

Polycystic Ovary Syndrome Among Patients of a University Hospital in Nicosia: A Retrospective Study

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Abstract

BACKGROUND/AIMS: Polycystic ovary syndrome (PCOS) is a heterogeneous endocrine disorder, characterized by hyperandrogenism, ovulatory dysfunction and polycystic ovarian morphology leading to health complications including infertility, hirsutism and metabolic syndrome. The aim of this study was to determine the status, features and treatments implemented for PCOS patients diagnosed in a university hospital of Nicosia, North Cyprus, where no previous data on this issue was available in the medical literature.

MATERIALS AND METHODS: This descriptive study was administered using the records of 45,677 patients presenting to the gynecology and obstetrics clinic for the time period of 2015-2019. The study group included 819 patients diagnosed as PCOS. The data were collected using a data collection form designed by the researchers and analyzed by IBM-SPSS 18.0 program, with a significance level accepted as $p < 0.05$.

RESULTS: European Society for Human Reproduction and Embryology/American Society for Reproductive Medicine Rotterdam Conference-2003 or the Androgen Excess and PCOS Society (AE-PCOS) Conference-2006 criteria were used for the diagnosis. The 819 patients diagnosed as PCOS comprised a frequency of 1.8%, lower than the expected average value reported among gynecologic patients. Family history existed in 0.7% of the cases. The characteristics of the patients were similar to those of other studies and treatments initiated were in accordance with PCOS consensuses in general, with the exception of a lower use of metformin.

CONCLUSION: The frequency of PCOS among North Cyprus women was low, indicating the disease was an under-recognized condition in this tertiary hospital compared to rates estimated in community samples globally. Further research is recommended to establish more valid data in order to improve women's health.

Keywords: Polycystic ovary syndrome, ovulation irregularity, hyperandrogenism, treatment, North Cyprus

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a heterogeneous endocrine disorder characterized by hyperandrogenism, ovulatory dysfunction and polycystic ovarian morphology, with excessive androgen production by the ovaries.¹ PCOS is the most frequent endocrinological disorder among women of reproductive ages leading to a number of health complications.^{1,2} An international consensus definition of PCOS has been published, which defines PCOS as at least two of the following criteria: Reduced or no ovulation; clinical and/or biochemical signs of excessive secretion of androgens; and/or polycystic ovaries (the presence of at

least 12 follicles measuring 2-9 mm in diameter, an ovarian volume in excess of 10 mL, or both).³

In terms of ovarian functions, PCOS is a syndrome of ovarian dysfunction characterized by an accumulation of incompletely developed follicles in the ovaries because of anovulation. Clinical manifestations include menstrual dysfunction, oligomenorrhea or amenorrhea, infertility, hirsutism and acne.⁴ Insulin resistance affects 50-70% of women with PCOS, gradually ending up with co-morbidities such as hypertension, dyslipidemia, glucose intolerance, leading to diabetes and metabolic syndrome.⁵

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Although the physiopathology of PCOS is unknown, most studies imply familial heritage. Some clinical genetic studies indicate an autosomal dominant inheritance, while others reveal a complex trait of oligogenic basis. On the other hand, the heterogeneity of phenotypic features point to the contribution of environmental factors.⁶ Genetically transmitted β -cell dysfunction and high androgens, dyslipidemia and insulin resistance serum markers in families of women with PCOS, including the male population have been demonstrated.^{7,8} The majority of PCOS patients exhibit metabolic dysfunction with insulin resistance, hyperinsulinaemia and an increased risk for type 2 diabetes mellitus, gestational diabetes and other pregnancy-related complications, cardiovascular events and endometrial cancer.⁹⁻¹³

PCOS is classified into four separate phenotypes (A-D), according to the presence or absence of three characteristics: hyperandrogenism (either biochemical or clinical), ovulatory dysfunction and polycystic ovarian morphology. Only phenotype A requires all three features of PCOS to be present. The various diagnostic criteria currently available for PCOS include a greater or fewer number of PCOS phenotypes.¹¹

The prevalence of PCOS is remarkably similar worldwide. The prevalence of clinically evident PCOS in women of reproductive ages from the United States, Europe, Asia and Australia ranges between 5% and 9% based on the original 1990 US National Institutes of Health (NIH) diagnostic criteria. Using the broader 2003 Rotterdam criteria now accepted internationally, the prevalence of PCOS ranges from 5.5% to 19.9%.¹¹

PCOS is reported to be diagnosed in 4-10% of women attending gynecology clinics in high income countries.¹⁴ In some European studies, the prevalence of PCOS has been reported as being 6.5-8%.^{14,15} The prevalence of PCOS may be in the range of 15-20% using the criteria of the European Society for Human Reproduction and Embryology/American Society for Reproductive Medicine (ESHRE/ASRM).⁵ However, among unselected general female populations of different ethnicities, PCOS rates using other criteria were found as follows: Caucasians 5.5% (NIH: 1990); African-American and Afro-Brazilian 7.4% (NIH: 1990); Chinese 2.2% (NIH: 1990), 5.6% (ESHRE/ASRM, Rotterdam 2003); and Middle East (Iranian and Turkish) 6.1% (NIH: 1990), 16.0% (ESHRE/ASRM, Rotterdam 2003), 12.6% (AES, 2006).^{4,16} Diagnostic criteria for PCOS include clinical or biochemical hyperandrogenism, oligo/anovulation and polycystic ovarian morphology according to ESHRE/ASRM 2012 criteria while clinical or biochemical hyperandrogenism and persistent oligo-/anovulation according to Endocrine Society 2013 criteria.¹⁶ As a consequence, the worldwide prevalence of PCOS shows variations according to the diagnostic criteria used. Greater estimates of PCOS prevalence with the ESHRE/ASRM Rotterdam 2003 and Androgen Excess and PCOS Society (AE-PCOS) 2006 criteria are largely attributed to their more expansive definition and inclusion of additional phenotypes.¹⁶ However, the results of PCOS studies largely depend on how the study population and the PCOS phenotypes were defined. Since the assessment of the PCOS phenotype is a complex process, study results may reflect underreporting due to the limitations of more intensive investigations.^{15,16}

Aim: The aim of this study was to determine the status and features of PCOS and to investigate the treatments provided to patients diagnosed in the Near East University Hospital in Nicosia, North Cyprus, where no previous data on this issue was available in a search of the literature. The time period of this study was set as 1st September, 2015 to 31st August, 2019.

MATERIALS AND METHODS

Study type: The study was a descriptive records-based study.

Diagnostic and inclusion criteria: In order to establish a diagnosis of PCOS, the criteria of the ESHRE/ASRM Rotterdam Conference of 2003 or the AE-PCOS Conference 2006 were used in the Near East University Hospital. According to these criteria, the following parameters were considered sufficient for the diagnosis of PCOS: Clinical and biochemical hyperandrogenism, ovulation irregularity and/or polycystic ovary morphology.¹⁰

Study design and setting: The study was conducted between the 2nd and 9th of August, 2019 via an investigation of the patient records of the Gynecology and Obstetrics Clinics of the Near East University Hospital. The study group included those patients diagnosed as PCOS starting 1st September, 2015 until 31st August, 2019. All of the patients registered with this diagnosis were admitted into this study without exclusion. The data were obtained from the information system of the Near East University Hospital with the permission of the chief physician of the hospital.

Study tool: The data were collected and recorded by a data collection form designed and structured by the researchers. The details of the records of each patient were entered into the data collection form individually.

Statistical Analysis

The data were analyzed using IBM-SPSS (Statistical Package for the Social Sciences) version 18 (SPSS Inc., Chicago, IL, USA). Descriptive statistics including frequency, percentage, mean, and standard deviation were calculated to describe the characteristics of the study sample. Bivariate analysis using the chi-squared test was performed to examine the relationships between independent variables with a significance level set at $p < 0.05$.

Permission from the Near East University Gynecology and Obstetrics Department and the Chief Physician of the Near East University Hospital was obtained and consent and approval of the Near East University Ethics Committee with report number YDU/2019/71-869 was provided.

RESULTS

In this descriptive study, the records of 819 patients diagnosed as PCOS among 45,677 patients presenting to the Gynecology and Obstetrics Clinics of the Near East University Hospital between 1st September, 2015 and 31st August, 2019 were studied. The detailed history of 80 patients were not recorded in the system, other than their diagnosis as PCOS.

The results are given under the headings of age distribution, family history, symptoms and findings, diagnosis and treatments. The age distribution, the status of family history and prior drug use history of the patients followed up with the diagnosis of PCOS are presented in Table 1.

Of the total patients, 41.5% were in the 20-24 year age group. The mean age of the PCOS patients was 27 years, with a minimum age of 15 and maximum age of 50. Only 5 patients (0.7%) had a family history according to their records. Of the 232 patients under drug therapy prior to admission, 42.2% were reported as taking contraceptive drugs and 78.0% as using other medications (Table 1).

The analysis of the patients followed up with the diagnosis of PCOS at the Near East University Hospital showed that 8.4% of the patients (69 patients) had undergone surgical interventions, while 2.2% (18 patients) of them had experienced gynecologic/obstetric operations prior to admission.

Table 2 indicates the presenting and later symptoms and signs of the PCOS patients diagnosed at the Near East University Hospital. Of the patients with recorded data, 45.9% were admitted to the hospital with complaints of menstrual irregularity, followed by the desire for offspring, hirsutism and dermatological problems as the major causes of presentation to the hospital. Leading symptoms at a later stage of the disease included oligomenorrhea, hirsutism and acne. In addition, data from the records showed that 78.6% of the patients diagnosed as PCOS had ultrasonographic findings of polycystic ovaries (Table 2).

The laboratory investigations requested of the patients followed up with the diagnosis of PCOS at the Near East University Hospital are given in Table 3. The patient records revealed that hormone profile, vaginal smear, thyroid function tests and HOMA-IR (insulin resistance) were the laboratory tests most commonly requested for those patients with PCOS, the leading test among the total being hormone profile with 83.5%, followed by vaginal smear with 14.4% (Table 3).

The details about drug therapies provided for the PCOS patients diagnosed at the Near East University Hospital are shown in Table 4. Among the records of the 819 PCOS patients registered, 759 patient records had pharmacotherapy information, 431 of whom were stated as receiving drug therapy and 328 as receiving no drug therapy. Of the total 431 records with information regarding pharmacologic therapies, 69.4% were taking oral contraceptives and progesterone. Oral contraceptive medications were prescribed for 39.2% of the patients while 29.0% received progesterone therapy. Antibiotics, metabolic drugs and supplements were the following groups of medications in order of frequency recommended for the PCOS patients.

Metformin was reported to be prescribed for 5.3% of the patients. Other ovulation stimulators used included clomiphene, dopamine agonists, estrogen agonists and aromatase inhibitors. Dermatologic and other medications were prescribed for 6% of the patients (Table 4).

Reporting of a PCOS symptom at first presentation to the hospital according to age groups is given in Table 5. A significant difference was illustrated between the age groups regarding the existence of symptoms at first presentation. Those patients under 25 years of age had symptoms regarding PCOS at their first visit to the hospital at significantly higher levels than those patients 25 years or older ($\chi^2=13.0$, $p<0.01$) (Table 5).

DISCUSSION

This study was conducted using the patient registration system of a university hospital in North Cyprus.

The frequency of PCOS was established as 1.8% among the gynecologic patients, lower than reported in the literature for the same age group of patients in similar settings. PCOS was reported to be diagnosed in 4-10% of women attending gynecology clinics in high income countries.¹⁴

According to our review of the literature, the prevalence of PCOS among women had not been investigated in North Cyprus until the present time. Therefore, a comparison with previous research was not possible and our study may be part of the initial research on this issue in this country.

The incidence and prevalence of PCOS among women seeking healthcare at primary healthcare settings was found to be low, indicating that PCOS is an under-recognized condition at the broadest level of the healthcare systems.¹³ Prevalence studies from several countries have reported PCOS frequencies, such as 6.6% for Spain, 5% for Türkiye, 2.2% for the Peoples Republic of China and 1.6% for the USA.⁹ A study in the UK found an overall incidence rate of 1.84% for the time period 2004-2014, with women aged 20-24 years and women living in deprived areas having the highest incidences. The prevalence of PCOS for the year 2014 was estimated to be approximately 2%, reflecting a lower level of this syndrome, similar to our study.¹⁷

Although our study group included gynecologic patients, the frequency of PCOS was 1.8%, lower than the reported 4-10% in the literature for the same age group of patients in similar settings.¹⁴ In a cross-sectional study representing the South Cyprus population, the overall prevalence

Table 1. Age distribution, family history and drug use history of those patients with a diagnosis of PCOS at Near East University Hospital (Nicosia: August, 2019)

Age group (n=814)		n	%
<20		36	4.4
20-24		338	41.5
25-29		218	26.8
30-34		137	16.8
35-39		61	7.5
≥40		24	3.0
Mean ± SD: 27±5.8	Median: 25	Minimum: 15	Maximum: 50
Family history (n=756)			
Yes		5	0.7
No		751	99.3
Drug use history on record (n=232)*			
PCOS-related drugs**		98	42.2
Other drugs (none PCOS-related)		181	78.0
*Limited to information in the patient records, **PCOS related drugs: Contraceptive drugs (cyproterone and estrogen, dienogest and ethinylestradiol, ulipristal, dienogest and estrogen, medroxyprogesterone, drospirenone and ethinylestradiol), PCOS: Polycystic ovary syndrome, SD: Standard deviation.			

of PCOS among women was found to be 6.1%, much higher than the results of our study. The age group with the highest rate in this study of the South Cyprus population was the 25-44 age group women with 16.0%, followed by the 18-24 age group with 8.6%.¹⁸

Additionally, the prevalence of PCOS was found to be higher using the ESHRE-ASRM Rotterdam Conference 2003 and AE-PCOS Society

conference 2006 criteria, as compared to the NIH 1990 criteria. Since the former two criteria were used in our clinics and the setting is a tertiary university hospital, the present frequency finding was much lower than the expected values, indicating an under-diagnosis of this syndrome, which may be attributed to the private status of the university hospital and also some missing data in the records. As PCOS is more a condition of deprived populations, more patients probably seek health

Table 2. The presenting and later symptoms and signs of patients followed up with a diagnosis of PCOS at the Near East University Hospital (Nicosia: August, 2019)

Presenting symptom (n=758)	n	%
Menstrual irregularity	348	45.9
Desire for offspring	57	7.5
Hirsutism	47	6.2
Dermatological problem	47	6.2
Pain	41	5.4
Amenorrhea	41	5.4
Vaginal secretion	35	4.6
Check-up	31	4.8
Pregnancy monitoring	27	3.5
Hemorrhage	25	3.2
PCOS control	20	2.6
Dysmenorrhea	13	1.7
Metabolic disorder	12	1.5
Infertility	5	0.7
Urinary infection	4	0.5
Other infection	2	0.3
Abdominal mass	2	0.3
Abortion	1	0.1
Later symptoms and signs		
Oligomenorrhea (n=759)	424	55.9
Hirsutism (n=759)	192	25.3
Acne (n=759)	87	11.5
Polycystic ovaries on ultrasound (n=760)	597	78.6

PCOS: Polycystic ovary syndrome.

Table 3. The records of the laboratory investigations requested of the patients followed up with a diagnosis of PCOS at the Near East University Hospital (Nicosia: August, 2019)

Investigation (n=480)	n	%
Hormone profile	401	83.5
Vaginal smear	69	14.4
Thyroid function tests	27	5.6
HOMA-IR (insulin resistance)	26	5.4
Complete blood count test	21	4.4
Urinary analysis	14	2.9
Hepatic function tests	7	1.5
Fasting blood glucose	7	1.5
Tumor markers	6	1.3
Glucose tolerance test	5	1
Magnetic resonance imaging	3	0.7
Chorionic villus sampling	3	0.7
Hysterosalpingography	2	0.4

PCOS: Polycystic ovary syndrome.

services at state institutions in Cyprus or in Türkiye. However, the socio-demographic features of the patients were not recorded in sufficient detail in the records used in the current study. Thus, further analysis in regard to other sociodemographic features other than age was not possible. Regarding family history, no evidence was found suggesting familial transmission among the majority of the patients.

Additionally, the assessment of the PCOS phenotype is a complex process and due to the unavailability of some investigations, study results may reflect lower prevalences.^{15,16} This may be one of the other reasons for the lower prevalence found in our study.

The findings of the current study were in agreement with previous studies conducted in other studies.¹⁸ Among the patients diagnosed as PCOS, two or more of the PCOS criteria of menstrual irregularity, polycystic ovary morphology, and/or hyperandrogenism-hirsutism were present in 80% of the cases. Similarly, 75% of the patients had two or more of these criteria in another study conducted in Denmark.¹⁹

According to the European survey of diagnosis and management of PCOS among European Society of Endocrinology members, NIH criteria were utilized for PCOS diagnosis by the majority of the respondents.²⁰ The respondents were most likely to select menstrual irregularity as the most frequent criteria used for PCOS diagnosis, followed by hirsutism and biochemical hyperandrogenism, similar to our study as menstrual irregularity was the first and hirsutism the third ranked findings reported (Table 2).

The most frequent biochemical parameters in the differential diagnosis of hyperandrogenism were total testosterone or free androgen index, contrary to our findings regarding laboratory tests, which did not include all of these tests.²⁰

Treatment is recommended to be in alignment with the complaints

and needs of the patients and should involve lifestyle changes targeting metabolic abnormalities, medications and surgery for the management of excess weight, androgen suppression and/or blockade, endometrial protection, reproductive therapy and the treatment of psychological features.^{11,20}

In the current study, 40.4% of the 431 patients prescribed medications were reported as receiving oral contraceptives and 29% as receiving progesterone. Totally, 16.6% of the patient records with pharmacotherapy information indicated the use of ovulation stimulators.

Metformin use was only 5.3% in our study, considerably less than reported in the literature. In a study from the USA, metformin comprised 75% of the drugs administered to PCOS patients.⁹ However, the rate of metformin use was lower in the UK study covering 2004-2014 at 10.2%. In this UK study, the proportion of women with a prescription in the 24 months after their PCOS index date varied by drug type: 10.2% metformin, 15.2% combined oral contraceptives, 18.8% acne-related treatments, and less than 5% for clomiphene, spironolactone, cyproterone and eflornithine.¹⁷ The use of oral contraceptives was much higher in our study than was found in the UK study, although metformin use was lower.

In the European survey, the most common treatments for patients with PCOS were metformin (33%), lifestyle modification (25%), oral contraceptives (22%), antiandrogens (13%), cosmetic procedures for hirsutism (8%) and a number of different combinations of these agents or methods. More direct treatments of infertility included clomiphene citrate alone or in combination with metformin, prescribed at rates of 9% and 23%, respectively, whereas only 6% used other methods for the induction of ovulation.²⁰ The treatment options in the present study were similar to the current literature, except for the low rate of metformin use.

Table 4. Drug therapies provided for the patients followed up with a diagnosis of PCOS at the Near East University Hospital (Nicosia: August, 2019)

Pharmacotherapies (n=431)	n	%
Oral contraceptives	174	40.4
Progesterone	125	29.0
Antibiotics	81	18.8
Metabolic drugs (anti-diabetics, thyroid hormones...)	54	12.5
Supplements (vitamins, ferrum...)	53	12.3
Ovulation stimulators		
Metformin	23	5.3
Dopamine agonists	19	4.4
Estrogen agonists (tamoxifen...)	17	3.9
Other ovulation stimulators (clomiphene, aromatase inhibitors)	13	3.0
Other drugs		
(Dermatologic agents and others)	26	6.0

Table 5. The distribution by age groups of the PCOS patients according to the existence of symptoms at first presentation to the hospital (Nicosia: August, 2019)

Age group	Under 25 years		25 years of age or over		Total	
	n	%	n	%	n	%
PCOS symptom at first presentation (n=758)						
Existent	309	88.5	322	78.7	631	83.2
Non-existent	40	11.5	87	21.3	127	16.8

$\chi^2=13.0$, $p<0.01$. PCOS: Polycystic ovary syndrome.

Regarding the lack of population level data on the prevalence and distribution of common benign women's health diseases, including PCOS in North Cyprus, the Cyprus Women's Health Research initiative will be the first cross-sectional study to evaluate these conditions, aiming to recruit 8,000 women of reproductive age and establish a cohort of women in North Cyprus. The results of this large-scale study are expected to shed light on the definite data on this condition of women as well as others.²¹

The current study has shown that only half of the patients diagnosed as PCOS continued their follow-up for this disease as recommended. Under-diagnosis and lack of monitoring may lead to rapid conversion of metabolic disorders for PCOS patients. This lack of treatment results in increased risks of type 2 diabetes, atherosclerosis and endometrium cancer.^{10,11} Therefore, there is a need for programs to effectively monitor and treat patients diagnosed as or suspected of PCOS through accurate data keeping and registration systems. These patients should be informed and monitored closely and regularly regarding the possible risks of this syndrome.

Study Limitations

The lack of full data of the patients' records in the system is considered to be a limitation of this study. The data and results of this study are limited by the information covered in the records. There was considerable missing data in the system. There is definitely a need for a more comprehensive record-keeping and monitoring system in order to allow for a better follow-up of these patients. Due to the descriptive nature of this study, the results may show hints of the actual situation, which may only be derived from representative studies. The lower PCOS rate may be attributed to the private status of the hospital, as well as the insufficiency of the records.

CONCLUSION

Based on the NIH's diagnostic criteria, there is a similar prevalence of PCOS across countries. Some studies have shown some differences between geographical locations and ethnic groups. However, the existing data is not conclusive enough to decide whether or not there are any significant differences in the prevalence of PCOS across geographical locations, racial or ethnic groups.⁹

Different diagnostic criteria may be one of the factors for the considerable variations in the prevalence of PCOS. In spite of the efforts for diagnosis, a large percentage of women are anticipated to remain undiagnosed even after visiting multiple health care providers. This finding points to the need for ethnicity-specific guidelines for PCOS in order to prevent under- or over-diagnosis of this condition because under-diagnosis may lead to rapid conversion of metabolic disorders for patients, whereas over-diagnosis may cause negative psychological effects on patients, worsening the major symptoms of PCOS.

This was a descriptive record-based study, covering only the patients of a university hospital; thus it was not representative of the North Cyprus population, but it shed light on the features of a group of women with PCOS in this community. Our findings point to the probability of under-diagnosis compared to the international data presented in the medical literature. There is a need for representative studies of the whole country for a full picture of this issue and to prevent patients from being undiagnosed. Further knowledge about this specific women's health

problem in the population of this geography may enlighten the road map in order to take effective measures for this issue and may be of assistance for interventions in similar communities.

What this paper contributes

The results of this study imply under-recognition of PCOS among the population of women in North Cyprus, which may lead to rapid conversion of metabolic disorders.

Only half of the patients diagnosed as PCOS continued their follow-up for this disease as recommended.

Under-diagnosis and a lack of monitoring result in increases in risks for type 2 diabetes, atherosclerosis and endometrium cancer.

Therefore, the results of this study point to a need for programs to effectively diagnose, treat and monitor those patients diagnosed as or suspected of PCOS, including accurate data keeping and registration systems, in order to improve women's health.

MAIN POINTS

- In the current study, the status of polycystic ovary syndrome (PCOS) was investigated retrospectively among patients of a university hospital in North Cyprus, where no previous research on this issue had been conducted.
- Among the 819 PCOS patients found for the time period of 2015-2019, 78.5% displayed polycystic ovary morphology via ultrasonography and a minority (0.7%) had a family history.
- PCOS patients comprised 1.8% of the total patients of the gynecology clinic, lower than the expected value, although ESHRE/ASRM Rotterdam Conference 2003 and AE-PCOS Conference 2006 criteria were used.
- The results point to the need for further research and effective interventions in this community for this specific women's health problem in order to prevent complications.

ETHICS

Ethics Committee Approval: Permission from the Near East University Gynecology and Obstetrics Department and the Chief Physician of the Near East University Hospital was obtained and consent and approval of the Near East University Ethics Committee with report number YDU/2019/71-869 was provided.

Informed Consent: It was obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: Ö.A., S.V., G.A., S.C., Design: Ö.A., S.V., G.A., S.C., Supervision: Ö.A., S.V., G.A., S.C., Fundings: S.C., Materials: Ö.A., S.V., G.A., S.C., Data Collection and/or Processing: S.V., S.C., Analysis and/or Interpretation: Ö.A., S.V., G.A., S.C., Literature Search: Ö.A., S.V., G.A., Writing: Ö.A., S.V., Critical Review: S.V., G.A., S.C.

DISCLOSURES

Conflict of Interest: No conflict of interest was declared by the authors.

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