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Original Research

Health-Related Quality of Life in perimenopausal women with PCOS

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Abstract

Background: Several studies have shown that younger women with polycystic ovary syndrome (PCOS) have decreased Health-Related Quality of Life (HRQoL) compared with women in general. **Method**: In this study peri- and postmenopausal women previously diagnosed with PCOS (n = 27) were compared with randomly selected, age-matched controls (n = 94). Mean age of the study participants was 52 years. Structured interviews and Short Form (SF)-36 questionnaires were used. **Results**: No differences in SF-36 scores were found, median for the physical summary score was 54 vs. 57, for women with PCOS and controls, respectively; and 53 vs. 53 for the mental summary score, with no differences in any of the eight dimensions of HRQoL. There were no significant difference in prevalence of depression and/or anxiety. The use of drugs for mood disorders was 22% in both groups. **Conclusion**: PCOS women of peri- and postmenopausal ages had similar HRQoL compared with age-matched controls.

Keywords: PCOS; Quality-of-life; Menopause; Depression; Anxiety

1. Introduction

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women of reproductive age, affecting between 9–18% depending on the diagnostic criteria used [1]. Typical symptoms associated with PCOS are hirsutism, acne and infertility, but the syndrome is also associated with obesity, insulin resistance, diabetes and hypertension [2]. There is also increasing evidence that women with PCOS of fertile age have reduced Health-Related Quality of Life (HRQoL) and increased prevalence of depression and anxiety symptoms [3].

HRQoL means how a disease, and it's treatment, have an effect on a persons ability to function, as sensed by that person. The importance of HRQoL is getting increased recognition. The National Health Service in Great Britain declared in 2008 that measures as HRQoL should be of equal importance in reporting outcomes, as more established outcomes, such as mortality or other somatic end points, both in clinical practice and in clinical trials. This further emphasizes the need for studies on HRQoL, as in the present study of PCOS, a common disorder in women. The current knowledge of HRQoL and depression/anxiety disorders in women with PCOS is based on studies performed on women during their reproductive years, where an impaired HRQoL both in mental and physical aspects is seen [4,5]. Previous studies of younger women with PCOS also showed an increased risk of depression and anxiety [6–10], as well as other psychiatric disorders [8]. A common genetic pathogenesis between PCOS and psychiatric disorders has also been proposed, based on the findings that siblings, including brothers, to women with PCOS also had an increased risk for psychiatric disorders [8,11]. Data on mood disorders in women with PCOS up at peri- and postmenopausal ages are sparse, and there are to our knowledge no reports on HRQoL at this age.

In this cross-sectional study, HRQoL and depression/anxiety were compared between women with PCOS around 50 years of age to age-matched controls. Since some of the stigmata for PCOS, e.g., hyperandrogenism, remain (albeit attenuated) with age [12,13], the hypothesis was that older women with PCOS would have a lower HRQoL and a higher proportion of mood disorders, than women in the general population.

2. Methods

2.1 Women with PCOS

In 1992, 33 women attending Sahlgrenska University Hospital for infertility or hirsutism, were diagnosed with PCOS according to the National Institute of Health (NIH) criteria [14]. They were then invited and accepted to participate in a study regarding hormonal treatment for hirsutism [15]. A follow-up was carried out in 2016 when the HRQoL questionnaire was added to the protocol. Five of the 33 women with PCOS were deceased and one declined partic-

ipation. Twenty-seven women with PCOS were included, mean age 52 $\pm$ 5 years, age range 42–63 years. All women in the PCOS group were previously diagnosed using NIH criteria.

2.2 Controls

A randomly selected population sample of women, previously participating in the World Health Organization (WHO) study, MONItoring of trends and determinants for CArdiovascular disease (MONICA) 1995, Gothenburg, Sweden [16], was re-examined in 2008, with a participation rate of 65% [17]. Out of the 317 women included in that study, 95 women were selected using a group matching model, according to age. The study journals from 2008 were revised and one woman was excluded due to elevated testosterone. The final control group was comprised of 94 women, mean age 52 $\pm$ 6 years, range 39–62 years.

2.3 Anthropometry and blood pressure

Height was measured to the nearest 0.5 cm, body weight to the nearest 0.5 kg. Waist and hip circumferences were measured to the nearest cm in the standing position over the umbilicus and the maximum circumference over the buttocks, respectively. Overweight was defined as BMI $\geq$25 kg/m^2 but $<$30 kg/m^2. Obesity was defined as BMI $>$30 kg/m^2.

2.4 Structured medical history and co-morbidity

Data was collected using a structured interview. Morbidity was self-stated, but all morbidity was also later verified in medical records. Postmenopausal is here defined as Follicle Stimulating Hormone (FSH) $>$50 IU/L.

Depression and/or anxiety: Current diagnosis of depression and anxiety were consolidated into one group to increase power and were defined according to medical records and use of psychopharmacological medications.

Psychopharmacological medications: Current medications were coded according to the Anatomical Therapeutic Chemical (ATC) Classification System. The proportion of patients using medications from ATC groups N05 and N06, denoting antidepressants, anxiolytic and sleeping pills, was analyzed.

The metabolic syndrome: It was defined as fulfilling at least three out of the five criteria: (1) waist $>$88 cm; (2) serum triglycerids (S-TG) $\geq$1.7 mmol/L; (3) serum high density lipoprotein (S-HDL) $\leq$ 1.3 mmol/L; (4) Systolic blood pressure $\geq$130 mm Hg and/or diastolic blood pressure $\geq$85 mm Hg and/or use of anti-hypertensive drugs; (5) fasting plasma glucose $\geq$5.6 mmol/L or use of antiglycemic drugs, in accordance with the harmonized definition [18].

2.5 The Short Form 36 questionnaire (SF-36)

The SF-36 is a multipurpose generic, not disease specific, health survey comprised of 36 questions, which yields an eight-scale profile of functional health and well-being scores [19]. It is a comonly used generic tool to measure HRQoL and are validated in several populations [19], and used in different diseases [20]. The eight dimensions are: Physical Functioning, Role Physical (limitations due to physical problems), Bodily Pain, General Health, Vitality, Social Functioning, Role Emotional (limitations due to emotional problems) and Mental Health (range for all 0–100, low to high HRQoL). It also generates psychometrically based physical and mental health summary measures. The Mental Component Summary Score is comprised of the subscales for Vitality, Social Functioning, Role Emotional, and Mental Health. The Physical Component Summary Score is comprised of the subscales for Physical Functioning, Role Physical, Bodily Pain, and General Health. The summary scores are designed to have a population mean score of 50 with a standard deviation of 10 and low scores indicate greater impairment of quality-of-life (range 0–100).

2.6 Statistical analyses

SF-36 scores were calculated using scoring software obtained from Optum^{TM} (Optum Inc., Eden Prairie, MN, USA) (license number QM03712), Mental and Physical component scores were calculated using 1998 US norms.

The SF-36 scores were compared with the Mann-Whitney U test. Categorical comparisons were calculated using Fischer's exact *t* test or chi square.

Odds ratios (OR) were computed with a multiple variate logistic regression analysis, no adjustments were done, due to the small samle size, so all OR presented are crude.

SPSS Statistics version 25 (IBM Corp., Armonk, NY, USA) was used for the analyses.

A post-hoc power calculation was done, using G*Power. Using a clinically important minimal difference of 7, the actual sample sizes and α = 0.05 gives a power = 0.89.

3. Results

Women with PCOS and controls had a mean age of 52 years, all women were Caucasians. The women with PCOS had higher BMI (31 vs. 26 kg/m^2) and higher WHR (0.90 vs. 0.83). Background characteristics are shown in Table 1. Possible confounders were identified, such as employment status, living alone, nulliparity and use of systemic hormone therapy, and there were no differences between the groups. Fewer of the women with PCOS were postmenopausal.

Co-morbidity in women with PCOS and controls is shown in Table 2. There were no significant differences in the proportion of women with depression and/or anxiety diagnosis or use of antidepressive and/or anxiolytic agents, sedatives and sleeping pills. Women with PCOS had a higher prevalence of other co-morbidities: hypertension (37 vs. 14%), type 2 diabetes (19 vs. 1%) and the metabolic syndrome (48 vs. 12%).

Table 1. Anthropometric data, background characteristics and medications in women with polycystic ovary syndrome (PCOS) and controls.

	PCOS (n = 27)	Controls (n = 94)	*p*-value
Age, years	52.4 ± 5.4	52.4 ± 6.3	0.68
BMI, kg/m^2	30.7 ± 7.4	25.5 ± 3.9	**<0.01**
Waist circumference, cm	101.7 ± 18	86.6 ± 10.6	**<0.01**
Hip circumference, cm	112.9 ± 15.3	103.7 ± 8.9	**<0.01**
WHR	0.90 ± 0.12	0.83 ± 0.06	**0.02**
Current smoker, n (%)	3 (11)	9 (10)	1.00
Never smoker, n (%)	12 (44)	49 (53)	0.51
Single/not in relationship, n (%)	8 (30.8)	15 (23.1)	0.44
In work	25 (92.6)	85 (92.4)	0.97
Null-parity, n (%)	5 (18.5)	18 (19.4)	1.00
Postmenopausal	5 (21.7)	47 (55.3)	**<0.01**
Systemic hormone therapy, n (%)	2 (7.4)	9 (9.6)	1.00

Means ± SD are given, or number and percentages (%) in parenthesis where so stated. Significant *p*-values are marked bold.

BMI, Body Mass Index; WHR, Waist/Hip Ratio.

N = 27 for PCOS, except for waist, hip, WHR, and postmenopausal where n = 25, and living single where n = 26.

N = 94 for controls except for nulliparity where n = 93, living single where n = 65.

There were no differences in SF-36 scores in any of the eight dimensions, mental or physical, between the women with PCOS and controls. Neither did the mental or physical summary scores differ between the groups. Mean, SD, median and IQR for the eight dimensions and the summary scores are shown in Table 3.

4. Discussion

The main finding of this study was that HRQoL did not differ between women of peri-menopausal age with PCOS and age-matched controls, despite the increased prevalence of other co-morbidities in the women with PCOS at this age. There was no difference in depression and/or anxiety, nor in social status or life style factors.

Although several studies and meta-analyses have shown lower HRQoL in women with PCOS in comparison to controls [4,5,9,21–24] these studies measured HRQoL in younger women with PCOS, with a mean age of less than 40 years. In a population-based cohort, women with a self-stated PCOS diagnosis had lower HRQoL at age 31 years and 46 years compared with women without symptoms common in PCOS [25]. PCOS was an independent risk factor for low HRQoL in that study, and the lower HRQoL in PCOS was similar to that of women with other chronic conditions, such as asthma, migraine, rheumatoid arthritis, and depression. The risk for low HRQoL in PCOS remained significant after adjusting for body mass index, hyperandrogenism, and socioeconomic status [25]. The age-distribution of the present PCOS population was higher and included peri- and postmenopausal women, and in addition, these women were diagnosed according to NIH criteria as young, when in contact with the healthcare system due to hirsutism or infertility. To our knowledge this is the first study of HRQoL in perimenopausal women with PCOS. To be able to compare with controls, a generic tool, SF-36, was used, which is the most commonly used generic instrument in PCOS. Previous studies have shown that symptoms associated with the typical phenotype in PCOS, such as obesity, hirsutism, and menstruation disturbances were associated with lower HRQoL in younger women with PCOS [22,26]. The similar parity, and especially nulliparity prevalence, in this cohort of PCOS and controls [27] might explain the satisfaction with their lives, comparable with controls, in these perimenopausal ages. The infertility fears in the young is a great existential problem in PCOS. Psychosocial factors are probably important, whereas older age may lead to a greater self-acceptance of high BMI and better coping with hirsutism which might attenuate the impact that these factors have on them in comparison to the general population. Furthermore, the decline in androgens, described earlier [28], which did not differ from controls any longer, might contribute to the similar HRQoL up in the postmenopausal ages in PCOS. The mean age of the women in the study groups (52 years) is similar to the reported mean menopausal age in the general population in Sweden, (51 years) [29]. As the menopausal age was higher in PCOS, a higher propor-

Table 2. Co-morbidity in women with PCOS and controls, n (%) and crude OR.

	PCOS (n = 27)	Controls (n = 94)	*p*-value	OR (95% CI)
Depression and/or anxiety	6 (22)	14 (15)	0.39	1.6 (0.6–4.7)
Psychopharmacological medications	6 (22)	23 (25)	1.00	0.9 (0.3–2.5)
Overweight or obese (BMI ≥25)	20 (74)	46 (49)	**0.03**	3.0 (1.2–7.7)
Hypertension	10 (37)	13 (14)	**0.01**	3.6 (1.4–9.6)
Type 2 diabetes mellitus	5 (19)	1 (1)	**<0.01**	21.1 (2.4–190.1)
Hypothyreosis	5 (19)	10 (11)	0.32	1.9 (0.6–6.2)
Gallbladder disease	1 (4)	9 (10)	0.46	0.4 (0.04–3.0)
Metabolic syndrome	12 (48)	11 (12)	**<0.01**	6.6 (2.4–18.1)
Myocardial infarction	1 (4)	1 (1)	0.40	3.5 (0.2–58.5)
Stroke	1 (4)	1 (1)	0.39	3.7 (0.2–60.9)

Significant *p*-values are marked bold.

Table 3. SF-36 scores in PCOS women and controls. Score range 0–100 (low to high HRQoL). Since the scores were not normally distributed, both mean (SD) and median (IQR) are shown. Mann-Whitney U test was used to compare groups.

	PCOS		Controls		*p*-value
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	
Physical Functioning	84.6 (20.6)	95.0 (75.0–100.0)	88.4 (17.8)	95.0 (80.0–100.0)	0.69
Role Physical	77.8 (37.6)	100.0 (50.0–100.0)	84.7 (30.0)	100.0 (75.0–100.0)	0.53
Bodily Pain	66.1 (26.4)	62.0 (51.0–100)	76.1 (23.4)	84.0 (62.0–100.0)	0.08
General Health	70.7 (25.3)	82.0 (55.0–87.0)	77.8 (20.4)	82.0 (62.0–96.0)	0.23
Vitality	57.6 (26.0)	55.0 (45.0–80.0)	64.5 (23.0)	70.0 (50.0–85.0)	0.24
Social Functioning	77.8 (29.9)	87.5 (62.5–100.0)	85.5 (23.0)	100.0 (75.0–100.0)	0.30
Role Emotional	71.6 (36.6)	100.0 (33.3–100.0)	86.7 (27.0)	100.0 (100.0–100.0)	0.06
Mental Health	71.6 (23.0)	80.0 (56.0–88.0)	76.9 (18.6)	80.0 (64.0–92.0)	0.44
Physical Component Score	51.0 (9.7)	53.5 (43.4–58.4)	53.0 (8.9)	56.3 (48.5–59.3)	0.31
Mental Component Score	46.8 (14.8)	53.2 (35.7–57.7)	51.0 (10.2)	53.2 (47.4–58.2)	0.50

The italic, bold scores indicate that these are summary scores.

tion of the controls were postmenopausal compared with the women with PCOS [27]. However, menopausal status has not been shown to correlate to HRQoL in women in the general population [30]. The finding that PCOS as such, did not affect the self-perceived functional health at this age, despite the increased co-morbidity, is encouring.

It has been reported that younger women with PCOS have a greater prevalence of depression and anxiety compared to controls and they are more often hospitalized due to mood disorders [7–10,31]. The Northern Finland Birth Cohort is, to our knowledge, the previous study with the highest mean age (46 years) to report on the prevalence of depression and anxiety in PCOS [10]. In that study, a self-reported PCOS diagnosis was associated with a higher prevalence of depression (25% compared to 14% for controls) and higher depression and anxiety scores. On the contrary, in another study, women with a mean age of 46 years and a history of oligomenhorrehea and hyperandrogenism at that age, did not have increased depressive symptoms compared with women with a history of regular menses and normal testosterone at age 46 [32]. A recent meta-analysis, on mostly younger women, calculated that the prevalence of moderate to severe depressive symptoms was 26% in the PCOS group compared to 15% in the control group [6]. The results presented in this study, with a mean age of 52 years, are similar to both of these studies (22% in PCOS vs. 15% in controls), even though the difference was not statistically significant, could be due to low power because of the small sample size of PCOS. However, the proportion of women taking psychopharmacological medication did not differ between PCOS and controls in the present study.

A strength of the present study was the well-characterized group of women with PCOS, which has been followed since 1992. The control group was based on a random sample from the general population. All women in the study, both controls and women with PCOS, originated

from the same geographic area and they were all of Caucasian ethnicity, which might be relevant for generalization to other ethnecities. One limitation is the small sample size of women with PCOS. Another limitation is that the women with PCOS were examined eight years later than controls. The women with PCOS in this study were initially included when they were in contact with the healthcare system due to infertility or hirsutism which may have introduced a selection bias that must be considered when interpreting the results.

5. Conclusions

HRQoL were similar in women with PCOS and controls at peri- and postmenopausal ages.

Author contributions

MF, KLW, JS, MB and ED designed the study. MF and EK analyzed the data under supervision of KLW and ED. MF wrote the first draft to the manuscript. MF, ED, PT and KLW performed the physical examinations and acquired the data from the controls. ED was the principal investigator for the PCOS group and KLW for the controls. MF, KLW, EK, PT, JS, MB and ED all reviewed the manuscript and provided critical scientific input. MF and ED had primary responsibility for the final content. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The study was approved by the Regional Ethical Review Board in Gothenburg (reg.no. 221-16, reg.no. 088-06, and reg.no. T282-11), and all the women gave their written informed consent. The study was conducted in accordance with the Declaration of Helsinki.

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Conflict of interest

The authors declare no conflict of interest.

Data availability

The data that support the findings of this study are available on reasonable request from the corresponding author (MF).

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