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Original Article

Clinical features of systemic cancer patients with acute cerebral infarction and its underlying pathogenesis

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Abstract: Background: The increased incidence of cerebral infarction in patients with systemic cancer has been reported; however, the underline mechanisms remain unclear. Investigation regarding the clinical features of cerebral infarction in cancer patients could be helpful to understand its underlying pathogenesis. Methods: A total of 537 patients were recruited and divided into three groups: 1) stroke and cancer group (SCG), defined as active cancer patients with acute cerebral infarction; 2) stroke group (SG), defined as acute cerebral infarction patients without cancer; and 3) Cancer group (CG), defined as active cancer patients without cerebral infarction. These patients were age and gender-matched among groups. Results: 179 patients, including 128 male subjects (73.68%) were enrolled in each group. Compared to SG patients, more SCG patients lacked conventional vascular risk factors (CRFs), and had elevated plasma D-dimer, cancer antigen (CA) 125 and 199 levels with multiple lesions in multiple cerebral arterial territories. In addition, SCG patients were found to have poorer prognosis. Compared to CG patients, more SCG patients' cancer had metastasized. Multiple logistic regression analysis showed that the elevated plasma D-dimer, CA125 and CA199 levels may independently increase, but chemoradiotherapy decreased the risk of cerebral infarction in cancer patients. Conclusions: Our study demonstrated that the clinical features of acute cerebral infarction in most active cancer patients can be identified as multiple lesions in multiple cerebral arterial territories with elevated plasma D-dimer and the elevated levels of cancer antigens.

Keywords: Clinical feature, cancer, cerebral infarction, pathogenesis

Introduction

The incidence of cerebral infarction increases in the patients with systemic cancer, such as breast, lung and neck, and ovarian cancer [1-3]. Previous studies have suggested that some cerebral infarcts were induced by cancer through an underlying physiopathologic mechanism, which were identified as cancer-related cerebral infarction [4, 5]. With improvement in anti-cancer therapies, cancer patients have lower mortality, which may lead to an increase in the incidence of cancer-related cerebral infarction [6, 7]. Therefore, it is important to explore the unique clinical features and the underlying mechanism of this type of cerebral infarction. Recent studies have shown that a considerable portion of cancer patients with cerebral infarction did not have conventional cardiovascular risk factors (CRFs), and that these patients first experienced cerebral infarction, but there were multiple lesions in multiple arterial territories in their brain [5-8]. Therefore, it was suggested that the pathogenesis of cerebral infarction in some of systemic cancer patients may markedly differ from conventional cerebral infarction. However, the physiopathologic mechanisms in which cancer results in cerebral infarction have not yet been elucidated.

In rare cases, it has been reported that systemic cancers can directly induce cerebral infarction. Stergiopoulos and his colleagues [9] used transesophageal echocardiography and Computed Tomography (CT) in a renal cancer patient with acute cerebral infarction to demonstrate that renal cancer cells invaded the wall of the inferior vena cava and entered the blood stream. These cells then invaded the heart through the right lower pulmonary vein, and for-

med an embolism that induced embolic cerebral infarction. Additionally, a carotid body tumor has been demonstrated to compress the right internal carotid artery to occlusion, and to induce a right middle and posterior cerebral artery territory infarction [10]. Non-bacterial thrombotic endocarditis (NBTE) has been demonstrated to exist in some of cancer patients by autopsy and echocardiography, and to be the cause of embolic cerebral infarction [11, 12]. Nevertheless, the pathogenesis of cerebral infarction in most cancer patients with cerebral infarction is unknown. Recent studies revealed that an elevated plasma D-dimer level was found in a considerable portion of systemic cancer patients with cerebral infarction, and that hypercoagulopathy may play a role in cerebral infarction in these patients [13-15]. The metastasis stage of cancer and a higher C protein level in external blood are common findings in cancer patients with multiple lesion cerebral infarction, suggesting that cancer may play an important role to occurrence of cerebral infarction in cancer patients [16]. However, since cancer cells are heterogeneous, and the local sites and status of cancer are diverse, the clinical features and the pathogenesis of cerebral infarction in cancer patients may be complicated.

In the present study, we performed a systemically retrospective study by reviewing the clinical data of active cancer patients with acute cerebral infarction. Meanwhile, we selected same number of acute cerebral infarction patients without active cancer as one control group to identify the unique features of cerebral infarction in active cancer patients. In addition, to explore the potential risk factors of cerebral infarction, we selected same number of active cancer patients without cerebral infarction as anther control group. Overall, we aimed to obtain a better understanding of the clinical features of cancer-related cerebral infarction and its potential pathogenesis.

Materials and methods

Subjects

This study was reviewed and approved by the Guangxi Medical University Review Board. All patients were recruited from the First Affiliated Hospital and the Affiliated Cancer Center of Guangxi Medical University during the period from January 2006 to December 2012. The diagnostic criteria of active cancer, active cancer with acute cerebral infarction, and acute cerebral infarction has been described previously [17, 18]. Briefly, the diagnosis of cancers for all patients was pathologically confirmed. Acute cerebral infarction was diagnosed by clinical symptoms, and signs of neurological deficits, such as sudden onset of loss of consciousness, slurred speech, paralysis and/or numbness of limbs, and a new brain lesion revealed on brain Magnetic Resonance Imaging (MRI) with hyper intensive lesions on MRI T_2 and diffusion weighted imaging (DWI). Cerebral hemorrhage was excluded with CT scan.

The recruitment criteria for active cancer patients with acute cerebral infarction (stroke and cancer group, SCG) includes: 1) patients with active non-cranial cancer (primary, recurring or metastasized) and an acute cerebral infarct that occurred during the hospital stay for cancer treatment; 2) patients admitted into the hospital due to acute cerebral infarction, and were confirmed to have non-cranial cancer during the hospital stay. The exclusion criteria includes: 1) Patients had primary or metastatic intracranial malignant tumors; 2) Cerebral infarction occurring more than five years after the cancer has been cured without the evidence of recurrence or metastasis.

Stroke group (SG) patients had confirmed acute cerebral infarction, but no somatic or neurological cancers and functional failure of major organs such as heart, lung, kidney, and liver. Cancer group (CG) patients had confirmed non-cranial cancer; but no cerebral infarction, hemorrhage, other neurological disorders, or failure of major organs such as heart, lung, kidney, and liver. The age and sex in both the SG and CG patients were matched with SCG patients. These recruitment criteria were determined by one oncologist and one neurologist who were blind to this study.

Collection of clinical data

We collected the general demographic characteristics, such as age and gender; clinical cancer-associated data, including cancer pathologic type, grading and staging; and treatment information, including radiotherapy, chemotherapy and surgical resection. We also collected data on CRFs for stroke, including hyperten-

Table 1. The clinical features of SCG Compared to SG

Characteristics	SCG (n = 179)	SG (n = 179)	*P value*
Age (Mean ± SD)	52.55 ± 10.27	53.14 ± 10.52	0.590[a]
Gender			
Male (n, %)	108 (60.3)	108 (60.3)	1.000[b]
Female (n, %)	71 (39.7)	71 (39.7)	
CRF			
Yes	81 (45.2)	145 (81.0)	< 0.001[b]
No	98 (54.8)	34 (19.0)	
Blood tests			
RBC ($\times 10^{12}$/L)	4.12 ± 0.83	4.26 ± 0.70	0.081[a]
HGB (g/L)	114.06 ± 16.39	121.67 ± 16.68	< 0.001[a]
PLT ($\times 10^{9}$/L)	207.96 ± 61.05	197.92 ± 59.25	0.115[a]
MPV (fl)	8.37 ± 1.77	8.26 ± 1.57	0.543[a]
TT (s)	13.20 ± 1.86	13.34 ± 1.87	0.463[a]
PT (s)	12.15 ± 1.47	11.94 ± 1.63	0.210[a]
APTT(s)	31.73 ± 3.42	31.91 ± 3.42	0.616[a]
INR	1.05 ± 0.14	1.08 ± 0.47	0.360[a]
FIB (g/l)	4.62 ± 1.09	4.57 ± 1.05	0.641[a]
D-dimer (ng/mL)	795.43 ± 287.92	411.41 ± 314.39	< 0.001[a]
CA 125 (U/ml)	570.23 ± 240.19	-	
CA 155 (U/ml)	81.73 ± 43.09	-	
CA 199 (U/ml)	261.19 ± 186.08	-	
MRI multiple lesions in multiple arterial territories			
Yes (n, %)	107 (59.8)	20 (11.2)	< 0.001[b]
No (n, %)	72 (40.2)	159 (88.8)	
Type of cerebral infarction (n, %)			
Atherosclerotic cerebral infarction	45 (25.1)	83 (46.4)	< 0.001[b]
Cardiogenic cerebral embolism	7 (3.9)	10 (5.6)	0.456[b]
Lacunar cerebral infarction	50 (27.9)	64 (35.8%)	0.112[b]
Cryptogenic cerebral infarction	73 (40.8)	17 (9.5)	0.000[b]
Others	4 (2.2)	5 (2.8)	1.000[b]
NHISS score	8.05 ± 5.16	4.57 ± 3.16	< 0.001[a]
Prognosis at the 30th day from cerebral infarction onset			
mRS (Mean ± SD)	2.69 ± 1.71	1.11 ± 1.07	< 0.001[a]
Survival (n, %)	166 (92.7)	176 (98.3)	0.021[b]
Death (n, %)	13 (7.3)	3 (1.7%)	0.021[b]

Compared to CG, [a], with two independent samples t-test; [b], with chi-square test. CRF, conventional risk factors; RBC, red blood cells; HGB, hemoglobin; PLT, platelet; MPV, mean platelet volume; TT, thrombin time; PT, prothrombin time; APTT, activated partial thromboplastin time; INR, international normalized ratio; FIB, fibrinogen; NHISS, National Institutes of Health Stroke Scale; mRS, modified Rankin Rating Scale; SD, standard deviation; '-' no datum.

sion, diabetes mellitus, hyperlipidemia, atrial fibrillation, tobacco and alcohol exposure, previous history of stroke, family history of stroke, as well as the history of thromboembolic events such as myocardial infarction, thrombosis of organ and limb arteries or deep veins, and pulmonary embolism. Data on acute cerebral infarction, including etiology, clinical signs and symptoms, as well as the severity of neurological deficits evaluated with the U.S. National Institutes of Health Stroke Scale (NIHSS) were collected. In addition, we collected data from blood tests, and imaging endpoints, including echocardiography (ECG), transcranial Doppler ultrasound, cranial CT, CT Angiography (CTA), MRI, and Magnetic resonance angiography

Table 2. The clinical features of SCG compared to CG

Characteristics	SCG (n = 179)	CG (n = 179)	*P value*
Age (Mean ± SD)	52.55 ± 10.27	52.23 ± 10.34	0.774[a]
Gender (Male)			
Female (n, %)	71 (39.7)	71 (39.7)	1.000[b]
Male (n, %)	108 (60.3)	108 (60.3)	
CRF			
Yes (n, %)	81 (45.2)	95 (53.1)	0.139[b]
No (n, %)	98 (54.8)	84 (46.9)	
Blood Tests			
RBC ($\times 10^{12}$/L)	4.12 ± 0.83	4.15 ± 0.71	0.671[a]
HGB (g/L)	114.06 ± 16.39	118.37 ± 21.51	0.034[a]
PLT ($\times 10^{9}$/L)	207.96 ± 61.05	195.27 ± 57.22	0.043[a]
MPV (fl)	8.37 ± 1.77	8.29 ± 1.46	0.651[a]
TT (s)	13.20 ± 1.86	12.99 ± 1.65	0.266[a]
PT (s)	12.15 ± 1.47	12.09 ± 1.40	0.724[a]
APTT(s)	31.73 ± 3,42	32.05 ± 3,46	0.378[a]
INR	1.05 ± 0.14	1.04 ± 0.12	0.607[a]
FIB (g/l)	4.62 ± 1.09	4.69 ± 1.16	0.527[a]
D dimmer (ng/mL)	795.43 ± 287.92	413.43 ± 265.71	< 0.001[a]
CA 125 (U/ml)	570.23 ± 240.19	107.10 ± 70.07	< 0.001[a]
CA 155 (U/ml)	81.73 ± 43.09	89.80 ± 44.53	0.082[a]
CA 199 (U/ml)	261.19 ± 186.08	83.65 ± 48.79	< 0.001[a]
Type of therapy (n = 164) (n, %)			
Chemoradiotherapy	53 (32.3)	101 (61.6)	< 0.001[b]
Surgery	111 (67.7)	63 (38.4)	
Cancer metastasis (n, %)			
Yes	86 (48.0)	25 (14.0)	< 0.001[b]
No	93 (52.0)	154 (86.0)	
Prognosis at the 30th day from cerebral infarction onset			
Survival (n, %)	166 (92.7)	174 (97.2)	0.053[b]
Death (n, %)	13 (7.3)	5 (2.8)	

Compared to CG, [a], with two independent samples t-test; [b], with chi-square test. CRF, Conventionalrisk factors; RBC, red blood cells; HGB, hemoglobin; PLT, platelet; MPV, mean platelet volume; TT, thrombin time; PT, pro-thrombin time; APTT, activated partial thromboplastin time; INR, international normalized ratio; FIB, fibrinogen; CA, cancer antigen; SD, standard deviation.

(MRA). The prognosis of patients at the 30th day from symptom onset of cerebral infarction was based on the modified Rankin Rating Scale (mRS) [19]. All data were abstracted from the patients' medical records after obtaining the written informed consent.

Statistical methods

Two independent samples t-test for quantitative data and a chi-square test for qualitative data were used for the comparisons of SCG *vs.* SG and SCG *vs.* CG. In SCG patients, the relationship between plasma D dimer and cancer markers (plasma D dimer vs. CA 125, plasma D dimer vs. CA 155, plasma D dimer vs. CA 199), and the relationship between plasma D dimer and the patients' mRS at the 30th day from diagnosis of cerebral infarction were analyzed with Spearman correlation. Multivariable logistic regression analysis was performed to predict the independent contribution of factors in SCG vs. CG. Variables with $P < 0.05$ on univariable analyses were considered as explanatory variables and were entered together into multivariable models. All data analyses were performed using SPSS version 18.0 (SPSS Inc. IBM Corp); and two sided *P* value < 0.05 was considered statistically significant.

Table 3. Multivariate Logistic regression analysis

Factors	β	SE (β_j)	Wals	*df*	*P*	OR	95% CI
D dimer	0.006	0.002	7.284	1	0.007	1.006	1.002-1.010
CA125	0.028	0.006	24.447	1	< 0.001	1.029	1.017-1.040
CA199	0.019	0.007	7.308	1	0.007	1.019	1.005-1.033
Chemoradiotherapy	-5.007	1.871	7.157	1	0.007	0.007	0.000-0.262
Constant	-13.022	3.089	17.777	1	< 0.001	< 0.001	

SE, standard error; OR, odds ratio; CI, confidence interval.

Results

Among 179 enrolled patients in each group, 128 patients were male (73.68%). The average age (Mean ± Standard deviation (SD) was 52.84 ± 10.54 years; 53.66 ± 11.02 years and 51.92 ± 10.69 years in the SCG, SG and CG patients, respectively. As expected, no significant differences in age or gender were observed among these three groups. The demographic characteristics are listed in **Tables 1** and **2**.

In SCG patients, there were 19 kinds of cancers, the top 3 of which were lung cancer (76 cases, 54.41%), followed by colorectal cancer (27 cases, 15.08%), liver cancer (21 cases, 11.73%). In the SCG, 163 out of 179 patients (90.06%) suffered from acute cerebral infarctions during cancer-related treatment. Sixteen cases (8.94%) were admitted to the hospital due to acute cerebral infarction, and the somatic cancers were confirmed during the hospital course.

No significant differences were observed between SCG and SG patients for the symptoms and signs of cerebral infarction, including sudden onset single-limb paralysis or hemiplegia, central facial, slurred speech, aphasia, ataxia, and disturbance of consciousness. However, compared to SG patients, more SCG patients lacked CRFs, and more patients had multiple lesions in multiple arterial territories in their brain. In addition, SCG patients had a higher plasma D dimer levels, and poorer prognosis (**Table 1**). Furthermore, in SCG subjects, the plasma D dimer levels were positively correlated to the levels of plasma CA 125 (r_s = 0.457, *P* < 0.001), CA199 (r_s = 0.329, *P* < 0.001) and the patients' mRS at the 30th day from diagnosis of cerebral infarction (r = 0.136, *P* = 0.031), but not the levels of CA 155 (r_s = 0.214, *P* = 0.082).

As a result of selected condition, there was no significant difference on the types of cancer between SCG and CG patients. When the clinical characteristics of SCG patients were compared to that of CG patients, most items of blood routine and coagulation, and the prognosis at the 30th day from cerebral infarction onset of SCG patients and that of CG patients at same time internal were not significantly different. However, blood test endpoints, including hemoglobin (HGB), platelet (PLT), D dimmer, CA125, CA155 and CA199 were significant different between SCG and CG. In addition, more SCG patients underwent surgical resection treatment and while fewer SCG patients received chemoradiotherapy (**Table 2**).

Multivariate logistic regression analysis was performed to further evaluate the independent predictors for SCG vs. CG (**Table 3**). Eight variables, including HGB (X1), PLT (X2), D dimmer (X3), CA125 (X4), CA199 (X5), surgery (X6), chemoradiotherapy (X7) and metastasis (X8), were entered together into the first model. However, only four factors, including D dimer (X3), CA125 (X4), CA199 (X5) and chemoradiotherapy (X7) were entered the final models, because their *P* values were less than 0.05 in the first regression model. The final regression equation was as follows: logit Pi = -13.022 + 1.029 X 4 + 1.019 X 5 + 1.006 X 3 + (-0.007) X 7. Our results showed that the plasma CA125 level per 1 U/ml elevation increases 2.9% (OR: 1.029; 95% CI: 1.017-1.040; *P* < 0.001), plasma CA199 level per 1 U/ml elevation increases 1.9% (OR: 1.019; 95% CI: 1.005-1.033; *P* = 0.007) and plasma D dimer level per 1 ng/ml elevation increases 0.6% the risk of cerebral infarction for cancer patients (OR: 1.006; 95% CI: 1.002-1.010; *P* = 0.007). However, chemoradiotherapy decreases the risk of cerebral infarction in cancer patients by 0.7% (OR: 0.007; 95% CI: 0-0.265; *P* = 0.007).

Discussion

Clinical features of cancer patients with acute cerebral infarction

The evidence that incidence of cerebral infarction in cancer patients is notably higher compared to the general population has been demonstrated for years [1-6]. To explore the clinical characteristics and their association with the risk of cerebral infarction in cancer patients may help us to make appropriate diagnosis and develop therapies for cancer patients with acute cerebral infarction. The clinical features of cancer patients with acute cerebral infarction have drawn more and more attentions. In a clinic-based cohort study with 2,562 cases of acute cerebral infarction, Kim *et al* [20] reported that among 348 patients with cryptogenic stroke, 71 (20.4%) patients were confirmed to have active cancer at the time of stroke. Compared to stroke patients without active cancer, or cancer patients without stroke, active cancer patients with acutely cryptogenic stroke had significantly elevated plasma D-dimer levels (both $P < 0.001$), and a greater portion of these patients had multiple lesions in multiple cerebral arterial territories (both $P < 0.001$). Similar clinical features, including an elevated plasma D-dimer level and multiple lesions in multiple cerebral arterial territories, had previously been observed in cancer patients with acute cerebral infarction [4, 5, 8, 9]. These clinical features revealed that some of the cerebral infarctions in cancer patients were distinct from conventional cerebral infarction, indicating that some of the cerebral infarctions in cancer patients were related to the cancers. Guo and Kim *et al* [4, 20] even asserted that the clinical features mentioned above might be regarded as clues to find out the occult cancer in cryptogenic cerebral infarction patients.

In present study, the manifestations between SCG and SG, including symptoms and signs of cerebral infarction, were similar. However, compared to SG patients, a greater portion of SCG patients had multiple lesions within numerous cerebral arterial territories; with elevated plasma D-dimer and cancer maker levels, but without any CRFs. From the present data, it was further suggested that if the higher levels of D-dimer and cancer markers existed in a cryptogenic cerebral infarction patient with multiple lesions within multiple arterial territories, cancer would most likely be the root cause.

Furthermore, in present study, 16 SCG patients without any vascular risk, were originally admitted into hospitals for their acute cerebral infarction, and were demonstrated to have active cancer during the hospital stay. In addition, a number of types of cancers, in particular adenocarcinoma including lung, ovarian and pancreatic cancer, have recently been found in patients with an initial presentation of cerebral infarction [21-23]. As suggested in prior work, our study confirmed that systemic cancer may impair remote organs to a greater extent than its adjacent organs or tissues, and that cancer may be the root cause of an acutely cryptogenic cerebral infarction.

Potential pathogenesis of cancer related cerebral infarction

In the present study, in term of clinical features, there were at least two different classifications of patients in the SCG cohort; patients with CRFs with a single lesion in their brain, or multiple lesions in multiple arterial territories but without any CRFs. For the former, the pathogenesis of cerebral infarction was hypothetically similar to the conventional cerebral infarction. However, for the second subgroup, because they lacked CRFs, the cause of cerebral infarction was less clear. Prior studies have demonstrated that cancer could cause cerebral infarction with a novel pathogenesis in specific patients, including compression of the internal carotid to occlusion, cellular invasion of the vessel wall to the cardiac cavity, and inducing NBTE [9-12].

However, the pathogenesis in most cancer patients with acute cerebral infarction has remained elusive. In 1988, Cornuz *et al.* [21] reported one case of a 42-year-old female patient with ovarian adenocarcinoma that was initially hospitalized for cerebral infarction but lacked CRFs. This patient developed chronic intravenous coagulation despite high dose vitamin K antagonists therapy, and hypercoagulopathy was suspected to be the pathogenesis of cerebral infarction. A number of studies have presented the clinical features of cancer patients with acute cerebral infarction. These patients' features including elevated D-dimer

levels and multiple lesions in multiple cerebral arterial territories [4, 5, 8, 9] suggested that some cerebral infarctions in active cancer patients were embolic infarctions and hypercoagulopathy was further suspected to be the pathogenesis. In order to test the hypothesis that cancer increased coagulable status of blood and induces miro-thrombus to cause embolic infarction, Seok *et al.* [18] prospectively recruited a total of 74 active cancer patients with cerebral infarction within the middle cerebral artery (MCA). The patients' coagulation status was assessed based on the serum D-dimer levels, and transcranial Doppler (TCD) monitoring was performed on both MCAs for 30 minutes to detect embolic signals (ES). It was found that ES was more commonly observed in patients without CRFs (22 of 38 patients, 57.9%) than in those with CRFs (12 of 36 patients, 33.3%) ($P = 0.034$). Moreover, ES was more commonly detected in patients with elevated serum D-dimer levels ($P < 0.001$), and serum D-dimer levels were significantly correlated with the number of ESs in patients without CRFs ($r = 0.732$, $P < 0.001$), but were poorly correlated in patients with CRFs ($r = 0.152$, $P = 0.375$). These data indicated that formation of tiny emboli due to hypercoagulation status may be one explanation of cerebral infarction in patients with active cancer.

In the present study, compared to SG and CG, as a greater portion of SCG patients had higher plasma D-dimer levels and multiple lesions in multiple arterial territories, hypothesized that the cerebral infarctions in a greater portion of SCG patients were embolic infarctions, and that hypercoagulophy may be the pathogenesis. Moreover, a greater portion of SCG patients had elevated plasma cancer marker levels, and further correlation analysis revealed that elevated cancer markers (including CA 125 and CA199) were significantly correlated to the plasma D-dimer levels. In addition, it was reported that markedly elevated levels of CA125 were involved in the recurrence of cerebral infarction in metastatic cancer patients [24]. Furthermore, a greater portion of SCG patients' cancers were in metastatic status in the present study. Multivariate Logistic regression analysis revealed that the elevated levels of plasma D-dimer and cancer markers may independently increase the risk of cerebral infarction for active cancer patients. Therefore, we speculate that cancer cells may produce some mucinous substances, such as CA125 and CA199, to induce a hypercoagulable state leading to embolic cerebral infarctions.

Prophylactic and therapeutical measures

In the present study, chemoradiotherapy may decrease the risk of cerebral infarction in cancer patients. In addition, it has been reported that cancer related treatment could decrease the risk of cerebral infarction in cancer patients [25]. Therefore, our data suggested that the best method for prevention of cerebral infarction in cancer patients may be to eliminate the cancerous cells. As embolic events were common complications in cancer patients due to the hypercoagulable status [26], with the use of anticoagulants and antiplatelet drugs the embolic events in cancer patients could be largely decreased [27, 28]. In addition, Seok *et al.* [18] had observed that the embolic signals in MCAs of cancer patients decreased notably after the anticoagulant therapy. Therefore, anticoagulants and antiplatelet therapies may play an important role to prevent cerebral infarction in active cancer patients. However, the efficiency and safety of anticoagulants therapy in this population is unclear, and further studies are warranted.

In the present study, cancer patients with cerebral infarction may have a poorer prognosis, which is consistent with previous results [16]. Improvement in treatment options for these patients is necessary. Although active cancers are commonly considered as a contraindication for thrombolytic therapy, it were reported that acute cerebral infarction in patients with no blood cancer had successfully undergone intravenous thrombolytic therapy [29, 30]. Novel therapies such as this should be encouraged through further exploration. As a retrospective study, our study has all the inherent problems related to this study design, such as potential for selection bias in the process of selecting patients in the control group. A prospective population-based cohort study is warranted to better address the clinical risk factors of cerebral infarction in cancer patients.

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Disclosure of conflict of interest

None.

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