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ORIGINAL ARTICLES

Analysis of risk factors affecting moderate and severe prognosis after discharge in patients with acute cerebral infarction

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Abstract

Objective: To investigate risk factors affecting short-term functional prognosis after discharge in patients with acute cerebral infarction and explore the correlation between relevant factors and National Institutes of Health Stroke Scale (NIHSS) scores. *Methods:* A retrospective analysis of 4,048 patients with acute cerebral infarction hospitalised between January 2014 and November 2018 in Department of Neurology, Renqiu Kangji Xintu Hospital, Hebei were conducted. The enrolled patients, including 2,506 men and 1,542 women, were divided into mild (n=3,696), moderate (n=278) and severe groups (n=74) based on NIHSS score. Baseline data (gender, history of hypertension, diabetes, hyperlipidaemia, drinking, cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, lipoprotein (a), urea nitrogen, creatinine) were compared among the three groups, and the relationship between relevant factors and NIHSS scores was studied. *Results:* Through single factor regression analysis, it was found that age, history of stroke, atrial fibrillation, coronary heart disease, antiplatelet medication usage, systolic blood pressure and uric acid were risk factors for the moderate group. Multivariate logistic regression analysis showed that, after adjusting for confounding factors, age, history of stroke and systolic blood pressure ($P<0.01$) were independent risk factors for the moderate group. Age (OR=1.089; , history of stroke, atrial fibrillation, diastolic blood pressure, fasting plasma glucose and uric acid ($P<0.05$) were independent risk factors for the severe group. *Conclusion:* Age, history of stroke, atrial fibrillation, systolic and diastolic blood pressure, fasting plasma glucose and uric acid levels are independent risk factors affecting the short-term post-discharge functional prognosis of patients with acute cerebral infarction and are related to the NIHSS scores of these patients after discharge.

Keywords: Acute cerebral infarction, NIHSS score, risk factors

INTRODUCTION

Acute cerebral infarction is a prevalent and serious cerebrovascular condition that causes a huge disease burden worldwide.[1] As the most common type of stroke (accounting for 60%–80% of all strokes), acute cerebral infarction possesses a high disease burden in East Asia, Southern/Eastern sub-Saharan Africa and Southeast Asia.[2] Due to population ageing in recent years, the incidence and mortality of acute cerebral infarction have increased, and it has turned into a principal cause of death among urban inhabitants. Thus, screening for and preventing stroke are becoming increasingly important.[3] The current methods for evaluating the severity of acute cerebral infarction are brain and neurovascular imaging and the National Institutes of Health Stroke Scale (NIHSS) score. However, these methods are time-consuming, resource intensive and subjective. Exploring independent risk factors can

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enhance stroke assessment, and understanding the associated risk factors can help tailor treatment strategies. Current epidemiological studies on acute cerebral infarction have identified some common risk factors such as hypertension, diabetes and hyperlipidaemia, that are closely related to the incidence and prognosis of acute cerebral infarction.[4,5]

The NIHSS is frequently utilised for neurological evaluation and supports the systematic quantification of assessment results, allowing for objective reflections of neurological deficits and severities caused by cerebral infarction.[6] The NIHSS assists in clinical decisions regarding diagnosis, prognosis prediction and treatment of acute cerebral infarction and has been shown to predict functional outcomes following revascularisation or mechanical thrombectomy in patients who experienced a stroke.[7,8] While the NIHSS can be proficient in evaluating the severity of acute cerebral infarction, we still lack a comprehensive understanding of specific risk factors contributing to moderate and severe acute cerebral infarction that have high NIHSS scores. Previous studies have revealed associations between factors such as age, stroke history and atrial fibrillation with severity prognosis[9], but understanding of other potential risk factors remains limited.

Therefore, this study aimed to investigate risk factors affecting short-term functional prognosis (indicated by the NIHSS score) after discharge in patients with acute cerebral infarction. Through a large-sample retrospective analysis based on patient data, this study examines the relationship between NIHSS scores and independent factors such as age, stroke history, atrial fibrillation, blood pressure and blood sugar. We hypothesized that these independent factors may have a prediction function regarding the severity of acute cerebral infarction. This study aims to fill in the current knowledge gap regarding risk factors related to moderate and severe prognosis, indicated by NIHSS scores, and further expand the current understanding of acute cerebral infarction. By gaining an in-depth understanding of the aforementioned risk factors, we hope to improve the accuracy of predictive instruments, provide more accurate guidance for clinical practice and improve rehabilitation and prognosis in patients with acute cerebral infarction.

METHODS

Study design and subjects

This was a single-centre, retrospective, large-sample observational study. The participants were 4,048 patients with acute cerebral infarction (212 patients received thrombolysis treatments) hospitalised in the Neurology Department of our hospital between January 2014 and November 2018 who were aged 22–98 years and had an average age of 65.00 (58.00–73.00) years. The inclusion criteria were: (1) Age was greater than 18 years; (2) stroke onset within 7 days; (3) symptoms met the revised diagnostic criteria for acute ischemic stroke in the 'Chinese Guidelines for Diagnosis and Treatment of Acute Ischemic Stroke 2014'[10,11] and confirmed by head computerized tomography or magnetic resonance imaging.

The exclusion criteria were: (1) Patients who were unable to cooperate with examinations due to conditions such as severe consciousness disorder, mental illness, aphasia or hearing loss; (2) patients who had a history of mental illness or psychological disorders; (3) haemorrhagic cerebrovascular disease; (4) concurrent chronic consumptive disease, malignancy, hyperthyroidism or hematologic disease; (5) autoimmune disease (such as Addison disease, inflammatory bowel disease, multiple sclerosis or myasthenia gravis). Based on the actual clinical situation and physician's diagnosis, the enlisted patients received conservative treatment or revascularisation. This study was approved by the Ethics Committee, and the patients informed consent was exempted for this study due to its retrospective nature.

Data collection

Eligible patients were surveyed by trained medical personnel using uniformly designed questionnaires. Relevant information such as survey questionnaires, physical examinations (baseline health data and diagnosis), laboratory test results (blood biochemistry test) and discharge outcomes (NIHSS scores) were collected. These results were the observation indicators.

Laboratory tests

For all patients who needed a laboratory test, 6 ml of fasting venous blood plasma specimens was routinely collected after fasting for 12 h upon admission. The Olympus 400 fully automatic biochemical analyser was used to

determine fasting plasma glucose (FPG), total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C), lipoprotein (a), homocysteine (Hcy), urea nitrogen (BUN), creatinine (SCr) and cystatin C (CysC) levels. Fibrinogen (FIB) was measured using the Sysmex SF-8000. All tests were carried out in strict accordance with the operating instructions of the reagent kits.

National Institutes of Health Stroke Scale scores

National Institutes of Health Stroke Scale (NIHSS) grading was conducted at patient upon discharge, comprising assessment components such as consciousness status, gaze, visual field, facial paralysis, limb motility, ataxia, sensation, speech, dysarthria and hemi-neglect. The scores ranged from 0–42, with higher scores indicating more severe neurological impairment.[12] Enrolled patients were divided into three groups according to their NIHSS score at discharge: the mild condition group (NIHSS score <7), the moderate condition group (7≤ NIHSS score <15) and the severe condition group (NIHSS score ≥15).[13]

Statistical methods

SPSS 21.0 statistical software was utilised for analysis. Count data were denoted as rates. The normality of measurement data was evaluated via histograms and Q-Q plots. Normally distributed measurement data were denoted as mean ± standard deviation, and non-normally distributed measurement data were denoted as median (Q25–Q75). Chi-squared ($\chi 2$) tests were employed for comparing multiple rates, and a one-way analysis of variance was utilised to compare normally distributed continuous variables between multiple groups. The Kruskal–Wallis test was applied to compare non-normally distributed continuous variables among multiple groups. The NIHSS scores at discharge and related risk factors were analysed by univariate and multivariate logistic regression, respectively. The logistic regression analysis examined the relationship between NIHSS scores and various risk factors in patients with acute cerebral infarction. The study compared the baseline characteristics and risk factors among groups. The odds ratios (ORs) and confidence intervals (CIs) for each risk factor were shown to express the magnitude and direction of their effects on NIHSS scores. P<0.05 was considered statistically significant.

RESULTS

Comparison of baseline information

Among the 4,048 participants, there were 3,696 patients in the mild group (91.30%), 278 in the moderate group (6.87%) and 74 in the severe group (1.83%). There were no statistically significant differences between the three groups in terms of baseline information, including for gender, history of hypertension, diabetes, hyperlipidemia, excessive drinking, TC, HDL-C, LDL-C, lipoprotein (a), BUN and SCr (P>0.05, Table 1). However, as the NIHSS score increased, statistically significant differences were identified among the three groups in terms of age, history of stroke, atrial fibrillation, coronary heart disease, smoking, antiplatelet medication usage, systolic blood pressure, diastolic blood pressure, FPG, TG, FIB, uric acid, Hcy and CysC (*P<0.05, **P<0.01, Table 1).

Univariate logistic regression analysis of National Institutes of Health Stroke Scale scores

For univariate logistic regression analyses, the moderate and severe groups were selected as dependent variables (the mild group was not analysed in this section), and gender, age, body mass index, hypertension, diabetes, hyperlipidaemia, stroke or transient ischaemic attack, atrial fibrillation, coronary heart disease, smoking, excessive alcohol consumption, antiplatelet medication usage, systolic blood pressure, diastolic blood pressure, FPG, TG, TC, LDL-C, HDL-C, lipoprotein (a), FIB, uric acid, Hcy, BUN, SCr and CysC were selected as the independent variables. The results showed that age, history of stroke, atrial fibrillation, coronary heart disease, antiplatelet medication usage, systolic blood pressure and uric acid levels were risk factors for the moderate group (P<0.05, P<0.01, Table 2). Age, history of stroke, atrial fibrillation, antiplatelet medication usage, systolic blood pressure, diastolic blood pressure, FPG, TG and uric acid levels were risk factors for the severe group (P<0.05, Table 2).

Multivariate logistic regression analysis of National Institutes of Health Stroke Scale scores

Using the mild group as a reference and the moderate and severe groups as dependent variables, multivariate logistic regression analyses were executed after adjusting for other risk factors. The results showed that age (OR=1.038;

Table 1: Baseline information

Parameters	Total (4048 cases)	Mild (3696 cases)	Moderate (278 cases)	Severe (74 cases)	P-VALUE
Demographic characteristics					
Male [Number of cases (%)]	2506 (61.91)	2308 (57.02)	155(3.83)	43 (1.06)	0.068
Age	65.00 (58.00-73.00)	65.00 (57.00-72.00)	69.00 (62.00-78.00)	72.00 (65.75-80.00)	0.000
BMI	24.73 (22.53-27.04)	24.73 (22.58-27.04)	24.34 (22.45-26.88)	24.92 (22.75-26.75)	0.539
Risk factors [Number of cases (%)]					
Hypertension	2831 (69.93)	2584 (63.83)	193 (4.77)	54 (1.33)	0.835
Diabetes	779 (19.24)	718 (17.74)	47 (1.61)	14 (0.35)	0.588
Hyperlipidemia	536 (13.24)	478 (1.81)	44 (1.09)	14 (0.35)	0.135
Previous stroke	1366 (33.75)	1211 (29.92)	117 (2.89)	38 (0.94)	<0.001
Atrial fibrillation	91 (2.25)	71 (1.75)	12 (0.30)	8 (0.20)	<0.001
Coronary heart disease	550 (13.59)	485 (11.98)	51(1.26)	14 (0.35)	0.020
Smoking	1918 (47.38)	1772 (43.77)	119 (2.94)	27 (0.67)	0.042
Excessive drinking	179 (4.42)	172 (4.25)	6 (0.15)	1 (0.02)	0.064
Antiplatelet medication usage	634 (15.66)	554 (13.69)	58 (1.43)	22 (0.54)	<0.001
Systolic blood pressure (mmHg)	162.00 (147.00-179.00)	161.00 (146.00-178.00)	166.00 (151.75-182.00)	168.00 (150.50-188.00)	<0.001
Diastolic blood pressure (mmHg)	87.00 (79.00-97.00)	87.00 (79.00-96.00)	90.00 (79.75.0-97.00)	93.00 (83.00-104.50)	<0.001
FPG (mmol/L)	5.42 (4.81-6.44)	5.40 (4.81-6.38)	5.51 (4.92-6.69)	6.42 (5.48-7.92)	<0.001
TG (mmol/L)	1.23 (0.88-1.76)	1.24 (0.89-1.78)	1.15 (0.83-1.62)	0.95 (0.74-1.50)	<0.001
TC (mmol/L)	4.72 (4.08-5.43)	4.72 (4.09-5.43)	4.77 (3.99-5.38)	4.75 (4.16-5.69)	0.735
LDL-C (mmol/L)	2.28 (1.85-2.86)	2.28 (1.84-2.85)	2.38 (1.88-3.01)	2.27 (1.93-2.86)	0.112
HDL-C (mmol/L)	1.08 (0.91-1.29)	1.08 (0.92-1.29)	1.06 (0.88-1.30)	1.04 (0.82-1.31)	0.397
Lipoprotein (a)	192.00 (98.00-330.90)	191.00 (98.25-326.00)	251.10 (95.33-371.48)	188.75 (109.25-400.60)	0.465
FIB (g/L)	2.94 (2.53-3.38)	2.93 (2.51-3.35)	3.04 (2.63-3.60)	3.10 (2.73-3.71)	<0.001
Uric acid (umol/L)	323.75 (266.80.-391.80)	324.65 (268.10-393.50)	310.05 (247.05-384.50)	307.00 (242.88-367.45)	0.018
Homocysteine	16.00 (12.00-21.00)	16.00 (12.00-21.00)	17.80 (13.00-21,00)	20.11 (14.08-24.75)	<0.001
Urea nitrogen	5.40 (4.42-6.62)	5.39 (4.43-6.58)	5.59 (4.32-7.01)	5.66 (4.31-7.25)	0.229
Creatinine	67.20 (57.40-78.90)	67.10 (57.33-78.90)	68.30 (58.05-79.98)	71.35 (57.40-84.85)	0.499
Cystatin-C	0.90(0.70-1.10)	0.90(0.70-1.10)	0.90 (0.80-1.00)	1.00 (0.80-1.20)	0.022

BMI, Body mass index; FPG, Fasting plasma glucose; TG, Triglycerides; TC, Total cholesterol; LDL-C, Low density lipoprotein cholesterol; HDL-C, High density lipoprotein cholesterol; FIB, Fibrinogen.

Table 2: Univariate logistic regression analysis of NIHSS scores for patients with acute cerebral infarction

Item	Moderate			Severe		
	OR	95%CI	P value	OR	95%CI	P value
Demographic characteristics						
Gender	1.320	1.032~1.087	0.027	1.199	0.752~1.911	0.446
Age	1.043	1.031~1.055	0.000	1.067	1.043~1.091	<0.001
BMI	0.984	0.950~1.018	0.354	0.980	0.918~1.047	0.552
Risk factors					~	
Hypertension	0.977	0.750~1.273	0.864	1.162	0.692~1.950	0.570
Diabetes	0.844	0.610~1.167	0.305	0.968	0.538~1.741	0.913
Hyperlipidemia	1.266-	0.905~1.772	0.169	1.571	0.871~2.833	0.133
Previous stroke	1.491	1.164~1.911	0.002	2.166	1.366~3.435	0.001
Atrial fibrillation	2.303	1.234~4.300	0.009	6.189	2.864~13.372	<0.001
Coronary heart disease	1.478	1.082~2.045	0.015	1.545	0.857~2.785	0.148
Smoking	1.231-	0.962~1.574-	0.099-	1.603	0.994~2.585	0.053
Excessive drinking	0.452	0.198~1.030	0.059	0.281	0.039~2.031	0.208
antiplatelet medication usage	1.495-	1.104~2.025-	0.009-	2.399	1.446~3.982	0.001
Systolic blood pressure (mmHg)	1.009	1.004~1.013	0.001	1.013	1.004~1.022	0.005
Diastolic blood pressure (mmHg)	1.008-	0.999~1.017-	0.067-	1.036	1.020~1.052	<0.001
FPG (mmol/L)	1.028	0.978~1.082	0.276	1.179	1.105~1.258	<0.001
TG (mmol/L)	0.986	0.896~1.084	0.769	0.691	0.499~0.973	0.034
TC (mmol/L)	0.986	0.886~1.099	0.803	1.095	0.902~1.328	0.359
LDL-C (mmol/L)	0.995-	0.968~1.023-	0.708-	0.982	0.861~1.121	0.791
HDL-C (mmol/L)	0.870-	0.615~1.232-	0.432-	0.815	0.408~1.629	0.502
Lipoprotein (a)	1.000	1.000~1.000	0.781	1.000	1.000~1.001	0.226
FIB (g/L)	1.049	0.995~1.107	0.079	1.058	0.980-1.143	0.147
Uric acid (umol/L)	0.999	0.997~1.000	0.031	0.997	0.995~1.000	0.035
Homocysteine	1.003	0.996~1.011	0.390	1.008	0.996~1.020	0.213
Burea nitrogen	1.015	0.9713~1.059	0.481	1.034	0.981~1.089	0.209
Creatinine	0.998	0.994~1.003	0.494	1.000	0.994~1.007	0.948
Cystatin-C	0.995	0.956~1.036	0.804	1.001	0.970~1.034	0.950

NIHSS, National Institutes of Health Stroke Scale; BMI, Body mass index; FPG, Fasting plasma glucose; TG, Triglycerides; TC, Total cholesterol; LDL-C, Low density lipoprotein cholesterol; HDL-C, High density lipoprotein cholesterol; FIB, Fibrinogen.

95% CI: 1.025–1.050; P<0.01), history of stroke (OR=1.351; 95% CI: 1.034–1.767; P<0.05) and systolic blood pressure (OR=1.007; 95% CI: 1.002–1.012; P<0.01) were independent risk factors for the moderate group. Age (OR=1.089; 95% CI: 1.061–1.118; P<0.01), history of stroke (OR=1.548; 95% CI: 1.025–2.593; P<0.05), atrial fibrillation (OR=2.983; 95% CI: 1.249–7.120; P<0.05), diastolic blood pressure (OR=1.053; 95% CI: 1.032–1.075; P<0.01), FPG (OR=1.240;

95%CI: 1.151–1.335; P<0.01) and uric acid levels (OR=0.997; 95%CI: 0.995–1.000; P<0.05) were independent risk factors for the severe group (Table 3).

DISCUSSION

In this study, the 4,048 enrolled patients with acute cerebral infarction were divided into three groups based on their NIHSS scores: mild, moderate, and severe, accounting for 91.30%, 7.87% and 1.83% of the total participants, respectively. According to this study's results, increased NIHSS scores were associated with multiple stroke-related risk factors, among which age, history of stroke, atrial fibrillation, diastolic blood pressure, FPG and uric acid levels were independent risk factors.

The results also showed that as the age of patients with acute cerebral infarction increased, the risk of elevated NIHSS scores increased, too. Previous studies have shown that older age is one of the risk factors for poor prognosis after stroke.[14] According to relevant studies outside China, people over 80 years are more likely to experience cardiogenic embolism and atherosclerosis, which are common causes of severe cerebral infarction and are associated with smoking and alcohol consumption.[15] Age is a very important factor affecting the prognosis of patients with acute cerebral infarction and can serve as an independent predictor of prognosis after acute cerebral infarction. Therefore, it is considered that the older the age, the poorer the prognosis of acute cerebral infarction and the more severe the neurological deficits, which would prompt continuous escalation of NIHSS scores.[16]

Existing research has also found that if a patient has had a previous cerebral infarction and the resulting neurological deficits have not been eliminated, the severity of a subsequent cerebral infarction will increase.[17] Thus, a history of previous cerebral infarction is an independent influencing factor for severe cerebral infarction.[18] This finding is consistent with the present study in that a history of stroke can lead to more severe neurological deficits, thus resulting in increased NIHSS scores. For patients with a history of previous cerebral infarction who experience a recurrent stroke, efforts should be made to strengthen monitoring and prevention of deterioration to improve prognosis.

Clinical studies have shown that among patients with acute cerebral infarction, those with concurrent atrial fibrillation have higher rates of haemorrhagic transformation, larger areas of cerebral infarction and more severe neurological impairments.[19-21] It was confirmed by previous research that atrial fibrillation increases the risk of cerebral infarction by four- to five-fold and aggravates the condition at the time of onset. The main reason is that atrial fibrillation-related cardiac arrhythmias or heart failure can lead to increased venous pressure or decreased cardiac output, which can result in reduced intracranial blood flow, hypoxia and ischemia in brain tissue and stroke.[22] The above findings are consistent with this study's results in that a history of atrial fibrillation is associated with more severe neurological damage, thus affecting NIHSS scores at discharge in patients with acute cerebral infarction.

Table 3: Multivariate logistic regression analysis of NIHSS scores for patients with acute cerebral infarction

Item	Moderate			Severe		
	OR	95%CI	P	OR	95%CI	P
Age	1.038	1.025~1.050	0.000	1.089	1.061~1.118	0.000
Previous stroke	1.351	1.034~1.767	0.028	1.548	1.025~2.593	0.047
Atrial fibrillation	-	-	-	2.983	1.249~7.120	0.014
Systolic blood pressure (mmHg)	1.007	1.002~1.012	0.009	-	-	-
Diastolic blood pressure (mmHg)	-	-	-	1.053	1.032~1.075	<0.001
FPG (mmol/L)	-	-	-	1.240	1.151~1.335	<0.001
Uric acid (umol/L)	-	-	-	0.997	0.995~1.000	0.039

NIHSS, National Institutes of Health Stroke Scale; FPG, Fasting plasma glucose.

With further Pearson linear correlation analysis, it was found that NIHSS scores in patients with acute cerebral infarction were positively correlated with 24-hour average systolic blood pressure, 24-hour average diastolic blood pressure, nighttime mean systolic blood pressure, nighttime mean diastolic blood pressure, daytime mean systolic blood pressure, daytime mean diastolic blood pressure, 24-hour pulse pressure, 24-hour systolic blood pressure variability. This is also consistent with this study[23] in that increased blood pressure levels can lead to increased NIHSS scores.

Statistics show that patients who experience an ischemic stroke with concurrent diabetes have a higher risk of mortality, which demonstrates that blood glucose levels can affect the development and prognosis of cerebral infarction.[24] For patients with acute cerebral infarction and concurrent diabetes mellitus, the higher the fasting blood glucose level, the more severe the neurological deficits and the worse the prognosis.[25] That is, blood glucose levels are positively correlated with prognosis in patients. This is also consistent with this study's results in that increased FPG can lead to increased neurological deficit scores, thereby affecting NIHSS scores at discharge in patients with acute cerebral infarction.

Studies have shown that hyperuricemia is an independent risk factor for poor prognosis in acute cerebral infarction, and blood uric acid levels are positively correlated with the disease's severity, therefore requiring special attention clinically.[26] The positive correlation between blood uric acid levels and NIHSS scores ($P<0.05$) concurs with other studies[27], indicating that blood uric acid levels should be actively controlled in patients with acute cerebral infarction. One study explored the risk factors of acute cerebral infarction (ACI) in patients with primary hypertension and found that higher uric acid content is an independent risk factor for ACI in patients with primary hypertension.[28] Another paper suggests a potential link between hyperuricemia and cardiovascular diseases.[29] This study's results confirm that increased uric acid levels can reflect increased NIHSS scores. However, after analysing the relationship between the presence or absence of chronic kidney disease during the acute phase and at admission and clinical outcomes in 412 patients with acute ischemic stroke, one study[30] showed that NIHSS scores decreased with increasing blood uric acid levels, there was a significant correlation between quantitative blood uric acid levels and NIHSS scores, and blood uric acid levels had an independent protective effect on stroke severity in the adjusted multivariate model.

Our study has some limitations, such as the retrospective design, the single-centre setting and the lack of long-term follow-up data. These may affect the generalisability and applicability of the results. Future studies may benefit from using prospective, multicentre and longitudinal designs to validate and extend this study's results.

In conclusion, through a large-sample retrospective analysis based on patient data, age, history of stroke, atrial fibrillation, diastolic blood pressure, FPG and uric acid levels were found to be independent risk factors affecting the short-term post-discharge functional prognosis of patients with acute cerebral infraction. These factors are related to the NIHSS scores of these patients after discharge.

DISCLOSURE

Data availability: All data generated or analyzed during this study are included in this published article.

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Conflict of interest: None

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