Clinical course of depression symptoms and predictors of enduring depression risk in women with polycystic ovary syndrome: Results of a longitudinal study

Eleni A. Greenwood, M.D., M.Sc.,[a] Lauri A. Pasch, Ph.D.,[a] Kanade Shinkai, M.D., Ph.D.,[b] Marcelle I. Cedars, M.D.,[a] and Heather G. Huddleston, M.D.[a]

[a] Department of Obstetrics, Gynecology and Reproductive Sciences, and [b] Department of Dermatology, University of California San Francisco, San Francisco, California

Objective: To [1] characterize depression symptoms over time and [2] test the hypothesis that adverse metabolic parameters would associate with risk of enduring depression risk in women with polycystic ovary syndrome (PCOS).
Design: Prospective cohort study.
Setting: University center.
Patient(s): One hundred sixty-three women with PCOS.
Intervention(s): The Beck Depression Inventory Fast Screen (BDI-FS) was self-administered at baseline and follow-up to identify depression risk, using a cutoff score >4.
Main Outcome Measure(s): BDI-FS scores.
Result(s): Median baseline age was 29.0 years, and median follow-up interval was 5.5 years. Fifty-nine of 163 women had positive depression screens at baseline (36%); 52 women (32%) screened positive at follow-up. Median change in BDI-II score was 0 (interquartile range, −2, 1) over the study period. Of the 59 women at risk for depression at baseline, 22 screened negative at follow-up (37%), while 37 women remained at risk (63%). Considering these 59 women with positive depression screens at baseline, higher body mass index (BMI) was associated with increased odds of enduring depression risk at follow-up (adjusted odds ratio = 1.09; 95% confidence interval, 1.00, 1.18), in a multivariate logistic regression model. Compared with women with normal body weight at baseline, obese women (BMI >30 kg/m^2) had five-fold increased odds of enduring depression risk at follow-up (adjusted odds ratio = 5.07; 95% confidence interval, 1.07, 24.0).
Conclusion(s): The prevalence of depression was relatively stable over time in a cohort of women with PCOS. Elevated BMI is a hallmark of enduring depression risk. These results may assist providers in developing targeted intervention strategies to reduce the prevalence of long-term depressive symptoms in women with PCOS. (Fertil Steril® 2019;111:147–56. ©2018 by American Society for Reproductive Medicine.)
El resumen está disponible en Español al final del artículo.

Key Words: Polycystic ovary syndrome (PCOS), depression, obesity

Polycystic ovary syndrome (PCOS) is a multisystem disorder associated with a variety of reproductive, metabolic, and psychological comorbidities (1). The prevalence of PCOS may exceed 15%, depending on diagnostic criteria (2), making it a common clinical entity imposing a substantial health care burden.

Recently, the adverse psychological correlates of PCOS have gained increasing attention as a key feature impairing quality of life. Depression is a primary concern; women with PCOS are disproportionately afflicted by depression, with three- to eight-fold increased prevalence compared with controls (3).

Received August 12, 2018; revised September 28, 2018; accepted October 1, 2018; published online November 17, 2018.
E.A.G. has nothing to disclose. L.A.P. has nothing to disclose. K.S. has nothing to disclose. M.I.C. has nothing to disclose. H.G.H. has nothing to disclose.
Reprint requests: Eleni Greenwood, M.D., M.Sc., Department of Obstetrics, Gynecology and Reproductive Sciences, Division of Reproductive Endocrinology and Infertility, University of California San Francisco School of Medicine, 499 Illinois Street, San Francisco, California 94158-2519 (E-mail: eleni.greenwood@ucsf.edu).

Fertility and Sterility® Vol. 111, No. 1, January 2019 0015-0282/$36.00

https://doi.org/10.1016/j.fertnstert.2018.10.004

However, our current understanding of depression risk in PCOS is predominantly from cross-sectional studies of subjects presenting for a single episode of clinical care (3). Very little is known about the evolution of depression symptoms over time in women with PCOS. Indeed, in a 2018 position statement, the Androgen Excess and PCOS Society emphasized this gap in knowledge and the explicit need for research in longitudinal cohorts (4).

Unfavorable metabolic factors, primarily obesity, are known correlates of depression risk in the general population (5, 6) as well as in women with PCOS (7). We have previously identified a link between insulin resistance and depressed mood in women with PCOS (8, 9), postulating a "metabolic pathway" for depression in this clinical population. Yet risk factors for enduring depression in women with PCOS have not been characterized.

With aging, several clinical features of PCOS are progressively attenuated (10, 11). Menses become more regular, and biochemical hyperandrogenism declines (10, 12). In contrast, the evolution of the metabolic symptoms of PCOS with aging is less clear. Recent studies have indicated that there is progression of insulin resistance and dyslipidemia over time in obese women with PCOS but limited changes for lean counterparts (10, 13, 14).

A better understanding of the trajectory of depression symptoms in women with PCOS will facilitate better counseling. Further, identifying baseline clinical characteristics that are risk factors for enduring depression might help clinicians identifying high-risk individuals for whom more intensive resources should be offered and potentially afford insights into pathophysiology of mood derangements in this population.

The objectives of this study were to [1] characterize depression symptoms over time and [2] test the hypothesis that adverse metabolic parameters are associated with risk of enduring depression in women with PCOS.

MATERIALS AND METHODS

This is a prospective cohort study of women with PCOS by the Rotterdam criteria (15) evaluated in an academic clinic. Institutional Review Board approval was obtained from the University of California at San Francisco Committee on Human Research. Subjects provided informed, written consent to participate in the research cohort.

Subjects

Women were consecutively recruited over 11 years (2006–2017) at a university-based multidisciplinary PCOS specialty clinic. Women were referred to the clinic primarily by community providers; approximately one third of women were self-referred. Clinical evaluations were motivated by [1] establishing and/or confirming a rigorous diagnosis (or lack thereof) of PCOS, [2] interacting with a multidisciplinary panel of experts, including reproductive endocrinologists, a psychologist, a dermatologist, a registered dietician, and a genetic counselor, to discuss clinical implications and management strategies of PCOS, and [3] participating in research opportunities available to the PCOS cohort. Details of subject recruitment and the clinic protocol have been described elsewhere (8, 16).

Of the PCOS cohort evaluated during the baseline study period (n = 478), 450 women had e-mail addresses available at the time of follow-up. Of the 450 surveys e-mailed, 27 were undeliverable; 179 of the remaining 423 women completed the follow-up survey (43%). Four women replied declining to participate.

Inclusion criteria required PCOS diagnosed by the Rotterdam criteria (15), age 16–45 at baseline, and complete Beck Depression Inventory Fast-Screen (BDI-FS) questionnaire data at baseline and follow-up. Sixteen women were excluded for missing BDI-FS items at either time point, resulting in a final study cohort of 163 women.

Baseline Clinical Evaluation

During the initial clinic intake, women completed a series of questionnaires addressing their medical history and health behaviors. Exercise was characterized using the validated International Physical Activity Questionnaire (17), which quantifies weekly moderate and vigorous intensity exercise expenditure.

Depression was assessed using the BDI-FS (18). The BDI-FS is a seven-item self-administered questionnaire derived from the precursor 21-item Beck Depression Inventory (BDI-II). The seven items were selected by factor analysis to emphasize anhedonia, dysphoria, and other major cognitive features of depression (18). The scale has been validated in a variety of clinic populations (18–21). Subjects are queried about characteristic symptoms of depression and the frequency with which they experienced the symptoms over the prior 2 weeks. Items are scored from 0 (absent symptom) to 3 (severe symptom), for a total summative score of 0–21. We considered BDI-FS scores as a dichotomized outcome, with a score >4 indicating a positive depression screen in accordance with prior literature (22). The following depression severity categories were considered: 0–4, no depression; 5–8, mild depression; 9–12, moderate depression; >12: severe depression (22).

During the baseline clinic visit, women underwent rigorous characterization with complete history and physical examinations, transvaginal ultrasound assessment of ovarian morphology, and dermatologic examination including modified Ferriman-Gallwey (mFG) scoring to quantify hirsutism.

Fasting metabolic and endocrine testing was performed at baseline at the university laboratory or two primary commercial laboratories, according to patients' insurance coverage. The 75 g 2-hour oral glucose tolerance test was administered with the laboratory panel. Women were required to abstain from hormonally active medications and glucose sensitizers such as metformin for at least 1 month before laboratory testing as well as before the clinic ultrasound. Additional details of the multidisciplinary clinic protocol have been described elsewhere (8, 16).

Follow-up Survey

At the time of follow-up, consenting PCOS cohort participants evaluated in clinic at least 6 months before were

recontacted via e-mail and invited to complete a follow-up questionnaire online, which included the BDI-FS to assess depression.

Additional survey questions were compiled by a panel of multidisciplinary PCOS experts to ascertain updated menstrual history, current height and weight, interval medical diagnoses, and current medication use. Follow-up body mass index (BMI) was calculated from self-reported height and weight. The International Physical Activity Questionnaire was repeated to assess follow-up exercise behavior. Finally, participants were asked to indicate their current level of concern about a set of PCOS-related issues, using a visual analog scale ranging from 0 (not concerned) to 50 (somewhat concerned) to 100 (very concerned). Queried concerns included irregular or absent menses, excessive hair growth, acne, hair loss, weight, fertility, mood or depression, and long-term health consequences.

Statistical Analysis

Data were tested for normality, and descriptive statistics were provided. Subjects were categorized as depression risk versus no depression risk at both time points (baseline and follow-up) on the basis of the BDI-FS threshold score >4 indicating risk for depression. Patient characteristics were compared between groups (e.g., depression risk vs. no depression risk) using Kruskal-Wallis, χ^2, or Fisher's exact testing as appropriate. To delineate potential predictors of enduring depression risk, attention was then focused on the subset of women (n = 59) who were classified as at risk for depression at baseline. The primary outcome, enduring versus resolved depression risk at follow-up, was coded as a binary outcome (1 vs. 0, respectively) on the basis of follow-up BDI-FS score. Logistic regression modeling evaluated the association between baseline characteristics of women and odds of enduring depression risk. A multivariate logistic regression model incorporated baseline age follow-up intervals as covariates, selected a priori as clinically important potential confounding variables. In a sensitivity analysis, we also included baseline BDI-FS score in the model. Finally, we alternatively considered change in BDI-FS score as a continuous outcome and examined linear regression models in an additional sensitivity analysis. Correction for multiple comparisons was not performed in light of the exploratory nature of this analysis.

Statistical analyses were performed with STATA, version 14.2.

RESULTS

Four hundred fifty emails were dispatched, of which 423 follow-up e-mails were delivered; a 42% survey response rate was achieved (179/423 women).

Responders versus Nonresponders

Considering the full cohort of e-mails dispatched (n = 450), a comparison of the 179 responders with the 271 e-mail addressees from whom no response was achieved revealed that the responders, on average, were older at their baseline visit (29.1 vs. 27.5 years, $P=.02$) and had a shorter time interval elapsed since their clinic visit (5.0 vs. 6.2 years, $P=.01$). Median baseline BDI-FS scores were similar between these two groups (3 vs. 4, $P=.37$). Baseline BDI-FS correlated with BMI in both responders (rho = 0.26, $P<.01$) and nonresponders (rho = 0.18, $P<.01$). The same patterns applied when restricting the analysis to the cohort of delivered e-mails (n = 423), as well as when additionally excluding the respondent women with incomplete BDI-FS data at either time point (n = 16).

Baseline Characteristics

At baseline, 59 of 163 (36%) women screened positive for depression risk. Compared with women screening negative, these at-risk patients showed a differential distribution of socioeconomic factors at baseline, including a lower proportion of Caucasian racial background, lower percentage attaining postgraduate degrees, and lower income category distribution (Table 1). Patients at risk for depression also had higher BMI (31.1 vs. 27.4 kg/m^2, $P<.01$), lower serum high-density lipoprotein (HDL) cholesterol (52 vs. 58 mg/dL, $P=.04$), and higher triglycerides (91 vs. 74 mg/dL, $P=.03$). Exercise behavior, as measured by weekly hours of physical activity, did not differ between groups.

Follow-up Characteristics

At follow-up, 52 of 163 (32%) women screened positive for depression risk. Compared with women with negative screens at follow-up, at-risk women had a shorter median follow-up interval (3.8 vs. 5.8 years, $P=.02$), higher BMI (32.6 vs. 26.6 kg/m^2, $P<.01$), and higher level of concern regarding all queried PCOS symptoms (Table 2). Similar exercise behavior was reported in both groups.

Depression Natural History

Of the 59 women with depression risk at baseline, 37 women (63%) remained at risk, while 22 (37%) no longer met the criteria for depression risk at follow-up. Conversely, of the 104 women free of depression risk at baseline, 15 (14%) were at risk for depression at follow-up. The median change in BDI-FS score was 0 (interquartile range [IQR], −2, 1), indicating relative stability of mood symptoms over the course of the study.

Predictors of Enduring Depression Risk

Restricting the analysis to those women with depression risk at baseline (n = 59), logistic regression modeling was used to identify variables associated with enduring depression risk at follow-up. In univariate analyses, increasing total and low-density lipoprotein (LDL) cholesterol was associated with marginally increased odds of enduring depression risk at the $P<.05$ statistical significance level (Table 3). Increasing baseline BDI-FS score (i.e., depression severity) was suggested to be associated with increased odds of enduring depression risk; however, this was not statistically significant (odds ratio [OR] = 1.22; 95% confidence interval [CI], 0.98, 1.51, $P=.07$).

TABLE 1

Patient characteristics at baseline.

	Overall (n = 163)	Negative depression screen (n = 104)	Positive depression screen ("at risk"; n = 59)	*P*
Demographics				
Age	29.0 (25.2, 32.2)	29.3 (25.0, 32.2)	28.7 (25.5, 31.9)	.66
Caucasian	65	74	49	<.01
Education				.04
High school	5	5	6	
College	62	55	74	
Postgraduate	33	40	20	
Income				.04
<$50,000	37	31	47	
$50,000–100,000	34	33	37	
$100,000–200,000	22	29	11	
>$200,000	7	8	5	
Parous	13	13	13	.98
BMI, kg/m^2	28.3 (24.1, 35.2)	27.4 (23.4, 33.3)	31.1 (25.5, 38.3)	<.01
Waist, inches	34 (29, 40)	34 (29, 38)	35 (30, 43)	.02
Systolic blood pressure, mmHg	112 (102, 120)	110 (100, 120)	116 (106, 122)	.09
Diastolic blood pressure, mmHg	70 (67, 80)	70 (66, 79)	74 (68, 80)	.13
PCOS diagnosis				
Oligomenorrhea	87	86	88	.77
Hirsute	57	57	57	1.00
Polycystic ovarian morphology	89	91	85	.25
Biochemical hyperandrogenism	66	64	69	.66
mFG score	8 (4, 13)	8 (4, 12)	9 (4, 14)	.57
Health behaviors				
Total exercise, hours/wk	3.3 (1.0, 6.0)	3.5 (1.5, 6.0)	3.2 (0.5, 5.9)	.40
Vigorous exercise, hours/wk	1.5 (0.0, 3.0)	2.0 (0.0, 3.0)	1.0 (0.0, 3.0)	.55
Smoker	13	8	20	.04
Antidepressant use	10	9	14	.42
Metabolics				
Total cholesterol, mg/dL	181 (165, 207)	185 (167, 214)	174 (161, 199)	.10
LDL cholesterol, mg/dL	107 (86, 133)	111 (90, 133)	101 (81, 123)	.13
HDL cholesterol, mg/dL	54 (46, 67)	58 (47, 70)	52 (44, 62)	.04
Triglycerides, mg/dL	80 (54, 125)	74 (53, 111)	91 (65, 147)	.03
Total T, ng/dL	48 (36, 68)	49 (35, 68)	46 (36, 68)	.97
Free T, ng/dL	5.0 (2.6, 7.5)	4.5 (2.1, 7.5)	5.3 (2.7, 7.8)	.34
Androstenedione, ng/dL	186 (125, 254)	188 (124, 261)	183 (125, 238)	.55
Fasting glucose, mg/dL	87 (82, 92)	87 (82, 92)	85 (81, 93)	.54
Fasting insulin, mg/dL	10.0 (4.3, 16.1)	8.0 (3.7, 15.8)	11.5 (6.0, 25.0)	.06
2-Hour glucose, mg/dL	94 (80, 117)	92 (80, 110)	103 (80, 124)	.14
2-Hour insulin, mg/dL	44 (21, 99)	40 (21, 75)	57 (21, 140)	.31
HOMA-IR	1.98 (0.97, 3.65)	1.72 (0.80, 3.38)	2.47 (1.16, 5.25)	.12
HOMA elevated (>2.2)	64	61	69	.26
Antimüllerian hormone, ng/mL	8.2 (5.4, 11.4)	8.9 (6.1, 14.5)	6.4 (3.2, 10.2)	.04
High-sensitivity C-reactive protein, mg/L	1.0 (0.2, 3.0)	1.3 (0.2, 3.0)	0.7 (0.1, 4.9)	.38
Aspartate aminotransferase, U/L	19 (15, 24)	19 (15, 24)	19 (16, 25)	.73
Alanine aminotransferase, U/L	18 (13, 29)	19 (13, 29)	18 (15, 32)	.50

Note: Data are reported as median (IQR) or %. *P* values were derived from Kruskal-Wallis, χ^2, or Fisher's exact testing as appropriate. Positive depression screen indicated by score >4 on BDI-FS. HOMA-IR = homeostatic model assessment of insulin resistance.

Greenwood. Predictors of enduring depression in PCOS. Fertil Steril 2018.

After adjustment for baseline age and duration of follow-up interval (defined as time elapsed between BDI-FS administrations), we observed an association between baseline BMI and odds of enduring depression risk; specifically, each 1 kg/m^2 unit increase in BMI was associated with a 9% increased odds of persistent depression risk over the course of the study period (adjusted OR [aOR] = 1.09; 95% CI, 1.00, 1.18; *P*=.04; Table 3, multivariate model 1). Considering BMI as a categorical predictor, obesity at baseline was associated with 5 times increased odds of enduring depression risk compared with having a lean baseline BMI (aOR = 5.07; 95% CI, 1.07, 24.00; *P*=.04; overall test for trend *P*=.04).

Additional baseline parameters that were associated with increased odds of enduring depression risk in the multivariate model included increasing serum total cholesterol, LDL cholesterol, and triglycerides; meanwhile, increasing HDL cholesterol was associated with reduced odds of ongoing depression risk (Table 3, multivariate model 1). Finally, higher serum 2-hour glucose after oral glucose challenge was associated with increased odds of enduring depression risk. Baseline age, income, and exercise were not associated with odds of enduring depression risk in this model.

Although baseline BMI was associated with odds of enduring depression risk over the study period, change in

TABLE 2

Patient characteristics at follow-up.

	Overall (n = 163)	Negative depression screen (n = 111)	Positive depression screen ("at-risk") (n = 52)	*P*
Demographics				
Age	34.2 (29.7, 38.7)	35.1 (30.3, 39.2)	33.5 (28.8, 38.0)	.14
Follow-up interval, years	5.5 (2.4, 8.1)	5.8 (3.1, 8.2)	3.8 (1.9, 7.1)	.02
BMI, kg/m^2	28.3 (23.5, 35.1)	26.6 (23.1, 32.6)	32.6 (26.9, 39.7)	<.01
Health behaviors				
Total exercise, hours/wk	4.0 (1.0, 7.6)	4.0 (1.5, 7.0)	3.5 (0.8, 5.0)	.86
Vigorous exercise, hours/wk	1.5 (0.0, 3.8)	1.5 (0.0, 3.8)	1.0 (0.0, 3.8)	.55
Medication usage				
Oral contraceptive pills	29	30	29	.91
Metformin	21	17	31	.05
Cholesterol-reducing agent	4	5	2	.44
Antidepressant	16	13	23	.09
Antianxiety agent	11	7	19	.02
Sleep medication	5	5	6	.71
Weight loss medication	1	1	2	.54
Spironolactone	17	14	23	.13
Medical history				
Prediabetes	18	13	31	<.01
Diabetes mellitus	4	3	6	.39
Depression	27	20	44	<.01
Anxiety	29	20	48	<.01
Obstructive sleep apnea	6	3	12	.03
Infertility	17	19	12	.24
None of the above	34	42	15	<.01
Concerns related to PCOS (0–100; 100 reflects extreme concern)				
Mood	64 (20, 88)	30 (5, 67)	91 (81, 100)	<.01
Long-term health consequences	79 (58, 96)	72 (50, 86)	91 (74, 100)	<.01
Hair growth	67 (28, 87)	62 (20, 80)	75 (63, 93)	<.01
Acne	28 (5, 65)	23 (2, 59)	50 (14, 74)	.01
Fertility	62 (10, 91)	51 (6, 80)	75 (14, 99)	.03
Weight	83 (44, 100)	74 (26, 95)	93 (80, 100)	<.01

Note: Data are reported as median (IQR) or %. *P* values are derived from Kruskal-Wallis, χ^2, or Fisher's exact testing as appropriate. Positive depression screen indicated by score >4 on BDI-FS.

Greenwood. Predictors of enduring depression in PCOS. Fertil Steril 2018.

BMI from baseline to follow-up was not associated with depression risk in the univariate or multivariate models.

Self-rated hirsutism scores do not always correlate with clinician ratings and are more strongly associated with negative quality of life impact (23). A subset of 70 women had self-rated mFG scores available at baseline. Yet, similar to clinician-rated mFG scores, self-rated mFG scores were not associated with risk of enduring depression in any model.

Antidepressant use at either baseline (Table 3) or follow-up (data not shown) was not associated with odds of enduring depression risk in this cohort. Interestingly, depression as indicated by active symptomatology per the BDI-FS did not correlate well with antidepressant use. Seventeen of 163 women (10%) reported antidepressant use at baseline: eight were classified as at risk for depression and nine as not at risk according to symptom screen via BDI-FS (Supplemental Fig. 1). Of the eight at-risk women taking an antidepressant at baseline, six remained at risk for depression at follow-up. Finally, at follow-up, 26 women (16%) reported antidepressant use: 12 screened positive for depression and 14 screened negative.

We acknowledge that effective antidepressant use may adequately control symptoms, resulting in negative depression screens. Upon excluding women taking antidepressants at baseline while screening negative for depression (n = 9), our primary results were unchanged.

To determine whether the baseline serum metabolic parameters, namely lipids and 2-hour glucose, that are associated with the odds of enduring depression risk were independent of baseline BMI, an additional multivariate regression model adding baseline BMI as a covariate was explored (Table 3, multivariate model 2). In this analysis, we observed attenuation of the linkage between serum metrics and odds of depression risk: total cholesterol (aOR = 1.02; 95% CI, 1.00, 1.05; *P*=.07), LDL cholesterol (aOR = 1.02; 95% CI, 1.00, 1.05; *P*=.08), triglycerides (aOR = 1.01; 95% CI, 1.00, 1.02; *P*=.08), HDL cholesterol (aOR = 0.98; 95% CI, 0.93, 1.02; *P*=.34), and 2-hour glucose (aOR = 1.02; 95% CI, 0.99, 1.05; *P*=.12). This suggests the associations between lipid parameters and odds of enduring depression risk in our cohort were explained at least in part by differences in baseline BMI.

To explore whether degree of depression risk at baseline is associated with enduring depression risk, we performed a sensitivity analysis incorporating BDI-FS as a continuous

TABLE 3

Baseline patient characteristics associated with enduring depression risk—logistic models.

	Univariate model, OR (95% CI)	P	Multivariate model 1, aOR (95% CI)	P	Multivariate model 2, aOR (95% CI)	P
Age	0.97 (0.88, 1.06)	.51	–	–	–	–
Follow-up interval, years	0.85 (0.71, 1.02)	.08	–	–	–	–
Baseline BDI-FS score	1.22 (0.98, 1.51)	.07	1.24 (0.98, 1.57)	.07	1.23 (0.96, 1.57)	.10
Baseline BDI-FS category						
Mild (5–8)	Ref	.31	Ref	.28	Ref	.41
Moderate (9–12)	1.94 (0.60, 6.31)	.27	2.44 (0.70, 8.54)	.16	2.18 (0.60, 7.93)	.24
Severe (13+)	4.17 (0.44, 39.68)	.22	3.20 (0.30, 34.00)	.33	2.75 (0.23, 32.66)	.42
BMI, kg/m^2	1.06 (0.99, 1.14)	.10	1.09 (1.00, 1.18)	.04	–	–
BMI category					–	–
Lean (<25)	Ref	.11	Ref	.04		
Overweight (25–30)	0.88 (0.19, 4.00)	.65	0.92 (0.18, 4.61)	.92		
Obese (≥30)	3.00 (0.75, 12.00)	.12	5.07 (1.07, 24.00)	.04		
Waist, inches	1.06 (0.98, 1.13)	.12	1.08 (1.00, 1.17)	.05	1.02 (0.86, 1.20)	.83
Caucasian, %	1.10 (0.37, 3.23)	.86	0.70 (0.20, 2.46)	.58	0.96 (0.25, 3.61)	.95
Income						
<$50,000	Ref	.99	Ref	.99	Ref	.98
$50–100,000	1.18 (0.36, 3.90)	.79	1.1 (0.29, 3.59)	.99	1.00 (0.27, 3.78)	.99
$100–200,000	1.18 (0.18, 7.62)	.87	1.30 (0.19, 8.99)	.79	1.48 (0.21 10.56)	.69
>$200,000	1.18 (0.09, 14.69)	.90	1.12 (0.09, 14.59)	.93	1.32 (0.08, 20.81)	.85
Smoker, yes	0.62 (0.16, 1.27)	.49	1.06 (0.24, 4.71)	.94	0.85 (0.17, 4.23)	.84
Antidepressant use, yes	1.94 (0.35, 10.55)	.44	1.36 (0.23, 8.06)	.74	1.18 (0.18, 7.93)	.86
mfG score	0.96 (0.88, 1.06)	.42	1.02 (0.92, 1.12)	.74	0.97 (0.87, 1.08)	.55
Hirsute, yes	0.65 (0.17, 2.42)	.52	0.37 (0.08, 1.67)	.20	0.41 (0.08, 1.97)	.26
Total exercise, hours/wk	1.00 (0.87, 1.15)	.97	0.97 (0.83, 1.14)	.72	1.01 (0.85, 1.21)	.88
Vigorous exercise, hours/wk	1.09 (0.87, 1.37)	.43	1.08 (0.85, 1.36)	.55	1.09 (0.84, 1.40)	.52
Total cholesterol, mg/dL	1.02 (1.00, 1.04)	.05	1.03 (1.00, 1.05)	.02	1.02 (1.00, 1.05)	.07
LDL cholesterol, mg/dL	1.02 (1.00, 1.04)	.05	1.03 (1.00, 1.05)	.02	1.02 (1.00, 1.05)	.08
HDL cholesterol, mg/dL	0.97 (0.93, 1.01)	.10	0.96 (0.92, 1.00)	.05	0.98 (0.93, 1.02)	.34
Triglycerides, mg/dL	1.01 (1.00, 1.02)	.08	1.01 (1.00, 1.02)	.04	1.01 (1.00, 1.02)	.08
Total T, ng/dL	1.01 (0.98, 1.03)	.59	1.01 (0.98, 1.03)	.68	1.01 (0.98, 1.03)	.66
Free T, ng/dL	1.14 (0.95, 1.38)	.16	1.15 (0.93, 1.43)	.19	1.12 (0.89, 1.41)	.32
Fasting glucose, mg/dL	1.01 (0.97, 1.06)	.56	1.02 (0.98, 1.07)	.31	1.01 (0.96, 1.06)	.75
Fasting insulin, mg/dL	0.99 (0.98, 1.01)	.50	1.00 (0.98, 1.01)	.61	0.99 (0.97, 1.01)	.41
2 Hour glucose, mg/dL	1.02 (1.00, 1.03)	.10	1.03 (1.00, 1.05)	.03	1.02 (0.99, 1.05)	.12
2 Hour insulin, mg/dL	1.00 (0.99, 1.01)	.89	1.00 (0.99, 1.02)	.42	1.00 (0.99, 1.01)	.70
HOMA-IR	0.98 (0.92, 1.04)	.48	0.98 (0.93, 1.04)	.60	0.96 (0.88, 1.06)	.45
HOMA elevated (>2.2)	2.15 (0.69, 6.70)	.19	2.07 (0.59, 7.27)	.26	1.11 (0.27, 4.61)	.89
Change in BMI, kg/m^2	0.98 (0.86, 1.11)	.78	1.00 (0.88, 1.13)	.96	1.02 (0.89, 1.18)	.73

Note: Multivariate model 1 is adjusted for baseline age and follow-up interval. Multivariate model 2 is adjusted for baseline age, follow-up interval, and baseline BMI. OR > 1 indicates increased odds of enduring depression risk during the study interval; OR < 1 indicates reduced odds of enduring depression risk. HOMA-IR = homeostatic model assessment of insulin resistance.

Greenwood. Predictors of enduring depression in PCOS. Fertil Steril 2018.

covariate in the multivariate model. The overall results remained effectively unchanged in this iteration.

We alternatively considered change in BDI-FS score from baseline to follow-up as a continuous outcome rather than a dichotomous approach, in an additional sensitivity analysis, to further explore the relationship between baseline clinical parameters and change in depression risk scores. A multivariate linear regression model adjusting for baseline age and follow-up interval revealed the following factors associated with change in BDI-FS score: baseline BDI-FS (coefficient –0.45; 95% CI, –0.57, –0.33; $P<.01$), Caucasian race (coefficient 1.88; 95% CI, 0.70, 3.06; $P<.01$), and weekly hours of vigorous exercise at baseline (coefficient 0.19; 95% CI, 0.02, 0.35; $P=.03$; Table 4, multivariate model 1). Upon adding baseline BDI-FS into this model, increasing BMI at baseline was associated with increasing BDI score during the study interval (coefficient 0.10; 95% CI, 0.04, 0.17; $P<.01$); obesity at baseline was associated with a 1.7-point increase in BDI-FS score (95% CI, 0.58, 2.83; $P<.01$) when compared with lean baseline BMI. Higher triglycerides and 2-hour glucose at baseline were again associated with increasing BDI scores in this model (Table 4, multivariate model 2).

Finally, we examined whether BMI also associated with converting from a negative depression screen at baseline (n = 104) to a positive depression screen at follow-up (n = 15, of 104) in an exploratory analysis. Indeed, after adjusting for baseline age and follow-up interval, each 1 kg/m^2 increase in BMI at baseline increased the odds of converting from a negative depression screen to a positive depression screen by 10% (aOR = 1.10; 95% CI, 1.01, 1.21; $P=.03$). Obese women screening negative for depression at baseline had four-fold increased odds of developing depression risk at follow-up compared with women with normal BMI and negative BDI screening at baseline (aOR = 4.42; 95% CI, 1.09, 17.91; $P=.04$).

TABLE 4

Baseline patient characteristics associated with change in depression risk scores—linear models.

	Univariate model, Coef (95% CI)	P	Multivariate model 1, aCoef (95% CI)	P	Multivariate model 2, aCoef (95% CI)	P
Age	–0.09 (–0.19, 0.01)	.08	–	–	–	–
Follow-up interval, years	–0.05 (–0.23, 0.12)	.56	–	–	–	–
Baseline BDI-FS score	–0.45 (–0.57, –0.33)	<.01	–0.46 (–0.59, –0.34)	<.01	–	–
Baseline BDI-FS category					–	–
Mild (5–8)	Ref	.01	Ref	<.01		
Moderate (9–12)	–1.71 (–4.02, 0.60)	.14	–1.33 (–3.58, 0.92)	.24		
Severe (13+)	–5.44 (–9.06, –1.82)	<.01	–6.07 (–9.63, –2.50)	<.01		
BMI, kg/m^2	0.02 (–0.05, 0.09)	.60	0.02 (–0.05, 0.10)	.53	0.10 (0.04, 0.17)	<.01
BMI category						
Lean (<25)	Ref	.42	Ref	.33	Ref	<.01
Overweight (25–30)	–0.34 (–1.84, 1.15)	.65	–0.46 (–1.95, 1.04)	.55	0.04 (–1.21, 1.29)	.95
Obese (≥30)	0.55 (–0.76, 1.86)	.41	0.58 (–0.72, 1.89)	.38	1.71 (0.58, 2.83)	<.01
Waist, inches	0.01 (–0.07, 0.09)	.83	0.02 (–0.07, 0.10)	.68	0.09 (0.02, 0.17)	.01
Caucasian %	1.88 (0.70, 3.06)	<.01	1.76 (1.57, 2.95)	<.01	0.72 (–0.37, 1.81)	.20
Income						
<$50,000	Ref	.21	Ref	.09	Ref	.64
$50–100,000	0.27 (–1.14, 1.67)	.71	0.43 (–0.97, 1.84)	.54	–0.06 (–1.30, 1.19)	.93
$100–200,000	1.20 (–0.40, 2.81)	.14	1.64 (0.02, 3.26)	.05	0.44 (–1.03, 1.91)	.56
>$200,000	2.21 (–0.28, 4.69)	.08	2.46 (–0.02, 4.94)	.05	1.24 (–0.98, 3.45)	.27
Smoker, yes	0.05 (–1.73, 1.84)	.95	0.11 (–1.67, 1.89)	.90	1.17 (–0.37, 2.71)	.14
Antidepressant use, yes	–0.83 (–2.66, 1.00)	.37	–0.95 (–2.79, 0.89)	.31	0.29 (–1.33, 1.91)	.73
mfG score	–0.02 (–0.12, 0.07)	.64	–0.03 (–0.13, 0.06)	.51	–0.00 (–0.09, 0.08)	.94
Hirsute, yes	–0.29 (–1.62, 1.04)	.67	–0.26 (–1.58, 1.07)	.70	–0.47 (–1.60, 0.66)	.41
Total exercise, hours/wk	0.09 (–0.00, 0.17)	.05	0.08 (–0.01, 0.17)	.07	0.04 (–0.04, 0.12)	.30
Vigorous exercise, hours/wk	0.19 (0.02, 0.35)	.03	0.18 (0.02, 0.35)	.03	0.11 (–0.03, 0.26)	.12
Total cholesterol, mg/dL	0.01 (–0.01, 0.03)	.20	0.02 (–0.00, 0.03)	.08	0.01 (–0.00, 0.03)	.12
LDL cholesterol, mg/dL	0.01 (–0.01, 0.03)	.25	0.02 (–0.00, 0.04)	.08	0.01 (–0.00, 0.03)	.14
HDL cholesterol, mg/dL	0.02 (–0.02, 0.05)	.29	0.02 (–0.02, 0.06)	.27	–0.00 (–0.03, 0.03)	.96
Triglycerides, mg/dL	0.00 (–0.01, 0.01)	.68	0.00 (–0.01, 0.01)	.50	0.01 (0.00, 0.02)	.03
Total T, ng/dL	0.01 (–0.01, 0.03)	.25	0.01 (–0.01, 0.04)	.23	0.01 (–0.01, 0.03)	.39
Free T, ng/dL	0.03 (–0.13, 0.19)	.69	0.02 (–0.14, 0.19)	.79	0.01 (–0.13, 0.15)	.85
Fasting glucose, mg/dL	0.00 (–0.05, 0.06)	.92	0.01 (–0.05, 0.07)	.71	0.03 (–0.02, 0.08)	.28
Fasting insulin, mg/dL	–0.01 (–0.03, 0.01)	.34	–0.01 (–0.03, 0.01)	.35	0.00 (–0.02, 0.02)	.79
2-Hour glucose, mg/dL	0.01 (–0.01, 0.02)	.52	0.01 (–0.01, 0.02)	.47	0.02 (0.00, 0.03)	.03
2-Hour insulin, mg/dL	–0.01 (–0.02, 0.00)	.24	–0.01 (–0.02 0.01)	.30	–0.00 (–0.01, 0.01)	.87
HOMA-IR	–0.05 (–0.14, 0.04)	.24	–0.05 (–0.14, 0.04)	.28	0.00 (–0.07, 0.08)	.92
HOMA elevated (>2.2)	0.62 (–0.54, 1.78)	.29	0.61 (–0.57, 1.78)	.31	0.77 (–0.23, 1.78)	.13
Change in BMI, kg/m^2	0.01 (–0.16, 0.19)	.90	0.03 (–0.15, 0.20)	.74	0.04 (–0.11, 0.20)	.56

Note: Multivariate model 1 is adjusted for baseline age and follow-up interval. Multivariate model 2 is adjusted for baseline age, follow-up interval, and baseline BDI-FS score. Coefficient > 0 indicates that index predictor is associated with increasing BDI-FS score (i.e., increasing depression symptoms) during the study interval; coefficient < 0 indicates that index predictor is associated with decreasing BDI-FS score during the study interval. Coef = regression coefficient; aCoef = adjusted regression coefficient; HOMA-IR = homeostatic model assessment of insulin resistance.

Greenwood. Predictors of enduring depression in PCOS. Fertil Steril 2018.

DISCUSSION

It is now well-known that women with PCOS represent a population of women disproportionately burdened by depression (3, 4); however, the trajectory of depression symptoms over time in PCOS has remained poorly understood, and there has been a call for studies to help fill this gap in knowledge (4). The current study used a longitudinal design to describe change in depression symptoms over time and to identify predictors of persistent depression symptomatology in this population. We report that depressive symptoms remain relatively stable over time and further found that the metabolic phenotype of PCOS, particularly obesity, was a strong predictor of enduring depression risk.

The predominance of our current understanding of mental health in PCOS results from studies of patients presenting for clinical care (3), where an approximately fourfold increased risk of depression symptoms has been observed at a single time point. We observed a relatively stable prevalence of positive depression screens over a median of 5.5 years of follow-up, from 35% to 40%. This is consistent with the only other longitudinal study of depression in American women with PCOS (n = 60), which reported a prevalence of 33% and 40% at baseline and follow-up, respectively, over an average of 1.8 years (24). Our findings extend this prior study by reporting on a larger population followed for a longer duration. Our findings also echo studies from the longitudinal population-based Northern Finland Birth Cohort 1966, where women with self-reported oligomenorrhea and hirsutism had a similar prevalence of depression at ages 31 and 46 years (25).

In the general population, evidence suggests that both the incidence of depression and the prevalence of depressive episodes decrease with aging (26, 27). However, because the decrement in depression symptoms in the community setting is reported after age 45 or later (27), it is possible that women with PCOS will demonstrate a similar

diminution of depression in studies with longer follow-up time than was achieved with this study. Indeed, among our cohort of 163 women completing the follow-up survey, those 59 women with positive depression screens at baseline had been seen in clinic more recently than those with negative depression screens at baseline (3.8 vs. 5.8 years, $P=.02$; Table 2). In the regression analysis, there was a trend toward increased follow-up interval being protective against enduring depression risk (OR = 0.85, 95% CI, 0.71, 1.02; $P=.08$); however, this did not reach statistical significance. Together, these data keep open the possibility that depression risk is mitigated over a more extended period of time than has been captured in our study. Alternatively, it is also possible that the lack of motivation intrinsic to depression resulted in the differential follow-up times we observed.

Importantly, we observed that several baseline metabolic features corresponded to an increased odds of enduring depression risk over time. In our adjusted logistic model, each 1 kg/m^2 increase in baseline BMI was associated with a 9% increased odds of enduring depression risk. Furthermore, women who were obese at baseline had over five-fold odds of persistent depression risk at follow-up compared with their lean counterparts. We found evidence that glucose intolerance and dyslipidemia were associated with increased odds of enduring depression risk; increased 2-hour serum glucose after oral glucose challenge as well as adverse lipid parameters (increased total cholesterol, LDL cholesterol and triglycerides, and decreased HDL) at baseline were associated with increased odds of enduring depression risk in the adjusted model. We have previously identified insulin resistance as a risk factor for depression in cross-sectional studies of women with PCOS (8, 9). Our current observation of five-fold increased odds of *persistent* depression in obese compared with lean women with PCOS is in line with the hypothesis that progression of insulin resistance with aging in obese but not lean women contributes to recalcitrant depression in this population (10, 13, 14). Similarly, at follow-up we observed that a greater proportion of women who were at risk for depression in the cohort at large reported a diagnosis of prediabetes (31% vs. 13%) and/or to be taking metformin (31% vs. 17%), compared with those not at risk for depression (Table 2), suggesting an increased prevalence of insulin resistance in those with positive BDI-FS screens.

Whether glucose intolerance and dyslipidemia, correlates of insulin resistance and systemic inflammation, function as risk factors for depression independent of obesity cannot be concluded from our data. After controlling for baseline BMI in the model, we noted an attenuation of the association between odds of enduring depression and 2-hour glucose and lipids. Notably, the P values remained between 0.07 and 0.12. It remains possible that with a larger sample size we might observe an independent effect of these metabolic markers on persistence of depressed mood.

In an adjusted linear model examining change in BDI-FS scores over time, higher BMI was associated with increasing BDI-FS scores, suggesting a dose-response effect. Similarly, higher 2-hour glucose and triglyceride levels correlated with increasing depression scores during the study interval. Unexpectedly, higher reported weekly hours of vigorous exercise and Caucasian race were also associated with increasing BDI scores. The exercise data are counterintuitive; given the well-documented panoply of positive metabolic and psychologic effects of exercise on mood, one would expect higher levels of exercise to abbreviate depression duration. Empirically we have noted obese women having difficulty with weight management, despite reportedly high levels of exercise, which may compound their frustration and depressed mood. It is possible that this association reflects this patient subset. The impact of race on changes in depression scores over time in women with PCOS warrants further attention.

The reciprocal risk imposed between depression and obesity has been well characterized in longitudinal studies in non-PCOS cohorts (28). It is less clear how obesity impacts the trajectory of depression symptoms after depression is established. We did not observe an association between change in BMI and odds of enduring depression risk in this cohort; however, the observational design does not preclude the possibility that weight loss might improve mood. In fact, evidence in non-PCOS groups suggest a bidirectional therapeutic opportunity whereby treatment of obesity (i.e., weight loss) improves mood (6, 29), and vice versa (30, 31).

In summary, our results indicate that for many women with PCOS, depression remains a persistent comorbid symptom. The results echo prior findings suggesting a "metabolic pathway" for depression in women with PCOS (8, 9) and further open the possibility that an adverse metabolic phenotype may predict enduring depression risk. In contrast, reproductive manifestations of PCOS including parity (a marker of fertility) and hyperandrogenism as manifested by hirsutism and serum androgens do not appear to correlate with depression risk or mood symptom trajectory.

Strengths, Limitations, and Future Directions

Strengths of our study include [1] a prospective longitudinal design, [2] repetition of the identical, validated screening tool at both time points, [3] acceptable response rate, [4] systematically characterized study cohort with a relatively large sample size, and [5] follow-up duration exceeding prior report.

Limitations of our study include [1] lack of a control cohort, [2] capturing of predominantly reproductive-age women limiting extrapolation of findings to later postmenopausal life, [3] use of a screening tool to identify depression risk rather than the gold standard diagnostic of a structured clinical interview, [4] lack of baseline data about body image, precluding our ability to assess whether the impact of obesity on enduring depression risk was mediated by disruptions in self-esteem, [5] lack of laboratory profiling at follow-up, [6] possible introduction of bias due to unequal distribution of follow-up times between respondents versus nonrespondents and between women with positive versus negative depression screens, and [7] clinical cohort composed of women seeking specialty care in a multidisciplinary setting, which might impede the representativeness of community-based samples.

Future studies should extend the follow-up duration beyond reproductive senescence, in a large cohort of women, incorporating psychiatric diagnostic modalities, to better understand the natural history of depression in women with PCOS. Ultimately, an enhanced understanding of the trajectory of symptoms and risk factors for persistent depression might facilitate both a deeper understanding of the pathophysiology of depression in women with PCOS and the clinical identification of high-risk individuals warranting aggressive up-front interventions.

Conclusions

Depression risk appears stable in reproductive-age women with PCOS over the course of 5+ years. Obesity may function as a risk factor for enduring depression. Clinicians should acknowledge and target this high-risk group accordingly. Additional research is warranted to confirm the long-term trajectory of depression symptoms and to identify opportunities for interrupting the pathways contributing to this persistent source of major morbidity in women with PCOS.

REFERENCES

1. Legro RS, Arslanian SA, Ehrmann DA, Hoeger KM, Murad MH, Pasquali R, et al. Diagnosis and treatment of polycystic ovary syndrome: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2013;98:4565–92.
2. Lizneva D, Suturina L, Walker W, Brakta S, Gavrilova-Jordan L, Azziz R. Criteria, prevalence, and phenotypes of polycystic ovary syndrome. Fertil Steril 2016;106:6–15.
3. Cooney LG, Lee I, Sammel MD, Dokras A. High prevalence of moderate and severe depressive and anxiety symptoms in polycystic ovary syndrome: a systematic review and meta-analysis. Hum Reprod 2017;32:1075–91.
4. Dokras A, Stener-Victorin E, Yildiz BO, Li R, Ottey S, Shah D, et al. Androgen Excess- Polycystic Ovary Syndrome Society: position statement on depression, anxiety, quality of life, and eating disorders in polycystic ovary syndrome. Fertil Steril 2018;109:888–99.
5. Stunkard AJ, Faith MS, Allison KC. Depression and obesity. Biol Psychiatry 2003;54:330–7.
6. Dixon JB, Dixon ME, O'Brien PE. Depression in association with severe obesity: changes with weight loss. Arch Int Med 2003;163:2058–65.
7. Cinar N, Kizilarslanoglu MC, Harmanci A, Aksoy DY, Bozdag G, Demir B, et al. Depression, anxiety and cardiometabolic risk in polycystic ovary syndrome. Hum Reprod 2011;26:3339–45.
8. Greenwood EA, Pasch LA, Shinkai K, Cedars MI, Huddleston HG. Putative role for insulin resistance in depression risk in polycystic ovary syndrome. Fertil Steril 2015;104:707–14.e1.
9. Greenwood EA, Pasch LA, Cedars MI, Legro RS, Eisenberg E, Huddleston HG. Insulin resistance is associated with depression risk in polycystic ovary syndrome. Fertil Steril 2018;110:27–34.
10. Brown ZA, Louwers YV, Fong SL, Valkenburg O, Birnie E, de Jong FH, et al. The phenotype of polycystic ovary syndrome ameliorates with aging. Fertil Steril 2011;96:1259–65.
11. Hsu MI. Changes in the PCOS phenotype with age. Steroids 2013;78:761–6.
12. Johnstone EB, Davis G, Zane LT, Cedars MI, Huddleston HG. Age-related differences in the reproductive and metabolic implications of polycystic ovarian syndrome: findings in an obese, United States population. Gynecol Endocrinol 2012;28:819–22.
13. Huddleston HG, Quinn MM, Kao CN, Lenhart N, Rosen MP, Cedars MI. Women with polycystic ovary syndrome demonstrate worsening markers of cardiovascular risk over the short-term despite declining hyperandrogenaemia: results of a longitudinal study with community controls. Clin Endocrinol 2017;87:775–82.
14. Livadas S, Kollias A, Panidis D, Diamanti-Kandarakis E. Diverse impacts of aging on insulin resistance in lean and obese women with polycystic ovary syndrome: evidence from 1345 women with the syndrome. Eur J Endocrinol 2014;171:301–9.
15. Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). Hum Reprod 2004;19:41–7.
16. Greenwood EA, Noel MW, Kao CN, Shinkai K, Pasch LA, Cedars MI, et al. Vigorous exercise is associated with superior metabolic profiles in polycystic ovary syndrome independent of total exercise expenditure. Fertil Steril 2016;105:486–93.
17. Craig CL, Marshall AL, Sjostrom M, Bauman AE, Booth ML, Ainsworth BE, et al. International physical activity questionnaire: 12-country reliability and validity. Med Sci Sports Exerc 2003;35:1381–95.
18. Beck ATSR, Brown GK. BDI: fast screen for medical patients manual. San Antonio, TX: Psychological Corp; 2000.
19. Benedict RH, Fishman I, McClellan MM, Bakshi R, Weinstock-Guttman B. Validity of the Beck Depression Inventory-Fast Screen in multiple sclerosis. Mult Scler 2003;9:393–6.
20. Neitzer A, Sun S, Doss S, Moran J, Schiller B. Beck Depression Inventory-Fast Screen (BDI-FS): an efficient tool for depression screening in patients with end-stage renal disease. Hemodial Int 2012;16:207–13.
21. Law M, Naughton MT, Dhar A, Barton D, Dabscheck E. Validation of two depression screening instruments in a sleep disorders clinic. J Clin Sleep Med 2014;10:683–738.
22. Smarr KL, Keefer AL. Measures of depression and depressive symptoms: Beck Depression Inventory-II (BDI-II), Center for Epidemiologic Studies Depression Scale (CES-D), Geriatric Depression Scale (GDS), Hospital Anxiety and Depression Scale (HADS), and Patient Health Questionnaire-9 (PHQ-9). Arthritis Care Res 2011;63(Suppl 11):S454–66.
23. Pasch L, He SY, Huddleston H, Cedars MI, Beshay A, Zane LT, et al. Clinician vs self-ratings of hirsutism in patients with polycystic ovarian syndrome: associations with quality of life and depression. JAMA Dermatol 2016;152:783–8.
24. Kerchner A, Lester W, Stuart SP, Dokras A. Risk of depression and other mental health disorders in women with polycystic ovary syndrome: a longitudinal study. Fertil Steril 2009;91:207–12.
25. Karjula S, Morin-Papunen L, Auvinen J, Ruokonen A, Puukka K, Franks S, et al. Psychological distress is more prevalent in fertile age and premenopausal women with PCOS symptoms: 15-year follow-up. J Clin Endocrinol Metab 2017;102:1861–9.
26. Eaton WW, Anthony JC, Gallo J, Cai G, Tien A, Romanoski A, et al. Natural history of Diagnostic Interview Schedule/DSM-IV major depression. The Baltimore Epidemiologic Catchment Area follow-up. Arch Gen Psychiatry 1997;54:993–9.
27. Kessler RC, Berglund P, Demler O, Jin R, Koretz D, Merikangas KR, et al. The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R). JAMA 2003;289:3095–105.
28. Luppino FS, de Wit LM, Bouvy PF, Stijnen T, Cuijpers P, Penninx BW, et al. Overweight, obesity, and depression: a systematic review and meta-analysis of longitudinal studies. Arch Gen Psychiatry 2010;67:220–9.
29. Mitchell JE, King WC, Chen JY, Devlin MJ, Flum D, Garcia L, et al. Course of depressive symptoms and treatment in the longitudinal assessment of bariatric surgery (LABS-2) study. Obesity 2014;22:1799–806.
30. Jantaratnotai N, Mosikanon K, Lee Y, McIntyre RS. The interface of depression and obesity. Obes Res Clin Pract 2017;11:1–10.
31. Jain AK, Kaplan RA, Gadde KM, Wadden TA, Allison DB, Brewer ER, et al. Bupropion SR vs. placebo for weight loss in obese patients with depressive symptoms. Obes Res 2002;10:1049–56.

Evolución clínica de los síntomas depresivos y predictores de riesgo de depresión prolongada en mujeres con síndrome de ovario poliquístico: Resultados de un estudio longitudinal.

Objetivo: (1) Caracterizar síntomas depresivos en el tiempo y (2) evaluar la hipótesis que los parámetros metabólicos adversos se asociarían con riesgo de depresión prolongada en mujeres con síndrome de ovario poliquístico (SOP).

Diseño: Estudio prospectivo de cohorte.

Ámbito: Centro Universitario.

Paciente(s): Ciento sesenta y tres mujeres con SOP.

Intervención(es): El Inventario de Depresión de Beck de Cribado Rápido (IDB-CR) fue auto-administrado al inicio y en el seguimiento para identificar riesgo de depresión, usando un punto de corte >4.

Principal(es) variable(s) de resultado(s): Puntuaciones de IDB-CR.

Resultado(s): La edad media al inicio fue 29 años, y la media de intervalo de seguimiento fue 5.5 años. Cincuenta y nueve de 163 mujeres tuvieron cribados de depresión positivos al inicio (36%); 52 mujeres (32%) dieron positivo durante el seguimiento. La media de cambio en la puntuación de IDB-II fue 0 (rango intercuartil, -2,1) durante el período de estudio. De las 59 mujeres con riesgo de depresión al inicio, 22 dieron negativo en el seguimiento (37%), mientras que 37 mujeres permanecieron en riesgo (63%). Considerando estas 59 mujeres con cribados de depresión positivos al inicio, un mayor índice de masa corporal (IMC) fue asociado con un aumento en la probabilidad de expresar depresión prolongada en el seguimiento (odds ratio ajustado = 1.09; intervalo de confianza 95%, 1.00, 1.18), en un modelo de regresión logístico multivariable. Comparadas con mujeres con peso normal al inicio, mujeres obesas (IMC > 30 Kg/m^2) tuvieron una probabilidad cinco veces mayor de riesgo de depresión prolongada en el seguimiento (odds ratio ajustado = 5.07; intervalo de confianza 95%, 1.07, 24.0).

Conclusión(es): La prevalencia de depresión se mantuvo relativamente estable a lo largo del tiempo en una cohorte de mujeres con SOP. El IMC elevado es un signo distintivo de riesgo de expresar depresión prolongada. Estos resultados podrían ayudar a los profesionales a desarrollar estrategias de intervención dirigidas a reducir la prevalencia de síntomas de depresión a largo plazo en mujeres con SOP.