



Lipid Accumulation Product as an Index for Visceral Obesity and Cardiovascular Risk among a Sample of Obese Egyptian Women

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Abstract

BACKGROUND: Lipid accumulation product (LAP) is one of the indices that can demonstrate cardiovascular risk factors according to international studies.

AIM: The aim of the study was to evaluate relationship between LAP, visceral obesity, and different cardio vascular risk factors among sample of obese Egyptian Women.

METHODS: A retrospective cross-sectional observational study included 350 obese Egyptian women; aged 25–55 years. They were subjected to blood pressure (BP) and anthropometric assessment (weight, height, and waist circumference [WC]), abdominal ultrasound (visceral fat), and laboratory tests (fasting blood sugar and lipid profile).

RESULTS: The majority of the participated women had wide WC (88.9%) and increased visceral fat (80.6%). Hyperglycemia was present among (47.4%), hypertension among 42.6%, high triglycerides among 26.6%, and low high-density lipoprotein among 44.3%. The odds of obtaining LAP >80.74 cm.mmol/L (4th quartile) are 2.7 times higher in individuals with hypertension (blood BP >130/85), and 6.79 times higher in individuals with visceral fat ≥5 cm. Depending on the visceral fat as a standard for classification of visceral obesity (>5 cm for women), revealed that the area under the curve of LAP was 0.752 (95% Confidence interval 0.697–0.806) in women. The cutoff point of LAP; for prediction of visceral obesity among Egyptian women, was 61.69; using receiver operating characteristic analysis; with sensitivity 68% and specificity 75% and positive predictive value/negative predictive value 1.05 and accuracy 71.5%.

CONCLUSION: LAP index had significant correlations with visceral obesity and hypertension. The cutoff point of LAP 61.69 can be used to predict visceral obesity among Egyptian women.

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Introduction

Obesity is the fifth leading cause of death worldwide. It is a documented risk factor for large number of metabolic abnormalities as insulin resistance, dyslipidemia, higher levels of blood pressure (BP), and cardiovascular diseases (CVD) [1].

Approximately 80% of all body fat is distributed subcutaneously, accumulated largely at gluteo-femoral regions, at the back and at anterior abdominal wall. The visceral fat represents only 10–20% of the total amount of fat in male and 5–8% in females [2]. Abdominal obesity, in particularly high visceral fat, plays a crucial role in the evolution of metabolic and CVD independent of generalized obesity [3].

Multiple anthropometric measurements are used regularly for assessment of obesity such as body mass index (BMI), waist circumference (WC), and waist-to-hip ratio, but most of them cannot distinguish between visceral fat and subcutaneous fat [4].

Recently, mathematically calculated indices have been considered reliable and effective [5]. These

methods are considered more applicable options, as they include formulas and biochemical measures that enable medical practice and research to enquire better tracking and risk factors prevention [6].

Lipid accumulation product (LAP) is one of these indices. It is described in the literature as sensitive and specific markers for assessment of visceral fat compared to other traditional parameters including WC and BMI. It is calculated as a combination of WC and fasting triglyceride (TG). Its superiority is the simultaneous reflection of the anatomical and physiological changes of fat over accumulation in adults. According to international studies, LAP can demonstrate risk factors associated with CVD fairly well [7].

In clinical practice, imaging modalities including computed tomography (CT) and magnetic resonance imaging are considered the gold standards for assessment of visceral and subcutaneous fat. Their high costs and radiation exposure in case of CT enormously limit their widely use in medical field. Therefore, it is crucial to establish a simple and effective method for the assessment of visceral obesity in adults [8].

Ultrasound (US) is considered one of the most vital methods for assessing fatty body layers [9]. It is considered cheap, non-invasive, reliable, and sensitive method to estimate the visceral fat making it excellent for visceral fat assessment in all population [10].

Aim of this work

The aim of this work was to evaluate the relationship between LAP, visceral fat measurement and different cardiovascular risk factors among a sample of obese Egyptian Women.

Subjects and Methods

Study subjects

This study is retrospective cross-sectional observational study started by screening a total of 598 Egyptian women, with age ranged between 25 and 60 years who visited "Management of visceral obesity and growth disturbance unit" in the "Medical Excellence Research Centre," National research Centre, Egypt. Those with incomplete medical histories or medication records, those with chronic diseases other than hypertension or diabetes, and those who had previously received cancer treatment or were diagnosed with cancer were excluded from the study. From them, 350 obese Egyptian women, were studied for evaluation of "Visceral and Central Obesity as an Early Estimator for Obesity Health Risk: Management and Intervention." The participants were recruited from the employee in the "National Research Centre." Participants were informed about the purpose of the study and their permission in the form of written informed consent was obtained. The protocol was approved by the "Ethical Committee" of the "National Research Centre." The agreement reference number is 10/119.

All participants subjected to full clinical examination, BP, anthropometric assessment, abdominal US, and laboratory tests:

BP was measured on the right arm after 10 min of rest using an automatic BP measurement device (BP-8800C; Colin Electronics Co., Ltd., Aichi, Japan). The BP measurement was repeated if the systolic BP (SBP) was >140 mmHg or the diastolic BP (DBP) was >90 mmHg. Average SBP and DBP were recorded.

Anthropometric evaluation

Anthropometric measurement was performed by trained personnel. Height, weight, waist, and hip circumferences were measured following the recommendations of the International Biological Program [11]. Height was measured to the nearest

0.1 cm using a Holtainportable anthropometer, and weight was determined to the nearest 0.01 kg using a Seca Scale Balance, with the subject wearing minimal clothing and no shoes. WC was measured at the level of the umbilicus with the subject standing and breathing normally, the face directed forward and shoulders relaxed using non-stretchable plastic tape to the nearest 0.1 cm. The BMI was calculated:

BMI as weight (in kilograms) divided by height (in meters²)

Abdominal US

US examination to each participant was done to evaluate visceral fat at the umbilicus (USVF) in cm. Intra-abdominal fat thickness measurement was obtained using the "MedisonSonoace X8" ultrasonography equipment. For visceral fat measurement, a 3.5 MHz transducer was transversely positioned 1 cm above the umbilical scar on the abdominal midline, without exerting any pressure over the abdomen. Visceral fat thickness attempted corresponding to the measurement in centimeters between the internal surface of the rectus abdominis muscle and the anterior aortic wall in the abdominal midline, during expiration. These parameters were based on the previous methodological descriptions [12].

Blood tests

Participants were fasted for at least 12 h; to get blood sample once for analysis of both FBS and lipid profile; and a blood sample was collected and analyzed under fasting conditions. The blood samples were left to clot; sera were separated by centrifugation for 10 min at 5000 rpm then stored at -80°C until assays. Serum concentration of fasting glucose, total cholesterol [13], TGs [14], and high-density lipoprotein-cholesterol (HDL-C) [15] was measured using commercially available kits provided by STANBIO Laboratory Inc. (1261 North Main Street Boerne Texas 78006 USA). Then total cholesterol/HDL-C ratio was calculated. Low-density lipoprotein-cholesterol (LDL-C) was calculated according to an equation developed by Friedewald [16] as follows:

$$\text{LDL-C} = \text{Total cholesterol} - \text{TGs}/5 + \text{HDL-C}$$

The LAP was categorized by quartiles and analyzed the relationship.

Definition of cardio vascular risk factors

The cardio vascular risk factors were defined; according to the modified National.

Cholesterol Education Program Adult Treatment Panel III [17]; as follow: WC >88 cm (for women), fasting blood sugar (FBS) >100 mg/dL; BP >130/85 mmHg; serum TG >150 mg/dL; and serum HDL-cholesterol <50 mg/dL (for women). These factors

were referred to as visceral obesity, hyperglycemia, high BP, high TG, and low HDL-C, respectively.

Defining the LAP

LAP is defined and calculated as follows [18]:

LAP for women=(WC [cm]-58)×(TG concentration [mmol/L])

N.B.: For TGs, to convert from mg/dL to mmol/L multiplies by 0.01129.

Statistical analysis

All statistical analyses were conducted with the Statistical Package for the Social Sciences (SPSS/Windows Version 18, SPSS Inc., Chicago, IL, USA). *P*-values of all the reported results were two-tailed, and the significance level was set at $p > 0.05$. Normality of data was tested using the Kolmogorov-Smirnov test, and they were not normally distributed. Descriptive statistics was expressed as mean \pm standard deviation. The participated women were divided into two groups according to the presence or absence of each cardiovascular risk factor (hypertension, high TG, low HDL-C, hyperglycemia, visceral obesity at umbilicus, and smoking). These categorical variables were expressed as numbers and percentages, and compared by using the Chi-square test.

The spearman's correlation was used to examine the significance of linear association between LAP and visceral fat on one side and the different variables. Calculation of the 4th quartile of LAP was done. The risk of presence of the 4th quartile of LAP according to the presence of different cardiovascular risk factors was examined using odd ratio, 95th confidence interval (CI) and Chi-square test. The predictive accuracy of LAP in identifying women with visceral obesity; diagnosed by US; was examined using a receiver operating characteristic (ROC) curve to assess the area under the curve (AUC), sensitivity, and specificity. Negative and positive predictive values (PPV/NPV) were calculated. Sensitivity was calculated as true-positives/(true-positives + false-negatives); specificity as true negatives/(true-negatives + false-positives). Maximal accuracy and PPV/NPV closest to 1 were used for cutoff level determination

Results

This study included 350 Egyptian obese women, aged 25 up to 60 years; their mean age was 43.4 ± 9.4 years. In respect to the cardiovascular risk indicators, the mean BP was within the prehypertensive level (SBP, 128.15 ± 19.10 mmHg; DBP,

83.41 ± 11.98 mmHg), and the means for lipid profile were within the normal levels (TG: 122.66 ± 54.29 mg/dL, HDL: 53.44 ± 23.34 mg/dL). While, the mean BMI (37.57 ± 7.13 kg/m²), WC (104.22 ± 13.95 cm), FBS ($103.76 + 37.83$), and visceral fat ($6.20 + 2.16$ cm) were above the normal level. The mean LAP was 63.95 ± 37.92 (Table 1).

Table 1: Base line characteristics of the study participants

Variables	Obese women (n=350)			
	Mean	SD	Minimum	Maximum
Age (years)	43.41	9.41	25	60
Blood pressure (mm Hg)				
SBP	128.15	19.10	90	200
DBP	83.41	11.98	60	130
Anthropometric				
BMI (Kg/m ²)	37.57	7.13	25	57
WC (cm)	104.22	13.95	37	145
Lab				
FBS (mg/dL)	103.76	37.83	60	265
Triglycerides (mg/dL)	122.66	54.29	40	316
Cholesterol (mg/dL)	201.98	47.33	50	381
HDL (mg/dL)	53.44	23.34	18	187
LDL (mg/dL)	129.27	44.05	27	260
Triglycerides/HDL	2.62	1.42	0	7.06
Cholesterol/HDL	4.16	1.32	0	8.1
LDL/HDL	2.66	1.15	0	5.9
LAP (cm.mmol/L)	63.95	37.92	-8.13	254.4
US findings				
VF at umbilicus (cm)	6.20	2.16	0.7	12.5

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, BMI: Body mass index, WC: Waist circumference, FBS: Fasting blood sugar, HDL-C: High-density lipoprotein-cholesterol, LDL-C: Low-density lipoprotein-cholesterol, LAP: Lipid accumulation product, US: Ultrasound, VF: Visceral fat.

The majority of the participated women had wide WC (88.9%) and increased visceral fat (80.6%), while half of them were smokers (48.8%) and had hyperglycemia (47.4%). Hypertension was present among 42.6% of them, high TG among 26.6% and low HDL among 44.3% of them (Table 2).

Table 2: Frequency distribution of the components of cardiovascular risk factors by sex

Variables	Normal Range	Women (n = 350)	
		n	%
Hypertension	SBP/DBP>130/85 mmHg	149	42.60
Hyperglycemia	>100 mg/dL	171	47.4
High TG	>150 mg/dL	96	26.6
Low HDL	<50 mg/dL	155	44.3
Wide WC	>88 cm (women)	321	88.9
Visceral fat	>5 cm	282	80.6
Smoking	>3 cigarettes/day	176	48.8

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, TG: Triglycerides, HDL-C: High-density lipoprotein-cholesterol, WC: Waist circumference.

Spearman's correlation test revealed that LAP had highly significant positive correlations with systolic and DBP, BMI, WC, TG, total cholesterol, TG/ HDL, cholesterol/HDL and visceral fat at umbilicus, and significant positive correlation with age (Table 3). While visceral fat at umbilicus had highly significant positive correlations with age, systolic and DBP, BMI, WC and LAP, and significant positive correlation with TG.

The LAP was categorized by quartiles and analyzed the relationship between the 4th quartile of the LAP (the highest values) and the different cardiovascular risk variables. Compared to that in individuals with BP <130/85, the odds of obtaining LAP >80.74 cm.mmol/L (4th quartile) is 2.7 times higher in individuals with BP >130/85 ($p < 0.000$). Furthermore, the odds of obtaining a LAP >80.74 was 6.79 times higher in individuals with visceral fat ≥ 5 cm compared to that in

Table 3: Spearman s correlations between LAP, visceral fat, and different cardiovascular risk factors

Variables	LAP		Visceral fat (VF)	
	r	p	r	p
Age (years)	0.116*	0.033	0.180**	0.001
Blood pressure (mmHg)				
SBP	0.235**	0.000	0.267**	0.000
DBP	0.227**	0.000	0.256**	0.000
BMI (Kg/m ²)	0.439**	0.000	0.599**	0.000
WC (cm)	0.609**	0.000	0.629**	0.000
Lab				
FBS (mg/dL)	0.066	0.229	0.032	0.558
Triglycerides (mg/dL)	0.821**	0.000	0.129*	0.017
Cholesterol (mg/dL)	0.154**	0.005	0.084	0.123
HDL (mg/dL)	-0.060	-0.280	0.074	0.173
LDL (mg/dL)	-0.030	-0.589	0.023	0.673
Triglycerides/HDL	0.730**	0.000	0.096	0.080
Cholesterol/HDL	0.145**	0.008	0.041	0.452
LDL/HDL	0.001	0.988	0.000	0.999
LAP (cm.mmol/L)			0.411**	0.000
US findings				
VFA at umbilicus (cm ²)	0.412**	0.000		

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, BMI: Body mass index, WC: Waist circumference, FBS: Fasting blood sugar, HDL-C: High-density lipoprotein -cholesterol, LDL-C: Low-density lipoprotein-cholesterol, LAP: Lipid accumulation product, US: Ultrasound, VF: Visceral fat. p<0.05= significant difference, p<0.01= highly significant difference

individuals with visceral fat <5 cm (p < 0.000). Moreover, the results showed that the presence or absence of hyperglycemia or low HDL was insignificantly associated with the LAP (Table 4).

Table 4: Risk of LAP (>80.74) according to the different cardiovascular risk factors

	OR	95% CI	p	
Hypertension	2.702	1.608	4.540	0.000**
High TG	34.244	17.626	66.532	0.000**
Low HDL	1.482	0.903	2.433	0.119
Hyperglycemia	1.394	0.852	2.281	0.187
VF at umbilicus (cm)	6.785	2.391	19.256	0.000**
Smoking	0.283	0.077	1.037	0.044*

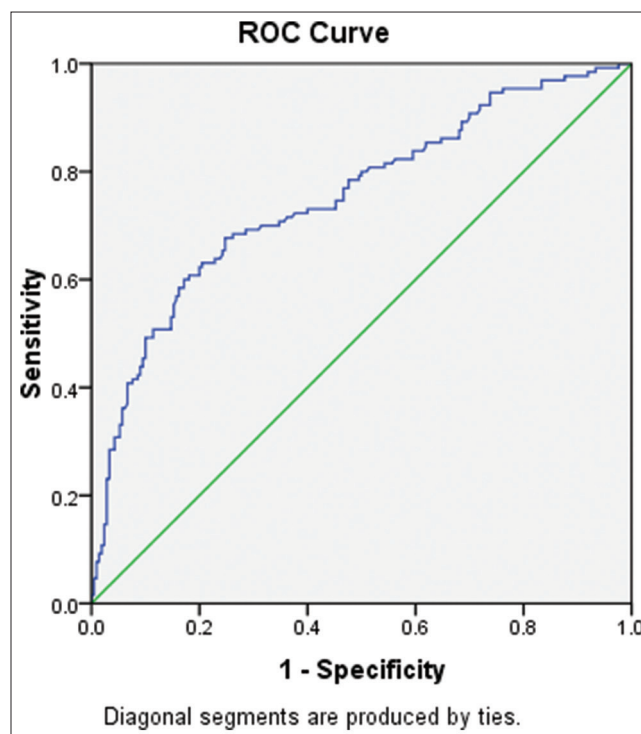
TG: Triglycerides, HDL-C: High-density lipoprotein-cholesterol, VF: Visceral fat. p<0.05= significant difference, p<0.01= highly significant difference

Depending on the visceral fat as a standard for classification of visceral obesity (>5 cm for women), revealed that the AUCs of LAP was 0.752 (95% CI 0.697–0.806) in women with statistical significance (p = 0.000) (Figure 1). The cutoff point of LAP was found to be 61.69 for centrally obese women; using ROC analysis; with sensitivity 68% and specificity 75% and PPV/NPV 1.05 and accuracy 71.5%

Discussion

Obesity is a significant public health problem with a reduced quality of life, multiple comorbidities, and multicausal mortality [19]. The frequency of obesity related cardiovascular risk factors has significantly increased both in developing and developed countries [20]. In defining obesity and its relevance in predicting cardiovascular risks, concern has changed from central obesity to visceral obesity [21].

Multiple indices are used to determine general and central obesity in clinical practice. Although BMI is the most widely used parameter for assessment of obesity, it is an indicator of general obesity rather



Area Under the Curve				
Test Result Variable (s):Lipid Accumulation Product				
Area	Std. Error ^a	Asymptotic Sig. ^b	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
0.752	0.028	0.000	0.697	0.806

Figure 1: Receiver operating characteristic curve for lipid accumulation product to identify visceral obesity among Egyptian women. The area under the curve is 0.752 (p < 0.000) with 95% confidence intervals ranged between 0.697 and 0.806. The straight line is the line of identity, corresponding to an area under the curve of 50%

than central obesity [22]. Clinicians are encouraged to use BMI and WC as monitoring tools for assessment of obesity in adults and children [19]. WC is better than BMI in evaluating visceral fat distribution and in anticipating CVD [22].

The LAP is one of the anthropometric indices that is built on a combination of two low-cost measurements, WC and serum TG implicating an over accumulation of lipids over time [1]. LAP can surmount BMI in the anticipation of CVD risk with positive correlation between it and long-standing CVD incidence in CVD-free Caucasian adults as documented by Kyrou [23].

Studies have shown that LAP Index is linked with hypertension, type-2 diabetes mellitus (T2DM), metabolic syndrome, and CVD. Most of these studies suggest that LAP is a strong indicator for prediction of a worse metabolic profile and CVD when matched with other long used anthropometric indices [1].

In the current study, LAP and visceral fat at umbilicus had highly significant positive correlations with BMI and WC. Evans [24] study showed that LAP index is a more sensitive tool than BMI and WC in the anticipation of cardio-metabolic risk among T2DM patients. Similar results were documented by Gao [25].

Measurements of visceral fat area of the abdomen were evaluated thoroughly for its value in anticipating the presence of cardiovascular risk factors [21]. CT is considered to be the “golden standard,” being able to exactly differentiate visceral fat from subcutaneous fat in anybody region. However, its great cost, the necessity of sophisticated machine, expert people and the exposure of the individual to radiation are the main restrictions for its use in routine practice and in observational studies [26]. US is considered one of the most hopeful methods for assessment of fat layers in the body [9].

There have been many studies on LAP and chronic metabolic and cardiovascular diseases, but the relationship between LAP and visceral fat measurement needs further assessment. Moreover, an index such as LAP can have different results based on ethnicity, and this study is valuable because it analyzes the relationship between LAP, visceral fat measurement and cardiovascular risk factors in Egyptian adults.

Hypertension is one of the most critical public health problems worldwide with an increased prevalence in last year’s [27]. It is considered as a leading risk factor for CVD [28]. High levels of visceral fat were observed in males and females suffering from arterial hypertension [2].

In current results both LAP and visceral fat at umbilicus had highly significant positive correlations with systolic and DBP. Ian [8] found a significant relationship between LAP and hypertension risk in Han Chinese adults. Similar results were found in Japanese population done by Wakabayashi [29] in Mongolians population by Gao [25].

The TG/HDL-C ratio is an unsophisticated tool to ascertain patients at increased risk for insulin resistance and CVD. It is used to determine subjects at risk and vary across ethnicity and race [7]. Ioachimescu [30] and Bruna [1] also detected correlations with LAP Index and fasting glucose, HDL-C and SBP in both general population and in patients at higher cardiovascular risk. In the current study, LAP had highly significant positive correlations with TG, total cholesterol, TG/HDL, and cholesterol/HDL.

Obesity is intimately related with a higher incidence of type 2 diabetes and is associated with the development of diabetic complications [31]. It has been found that subjects with increased visceral fat have greater degree of insulin resistance [32]. Visceral fat is considered a metabolically active endocrine organ, secreting multiple pro-inflammatory adipokines with subsequent occurrence of a number of cardio-metabolic disorders [32]. LAP can be used as a non-invasive tool for assessing insulin resistance and diabetes as it can reflect visceral fat accumulation [33].

Pontes [34] conducted that LAP was a better indicator of glucose imbalance and a stronger predictor

of DM than BMI. Flavia [35] had confirmed that LAP is sensitive to identify impairment related to glucose metabolism even after correction for drug use. However, in our study, the results showed that the presence or absence of hyperglycemia is insignificantly associated with the LAP.

Freedman [36] and Snijder [37] have found that visceral obesity determined by WC is more strongly associated with cardiovascular risk factors than BMI. Porter [38] and McLaughlin [39] identified that several CVD risk factors, including hypercholesterolemia and low HDL-C, were associated only with VAT volume change but not with SAT volume change. Our outcome documented that visceral fat at umbilicus had highly significant positive correlations with TG and LAP.

In many populations, the body composition differs substantially according to several ethnics, and most of the studies that evaluated LAP Index were made among Americans, European, and Eastern people. In this study, we use 5 cm as the best cutoff points of measurement of visceral fat by US for women as concluded by Hassan [40] study done on a sample of adult Egyptian women. We use it to document the cutoff of LAP among our subjects.

Wakabayashi [29] 2014 evaluated 10,170 Japanese workers (35–40 years old) and proposed cutoff values for the LAP index of 21.1 cm.mmol/l and 37.2 cm.mmol/l for women and men, respectively.

Nascimento [41] found a high cutoff point through using an ROC curve in a cross-sectional study conducted on 78 women aged 18–42 years who presented polycystic ovarian syndrome and were attended at a university hospital in Brazil. They showed that all cardiovascular risk markers presented a higher chance of being altered when the LAP index was above the cutoff value of 37.9 cm.mmol/l. This higher value may have been found because women with polycystic ovarian syndrome already present higher cardiovascular risk than that of the general population. Finally, in a regional hospital in southern Taiwan, Chiang [42] evaluated 513 individuals and showed that the optimal cutoff for the LAP index was 28.4 cm. mmol/l, for both sexes.

The cutoff point of LAP in our study was found to be 61.69 cm.mmol/l for centrally obese women with sensitivity 68% and specificity 75% and accuracy 71.5%.

In conclusion, the results from the present study showed that the LAP index presented good correlations with visceral fat and cardiovascular risk factors. The cutoff point of LAP 61.69 can be used to predict visceral obesity among Egyptian women.

It proves the assumption that it is a practical indicator for detecting interactions between excess body fat and its related risk factors. Therefore, it will be helpful in primary medical care services that face

financial difficulty that hinder access to cardiovascular risk markers.

Limitation of this study

This study was done on women only. In future, further research should be done on men, to have equation for each sex.

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Author Contribution

Nayera E. Hassan and Mohamed S. El Hussieny, designed the study; Nayera E. Hassan, supervisor on anthropological assessment; Sahar A. El-Masry performed the statistical analysis and publication process; Mohamed S. El Hussieny responsible for radiological assessment of visceral obesity; Gamila S. M. El-Saeed responsible for laboratory investigations. All authors contributed to the collection of references, drafting of the article, and final approval of the version to be submitted. All the authors have accepted responsibility for the entire content of this submitted manuscript and approved submission.

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