Polycystic ovary syndrome. Are we overlooking something?

To the Editor,

The article by Özkeçeci et al. (1) entitled "Heart rate variability and heart rate turbulence in patients with polycystic ovary syndrome" published in the Anatol J Cardiol 2016; 16: 323-7, draws attention to discussion of the role of the autonomic nervous system in patients with polycystic ovary syndrome (PCOS). Although there are overwhelming data that PCOS is associated with augmented sympathetic activity and depressed vagal tonus (2), there are few data supporting the observation of Özkeçeci et al. (1) demonstrating neutral effect of this disorder on autonomic nervous activity. This is similar to the debate surrounding interpretation of lipid metabolism disorders in PCOS. Many studies have described hypertriglyceredemia, low high-density lipoprotein cholesterol, and high low-density lipoprotein cholesterol. But these findings have not been consistently confirmed by other researchers. The question is, why? What are we missing?

High prevalence of central obesity, insulin resistance, and obstructive sleep apnea have led to speculation that sympathetic activity may be increased in PCOS (2). Targeting sympathetic nervous system might even be considered part of treatment protocol (2). Lean women with PCOS might have normal insulin levels and sensitivity (3). Meanwhile, majority of women with body mass index (BMI) >30 kg/m^2 have insulin resistance (3). Orio et al. (4) reported that patients with PCOS having BMI of 18–25 kg/m^2 had fasting insulin levels 5 times higher and homeostatic model assessment (HOMA) insulin resistance values 6 times higher than BMI-matched controls. These ratios were even larger for those with BMI >30 kg/m^2. Thus, even lean patients with PCOS may have insulin resistance. It is well-known that insulin resistance and hyperinsulinemia lead to elevated sympathetic outflow through actions in central brain receptors (5). Sympathetic activity might contribute to increased resistance (5). Özkeçeci et al. (1) failed to present HOMA values. Therefore, it is very probable, though not certain, that presence, absence, or degree of insulin resistance determines autonomic nervous activity, with particular emphasis on sympathetic system, in PCOS. Insulin resistance may, in part, also be the explanation for observed variability in lipid levels in different studies.

Definition and diagnostic criteria of PCOS are not uniform across the studies. The flexibility of Rotterdam criteria generated the possibility of 4 phenotypes. Phenotype D, which is without overt hyperandrogenism, is of particular concern. Androgens are generally considered to induce insulin resistance, and insulin resistance might contribute to hyper-androgenic and ovulatory dysfunction through multiple mechanisms (5). Phenotype-based separate analyses are not usually reported in literature. As a result, we don't know the relative contribution of each phenotype to the reported findings, which might, in part, have the potential to reveal the discrepancy in the research.

Finally, a simple marker of autonomic activity of cardiovascular system would be attractive, but human autonomic nervous system is highly complex structure rendering it inaccessible for examination with such an easy assay. Unfortunately, there is no gold-standard technique available to determine autonomic activity. In conclusion, one should consider the aforementioned discussion in order to interpret findings of a study investigating autonomic nervous system activity in patients with PCOS.

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