

A Bayesian look at the new 2019 guidelines for imaging of pheochromocytoma/paraganglioma with emphasis on extra-adrenal disease

Dear Editor,

In this journal [1], a few years ago, we presented a Bayesian (critical) appraisal of the then recent-American Endocrine Society's guidelines regarding the diagnosis and management of pheochromocytoma/paraganglioma (PPG) [2]. This year, the European Society of Nuclear Medicine and the Society of Nuclear Medicine and Molecular Imaging have introduced new guidelines regarding functional imaging (i.e. by means of Nuclear Medicine modalities) of PPG [3]. In light of this, we believe that it is appropriate to present a new relevant Bayesian assessment. In the new guidelines the following functional imaging modalities are covered [3]: iodine-123-metaiodobenzylguanidine (^{123}I -MIBG) single photon emission tomography (SPET), indium-111-diethylenetriamine pentaacetic acid (^{111}In -DTPA)-pentetretotide (^{111}In -pentetretotide) SPET, fluorine-18-fluorodihydroxyphenylalanine (^{18}F -FDOPA) positron emission tomography (PET), ^{18}F -fluorodeoxyglucose (^{18}F -FDG) PET and PET with various gallium-68-1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (^{68}Ga -DOTA)-coupled somatostatin agonists (^{68}Ga -SSTa). Based on a pretest probability of 15% for extra-adrenal disease and the reported sensitivity and specificity for

each modality, we calculated likelihood ratios (LR) for a positive and a negative test (LR+ and LR-, respectively). In the absence of a given specificity in the guidelines we used levels of 55% for ^{18}F -FDG and 85% for ^{68}Ga -SSTa (the latter is a level that we used in our previous assessment [1]), which have been validated in a recent meta-analysis [4]. Using LR+ and LR- with Fagan's nomograms we calculated the post-test probability of extra-adrenal PPG (Table 1). Only the LR+ for ^{18}F -FDOPA was over 10 and no LR- was lower than 0.1, shifting to an important degree the probability of a diagnosis (clinicians have to bear in mind that an LR- may not be useful, since absence of radionuclide uptake does not imply absence of PPG if biochemistry is positive) [5]. It is evident that functional imaging of PPG has become more diversified and tailored according to each patient's history and genetic background. Nevertheless, the diagnostic characteristics of all methods (biochemical and imaging) are still not perfect; they are rather complimentary to each other. Biochemical evaluation should be done first, since functional imaging of PPG is advised to be performed in patients with biochemically proven disease.

The authors declare that they have no conflicts of interest.

Table 1. Diagnostic accuracy of various functional imaging modalities for PPG for a given pre-test probability of 15% for extra-adrenal PPG.

Radiotracer	Sensitivity	Specificity	LR+ (post-test probability)	LR- (post-test probability)
^{123}I -MIBG				
XAP & HeredPG	64%	85%	4.27 (43%)	0.42 (7%)
HNPGLs	34%	85%	2.27 (29%)	0.78 (12%)
^{111}In -Pentetretotide	95%	34%	1.44 (20%)	0.15 (3%)
^{18}F -FDOPA	79%	95%	15.80 (74%)	0.22 (4%)
^{18}F -FDG	90%	55%*	2.00 (26%)	0.18 (3%)
^{68}Ga -SSTa	89%	85%*	5.93 (51%)	0.13 (2%)

PPG: pheochromocytoma/paraganglioma; ^{123}I -MIBG: iodine-123-metaiodobenzylguanidine; ^{111}In -Pentetretotide: indium-111-diethylenetriamine pentaacetic acid-pentetretotide; ^{18}F -FDOPA: fluorine-18-fluorodihydroxyphenylalanine; ^{18}F -FDG: fluorine-18-fluorodeoxyglucose; ^{68}Ga -SSTa: gallium-68-1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid-coupled somatostatin agonists; XAP: extra-adrenal pheochromocytomas; HeredPG: hereditary paragangliomas; HNPGLs: head and neck paragangliomas; LH+: likelihood ratio for a positive test; LR-: likelihood ratio for a negative test; *specificity not given in the guidelines - see text for details

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