ORIGINAL ARTICLE

The Incidence of Ischemic Stroke in Cancer Patients in Thailand

Krongkamol Ponglikitmongkol, MD[1], Arthita Choolam, MD[1]

[1] Department of Medicine, Chulabhorn Hospital, HRH Princess Chulabhorn College of Medical Science, Chulabhorn Royal Academy, Bangkok, Thailand

Objective: Cancer and stroke are leading causes of morbidity and mortality in Thailand. The objectives of the present study were 1) to determine the incidence of ischemic stroke in cancer patients in Thailand, 2) to identify the cancer subtypes most associated with ischemic stroke, and 3) to compare the etiology of stroke in two groups of patients, those who had conventional risk factors for stroke and those without conventional risk factors or cryptogenic stroke.

Materials and Methods: The present study was a retrospective descriptive study. The authors collected data on cancer patients hospitalized between 2008 and 2020 according to International Classification of Disease and Related Health Problem Tenth Revision (ICD-10) and identified the number of ischemic stroke patients and the cancer subtype for each patient. Risk factors for stroke were identified as conventional risk factors (hypertension, diabetes mellitus, dyslipidemia, atrial fibrillation, smoking, and imaging evidence of atherosclerosis) and cryptogenic risk factors (none of the conventional risk factors).

Results: Sixteen thousand six hundred forty-seven cancer patients were included in the present study and 85 of these patients were diagnosed with ischemic stroke. Therefore, the incidence of ischemic stroke in cancer patients was 0.51%. The cancer subtypes most often associated with ischemic stroke were thoracic as predominantly lung, lower gastrointestinal tract, and hepatobiliary cancer. Most patients (88.24%) had at least one conventional risk factor. Hypertension was the most common conventional risk factor. Cryptogenic stroke was found in 5.88% of the patients and 5.88% of the patients had insufficient data on risk factors.

Conclusion: The incidence of ischemic stroke in Thai cancer patients is low. Lung cancer is the cancer type most associated with ischemic stroke. Most cancer patients with ischemic stroke had multiple vascular risk factors.

Keywords: Stroke; Cancer; Incidence

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Cancer and stroke are leading causes of morbidity and mortality in Thailand[1,2]. When these two conditions occur together, they will have a serious impact on patients' quality of life. There are limited data about the prevalence of ischemic stroke in cancer patients[3,4], and the incidence of ischemic stroke in cancer patients in Thailand is not known. Moreover, it is important to identify the risk of ischemic stroke in each subtype of cancer.

Cancer patients tend to have a higher risk of ischemic stroke compared with the general population[5-7]. While cancer-related risk factors for stroke involve various mechanisms, hypercoagulability is one of the cancer-related factors associated with increased stroke risk[8]. However, a review of the etiology of stroke in cancer patients found that most patients had combined vascular risk factors for stroke[9,10]. Because both cancer and ischemic stroke are often found in older people, the vascular risk factors may develop over time[11]. It is important to study the underlying mechanisms of stroke in cancer patients because there is conflicting evidence as to whether antiplatelet or anticoagulant therapy is more appropriate[12]. On the one hand, if atherosclerosis played an important role in the mechanism of ischemic stroke, antiplatelet therapy could be beneficial. On the other hand, anticoagulant therapy might be the better option in patients with underlying hypercoagulability. The objectives of the present study were 1) to determine the incidence of ischemic stroke in cancer patients in Thailand, 2) to identify the cancer subtypes most associated with ischemic stroke, and 3) to compare the incidence

Correspondence to:

Ponglikitmongkol K.

Department of Medicine, Chulabhorn Hospital, Chulabhorn Royal Academy, 906 Khamphaengphet 6 Road, Laksi, Bangkok 10210, Thailand.

Phone: +66-2-5766791

Email: Krongkamol.pong@gmail.com

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Table 1. The incidence of stroke in patients with different cancer subtypes admitted to Chulabhorn Hospital between 2008 and 2020

Cancer subtypes	Total cancer patients (n)	Patients with ischemic stroke (n)	Incidence of ischemic stroke in cancer patients (%)
Thoracic	1,834	22	1.20
Hepatobiliary	2,343	16	0.68
Breast	2,376	1	0.04
Lower Gastrointestinal Tract	2,196	16	0.73
Female Reproductive Organ	2,143	10	0.47
Hematologic Malignancies	833	0	0.00
Other	4,922	20	0.41
Total	16,647	85	0.51

of ischemic stroke associated with conventional risk factors to that of cryptogenic stroke.

Materials and Methods

The present study was conducted at Chulabhorn Hospital, a well-known cancer institute in Thailand. The present study complied with the Declaration of Helsinki Guidelines for human subjects. The study protocol was ethically reviewed and approved by the Ethics Committee for Human Research, Chulabhorn Research Institute (Certificate No. 068/2564). The authors retrospectively collected the data of cancer patients diagnosed with ischemic stroke during admission according to ICD-10 from 2008 to 2020. The diagnosis of ischemic stroke was also approved by the imaging of the brain including computerized tomography (CT) scan, magnetic resonance imaging (MRI) scan, and positron emission tomography (PET) scan.

Age, gender, cancer type, and vascular risk factors were identified for each patient. Conventional risk factors for stroke included hypertension, diabetes mellitus, dyslipidemia, atrial fibrillation, smoking, and imaging evidence of cranial atherosclerosis[11,13,14]. Patients with one or more conventional risk factors were included in the conventional risk factors group and patients without conventional risk factors were identified as having cryptogenic stroke.

Results

The present study population comprised 16,647 cancer patients admitted to Chulabhorn Hospital between 2008 and 2020. There were 85 patients diagnosed with ischemic stroke during hospitalization. Therefore, the incidence of ischemic stroke in the cancer patients was 0.51%. Most of the patients were male. The mean age at diagnosis of cancer was 66 years and the mean age at onset of ischemic stroke was 67 years. The subtypes of cancer most often associated with ischemic stroke were thoracic (predominantly lung), lower gastrointestinal tract, and hepatobiliary cancer (Table 1). The incidences of thoracic cancer, lower gastrointestinal tract cancer, and hepatobiliary tract cancer in ischemic stroke patients were 1.2%, 0.73%, and 0.68%, respectively. Most of the cancer patients with ischemic stroke (88.24%) had at least one conventional risk factor, 5.88% of the patients did not have any conventional risk factors and were identified as having cryptogenic stroke, and 5.88% of the patients had insufficient data to subgroup in either conventional risk factors group or cryptogenic stroke group. The patient risk factors, and cancer subtypes are listed in Table 2. The most common conventional risk factor was hypertension. Other risk factors included diabetes and dyslipidemia. Unfortunately, data on atrial fibrillation, smoking, and imaging evidence of atherosclerosis were incomplete, so the authors could not analyze these risk factors in the patient population.

Discussion

The incidence of ischemic stroke in cancer patients varies in different countries[5-7]. In the present study, the incidence of ischemic stroke in cancer patients in Thailand was 0.51%. This is the first, and by far, the largest report assessing ischemic stroke in cancer patients in Thailand. The present study results are similar to those previous studies showing that 0.12% of patients admitted to a major cancer institute in a Western country presented with ischemic stroke[15]. These data suggest that the incidence of ischemic stroke in patients presenting to cancer institutes is low. Possible reasons for the low incidence found in the present study include the single-center, retrospective nature of the study, and that most of the data were excluded due to incomplete medical records. Furthermore, patients with ischemic stroke admitted to larger hospitals or other general medical centers were not included.

Nevertheless, the present study data shows the

Table 2. Patient characteristics and vascular risk factors in different cancer subtypes

Number of patients	Total	Thoracic cancer	Hepatobiliary cancer	Breast cancer	Lower gastrointestinal tract cancer	Female reproductive organ cancer	Other cancer
Sex; n (%)							
Male	52 (61.18)	16 (72.73)	14 (87.50)	0 (0.00)	8 (50.00)	0 (0.00)	14 (70.00)
Female	33 (38.82)	6 (27.27)	2 (12.50)	1 (100)	8 (50.00)	10 (100)	6 (30.00)
Age at diagnosis of cancer; mean±SD	66.07±11.02	67.59±8.93	66.38±8.00	62	70.25±9.64	58.40±18.53	64.85±10.56
Age at onset of stroke; mean±SD	67.31±10.95	68.59±8.96	66.88±8.02	63	71.94±10.80	59.90±17.97	66.45±9.74
Etiology; n (%)							
Conventional	75 (88.24)	21 (95.45)	13 (81.25)	0 (0.00)	13 (81.25)	9 (90.00)	19 (95.00)
Cryptogenic	5 (5.88)	1 (4.55)	1 (6.25)	1 (100)	1 (6.25)	0 (0.00)	1 (5.00)
Incomplete data	5 (5.88)	0 (0.00)	2 (12.50)	0 (0.00)	2 (12.50)	1 (10.00)	0 (0.00)
Hypertension; n (%)							
No	24 (28.24)	5 (22.73)	5 (31.25)	1 (100)	4 (25.00)	2 (20.00)	7 (35.00)
Yes	53 (62.35)	14 (63.64)	9 (56.25)	0 (0.00)	10 (62.50)	8 (80.00)	12 (60.00)
Incomplete data	8 (9.41)	3 (13.64)	2 (12.50)	0 (0.00)	2 (12.50)	0 (0.00)	1 (5.00)
Diabetes; n (%)							
No	42 (49.41)	12 (54.55)	7 (43.75)	1 (100)	6 (37.50)	3 (30.00)	13 (65.00)
Yes	26 (30.59)	5 (22.73)	5 (31.25)	0 (0.00)	4 (25.00)	7 (70.00)	5 (25.00)
Incomplete data	17 (20.00)	5 (22.73)	4 (25.00)	0 (0.00)	6 (37.50)	0 (0.00)	2 (10.00)
Dyslipidemia; n (%)							
No	25 (29.41)	6 (27.27)	5 (31.25)	1 (100)	3 (18.75)	4 (40.00)	6 (30.00)
Yes	35 (41.18)	11 (50.00)	4 (25.00)	0 (0.00)	8 (50.00)	5 (50.00)	7 (35.00)
Incomplete data	25 (29.41)	5 (22.73)	7 (43.75)	0 (0.00)	5 (31.25)	1 (10.00)	7 (35.00)
Atrial fibrillation; n (%)							
No	57 (67.06)	13 (59.09)	9 (56.25)	1 (100)	9 (56.25)	8 (80.00)	17 (85.00)
Yes	9 (10.59)	3 (13.64)	2 (12.50)	0 (0.00)	3 (18.75)	1 (10.00)	0 (0.00)
Incomplete data	19 (22.35)	6 (27.27)	5 (31.25)	0 (0.00)	4 (25.00)	1 (10.00)	3 (15.00)
History of smoking; n (%)							
No	7 (8.24)	3 (13.64)	1 (6.25)	1 (100)	1 (6.25)	0 (0.00)	1 (5.00)
Yes	20 (23.53)	10 (45.45)	5 (31.25)	0 (0.00)	0 (0.00)	0 (0.00)	5 (25.00)
Incomplete data	58 (68.24)	9 (40.91)	10 (62.50)	0 (0.00)	15 (93.75)	10 (100)	14 (70.00)
Imaging evidence of atherosclerosis; n (%)							
No	10 (11.76)	2 (9.09)	5 (31.25)	0 (0.00)	0 (0.00)	1 (10.00)	2 (10.00)
Yes	18 (21.18)	5 (22.73)	1 (6.25)	0 (0.00)	5 (31.25)	3 (30.00)	4 (20.00)
Incomplete data	57 (67.06)	15 (68.18)	10 (62.50)	1 (100)	11 (68.75)	6 (60.00)	14 (70.00)

SD=standard deviation

subtypes of cancer most commonly associated with ischemic stroke are thoracic (predominantly lung), lower gastrointestinal tract, and hepatobiliary cancer. These data are similar to the western reports showing that stroke risk was higher in patients with lung and gastrointestinal tract cancers[5,16-19]. The incidence of stroke was highest in lung cancer patients in the present study cohort. This may be because lung cancer and ischemic stroke share common risk factors such as smoking, hypertension, obesity, and diabetes[20-23].

The etiology of ischemic stroke in cancer patients is unclear. Cryptogenic stroke is diagnosed more often in cancer patients than in patients without cancer[16]. Many cancer-related risk factors that are thought to contribute to the pathogenesis of ischemic stroke are blood vessel compression or infiltration by tumors, abnormal coagulation, treatment complications such as chemotherapy-induced endothelial toxicity, and post-radiation vasculopathy in both intracranial and extracranial vessels[8,18]. The presence of cancer and anti-cancer treatment complications can both exacerbate conventional risk factors for stroke. For example, radiation can lead to atherosclerosis or small vessel disease and hypercoagulable

states can increase the risk of cardiac thrombosis. A hypercoagulable state is associated with an increased risk of cancer-related stroke and D-dimer levels are high in cancer patients with ischemic stroke[16,24]. However, atherosclerosis is the most common cause of cerebrovascular disease identified at autopsy of cancer patients[4]. Furthermore, more stroke patients present with conventional risk factors than with cryptogenic stroke[9,10,25]. As the raise of awareness of cryptogenic stroke in cancer patients worldwide, the authors compare the number of patients with conventional risk factors and cryptogenic stroke in Thai cancer population. The present study result showed that most Thai cancer patients have at least one conventional risk factors of ischemic stroke. The most common conventional risk factor for stroke in the present study was hypertension. These data were similar to results from other cancer institutes that identified hypertension as the most common vascular risk factor[15,25]. Hypertension is also a risk factor for stroke in Thailand[13]. Hypertension leads to atherosclerosis and small vessel disease, the major cause of ischemic stroke.

The number of cryptogenic stroke patients in the present study was low and cancer-related risk factors could not be identified in this group due to incomplete data. Therefore, further studies are needed to confirm whether Thai patients have a lower risk of cancer-related conditions such as coagulopathies or other mechanisms of stroke than Western populations.

The present study data suggests that cancer patients should be evaluated for vascular risk factors to help prevent ischemic stroke. Further studies are required to better understand the cancer-related mechanisms leading to ischemic stroke and the most appropriate antithrombotic therapies for cancer patients.

Conclusion

To the authors knowledge, the present study is the first study of ischemic stroke in cancer patients in Thailand. The data showed the incidence of ischemic stroke in cancer patients presenting to a major Thai cancer institute is low. Lung cancer patients had the highest incidence of ischemic stroke in the present study. Moreover, most cancer patients had at least one vascular risk factor, most commonly hypertension. These data suggest that evaluating and optimizing treatment for vascular risk factors may lower the risk of stroke in cancer patients.

What is already known on this topic?

The incidence of ischemic stroke in cancer patients varies worldwide[5-7]. The subtypes of cancer most associated with stroke are lung and gastrointestinal tract cancer(5,16-19). The conclusion for the etiology of stroke in cancer patients is still unclear. However, the data on ischemic stroke in cancer patients in Thailand has never been reported.

What does this study add?

This study is the first and by far, the largest study of the incidence of ischemic stroke in cancer patients in Thailand. The study shows that lung, lower gastrointestinal, and hepatobiliary tract cancers are the most common cancers with comorbidity of ischemic stroke. Furthermore, this study also provides information that most cancer patients had at least one conventional risk factor of stroke. Only few patients had cryptogenic stroke.

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Authors' contributions

KP was responsible for statistical analyses and for drafting, reviewing, and editing the manuscript. AC was responsible for the study design and editing the manuscript.

Availability of data

The data of the present study is not publicly available because some patient information is private. However, the data may be made available upon reasonable request to the corresponding author.

Conflicts of interest

The authors have no conflict of interest to report.

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