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Original Article

Association between Spirometric Data and Cognitive Function in Middle-Aged and Older Adults

Yen-Huey Chen [a,b,c], Chia-Hsuan Yu [d,e], Hui-Ling Lin [a,c], Chung-Chi Huang [a,b] *

[a] *Department of Respiratory Therapy, College of Medicine, Chang Gung University, Taoyuan, Taiwan,* [b] *Department of Pulmonary and Critical Care Medicine, Linkou Chang Gung Memorial Hospital, Taoyuan, Taiwan,* [c] *Department of Respiratory Care, Chang Gung University of Science and Technology, Chiayi Branch, Chiayi, Taiwan,* [d] *Department of Respiratory Therapy, Graduate Institute of Medicine Science, College of Medicine, Chang Gung University, Taoyuan, Taiwan,* [e] *Department of Nursing, MacKay Memorial Hospital, Taipei, Taiwan*

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SUMMARY

Background: Pulmonary function declines with aging impairs the capabilities of oxygen delivery to the brain and may affect on cognitive performance. The purpose of this study was to examine the relationship between spirometric data, cognitive function and cerebral oxygenation in middle-aged and elderly individuals.
Methods: Subjects who were older than 45 years old were recruited from long-term care facilities. The pulmonary function was measured through forced expiratory volume in 1 second (FEV_1), forced vital capacity (FVC) and peak expiratory flow (PEF). The cognitive function was assessed by the Montreal Cognitive Assessment (MoCA) and Mini-Mental State Examination (MMSE). The cerebral oxygenation status was assessed by the near-infrared spectroscopy (NIRS).
Results: Sixty subjects participated in the study. The cognitive function (MMSE score) was also significantly related to FEV_1 ($r = 0.374$, $p = 0.003$), FEV_1/FVC ($r = 0.319$, $p = 0.013$), and PEF ($r = 0.482$, $p < 0.001$). The MoCA scores were significantly related to FEV_1 ($r = 0.418$, $p = 0.001$), FEV_1/FVC ($r = 0.319$, $p = 0.013$), and PEF ($r = 0.508$, $p < 0.001$). Subjects in normal lung function group have significantly higher MMSE scores (24.0 ± 9.1) than those in abnormal lung function group (17.2 ± 7.2, $p = 0.006$). No difference in the measurements of cerebral oxygenation was found between normal and abnormal lung function group (> 0.05).
Conclusion: In this cross-sectional study, the pulmonary function and cognitive function declined with aging. A better pulmonary function was associated with better cognitive function. However, longitudinal studies were required to determine the possible causation between cognition and pulmonary function.

1. Introduction

Societies worldwide are experiencing a rapid increase in the older population.[1] The aging process induces anatomical and physiological changes in the brain, affecting aspects of cognition, particularly processing speed, working memory, and executive functions.[2,3] Older adults may experience a decline in cognitive function as they age, which impact their independence in performing daily activities (ADL) and their overall quality of life.[2,3] In a cross-sectional study, Chiu et al. reported that specific aspects of cognitive function, such as language, processing speed, and orientation, were significantly correlated with independence in ADL.[4] Identifying factors influencing cognitive function may help improve the health outcomes for older adults and enhance their independence and quality of life.

Cognitive function is influenced by the oxygen utilization status of brain tissue.[5,6] Although the brain accounts for only 2% of body weight, it consumes nearly 20% of total body oxygen.[7] The respiratory system plays an important role in regulating the whole-body oxygen supply.[8] Aging alters the structure and characteristics of the lungs and chest wall.[8] Loss of elastic tissue and alveolar integrity reduces gas exchange and diffusion capacity, resulting in decreased peak expiratory flow (PEF), increased residual volume, and decrease dvital capacity.[8] These age-related changes in lung function impair the body's ability to provide adequate oxygen, including to the brain.[8] Guo et al. reported that a decline in pulmonary function during middle age was associated with a high risk of developing dementia and Alzheimer's disease later in life.[9] However, as poor pulmonary function is associated with increased mortality in middle-aged and older adults,[10] individuals with lower pulmonary function may not survive to an age when dementia manifests. Consequently, the relationship between pulmonary function and cognition may have been underestimated in Guo's longitudinal study.[9] Therefore, this study aimed to examine the relationship between pulmonary and cognitive functions in middle-aged and older adults.

Incentive spirometry (IS) is a lung expansion therapy device designed to help individuals achieve sustained and maximal inspiration.[11] During deep inspiration, IS increases the transpulmonary pressure gradient by decreasing the pleural pressure which enhances alveolar expansion and lung volume.[11] IS therapy effectively im-

* Corresponding author. Department of Pulmonary and Critical Care Medicine, Linkou Chang Gung Memorial Hospital, No. 5, Fu-Hsin St., Kweishan, Taoyuan 333, Taiwan.
E-mail address: cch4848@cgmh.org.tw (C.-C. Huang)

proves lung compliance and oxygenation while preventing atelectasis.[11,12] Ferreira et al. reported that IS training improves pulmonary function and specific cognitive aspects in older individuals.[13] However, the detailed mechanisms underlying this relationship remain unclear. Therefore, this study also examined the acute effect of a single IS training session on cerebral oxygenation in this population.

2. Population and methods

2.1. Participants and study procedures

This was a prospective, cross-sectional study. Participants were recruited from a nursing home. The inclusion criteria for the present study were: 1) age $\geq$ 45 years,[14] 2) hemodynamic stability, and 3) ability to provide written informed consent. Exclusion criteria included: 1) Subjects with conditions that were adversely affected by increasing intrathoracic pressure (eg. Acute myocardial infarction within 1 week, systemic hypotension or sever hypertension, significant atrial ventricular arrythmia, presence of pneumothorax); increasing intraabdominal pressure (eg. abdominal surgery within 4 weeks, late-term pregnancy); increasing of intracranial/ocular pressure (eg. cerebral aneurysm, recent concussion with continuing symptoms, brain surgery within 4 weeks, eye surgery within 1 week; increasing sinus and middle ear pressures (eg. sinus surgery or middle ear surgery or infection within 1 week); infection control issues (eg. active or suspected transmissible respiratory or systemic infection, including tuberculosis;[15] 2) having any disease that was at the acute stage, such as acute pneumonia, acute bronchitis, acute stroke, acute myocadiac infarction, or acute bacterial infection; 3) inability to complete the cognition assessment owing to conditions like inability to speak or vision loss; 4) inability to complete the spirometry test because of difficulty following instructions, and 5) current use of psychiatric medication that could affect consciousness or cognition status. This study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Review Board of Chang Gung Medical Foundation (201901594B0). Written informed consent was obtained from all participants. A registered nurse conducted the interviews with the participants, during which demographic data were collected, spirometry data and cognitive performance were assessed.

After pulmonary and cognitive function assessments, participants performed a single breathing exercise session using an IS device (Triflo II, Teleflex, Inc, USA). Participants exhaled normally before placing the mouthpiece in their mouth. They then inhaled to the target level through the IS device, held their breath for at least 3 s at the end of inspiration, exhaled normally, and rested for 10–30 s. This process was repeated 10–15 times (approximately 5–10 min).[12] Cerebral oxygenation status was monitored using near-infrared spectroscopy (NIRS) during the IS session.

2.2. Measurements

2.2.1. Spirometry test

Pulmonary function was assessed using a spirometry test. Forced vital capacity (FVC) and forced expiratory volume in one second (FEV_1) were measured three times using computerized spirometry (Spirometry, MD Spiro, Inc., Lewiston., USA), and the best trial was reported. All measurements were performed according to American Thoracic Society recommendations.[15] The predicted FVC and FEV_1 values were calculated based on body height, age, and sex.

2.2.2. Cognitive performance measurement

Cognitive status was assessed using the Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA). This MMSE test measured various cognitive functions, including learning and memory, orientation, attention executive functions, temporal-spatial language, and visual-constructive abilities. Scores ranged from 0 to 30 points, with higher scores indicating higher cognitive abilities.[16]

The MoCA comprised 11 items spanning 8 cognitive dimensions (i.e., visual-spatial executive ability, naming, memory, attention, language fluency, abstract thinking, delayed memory, and orientating function). Scores ranged from 0 to 30, with higher score indicating better cognitive function.[17] The validity of the MMSE and MoCA tests in assessing cognition function has been established in previous studies.[17,18]

2.3. Cerebral oxygenation measurement

Cerebral oxygenation status was measured using portable NIRS devices (PortaMon, Artinis, the Netherlands). NIRS technology emits near-infrared (700–1000 nm) light into tissues, where it is either scattered or absorbed by chromophores such as deoxygenated hemoglobin (HHb) and oxygenated hemoglobin (O2Hb). O2Hb indicated tissue oxygenation status, whereas HHb represented the level of tissue deoxygenation from O_2 extraction. Total hemoglobin (TotHb), the sum of O2Hb and HHb, serves as an index of regional blood volume.[19] The probe was placed on the left forehead, secured with elastic bandages to shield from ambient light. The distance between the opcodes and the receptor was $\geq$ 4 cm, allowing signal penetration of approximately 2 cm. Continuous measurements were taken every 10 s. A sampling rate of 10 Hz was used for the analog-to-digital conversion, and subsequent analyses were conducted.

2.4. Statistical analysis

Sample size was calculated based on a previous study,[20] assuming an effect size 0.44, α error of 0.05 and a statistical power of 0.9, resulting in a sample size of 55 participants. Considering a potential dropout rate of 10%–20%, the sample size was increased to 65 participants.

Statistical analysis was conducted using SPSS v.22. The Shapiro-Wilk test was used to examine the normality of distribution. The results are expressed as the mean $\pm$ SD for normal distributions and the median (25^{th}–75^{th} percentiles) for nonparametric distributions. The relationship between spirometry data and cognitive performance was examined using Pearson correlation analysis for parametric distribution sample, and using Spearman's correlation analysis for nonparametric distribution. Partial correlation analysis, controlling for age, was conducted to further examine these relationships.

The participants were divided into normal (NML) and abnormal (ABN) pulmonary function groups based on the spirometry data (NML group: $FEV_1 \geq 80\%$ and $FEV_1/FVC \geq 70\%$; ABN group: FEV_1 or FEV_1/FVC below the thresholds).[15] Differences in variables between groups were analyzed using the Student's *t*-test or the Mann-Whitney *U* test in cases of nonparametric distribution. Statistical significance was set at $p < 0.05$.

3. Results

From November 2019 to November 2020, 65 participants volunteered for this study. Five participants were excluded because they could not comply with the cognitive function assessment, resulting in a total of 60 participants. The participants' characteristics were presented in Table 1. The mean age of the participants was

75.7 ± 1.0 years, and 63.6% were females (n = 38). The mean predicted FEV_1 value was 49.3 ± 27.6%. The mean MMSE and MoCA scores were 17.6 ± 8.1 and 13.5 ± 9.0, respectively. A total of 16.7% of the participants were middle-aged individuals.

The relationship between age and pulmonary function is presented in Table 2. There was a negative correlation between age and FVC (r = -0.319, p = 0.013), FEV_1 (r = -0.520, p = 0.378), and PEF (r = -0.469, p = 0.000). The age was also inversely related to tidal volume (VT) (r = -0.368, p = 0.004) (Table 2). These findings indicate that lower expiratory flow and lung volume were associated with higher age.

Table 3 presents the relationship between lung function and cognitive performance. MoCA scores were positively correlated with FEV_1 (r = 0.418, p = 0.001), FEV_1% (r = 0.294, p = 0.023), FEV_1/FVC (r = 0.319, p = 0.013), PEF (r = 0.508, p < 0.001), and VT (r = 0.434, p = 0.001). Similarly, MMSE scores showed positive correlations with FEV_1 (r = 0.374, p = 0.003), FEV_1/FVC (r = 0.319, p = 0.013), and PEF (r = 0.482, p < 0.001). After controlling for age, the MMSE scores were positively related to FEV1 (r = 0.265, p = 0.042) and PEF (r = 0.350, p = 0.007). The MoCA scores were positively related to FEV1/FVC (r = 0.275, p = 0.035), PEF (r = 0.394, p = 0.002), and VT (r = 0.335, p = 0.009). A better cognitive performance (higher MMSE, MoCA scores) was associated with higher pulmonary function (FEV1, PEF) (Table 4).

Patients were subdivided into NML (n = 9) and ABN groups (n = 51) according to their spriometric data (Table 5). No differences in age, height, or weight were observed between groups. Spriometric data in the NML group were significantly better than those in the ABN group. Cerebral O2Hb in the NML group (28.1 ± 23.8 μmol/L) was higher than those in the ABN group (12.4 ± 5.8 μmol/L) (p = 0.099). Similarly, cerebral TotHb in the NML group (49.5 ± 43.4 μmol/L) was higher than those in the ABN group (20.9 ± 10.1 μmol/L) (p = 0.079) (Table 3). However, these differences were not statistically significant. Regarding cognitive function, the MoCA scores in

Table 1
Demographic data.

	Total	Middle age	Old age
N (%)	60 (100%)	10 (16.7%)	50 (83.3%)
Age (year)	75.7 ± 10.9	56.7 ± 3.2	78.8 ± 7.9
Body height (cm)	156.1 ± 9.1	166.1 ± 6.0	164.8 ± 8.6
Body weight (kg)	58.9 ± 11.3	66.5 ± 14.2	58.2 ± 10.7
BMI (kg/m^2)	24.1 ± 3.9	24.0 ± 4.8	24.2 ± 3.7
Gender (M/F) (n)	22/38	8/2	14/36

Middle age: 45 years ≤ age < 60 years; Old age: age ≥ 60 years.

Table 3
Correlation between spirometry data and cognition.

	MoCA		MMSE	
	r	p	r	p
FEV_1	0.418	0.001	0.374	0.003
FEV_1%	0.294	0.023	0.227	0.081
FVC	0.114	0.384	0.091	0.490
FVC%	0.004	0.978	-0.027	0.835
FEV_1/FVC	0.319	0.013	0.319	0.013
PEF	0.508	0.000	0.482	0.000
MVV	0.398	0.002	0.354	0.006
VT	0.434	0.001	0.350	0.006
Age	-0.346	0.001	-0.342	0.001

FEV_1: forced expiratory volume in 1 second; FVC: forced vital capacity; MMSE: Mini-Mental State Examination; MoCA: Montreal Cognitive Assessment; MVV: maximal voluntary ventilation; PEF: peak expiratory flow; VT: tidal volume.

Table 5
Comparison between normal and abnormal lung function groups.

Characteristics	Normal (n = 9)	Abnormal (n = 51)	p
Basic data			
Age (year)	65.6 ± 12.4	78.0 ± 9.3	0.167
Body height (cm)	164.3 ± 6.9	154.5 ± 8.5	0.495
Body weight (kg)	67.2 ± 13.5	57.5 ± 10.3	0.763
BMI (kg/m^2)	24.8 ± 4.4	24.0 ± 3.8	0.784
Gender (M/F) (n)	7/2	15/36	0.005
Cerebral oxygenation			
O2Hb (μmol/L)	28.1 ± 23.8	12.4 ± 5.8	0.099
HHb (μmol/L)	21.4 ± 19.1	17.1 ± 8.7	0.742
TotHb (μmol/L)	49.5 ± 43.4	20.9 ± 10.1	0.079
TSI (%)	60.3 ± 4.7	60.6 ± 9.7	0.884
Cognitive function			
MoCA (scores)	21.5 ± 10.7	12.8 ± 8.0	0.016
MMSE (scores)	24.0 ± 9.1	17.2 ± 7.2	0.006
Spirometry data			
FVC (L)	2.9 ± 1.4	1.5 ± 1.2	0.001
FVC (% predicted)	100.2 ± 26.4	64.9 ± 53.0	0.056
FEV_1 (L)	2.5 ± 1.3	0.9 ± 0.4	< 0.001
FEV_1 (% predicted)	77.8 ± 40.1	44.2 ± 21.6	< 0.001
PEF (L/s)	203.6 ± 104.1	71.2 ± 49.3	< 0.001
FEV_1/FVC (%)	82.9 ± 7.1	68.0 ± 22.7	0.057

FEV1: forced expiratory volume in 1 second; FVC: forced vital capacity; HHb: deoxygenated hemoglobin; MMSE: Mini-Mental State Examination; MoCA: Montreal Cognitive Assessment; O2Hb: oxygenated hemoglobin; PEF: peak expiratory flow; TotHb: total hemoglobin; TSI: tissue saturation index.

Table 2
Correlation between age and spirometry data.

	FVC	FVC% predicted	FEV1	FEV1% predicted	FEV1/FVC	PEF	MVV	VT
Age *r*	-0.319	-0.116	-0.520	-0.161	-0.172	-0.469	-0.477	-0.368
p	0.013	0.378	0.000	0.220	0.189	0.000	0.000	0.004

FEV_1: forced expiratory volume in 1 second; FVC: forced vital capacity; MVV: maximal voluntary ventilation; PEF: peak expiratory flow; VT: tidal volume.

Table 4
Correlation between spirometry data and cognition after controlling for age.

	FVC	FVC%	FEV1	FEV1%	FEV1/FVC	PEF	MVV	VT
Control for age								
MMSE								
r	-0.17	-0.048	0.265	0.253	0.277	0.350	0.186	0.228
p	0.897	0.720	0.042	0.053	0.344	0.007	0.159	0.083
MoCA								
r	-0.055	-0.087	0.194	0.177	0.275	0.394	0.254	0.335
p	0.677	0.514	0.142	0.180	0.035	0.002	0.052	0.009

FEV_1: forced expiratory volume in 1 second; FVC: forced vital capacity; MMSE: Mini-Mental State Examination; MoCA: Montreal Cognitive Assessment; MVV: maximal voluntary ventilation; PEF: peak expiratory flow; VT: tidal volume.

the NML group (21.5 ± 10.7) were significantly higher than those in ABN group (12.8 ± 8.0) ($p = 0.016$). Likewise, MMSE scores were significantly higher in the NML group (24.0 ± 9.1) compared to the ABN group (17.2 ± 7.2) ($p = 0.006$).

After the 5–10 min of IS training, cerebral O2Hb increased from 14.8 ± 6.1 μmol/L to 18.5 ± 6.7 μmol/L ($p = 0.252$), and cerebral TotHb increased from 25.2 ± 10.7 μmol/L to 34.5 ± 13.2 μmol/L ($p = 0.245$). However, these changes did not achieve statistical significance (Figure 1).

4. Discussion

This study examined the relationship between pulmonary function and cognition in middle-aged and older individuals. Our results demonstrated a significant relationship between spirometry data and cognitive performance. Participants with normal pulmonary function exhibited superior cognitive performance compared to those with abnormal pulmonary function. Although cerebral oxygenation levels improved after single IS session, the improvement did not reach statistical significance.

Several physiological changes occur in the respiratory systemas aging, which can affect pulmonary function. The chest wall becomes less elastic, supporting muscles weaken, and the rib cage stiffens, resulting in reduced chest wall movement during breathing. These changes contribute to a decreased lung volume.[21,22] Consistent with the findings of Ren et al., our study showed that lung function parameters such as FVC, FEV_1, and PEF decline with age.[23] This inverse relationship between age and pulmonary function highlights the impact of aging on respiratory health.

Our study also found a positive correlation between spirometry data and cognition performance. Higher lung volumes (VT) and greater expiratory flow (FEV_1, PEF) were associated with higher cognitive test scores (MMSE, MoCA scores). According to Qiao et al. FEV_1 in middle-aged adults significantly predicted late-life cognitive function.[24] They also reported that decreased FEV_1 and FVC in midlife were associated with higher risks of impaired memory capacity, reaction speed, and executive function among older population.[24] Similarly, Guo et al. reported that improved pulmonary function in midlife lowered the risk of developing dementia and Alzheimer's disease in later life.[9] For every one standard deviation increase in PEF, FVC, and FEV_1, the risk for incident dementia decreased by > 20%.[9] While previous longitudinal studies indicated that a better pulmonary function in middle age may have a protective effect for preventing the development of dementia in old age, our cross-sectional study showed the potential for using a spirometry test to identify individuals who could also have impaired cognition at a single time point. Although our cross-sectional study may not be able to determine the causality, the results complemented longitudinal evidence by underscoring the potential use of the spirometry test as a concurrent indicator for cognitive health.

In NIRS measurement, O2Hb reflects oxygen supply to the brain tissue, whereas TotHb indicates overall blood volume and blood flow changes.[19] According to Wijnant et al., cerebral blood flow (mL/min) was significantly lower in participants with moderate to severe chronic obstructive pulmonary disease (COPD) than in participants with normal spirometry tests.[25] In our study, the O2Hb and TotHb in the normal lung function group were higher than those in the abnormal lung function group; however, the difference did not reach statistical significance ($p = 0.099$ and 0.079, respectively), likely because of the small sample. Declines in cerebral blood flow may precede brain atrophy in older adults, potentially leading to cognitive deficits.[5,6] We also observed that cognitive performance (MMSE and MoCA scores) in the normal lung function group was significantly better than in the abnormal lung function group. Proper lung function ensures efficient gas exchange, supplying oxygen to the bloodstream for tissue distribution and removing carbon dioxide. Impaired lung function leads to decreased oxygen availability, affecting the status of various systemic oxygenation functions, such as the brain, potentially affecting cognitive performance.

The IS device facilitates sustained maximal inspiration, promoting lung expansion and enhanced pulmonary ventilation. Previous studies showed that IS training improved lung function and oxygenation over time. In patients with coronary artery bypass graft surgery, IS training over 3 days significantly increased arterial oxygen pressure and reduced carbon dioxide pressure.[26] In our study, a single IS session led to improvements in cerebral oxygenation (O2Hb and TotHb levels), though these changes did not reach statistical significance. The lack of significance could be attributed to the limited duration of training, as earlier studies have demonstrated benefits after repeated sessions over several days.[26]

4.1. *Limitation*

Our study had certain limitations. First, this was a cross-sectional study. We could not determine causality or assess whether improvements in pulmonary function could directly enhance cognitive performance. Second, cognitive function was evaluated using MoCA and MMSE, which assess general cognitive status. We did not investigate specific cognitive domains, such as memory, language, vasoconstriction, attention, or executive functions.[4] Therefore, our study may be unable to determine which specific cognitive domains were more related to lung function during aging. The third limitation is the sample size. While the study may not have missed major associations, a larger sample size might have detected smaller associations. Fourth, the lack of information on participants' comorbidities, such as COPD or neurological conditions, may have influenced both

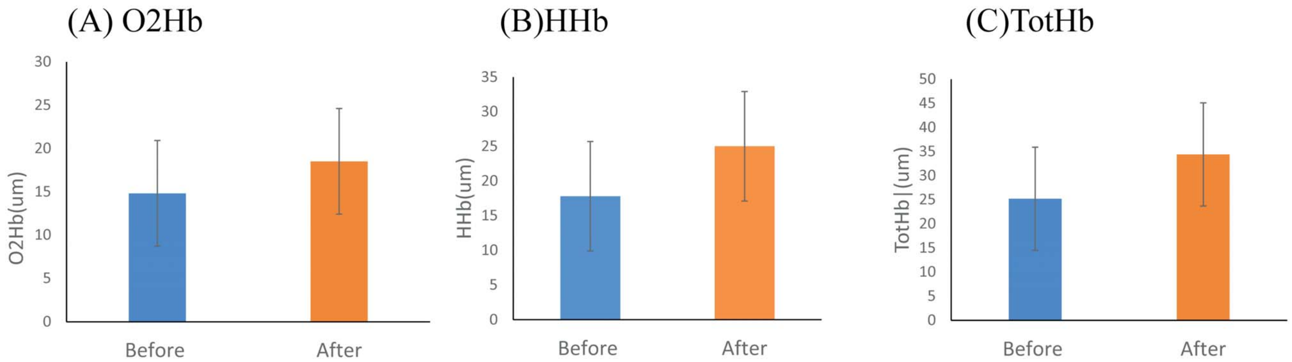

Figure 1. Cerebral oxygenation status before and after IS training. (A) O2Hb; (B) HHb (deoxygenated Hb); (C) TotHb.

pulmonary and cognitive functions, potentially affecting the interpretation of our findings.

5. Conclusion

Lung and cognitive functions were interconnected in older adults. This study observed cognitive impairment in individuals with lower pulmonary function, highlighting the importance of maintaining good respiratory health to support cognitive abilities and overall well-being. Promoting lung health through interventions such as breathing exercises may help mitigate the potential negative impacts of reduced pulmonary function on cognition, ultimately contributing to healthier aging. Future studies will be required to examine the effects of pulmonary function improvement on the cognitive function.

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Conflicts of interest

The authors declare no conflict of interest.

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