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Original Research

European survey of diagnosis and management of the polycystic ovary syndrome: full report on the ESE PCOS Special Interest Group's 2023 Questionnaire

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Abstract

Background: Although polycystic ovary syndrome (PCOS) is a very common endocrinopathy, there are several issues related to this disorder which perplex clinicians in their everyday practice.

Objective: To determine the current state of knowledge among European endocrinologists concerning the full spectrum of PCOS.

Methods: An online survey comprising 41 items covering various aspects of PCOS diagnosis and management was distributed to members of the European Society of Endocrinology.

Results: A total of 505 European endocrinologists (64% females), with a mean age of 47 ± 11.6 years, participated in the survey. The Rotterdam criteria were the primary diagnostic tool for 85% of respondents. Most referrals (87.1%) occurred between ages 20 and 40 years. Twenty-five percent of physicians have access to mass spectrometry for the evaluation of androgen levels. While an extended metabolic profile was commonly employed as part of the workup, there was uncertainty regarding chronic anovulation diagnosis. Diabetes, including gestational or type 2, was recognized as a significant risk factor with universal screening irrespective of BMI status. Lifestyle modification and metformin were considered as standard interventions by all participants alongside oral contraceptives, though there was significant discrepancy in treatment duration.

Conclusions: The Rotterdam diagnostic criteria are widely adopted for PCOS diagnosis among European endocrinologists. The current updated survey shows an emphasis on steroid profiling as an important part of diagnostic workup and a strong position held for recognition of PCOS as a metabolic condition with potentially serious implications. Current therapy thus shifted to the demand for prioritizing lifestyle interventions and metabolic therapies, either as monotherapy or in combination with standard hormone compounds.

Keywords: PCOS, questionnaire, anovulation, androgens, ovary

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Significance

This survey highlights gaps of knowledge and areas of confidence in the diagnosis and management of women suffering from polycystic ovary syndrome. Specifically, in a sample of 500 European endocrinologists, ambiguity regarding the diagnosis of chronic anovulation, hyperandrogenemia, and the ideal duration of oral contraceptives administration or the management of anovulatory women was revealed. On the contrary, this group of physicians evaluates thoroughly potential metabolic risk as well as psychological profile and everyday life habits. Furthermore, lifestyle modification and multidisciplinary approach are considered 2 important steps in management. Accordingly, several steps are needed to resolve the unmet needs in PCOS diagnosis and management and further underline the outstanding procedures already adopted.

Introduction

Polycystic ovary syndrome (PCOS) is the most common endocrinopathy of women of reproductive age, affecting 8%-24% of this population and impacting their life with a significant burden of disease, defined as increased disability-adjusted life-years.[1,2] Despite the fact that extensive research has shed much light on several issues regarding the underlying pathogenetic mechanisms, associated comorbidities, and therapeutic modalities, its management remains an area of uncertainty in everyday practice.[3] One of the main reasons for this vexatious situation is the discrepancy between the current guidelines and the practical implementation of the recommendations.[4] Other reasons for the inconsistency are the several criteria applied in the diagnosis of the syndrome, the different medical specialties dealing with the disease, the multifaceted nature of the disorder, and the effect of age on PCOS subtypes.[5-7] It is a discrepancy that is reflected clearly in the diverse methods of diagnostic evaluation according to each physician's specialty.[8] All of the above contribute to a frequently large degree of disappointment among some patients as regards their management, very often leading to discontinuation of regular follow-up and/or therapy withdrawal.[9] Moreover, such cessation of endocrine therapy is highly likely to have a detrimental effect on the woman's general health status given the long-term consequences and comorbidities related to the syndrome.[10]

The European Society of Endocrinology (ESE), having drawn attention to this problem over a decade ago, carried out a detailed study addressing the strategies applied by European endocrinologists regarding diagnosis and management of PCOS.[11] However, despite this excellent endeavor, continuous medical education, and massive research conducted concerning virtually every aspect of PCOS over the last decade, several issues related to the PCOS spectrum remain unfamiliar to many endocrinologists. On the other hand, several previously uncertain aspects of the syndrome have been elucidated and extensively studied, while a number of perceptions regarding PCOS diagnosis and management have been substantially revised,[12-15] thus bringing to the clinical endocrinologist a formerly unmet need for enhanced understanding of the syndrome.

Therefore, we designed the present survey in an attempt to delineate the current status of the European endocrine community regarding the diagnosis and management of this hormonal disorder as well as the degree of insight into the complex nature of the syndrome.

Methods

The present study was organized by the ESE and designed to be distributed among European endocrinologists. The research was an electronic survey conceived by the ESE PCOS Special Interest Group (SIG). The questionnaire was originally drafted by one of the authors (S.L.), and was finalized and approved in October 2022. The final questionnaire consisted of 33 questions which were either multiple choice questions (presenting participants with either single select options or multi-select options, where more than 1 answer could be chosen from a list), or open-ended questions. The questionnaire is presented in Appendix.

For the online survey, the Google Forms platform was used and one of the contributors (ES) designed and developed the web-based questionnaire. Google Forms is a cloud-based data management tool used for the design and development of web-based questionnaires. The tool is provided by Google Inc. (https://docs.google.com/forms/) and is freely available online.

The survey was promoted at the 25th European Congress of Endocrinology (ECE 2023) in Istanbul, Turkey, and was disseminated by email to the entire ESE mailing list from May to August 2023. Survey participation was voluntary, and participants were free to withdraw their participation from the study at any time. In total, 505 ESE members participated in the study and filled in the online survey. Data were extracted in a spreadsheet form for statistical analysis.

According to the Rotterdam criteria, 4 phenotypes were defined, as follows: (A) Oligomenorrhea, hyperandrogenism, and polycystic ovarian morphology (PCOM), (B) hyperandrogenism, PCOM, and regular menstrual cycles, (C) oligomenorrhea, hyperandrogenism, and normal ovaries, and (D) oligomenorrhea, PCOM, and no hyperandrogenism.

Statistical analysis

There was no sample size calculation, and the survey invitation for participation in the study was sent out to all ESE members. Missing data that occurred in the study were not imputed or replaced. Additionally, no outlier detection and analysis were performed. Descriptive statistics were applied to the data collected. Qualitative variables were expressed as absolute and relative (%) frequencies (which describe the total number of participants in the study). Quantitative variables are expressed as means of central tendency (mean and median) and means of dispersion (SD, minimum, and maximum) measurements, including the percentage of valid responses. In terms of graphical representation, qualitative data are presented using bar charts, while quantitative data are presented using boxplots. Statistical processing and analysis of data were conducted using IBM SPSS software (version 28.0)[16] or RStudio (version 2023.06.0 Build 421).[17]

Results

From the total group of 505 responders, 64% were females and the mean age was 47 ± 11.6 years, most of them (56%) being

Table 1. Diagnostic approach to and assessment of women with PCOS.

Diagnostic criteria (%)				Most frequent age at referral (years)			
NIH	Rotterdam	AE-PCOS	n/a	<20	20-40	>40	n/a
4.2	85	7.3	3.6	8.5	87.1	.8	3.6

Evaluation of clinical hyperandrogenism (%)				Evaluation of biochemical hyperandrogenism (%)				
FG score	Acne	Androgenic alopecia	Others	Testosterone	DHEAS	17-OHP	D4	FAI
84.4	62.2	59		78.6	73.7	56.2	55.8	56.4

Evaluation of chronic anovulation (%)			PCOS diagnosis exclusion				
Cycles > 35 days	<8 cycles per year	Progesterone evaluation in/ during 3 consecutive cycles	TSH	Prolactin	17-OHP	Overnight DSST	IGF-1
41.2	38.6	11.5	75.2	70.9	74.7	53.9	21.8

Assessment of family history (%)					
DM2	CV	Hypertension	Dyslipidemia	PCOS	Premature pubarche/adrenarche
93.9	82.4	76.6	73	85	73

Assessment of everyday habits (%)					
Dietary habits	Exercise	Smoking	Alcohol consumption	Sleep	Sexual activity
93.7%	92.5%	81.4%	72.5%	57.6%	43%

Assessment of psychological status (%)			Endometrial cancer (%)		
Eating disorders	Depression	Anxiety	Assessment	Pelvic U/S	n/a
80%	63.4%	55.4%	56.4	22%	65%

between 35 and 55 years. In total, 69% of the participants defined themselves as clinicians. The vast majority apply the Rotterdam criteria for diagnosis (85%) and the most frequent age at referral of women with PCOS is between 20 and 40 years (87.1%). According to the replies received, the most prevalent phenotypes in clinical practice were phenotypes B (60.8%) and A (57.4%), followed by phenotypes C (21.2%) and D (21.0%). The most common reason for clinical presentation of patients diagnosed with PCOS was either clinical hyperandrogenism (40%) or menstrual disturbances (32%). Gynecologists (75.0%), self-referral (52.9%), general physicians (48.5%), dermatologists (44.2%), and social media (7.7%) were reported as referral sources of women with PCOS.

The most common symptoms for the assessment of clinical hyperandrogenism were hirsutism (84.4%) (by application of the Ferriman-Gallwey score), acne (62.2%), and androgenic alopecia (59%). Of note, 27.7% of participants evaluated the degree of hirsutism by patient assessment. The evaluation of biochemical hyperandrogenaemia at diagnosis was carried out based on assessment of total testosterone (78.6%), DHEAS (73.7%), 17-hydroxyprogesterone (17-OHP) (56.2%), free androgen index (FAI, total testosterone/SHBG values, 56.4%), and androstenedione levels (55.8%). Interestingly, in everyday practice, 25% of participants used LC/MS for steroid excess evaluation at diagnosis.

Evaluation of chronic anovulation was based on either menstrual cycle longer than 35 days (41.2%) or if the patient reported fewer than 8 cycles per year (38.6%), whereas the gold standard of progesterone evaluation based on 3 consecutive menstrual cycles was reported by 11.5%. Ultrasonography of the ovaries at diagnosis was requested by 83.4% of the responders, while 67.9% of the reports mentioned the number of ovarian cysts. Responders excluded PCOS diagnosis based on assessment of TSH (75.2%), 17-OHP (74.7%), and prolactin (70.9%). The overnight dexamethasone suppression test (DSST) (53.9%) and IGF-1 values (21.8) were recommended by the participants.

The doctors evaluated lifestyle behaviors by enquiring about dietary habits (93.7%), exercise (92.5%), smoking (81.4%), and alcohol consumption (72.5%). Of note, sleep (57.6%) and sexual activity (43%) were recognized as important parameters by almost half of the participants. From the same point of view, questions regarding eating disorders (80%), depression (63.4%), and anxiety (55.4%) were important among a significant percentage of participants. Endometrial cancer evaluation was carried out by 41% of participants at 1-3-year intervals (Table 1).

Regarding which are considered the 3 most important problems of women with PCOS, subfertility (incidence 54.1%), hyperandrogenism (51.7%), obesity (45.9%), anovulation (43.6%), and diabetes risk (41%) were the most common. However, none of them is predominant significantly. Considering the metabolic abnormalities associated with PCOS, the majority of health providers ordered an extensive metabolic profile including lipids (88.9%), oral glucose tolerance test (OGTT) (79.8%), liver enzymes (75.8%), fasting glucose (78.4%), insulin levels (60.6%), and HbA1c (68.5%). Metabolic profile was evaluated not only in obese (89.9%) and overweight (87.5%) individuals but also in normal weight subjects (60.4%), while 86% of the group considered that lean women with PCOS are at risk of developing type 2 diabetes (T2D). Concerning whether pregestational diabetes screening is important, 87.7% are positive and 89.7% believe that PCOS represents an independent risk factor for gestational diabetes mellitus (GDM) resulting among half of the respondents in early (16-18 weeks pregnancy) screening for GDM (Table 2).

The major choice for treatment in the case of hyperandrogenism were combined oral contraceptive pills (OCPs), with

Table 2. Assessment of the spectrum of PCOS comorbidities.

Which do you consider the 3 most important PCOS problems (%)						
Subfertility	Hyperandrogenism	Obesity	Anovulation	Diabetes risk	CV risk	Psychological problems
54.1	51.7	45.9	43.6	41	37.0	17.9

Evaluation of metabolic abnormalities (%)						
Lipids	OGTT	HbA1c	Glucose	Insulin	Liver enzymes	Liver ultrasound
88.9	79.8	68.5	74.8	60.6	75.8	21.8

Evaluation of metabolic profile according to BMI status (%)			Gestational diabetes (%)		
Obese	Overweight	Normal weight	Pregestational diabetes screening	PCOS as an independent risk factor for GDM	Early (16-18 weeks pregnancy) screening
89.9	87.5	60.4	87.7	89.7	50

Table 3. Management of PCOS by endocrinologists.

Treatment in the case of hyperandrogenism (%)					
OCPs	OCPs with antiandrogenic properties	Lifestyle modification	Antiandrogens	Metformin	Laser
39.6	49.1	80.8	8.9	6.7	5

Do you modify your approach according to BMI status?			For how long do you use OCPs?		
Yes	No	n/a	<1 year	1-3 years	>3 years
89.7	6.3	4	24	31	38

OCP's discontinuation (%)				
Once the clinical endpoint has been reached	Adoption of healthy lifestyle	>30 years of life	If they become obese	Post-pregnancy
50.7	33.1	28.9	22	18.0

Treatment in the case of chronic anovulation (%)			
Metformin	Lifestyle modification	OCPs	OCPs with antiandrogenic properties
86	82.4	44.6	32.1
Inositols	GLP-1 agonists	Pioglitazone	SGLT-2 inhibitors
31.7	13.9	4.8	1.9

(49.1%) or without antiandrogenic properties (39.6%), in combination with lifestyle modification (80.8%). Question 27 asked: "Do you modify your approach according to their BMI status?", with 90% of respondents beeing positive to this question. The latter response emphasizes the impact of weight on the management of women with PCOS and, additionally, the heterogeneity of this disorder. The duration of OCP administration was shown to be 3 years in 38% of respondents, and is 1 to 3 years in 31%. Half of them is discontinuing OCPs once the clinical outcome has been achieved. Nevertheless, the adoption of a healthy lifestyle (33%), the third decade of life (28.9%), and development of obesity (22%) are also considered substantial reasons to cease OCP administration.

In the case of chronic anovulation, the administration of metformin (86%) accompanied by lifestyle modification (82.4%) is the preferred approach. However, OCPs with (32%) or without (44.6%) antiandrogenic properties are chosen by several responders, while inositol (31.7%) has been regarded as an alternative option (Table 3).

Interaction with other specialties is shown by the fact that endocrinologists frequently refer their patients to dieticians (83.8%), gynecologists (76.4%), and dermatologists (47.9%). Furthermore, consultation of either a psychologist (40.6%) or a psychiatrist (22.8%) was often suggested. The importance of exercise in the management of the disorder is highlighted by the fact that 42.6% recommended regular engagement in physical activity.

Discussion

The present survey clearly illustrates current status of knowledge of PCOS among European endocrinologists and underlines several unresolved issues in PCOS diagnosis and management. It has, however, become clear that currently, our colleagues possess, or else are gradually developing, broader and deeper knowledge of the PCOS spectrum than that of their peers during the previous decade. Indeed, the ESE PCOS conducted a similar study 10 years ago on the diagnostic and therapeutic approach applied in PCOS.[11] It is of note that the mainly European endocrinologists to whom these 2 questionnaires were addressed comprised virtually the same population as that of the 2013 ESE PCOS survey, since the mean age and gender distribution were practically identical among the 2 surveys (47 ± 11.6 vs 48.8 ± 11.2 years, 56 vs 64% female). Furthermore, it is apparent that the

physicians managed the same age groups of PCOS patients given that in the present study, the most prominent age range was from 20 to 40 years (87%), comparable to the main age group of 20 and 30 years (76%) in the former study. On the other hand, the previous questionnaire included 23 questions, whereas that applied in the present survey had 41 items. However, in both questionnaires, the majority of responders associated the syndrome with the reproductive years despite the fact that PCOS should be considered as a continuum, with symptoms and consequences lasting for years post-menopause.

Comparison of these 2 surveys revealed a number of differences, this emphasizing the knowledge that has accrued over the past decade as well as the current more holistic perspective. One major difference is the shift from application of the NIH criteria, these being the main criteria used in 2014, toward application of the Rotterdam criteria, which are also endorsed by the International PCOS guidelines. It was in fact observed that 85% of responders use the Rotterdam criteria in their everyday practice and consider that phenotypes A (57.4%) and B (60.8%) are the most prevalent. The referral for PCOS was made not only through expected sources, such as gynecologists, dermatologists, general practitioners, and self-referral but also via the social media (7.7%), highlighting the impact of internet information on the health status of women, an aspect which should not be neglected.[18,19]

The diagnosis of clinical hyperandrogenism was made based on the clinical manifestation of hirsutism in both surveys, but the diagnosis of biochemical hyperandrogenism revealed some contradictory results. In the present study, the key androgens (total testosterone, DHEAS, 17-OHP, D4) and FAI were requested by the vast majority of participants. However, a decade ago, the response to the question "Which are the two most common biochemical parameters you use in the differential diagnosis of hyperandrogenism in your patients" comprised more than 20 combinations. Most interestingly, 21.4% of the respondents reported direct measurement of free testosterone, which was not even mentioned in the present study. On the other hand, in both surveys, a significant body of responders (73.7%) requested DHEAS level evaluation despite the fact that the clinical significance of this measurement has not to date been substantiated. In fact, DHEA sulfation is formed mainly in the adrenals and a favorable association between DHEAS levels and metabolic abnormalities has been reported in women with PCOS.[20,21] Since DHEAS is however the most abundant circulating steroid, its measurement is of clinical significance.

On the other hand, a very interesting finding of the present study was the use at diagnosis of LC/MS for steroid evaluation reported by 25% of participants, this demonstrating the implementation of gold standard techniques in everyday practice. This method is important since it allows for more accurate and precise diagnosis.[22] Furthermore, the emerging role of 11-oxygenated steroids in PCOS pathophysiology will probably lead to different diagnostic and treatment modalities in the future.[23] However, more data are needed to further substantiate the role of 11-ketosteroids in PCOS development and management.

The evaluation of chronic anovulation was based mainly on menstrual history, namely, the existence of cycles longer than 35 days (41.2%) or fewer than 8 cycles per year (38.6%), with only a small percentage (11.5%) recommending the golden standard of progesterone levels assessment during 3 consecutive cycles. This response represents an improvement over the answers of 10 years ago to: "Do you routinely use menstrual disturbances in the diagnostic criteria for PCOS?", with positive answers now provided by 87% of the participants. However, it is clear that in clinical practice, the definition of chronic anovulation is still a matter of debate and more research is needed to elucidate this issue.

The implementation of the Rotterdam criteria was reflected in the requirement of ovarian ultrasound at diagnosis, which has risen from 60% of respondents in the former survey to 83% in the present study. This finding may be related to the fact that access to ovarian ultrasound is easier nowadays compared to the previous decade. Moreover, today, 67.9% of reports mention the number of ovarian follicles, this translating to more detailed and precise ovarian morphology assessment. Of note, AMH values were recommended by less than 1% of respondents, significantly lower than in the previous survey (5%). This finding points to the uncertainty, on clinical grounds, surrounding the use of AMH concentrations as a surrogate marker of ovarian function in PCOS diagnosis.[24] Regarding the differential diagnosis of PCOS, 70%-75% of responders requested evaluation of TSH, prolactin, and 17-OHP values, followed by overnight DSST (54%) and IGF-1 (22%) levels, which evidences the present-day implementation of the current guidelines in diagnosis.

One of the major complaints voiced by women with PCOS is the frequent disharmony between their actual needs and the doctor's priorities.[9] This discrepancy, occurring when the woman feels disheartened by the physician's approach, often erodes the patient's compliance with and adherence to a given therapeutic plan: The physician's lack of acknowledgement of his patients' special needs will, unfortunately, result in a less patient-centered approach. As a consequence, it is of utmost importance that European endocrinologists adopt a more personalized approach by carefully questioning their patients concerning a number of aspects of their everyday life, such as dietary habits (93.7%), exercise (92.5%), smoking (81.4%), alcohol consumption (72.5%), sleep (57.6%), and sexual activity (43%). Moreover, since the assessment of patients' psychological status is indeed critical, it is recommended that the participants should ask their patients about eating disorders (80%), depression (63.4%), and anxiety (55.4%), the current available data certainly supporting these types of queries.[25] This kind of information provides greater and more detailed information and highlights those areas where improvement of medical care and special aid is needed. At the same time, such a holistic approach enables the patient to feel more confidence and satisfaction, which will most likely encourage her to follow the therapeutic plan. It is important to stress that this type of information was not assessed in the former survey, emphasizing the deeper and more thorough current perception of the PCOS spectrum.

Similarly, family history in the earlier questionnaire focused on PCOS, T2D, and cardiovascular disease (CVD), with almost all respondents reporting that they asked about these issues. By contrast, in the present study, the vast majority also asked about family history of hypertension and dyslipidemia, clearly demonstrating greater awareness of the interplay of these disorders with the PCOS spectrum, as this has more recently been substantiated.[26,27] Of interest, a significant percentage (73%) enquired about any personal history of premature pubarche/adrenarche, which displays present-day physicians' more comprehensive approach to the natural history of PCOS.[28]

In the present study, the question concerning which are regarded as the 3 most important problems of PCOS provided

quite similar results to those of the previous survey, with, however, subfertility (54.1%) and hyperandrogenism (51.7%) predominating, followed by obesity (45.9%), anovulation (43.6%), T2D risk (41.5%), CVD risk (37%), and psychological problems (17.9%). These findings underline the impact of PCOS on the risk for morbidity and mortality among this population and the compelling need for long-term follow-up, compatible with the available literature data.[29] Intriguingly, although endometrial cancer was not considered a major risk, half of the respondents evaluated this probability mainly by regular pelvic ultrasound. In contrast, in the former study, the long-term concerns pertaining to PCOS were obesity and T2D (64%), followed by infertility (20%), CVD risk (12%), psychosocial problems (3%), and endometrial cancer (1%).

The undisputed role of insulin resistance in PCOS pathophysiology and the elevated T2D risk reported in this population underscored the metabolic aspects of the syndrome as being of crucial importance at the time of the initial evaluation of women with PCOS. The respondents, armed with this knowledge, therefore insisted on a detailed metabolic profile, which included assessment of lipids (88.9%), OGTT (79.8%), liver enzymes (75.8%), fasting glucose (78.4%) insulin (60.6%), and HbA1C levels (68.5%). It is noteworthy that due to deepening insight over the years into the development of PCOS, the vast majority of participants (86%) today believe that normal weight women with PCOS have an increased risk of developing T2D, albeit the available data do not fully support this hypothesis.[30,31] Nevertheless, the latter proposition is further strengthened by the observation that metabolic profile should be assessed not only in obese (89.9%) or overweight (87.5%) but also in lean subjects (60.4%). As a consequence, the respondents are particularly sensitive regarding pregestational diabetes screening, which is virtually universally requested (87.7%) since the majority (89.7%) consider PCOS as an independent risk factor for GDM development. This conception leads to early (16-18 weeks pregnancy) screening for GDM in half of the group, in accordance with the current guidelines which recommend OGTT at the first antenatal visit.[32]

The recognition of the ever-changing phenotype of women with PCOS and the unraveling of the natural history of the syndrome, from an early stage when hyperandrogenic symptoms dominate the clinical spectrum to a latter phase when metabolic disorders are more prevalent, led us to provide the respondents with 2 different scenarios regarding treatment. Specifically, it was asked what their approach would be if hyperandrogenic symptoms prevailed and what treatment they would prefer in the case of chronic anovulation. It must be emphasized that in both circumstances, the same therapeutic options were available, but diverse results were obtained. In the case of hyperandrogenism, the majority preferred the use of OCPs with or without antiandrogenic properties, combined with lifestyle modification (80.8%). However, consideration of body weight has an impact on this approach in 90% of respondents; thus, several different responses were given regarding OCP duration, ranging from less than 1 year among 24%, 1-3 years in 31%, and even more than 3 years in 38%. Another area of uncertainty is the timing of OCP discontinuation. While some suggest ceasing therapy once the clinical endpoint has been reached (50.7%), others consider this advisable once a healthy lifestyle has been adopted (33.1%), after 30 years of age (28.9%), if obesity prevails (22%), or after a successful pregnancy (18%). It is obvious that in spite of the widespread use of OCPs, there is to date no clear indication of which formulation is the most suitable; additionally, until now, the duration of therapy is based only on personal experience rather than on currently updated guidelines.[32] In any case, this approach is not advised given that early OCP discontinuation will be followed by symptom recurrence, namely, anovulation and clinical hyperandrogenism.

In the case of chronic anovulation, the administration of metformin (86%) accompanied by lifestyle modification (82.4%) was the preferred approach. However, combined OPCs with (32%) or without antiandrogen properties (44%) were suggested. Interestingly, the use of inositol (31.7%) has emerged, although the evidence supporting its use is sparse and inconclusive. In comparison to the former study wherein a more generic question regarding treatment together with a more specific one regarding fertility were posed, there is a similar approach regarding OCPs and metformin, although lifestyle modification was today strongly indicated as a major therapeutic step. Piltonen et al.[33] carried out a mixed survey using a sample of 382 endocrinologists and gynecologists where they showed that lifestyle management was mostly recommended by younger physicians (<35 years) and OCPs by older ones (>56 years), though this was not confirmed in the current survey.

The perception of PCOS as a multifaceted disorder led most European endocrinologists to implementing a multidisciplinary approach, including gynecologists (76.4%), dermatologists (47.9%), and psychiatrists (22.8%), as well as dieticians (83.8%), physical activity trainers (42.6%), and psychologists (40.6%). This is a significant improvement, since in the former survey, only 42% entertained this perception, mainly collaborating with gynecologists (86.6%), dermatologists (39.1%), and nutritionists (35.9%). Taking the above as a whole, it is clear that the long-term management of PCOS requires the combination of several health providers, with endocrinologists preferably playing a central role in the coordination of different disciplines to provide our patients with optimal care via a tailored approach.

In conclusion, the present survey has clearly shown that European endocrinologists have today a deeper and broader understanding regarding PCOS diagnosis and treatment than their peers a decade ago. However, there are several areas which should be further investigated and elucidated, such as the definition of chronic anovulation, the hormonal assessment of hyperandrogenism, the duration of OCP administration, and the regular long-term follow-up of this population. Meanwhile, the holistic and multidisciplinary approach supported by the responders and the recognition of PCOS not only as a reproductive but also as a metabolic disorder are substantial modern-day advancements.

ESE PCOS Special Interest Group

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Conflict of interest: Coauthor A.G. is on the editorial board of EJE. A.G. was not involved in the review or editorial process for this paper, on which A.G. is listed as an author. The other authors have nothing to disclose.

Ethical approval/considerations

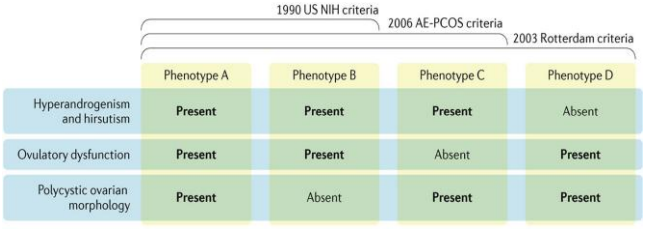
This study was compatible with the Declaration of Helsinki and since no patients were involved, no ethical approval was needed.

Appendix

The final form of the questionnaire

1. Age
2. Gender
3. I am practicing endocrinology in _____ [country]
4. Type of practice (Clinician; Clinician Scientist; Allied Health Professional; Nurse; Scientist) *based on ECE classification*
5. What is the most frequent age at referral of women with PCOS in your practice?
   - 20 years
   - 20-40 years
   - 40 years - post menopause
   - [Total percentage: 100%]
6. What percentage of your patients are:
   - Obese [BMI >30 kg/m^2]
   - Overweight [BMI 25-30 kg/m^2]
   - Normal weight [BMI <25 kg/m^2] at diagnosis
     - (total 100%)
7. Which criteria do you use for the diagnosis?
   - NIH
     (chronic anovulation and hyperandrogenism/ hyperandrogenemia)
   - Rotterdam
     (presence of two of these three: chronic anovulation, hyperandrogenism/hyperandrogenemia, and polycystic ovaries on ultrasonography)
   - Androgen Excess Society
     (hyperandrogenism/hyperandrogenemia and anovulation or polycystic ovarian morphology).
8. How do you define chronic anovulation in your everyday practice?
   - Menstrual cycles longer than 35 days?
   - Less than 8 cycles per year?
   - Progesterone evaluation in/during three consecutive menstrual cycles?
   - Other
9. How do you define clinical hyperandrogenism? (*Please tick everything that applies*)
   - Hirsutism according to the Ferriman Gallwey score
   - Hirsutism according to patient assessment
   - Acne
   - Androgenic alopecia
   - Other
10. How do you evaluate biochemical hyperandrogenism at diagnosis? *(Please tick everything that applies)*
    - Total testosterone
    - Free testosterone
    - Free androgen index (testosterone/SHBG)
    - Androstenedione
    - 17-hydroxyprogesterone
    - DHEAS
    - Other
11. Do you request ultrasonography of the ovaries at diagnosis? [Yes or No]
    - IF YES => Do the reports mention the number of cysts
      (i) Always
      (ii) Never
      (iii) Sometimes
12. Which are the two most prevalent phenotypes in clinical practice
    - Phenotype A
    - Phenotype B
    - Phenotype C
    - Phenotype D

    Please see Figure



13. Which assessments do you use for the exclusion of PCOS diagnosis *(Please tick everything that applies)*
    - TSH
    - Prolactin
    - 17-hydroxyprogesterone
    - IGF-1
    - Overnight dexamethasone suppression test
    - Other
14. In everyday practice, do you use LC/MS for steroids evaluation at diagnosis? [Yes or No]

15. How do you perform metabolic assessment at diagnosis? *(please tick everything that applies)*
    - Fasting glucose
    - HbA1C
    - Lipids (cholesterol, HDL, LDL, triglycerides)
    - Liver enzymes (AST, ALT, γGT)
    - Uric acid
    - hsCRP
    - Fasting insulin
    - Oral glucose tolerance test (0' and 120')
    - Oral glucose tolerance test (0', 30', 60', 90', 120')
    - Oral glucose tolerance test and evaluation of glucose and insulin (0', 30', 60', 90', 120')
    - Liver ultrasound
    - Other
16. Do you perform metabolic profile at diagnosis? *(Please tick everything that applies)*
    - In obese [BMI >30 kg/m^2]
    - In overweight [BMI 25-30 kg/m^2]
    - In normal weight [BMI <25 kg/m^2]
    - All of them
17. Do you ask your patients about their habits? *(Please tick everything that applies)*
    - Dietary habits
    - Exercise
    - Sleep
    - Alcohol consumption
    - Smoking
    - Sexual activity
18. Do you ask your patients about of these conditions? *(Please tick everything that applies)*
    - Anxiety
    - Depression
    - Obsessive compulsive disorder
    - Eating disorders
    - Poor self-esteem
    - Other
19. Do you ask your patients about any family history of … *(Please tick everything that applies)*
    - Polycystic ovary syndrome
    - Diabetes type 2
    - Cardiovascular disease
    - Dyslipidemia
    - Hypertension
    - Thromboembolic episodes
    - Endometrial cancer
    - Breast cancer
    - Other [blank space]
20. Do you consider that lean women with PCOS are at risk of developing DM2? (Yes or No)
21. Do you evaluate for endometrial cancer?
    - No
    - Yes [If yes, how (empty space) and how often (1-2-3 year)?
22. Do you ask your patients about any history of premature pubarche/adrenarche at diagnosis? [Yes or No]
23. Of those patients that YOU have diagnosed with polycystic ovary syndrome, what was the most common reason for clinic attendance?
    - Clinical hyperandrogenism
    - Biochemical hyperandrogenism
    - Menstrual disturbances
    - Infertility
    - Metabolic disorders [dyslipidemia/dysglycemia]
    - Obesity
    - Insulin resistance
    - PCO morphology on ultrasound
    - Other
24. Who refers to you women with PCOS? *(Please tick everything that applies)*
    - Self referral
    - Gynaecologist/Obstetrician
    - Dermatologist
    - GP
    - Internal medicine
    - Psychiatrist
    - Dietician
    - Social media
    - Other
25. In your opinion, which are the three most important PCOS problems?
    - Anovulation
    - Hyperandrogenism
    - Psychological problems
    - Subfertility
    - Obesity
    - NASH
    - Cardiovascular risk
    - Diabetes risk
    - Endometrial cancer
    - Other
26. In the case of hyperandrogenism, your approach consists in: *(please tick everything that applies)*
    - Lifestyle modification
    - Combined oral contraceptive pills
    - Combined oral contraceptive pills with antiandrogenic properties [desogestrel, chlormadinone, cyproterone, drospirenone]
    - Antiandrogens (cyproterone acetate/finasteride/bicutalamide/flutamide/spironolactone)
    - Laser
    - Metformin
    - GLP-1 agonists
    - SGLT-2 inhibitors
    - DDP-4 inhibitors
    - Pioglitazone
    - Inositols
    - Other
27. Do you modify your approach according to their BMI status? [Yes or No]
28. For how long do you use OCPs?
    - Up to 1 year
    - Up to 3 years
    - More than 3years

    IN THOSE WHO RESPONDED POSITIVELY TO OCPs
29. When do you stop OCPs [as many options]
    - Once the clinical endpoint has been reached
    - After the third decade of life due to substantial decrease of androgens
    - If they become obese (BMI > 30)
    - Post-pregnancy
    - When they have adopted a healthy lifestyle

30. In the case of chronic anovulation, your approach consists in:
    (Please tick everything that applies)
    - Lifestyle modification
    - Combined oral contraceptive pills
    - Combined oral contraceptive pills with antiandrogenic properties [desogestrel, chlormadinone, cyproterone, drospirenone]
    - Metformin
    - Antiandrogens (cyproterone acetate/finasteride/bicutalamide/flutamide/spironolactone)
    - Laser
    - Metformin
    - GLP-1 agonists
    - SGLT-2 inhibitors
    - DDP-4 inhibitors
    - Pioglitazone
    - Inositols
    - Other
31. If needed, do you consider referring your patients to:
    (Please tick everything that applies)
    - Dietician
    - Physical activity trainer
    - Psychologist
    - Psychiatrist
    - Dermatologist
    - Obstetrician/Gynaecologist
    - Other (please specify)
32. Do you consider pregestational diabetes screening? [YES or NO]
33. Do you consider that PCOS represents an independent risk factor for GDM development, irrespectively of BMI
    (a) (Yes or No)
    (b) Do you make an early (16-18 weeks pregnancy) or regular screening (24-28 weeks pregnancy)?

References

1. Chiaffarino F, Cipriani S, Dalmartello M, *et al.* Prevalence of polycystic ovary syndrome in European countries and USA: a systematic review and meta-analysis. *Eur J Obstet Gynecol Reprod Biol*. 2022;279:159-170. https://doi.org/10.1016/j.ejogrb.2022.10.020
2. Liu J, Wu Q, Hao Y, *et al.* Measuring the global disease burden of polycystic ovary syndrome in 194 countries: Global Burden of Disease Study 2017. *Hum Reprod*. 2021;36(4):1108-1119. https://doi.org/10.1093/humrep/deaa371
3. Hoeger KM, Dokras A, Piltonen T. Update on PCOS: consequences, challenges, and guiding treatment. *J Clin Endocrinol Metab*. 2021;106(3):e1071-e1083. https://doi.org/10.1210/clinem/dgaa839
4. Lee IT-L, Sansone S, Irfan M, Copp T, Beidas R, Dokras A. Implementation of international guidelines for polycystic ovary syndrome: barriers and facilitators among gynecologists and primary care providers. *F S Rep*. 2022;3(2):94-101. https://doi.org/10.1016/j.xfre.2022.01.005
5. 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(3):301-309. https://doi.org/10.1530/EJE-13-1007
6. Azziz R, Carmina E, Chen Z, *et al.* Polycystic ovary syndrome. *Nat Rev Dis Primers*. 2016;2(1):16057. https://doi.org/10.1038/nrdp.2016.57
7. Blackshaw LCD, Chhour I, Stepto NK, Lim SS. Barriers and facilitators to the implementation of evidence-based lifestyle management in polycystic ovary syndrome: a narrative review. *Med Sci (Basel)*. 2019;7(7):76. https://doi.org/10.3390/medsci7070076
8. Cussons AJ, Stuckey BGA, Walsh JP, Burke V, Norman RJ. Polycystic ovarian syndrome: marked differences between endocrinologists and gynaecologists in diagnosis and management. *Clin Endocrinol (Oxf)*. 2005;62(3):289-295. https://doi.org/10.1111/j.1365-2265.2004.02208.x
9. Gibson-Helm M, Teede H, Dunaif A, Dokras A. Delayed diagnosis and a lack of information associated with dissatisfaction in women with polycystic ovary syndrome. *J Clin Endocrinol Metab*. 2017;102(2):604-612. https://doi.org/10.1210/jc.2016-2963
10. Helvaci N, Yildiz BO. Polycystic ovary syndrome and aging: health implications after menopause. *Maturitas*. 2020;139:12-19. https://doi.org/10.1016/j.maturitas.2020.05.013
11. Conway G, Dewailly D, Diamanti-Kandarakis E, *et al.* European survey of diagnosis and management of the polycystic ovary syndrome: results of the ESE PCOS Special Interest Group's Questionnaire. *Eur J Endocrinol*. 2014;171(4):489-498. https://doi.org/10.1530/EJE-14-0252
12. Dapas M, Lin FTJ, Nadkarni GN, *et al.* Distinct subtypes of polycystic ovary syndrome with novel genetic associations: an unsupervised, phenotypic clustering analysis. *PLoS Med*. 2020;17(6):e1003132. https://doi.org/10.1371/journal.pmed.1003132
13. Pandurevic S, Mancini I, Mitselman D, *et al.* Efficacy of very low-calorie ketogenic diet with the Pronokal® method in obese women with polycystic ovary syndrome: a 16-week randomized controlled trial. *Endocr Connect*. 2023;12(7):e220536. https://doi.org/10.1530/EC-22-0536
14. Soldat-Stanković V, Popović-Pejičić S, Stanković S, *et al.* The effect of metformin and myoinositol on metabolic outcomes in women with polycystic ovary syndrome: role of body mass and adiponectin in a randomized controlled trial. *J Endocrinol Invest*. 2022;45(3):583-595. https://doi.org/10.1007/s40618-021-01691-5
15. Kakoly NS, Moran LJ, Teede HJ, Joham AE. Cardiometabolic risks in PCOS: a review of the current state of knowledge. *Expert Rev Endocrinol Metab*. 2019;14(1):23-33. https://doi.org/10.1080/17446651.2019.1556094
16. IBM Corp. *IBM SPSS Statistics For Windows, Version 28.0*. Armonk, NY: IBM Corp; Released 2021.
17. RStudio Team. *RStudio: Integrated Development for R*. Boston, MA: RStudio, PBC; 2020.
18. Malhotra K, Kempegowda P. Appraising unmet needs and misinformation spread about polycystic ovary syndrome in 85,872 YouTube comments over 12 years: big data infodemiology study. *J Med Internet Res*. 2023;25:e49220. https://doi.org/10.2196/49220
19. Elhariry M, Malhotra K, Solomon M, Goyal K, Kempegowda P. Top 100 #PCOS influencers: understanding who, why and how online content for PCOS is influenced. *Front Endocrinol (Lausanne)*. 2022;13:1084047. https://doi.org/10.3389/fendo.2022.1084047
20. Goodarzi MO, Carmina E, Azziz R. DHEA, DHEAS and PCOS. *J Steroid Biochem Mol Biol*. 2015;145:213-225. https://doi.org/10.1016/j.jsbmb.2014.06.003
21. Lerchbaum E, Schwetz V, Giuliani A, Pieber TR, Obermayer-Pietsch B. Opposing effects of dehydroepiandrosterone sulfate and free testosterone on metabolic phenotype in women with polycystic ovary syndrome. *Fertil Steril*. 2012;98(5):1318-1325.e1. https://doi.org/10.1016/j.fertnstert.2012.07.1057
22. Keevil B. Steroid mass spectrometry for the diagnosis of PCOS. *Med Sci (Basel)*. 2019;7(7):78. https://doi.org/10.3390/medsci7070078
23. O'Reilly MW, Kempegowda P, Jenkinson C, *et al.* 11-Oxygenated C19 steroids are the predominant androgens in polycystic ovary syndrome. *J Clin Endocrinol Metab*. 2017;102(3):840-848. https://doi.org/10.1210/jc.2016-3285
24. Bozdag G, Mumusoglu S, Coskun ZY, Yarali H, Yildiz BO. Anti-Müllerian hormone as a diagnostic tool for PCOS under different diagnostic criteria in an unselected population. *Reprod Biomed Online*. 2019;39(3):522-529. https://doi.org/10.1016/j.rbmo.2019.04.002
25. Dokras A, Stener-Victorin E, Yildiz BO, *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(5):888-899. https://doi.org/10.1016/j.fertnstert.2018.01.038
26. Gomez JMD, VanHise K, Stachenfeld N, Chan JL, Merz NB, Shufelt C. Subclinical cardiovascular disease and polycystic ovary syndrome. *Fertil Steril*. 2022;117(5):912-923. https://doi.org/10.1016/j.fertnstert.2022.02.028
27. van der Ham K, Louwers YV, Laven JSE. Cardiometabolic biomarkers in women with polycystic ovary syndrome. *Fertil Steril*. 2022;117(5):887-896. https://doi.org/10.1016/j.fertnstert.2022.03.008
28. Witchel SF, Azziz R, Oberfield SE. History of polycystic ovary syndrome, premature adrenarche, and hyperandrogenism in pediatric endocrinology. *Horm Res Paediatr*. 2022;95(6):557-567. https://doi.org/10.1159/000526722
29. Glintborg D, Rubin KH, Nybo M, Abrahamsen B, Andersen M. Cardiovascular disease in a nationwide population of Danish women with polycystic ovary syndrome. *Cardiovasc Diabetol*. 2018;17(1):37. https://doi.org/10.1186/s12933-018-0680-5
30. Anagnostis P, Paparodis RD, Bosdou JK, *et al*. Risk of type 2 diabetes mellitus in polycystic ovary syndrome is associated with obesity: a meta-analysis of observational studies. *Endocrine*. 2021;74(2):245-253. https://doi.org/10.1007/s12020-021-02801-2
31. Glintborg D, Kolster ND, Ravn P, Andersen MS. Prospective risk of type 2 diabetes in normal weight women with polycystic ovary syndrome. *Biomedicines*. 2022;10(6):1455. https://doi.org/10.3390/biomedicines10061455
32. Teede HJ, Tay CT, Laven JJE, *et al*. Recommendations from the 2023 international evidence-based guideline for the assessment and management of polycystic ovary syndrome. *Eur J Endocrinol*. 2023;189(2):G43-G64. https://doi.org/10.1093/ejendo/lvad096
33. Piltonen TT, Ruokojärvi M, Karro H, *et al*. Awareness of polycystic ovary syndrome among obstetrician-gynecologists and endocrinologists in Northern Europe. *PLoS One*. 2019;14(12):e0226074. https://doi.org/10.1371/journal.pone.0226074