Score for Predicting Active Cancer in Patients with Ischemic Stroke: A Retrospective Study

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Abstract

Background: We aimed to examine the differences between the clinical characteristics of patients with ischemic stroke and active cancer and those without cancer and develop a clinical score for predicting occult cancer in patients with ischemic stroke.

Methods: This retrospective study enrolled consecutive adult patients with acute ischemic stroke, who were admitted to our department between December 2017 and January 2019. The demographic, clinical, laboratory, and neuroimaging characteristics of patients with ischemic stroke with active cancer and those without cancer were compared. Multivariate analysis was performed to identify independent factors associated with active cancer. Subsequently, a predictive cancer-risk score was developed using the area under the receiver operating characteristic curve.

Results: Fifty-three (6.63%) of 799 patients with ischemic stroke had active cancer. The absence of a history of hyperlipidemia [odds ratio (OR)=0.17, 95% confidence interval (CI): 0.06–0.48, *P*<0.01], elevated serum fibrinogen (OR=1.72, 95% CI: 1.33–2.22, *P*<0.01) and D-dimer levels (OR=1.43, 95% CI: 1.24–1.64, *P*<0.01), and stroke of undetermined etiology (OR=22.87, 95% CI: 9.91–52.78, *P*<0.01) were independently associated with active cancer. Thus, a score based on the absence of hyperlipidemia and serum fibrinogen ≥4.00 g/L and D-dimer ≥2.00 μg/mL predicted active cancer with an area under the curve of 0.83 (95% CI: 0.77–0.89, *P*<0.01). The probability of active cancer was 59% at a supposed prevalence of 6.63%, if all three independent factors were present in a patient with ischemic stroke.

Conclusions: We devised a score to predict active cancer in patients with ischemic stroke based on the absence of a history of hyperlipidemia and elevated serum D-dimer and fibrinogen that highlights the importance of hypercoagulability in these patients and may help determine early intervention and management.

Background

Malignant tumors and stroke are the most common causes of disability and mortality worldwide [1]. The concomitance of both conditions has serious repercussions on the quality of life with a substantial increase in the socioeconomic burden on the individual and societal levels. Previous studies have reported that approximately 15% of patients with cancer are at risk of developing ischemic stroke (IS) later in life [2], and 10% of patients hospitalized with IS could have cancer as a comorbidity [3]. In some instances, IS is the initial manifestation of occult cancer [4]. Moreover, new diagnoses of solid tumors are related to a considerably increased short-term risk of stroke, and the risk of stroke varies according to the type of cancer, histopathological features, and stage [5, 6]. These previous studies revealed a close association between cancer and stroke. Thus, diagnosing occult malignancies at an early stage in patients with IS with appropriate interventions could help improve the chances of survival and functional outcomes [7].

The characteristics of patients with IS with a higher risk of developing malignancies remain unclear, despite the increasing knowledge in this field. Some studies have shown that the absence of classical vascular risk factors, higher rates of stroke of undetermined etiology (SUE), elevated C-reactive protein (CRP) and D-dimer levels, and lesions involving multiple vascular territories on diffusion-weighted imaging (DWI) are indicative of a hypercoagulable state [8–11]. However, other studies did not find significant differences in these stroke-related characteristics of patients with IS with cancer and those with IS but without cancer [12–14].

There is a surprising lack of research focusing on the appropriate time for screening patients with IS for active cancer. To the best of our knowledge, only one study has reported a score for occult malignancy prediction in patients with IS; however, the overall predictive strength calculated by that study yielded an area under the curve (AUC) of 0.73 [15]. Therefore, we conducted a retrospective study to identify the differences between the clinical characteristics of patients with IS either with active cancer or without cancer, and develop a more reliable, clinically relevant predictive score for cancer evaluation in patients with IS.

Methods

Patient selection and data collection

This retrospective study enrolled consecutive patients with acute IS from the Department of Neurology at the First Affiliated Hospital of China Medical University, a comprehensive academic hospital in a large urban area, between December 2017 and January 2019. Our inclusion criteria were as follows: (1) patients aged 18 years or above, (2) IS that met the Baltimore-Washington Cooperative Young Study Criteria, (3) neurologic deficit lasting longer than 24 h, and (4) computed tomography (CT) or magnetic resonance imaging (MRI) scans that depicted infarctions related to the clinical findings [16]. Patients were excluded from the study if they: (1) lacked information regarding the etiological examination of stroke, including Holter electrocardiography (ECG), transthoracic or transesophageal echocardiography, and magnetic resonance angiography (MRA), CT angiography (CTA), or Doppler ultrasonography; (2) were diagnosed with transient ischemic attack (TIA) or cerebral hemorrhage; (3) had a previous history of brain tumor, cerebral metastases, or intracranial surgery; and (4) had indications of inactive cancer (patients with IS and cancer that did not meet the description of active cancer) or hematological malignancies. Active cancer was defined as the diagnosis of cancer or administration of cancer treatment within the past 6 months or the metastasis or recurrence of known cancer [17, 18]. Patients with IS and active cancer were categorized into the cancer group, while those without cancer were assigned to the control group.

Clinical assessment

Trained personnel reviewed the patients' demographic data (age, sex, and medical history), vascular risk factors [hypertension (previously diagnosed and treated, or blood pressure ≥140/90 mmHg)], diabetes mellitus (previously diagnosed and treated, or fasting glucose level ≥7.00 mmol/L), hyperlipidemia

(previously diagnosed and treated, fasting total serum cholesterol level ≥5.72 mmol/L, triglyceride level ≥1.7 mmol/L, or low-density lipoprotein level ≥3.64 mmol/L), atrial fibrillation (previously diagnosed and treated, or ECG suggested), history of coronary heart disease, ischemic stroke or TIA, and obesity status (body mass index ≥28 kg/m^2), current smoking habit, stroke severity on admission [obtained using the National Institute of Health Stroke Scale (NIHSS) score] [19], and the results of diagnostic investigations. Two board-certified neurologists consensually determined the stroke etiology subtype as large-artery atherosclerosis (LAA), cardioembolism (CE), small-vessel occlusion (SVO), stroke of other determined etiology (SOE), or SUE, according to the Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria [20].

Routine investigations included neuroimaging (MRI, especially contrast-enhanced MRI and DWI, and angiography, including MRA, CTA, or Doppler ultrasonography), ECG or 24 h-ECG, and transthoracic or transesophageal echocardiography. Acute multiple cerebral infarctions (AMCIs) were selected based on the findings of DWI and defined as multiple acute infarcts, either in the bilateral anterior or posterior circulation or in the anterior and posterior circulation simultaneously, which suggested an embolic etiology. Routine laboratory data, including serum platelet, hemoglobin, fibrinogen, D-dimer, CRP, lipid, and glucose levels, were also obtained. The diagnosis of cancer was confirmed based on histopathological evidence and the oncologist's opinion. Furthermore, the oncological records were carefully reviewed for cancer-specific details, including tumor type, histology, and stage.

Statistical analysis

All statistical analyses were performed using SPSS 22.0 statistical software (SPSS Inc., Chicago, IL, USA). Categorical variables are presented as the total number (n) and percent (%) per group, and the χ^2 or Fisher's exact test was used to assess the statistical differences between them. The mean and standard deviations (SDs) were calculated for continuous variables with normal distribution, while the median and interquartile range (IQR) were used for continuous variables lacking normal distribution. Similarly, the Student's t-test was used for normally distributed data. The Mann-Whitney U test was used for data without normal distribution. Risk factors ($P \leq 0.05$) were further analyzed using univariate and multivariate logistic regression. The chosen clinical markers were dichotomized using cut-off points prior to score entry, based on the variables independently associated with active cancer. We compared the diagnostic performance of the different scores using the area under the receiver operating characteristic (AUC-ROC) curve. Bayesian decision theory was used to calculate the posterior probability of active cancer for the different scores. All *P*-values were two-tailed. *P*-values <0.05 were considered statistically significant.

Results

Baseline characteristics of patients with ischemic stroke in both groups

Of the initial 1889 patients with IS, 799 were included in the final analysis (Fig. 1). Of these, 53 (6.63%) were diagnosed with active cancer at the time of stroke onset and were assigned to the cancer group, while 746 (93.37%) did not have a history of cancer and were assigned to the control group. Patients with inactive cancer were not included in this study.

Table 1 shows the patient characteristics for both groups. Patients in the cancer group had a significantly higher mean age than those without cancer (mean ± SD: 67.21 ± 10.11 years versus 62.11 ± 12.09 years, respectively; t = 3.00, $P < 0.01$). The frequency of hyperlipidemia was lower in patients with active cancer than that of the control group (22.6% versus 49.3%, respectively; $\chi^2 = 14.13$, $P < 0.01$). The prevalence of other vascular risk factors did not differ significantly between the two groups. We observed that 35 (66.04%) patients with active cancer had SUE compared to 31 (4.16%) patients in the control group ($\chi^2 = 250.06$, $P < 0.01$), while the LAA subtype was less common in the active-cancer group than that in the control group (9.43% versus 60.99%, respectively; $\chi^2 = 53.85$, $P < 0.01$), as per the TOAST criteria. There were no significant differences in the CE, SVO, and SOE subtypes. We found that the average NIHSS score at admission was higher in the cancer group than that of the control group (mean ± SD 6.13 ± 4.10 versus 4.30 ± 4.48; t = 2.89, $P < 0.01$). AMCIs were observed more frequently in patients with active cancer than in those without cancer (56.60% versus 19.84%; $\chi^2 = 38.63$, $P < 0.01$). The incidence of deep vein thrombosis or pulmonary embolism during hospitalization was higher in the cancer group than in the control group (13.21% versus 3.75%, respectively; $\chi^2 = 10.56$, $P < 0.01$). Patients with active cancer had significantly higher serum levels of fibrinogen (mean ± SD, 4.44 ± 1.82 versus 3.56 ± 1.02, respectively; t = 3.49, $P < 0.01$), D-dimer [median (IQR): 2.23 (0.98–10.76) versus 0.35 (0.27–0.48), respectively; Z=-9.55, $P < 0.01$] and CRP [median (IQR): 18.40 (5.45–46.00) versus 3.90 (2.80–6.33), respectively; Z=-7.35, $P < 0.01$], but lower levels of hemoglobin (mean ± SD: 119.79 ± 25.68 versus 143.61 ± 18.57, respectively; t=-6.63, $P < 0.01$) than those in the control group.

Table 1
Baseline characteristics of patients with ischemic stroke and active cancer versus those without cancer

Variables	Cancer Group n = 53	Control Group n = 746	t/χ^2	*P*-value
Demographics				
Age, Years	67.21 ± 10.11	62.11 ± 12.09	3.00	< 0.01
Sex (% Male)	34 (64.2)	522 (70.0)	0.79	0.37
Vascular Risk Factors				
Hypertension	30 (56.6)	508 (68.1)	2.97	0.09
Diabetes Mellitus	14 (26.4)	286 (38.3)	3.00	0.08
Hyperlipidemia	12 (22.6)	368 (49.3)	14.13	< 0.01
Atrial Fibrillation	4 (7.6)	46 (6.2)		0.57
Coronary Heart Disease	8 (15.1)	106 (14.2)	0.03	0.86
Previous Stroke/TIA	7 (13.2)	129 (17.3)	0.59	0.45
Smoking	25 (47.2)	351 (47.1)	0.00	0.99
Obesity	6 (11.3)	121 (16.2)	0.89	0.35
TOAST Classification				
Large Artery Atherosclerosis	5 (9.4)	455 (61.0)	53.85	< 0.01
Cardioembolism	2 (3.8)	33 (4.4)		1.00
Small Vessel Occlusion	9 (17.0)	216 (29.0)	3.51	0.06
Other Determined Etiology	2 (3.8)	11 (1.5)		0.21
Undetermined Etiology	35 (66.0)	31 (4.2)	250.6	< 0.01
Ischemic Stroke Characteristics				
Initial NIHSS Score	6.13 ± 4.10	4.30 ± 4.48	2.89	< 0.01
AMCI	30 (56.6)	148 (19.8)	38.63	< 0.01
With VTE or PE	7 (13.2)	28 (3.8)	10.56	< 0.01
Laboratory Markers				

Data are represented as mean ± SD, median (IQR), or n (%).

Abbreviations: AMCI, acute multiple cerebral infarction; VTE, venous thromboembolism; PE, pulmonary embolism; CRP, C-reactive protein; NIHSS, National Institute of Health Stroke Scale; TOAST: Trial of Org 10172 in Acute Stroke Treatment, TIA: transient ischemic attack

Variables	Cancer Group n = 53	Control Group n = 746	t/χ^2	*P*-value
Hemoglobin (g/L)	119.79 ± 25.68	143.61 ± 18.58	-6.63	< 0.01
Platelet	213.28 ± 99.86	222.17 ± 66.55	-0.64	0.53
Fibrinogen (g/L)	4.44 ± 1.82	3.56 ± 1.02	3.49	< 0.01
D-Dimer (mg/mL)	2.23 (0.98–10.76)	0.35 (0.27–0.48)	-9.55	< 0.01
CRP (mg/L)	18.40 (5.45–46.00)	3.90 (2.80–6.33)	-7.35	< 0.01
Data are represented as mean ± SD, median (IQR), or n (%).				
Abbreviations: AMCI, acute multiple cerebral infarction; VTE, venous thromboembolism; PE, pulmonary embolism; CRP, C-reactive protein; NIHSS, National Institute of Health Stroke Scale; TOAST: Trial of Org 10172 in Acute Stroke Treatment, TIA: transient ischemic attack				

Type, histology, and stage of active cancer

The most commonly observed cancer diagnoses among the patients with IS and active cancer were as follows: lung cancer (n=16, 30.19%), followed by gastric cancer (n=8, 15.09%), liver cancer (n=6, 11.32%), colorectal cancer (n=5, 9.43%), breast cancer (n=5, 9.43%), genitourinary cancers (bladder, prostate, and ovarian cancers; n=5, 9.43%), biliary tract cancer (n=4, 7.55%), and pancreatic cancer, nasopharyngeal cancer, renal cancer, and adrenal cancer (n=1, 1.89% each). Thirty-one (58.49%) patients were diagnosed with adenocarcinoma, and 21 (39.62%) were diagnosed with metastatic disease (Table 2).

Univariate and multivariate logisticregression analyses

We assessed all the risk factors with *P*-values ≤0.05 (Table 1) using a univariate logistic regression model (including age, hyperlipidemia, LAA, SUE, NIHSS score, AMCI, hemoglobin, fibrinogen, D-dimer, and CRP). The results are shown in Table 3. Notably, we observed that the odds ratios (OR) for age, NIHSS score, hemoglobin, and CRP were approximately 1 based on the findings of univariate logistic regression. Therefore, we considered only the remaining risk factors, including hyperlipidemia, SUE, AMCI, presence of venous thromboembolism or pulmonary embolism, and fibrinogen and D-dimer levels, in the multivariate logistic regression model. This analysis showed that the absence of a history of hyperlipidemia [OR=0.17, 95% confidence interval (CI): 0.06–0.48, *P*<0.01], elevated serum fibrinogen levels (OR=1.72, 95% CI: 1.33–2.22, *P*<0.01) and D-dimer (OR=1.43, 95% CI 1.24–1.64, *P*<0.01), and SUE (OR=22.87, 95% CI: 9.91–52.78, *P*<0.01) were independently associated with active cancer (Table 3).

Predictive score using the area under the receiver operating characteristic curve

We developed a scoring system to predict active cancer in patients with IS, based on the findings of the multivariate analysis, particularly in the subset of patients with SUE. The final score, ranging from 0–3, comprised the sum of individual scores of the history of hyperlipidemia, serum D-dimer levels, and serum fibrinogen levels. We reviewed and compared several studies to determine the appropriate cut-off values

for D-dimer and fibrinogen levels for the scoring system. The OASIS-CANCER study conducted by Lee et al. determined the first quartile of the pre-treatment D-dimer concentration as 2.08 μg/mL and the median fibrinogen concentration as 399 mg/dL [10]. Moreover, Quintas et al. found that the median fibrinogen value of patients with IS without cancer was 408.5 mg/dL [21]. They demonstrated that fibrinogen values were associated with the diagnosis of cancer after IS. Therefore, we analyzed multiple data conditions and assigned the following final scores, according to the findings of previous studies, our clinical experience, and the findings of this study: history of hyperlipidemia=0 points, no history of hyperlipidemia=1 point; D-dimer level ≤2.00 μg/mL=0 points, D-dimer level >2.00 μg/mL=1 point; and fibrinogen level ≤4.00 g/L=0 points, fibrinogen level >4.00 g/L=1 point. Table 4 presents the sensitivity, specificity, and posterior probability for each cut-off point based on the supposed cancer prevalence value of 6.63% in our study. Figure 2 shows that the probability of active cancer was 59%, if a patient with IS had a clinical score of 3 points, with a reliable AUC-ROC curve value of 0.83 (95% CI: 0.77–0.89, P<0.01).

Table 2
Characteristics of patients with ischemic stroke and active cancer

Cancer Location	Histological Type	Number
Lung Cancer	Adenocarcinoma	15
	Small Cell Carcinoma	1
Gastric Cancer	Adenocarcinoma	8
Liver Cancer	Hepatocellular Carcinoma	6
Colon Cancer	Adenocarcinoma	3
Rectal Cancer	Adenocarcinoma	2
Breast Cancer	Infiltrating Ductal Carcinoma	4
	Medullary Carcinoma	1
Biliary Tract Cancer	Epithelial Cell Carcinoma	3
	Adenocarcinoma	1
Bladder Cancer	Transitional Epithelial Carcinoma	3
Prostate Cancer	Adenocarcinoma	1
Ovarian Cancer	Serous Carcinoma	1
Pancreatic Cancer	Adenocarcinoma	1
Nasopharyngeal Cancer	Squamous Cell Carcinoma	1
Renal Cancer	Clear Cell Carcinoma	1
Adrenal Cancer	Cortical Carcinoma	1
Metastatic Disease		21

Table 3
Univariate and multivariate logistic regression analyses of risk factors in patients with ischemic stroke with active cancer and those without cancer

	Univariate Logistic Regression Analysis		Multivariate Logistic Regression Analysis	
Variables	**OR (95% CI)**	**P-value**	**OR (95% CI)**	**P-value**
Age	1.04 (1.01, 1.07)	< 0.01		
Hyperlipidemia	0.30 (0.16, 0.58)	< 0.01	0.16 (0.06, 0.45)	< 0.01
LAA	0.07 (0.02, 0.17)	< 0.01		
SUE	44.85 (22.89, 87.88)	< 0.01	19.30 (7.93, 48.96)	< 0.01
NIHSS score	1.06 (1.02, 1.11)	< 0.01		
AMCI	5.27 (2.97, 9.34)	< 0.01	1.58 (0.66, 3.81)	0.31
with VTE or PE	4.56 (1.97, 10.58)	< 0.01	0.92 (0.21, 3.94)	0.91
Hemoglobin (g/L)	0.95 (0.94, 0.96)	< 0.01		
Fibrinogen (g/L)	1.63 (1.35, 2.00)	< 0.01	1.70 (1.31, 2.21)	< 0.01
D-dimer (μg/mL)	1.72 (1.45, 2.03)	< 0.01	1.42 (1.23, 1.65)	< 0.01
CRP	1.03(1.02, 1.04)	< 0.01		

Abbreviations: LAA, large-artery atherosclerosis; SUE, stroke of undetermined etiology; NIHSS, National Institute of Health Stroke Scale; AMCI, acute multiple cerebral infarction; VTE, venous thromboembolism; PE, pulmonary embolism; CRP, C-reactive protein

Table 4
Predictive score values and posterior probabilities for cancer in patients with ischemic stroke

Score	Sensitivity	Specificity	Posterior probability
1	0.96	0.37	0.09
2	0.68	0.88	0.27
3	0.19	0.99	0.59

Discussion

This study showed that the absence of a history of hyperlipidemia, increased serum levels of D-dimer and fibrinogen, and SUE were independent risk factors associated with active cancer in patients with IS. Adenocarcinoma was the most commonly observed histological manifestation, which was consistent with the results of several previous studies [10, 22, 23]. However, recent studies evaluating underlying cancer in patients with IS have simply focused on the differences in the epidemiological and biochemical

parameters. To date, there has been no consensus on the ideal method for the identification of active occult cancer in patients with IS or the optimal time for screening such patients for cancer. Thus, in light of our findings, we developed a predictive and reliable score to help clinical neurologists rapidly assess the occult risk of cancer in patients with IS at the early stage, which could ultimately improve their quality of life and survival outcomes.

Our systematically developed predictive score consisted of increased serum levels of D-dimer and fibrinogen and the absence of a history of hyperlipidemia, especially in patients with SUE. Our final scoring system demonstrated that if a patient with IS had a total score of 3/3, the probability of active cancer was 59% [with a high specificity (99%)], based on an assumed cancer prevalence of 6.63%, which was similar to that of previous studies [21, 24, 25]. The probability of active cancer was 27% if the score was 2 points. We compared the predictive capabilities of our scoring system with those of a previously reported system and found that our system was significantly superior; the AUC of the scores described by Selvik et al. was 0.73 [15], while the AUC of our scoring system was 0.83.

The differences between the associations of classical vascular risk factors in patients with IS with and without cancer remain unclear. Some studies reported that the prevalence of classical vascular risk factors was similar between these patient groups [8, 18, 26], while others have demonstrated that the frequency of occurrence of risk factors, especially hyperlipidemia, was lower in patients with IS and active cancer [27–29]. Our analyses demonstrated that the absence of a history of hyperlipidemia was independently associated with the presence of active cancer. Several studies suggested that low cholesterol levels were associated with an elevated risk of cancer-related mortality, and an inverse association has been well-demonstrated in patients with lung, liver, and stomach cancers [30–32]. The findings of these studies are generally in accordance with those of our study. Moreover, we found a significant difference in the classification of stroke etiology between the two groups. Similar to previous studies, we observed a lower frequency of the LAA subtype and higher prevalence of SUE in patients with IS and active cancer compared to those without cancer [12, 27]. Thus, previous studies and our study indicate that a specific stroke mechanism, differing from that associated with traditional IS, may exist in patients with active cancer.

We compared the differences in blood coagulation biomarkers between the two groups, including an analysis of platelet, fibrinogen, and D-dimer levels to further explore the possible mechanisms underlying cancer-associated IS. We found higher serum levels of fibrinogen and D-dimer in patients with IS and active cancer compared to those without cancer, similar to most recent studies [10, 11, 21, 33]. These factors are considered to be predictors of active cancer in patients with IS. Earlier studies reported that D-dimer levels, which reflect extensive fibrin turnover associated with an activated coagulation system, were correlated with the degree of hypercoagulability [10] and widespread dissemination of microthrombi [34]. Moreover, malignancies can induce a hypercoagulable state and promote the formation of microthrombi by promoting the secretion of mucins, release of tissue factors, and production of procoagulant cytokines [35], which may explain the elevated levels of blood coagulation biomarkers in the present study. Therefore, it is necessary to identify the specific cancer types that tend to induce hypercoagulable states

and thrombosis. Our data demonstrated that active lung cancer and gastric cancer were the most common cancer types, and adenocarcinoma was the most commonly observed histopathological subtype. These findings are also consistent with those of previous studies, which revealed a higher prevalence of thromboembolic events in patients with lung cancer [24, 36]. Furthermore, studies have shown that patients with adenocarcinoma were prone to developing cancer-mediated hypercoagulability and microemboli [18, 37]. Several studies have suggested that some epithelium-derived tumors, such as those originating from the lung, stomach, and bile ducts, are frequently adenocarcinomas and could systematically secrete mucins that bind to P- and L-selectins, inducing the formation of platelet-rich microthrombi [38, 39]. Moreover, these cancers usually remain undiagnosed until they reach an advanced or metastatic stage. The histologic and natural characteristics of these tumors underline the potential increase in the risk of IS, further revealing the role of hypercoagulability in cancer-related IS.

Our study has several limitations. First, this single-center retrospective study used consecutively collected data. Therefore, our findings may not be applicable to other settings due to the inherent selection bias. Second, comparing the characteristics of patients with different cancer types separately would have been ideal, as patients with IS may have different types of cancer. However, further categorization by cancer type did not allow for appropriate statistical subgroup analyses, because this study included a relatively limited number of patients with active cancer.

Conclusion

This study systematically developed a scoring system comprising the history of hyperlipidemia and fibrinogen and D-dimer levels for the prediction of active cancer in patients with IS, especially in those with SUE. Our findings indicate the importance of hypercoagulability in assessing active cancer in patients with IS, which could support early decision making for intervention and management at the time of admission. Prospective multicenter studies are needed to evaluate the effectiveness of this clinical scoring system prior to implementation in clinical practice.

List Of Abbreviations

AMCIs, Acute multiple cerebral infarctions; AUC-ROC, the area under the receiver operating characteristic curve; CE, cardioembolism; CRP, C-reactive protein; CT, computed tomography; CTA, computed tomography angiography; DWI, diffusion-weighted imaging; ECG, electrocardiography; IQR, interquartile range; IS, ischemic stroke; LAA, large-artery atherosclerosis; MRA, magnetic resonance angiography; MRI, magnetic resonance imaging; OR, odds ratio; SDs, standard deviations; SVO, small-vessel occlusion; SOE, stroke of other determined etiology; SUE, stroke of undetermined etiology; TIA, transient ischemic attack

Declarations

Ethics approval and consent to participate

This study was performed in accordance with the principles of the Declaration of Helsinki. The First Affiliated Hospital of China Medical University Medical Science Research Ethics Committee approved this study {committee's reference number: [2019]325}. The need for informed consent (prior to participation) was waived because of the retrospective nature of this study and the minimal risk posed to patients in this study.

Consent for publication

Not applicable

Availability of data and materials

Data has not been made accessible in the interest of protecting patients' privacy.

Competing interests

The authors have no competing interests to declare.

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Authors' contributions

JJ: conceptualization and design of the study, interpretation of data, drafting and revising the manuscript

JW: critical revision of the manuscript for important intellectual content, ethics submission and data analyses

MC: data collection and analyses

JZ: data collection and analyses

XS: critical revision of the manuscript for important intellectual content, study supervision and fund support

All authors have read and approved the manuscript.

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Figures

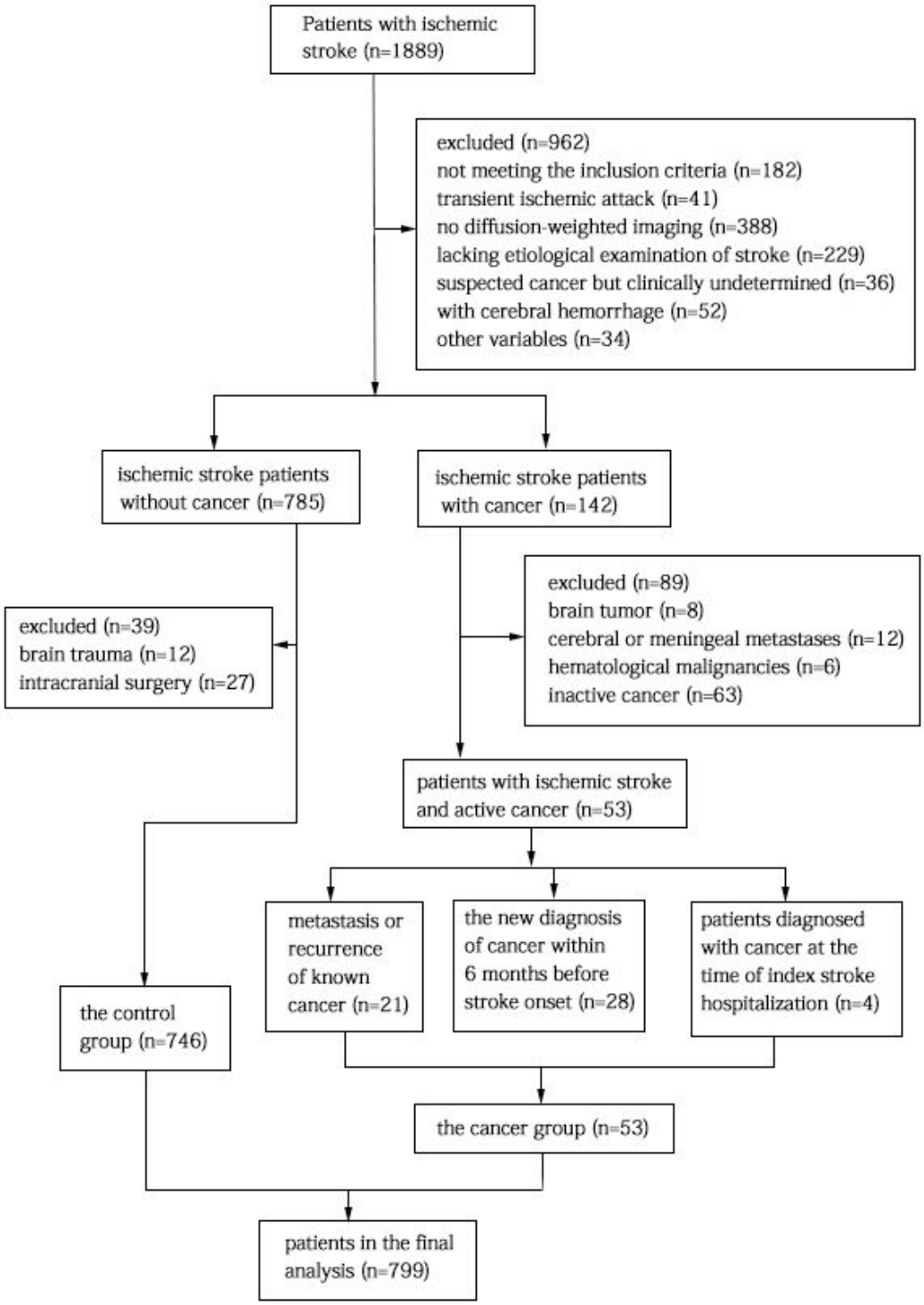

Figure 1

Flow diagram explaining the inclusion and exclusion criteria

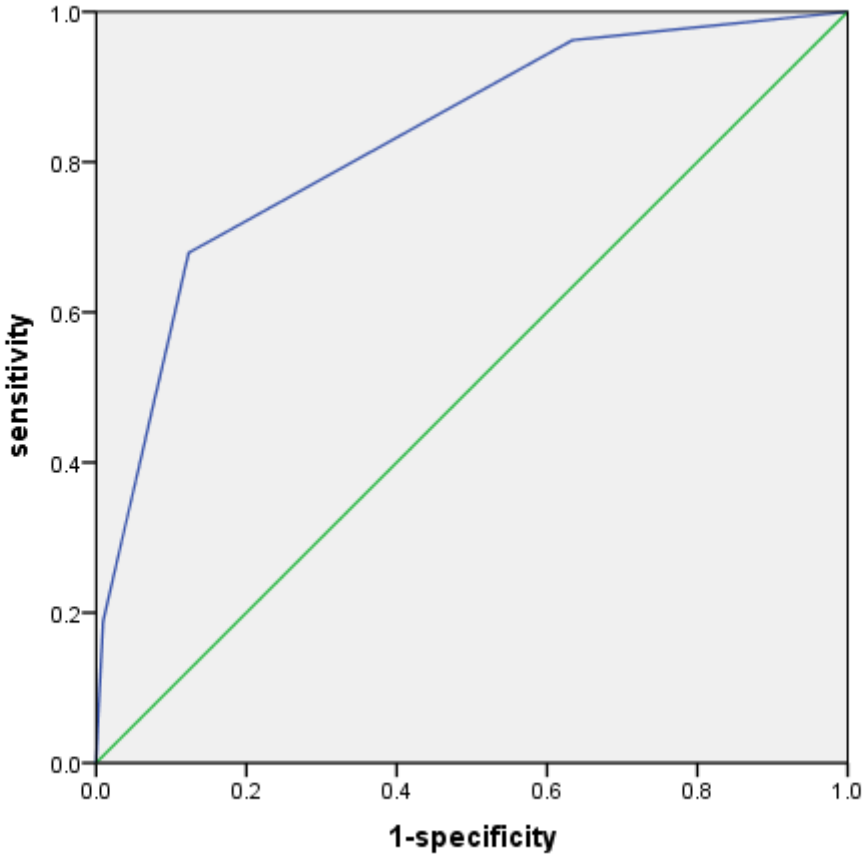

Figure 2

Receiver operating characteristics (ROC) curves of the clinical scores. The final scores were as follows: history of hyperlipidemia=0 points, no history of hyperlipidemia=1 point; D-dimer level ≤2.00 μg/mL=0 points, D-dimer level >2.00 μg/mL=1 point; and Fibrinogen level ≤4.00 g/L=0 points, Fibrinogen level >4.00 g/L=1 point

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