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EDITORIAL

The use of positron emission tomography with ^{11}C-methionine in patients with primary hyperparathyroidism

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Primary hyperparathyroidism (PHPT) is a common endocrine disorder, which is nowadays often discovered incidentally by the finding of increased serum calcium and PTH in routine blood tests [1]. PHPT is due to a single adenoma in the majority of cases (85–90 %), whereas hyperplasia of all parathyroid glands occurs in 10–15 % and carcinoma is found in less than 1 %. PHPT may occur sporadically or as a part of hereditary forms [2]. Pathological parathyroid glands are mainly located close to the thyroid gland, but ectopic localization in the mediastinum, or lateral to the carotid sheath, in the carotid bifurcation and very rarely within the thyroid or the thymus may occur in up to 20 % of cases [3].

Parathyroidectomy (PTx) is the only definitive cure of PHPT and, if performed by an experienced endocrine surgeon, is successful in up to 95 % of cases. In recent years, the minimally invasive PTx (MIP) has almost replaced the traditional full neck exploration [4]. A preoperative identification of the enlarged parathyroid lesion(s) is required to perform MIP [5]. Many imaging techniques are available for locating enlarged parathyroid glands, but ^{99m}Tc sestamibi scan and cervical ultrasound are the most commonly used [5]. Sestamibi is taken up both by thyroid and parathyroid tissues, but it persists longer in the latter; thus a late scan can show an uptake which is rather specific for the parathyroid gland. Planar parathyroid scintigraphy may miss small or ectopic lesions. The single photon emission computed tomography (SPECT) may be helpful for giving a more precise localization of enlarged parathyroid gland(s). The sensitivity varies in different series and may reach 90–95 % using SPECT, but may be lower using planar scintigraphy [6]. The sensitivity for small adenomas, double adenomas or hyperplasia is much lower, and in the latter case computed tomography (CT)-sestamibi SPECT image fusion is superior to CT or sestamibi SPECT alone [7]. Neck ultrasound is a widely available, safe and low-cost technique and may identify a coexisting thyroid disease. The accuracy of neck ultrasound is operator-dependent. Its sensitivity can range from 42 to 82 % with a specificity of approximately 90 % [8].

CT of the neck and mediastinum and magnetic resonance imaging (MRI) are generally used in patients with persistent or recurrent PHPT, or when ultrasound and sestamibi imaging studies are negative or contradictory [5]. The TC sensitivity ranges from 50 to 88 % [5]. MRI is time-consuming and less sensitive than TC.

Invasive localization techniques such as arteriography and selective venous sampling for PTH assay in the draining thyroid veins are nowadays rarely used and could be reserved to patients with prior PTx and negative imaging studies [5].

Positron emission tomography (PET) has a spatial resolution higher than that of sestamibi scintigraphy and, alone or with simultaneous CT scan (PET/CT), could be an useful tool for the identification of enlarged parathyroid glands in patient with persistent or recurrent PHPT when the results of other imaging techniques are negative or conflicting. In patients with PHPT, the PET with ^{18}F-fluorodeoxyglucose (FDG-PET) showed a diagnostic accuracy lower than that of sestamibi SPECT. On the other hand, PET with ^{11}C-methionine (C-Met-PET) has a sensitivity higher than that of FDG-PET [9]. C-methionine is considered to be more specific, since C-methionine seems to concentrate specifically in the enlarged parathyroid

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glands. The mechanism underlying the increased uptake of this tracer is still not clear and C-methionine is probably involved in the synthesis of the precursor of PTH. Few studies have evaluated the accuracy of C-Met PET in patients with PHPT. Most of the studies are retrospective, include small series, some use C-Met-PET alone and other C-Met PET/CT. Most, but no all studies, suggest that PET has a higher sensitivity than either planar ^{99m}Tc sestamibi or SPECT in patients with newly diagnosed PHPT [6], and persistent and recurrent PHPT [10, 11].

In the previous issue of the journal, Caldarella et al. [12] report a meta-analysis on the diagnostic performance of C-Met-PET in patients with PHPT. A computer literature search of PubMed/MEDLINE, Scopus, and Embase databases was performed to identify the pertinent articles. Only articles including patients in a preoperative setting, series of at least five patients with PHPT, and available histological/clinical follow-up were selected for the meta-analysis. A total of nine studies (5 retrospective and 4 prospective) including 258 patients was found. The pooled sensitivity and detection rate values of C-Met PET were 81 and 70 %, respectively, on a per patient-based analysis. The studies had a high statistical heterogeneity in their estimate and sensitivity. In some studies PET with simultaneous CT was carried out, but it was not possible to perform a sub-analysis due to the small number of cases. The authors conclude that C-Met-PET seems to be a sensitive and reliable technique for the identification of enlarged parathyroid glands in patients with PHPT, but its diagnostic performance does not differ from that of ^{99m}Tc sestamibi scan and cervical ultrasound. However, it is worth noting that in one of these studies performed in patients with persistent or recurrent hyperparathyroidism after surgery, C-Met-PET was able to correctly localize abnormal parathyroid glands in the majority of patients in whom conventional scintigraphy was negative [11].

This meta-analysis gives an useful update on the clinical utility of C-Met PET in patients with PHPT. Preoperative localization studies are a prerequisite of MIP, which is the modern surgical approach of newly diagnosed PHPT. ^{99m}Tc-sestamibi and cervical ultrasound are nowadays the first line imaging techniques for the preoperative localization of enlarged parathyroid glands. In the recent years, FDG-PET and, more frequently, C-Met PET have been used either in patients with newly diagnosed or recurrent and persistent PHPT. The results of the meta-analysis of Caldarella et al. [12] suggest that the sensitivity of C-Met-PET is not greater than that of parathyroid scintigraphy and ultrasound. Furthermore, the use of C-Met PET is limited mainly for the scarceness of PET centers and the high costs of the procedure.

Given these considerations, in our opinion, C-Met PET should not be used in the routine workup of patients with PHPT. This procedure could be considered in very selected cases, such as a patient with persistent/relapsing PHPT after multiple neck explorations, severe hypercalcemia not manageable with medical therapy, and negative conventional parathyroid imaging studies. Indeed in this particular setting, C-Met PET has been shown to be able to localize the abnormal parathyroid tissue.

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References

1. C. Marcocci, F. Cetani, Primary hyperparathyroidism. N. Engl. J. Med. **365**, 2389–2397 (2012)
2. F. Cetani, E. Pardi, S. Borsari, C. Marcocci, Molecular pathogenesis of primary hyperparathyroidism. J. Endocrinol. Invest. **34**(7 Suppl), 35–39 (2011)
3. G. Akerström, J. Malmaeus, R. Bergström, Surgical anatomy of human parathyroid glands. Surgery **95**, 14–21 (1984)
4. P. Miccoli, P. Berti, G. Materazzi, C.E. Ambrosini, L. Fregoli, G. Donatini, Endoscopic bilateral neck exploration versus quick intraoperative paratormone assay (qPTHa) during endoscopic parathyroidectomy: a prospective randomized trial. Surg. Endosc. **22**, 398–400 (2008)
5. R. Udelsman, J.L. Pasieka, C. Sturgeon, J.E. Young, O.H. Clark, Surgery for asymptomatic primary hyperparathyroidism: proceedings of the third international workshop. J. Clin. Endocrinol. Metab. **94**, 366–372 (2009)
6. M.O. Oksüz, H. Dittmann, C. Wicke, K. Müssig, R. Bares, C. Pfannenberg, S.M. Eschmann, Accuracy of parathyroid imaging: a comparison of planar scintigraphy, SPECT, SPECT-CT, and C-11 methionine PET for the detection of parathyroid adenomas and glandular hyperplasia. Diagn. Interv. Radiol. **17**, 297–307 (2011)
7. G. Wimmer, C. Profanter, P. Kovacs, M. Sieb, M. Gabriel, D. Putzer, R. Bale, R. Margreiter, R. Prommegger, CT-MIBI-SPECT image fusion predicts multiglandular disease in hyperparathyroidism. Langenbecks Arch. Surg. **395**, 73–80 (2010)
8. R. Van Husen, L.T. Kim, Accuracy of surgeon-performed ultrasound in parathyroid localization. World J. Surg. **28**, 1122–1126 (2005)
9. D. Otto, A.R. Boerner, M. Hofmann, T. Brunkhorst, G.J. Meyer, T. Petrich, G.F. Scheumann, W.H. Knapp, Pre-operative localisation of hyperfunctional parathyroid tissue with 11C-methionine PET. Eur. J. Nucl. Med. Mol. Imaging **31**, 1405–1412 (2004)
10. A. Sundin, C. Johansson, P. Hellman, M. Bergström, H. Ahlstrom, G.B. Jacobson, B. Långström, J. Rastad, PET and parathyroid L-[Carbon-11]methionine accumulation in hyperparathyroidism. J. Nucl. Med. **37**, 1766–1770 (1996)
11. G.J.R. Cook, J.C.H. Wong, W.J.B. Smellie, A.E. Young, M.N. Maisey, I. Fogelman, [^{11}C]Methionine positron emission tomography for patients with persistent or recurrent hyperparathyroidism after surgery. Eur. J. Endocrinol. **139**, 195–197 (1998)
12. C. Caldarella, G. Treglia, M.A. Isgrò, A. Giordano, Diagnostic performance of positron emission tomography using (11) C-methionine in patients with suspected parathyroid adenoma: a meta-analysis. Endocrine **43**, 78–83 (2013)