However, the lymph nodes present a maximum enhancement 70 seconds after the beginning of the injection (Table 1). Forty-five seconds after injection, both the parathyroid adenomas and the thyroid parenchyma present a maximum enhancement (187 HU versus 218 HU). However, this difference is not significant \((P > 0.05)\). On the contrary, the enhancement of the parathyroid adenomas differs significantly from that of the lymph nodes (187 HU versus 80 HU, \(P < 0.01\)). A threshold of 114 HU determined on the ROC curves distinguishes the density of the adenomas and lymph nodes at 45 seconds with a sensitivity and specificity of 96% (Figs. 2–3).

The relative enhancement is also significantly higher for the adenomas than for the lymph nodes (315% versus 60%, \(P < 0.01\)). The threshold determined on the ROC curves to distinguish between the adenomas and lymph nodes is 125%. With both the density and the relative enhancement at 45 seconds, one parathyroid adenoma and one lymph

Material and methods

Patients

This retrospective study comprises 37 consecutive patients who underwent surgery for a single parathyroid adenoma between July 2006 and July 2007. They previously had a 99mTc-sestamibi scintigraphy, a cervical sonography and a multi-phase cervico mediastinal computed tomography. Seven patients were excluded due to major artefacts in the computed tomography preventing a proper measurement of the densities. The study therefore included 30 patients (14 men, 16 women), average age: 61 years (40 to 86 years). Six patients presented a past history of cervical disease such as goitre (2), thyroidectomy (2), multiple endocrine neoplasia type 1 (1) and cervical lymphoma in clinical remission (1).

CT protocol

The examinations were carried out with a 40 section CT scanner (Philips brilliance 40) with the following parameters: 140kV, 350 mAs, 1.5 mm section thickness. Three acquisitions were carried out, from the mandible to the carena, without injection of contrast product, then 45 and 70 seconds after the injection of 150 cc of iodine based contrast product (350 mgI/mL) at 3 mL/s. The arms of the patients were kept extended along their bodies during all of the examinations.
Computed tomography of the parathyroids

Figure 1. Left parathyroid adenoma. a: before injection of contrast product, the density of the parathyroid adenoma is 40 HU while the density of the thyroid is 83 HU; b: the density of the adenoma reaches 168 HU 45 seconds after the injection of iodine based contrast product; c: seventy seconds after injection, the density of the adenoma decreases to 136 HU.

The node were poorly classified with the determined thresholds. Between the phases acquired 45 seconds and 70 seconds after injection, the density of the parathyroid adenomas and the thyroid parenchyma was reduced by 60 HU and 38 HU respectively ($P > 0.05$). However, the density of the lymph nodes increased by 13 HU. This is significant with respect to the reduction in density of the parathyroid adenomas ($P < 0.01$).

Table 1  Measurement of the CT density of parathyroid adenomas, the thyroid gland and lymph nodes before and after injection of iodine based contrast product.

<table>
<thead>
<tr>
<th></th>
<th>Parathyroid adenoma HU</th>
<th>Thyroid HU</th>
<th>Lymph node HU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Without injection</td>
<td>45 (±13)</td>
<td>90 (±14)$^a$</td>
<td>50 (±16)</td>
</tr>
<tr>
<td>45 s after injection</td>
<td>187 (±46)</td>
<td>218 (±35)</td>
<td>80 (±22)$^a$</td>
</tr>
<tr>
<td>70 s after injection</td>
<td>127 (±27)</td>
<td>180 (±30)</td>
<td>93 (±22)</td>
</tr>
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HU: hounsfield units.

$^a$ Significant difference with the adenomas: $P < 0.05$.  

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Discussion

Until the beginning of the 2000s, the classic surgical treatment of hyperparathyroidism involved a per-surgical exploration of four glandular sites. Computed tomography was little used and mainly reserved for failures in surgical treatment or if atomic reasons were likely to modify the surgical strategy [5–7]. Mini-invasive surgery appeared at the beginning of the 2000s. It consists of a small approach, with the shortest possible path, in order to remove the parathyroid adenoma, without exploring other glands [8]. It became primordial to perfectly locate the adenoma. Since then, computed tomography has been widely developed in the exploration of hyperparathyroidism [9]. In 2004, Lumachi et al. published a series of 44 examinations carried out 40 to 50 seconds after injection of contrast products compared with scintigraphy results [10]. The CT results were similar to those of the scintigraphy with a sensitivity and specificity of 88 and 95% for the CT and 86 and 96% for the scintigraphy. In this series, the CT helped diagnose 36 of the 40 adenomas, of which 13 were ectopic. However, two cases of false positives were noted. In 2006, a series of 75 patients with a triphasic CT scan (4D CT) was published by Rodgers et al. [11]. The examination protocol included a study carried out 25 seconds after the beginning of injection followed by a phase of equilibrium. The analysis was based on the enhancement characteristics of the parathyroid adenomas: fast intense enhancement followed by a washing. In this study, the sensitivity of the CT (87%) exceeded that of the scintigraphy (65%) and the sonography (57%) in the location.
Computed tomography of the parathyroids

Figure 3. Left laterotracheal lymph node. a: before injection of contrast product, the density of the lymph node is 21 HU; b: forty-five seconds after injection of contrast product, the density of the lymph node increases to 42 HU; c: seventy seconds after injection, the density of the lymph node continues to increase to reach 78 HU.

of parathyroid adenomas. Even with a specificity of 89%, due to false positives, the CT was the most effective technique in locating adenomas after the failure of the sonography. In 2008, Zald et al. published similar results with a sensitivity of 60% and a positive predictive value of 77% for CT [12]. Chazen et al., in a series of 27 adenomas, using the 4D CT technique with two acquisitions 25 and 55 seconds after injection, obtained a correct location in 25 cases and an error in two cases [13].

In 2009, Randall et al. published a series of 77 patients that benefited from a CT examination 50 to 70 seconds after the beginning of the injection of contrast product [4]. In this series, 92% of the parathyroid adenomas presented a major enhancement with a density close to that of the arteries. A recent meta-analysis assessed the sensitivity and positive predictive value of the CT at 89% and 93% respectively [14]. It is primordial to perfectly locate the adenomas in the pre-surgical period and not confuse them with other structures before a mini-invasive surgical treatment. In CT, certain thyroid prolongations or certain lymph nodes may be responsible for false positives [4]. The purpose of our study was therefore to determine whether the CT measurement of the density of parathyroid adenomas, before and after the injection of iodine based contrast product, distinguished them from the lymph nodes or thyroid parenchyma. In our series, the same major enhancement of the parathyroid adenomas was found as that described by Randall et al. [4]: a fast and major enhancement after injection...
of the contrast product immediately followed after a washing. However, the lymph nodes were progressively enhanced until 70 seconds after an injection. The enhancement curve also distinguishes the adenomas from the lymph nodes. Measurement of the density 45 seconds after the beginning of the injection also helps differentiate them by using the threshold of 114 HU. In a similar way, a relative enhancement of 125% between the spontaneous density and the density measured 45 seconds after injection distinguishes the parathyroid adenomas from the lymph nodes. Similar results for the adenomas and the lymph nodes have been reported by Beland et al. with means values of 128/138/109 HU for the adenomas and 58/92/100 HU for the lymph glands on the phases acquired 30/60/90 seconds after the beginning of the injection respectively [19].

In our study, the spontaneous density distinguishes the thyroid parenchyma and parathyroid adenomas. A density exceeding 75 HU is characteristics of the thyroid parenchyma while the density is lower for the adenomas. This result complies with that published by Vu [16], the mean density of the adenomas being 35 HU in his series and that of the thyroid parenchyma being 94 HU. However, as opposed to this study, we did not note a significant difference after injection of contrast product.

Therefore, density measurements easily distinguish parathyroid adenomas from the lymph glands and the normal thyroid parenchyma. Nevertheless, there are several limits to our study. The main limit is represented by the star artefacts mainly found in the sections passing through the shoulders due to a high absorption of X-rays. These star artefacts alter the density measurements. They are mainly due to the bone structures and the highly concentrated contrast product in the vascular structures. Seven of the 37 patients had to be excluded from our study. Another limitation is the measurement of the normal thyroid parenchyma. In fact, thyroid nodules are extremely polymorphous and sometimes their spontaneous density is low, under 75 HU [17]. Therefore, in certain cases, it may be extremely difficult to distinguish an exophytic thyroid nodule from a parathyroid adenoma in contact with the thyroid. There are other limits to our study such as the determination of density in zones of small surfaces, modifications in enhancement due to a different hemodynamic state or even variations in the vascularisation of parathyroid adenomas. These elements may account for the several errors obtained with the density thresholds defined in our study. Cystic adenomas are rare, thereby accounting for their absence in our series. Due to the cystic component, these adenomas may not present the enhancement characteristics observed in our study. The sonography associated with the guided puncture to measure the PTH concentration then remains the key examination [18]. Another cause of error may be due to the presence of adenopathies hypervascularised consecutive to another disease.

The acquisition protocol described is now used routinely on our site. Practice has confirmed its efficacy. The measurement of densities helps characterise parathyroid adenomas except in patients presenting major CT artefacts. Due to the use of X-rays and the injection of a contrast product, this technique to localise parathyroid adenomas is indicated after a difference or insufficient results in the cervical sonography and the 99mTc-sestamibi scintigraphy.

Conclusion

The acquisition of triphasic CT data without and then 45 and 70 seconds after injection of iodine based contrast product distinguishes parathyroid adenomas from the thyroid parenchyma and the cervical lymph nodes. The thyroid parenchyma spontaneously presents a density exceeding 75 HU while the density of parathyroid adenomas is lower. After injection of contrast product, the enhancement of the parathyroid adenomas is intense and rapid exceeding a density threshold of 114 HU, 45 seconds after injection. Their density decreases during the third acquisition. However, the enhancement of the lymph nodes is slow and progressive. Their density does not usually exceed 114 HU during the phase acquired at 45 seconds and then continues to progress between 45 and 70 seconds.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.
Computed tomography of the parathyroids

603


