



**HAL**  
open science

**Response to Letter to the Editor from Soghomonian:  
“Epicardial and Pericardial Adiposity Without  
Myocardial Steatosis in Cushing Syndrome”**

Peter Wolf, Benjamin Marty, Khaoula Bouazizi, Nadja Kachenoura, Céline Piedvache, Anne Blanchard, Sylvie Salenave, Mikaël Prigent, Christel Jublanc, Christiane Ajzenberg, et al.

► **To cite this version:**

Peter Wolf, Benjamin Marty, Khaoula Bouazizi, Nadja Kachenoura, Céline Piedvache, et al.. Response to Letter to the Editor from Soghomonian: “Epicardial and Pericardial Adiposity Without Myocardial Steatosis in Cushing Syndrome”. *Journal of Clinical Endocrinology and Metabolism*, 2022, 107 (1), pp.e443-e444. 10.1210/clinem/dgab678 . hal-03942111

**HAL Id: hal-03942111**

**<https://hal.science/hal-03942111v1>**

Submitted on 4 Sep 2024

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

## Letter to the Editor Response

# Response to Letter to the Editor from Soghomonian: “Epicardial and Pericardial Adiposity Without Myocardial Steatosis in Cushing Syndrome”

Peter Wolf,<sup>1,2</sup> Benjamin Marty,<sup>3</sup> Khaoula Bouazizi,<sup>4,5</sup> Nadja Kachenoura,<sup>4,5</sup> Céline Piedvache,<sup>6</sup> Anne Blanchard,<sup>7</sup> Sylvie Salenave,<sup>1</sup> Mikaël Prigent,<sup>4</sup> Christel Jublanc,<sup>8</sup> Christiane Ajzenberg,<sup>9</sup> Céline Droumaguet,<sup>9</sup> Jacques Young,<sup>1</sup> Anne-Lise Lecoq,<sup>1</sup> Emmanuelle Kuhn,<sup>1</sup> Helene Agostini,<sup>6</sup> Severine Trabado,<sup>10</sup> Pierre G. Carlier,<sup>3</sup> Bruno Fève,<sup>11</sup> Alban Redheuil,<sup>5,12</sup> Philippe Chanson,<sup>1</sup> and Peter Kamenický<sup>1</sup>

<sup>1</sup>Université Paris-Saclay, Inserm, Physiologie et Physiopathologie Endocrinienne, Assistance Publique-Hôpitaux de Paris, Hôpital Bicêtre, Service d'Endocrinologie et des Maladies de la Reproduction, Centre de Référence des Maladies Rares de l'Hypophyse, 94275 Le Kremlin-Bicêtre, France; <sup>2</sup>Medical University of Vienna, Department of Internal Medicine III, Division of Endocrinology and Metabolism, 1090 Vienna, Austria; <sup>3</sup>Institut de Myologie, CEA, Laboratoire de Résonance Magnétique Nucléaire, 75013 Paris, France; <sup>4</sup>Institut de Cardiométabolisme et Nutrition (ICAN), 75013 Paris, France; <sup>5</sup>Sorbonne Université, CNRS, Inserm, Laboratoire d'Imagerie Biomédicale, LIB, 75006 Paris, France; <sup>6</sup>Assistance Publique-Hôpitaux de Paris, Hôpital Bicêtre, Unité de Recherche Clinique, 94275 Le Kremlin-Bicêtre, France; <sup>7</sup>Université de Paris, Assistance Publique des Hôpitaux de Paris, Hôpital Européen Georges-Pompidou, Centre d'Investigations Cliniques, Inserm CIC1318 et UMR 1138, 75015 Paris, France; <sup>8</sup>Assistance Publique-Hôpitaux de Paris, Hôpital Pitié-Salpêtrière, Service d'Endocrinologie-Métabolisme, 75013 Paris, France; <sup>9</sup>Assistance Publique-Hôpitaux de Paris, Hôpital Henri-Mondor, Service de Médecine Interne, 94000 Créteil, France; <sup>10</sup>Assistance Publique-Hôpitaux de Paris, Hôpital Bicêtre, Service de Génétique Moléculaire, Pharmacogénétique et Hormonologie, 94275 Le Kremlin-Bicêtre, France; <sup>11</sup>Assistance Publique-Hôpitaux de Paris, Hôpital Saint-Antoine, Service d'Endocrinologie et Métabolisme, Centre de Référence des Maladies Rares de l'Insulino-Sécrétion et de l'Insulino-Sensibilité (PRISIS), Sorbonne Université, Inserm, Centre de Recherche Saint-Antoine, UMR-S938, IHU ICAN, 75012 Paris, France; and <sup>12</sup>Assistance Publique-Hôpitaux de Paris, Hôpital Pitié-Salpêtrière, Unité d'Imagerie Cardiovasculaire et Thoracique, APHP.SU, 75013 Paris, France

**ORCID numbers:** 0000-0001-6779-734X (P. Wolf); 0000-0002-4983-647X (B. Marty); 0000-0002-0815-0586 (A. Blanchard); 0000-0001-9286-5631 (J. Young); 0000-0001-5096-5722 (P. Chanson); 0000-0002-1994-4226 (P. Kamenický).

Received: 31 August 2021; Editorial Decision: 9 September 2021; First Published Online: 14 September 2021; Corrected and Typeset: 29 September 2021.

Dear Editor,

We thank Soghomonian et al (1) for their interest in our manuscript and for their supportive comments. We fully agree that epicardial adipose tissue may play an important

role in the development of cardiovascular comorbidities in patients with Cushing syndrome.

Their letter highlights the important question of who are “appropriate” controls in order to identify the impact

of cortisol per se on epicardial adiposity. In our study, we matched patients and controls for sex, age, and body mass index, and made the choice not to match them for cardiovascular risk factors (like hypertension or diabetes mellitus) as these could directly affect the heart function and heart fat stores (2, 3). In contrast to the study published by Maurice and colleagues (4), we investigated patients not only cross-sectionally, but also longitudinally before and after biochemical disease remission, so that each patient was his or her own appropriate control. This allowed us to evaluate the direct impact of normalizing hypercortisolism. In addition, in the multiple regression model, we adjusted the cross-sectional analysis for confounding factors, and hypercortisolism remained a strong independent predictor of epicardial adiposity.

With regard to the methodological aspects, we are aware that the intramyocardial lipid percentages that we obtained by  $^1\text{H}$  magnetic resonance spectroscopy were rather high. However, all spectra were reviewed by 2 experts before inclusion in the analysis.  $^1\text{H}$  magnetic resonance spectroscopy of the heart is a technically challenging and time-demanding procedure. Especially in patients with vertebral fractures, frequently observed in patients with Cushing syndrome, these long examinations are often not well tolerated, which explains artifacts by movements and premature interruption. These technique- and disease-related difficulties probably explain why our study is the first study to apply  $^1\text{H}$  magnetic resonance spectroscopy in patients with Cushing syndrome. Of note, we also used a second, independent Dixon method-based assessment of myocardial fat content, which yielded equivalent results.

We provided the first systematic mapping of all different cardiac fat depots, including intramyocardial, epicardial, and pericardial adipose tissue in patients with Cushing syndrome. The decorrelation between the epicardial adipose tissue and visceral adipose tissue may at first glance appear surprising. However, the strong correlation between visceral adipose tissue and epicardial fat is described in the general population and in community obesity (5), but not in hypercortisolism. The strong association of epicardial fat with hypercortisolism and the significative variation induced by its treatment demonstrate that epicardial adipose tissue is highly sensitive to glucocorticoids, probably due to a different expression of glucocorticoid, mineralocorticoid, or  $\beta$ -adrenergic receptors compared to the classic visceral tissue. Last, pericardial adiposity was not independently associated with hypercortisolism in multiple regression analysis. It correlated with visceral fat mass and thus represents a more “classical” visceral adipose tissue. The mentioned high expression of 11 $\beta$ -hydroxysteroid dehydrogenase

type 1 (11 $\beta$ -HSD1) in mediastinal adipose tissue was described in patients with conventional obesity (6). In contrast, studies in patients with Cushing syndrome rather showed a downregulation of 11 $\beta$ -HSD1 in visceral adipose tissue, probably as a response to chronic overstimulation (7). Furthermore, chronic stimulation of the glucocorticoid and/or mineralocorticoid receptors may lead to fibrosis and remodeling and consequently alter visceral adipose tissue expansibility in Cushing syndrome patients (8). This could explain the missing changes after biochemical disease remission of hypercortisolism on pericardial fat in short-term follow-up.

In conclusion, we are convinced that hypercortisolism differentially affects distinct cardiac fat depots. The link between cardiac adiposity and cardiovascular morbidity warrants further investigations.

## Additional Information

**Correspondence:** Peter Kamenický, MD, PhD, Faculté de Médecine Paris-Saclay, 63 rue Gabriel Péri, 94276 Le Kremlin Bicêtre Cedex, France. Email: [peter.kamenicky@universite-paris-saclay.fr](mailto:peter.kamenicky@universite-paris-saclay.fr)

## References

1. Soghomonian A, Dutour A, Maurice F, Castinetti F, Gaborit B. Letter to the editor from Soghomonian: “Epicardial and pericardial adiposity without myocardial steatosis in Cushing syndrome.” *J Clin Endocrinol Metab*. 2021.
2. McGavock JM, Lingvay I, Zib I, et al. Cardiac steatosis in diabetes mellitus: a  $^1\text{H}$ -magnetic resonance spectroscopy study. *Circulation*. 2007;**116**(10):1170-1175.
3. Wolf P, Winhofer Y, Krššák M, Krebs M. Heart, lipids and hormones. *Endocr Connect*. 2017;**6**(4):R59-R69.
4. Maurice F, Gaborit B, Vincentelli C, et al. Cushing syndrome is associated with subclinical LV dysfunction and increased epicardial adipose tissue. *J Am Coll Cardiol*. 2018;**72**(18):2276-2277.
5. Gaborit B, Kober F, Jacquier A, et al. Assessment of epicardial fat volume and myocardial triglyceride content in severely obese subjects: relationship to metabolic profile, cardiac function and visceral fat. *Int J Obes (Lond)*. 2012;**36**(3):422-430.
6. Atalar F, Gormez S, Caynak B, et al. The role of mediastinal adipose tissue 11 $\beta$ -hydroxysteroid dehydrogenase type 1 and glucocorticoid expression in the development of coronary atherosclerosis in obese patients with ischemic heart disease. *Cardiovasc Diabetol*. 2012;**11**:115.
7. Mariniello B, Ronconi V, Rilli S, et al. Adipose tissue 11 $\beta$ -hydroxysteroid dehydrogenase type 1 expression in obesity and Cushing's syndrome. *Eur J Endocrinol*. 2006;**155**(3):435-441.
8. Hayashi R, Okuno Y, Mukai K, et al. Adipocyte GR inhibits healthy adipose expansion through multiple mechanisms in Cushing syndrome. *Endocrinology*. 2019;**160**(3):504-521.