Journal of Clinical Densitometry: Assessment & Management of Musculoskeletal Health, vol. ■, no. ■, 1–7, 2016

1094-6950/■:1–7/$36.00
http://dx.doi.org/10.1016/j.jocd.2016.10.007

Original Article

Women With Polycystic Ovary Syndrome Have Comparable Hip Bone Geometry to Age-Matched Control Women

Laura E. McBreairty,[1] Gordon A. Zello,[1] Julianne J. Gordon,[2] Shani B. Serrao,[3] Roger A. Pierson,[3] Donna R. Chizen,[3] and Philip D. Chilibeck[2,]*

[1]College of Pharmacy and Nutrition, University of Saskatchewan, 110 Science Place, Saskatoon, SK S7N 5C9, Canada; [2]College of Kinesiology, Physical Activity Complex, University of Saskatchewan, 87 Campus Drive, Saskatoon, SK S7N 5B2, Canada; and [3]Obstetrics, Gynecology and Reproductive Sciences, College of Medicine, 103 Hospital Drive, Saskatoon, SK S7N 0W8, Canada

Abstract

Polycystic ovary syndrome (PCOS) is an endocrine disorder affecting women of reproductive age manifesting with polycystic ovaries, menstrual irregularities, hyperandrogenism, hirsutism, and insulin resistance. The oligomenorrhea and amenorrhea characteristic to PCOS are associated with low bone mineral density (BMD); conversely, the hyperandrogenism and hyperinsulinemia may elicit a protective effect on BMD. As bone geometric properties provide additional information about bone strength, the objective of this study was to compare measures of hip geometry in women with PCOS to a healthy female population. Using dual-energy X-ray absorptiometry, BMD and measures of hip geometry were determined in women with PCOS (n = 60) and healthy controls (n = 60) aged 18–35 years. Clinical biochemical measures were also determined in women with PCOS. Measures of hip geometry, including cross-sectional area, cross-sectional moment of inertia, subperiosteal width (SPW), and section modulus, were similar between groups following correction for body mass index (BMI) (all $p > 0.05$) with intertrochanter SPW significantly lower in women with PCOS ($p < 0.05$). BMI-corrected whole body BMD as well as the lumbar spine and regions of proximal femur were also comparable between groups. In women with PCOS, BMI-corrected correlations were found between insulin and femoral shaft SPW ($r = 0.322$, $p < 0.05$), glucose and femoral neck ($r = 0.301$, $p < 0.05$), and trochanter BMD (0.348, $p < 0.05$), as well as between testosterone and femoral neck BMD (0.376, $p < 0.05$) and narrow neck cross-sectional area (0.306, $p < 0.05$). This study demonstrates that women with PCOS may have compromised intertrochanter SPW while oligomenorrhea appears to have no detrimental effect on bone density or geometry in women with PCOS.

Key Words: Bone mineral density; hip geometry; polycystic ovary syndrome.

Introduction

Polycystic ovary syndrome (PCOS) is a common endocrine disorder affecting 6%–8% of women of reproductive age *(1)*. The heterogeneity of PCOS is evident from the spectrum of associated clinical symptoms including polycystic ovaries, menstrual irregularities, hyperandrogenism, hirsutism, and insulin resistance *(1)*. Approximately 65%–80% of women with PCOS have menstrual cycle disturbances and experience either oligomenorrhea or amenorrhea *(2)*. Oligomenorrhea or amenorrhea are typically associated with low bone mineral density (BMD) due to concurrent estrogen deficiency; however, amenorrheic women with PCOS have higher BMD than age- and body mass index (BMI)-matched women with amenorrhea not related to PCOS *(3)*. Body weight positively affects BMD, and approximately 60% of women with PCOS are obese *(4)*; therefore, most studies adjust for BMI when comparing BMD between women with

Received 08/3/16; Revised 10/20/16; Accepted 10/25/16.
*Address correspondence to: Philip D. Chilibeck, PhD, College of Kinesiology, Physical Activity Complex, University of Saskatchewan, 87 Campus Drive, Saskatoon, SK S7N 5B2, Canada. E-mail: phil.chilbeck@usask.ca

PCOS and controls. Studies are conflicting and demonstrate either lower BMD *(5)*, no difference *(6)*, or higher BMD in women with PCOS compared to BMI-matched controls *(7)*. This suggests that factors other than body weight, such as hyperandrogenism and hyperinsulinemia, may contribute to the maintenance of BMD in women with PCOS.

BMD is a valuable measure to assess fracture risk; however, BMD can only be used as a surrogate marker of bone fragility, and bone geometry must also be accounted for when evaluating bone strength *(8)*. Measures of geometric properties provide additional information about the distribution of mass that can affect the ability of bone to resist stress *(9)*. Although BMD has been assessed in women with PCOS, few studies have measured geometric properties in this population, with no assessment of geometric parameters of the hip or differences between obese and nonobese women with PCOS. Hip fractures are associated with higher cost and disability than other types of osteoporotic fracture *(10)*, making it important to determine whether the protective effects of PCOS on BMD are also found on hip geometric properties.

Our objective was to compare measures of hip bone geometry in obese and nonobese women with PCOS to a control female population. In addition, we assessed the effect of menstrual cycle irregularities and hormonal influences on hip geometric properties in women with PCOS. Furthermore, because the inulin-sensitizing drug metformin positively affects bone *(11)*, we wanted to determine whether women with PCOS taking metformin had improved measures of BMD or bone strength. We hypothesized that women with PCOS would have similar (i.e., nonobese) or improved measures (i.e., obese) of hip geometry compared to control females of reproductive age. We also hypothesized that these measures would be more favorable in eumenorrheic compared to amenorrheic women with PCOS, and that bone measurements would be positively associated with androgen (i.e., testosterone) levels.

Materials and Methods

Participants

The results presented in the present report are baseline measures from participants involved in a larger ongoing study determining the effect of a pulse-based diet (e.g., beans, lentils, chickpeas) and exercise intervention in women with PCOS. Sixty women with PCOS had been recruited for the intervention and 60 healthy control women were recruited for this study as a comparison group. All participants were between 18 and 35 years old. The study was approved by the University of Saskatchewan Biomedical Research Ethics Board and all women gave written informed consent before participation in the study. Control participants were recruited via postings on the university website and women with PCOS were recruited via posters, contacting doctors' offices, and postings on the university website. Control women had not been diagnosed with any chronic medical conditions, were not pregnant, and had regular menstrual cycles. A diagnosis of PCOS was made by an obstetrics-gynecologist using criteria specified in the PCOS report of the Androgen Excess-PCOS Society Task Force *(1)*. A diagnosis of PCOS required presence of 2 of the 3 diagnostic criteria as defined by the Rotterdam consensus: a self-reported history of cycles >35 days in length, hyperandrogenism as defined by a Ferriman and Gallwey score of >6 or hyperandrogenemia *(1)*, as well as polycystic ovaries, defined as >25 follicles visualized by transvaginal ultrasonography, reflecting newest guidelines recommended by the Androgen Excess and Polycystic Ovary Syndrome Society *(12,13)*. Women using hormonal birth control methods or who had a medical condition limiting exercise or consumption of a pulse-based diet (allergies or intolerances) were excluded. A diagnosis of PCOS was excluded in women with the following conditions: taking antiseizure or antipsychotic medications known to induce development of PCOS; untreated hyperprolactinemia or thyroid disease; or excessive adrenal androgen production confirmed by a diagnosis of congenital adrenal hyperplasia or an adrenal tumor. Women were also excluded from the study if they had an uncontrolled medical condition that interfered with ovarian or systemic hormone production, were pregnant or breastfeeding, or resided outside of the local geographic area. Eleven PCOS women were categorized as eumenorrheic, which was defined as having an average of 26–35 days between cycles during the 6 months prior to baseline measures. Forty-three PCOS women were classified as oligoamenorrheic. Twenty PCOS women were taking metformin upon entry into the study and 40 PCOS women were not receiving metformin.

Dual-Energy X-Ray Absorptiometry (DXA)

BMD scans using DXA (Hologic Discovery Wi; Bedford, MA) were performed and analyzed by a certified radiology technologist. A quality-control phantom scan was performed daily. BMD and measures of hip bone geometry were determined as previously described *(14,15)*. Whole body (WB) BMD and bone mineral content (BMC), as well as BMD of the lumbar spine (LS) (L1–L4 vertebrae) and proximal femur regions including the femoral neck, trochanter, intertrochanteric, and total hip were also determined. DXA scans were used to determine geometric measures at the narrow neck (NN) region that is located across the narrowest segment of the femoral neck; the intertrochanter region along the bisector of the neck-shaft angle; and the femoral shaft (FS) located 2 cm distal to the midpoint of the lesser trochanter *(14)*. In these regions, the subperiosteal width (SPW), bone cross-sectional area (CSA), cross-sectional moment of inertia (CSMI), and section modulus (Z) were determined. Bone CSA is representative of BMC and expresses the amount of bone within a cross-section in terms of cortical equivalent surface area opposed to mineral mass. Measures of Z take into account the mass distribution whereas CSMI further accounts for the maximum distance of mass distribution. The CSA is indicative of bone compressive strength whereas