Eastern Cooperative Oncology Group Performance Status Scale as a Screening Tool for Sarcopenia in Onco-Hematology Patients

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Abstract

The present study aimed to assess the sensitivity of the Eastern Cooperative Oncology Group Performance Status (ECOG-PS) scale for scores other than 0 as a screening tool for sarcopenia in onco-hematology patients. A retrospective cohort study of 104 onco-hematology patients aged >19 years and treated at the Diagnostic and Imaging Center and at an outpatient clinic of a private tertiary hospital was conducted. Sarcopenia was defined as a skeletal muscle index (SMI) of $\leq 38.5\,cm^2/m^2$ for women and $\leq 52.4\,cm^2/m^2$ for men based on positron emission tomography-computed tomography scans. Functional status was assessed using an ECOG-PS score of 0 (indicating no dysfunction) or a score of ≥ 1 (indicating dysfunction). Accuracy analysis was conducted to determine the sensitivity and specificity of the ECOG-PS as a screening tool for sarcopenia. Sarcopenia was observed in 57.7% of patients. The median SMI was 43.3 (55.1) kg/m^2. Sarcopenia diagnosis was positively associated with male sex ($p = 0.027$) and an ECOG-PS score of ≥ 1 ($p = 0.048$). As a screening tool for sarcopenia, the ECOG-PS had sensitivity and specificity of 40.7% (95% confidence interval [CI] 30.6–50.8) and 83.8% (95% CI 75.1–92.9), respectively. Sarcopenia is a challenge in cancer. The association of sarcopenia with an ECOG-PS score of ≥ 1 observed in this study reinforces the study hypothesis and importance of further studies on the subject.

Keywords
- hematology
- sarcopenia
- physical functional performance
- nutritional status

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Introduction

Currently defined by the European Working Group on Sarcopenia in Older People (EWGSOP2) as a progressive and generalized skeletal muscle disorder associated with increased likelihood of adverse outcomes, sarcopenia is a formally recognized muscle disease with an International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM]M62.84]) diagnosis code.[1] A prognostic factor consistently reported in the literature as potentially modifiable for adverse clinical outcomes in solid tumors,[2–7] some studies also indicate that sarcopenia has an impact on hematologic cancer, showing an association with lower overall survival in patients diagnosed with non-Hodgkin lymphoma and undergoing chemotherapy.[8,9] In patients submitted to hematopoietic stem cell transplantation (HSCT), sarcopenia can be associated with lower overall survival and higher non-relapse mortality.[10]

Computed tomography (CT) of the third lumbar vertebra level is the gold standard for assessing muscle mass and diagnosing sarcopenia in patients with cancer,[1,11] although positron-emission tomography-CT (PET-CT) can also be used since it is often performed in cases of hematologic diseases.[12,13] However, such tests are not usually requested to assess body composition alone and have a high cost, thus preventing the adequate follow-up of patients in all institutions and on a routine basis.[14] Moreover, given the importance of detecting sarcopenia in patients with hematologic cancer, screening tools with adequate sensitivity and specificity that are affordable and feasible in different institutions are essential and can guide the diagnostic process in clinical practice.

Currently, the EWGSOP2 proposes the use of the Strength, Assistance with walking, Rising from a chair, Climbing stairs, and Falls (SARC-F) questionnaire as a screening tool for sarcopenia in clinical practice.[1,15,16] Although it has low-to-moderate sensitivity (3–10%) and high specificity (94–99%), this tool can efficiently predict more severe sarcopenia cases and was validated for the elderly population.[17]

Functional and self-care capacity are potentially compromised in sarcopenia and are assessed in clinical practice using tools such as the functional status scale proposed by the Eastern Cooperative Oncology Group Scale of Performance Status (ECOG-PS), which ranges from 0 (asymptomatic, fully active) to 5 (death).[18–20] Since previous studies have shown an association of ECOG-PS scores with cancer outcomes,[21,22] the feasibility and validity of the ECOG-PS for an early sarcopenia screening have been debated, particularly in cases of anemia, a frequent condition in onco-hematology patients and potentially harmful in those with sarcopenia.[23–26]

Considering the above, the objective of the present study was to assess the sensitivity of the ECOG-PS with scores other than 0 as a screening tool for sarcopenia and to characterize the prevalence of sarcopenia as well as the factors associated with it in onco-hematology patients, according to ►**Fig. 1**.

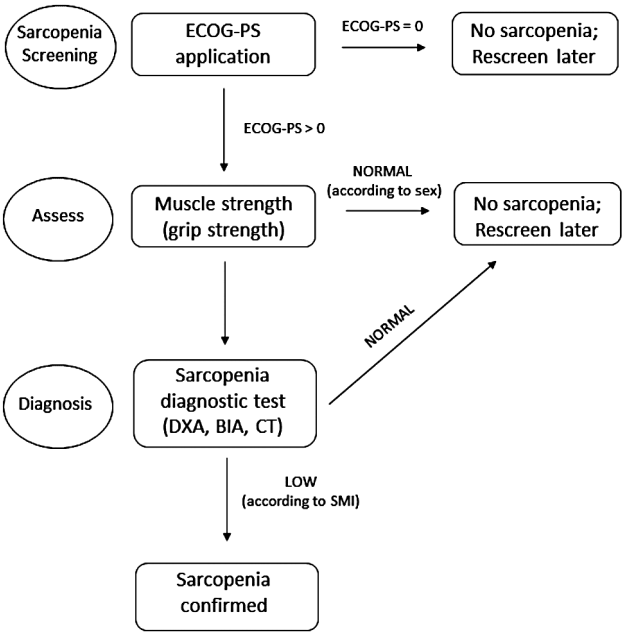

Fig. 1 Proposed flowchart for screening and diagnosis of sarcopenia. **Abbreviations:** DXA, dual X-ray absorptiometry; BIA, bioelectrical impedance analysis; CT, computed tomography.

Materials and Methods

Study Design

This was a retrospective cohort study that included patients diagnosed with hematologic cancer and treated at the Diagnostic and Imaging Center and at an outpatient clinic at the Oncology Center of a private tertiary hospital in São Paulo.

Sampling

A consecutive sample was obtained by searching institutional electronic health records. The outpatient electronic agenda of all hematologist physicians affiliated with the institution was accessed, and all patients who underwent treatment at the above-mentioned clinics between January 2019 and May 2021 were screened for potential inclusion in the current study.

Patients diagnosed with onco-hematologic diseases, adults (aged >19 years), and the elderly (aged ≥ 60 years), with data available on the ECOG-PS functional status scale, within a maximum time interval of 1 week in relation to PET-CT and the hemoglobin (Hb) test, were included. The ECOG-PS was collected by the medical team on the day of the clinical follow-up and at different stages throughout the follow-up, as listed in the results. Patients who had undergone hematopoietic stem cell transplant (HSCT) within a period of <1 year were excluded due to the preexistence of institutional protocols for periodic nutritional and body composition assessment of the patients according to the available literature.[27,28]

Overall, 1,254 patients were observed by the team of hematologists from January 2019 to May 2021. Of these, 1,144 were not eligible, including those with age <19 years

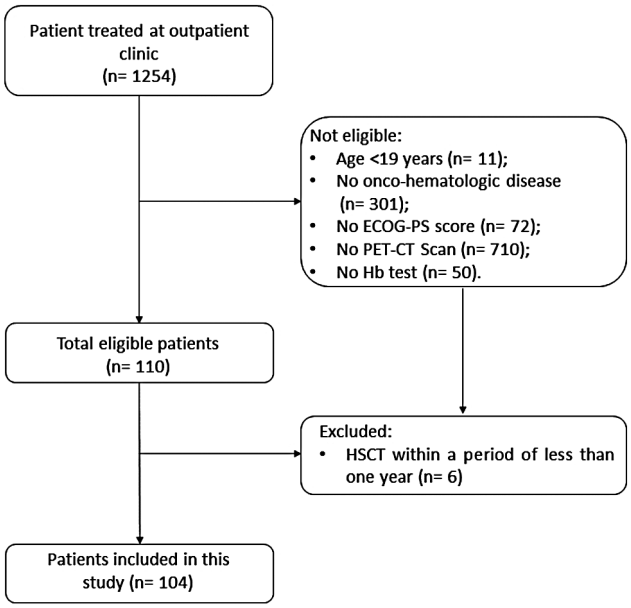

Fig. 2 Flowchart of the sampling of 104 onco-hematology patients. **Abbreviation:** n, number.

(n = 11), those with no onco-hematologic disease (n = 301), without an ECOG-PS score (n = 72), without PET-scan (n = 710), and without a biochemical hemoglobin (Hb) test result (n = 50), thus resulting in a total of 110 patients. Subsequently, 6 patients were excluded due to previous HSCT within a period of < 1 year in relation to the available PET-CT image. Therefore, 104 patients were included in the study as depicted in ►**Fig. 2**, with a total of 159 PET-CT images. All images were considered suitable for assessing body composition and diagnosing sarcopenia.

Data Analysis

The body mass index (BMI) was categorized according to the World Health Organization (WHO)[29] criteria for adults and the Pan American Health Organization[30] criteria for the elderly. Serum Hb levels were categorized according to the WHO's references for non-pregnant women and men aged ≥ 15 years.[31]

Body composition was assessed by analysis of the cross-sectional area (cm^2) resulting from the sum of the psoas, paraspinal, and abdominal wall muscles in the third lumbar vertebra (L3) region by a trained radiologist using the 3D Slicer software (version 4.7.0-2017-04-04 r25903). The total transverse muscle area measured in the analysis in the L3 region is linearly related to whole-body muscle mass[7] and was adjusted using the patient's height squared (m^2) to then calculate the skeletal muscle index (SMI, cm^2/m^2). Sarcopenia was defined as an SMI of ≤ 38.5 cm^2/m^2 for women and ≤ 52.4 cm^2/m^2 for men,[7,11,32] based on a Canadian population and CT scans, since no specific and validated values were available for the Brazilian population. The SMI was calculated three times for each PET-CT image by the same radiologist, with subsequent calculation of the mean to minimize possible intraobserver variations.

Statistical Analyses

Two different databases were used in the present study, depending on the objective of the analysis.

Information obtained from a database on the 104 patients observed by the team of hematologists from January 2019 to May 2021 was used to assess the prevalence of sarcopenia in patients with PET-CT images, ECOG-PS scores, and biochemical Hb test results in the relevant period and to assess factors associated with the diagnosis of sarcopenia. In the current study, the date of the last medical appointment was standardized for patients who had more than one appointment in the analyzed period.

An image database related to the 159 PET-CT images collected from 104 patients was used to assess the sensitivity, specificity, and positive and negative predictive values of the ECOG-PS as a screening tool for sarcopenia.

Descriptive statistical analysis was performed for all variables. Categorical data were presented as percentages, and continuous data as medians and intervals.

The Shapiro-Wilk test was applied to determine whether the data set followed a normal distribution. Inferential analysis of the association of a sarcopenia diagnosis with the qualitative or categorical variables of the current study was performed using the Chi-squared or Fisher's exact test.

The association of a sarcopenia diagnosis with the other variables was investigated in a final model that was developed by stepwise regression, adjusting for patient-related variables included in the univariate analyses. The level of significance for all the analyses was 5%, and all statistical analyses were performed using the IBM SPSS Statistics for Windows (IBM Corp., Armonk, NY, USA) software, version 22.0.

The ECOG-PS was stratified by score, either 0 or ≥ 1, according to the description of the functional status.[18–20]

Results

The results of the descriptive analysis of the 104 patients are summarized in ►**Table 1**.

The ECOG-PS was collected during outpatient follow-up visits and, for patients with more than one appointment within the analyzed period, the score from the most recent visit was considered for the following results. During this period, 71 patients (68.3%) were not undergoing treatment, and, of these, 39.4% were at the time of diagnosis.

The prevalence of sarcopenia was 57.7%, while 71.2% of the patients were classified based on the ECOG-PS as being without functional impairment.

An ECOG-PS score of ≥ 1 was significantly associated ($p = 0.016$) with a sarcopenia diagnosis when considering a level of significance of 5%.

►**Table 2** shows the results of the univariate and final regression model.

The univariate analysis showed that age ≥ 60 years, male sex, targeted therapy for cancer, and an ECOG-PS score of ≥ 1 were positively associated with a sarcopenia diagnosis. A higher body mass index (BMI) value was negatively associated

Table 1 Descriptive analysis of the 104 onco-hematology patients included in the study

		Sarcopenia	
	Total	**n (%)**	***p***
Number of patients	104		
Age (years): mean(± SD)	56.3(± 74.0)		
Age group: n (%)			
Elderly	48 (46.2)	36 (75.0)	< 0.01
Adult	56 (53.8)	24 (42.9)	
Sex: n (%)			
Male	70 (67.3)	46 (65.7)	0.021
Female	34 (32.7)	14 (41.2)	
Diagnosis: n (%)			
Lymphoma	79 (76.0)	43 (54.4)	0.209
Leukemia	8 (7.7)	7 (87.5)	
Others	17 (16.3)	10 (58.8)	
Disease status on PET scan: n (%)			
Not active/CR	55 (52.9)	32 (58.2)	0.830
Active	37 (35.6)	20 (54.1)	
Missing	12 (11.5)		
Treatment: n (%)			
No treatment	71 (68.3)	38 (53.5)	0.049
Targeted therapy[a]	15 (14.4)	13 (86.7)	
Chemotherapy	15 (14.4)	7 (46.7)	
Missing	3 (2.9)		
Corticosteroid use: n (%)			
No	91 (87.5)	54 (59.3)	1.00
Yes	5 (4.8)	3 (60.0)	
Missing	8 (7.7)		
Hemoglobin (g/dL): mean(± SD)	12.7(± 8.8)		
Anemia classification: n (%)			
Normal	62 (59.6)	30 (48.4)	0.092
Mild	24 (23.1)	16 (66.7)	
Moderate	15 (14.4)	11 (73.3)	
Severe	3 (2.9)	3 (100.0)	
BMI (kg/m^2): mean(± SD)	26.2(± 23.1)		
BMI classification: n (%)			
Underweight	5 (4.8)	4 (80.0)	< 0.01
Normal range	38 (36.5)	31 (81.6)	
Overweight	27 (26.0)	7 (25.9)	
Obese	12 (11.5)	5 (41.7)	
Missing	22 (21.2)		
SMI (kg/m^2) mean(± SD)	43.3(± 55.1)		
Prevalence of sarcopenia: n (%)	60 (57.7)		

Table 1 (*Continued*)

		Sarcopenia	
	Total	**n (%)**	***p***
ECOG-PS score: n (%)			
0	74 (71.2)	37 (50.0)	0.016
≥ 1	30 (28.8)	23 (76.7)	

Abbreviations: BMI, body mass index; ECOG-PS, Eastern Cooperative Oncology Group Scale of Performance Status; N, number; SD, standard deviation; SMI, skeletal muscle index; PET, positron-emission tomography.
Notes: [a]Targeted therapy includes monoclonal antibodies, small molecule inhibitors, and immunotherapy, as rituximab, bentruximab, denosumab, imatinib, and acalabrutinib.

Table 2 Factors associated with sarcopenia diagnosis in 104 onco-hematology patients in univariate and final regression models

	Univariate		Final	
	OR	***p***	**OR**	***p***
Age				
Adult	1.0			
Elderly	4.0	0.001		
Sex				
Female	1.0		1.00	
Male	2.74	0.019	4.11	0.027
Diagnosis				
Lymphoma	1.0			
Leukemia	5.86	0.106		
Others	1.2	0.741		
Treatment				
No treatment	1.0			
Targeted therapy[a]	5.64	0.030		
Chemotherapy	0.76	0.630		
BMI classification				
Underweight	1.0		1.00	
Normal range	1.11	0.932	1.25	0.859
Overweight	0.09	0.043	0.13	0.098
Obese	0.18	0.172	0.14	0.133
Hemoglobin	0.81	0.055		
ECOG-PS				
0	1.0		1.00	
≥ 1	3.29	0.015	3.93	0.048

Abbreviations: BMI, body mass index; ECOG-PS, Eastern Cooperative Oncology Group Scale of Performance Status; OR, odds ratio.
Notes: [a]Targeted therapy includes monoclonal antibodies, small molecule inhibitors, and immunotherapy, such as rituximab, bentruximab, denosumab, imatinib, and acalabrutinib.

with sarcopenia, and lower SMI values were related to sarcopenia.

The multivariate model did not obtain significant associations. The final stepwise model was conducted to evaluate the response of the ECOG-PS variable to the association considering the objectives of this article.

The final model showed that male sex was positively associated with a sarcopenia diagnosis, with male individuals having a 4.11 higher chance of developing muscle disease than female individuals. Similarly, an ECOG-PS score of ≥ 1 was also positively associated with sarcopenia, with a level of significance of 5%.

The variable "anemia" showed a casuistic incompatibility with the statistical model and multicollinearity with the other variables and was, thus, not included. Corticosteroid use ($p = 1.000$) and disease status ($p = 0.830$) showed a

Table 3 Accuracy analysis of the ECOG-PS scale as a screening tool for sarcopenia based on 159 PET-CT scans

	ECOG-PS score ≥ 1	95%CI
Sensitivity (%)	40.7	(30.6–50.8)
Specificity (%)	83.8	(75.1–92.6)
PPV (%)	77.1	(65.2–84.9)
NPV (%)	51.4	(42.1–60.6)
Accuracy (%)	59.1	(51.5–66.8)

Abbreviations: 95%CI, 95% confidence interval; ECOG-PS, Eastern Cooperative Oncology Group Scale of Performance Status; NPV, negative predictive value; PET-CT, positron-emission tomography-computed tomography; PPV, positive predictive value.

highly non-significant association and were not included in the models. Based on these results, a Spearman's correlation was conducted between SMI value, which is essential for sarcopenia diagnosis, and the classification on the ECOG-PS scale, obtaining a negative correlation (-0.296; $p < 0.01$).

Based on the association of an ECOG-PS score of $\geq$1 with a sarcopenia diagnosis, the accuracy of the scale as a screening tool for sarcopenia was calculated in a sample of mostly onco-hematology patients with sarcopenia, as shown in ►**Table 3**.

The ECOG-PS showed a sensitivity and specificity of 40.7% and 83.8%, respectively, as a screening tool for sarcopenia in this sample of onco-hematology patients, showing a greater ability to detect the absence of sarcopenia.

Discussion

In the present retrospective cohort study, we showed a considerable prevalence of sarcopenia among onco-hematology patients, a condition also associated with physical dysfunction on the ECOG-PS scale. A sarcopenia diagnosis in onco-hematology patients has been previously reported. A systematic review that included 6,894 patients diagnosed with solid and hematologic tumors found a prevalence of pretherapeutic sarcopenia of 38.6% (95% confidence interval [CI] 37.4–39.8) based on CT scans, associating the condition with an increased mortality risk and impact on antineoplastic treatment,[3] while a meta-analysis of 1,578 patients found a prevalence of 39.1% in onco-hematology patients based on CT scans and association with lower overall survival of individuals diagnosed with non-Hodgkin lymphoma.[33] Regarding the 104 onco-hematology patients included in the current study, most were diagnosed with lymphoma (76.0%), were not undergoing treatment at the time of the PET-CT examination (68.3%), and had sarcopenia (57.7%), with a prevalence higher than that reported in the literature. Although caution should be taken when comparing results obtained by different assessment methods, prior studies diagnosing sarcopenia based on PET-CT are scarce. However, the prevalence of sarcopenia in the patients included in the present study was significant.

Considering sarcopenia as a multifactorial diagnosis potentially associated with hematologic cancer and its related inflammatory and metabolic changes[1,3] and the importance of early detection, screening instruments that facilitate the diagnosis of this muscle disease are crucial; such tools help to reveal the patient population that would benefit from a more detailed sarcopenia assessment.

Our study found an association of sarcopenia diagnosis with male sex ($p = 0.027$). A study of 122 individuals aged $\geq$ 70 years living in a nursing home detected sarcopenia in 32.8% of the population, with the condition most often found in men (68%) rather than in women (21%) ($p < 0.001$).[34] Another study investigated the prevalence of sarcopenia diagnosed by bioelectrical impedance analysis in 164 patients who had hematologic diseases and were scheduled for HSCT. Sarcopenia was found in 50.6% of patients and was associated with the lower BMI (odds ratio 0.70; $p < 0.01$) and sex (odds ratio 3.09; $p < 0.01$); this led to the conclusion that male patients can be more susceptible to sarcopenia,[35] with a potential reduction in daily life activity compared with female patients.

Furthermore, an ECOG-PS score of $\geq$ 1 proved to be a good predictor of a sarcopenia diagnosis based on a significant association between the 2 variables ($p = 0.048$). Other studies have also investigated the association of the ECOG-PS scores with a sarcopenia diagnosis. A retrospective study of 42 patients, who were diagnosed with advanced non-small cell lung cancer and had received previous treatment, detected sarcopenia in 52.4%; however, the ECOG-PS scores were not significantly different in patients with or without sarcopenia ($p = 0.13$), possibly due to the reduced sample size.[36] However, although not significant, patients with worse PS tended to have reduced muscle mass compared with those with good PS, thus reinforcing the need for further studies on this subject.[36] Another retrospective study of 100 patients with advanced cancer treated with immunotherapy found a significant association between the SMI determined in the sarcopenia assessment and ECOG-PS ($p = 0.0324$). The majority of individuals had non-small cell lung cancer (NSCLC), melanoma, or kidney as their primary tumor.[37] Although the hypothesis of predicting sarcopenia using the ECOG-PS is promising, studies assessing the relationship between these variables are scarce. As previously mentioned, the ECOG-PS also considers functional and self-care capacity, which are potentially compromised in sarcopenia, thus resulting in an increased risk of falls and fractures, as well as motility disorders, and greater restrictions on the individual's daily living activities.[1,38]

In this context, a cut-off score of $\geq$ 1 was used when analyzing the ECOG-PS as a screening tool for sarcopenia, as, according to the scale, any score other than 0 already indicates some degree of functional impairment.

Questionnaires, such as the SARC-F, were created to screen patients at risk of sarcopenia, and were previously characterized with low-to-moderate sensitivity (3–10%) and high specificity (94–99%) in an elderly Chinese population[17] has since then been used in the elderly population.[1,15] In a cross-sectional study of 179 non-institutionalized elderly individuals, the SARC-F showed a sensitivity of 33.3% and a specificity of 84.2% and was associated with the anthropometric measurement of the calf circumference; then, these results were compared with sensitivity and specificity associated

with a diagnosis of sarcopenia by dual-energy X-ray absorptiometry.[39] An improved performance and sensitivity (66.7%) of the SARC-F as a screening tool for sarcopenia was observed when associating it with calf circumference measurements (area under the curve: 0.736 [95% CI 0.575–0.897]; comparing with SARC-F alone: $p = 0.027$), without compromising its specificity (82.9%).[39] However, similar to the SARC-F, this tool is also aimed at the elderly population.

Our study has several limitations, including its retrospective design with simultaneous data collection, and the use of the ECOG-PS variable taken from electronic medical records, whose classification permeates the evaluator's subjectivity, although following intrinsic instructions to the scale.

In conclusion, the ECOG-PS tool showed a sensitivity of 40.7% and, consequently, an increased negative predictive value (51.4%), indicating a high probability of false negatives. Although our results do not demonstrate adequate accuracy for using the scale as a screening tool for sarcopenia in onco-hematology patients, the study hypothesis remains relevant considering the association found between the variables and a sarcopenia diagnosis. Furthermore, the intrinsic characteristics of the ECOG-PS, such as simplicity, speed of use, and low cost, support its use in diverse health centers and by different members of a multidisciplinary team, but we reinforce the need for further studies.

Ethics Declaration

The current study was approved by the Research Ethics Committee (approval no.: 4.971.257) on September 13, 2021. Owing to the retrospective design study, the respective ethics committee waived the need for the Free and Informed Consent Form.

Clinical Trials

None.

Authors' Contribution

TG,: collection and assembly of data, conception and design, data analysis and interpretation, final approval of the manuscript, and writing of the manuscript; TTO, ACLS, and EYHN: conception and design, data analysis and interpretation, final approval of the manuscript, and writing of the manuscript; ALCCR: conception and design, data analysis and interpretation, and and final approval of the manuscript; DSR: collection and assembly of data, data analysis and interpretation, and final approval of the manuscript; TGR: conception and design, data analysis and interpretation, and final approval of the manuscript; LT, YN, and CAR: data analysis and interpretation, final approval of the manuscript, and provision of study materials or patient.

Ethics Committee Number

4.971.257.

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Conflict of Interests

The authors have no conflict of interests to declare.

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