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Original Article

# A Single-Center Experience of Mechanical Thrombectomy for Cancer-Associated Ischemic Stroke

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**Objectives:** Cancer-associated ischemic stroke tends to extend over multiple vascular territories and develops under poor general conditions. Owing to the rarity of such cases and poor prognoses, no comprehensive studies on mechanical thrombectomy for cancer-associated ischemic stroke have been reported in Japan. The present study investigated the radiological and clinical characteristics of mechanical thrombectomy in patients with cancer-associated ischemic stroke at our institution.

**Methods:** We retrospectively reviewed 108 patients who underwent mechanical thrombectomy for large cerebral artery occlusion between January 1, 2021, and October 31, 2022, at our institution. The characteristics of mechanical thrombectomy in the cancer-associated ischemic stroke group were compared with those in the control group.

**Results:** Of the 108 patients (112 procedures), seven patients (eight procedures) with clinically diagnosed cancer-associated ischemic stroke underwent mechanical thrombectomy. Of the eight procedures, six were performed during hospitalization. In contrast, only 10 of 104 procedures were performed in the control group. The in-hospital onset rate was higher in the cancer-associated ischemic stroke group (75.0%) compared to that in the controls (9.6%); $p < 0.001$. The puncture-to-reperfusion time was significantly longer in the cancer-associated ischemic stroke group in comparison to that in the controls with a median interquartile range of 69 minutes (60.0–82.0 minutes) and 59.5 minutes (44.5–69.3 minutes), respectively ($p < 0.01$). However, the rates of successful recanalization defined as thrombolysis in cerebral infarction ≥2b were not significantly different between the cancer-associated ischemic stroke group and controls with values of 62.5% and 79.8%, respectively ($p = 0.250$). Of the eight cases in the cancer-associated ischemic stroke group, only one (12.5%) had a good outcome on a modified Rankin Scale score of 0 to 2 at discharge, in contrast to 23 of the 104 (23.1%) cases in the controls ($p = 0.523$). Histopathological examination of six retrieved thrombi in the cancer-associated stroke group using hematoxylin and eosin staining revealed that only one case showed an erythrocyte-dominant thrombus while five displayed a fibrinoplatelet-dominant component. Conversely, 65 of 92 retrieved thrombi in the control group were erythrocyte dominant. Cancer was pathologically diagnosed in four of seven patients, all of which were adenocarcinomas.

**Conclusion:** Cancer-associated ischemic stroke tends to occur during hospitalization. Coagulation disorders associated with cancer, especially adenocarcinoma, may be related to the formation of thrombi with fibrinoplatelet-dominant components, leading to ischemic stroke. The procedural time for mechanical thrombectomy in cancer-associated ischemic stroke tends to be longer.

**Keywords ▸** cancer-associated ischemic stroke, mechanical thrombectomy, histological examination, large cerebral artery occlusion, adenocarcinoma

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## Introduction

Cancer-associated ischemic stroke is a systemic thromboembolism caused by coagulation disorders related to cancer.[1,2] Acute recanalization therapy is rarely indicated for cancer-associated ischemic stroke due to the extent of occurrence of infarction over multiple vascular territories[3] and the poor general condition of the patients with cancer.[4] Several recent case reports have described patients with cancer-associated ischemic stroke who underwent mechanical thrombectomy for large cerebral artery occlusions.[5–7] However, because of the rarity of such cases and their poor prognoses, no comprehensive studies of mechanical thrombectomy have been reported in Japan. Currently, one in 10 patients with ischemic stroke patients develop cancer.[8] Even in Japan, where the average lifespan is increasing, the incidence of cancer-associated ischemic stroke may increase owing to progress in cancer treatment. As the possibility of occurrence of these cases during acute recanalization therapy increases, it is important to understand the pathological conditions and clinical findings when considering treatment strategies. We retrospectively investigated the radiological and clinical features of mechanical thrombectomy in patients with cancer-associated ischemic stroke at our institution.

## Materials and Methods

### Subjects

Cancer-associated ischemic stroke is defined as an acute cerebrovascular disease in patients with active cancer.[9] Active cancer is defined as a diagnosis of cancer or cancer treatment within 6 months before from the onset of ischemic stroke.[9] Patients suspected of having acute cerebrovascular disease were initially diagnosed at our institution using CTA, within 6 hours of onset. MRI was performed in patients 6 hours after onset. Based on the Japanese clinical guidelines, thrombolysis with intravenous tissue plasminogen activator (0.6 mg/kg) was initiated for acute cerebral infarction within 4.5 hours following onset.[10] Mechanical thrombectomy was performed for acute ischemic stroke with the following eligibility conditions at our institution[11]: (1) within 6 hours of onset; (2) large cerebral artery occlusion (internal carotid artery, middle cerebral artery [MCA] horizontal [M1], Sylvian [M2] segment, basilar artery, vertebral artery); and (3) premorbid modified Rankin Scale (mRS) score of 0 to 2. In addition, mechanical thrombectomy was performed for patients within 24 hours of the time last known well if they had a mismatch between the ischemic core volume determined by CT perfusion or MRI, and neurological deficit or hypoperfusion lesions observed by perfusion imaging.[11] In particular, the diffusion-weighted imaging–Alberta Stroke Program Early CT Score (DWI-ASPECTS) was not considered an indication for mechanical thrombectomy because cancer-associated ischemic stroke tends to have a low DWI-ASPECTS due to multiple small infarctions. For patients with occlusion of the M2 segment or posterior circulation or with a premorbid mRS score of 2, the indication was carefully considered for the benefits and safety risks of the treatment.[11] We retrospectively analyzed the clinical and radiological assessments of mechanical thrombectomy in the cancer-associated ischemic stroke and control groups. We compared the onset-to-puncture time, puncture-to-reperfusion time, and rate of successful recanalization between the two groups. Moreover, we focused on the onset-to-puncture time of the in-hospital onset in both groups. A successful reperfusion is considered as thrombolysis in cerebral infarction (TICI) grade ≥2b. The retrieved thrombi from both groups were subjected to pathological examination. A qualified pathologist determined erythrocyte-dominant thrombus or other thrombi with fibrin- and platelet-dominant components using hematoxylin and eosin staining. The mRS score at discharge was considered as the endpoint of this study. For patients who underwent mechanical thrombectomy twice during hospitalization, the mRS scores before the second ischemic attack and at discharge were investigated. An mRS score of 0 to 2 indicated a good outcome. This study was approved by the Institutional Review Board (IRB) of Juntendo University (IRB approval number: E22-0402). Informed consent was waived due to the retrospective nature of the study.

### Endovascular procedures

In acute recanalization therapy for acute ischemic stroke due to large cerebral artery occlusion, intravenous infusion of tissue plasminogen activator is initiated if indicated, followed by mechanical thrombectomy. Mechanical thrombectomy was performed under local anesthesia. A 9-French balloon guiding catheter was inserted proximal to the internal carotid artery in cases of large cerebral artery occlusion of the anterior circulation. Otherwise, a 6-French guiding sheath was placed on the dominant side of the vertebral artery in the large cerebral artery occlusion of the posterior circulation. A thrombus is usually retrieved using a combination of a stent retriever and an aspiration catheter as a combined technique.[12] However, the method was changed to a simple stent retriever, direct aspiration technique,[13] or local thrombolysis, if distal occlusion persisted.

### Statistical analysis

Data were presented as medians with median interquartile ranges (IQRs). Mann–Whitney *U* tests for continuous variables and chi-squared ($\chi^2$) tests for categorical variables were performed as univariate analyses. Statistical analyses were performed using StatMate version 3.06 (ATMS, Chiba, Japan). $p$ <0.05 denoted statistical significance.

## Results

Among 108 patients who underwent 112 procedures at our institution between January 2021 and October 2022, seven patients with cancer-associated ischemic stroke underwent a total of eight mechanical thrombectomy procedures. Some patients underwent mechanical thrombectomy more than once, and therefore, the number of patients and procedures differ. The clinical features of all the patients with cancer-associated ischemic stroke are shown in **Table 1**. Three of the seven patients experienced a recurrence of large cerebral artery occlusion during hospitalization for cancer-associated ischemic stroke. Case 1 underwent mechanical thrombectomy again with anticoagulant therapy, while Cases 2 and 3 received conservative therapy due to an elevated risk of bleeding, owing to poor general health. Case 5 had an atypical course of cancer-associated ischemic stroke. The patient developed internal carotid artery occlusion due to an erythrocyte-dominant thrombus; the D-dimer level was not high and three territories sign was negative.[3] Abdominal CT scan revealed malignant gastric cancer, leading to a diagnosis of cancer-associated ischemic stroke. Atrial fibrillation, which has been associated with an increase in cancer,[14] was not detected by Holter electrocardiography. The baseline characteristics of cases with cancer-associated ischemic stroke and controls are shown in **Table 2**. Patients in the cancer-associated ischemic stroke group were younger in comparison to the controls with a median IQR of 72.5 years (65.3–77 years) and 78.5 years (73–85 years), respectively ($p$ <0.001). Higher National Institutes of Health Stroke Scale (NIHSS) scores of the cancer-associated ischemic stroke group in comparison to those of controls were calculated with median IQR of 21.5 (13.0–24.8) and 17.0 (11.8–23.0), respectively ($p$ <0.001). Lower DWI-ASPECTS were calculated with median IQR of 5.0 (4.5–5.8) in cancer-associated ischemic

**Table 1** Clinical features of all cases in the cancer-associated ischemic stroke group

| | Sex | Age | HT | DL | DM | Af | D-dimer | Three territories sign | Onset in hospital | NIHSS | DWI-ASPECTS | O-P | iv. tPA | P-R | Occlusion site | TICI | Macroscopic appearance of retrieved thrombi | Technique | Cancer | Pathology | Recurrence | mRS |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | F | 63 | – | – | – | – | 85 | + | + | 10 | 3 | Unknown | – | 65 | Rt. MCA | 2b | White with red | S UK | Lung | Adenocarcinoma | + | 3 |
| | F | 63 | | | | | | – | + | 24 | 8 | 40 | – | 40 | Lt. MCA | 3 | White | S | Lung | | – | 1 |
| 2 | F | 72 | + | – | – | – | 23.7 | + | + | 27 | 3 | 180 | – | 70 | Lt. MCA | 1 | None | S A | Stomach | Adenocarcinoma | + | 6 |
| 3 | M | 73 | – | – | – | – | 5.7 | – | + | 14 | 10 | 148 | – | 68 | Lt. MCA | 3 | Red with white | S A | Lung | Adenocarcinoma | + | 5 |
| 4 | F | 83 | – | – | – | – | 47.8 | Unknown | – | 10 | 5 | 160 | + | 200 | Rt. MCA | 2a | None | S A | Lung | Unknown | – | 6 |
| 5 | M | 83 | + | – | + | – | 2.3 | – | + | 23 | 5 | 45 | – | 85 | Lt. ICA | 2a | Red | S | Stomach | Unknown | – | 5 |
| 6 | M | 75 | + | + | – | – | 40.1 | + | + | 20 | 5 | 72 | – | 81 | Rt. MCA | 2b | White | S A | Lung | Adenocarcinoma | – | 3 |
| 7 | M | 66 | – | – | – | – | 40.8 | + | – | 35 | 5 | Unknown | – | 45 | BA tip | 3 | White with red | A | Liver | Unknown | – | 5 |

A: aspiration catheter; Af: atrial fibrillation; BA: basilar artery; DL: dyslipidemia; DM: diabetes mellitus; DWI-ASPECTS: diffusion-weighted imaging–Alberta Stroke Program Early CT Score; F: female; HT: hypertension; ICA: internal carotid artery; iv. tPA: intravenous infusion of tissue plasminogen activator; Lt.: left; M: male; MCA: middle cerebral artery; mRS: modified Rankin Scale; NIHSS: National Institutes of Health Stroke Scale; O-P: onset-to-puncture time (minutes); P-R: puncture-to-reperfusion time (minutes); Rt.: right; S: stent retriever; TICI: thrombolysis in cerebral infarction; UK: intra-arterial infusion of urokinase

**Table 2** Baseline characteristics of cancer-associated ischemic strokes and controls

| | Cancer-associated ischemic stroke, n (%) or median (IQR) | Control, n (%) or median (IQR) | *p* value |
|---|---|---|---|
| Total number of procedures | 8 | 104 | |
| Age, years | 72.5 (65.3–77.0) | 78.5 (73.0–85.0) | <0.001 |
| Sex | F: 4 (50.0) | F: 47 (45.2) | 0.792 |
| | M: 4 (50.0) | M: 57 (54.8) | |
| NIHSS | 21.5 (13.0–24.8) | 17.0 (11.8–23.0) | <0.001 |
| DWI-ASPECTS | 5.0 (4.5–5.8) | 7.0 (6.0–9.0) | <0.001 |
| iv. tPA | 1 (12.5) | 49 (47.1) | 0.057 |
| Occlusion site | MCA: 6 (75.0) | MCA: 58 (55.8) | 0.290 |
| | ICA: 1 (12.5) | ICA: 34 (32.7) | 0.235 |
| | BA: 1 (12.5) | BA: 12 (11.5) | 0.935 |
| sICH | 0 (0) | 12 (11.5) | 0.309 |

BA: basilar artery; DWI-ASPECTS: diffusion-weighted imaging–Alberta Stroke Program Early CT Score; F: female; ICA: internal carotid artery; IQR: interquartile range; iv. tPA: intravenous infusion of tissue plasminogen activator; M: male; MCA: middle cerebral artery; NIHSS: National Institutes of Health Stroke Scale; sICH: symptomatic intracranial hemorrhage

**Table 3** Outcomes following mechanical thrombectomy for cancer-associated ischemic stroke patients and controls

| | Cancer-associated ischemic stroke, n (%) or median (IQR) | Control, n (%) or median (IQR) | *p* value |
|---|---|---|---|
| Total number of procedures | 8 | 104 | |
| In-hospital onset | 6 (75.0) | 10 (9.6) | <0.001 |
| In-hospital onset-to-puncture time, minutes | 72.0 (45.0–148.0) | 41.5 (30.8–131.3) | <0.01 |
| Puncture-to-reperfusion time, minutes | 69.0 (60.0–82.0) | 59.5 (44.5–69.3) | <0.001 |
| Rate of effective recanalization | 5 (62.5) | 83 (79.8) | 0.250 |
| Number of pass | 2.00 (1.00–2.25) | 1.00 (1.00–2.00) | 0.201 |
| Good outcome (mRS: 0–2) | 1 (12.5) | 23 (23.1) | 0.523 |

IQR: interquartile range; mRS: modified Rankin Scale

stroke group in comparison to 7.0 (6.0–9.0) in the control group ($p$ <0.001). The proportion of cases who underwent intravenous tissue plasminogen activator thrombolysis tended to be lower in the cancer-associated ischemic stroke group (12.5%) than controls (47.1%), although the difference was not statistically significant ($p$ = 0.057). The radiological and clinical characteristics of mechanical thrombectomy in the cancer-associated ischemic stroke and control groups are shown in **Table 3**. Six of the eight procedures were performed during hospitalization in the cancer-associated ischemic stroke group. However, only 10 of the 104 procedures were performed in the control group. In-hospital stroke onset rate was higher in the cancer-associated ischemic stroke group (75.0%) compared to that in the control group (9.6%); $p$ <0.001. In-hospital onset-to-puncture time was significantly longer in procedures for the cancer-associated ischemic stroke group with median IQR of 72 minutes (45.0–148.0 minutes) and 41.5 minutes (30.8–131.3 minutes) for the control group ($p$ <0.01). The puncture-to-reperfusion time was significantly longer in the cancer-associated ischemic stroke group with median IQR of 69.0 minutes (60.0–82.0 minutes) in comparison to that in the control group showing 59.5 minutes (44.5–69.3 minutes) ($p$ <0.01). However, the rates of successful recanalization were not significantly different between the cancer-associated ischemic stroke group (62.5%) and controls (79.8%), $p$ = 0.250. The median number of passes in which the retrieval devices were used in the occluded vessels during treatment was twice in the cancer-associated ischemic stroke group with median IQR of 2.00 (1.00–2.25) in comparison to that in the control group with 1.00 (1.00–2.00), $p$ = 0.201. In our series, only one of eight cases (12.5%) with cancer-associated ischemic stroke had a good outcome in terms of mRS at discharge, in contrast to 23 of 104 (23.1%) in the controls ($p$ = 0.523). Retrieved thrombi were subjected to pathological examination in six of eight procedures in the cancer-associated ischemic stroke group and in 92 of 104 procedures in the control group. Of the six retrieved thrombi from the cancer-associated stroke group, hematoxylin and eosin staining revealed that only one was an erythrocyte-dominant thrombus and five were thrombi with a fibrinoplatelet-dominant component. Conversely, 65 of 92 retrieved thrombi in the control group were erythrocyte dominant. A pathological diagnosis of cancer made

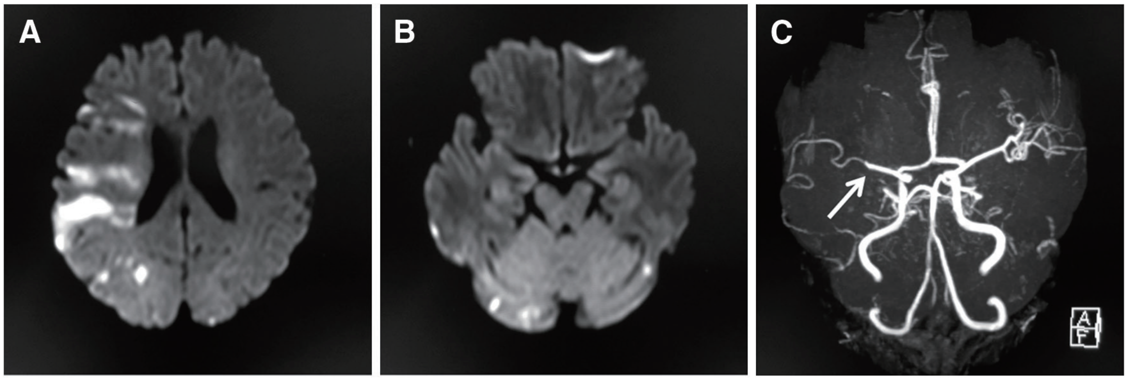


**Fig. 1** (**A** and **B**) DWIs showing multiple acute infarctions in the right MCA territory and small infarctions in both cerebellar hemispheres. (**C**) MRA demonstrating occlusion of the right MCA (white arrow). DWIs: diffusion-weighted images; MCA: middle cerebral artery

in four of seven patients showed that all of these were adenocarcinomas.

### Illustrative case (Case 1)

A 63-year-old woman presented with respiratory distress due to a cardiac tamponade. The patient was diagnosed with carcinomatous pericarditis caused by primary lung adenocarcinoma (T1cN1M1 stage IVb). On day 8 after emergent admission, she suddenly developed left-sided hemiparesis, and acute cerebral infarctions were detected in multiple territories on diffusion-weighted imaging (DWI) (**Fig. 1A** and **1B**). MRA revealed an occlusion of the horizontal segment (M1) of the right MCA (**Fig. 1C**). Mechanical thrombectomy was subsequently performed using a stent retriever (**Fig. 2A** and **2B**), and selective transarterial infusion of urokinase resulted in reperfusion with TICI grade 2b (**Fig. 2C** and **2D**). The retrieved pale-red thrombus was subjected to pathological examination. The patient's postoperative neurological symptoms improved, although mild hemiparesis persisted without any disturbances in the activities of daily living. Anticoagulant therapy with continuous intravenous unfractionated heparin injections was initiated upon confirmation of no hemorrhagic complications. On day 11, the patient suddenly developed total aphasia and severe right-sided hemiparesis. DWI revealed pale hyperintensity in the left MCA territory (**Fig. 3A**). MRA revealed a left M1 occlusion (**Fig. 3B**). Mechanical thrombectomy resulted in reperfusion with TICI grade 3 (**Fig. 3C** and **3D**). Macroscopically, the retrieved thrombus appeared white. The postoperative symptoms gradually improved, and the patient recovered with only slight dysarthria. No verrucous vegetation or right-left shunts, such as a patent foramen ovale, were noted on transthoracic echocardiography. Moreover, other risk factors for ischemic stroke such as hypertension, dyslipidemia, diabetes, and atrial fibrillation were not detected. The patient was discharged on day 33 with an mRS score of 1. Hematoxylin and eosin staining revealed the presence of different components in the first thrombus. The main component was a fibrinoplatelet-dominant area, which stained pink with eosin. The remaining areas were erythrocyte dominant with inflammatory cells, in which the nuclei were stained purple with hematoxylin (**Fig. 4A** and **4B**). The second thrombus was uniformly stained pink by eosin and comprised fibrin and platelets with few inflammatory cells and erythrocytes (**Fig. 4C** and **4D**).

## Discussion

Cancer-associated ischemic stroke has various manifestations including nonbacterial thrombotic endocarditis due to coagulation disorders, dehydration, malnutrition, tumor embolization, and atrial fibrillation, among others.[15,16] Systemic thromboembolism, which includes cerebral infarction due to coagulation disorders associated with cancer, is similar to disseminated intravascular coagulation (DIC).[17] Watanabe et al. reported that the D-dimer level could be a predictive marker of vascular events in patients with cancer because it was significantly higher in patients with cancer than in those without cancer.[18] In our study, five out of seven cases had D-dimer levels exceeding 20 µg/mL, and the retrieved thrombi in five of six cases had fibrinoplatelet-dominant component, closely resembling those formed in DIC.[19] This suggests that the patients developed cerebral infarction due to coagulation disorders with cancer. In the present study, cancers were pathologically diagnosed in four of seven patients, and all were adenocarcinomas. Adenocarcinomas produce

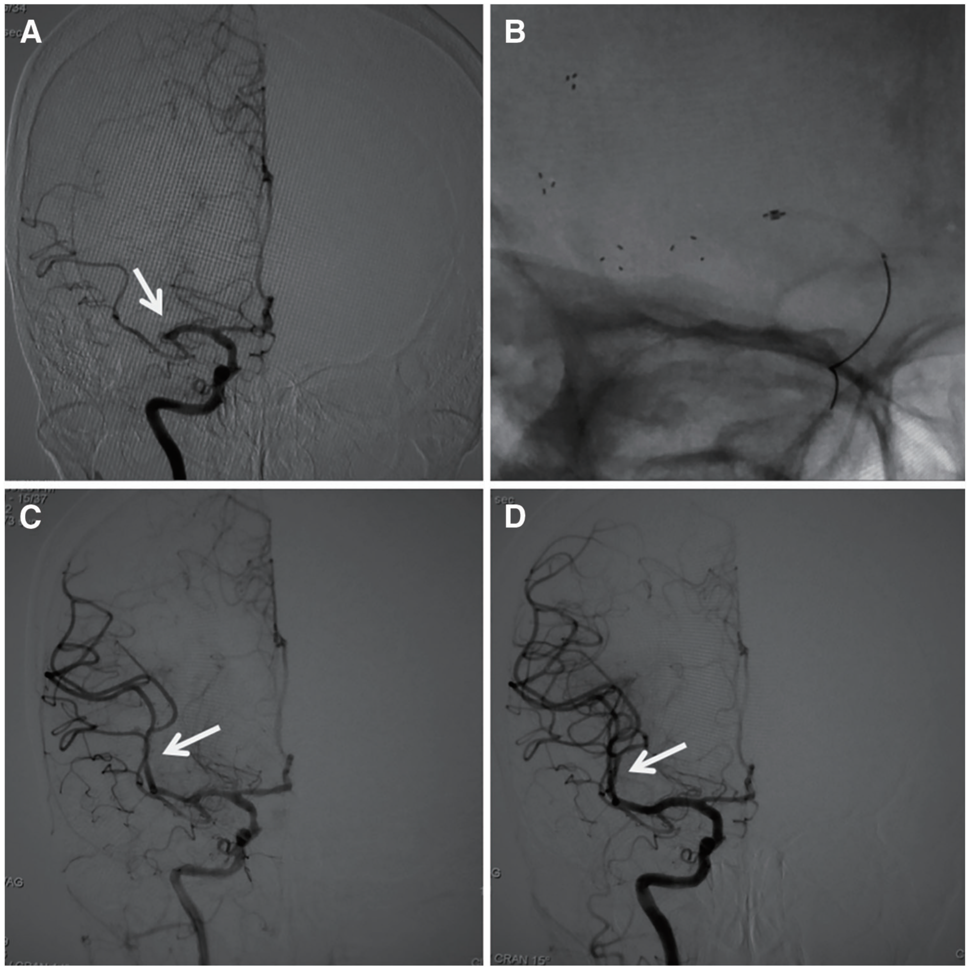


**Fig. 2** (**A**) Angiogram of the right internal carotid artery, anteroposterior view. The right MCA is occluded at the horizontal segment (M1) (white arrow). (**B**) A stent retriever was deployed in the right MCA. (**C**) Angiogram of the right internal carotid artery, anteroposterior view, showing partial recanalization after thrombectomy. Persistent obstruction of the insular segment (M2) persists (white arrow). (**D**) Angiogram of the right internal carotid artery, anteroposterior view, showing MCA recanalization after transarterial infusion of urokinase (white arrow). MCA: middle cerebral artery

mucin, which is associated with hypercoagulopathy and thrombus formation due to the activation of coagulation factors.[20] Furthermore, interactions between endothelial, phagocytic, platelet, and tumor cells are associated with coagulation disorders concomitant with cancer.[21,22] Pathological diagnoses confirmed adenocarcinomas in the five cases, suggesting that these molecular interactions induce coagulation disorders in the presence of adenocarcinomas, eventually leading to large cerebral artery occlusion.

Several studies have reported on acute recanalization therapies, including mechanical thrombectomy, for cancer-associated ischemic stroke overseas.[23–25] Intravenous tissue plasminogen activator thrombolysis is often not indicated due to hematological problems and recent surgery of cancer.[2,26] Instead, a mechanical thrombectomy was performed. Intravenous tissue plasminogen activator thrombolysis tended to be less common in the cancer-associated ischemic stroke group and only one patient was discharged with a good outcome and an mRS score of 1. These data are similar to results reported in previous studies.[27,28] The puncture-to-recanalization time was longer, although the successful recanalization rate did not differ significantly from that in controls. No postoperative symptomatic intracranial hemorrhage was observed. Thrombi with a fibrinoplatelet-dominant component accounted for five of six cases in the cancer-associated ischemic stroke group. Thrombi with fibrin- and platelet-dominant components commonly have high friction and are hard, which may contribute to the difficulty of successful recanalization.[27] In the present study, the median number of passes in which the retrieval devices were used in the occluded vessels during treatment tended to be larger in the cancer-associated ischemic stroke group than

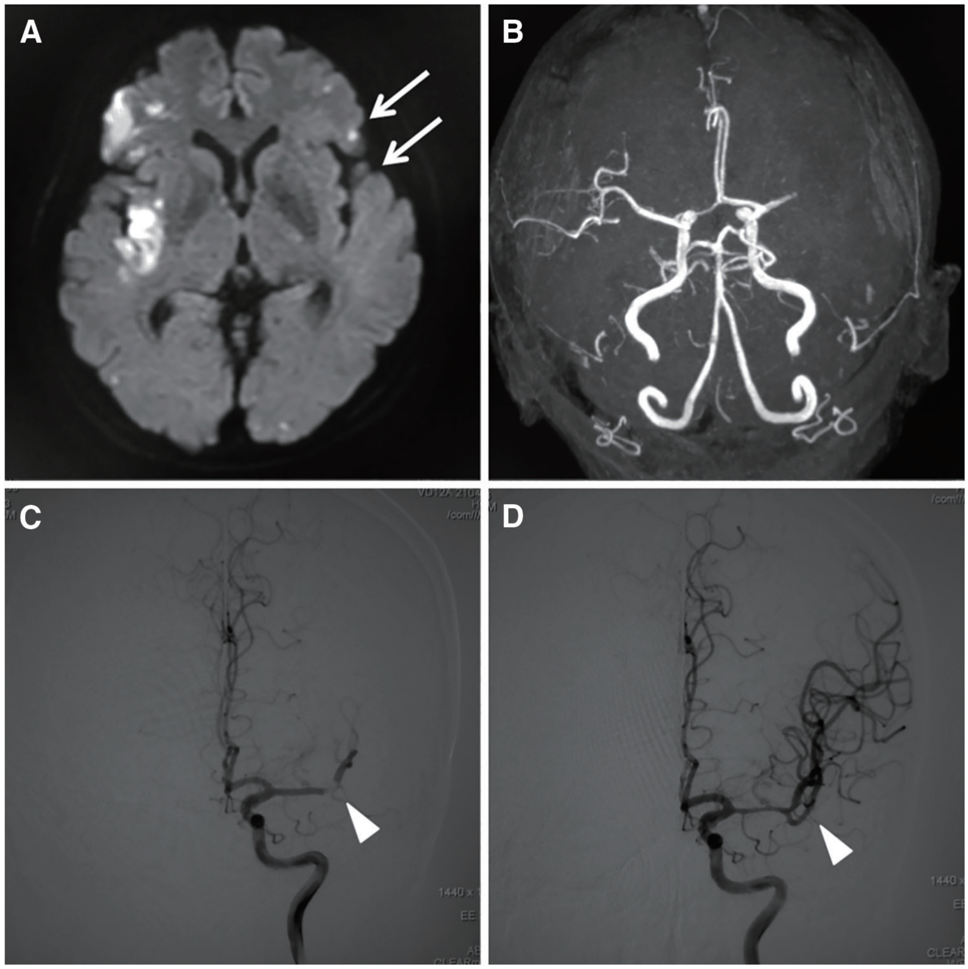


**Fig. 3** (**A**) DWIs representing very pale hyperintensity in the left MCA territory (double white arrow). (**B**) MRA representing occlusion of the left MCA. (**C**) Angiogram of the left internal carotid artery, anteroposterior view. The left MCA is occluded at the horizontal segment (M1) (white arrowhead). (**D**) Angiogram of the left internal carotid artery, anteroposterior view, showing MCA recanalization after thrombectomy (white arrowhead). DWIs: diffusion-weighted images; MCA: middle cerebral artery

that in the control group, although this difference was not statistically significant. This indicates that multiple passes through a vessel occluded by a hard thrombus may lead to longer procedure times.

In-hospital stroke onset is more common in patients with cancer-associated ischemic stroke.[28] Moreover, our study showed that the time to imaging diagnosis at in-hospital onset in the cancer-associated ischemic stroke group was longer than that in the control group. At our institution, patients with cancer are often admitted to the wards of each department, and the staff may not have been accustomed to managing ischemic stroke. Deterioration of neurological symptoms should be noted when patients are hospitalized for cancer, particularly with adenocarcinoma. It is important to establish a hospital system that enables prompt diagnosis and treatment by specialists. Patients with cancer are at elevated risk of recurrent stroke due to cancer-associated coagulation disorder.[23] Three of the seven patients in our series experienced major ischemic stroke recurrence with high D-dimer levels during hospitalization. Two of these patients could not be treated with anticoagulant therapy because of a substantial risk of cancer-related bleeding. Secondary preventive treatments for cancer-associated ischemic stroke vary depending on etiology. In particular, low-molecular weight heparin should be considered for the treatment of ischemic stroke in patients with cancer-associated coagulation disorders resembling DIC.[29] However, because its use for preventing cerebral infarction has not been authorized by the Japanese insurance system, continuous intravenous unfractionated heparin injections are often administered at our institution considering the risk of bleeding. Further studies are needed to develop

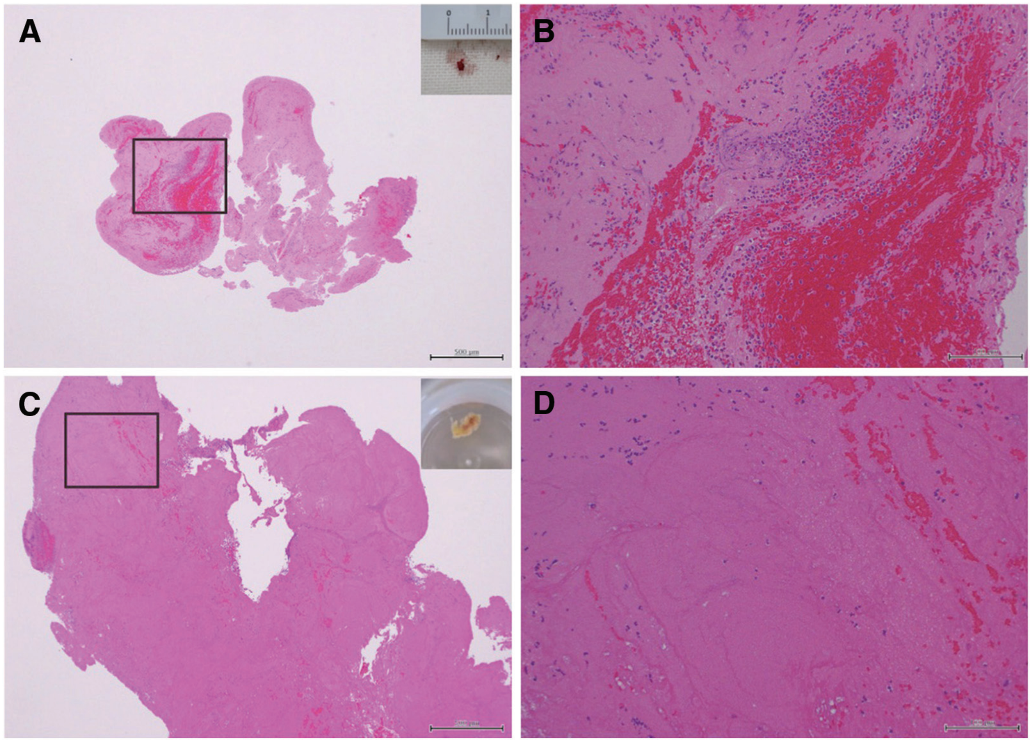


**Fig. 4** (**A** and **B**) The pathological image of a retrieved thrombus during the initial thrombectomy. The appearance of the retrieved thrombus is shown in the upper right panel of image A. The main component was the fibrinoplatelet-dominant area that was stained pink by eosin; the remaining parts were red-colored erythrocyte-dominant areas with inflammatory cells in which the nuclei were stained purple by hematoxylin and eosin staining. Scale bar: (**A**) 500 µm and (**B**) 100 µm. (**C** and **D**) Pathological images of the thrombus retrieved during the second thrombectomy. The retrieved thrombus is shown on the upper right side of (**C**). Thrombus length was 4 mm. Fibrinoplatelet-dominant thrombi were uniformly stained pink with eosin, and only a small number of inflammatory cells and erythrocytes were observed after hematoxylin and eosin staining. Scale bar: (**C**) 500 µm and (**D**) 100 µm

anticoagulant therapies for the secondary prevention of cancer-associated ischemic stroke. The cancer-associated ischemic stroke group tended to have poor outcomes at discharge, although there was no significant difference between the two groups because of the small number of cases in the cancer-associated ischemic stroke group. This may be because the neurological symptoms were more severe, the DWI-ASPECTSs were lower, and the recurrence of large cerebral artery occlusion was more common in the cancer-associated ischemic stroke group than those in the control group. Moreover, a poor general condition, including coagulation disorders, may be involved in the outcome at discharge in the cancer-associated ischemic stroke group.

This study has some limitations. First, the sample size differed between the cancer-associated ischemic stroke and control groups owing to the rarity of large cerebral artery occlusions in cancer-associated ischemic stroke. However, we believe that this was worthy of a comparative study, because the treatment process for large cerebral artery occlusions and the evaluation of vascular risks other than cancer were standardized in both groups at a single institution. Second, two cases of cancer-associated ischemic stroke were diagnosed with cancer for the first time during the examination of embolic sources. In such cases, the pathological diagnosis of the cancer remains unclear. Third, it may have been difficult to diagnose the extent of involvement of the cancer in the onset of cerebral infarction in our study. High D-dimer levels and the three territories sign were observed in many cases in our study; however, there were also atypical cases, such as Case 5. Further research is required to clarify the diagnostic criteria and mechanisms underlying coagulation disorders caused by cancer. Finally, pathological examination of the thrombi consisted of hematoxylin and eosin staining and microscopic observation by a pathologist. It is difficult to accurately distinguish between fibrin and platelets when measuring the area of each thrombus component.

Patients with cancer and comorbid ischemic stroke may have a poor prognosis owing to coagulation disorders and poor general conditions. Therefore, it is difficult to evaluate the efficacy of mechanical thrombectomy based on the mRS scores after 3 months.[30] We believe that improving neurological symptoms as much as possible by reducing the infarction volume may maintain the quality of life of patients, such that their remaining time may be meaningful. However, excessive trials and rough procedures in mechanical thrombectomy may cause hemorrhagic complications and worsen symptoms. Mechanical thrombectomy may be necessary when considering flexible strategies for cancer-associated ischemic stroke such as transarterial local fibrinolysis.

## Conclusion

Large cerebral artery occlusions during hospitalization of patients with cancer require careful attention. Coagulation disorders associated with cancer, particularly adenocarcinoma, may be due to the formation of thrombi with fibrinoplatelet-dominant components in cancer-associated ischemic stroke. The procedure time tended to be longer with mechanical thrombectomy for cancer-associated ischemic stroke. Further investigations are necessary to determine the effectiveness of mechanical thrombectomy in patients with cancer-associated ischemic stroke.

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## Disclosure Statement

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