



## Response to “Reproductive Function Abnormalities and Bariatric Surgery: is a Matter of Time?”

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In this interesting commentary entitled “Reproductive function abnormalities and bariatric surgery: is a matter of time?” the authors postulate that duration of reproductive and metabolic disease among women with polycystic ovary syndrome (PCOS) may inform likelihood of success after bariatric surgery. In our retrospective review of women with PCOS that underwent bariatric surgery at the Cleveland Clinic Foundation, most but not all women had improvements in reproductive and cardio-metabolic disease postoperatively. Preoperative free testosterone and ovarian volume appeared to have relevance in predicting benefits postoperatively. Duration of disease, however, was not considered and, as highlighted by this commentary, few have previously evaluated this feature in considering long-term health outcomes among women with PCOS.

Duration of PCOS is a challenging parameter to study as it requires determination of when PCOS first manifests in a woman. Pathogenesis of PCOS may have its origins in utero. Maternal hypertension and diabetes may result in fetal programming which predisposes children to metabolic dysfunction, hyperandrogenism, and PCOS [1]. Indeed, children of women with PCOS have subtle abnormalities in cardio-metabolic profiles detectable within the first 8 years of life [2]. Furthermore, PCOS commonly presents in adolescence but diagnosis during this time period is challenging due to normal increased rates of acne and irregular menses among adolescent girls. New methods of diagnosis

are needed in this age group to help standardize diagnosis at a younger age [3]. Even in adulthood, time of initial diagnosis will likely be greatly influenced by history of hormonal contraceptive use, which will mask ovulatory dysfunction, and desire for fertility as this is often when women with PCOS first present for evaluation.

While challenging to assess, length of disease presence may represent a good marker of the underlying pathology characterizing a woman’s PCOS diagnosis. Why some, but not all, women with PCOS have increased central adiposity and metabolic dysfunction is hypothesized to relate to the degree of baseline abnormalities in androgen synthesis. Those women with severe dysfunction in androgen production may not require significant metabolic disarray to exhibit the PCOS phenotype. Contrastingly, women with a minimal amount of androgen synthesis dysfunction may have the same reproductive phenotype if they also have increased central adiposity, insulin resistance, and hyperinsulinemia which is known to exacerbate hyperandrogenism [1, 4]. Thus, those women that only manifest features of PCOS after developing metabolic dysfunction may be diagnosed later in life, have a shorter duration of PCOS symptoms, and benefit most from weight loss surgery. Alternatively, a more direct correlation may exist between prolonged hyperandrogenism and cardio-metabolic disease [5]. Long-term androgen exposure may cause irreversible changes obesity surgery is unable to ameliorate.

Regardless of mechanism, the authors raise an important question that has not yet been addressed in the PCOS literature. To properly assess the impact of length of disease presence, prospective cohort studies are required, utilizing standardized phenotyping and diagnostic criteria. Better elucidation of when PCOS first manifests, the length of time disease is present, and interventions aimed at improving reproductive and metabolic outcomes will help shed light on the most effective methods to improve long-term health outcomes among these women.

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## Compliance with Ethical Standards

**Conflict of Interest** The authors declare that they have no conflict of interest.

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