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Letter to the Editor Response

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

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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 ^1H magnetic resonance spectroscopy were rather high. However, all spectra were reviewed by 2 experts before inclusion in the analysis. ^1H 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 ^1H 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 β -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 β -hydroxysteroid dehydrogenase

type 1 (11 β -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 β -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

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