Response to Letter to the Editor: "CT Characteristics of Pheochromocytoma: Relevance for the Evaluation of Adrenal Incidentaloma"

Letizia Canu,[1,2] Janna A. W. Van Hemert,[1] Michiel Kerstens,[3] Robert P. Hartman,[4] Aakanksha Khanna,[5] Ivana Kraljevic,[6] Darko Kastelan,[6] Corin Badiu,[7,23] Urszula Ambroziak,[8] Antoine Tabarin,[9] Magalie Haissaguerre,[9] Edward Buitenwerf,[3] Anneke Visser,[10] Massimo Mannelli,[2] Wiebke Arlt,[11] Vasileios Chortis,[11] Isabelle Bourdeau,[12] Nadia Gagnon,[12] Marie Buchy,[13] Francoise Borson-Chazot,[13] Timo Deutschbein,[14] Martin Fassnacht,[14,15] Alicja Hubalewska-Dydejczyk,[16] Marcin Motyka,[16] Ewelina Rzepka,[16] Ruth T. Casey,[17] Benjamin G. Challis,[17] Marcus Quinkler,[18] Laurent Vroonen,[19] Ariadni Spyroglou,[20,21] Felix Beuschlein,[20,21] Cristina Lamas,[22] William F. Young,[5] Irina Bancos,[5] and Henri J. L. M. Timmers[1]

[1]Department of Internal Medicine, Division of Endocrinology, Radboud University Medical Center, Nijmegen, 6500 HB, The Netherlands; [2]Department of Experimental and Clinical Biomedical Sciences, University of Florence, Florence, 59100, Italy; [3]Department of Endocrinology, University of Groningen, University Medical Center Groningen, Groningen, 9713 GZ, The Netherlands; [4]Department of Radiology, Mayo Clinic, Rochester, Minnesota 55905; [5]Division of Endocrinology, Diabetes, Metabolism, and Nutrition, Mayo Clinic, Rochester, Minnesota 55905; [6]Department of Endocrinology, University Hospital Center Zagreb, Zagreb, Croatia 10000; [7]National Institute of Endocrinology C. I. Parhon, Bucharest, Romania, Bucharest, 011863, Romania; [8]Department of Internal Medicine and Endocrinology, Medical University of Warsaw, Warsaw, 02-097, Poland; [9]Service d'Endocrinologie Hôpital Haut-Lévêque, CHU de Bordeaux, Pessac, 33600, France; [10]Department of Applied Health Research, University of Groningen, University Medical Center Groningen, Groningen, 9713 GZ, The Netherlands; [11]Institute of Metabolism and Systems Research, University of Birmingham, Birmingham, B15 2TT, UK; [12]Division of Endocrinology, Center Hospitalier de l'Université de Montréal (CRCHUM), Montreal, Quebec, H2X 0A9, Canada; [13]Fédération d'Endocrinologie, Groupement Hospitalier Est, Hospices Civils de Lyon, Bron 69500, France; [14]Department of Internal Medicine I, Division of Endocrinology and Diabetes, University Hospital, University of Wuerzburg, Wuerzburg, D-97080, Germany; [15]Comprehensive Cancer Center Mainfranken, University of Wuerzburg, Wuerzburg, D-97080, Germany; [16]Chair and Department of Endocrinology, Jagiellonian University, Collegium Medicum, Krakow, 31-501, Poland; [17]Addenbrooke's Hospital, Metabolic Research Laboratories, Wellcome Trust-MRC Institute of Metabolic Science, University of Cambridge and NIHR Biomedical Research Center, Cambridge, CB2 OQQ, UK; [18]Endocrinology in Charlottenburg, Berlin, 10627, Germany; [19]Department of Endocrinology, Center Hospitalier Universitaire de Liège, Liège, 4000, Belgium; [20]Medizinische Klinik und Poliklinik IV Ludwig-Maximilians-Universität München, Munich, 80336, Germany; [21]Klinik für Endokrinologie, Diabetologie und Klinische Ernährung, UniversitätsSpital Zürich, Zurich, 8091, Switzerland; [22]Endocrinology Department, Hospital General Universitario de Albacete, Albacete, 02006, Spain; and [23]Carol Davila University of Medicine and Pharmacy, Chair of Endocrinology, Bucharest, 011863, Romania

ORCiD numbers: 0000-0003-4995-8108 (L. Canu); 0000-0003-1231-3306 (A. Tabarin); 0000-0001-5106-9719 (W. Arlt); 0000-0001-6170-6398 (M. Fassnacht); 0000-0003-4028-1671 (M. Quinkler); 0000-0001-7826-3984 (F. Beuschlein); 0000-0001-9332-2524 (I. Bancos).

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We gladly respond to the interesting letter by Sweeney and Blake (1) regarding our recent paper on the Computed Tomography (CT) characteristics of pheochromocytoma, with relevance for the evaluation of adrenal incidentaloma (2). Our findings suggest

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that a low unenhanced attenuation of an adrenal lesion (≤ 10 Hounsfield Unit [HU]) has a high negative predictive value (> 99%) for pheochromocytoma (3). On the other hand, we found that a high absolute or relative washout of an adrenal lesion with an unenhanced attenuation of > 10 HU by no means rules out this disease, since the latter was the case in as many as 29% of evaluable pheochromocytomas. This is in line with a previous meta-analysis of 10 studies, which indicated a rate of pheochromocytomas with a high washout pattern of 35% (4).

In their letter, the authors point out that rather than washout, portal venous phase (PVP) CT attenuation, that is, the maximum attenuation at 60–75 seconds after the injection of contrast, could be used to facilitate the distinction between pheochromocytoma and adrenocortical adenoma. Based on 2 publications (5, 6), they emphasize that pheochromocytomas have a higher PVP attenuation than adenomas. In the first study, comparing 43 histologically proven adrenal adenomas with 34 pheochromocytomas, applying a cut-off of > 85 HU to diagnose pheochromocytoma yielded a sensitivity of 88% (5). However, in the setting of the evaluation of adrenal incidentalomas, it is of the utmost importance to rule out pheochromocytoma with a high level of certainty, since, obviously, missing this diagnosis potentially has deleterious consequences for the patient. When using the suggested approach to apply contrast-enhanced attenuation for lesions with an unenhanced attenuation of > 10 HU, 12% of pheochromocytomas would, in fact, be missed. The sensitivity of PVP attenuation is therefore clearly inferior to that of plasma-free metanephrines, established at 98% (7). In the second study, again in pheochromocytomas versus adenomas, applying a PVP threshold of > 130 HU resulted in a specificity of 100%, but this was at the cost of a sensitivity of only 38% (6). To find out whether this parameter is truly specific for pheochromocytomas as suggested, adrenocortical carcinomas and other malignant adrenal lesions should also be investigated.

Prompted by the authors' interesting suggestions, we re-analyzed our data regarding PVP values. Among 76 pheochromocytomas with unenhanced HU > 10 and available washout data, PVP was available from the radiology reports in only 6 cases, and among those lesions, only 2 exhibited a PVP of > 85 HU. This could be related to differences in contrast protocols among different centers.

Taking into account these considerations, it is our strong opinion that until PVP attenuation is systematically evaluated in a larger population of patients with a mix of different adrenal tumor types, any adrenal lesion with an unattenuated HU > 10 should prompt biochemical evaluation to rule out pheochromocytoma by the measurement of catecholamine metabolites.

Additional Information

Correspondence and Reprint Requests: Letizia Canu, Department of Experimental and Clinical Biomedical Sciences, University of Florence, 50139, Florence, Italy. E-mail: letizia.canu@unifi.it

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