Three-Month Outcomes Are Poor in Stroke Patients with Cancer Despite Acute Stroke Treatment

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Introduction: Stroke risk is increased in cancer patients. Prognosis in these patients is poor, with higher in-hospital mortality and increased subsequent mortality. However, data on stroke in cancer patients are limited, specifically regarding acute stroke treatment and functional outcomes. We aim to determine the functional outcomes of cancer patients admitted with acute stroke. *Materials and Methods:* We retrospectively reviewed patients carrying a diagnosis of cancer who were admitted with acute ischemic stroke between March 2013 and February 2016. Demographics, cerebrovascular risk factors, stroke characteristics including acute treatment, and characteristics of their cancer history and treatment were abstracted. The primary outcome measures included in-hospital mortality and 3-month functional outcome (as assessed by the modified Rankin Scale [mRS] score, with mRS scores of 3-6 considered poor functional outcome). Further outcome measures included length of stay and discharge destination. *Findings:* Forty-nine patients met the inclusion criteria, with a median admission National Institutes of Health Stroke Scale score of 8. Twelve patients (24.4%) underwent acute stroke treatment. The most common stroke etiology was hypercoagulability of malignancy (21, 42.9%). The three-month mortality was 46.9%; half of survivors had poor functional outcome. Functional outcomes did not differ by cancer type, stage, or year since diagnosis; on multivariate analysis only high admission NIHSS score was associated with poor functional outcome ($P = .002$). *Conclusion:* Nearly half of patients with cancer and stroke die within 3 months, and functional outcome is poor for 50% of 3-month survivors despite consideration of acute stroke treatment. Future research should address the role of hypercoagulability in the outcome prediction of stroke patients with cancer. **Key Words:** Acute ischemic stroke—cancer—hypercoagulability—malignancy—outcome—mortality—thrombolysis.

Introduction

Ischemic stroke (IS) and malignant cancer both represent leading causes of death and disability. Stroke risk and stroke recurrence are increased in cancer patients.[1,2] Next to traditional stroke risk factors, malignancy-related hypercoagulability, tumor embolism, and adverse effects from oncological treatment can contribute to the occurrence of IS.[3-6] Post-stroke prognosis in cancer patients has been reported to be poor, with higher in-hospital mortality[6,7] and higher subsequent mortality for cryptogenic stroke.[8] However, the majority of studies evaluating stroke in cancer patients do not distinguish between different stages of cancer, are limited to active cancer,[5,6,8-11]

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and do not take into account acute stroke treatment.[7,8] Furthermore, data are slim on functional outcomes in this patient population.

We aim to determine the functional outcomes of cancer patients admitted with acute stroke, and hypothesize that despite consideration of acute stroke treatment and safe application if appropriate, functional outcomes at 3 months after admission with stroke are poor for cancer patients.

Materials and Methods

Patient Population

We retrospectively identified all patients who were admitted with acute IS to our tertiary care referral and comprehensive stroke center between March 2013 and February 2016 and also carried a diagnosis of cancer. IS was defined as the presence of neurologic deficit that was either persistent for >24 hours with an imaging correlate or lasting less than 24 hours but confirmed by computed tomography (CT) or magnetic resonance imaging (MRI) of the brain. We extracted patient demographics, presence of cerebrovascular risk factors, previous vascular events, use of antiplatelet or anticoagulant medications prior to admission, and the National Institutes of Health Stroke Scale (NIHSS) and modified Rankin Scale (mRS) scores on admission. Diagnostic stroke work-up consisted of brain MRI or CT with angiogram if appropriate, extracranial duplex sonography, electrocardiography, prolonged electrocardiography monitoring if indicated, routine laboratory tests (including coagulation tests and fasting lipid profile), and transthoracic or transesophageal echocardiography. Acute stroke intervention was defined as use of intravenous tissue plasminogen activator (IV tPA), mechanical thrombectomy, or interventional clot retrieval.

The medical record was further reviewed for type and stage of cancer, location of metastasis if present, cancer treatment, and year of cancer diagnosis. Patients with brain tumors or cerebral metastatic disease were excluded.

Stroke Etiology and Stroke Pattern

Stroke etiology was defined according to the Trial of ORG 10172 in Acute Stroke Treatment (TOAST) classification.[12] If the cause of stroke could not be determined confidently or if at least two possible causes of stroke were present, the stroke etiology was classified as cryptogenic. Hypercoagulability of malignancy was considered a distinct stroke etiology if determined to be the most likely cause by the attending stroke physician after evaluation of all diagnostic data.

The infarct patterns were classified into four groups based on brain MRI or CT: (1) single lesion in one vascular territory, (2) scattered lesions in one vascular territory, (3) border zone infarction, and (4) infarcts in multiple vascular territories of the brain.[13] The presence of hemorrhagic transformation (HT) was determined by examining follow-up CT brain images. HT was characterized using established imaging subtypes[14]: HI type 1 consists of small petechiae along the border of the infarct, HI type 2 is more confluent petechiae without space-occupying effect, PH type 1 is classified when <30% of the infarct has confluent hemorrhage with some space-occupying effect, and PH type 2 is classified when >30% of the infarct has hemorrhage with substantial space-occupying effect or if any hemorrhage is located outside the infarct. Symptomatic HT was defined as a worsening of clinical examination by 4 points or greater on the NIHSS. Post-tPA coagulopathy was defined as a rise in the international normalized ratio (INR) of above 1.5 or reversal of tPA due to hemorrhagic complications.

Outcomes

Our primary outcome was defined as mortality, either in-hospital or at 3 months, and functional outcome at 3 months, as measured by the mRS. mRS scores of 3-6 were considered poor functional outcome. The outcome was obtained through inpatient chart review, outpatient records, and public records of death. Further outcome measures that were considered included discharge destination (favorable: home or home with health aid, acute rehabilitation; unfavorable: in-hospital death, hospice, skilled nursing facility, or long-term-acute care facility) and length of stay in the hospital.

Statistical Analysis

All analyses were done with SAS version 9.3 (Cary, NC). Continuous variables were compared with either two sample *t*-test or Mann–Whitney *U*-test. Categorical variables were compared with chi-square test or Fisher's exact test. A *P* value of .05 or less was considered statistically significant.

This study was approved by the local institutional review board and included a waiver of consent.

Results

There were 66 patients with acute IS and cancer. Seventeen of these were excluded due to the presence of brain metastasis or the cancer being a primary brain malignancy, as previously stated. Of the 49 patients included in the final analysis, the mean age was 71 years (±10.7 years) and 27 (55.1%) were female. The baseline characteristics are shown in Table 1. The most common stroke risk factors were hypertension, dyslipidemia, active smoking, and prior cerebrovascular event. The median NIHSS score on admission was 8 (interquartile range [IQR]: 9), and the median mRS score on admission was 1. Twenty-one patients (42.9%) were classified as having suffered a stroke due to hypercoagulability of malignancy. The next most common etiology was cardioembolic (9, 18.4%), followed by cryptogenic (8, 16.3%). Twelve patients (24.4%)