



The Modified Ferriman-Gallwey Score and Hirsutism among Filipino Women

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Background: The modified Ferriman-Gallwey (mFG) score is the gold standard for the clinical evaluation of hirsutism. However, racial variations in terminal hair growth limit this tool. This study aimed to determine the mFG cut-off score among Filipino women and its association with biochemical hyperandrogenism.

Methods: A total of 128 Filipino women were included in this prospective cross-sectional study and were divided into two groups: a polycystic ovary syndrome (PCOS) group ($n=28$) and a non-PCOS group ($n=100$). The participants underwent mFG score determination, ovarian ultrasound conducted by a single sonographer, and hormone testing. The mFG cut-off score was determined based on the 95th percentile of the non-PCOS group. Logistic regression was used to analyze the relationship between mFG score and biochemical hyperandrogenism.

Results: Although the mFG score was generally low in both the PCOS and non-PCOS groups, the former exhibited a higher mean score than the latter (4.3 ± 3.0 vs. 2.0 ± 2.2 , $P < 0.001$). Normal values for the total mFG score ranged from 0 to 7. Using a cut-off score of 7, a higher proportion of hirsute women (mFG score ≥ 7) was observed in the PCOS group versus the non-PCOS group (17.9% vs. 5.0%, $P = 0.025$). Elevated calculated free testosterone (FT) was also found to be significantly associated with hirsutism (odds ratio, 6.2; 95% confidence interval, 1.2 to 32.4 pmol/L; $P = 0.030$).

Conclusion: A score of 7 and above constitutes hirsutism in this population of Filipino women. Hirsute women are more likely than non-hirsute women to have elevated calculated FT.

Keywords: Hirsutism; Gonadal disorders; Polycystic ovary syndrome; Hyperandrogenism

INTRODUCTION

Hirsutism is defined as excessive terminal hair that appears in a male pattern or in androgen-sensitive areas in women [1]. It is present in 5% to 20% of the general population, and current data suggest that the majority of hirsute patients have polycystic ovary syndrome (PCOS), a common endocrine problem among

women of reproductive age. PCOS is associated with an increased risk of infertility, endometrial carcinoma, and multiple metabolic abnormalities [2,3]. Early identification and diagnosis of at-risk women can lead to timely management that can potentially reverse or prevent the progression of the metabolic complications associated with this syndrome.

At present, there are three acceptable criteria for the diagnosis

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of PCOS, all of which include hyperandrogenism. Hyperandrogenism can present either clinically or biochemically. Biochemical hyperandrogenism refers to an elevated serum level of androgens, including total testosterone (TT), free testosterone (FT), androstenedione, dehydroepiandrosterone (DHEA), and the DHEA metabolite dehydroepiandrosterone sulfate (DHEAS), while clinical hyperandrogenism refers to the presence of signs such as hirsutism, acne, and male-pattern alopecia [4]. In a large study of 950 women with clinical evidence of hyperandrogenism, more than half were diagnosed with PCOS, with hirsutism being the most common presentation [5]. The presence of hirsutism can easily be detected through a physical examination. Its presence in premenopausal women not only fulfills a criterion for the diagnosis of PCOS, but also warrants further investigation for other causes of hyperandrogenism [3].

The clinical evaluation of hirsutism entails the use of visual scoring tools, of which the most widely used is the modified Ferriman-Gallwey (mFG) score. The mFG score evaluates hair growth in nine androgen-sensitive body areas: the upper lip, chin, chest, upper and lower back, upper and lower abdomen, upper arm, and thigh. A score of 0 represents the absence of terminal hair growth, and a score of 4 represents extensive growth. A total score of 8 or higher constitutes hirsutism [6]. This cut-off value was based on a predominantly Caucasian cohort, and since it is now known that terminal hair growth exhibits substantial racial variability, it may not be applicable to other populations. Thus, it is important to establish race-specific normative ranges to determine whether a particular woman has excessive amounts of hair [7-9].

Among Asian women, studies have shown conflicting results regarding whether a lower cut-off score should be recommended. Studies conducted by Wang et al. [10] among Asian women living in the United States and by Leerasiri et al. [11] in a Thai

population still recommend a total mFG cut-off score of 8. However, both studies only examined women with PCOS. To date, no studies have defined the mFG cut-off score for hirsutism in a Filipino population. The present study was designed primarily to determine the mFG cut-off score among Filipinos and secondarily to determine its association with biochemical hyperandrogenism in the local setting.

METHODS

Study population

Between August 2018 and January 2019, Filipino women aged 18 to 45 years old were recruited and divided into a PCOS group and a non-PCOS group. The subjects in the PCOS group were recruited from private clinics and the outpatient department of The Medical City (TMC), a private tertiary hospital in Metro Manila, Philippines, whereas subjects in the non-PCOS group were healthy women—including hospital employees, physicians, and medical students—obtained from the general population using convenience sampling. Race was determined using a two-question format wherein subjects were asked to choose from certain categories. Information regarding ancestry, geographical origin, and parental race was also obtained [12].

Inclusion criteria

For subjects to be classified as part of the PCOS group, they first needed to fulfill the 2003 Rotterdam criteria for the diagnosis of PCOS (Table 1). Among subjects who met the Rotterdam criteria, those with the following diseases that can mimic PCOS were excluded:

(1) Hyperprolactinemia, defined as a prolactin level above the TMC laboratory reference range (5.18 to 26.53 ng/mL). Although elevated prolactin levels have been reported in women

Table 1. 2003 Rotterdam Criteria for the Diagnosis of Polycystic Ovary Syndrome

Rotterdam criteria (must meet 2 out of 3 of the following)			
(1) Hyperandrogenism		(2) Oligo-ovulation or anovulation	(3) Polycystic ovaries on ultrasound
Clinical and/or	Biochemical		
Hirsutism (mFG score \geq 8)	Elevated TT or FT	Bleeding interval <21 days	Presence of 12 or more follicles 2–9 mm in diameter in either ovary and/or increased ovarian volume >10 mL (without a cyst or dominant follicle) in either ovary
Acne	Elevated A4	Bleeding interval >35 days <8 episodes of menses/year	
Male-pattern alopecia	Elevated DHEA	Infertility	
	Elevated DHEAS	No menstruation for 3 consecutive months in the last 12 months	

mFG, modified Ferriman-Gallwey; TT, total testosterone; FT, free testosterone; A4, androstenedione; DHEA, dehydroepiandrosterone; DHEAS, dehydroepiandrosterone sulfate.

with PCOS, hyperprolactinemia and PCOS should be treated as two distinct clinical entities. A study of 474 Taiwanese women reported that the average prolactin level in women with PCOS is not significantly different from that in healthy controls [13]. Hence, further investigation into other causes of hyperprolactinemia should be performed in all women with elevated prolactin levels.

(2) Thyroid disease, as measured by levels of thyroid-stimulating hormone (TSH). Subjects with elevated or low TSH based on the TMC laboratory range (0.35 to 4.94 μ IU/mL) were recommended to undergo further work-up and were excluded from the study.

(3) Non-classical congenital adrenal hyperplasia, as measured by early-morning basal 17-hydroxyprogesterone (17-OHP). Subjects with a level of >2 ng/mL (>6 nmol/L) were recommended to undergo further work-up and were excluded from the study.

In contrast, subjects in the non-PCOS group did not meet the 2003 Rotterdam criteria for PCOS and were considered healthy controls.

Exclusion criteria

Women with diseases known to mimic PCOS, such as diseases of the pituitary gland, adrenal gland, and thyroid gland, as well as functional ovarian tumors, were excluded from the study. Likewise, subjects for whom the diagnosis of PCOS could not be accurately determined, such as those who were pregnant, were lactating, or had undergone the surgical removal of an ovary, were excluded. Lastly, subjects who were unable to give a reliable menstrual history, such as those who had undergone hysterectomy or those with primary ovarian failure, were also excluded from the study.

Sample size

Using Epi Info version 7 (Centers for Disease Control and Prevention, Atlanta, GA, USA), the minimum sample size was determined to be at least 126 based on the 91% specificity of mFG in detecting hyperandrogenism [14], with a margin of error of 5% and a confidence level at 95%. The total sample was divided into the PCOS and non-PCOS groups using a ratio of approximately 1:4 to achieve maximum statistical efficiency (26 PCOS and 100 non-PCOS subjects).

Study protocol

All participants underwent an interview using a standardized questionnaire, a physical examination, a blood draw for hor-

monone testing, and ovarian ultrasonography. Anthropometric variables, such as body mass index (BMI), waist-to-hip ratio, and blood pressure, were measured. The participants were screened for signs and symptoms of PCOS and diseases that can mimic PCOS. Participants with a history of hair removal in any of the nine androgen-sensitive sites were asked to return for evaluation according to the following timeline: after 12 weeks for those who underwent laser treatment or electrolysis, after 4 weeks for those who underwent depilation or waxing, and after 5 days for those who underwent shaving [9]. Patients who were taking spironolactone or other anti-androgens, oral contraceptive pills, or any form of hormone therapy as treatment for hirsutism were asked to discontinue that medication, if possible, and return after 60 days from the time of drug discontinuation. Two endocrinology fellows, who were trained to use the mFG scoring system, simultaneously obtained the mFG score of each participant and were expected to be in agreement with each other. Discrepancies between the two investigators were resolved by the supervising endocrinologist.

Venous blood samples were obtained on or before 8:00 AM, after a fast of at least 8 hours, and independently of menstrual cycle state. Investigators tested levels of the following hormones: TT, sex hormone-binding globulin (SHBG), prolactin, TSH, and 17-OHP. TT was assessed using the Abbott ARCHITECT[®] testosterone assay (Abbott Laboratories, Abbott Park, IL, USA), which is a chemiluminescent microparticle immunoassay. Elevated TT was defined as a level above the TMC reference range of 0.11 to 0.57 ng/mL. Participants with abnormal levels of prolactin, TSH, or 17-OHP, as previously defined, were excluded from this study. As surrogate markers for FT, calculated FT and the free androgen index (FAI) were derived from measurements of TT and SHBG. Assuming an albumin level of 43 g/L in all women, calculated FT was determined using the Vermeulen equation (<http://www.issam.ch/freetesto.htm>). FAI is a unitless measurement derived from the following equation: $(TT \text{ in nmol/L} \times 100) / \text{SHBG in nmol/L}$ [15]. In this study, an FT level of ≥ 35.3 pmol/L constituted elevated calculated FT, and an FAI level of ≥ 7.1 constituted elevated FAI [16].

Transvaginal or transrectal ovarian ultrasonography was performed by a single gynecologic sonographer using a Samsung R3 ultrasound device (Pasig, Philippines) with a 5- to 7-MHz endovaginal probe to determine the presence or absence of polycystic ovaries. Ultrasound diagnosis of polycystic ovaries was also based on the 2003 Rotterdam criteria.

The primary outcome of this study was to determine the mFG

cut-off score for hirsutism among Filipinos. Secondly, it aimed to determine the association of this derived mFG cut-off score with serum androgen levels, specifically TT, calculated FT, and FAI, among Filipinos.

Data analysis

Data were analyzed using Stata SE version 13 (StataCorp, College Station, TX, USA). Quantitative variables such as age, mFG score, and TT levels were summarized as mean and standard deviation, while qualitative variables were tabulated as frequency and percentage. Normal values of mFG were computed based on the fifth and 95th percentiles of non-PCOS patients. Characteristics were compared between the PCOS and non-PCOS groups using the independent *t* test for quantitative variables and the Fisher exact test for qualitative variables. The association between the derived total mFG score and androgen levels among Filipinos was determined via binary logistic regression using the adjusted odds ratio (OR) for continuity. All tests were performed using a *P* value of 0.05 to indicate statistical significance.

Ethical considerations

This study underwent full board review and was approved by the TMC Institutional Review Board (GCS Med 2017-187). Informed consent was obtained from each subject. Patient confidentiality and data privacy were ensured. This study was conducted in accordance with the Ethical Principles for Medical Research Involving Human Subjects as outlined in the Declaration of Helsinki.

RESULTS

A total of 134 participants were initially recruited for this study, of whom six were excluded. One participant was excluded from the study due to hyperprolactinemia (a prolactin level of 80 ng/mL) and refused further work-up, one participant became pregnant during the study period, and four participants withdrew their consent. Table 2 shows the characteristics of the 128 participants included in this study. Both groups had a similar mean age, history of hair removal, history of parity, and age of menarche. Patients in the PCOS group had a significantly higher frequency of diabetes, family history of PCOS, mean BMI, mean waist-to-hip ratio, and mean blood pressure.

Subjects in the PCOS group also had a significantly higher frequency of clinical hyperandrogenism, specifically acne and hirsutism. All four patients in the non-PCOS group who dis-

Table 2. Clinical Characteristics of the Study Population

Characteristic	PCOS (n=28)	Non-PCOS (n=100)	<i>P</i> value
Age, yr	27.7±4.7	27.5±4.4	0.808
History of hair removal	3 (10.7)	16 (16.0)	0.764
History of parity	4 (14.3)	17 (17.0)	1.000
Age of menarche, yr	12.0±1.3	11.7±1.2	0.198
Co-morbidities			
Diabetes	4 (14.3)	0	0.002
Hypertension	0	0	-
Dyslipidemia	1 (3.6)	1 (1.0)	0.391
Family history of polycystic ovary syndrome	10 (35.7)	17 (17.0)	0.039
Body mass index ^a , kg/m ²	28.5±5.9	23.9±4.5	<0.001
Waist-to-hip ratio	0.9±0.1	0.8±0.1	<0.001
Systolic blood pressure, mm Hg	110±11.9	102.6±11.8	0.004
Diastolic blood pressure, mm Hg	76.4±8.7	71.6±10.1	0.023
Clinical hyperandrogenism	13 (46.4)	4 (4.0)	<0.001
Acne	9	0	
Hirsutism	4	4	
Biochemical hyperandrogenism	6 (21.4)	0	<0.001
Oligo-ovulation or anovulation	27 (96.4)	0	<0.001
Polycystic ovaries on ultrasound	26 (92.9)	20 (20.6)	<0.001

Values are expressed as mean±standard deviation or number (%).

PCOS, polycystic ovary syndrome.

^aBody mass index was calculated as the participant's weight in kilograms divided by the square of the participant's height in meters.

played clinical hyperandrogenism presented with hirsutism. Ultrasound findings of polycystic ovaries were also significantly more frequent among subjects in the PCOS group than in the non-PCOS group. Both biochemical hyperandrogenism and oligo-ovulation or anovulation were observed only in the PCOS group (Table 2).

Table 3 details the biochemical characteristics of the study population. As expected, subjects in the PCOS group displayed significantly higher levels of TT, FAI, and calculated FT, as well as significantly lower levels of SHBG. The mean values for TSH, prolactin, and 17-OHP were within normal levels and were similar for both groups.

The mFG score for both groups was determined (Table 4, Fig. 1). The PCOS group showed a significantly higher mean total mFG score than the non-PCOS group (4.3 ± 3.0 vs. 2.0 ± 2.2 , $P<0.001$). The following sites also had significantly higher mFG scores in the PCOS group than in the non-PCOS group: the upper lip, upper back, upper and lower abdomen, and thighs.

Table 3. Mean Biochemical Characteristics of the Study Population

Characteristic	PCOS (n=28)	Non-PCOS (n=100)	P value
Total testosterone, ng/mL	0.5±0.1	0.3±0.1	<0.001
Sex hormone-binding globulin, nmol/L	23.5±16.0	41.9±28.0	0.001
Free androgen index	10.4±7.6	3.2±2.2	<0.001
Calculated free testosterone, pmol/L	39.8±18.2	16.8±8.5	<0.001
Thyroid-stimulating hormone, µIU/mL	1.8±0.6	1.6±0.8	0.282
Prolactin, ng/mL	12.4±5.5	14.9±5.3	0.089
17-Hydroxyprogesterone, ng/mL	1.4±0.3	1.4±0.4	0.931

Values are expressed as mean±standard deviation.
PCOS, polycystic ovary syndrome.

Table 4. Modified Ferriman-Gallwey Score of the Study Population

Site	PCOS (n=28)	Non-PCOS (n=100)	P value
Upper lip	1.2±0.7 (0.9–1.4)	0.7±0.6 (0.5–0.8)	<0.001
Chin	0.1±0.3 (0–0.2)	0.1±0.3 (0–0.1)	0.882
Chest	0.0±0.2 (0–0.1)	0.0±0.2 (0–0.1)	0.879
Upper back	0.5±0.7 (0.3–0.8)	0.3±0.5 (0.2–0.4)	0.029
Lower back	0.2±0.4 (0.1–0.4)	0.1±0.3 (0–0.2)	0.093
Upper abdomen	0.6±0.7 (0.3–0.8)	0.2±0.4 (0.1–0.3)	0.001
Lower abdomen	0.8±1.1 (0.4–1.2)	0.3±0.5 (0.2–0.4)	0.001
Upper arm	0.2±0.5 (0–0.4)	0.1±0.3 (0–0.1)	0.093
Thighs	0.7±1.0 (0.3–1)	0.3±0.6 (0.2–0.4)	0.012
Total	4.3±3.0 (3.2–5.4)	2.0±2.2 (1.6–2.4)	<0.001

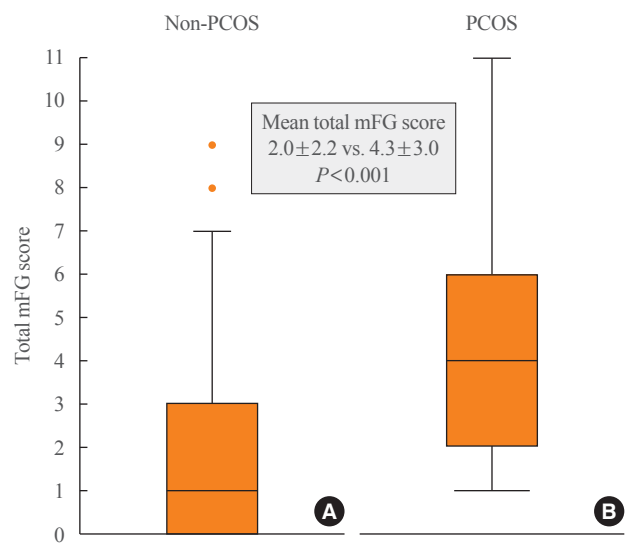
Values are expressed as mean±standard deviation (95% confidence interval).

PCOS, polycystic ovary syndrome.

The upper lip was the most severely affected site in both groups.

In this study, the fifth to the 95th percentile of the computed total mFG scores identified for the normal population (the non-PCOS group) ranged from 0 to 7. Based on the 95th percentile of the total mFG score of this group, a cut-off value of 7 and above represented hirsute women in this population. A total of 10 women had total mFG scores of ≥7. Using this score, there was still a significantly higher number of hirsute women in the PCOS group than in the non-PCOS group (5 of 28 [17.9%] vs. 5 of 100 [5.0%], $P=0.025$).

The association of a total mFG score of ≥7 with three biomarkers of hyperandrogenism using logistic regression is shown in Table 5. Subjects with a score of ≥7 displayed a higher frequency of elevated TT, FAI, and calculated FT. However, only calculated FT showed a significant association (OR, 6.2; 95%

**Fig. 1.** Boxplots representing the distribution of total modified Ferriman-Gallwey (mFG) scores in the non-polycystic ovary syndrome (PCOS) group (A) and the PCOS group (B). The mean total mFG scores for the two groups were: non-PCOS group, 2.0±2.2; PCOS group, 4.3±3.0.**Table 5.** Associations of Hirsutism with Biochemical Test Results

Variable	Total mFG ≥7 (n=10)	Total mFG <7 (n=118)	Adjusted odds ratio ^a (95% CI)	P value
Elevated TT	1 (10.0)	5 (4.2)	2.248 (0.232–21.765)	0.423
Elevated FAI	4 (40.0)	18 (15.3)	3.564 (0.735–17.296)	0.115
Elevated calculated FT	4 (40.0)	12 (10.2)	6.209 (1.190–32.398)	0.030

Values are expressed as number (%).

mFG, modified Ferriman-Gallwey; CI, confidence interval; TT, total testosterone; FAI, free androgen index; FT, free testosterone.

^aAdjusted for its covariates (age and body mass index).

Table 6. Comparison of Modified Ferriman-Gallwey Cut-off Scores across Various Asian Populations

Study	Country	Population	Suggested mFG cut-off score
Karimah et al. (2016) [17]	Indonesia	30	≥2
Li et al. (2012) [14]	China	10,120	≥5 ^a
Kim et al. (2011) [18]	Korea	1,010	≥6 ^a
Cheewadhanaraks et al. (2004) [19]	Thailand	531	≥3 ^a

mFG, modified Ferriman-Gallwey.

^aCut-off value based on the 95th percentile of an unselected population.

confidence interval [CI], 1.2 to 32.4; $P=0.030$). All ORs were adjusted using the covariates of age and BMI to account for these confounding variables.

DISCUSSION

The mFG score is considered the gold standard for evaluating hirsutism. While it is inexpensive and easy to use, a significant limitation of this tool is the variation in hair distribution among racial groups. Thus, it is currently recommended to define hirsutism according to race-specific mFG cut-off scores determined in unselected populations of premenopausal women. Guidelines recommend that the mFG cut-off value and subsequent diagnosis of hirsutism be based on the 95th percentile of the mFG score of the general population of the specific race under study. If this value is not available, a cut-off value of 8 or above should be used [3,9].

This study found that the fifth to the 95th percentile of the total mFG score among women in the non-PCOS group ranged from 0 and 7. Based on the 95th percentile of the total mFG score in this group, a cut-off value of 7 or above constituted hirsutism in this population. The findings of this study are consistent with reports that Asians have a lower mFG score than Caucasian populations, as obtained from studies of other Asian populations (Table 6) [14,17-19]. The number of hair follicles per unit of skin area has been found to be lower in Asians than in black or white individuals, and this may result in lower mFG cut-off scores [20]. This study is also consistent with findings that hirsutism is more frequent in patients with PCOS than in the normal population. Although the mean total mFG score of the PCOS group was lower than the proposed cut-off score of 7, the range of the total mFG scores in these 28 participants was between 1 and 11. In a study conducted by Pacioles-Flavier and

Aguilar [21] among 70 Filipinos diagnosed with PCOS at the Philippine General Hospital—a public tertiary hospital—the mean mFG score was 8. Compared to that study, the lower hirsutism score observed in the present study could be due to the different patient populations at the two institutions.

In addition, specific body areas were also shown to have significantly higher mFG scores in the PCOS group than in the non-PCOS group. These sites were the upper lip, upper back, upper and lower abdomen, and thighs. These findings are similar to those of a large cross-sectional study conducted in China in which the strongest contributors to the total mFG score were the upper lip, lower abdomen, and thighs [14]. Thus, these areas should be examined thoroughly in Filipino women. Future studies are warranted to determine the accuracy of these areas in defining hirsutism, which may further simplify the use of the mFG visual scoring tool.

Measuring FT levels is ideal for the diagnosis of hyperandrogenism, but measurements by direct radioimmunoassay, which was the method used in our setting, are highly inaccurate and does not reflect actual unbound testosterone levels. The most accurate method of measuring FT is directly via equilibrium dialysis. However, this method is expensive, tedious, and not widely available, which makes it impractical for use in clinical settings. Current guidelines recommend instead calculating FT based on accurate measurements of TT and SHBG [2]. In our setting, measurement of FT by equilibrium dialysis was unavailable; hence, we opted to measure TT and SHBG, and then subsequently compute FAI and calculated FT as surrogate markers of free testosterone. In this study, only elevated calculated FT (OR, 6.2; 95% CI, 1.2 to 32.4 pmol/L; $P=0.030$) was significantly associated with a total mFG score of ≥ 7 . Calculated FT is a simple and reliable index of bioavailable testosterone and is comparable to FT as determined via equilibrium assay [15]. Although hirsutism scores have been shown to have a poor correlation with serum androgen levels, it is also known that serum FT levels are still higher in hirsute women than in non-hirsute women, and high serum FT remains a potential indicator of an underlying hyperandrogenic disorder [3]. Our findings showed that hirsute women, or those with a total mFG score of ≥ 7 , were six times more likely than non-hirsute women to have elevated calculated FT; thus, in such patients, further investigation into the underlying cause is warranted.

Since this is a pilot study, a limitation is that it was performed at a single center. A multi-center study could be performed to validate the findings of the present study and to ensure that they are reflective of the general Filipino population.

In conclusion, among normal Filipino women, the fifth to 95th percentile of total mFG scores fell between 0 and 7. Thus, a total mFG score of 7 or higher represented hirsutism in this population. This cut-off score was significantly associated with calculated FT, and Filipino women with a total mFG score of 7 and above were six times more likely than non-hirsute women to have elevated calculated FT.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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AUTHOR CONTRIBUTIONS

Conception or design: M.K.C.C.I., E.P.P. Acquisition, analysis, or interpretation of data: M.K.C.C.I., E.P.P., D.Z.T., L.R.C.C., J.R.K.J. Drafting the work or revising: M.K.C.C.I., E.P.P. Final approval of the manuscript: M.K.C.C.I., E.P.P.

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