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Accuracy of Dual Phase Single-Photon Emission Computed Tomography/Computed Tomography in Primary Hyperparathyroidism: Correlation with Serum Parathyroid Hormone Levels

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Abstract

Purpose: The objectives of this study were: 1) to determine the accuracy of dual-phase ^{99m}Tc -methoxyisobutylisonitrile (MIBI) with single-photon emission computed tomography/computed tomography (SPECT/CT) for the preoperative localization of parathyroid adenomas in the setting of primary hyperparathyroidism; 2) to determine the accuracy of localization for ectopic glands; and 3) to assess the relationship between accuracy and serum parathyroid hormone (PTH) levels.

Methods: Eighty-eight patients who underwent ^{99m}Tc -MIBI SPECT/CT imaging for primary hyperparathyroidism at our institution over a 27-month period were retrospectively assessed. The preoperative SPECT/CT results were compared to intraoperative findings (within 1 year of imaging). The relationship between serum PTH level (within 3 months) and SPECT/CT accuracy was then evaluated.

Results: Accuracy indices for the retrothyroid subgroup were sensitivity 86.7%, specificity 96.4%, positive predictive value 98.1%, negative predictive value 77.1%, and accuracy 89.8%. Accuracy indices for ectopic parathyroid adenomas were sensitivity 81.5%, specificity 100%, positive predictive value 100%, negative predictive value 92.4%, and accuracy 94.3%. For the overall group, SPECT/CT demonstrated a sensitivity of 85.1% and a PPV of 98.7%. SPECT/CT correctly identified the abnormal parathyroid gland in 60% of patients with a normal serum PTH (<6.9 pmol/L), 73% between 6.9-9.9 pmol/L, 86% between 10.0-14.9 pmol/L, 100% between 15.0-19.9 pmol/L, 88% between 20.0-24.5 pmol/L, and 100% of patients with a PTH greater than 25.0 pmol/L.

Conclusions: Dual-phase ^{99m}Tc -MIBI with SPECT/CT is an accurate and reliable means to correctly localize both retrothyroid and ectopic parathyroid adenomas for the purpose of surgical planning. The accuracy of SPECT/CT increases with increasing serum PTH levels.

Résumé

Objet : L'étude avait pour objectif 1) de déterminer la précision de la méthode de double phase par tomographie d'émission à photon unique (TEPU-TDM) au technétium 99 m (^{99m}Tc) avec isocyanure de méthoxyisobutyle (MIBI) pour la localisation préopératoire des adénomes parathyroïdiens menant à l'hyperparathyroïdie primaire, 2) de déterminer la précision des examens de localisation des glandes ectopiques et 3) d'évaluer le lien entre la précision des examens et les niveaux de parathormone (PTH) dans le sérum.

Méthodes : Quatre-vingt-huit patients qui ont subi un examen TEPU-TDM ^{99m}Tc -MIBI pour hyperparathyroïdie primaire dans notre établissement sur une période de 27 mois ont fait l'objet d'une évaluation rétrospective. Les résultats des examens TEPU-TDM préopératoires ont été comparés avec les observations peropératoires (durant l'année suivant les examens). Le lien entre les niveaux de PTH dans le sérum (dans les trois mois suivants) et l'exactitude des examens TEPU-TDM a ensuite été évalué.

Résultats : Pour le sous-groupe de localisation d'adénomes rétro-thyroïdiens, les indices de précision étaient les suivants: sensibilité 86,7 %, spécificité 96,4 %, valeur prédictive positive 98,1 %, valeur prédictive négative 77,1 % et précision 89,8 %. Pour les examens de localisation des adénomes parathyroïdiens ectopiques, les indices de précision étaient les suivants: sensibilité 81,5 %, spécificité 100 %, valeur prédictive positive 100 %, valeur prédictive négative 92,4 % et précision 94,3 %. Pour l'ensemble du groupe, les résultats relatifs à la TEPU-TDM ont indiqué une sensibilité de 85,1 % et une valeur prédictive positive de 98,7 %. La TEPU-TDM a révélé des glandes parathyroïdes anormales chez 60 % des patients au niveau de PTH normal (<6,9 pmol/L), 73 % des patients au niveau de PTH entre 6,9 et

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9,9 pmol/L, 86 % entre 10,0 et 14,9 pmol/L, 100 % entre 15,0 et 19,9 pmol/L, 88 % entre 20,0 et 24,5 pmol/L et 100 % des patients au niveau de PTH supérieur à 25,0 pmol/L.

Conclusions : Les examens par la méthode de double phase par TEPU-TDM ^{99m}Tc -MIBI sont un moyen fiable et précis de localiser correctement les adénomes rétro-thyroïdiens et parathyroïdiens ectopiques à des fins de planification opératoire. La précision des examens par TEPU-TDM augmente avec la hausse des niveaux de PTH dans le sérum.

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Key Words: Primary hyperparathyroidism; Parathyroid adenoma; ^{99m}Tc -methoxyisobutylisonitrile; Single-photon emission computed tomography/computed tomography; Parathyroid hormone

Primary hyperparathyroidism (HPT), caused by hypersecretion of parathyroid hormone (PTH) from autonomously functioning parathyroid tissue, is a common endocrine disorder affecting 0.3% of the general population with a strong female predominance (4:1 female:male) [1].

In up to 90% of cases, primary HPT is caused by a single parathyroid adenoma, however primary HPT may also occur as the result of sporadic parathyroid carcinoma (<1%), multiple endocrine neoplasias, or as a sequelae of metabolic diseases or genetic syndromes [2,3]. A total of 80%-85% of parathyroid adenomas are located immediately posterior to the thyroid gland (retrothyroid); however, 15%-20% are ectopically positioned. Ectopic parathyroid glands can be found in a number of locations including the tracheo-oesophageal groove, adjacent to or within the carotid sheath, within the thyroid gland, or within the mediastinum [4].

Histopathologic distinction between parathyroid hyperplasia and a parathyroid adenoma is not well defined. Single gland disease is often felt to represent a parathyroid adenoma while multi gland disease is thought reflect parathyroid hyperplasia. Mariani et al [4] suggest these may reflect variable phenotypic expression of the same disease entity.

Management of primary HPT is routinely surgical. Due to a number of factors including improved cosmesis, decreased postsurgical pain, shorter operating time, decreased hospitalization, and comparable success rates, minimally invasive parathyroidectomy has replaced conventional bilateral neck dissection as the standard approach. Preoperative localization of hyperfunctioning parathyroid adenomas is critical in planning for minimally invasive surgery [5]. Despite this necessity there remains a high degree of variability in the clinical management of primary HPT in Canada [6].

^{99m}Tc -methoxyisobutylisonitrile (MIBI) scintigraphy is the mainstay molecular imaging technique for this clinical problem utilizing either dual-phase or subtraction techniques [7,8]. Recently, incorporation of single-photon emission computed tomography/computed tomography (SPECT/CT) into this imaging technique has become common practice, improving localization and resulting in increased utilization of minimally invasive surgical techniques [9].

PTH is a polypeptide released from parathyroid glands, which has multiple actions in calcium metabolism including increased renal tubular calcium absorption, stimulation of renal 1,25 dihydroxyvitamin D production, and regulation of bone remodelling [10]. Inappropriately

elevated serum PTH is a marker of primary HPT [11]. One report has suggested increased PTH levels in patients with positive MIBI scans compared to those with negative MIBI scans [12]. This report did not evaluate SPECT/CT.

The goals of our study were 3-fold: (a) to determine the overall accuracy of dual-phase MIBI scintigraphy with SPECT/CT for the preoperative localization of parathyroid adenoma in the setting of primary HPT, (b) to determine the accuracy of localization for ectopic glands, and (c) to assess the relationship between accuracy and serum PTH levels.

Methods

Study Population

Four hundred consecutive patients who underwent ^{99m}Tc -MIBI SPECT/CT imaging for HPT over a 27-month period at our institution were retrospectively reviewed. The study protocol was approved by our institutional ethics review board. Patients were excluded from analysis based on the following criteria: no surgery after the SPECT/CT study, delay between the SPECT/CT study and surgery of greater than 1 year, history of previous parathyroid or thyroid surgery prior to the SPECT/CT study, or history of end-stage renal disease or dialysis.

Data Collection

Data parameters obtained from the patient medical record included: gender, date of birth, imaging findings, surgical findings, pathology findings, pre-SPECT/CT PTH levels, past surgical history, and the surgical approach chosen. The surgical report, outlining the intraoperative findings, was used as the reference standard with respect to parathyroid gland localization. Glands were categorized as retrothyroid left, retrothyroid right, or ectopic in location. The preoperative SPECT/CT report was then compared with surgical findings to determine the detection and localization accuracy. For the purpose of the results, ectopic parathyroid glands were not subcategorized based on their specific location. Any parathyroid gland not located in the classical immediate retrothyroid location was considered ectopic. In order to ensure correct categorization of the imaging findings, the images were reviewed in the event of a discrepancy between the imaging report and the surgical report. The images were also reviewed if the described location

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