

ORIGINAL ARTICLES

Complication of acute stroke: A study in ten Asian countries

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Abstract

Background and Objective: There is a paucity of studies looking into the frequency of complications after stroke among Asians. We sought to determine the frequency and rate of complications among Asians after acute stroke. **Methods:** Consecutive patients with acute stroke among 10 participating Asian countries were included in the study. The frequency and timing of pre-determined complications, and their relation to area of admission were noted. **Results:** Of the 1,153 patients included in the study, 423 (41.9%) developed complications within the first 2 weeks of stroke. Recurrent stroke, chest infections and urinary tract infections were most commonly encountered, and were most frequent within the first week of stroke onset. A lower rate of complications was noted among patients admitted at an organized stroke unit.

Conclusion: There is a similar rate of frequency and timing of complications after acute stroke among Asians as compared with other populations.

INTRODUCTION

The hospital mortality and morbidity rate of patients with acute stroke ranges from 7.6% to 30%.¹⁻³ Of these, neurological deaths constitute about 80% and non-neurological deaths constitute about 17%.² The Stroke Unit Trialists' Collaboration study showed that there was no difference in the mortality rate during the first few days among patients admitted in the stroke unit and general neurology or conventional ward.⁴ Neurological deaths such as progressive increased intracranial pressure and subsequent herniation were the most common causes of death in both groups within the first 3 days of admission. In the subsequent days, however, a significant increase

in the number of deaths was seen among patients who were not admitted in the acute stroke unit. These mortalities were due to non-neurologic complications.⁵

Previous studies have demonstrated that complications following the occurrence of stroke range from 40% to 96%.⁵⁻¹⁴ These complications have been fatal in some cases, contributing to the hospital mortality and morbidity.^{5,12,13} At present, options for intervention for acute stroke remain limited; hence, in most cases, the outcome for survival and disability depends on prevention, recognition and early treatment of complications. Prevention of these complications would entail awareness of the types of complications that may occur as well as their time of occurrence,

particularly those complications that are encountered during the course of hospitalization.

In 1996, the Asian Stroke Advisory Panel (ASAP) was organized to address some common issues encountered among stroke patients in the region. One of the objectives of the group was to carry out researches that would be relevant to the region. We wanted to find out whether the nature of complications among Asian stroke patients differed from that of their Caucasian counterparts. Hence, the purpose of this paper is to determine the frequency of complications among stroke patients in the region. These complications would then be compared to retrospective and prospective published data on complications of stroke. We likewise sought to determine the time of occurrence of these complications so that more effective preventive strategies can be formulated and subsequently implemented.

METHODS

One hundred consecutive patients who had cranial CT scan or MRI to confirm the diagnosis of acute stroke (infarction or hemorrhage except subarachnoid hemorrhage) occurring within 7 days were recruited from each member country during the years 2003 and 2004. A data collection form was utilized to monitor the incidence of complications and the time of its occurrence. Demographic data such as age, sex, and date of recruitment were collected. The presence of the various risk factors, defined as follows, were noted: arterial hypertension (BP >160/90 mmHg or on antihypertensive medications), diabetes mellitus (elevated fasting blood glucose or HbA1c \geq 7.5% or on hypoglycemic medications), hypercholesterolemia (blood cholesterol >220mg% or on lipid lowering medication), elevated triglyceride levels, low density lipoprotein levels, current smokers (patients who smoke more than 10 sticks per day for more than a year) and significant alcohol intake (>30 grams of ethanol per day). Glasgow Coma Scale (GCS) and modified Rankin scale were also recorded. The subtypes of stroke were classified following the Oxfordshire classifications.¹⁶ The place of confinement was classified according to whether the patient was admitted to a general neurology ward, an organized stroke unit, or a general medical ward. Following the work by Langhorne, *et al*, modified predefined complications were utilized to monitor the occurrence of complications (Appendix 1).¹⁴ These complications were monitored daily by the

physician-in-charge during the first two weeks of admission and recorded as to its type and time of occurrence. The number of patients who had selected life-threatening complications during the following times was determined: within the first 3 days, 4-7 days, and 8-14 days. Subsequently, the types of complications and number of patients having such complications on a particular time were noted. The selected potentially life-threatening complications are as follows: recurrent stroke, epileptic seizure, chest infections, falls, deep vein thrombosis, pulmonary embolism, acute congestive heart failure, cardiac arrhythmias and aspiration pneumonia. The patient's condition, whether he survived or succumbed to his illness, was noted upon discharge.

RESULTS

One thousand one hundred and fifty three consecutive patients were recruited from 10 ASAP member countries. There were 666 (57%) males. Mean age was 62 ± 13.5 years and 919 (80%) had their first-ever stroke.

On admission, the following risk factors were noted among the subjects: hypertension in 352 (30.0%), diabetes mellitus in 312 (27.7%), alcohol consumption >30g/day in 209 (23.1%) and current cigarette smoking in 236 (26.0%). Eight hundred sixty seven (95.0%) had a GCS \geq 8. Four hundred seven (67.0%) had a modified Rankin score of 1-3, while the remainder had a modified Rankin score of 4-6. Nine hundred thirty six underwent a cranial CT scan (81%), 26 (2%) had a cranial MRI, and 191 (17%) underwent both modalities of imaging studies. The following subtypes of stroke were noted: Partial anterior circulation infarct - PACI 274 (27%), total anterior circulation infarct - TACI 115 (12%), lacunar infarct - LACI 247 (25%), posterior circulation infarct - POCI 99 (10%) and primary intracerebral hemorrhage - PICH 258 (26%). Four hundred ninety five (46%) were admitted to an organized stroke unit, 449 (42%) to a general neurology ward and 130 (12%) to a general medical ward. Nine hundred forty nine (93.9%) were discharged alive and 70 (6.9%) died during confinement. Most of these deaths occurred during the first week from admission.

Table 1 shows the overall rates of complications in the Asian region and compares it to other previously published retrospective and prospective papers. A total of 495 (42.9%) complications was seen in this cohort of patients. Among the neurological complications, 49 (4.8%) patients developed recurrent stroke and 13 (1.2%) had

Table 1: Frequencies of complications compared with previous retrospective and prospective studies

Complications	Present study (%)	Frequency in published retrospective studies, percent ^{6,9-11,14}	Frequency in published prospective studies, percent ^{7,14}
Recurrent stroke	50 (4.9%)	5	9-18
Epileptic seizure	14 (1.3%)	2-5	3
Urinary tract infection	50 (4.9%)	7-25	11-28
Chest infection	95 (9.4%)	7-21	10-22
Falls	25 (2.4%)	22-25	25
Pressure sore	26 (2.6%)	3-18	5-21
Deep vein thrombosis	5 (0.5%)	1-2	0-1
Pulmonary embolism	1 (0.1%)	2-18	0-2
Depression	40 (4.0%)	5-33	16
Upper gastrointestinal bleeding	17 (1.6%)	N/R	N/R
Other bleeding	11 (1.1%)	N/R	N/R
Congestive heart failure	2 (0.2%)	N/R	2.9
Constipation	75 (7.9%)	N/R	N/R
Cardiac arrhythmias	3 (0.3%)	N/R	3.4
Arthritis	7 (0.7%)	N/R	N/R
Retention of urine	49 (5.0%)	N/R	N/R
Aspiration	25 (2.5%)	N/R	N/R
Total	495 (42.9%)	40-96	63-95

N/R not reported

epileptic seizure. Among the non-neurologic complications, the most commonly encountered were chest infections, constipation, and urinary retention with a rate of 9.0%, 7.9%, and 5.0% respectively.

The number of patients developing selected life-threatening complications was determined during the first 3 days of confinement, on days 4-7 and on days 8-15 of confinement (Table 2). Recurrent stroke and seizure were more frequent during the first week. Chest infection was the most common complication during the entire two weeks of observation, with a peak incidence during the first week.

The complication rate was noted according to the different areas of confinement (Table 3). The rate of complications tended to be lower among patients admitted in a stroke unit, compared with those admitted in a general medical ward or a

general neurology ward.

DISCUSSION

Our study showed that the complication rate (42.9%) in this cohort of patients is comparable to the previously reported retrospective and prospective papers from Caucasian stroke patients.⁵⁻¹³ This would indicate that there is not much racial and ethnic difference with regard to the total rate of occurrence and the type of complications among stroke patients.

The frequencies of neurologic complications (such as recurrent stroke and epileptic seizure) and medical complications (such as pressure sores and urinary tract infection) were similar to rates noted in previous studies.⁵⁻¹⁵ Falls, deep vein thrombosis and pulmonary embolism were less frequent among Asian stroke patients. Cardiac complications, like congestive heart failure

Table 2: Rates and timing of complications during hospitalization

	N	<4 days		4-7 days		8-14 days	
		n	%	n	%	n	%
Recurrent stroke	1020	34	3.3	13	1.3	3	0.3
Seizure	1083	10	0.9	2	0.2	2	0.2
Chest infection	1013	44	4.3	40	4.1	11	1.2
Falls	1052	20	1.9	1	0.1	2	0.2
Deep vein thrombosis	1000	0	0.0	4	0.4	1	0.1
Pulmonary embolism	1000	1	0.1	0	0.0	0	0.0
Congestive heart failure	1000	1	0.1	1	0.1	0	0.0
Cardiac arrhythmias	1000	15	1.5	2	0.2	1	0.1
Aspiration	1000	19	1.9	3	0.3	3	0.3

and arrhythmias likewise occurred at a lower rate compared to other studies. Falls, though infrequent, occurred in most instances during the first 3 days of admission. The combination of impaired balance and gait, often with perception difficulties contributes to this complication.¹⁷ The low rate of occurrence may be due to the short period of follow-up in this study. The low risk of deep vein thrombosis and pulmonary embolism among Asians has long been noted in previous studies^{18,19} and is further underscored by results of this study. This has been attributed to the low rate of hazardous mutations (such as the factor V Leiden mutation and the prothrombin G20210A mutation) or unspecified pulmonary embolism / deep vein thrombosis protective traits among Asians.^{18,20} The low rate of cardiac complications in this study may be attributed to the lack of extensive cardiac work-ups.

Certain life-threatening complications occurred at different times during the course of hospitalization. The risk of neurologic complications such as recurrent stroke and seizures appear to be elevated within the first three days of admission. This is similar to earlier published data which noted that neurologic complications were more likely to occur in the first week.⁵ Pulmonary complications such as pneumonia and aspiration were more likely to occur during the first week in this study. The timing of these pulmonary complications in this study is earlier than expected, as Kelly noted that pulmonary embolism and pneumonia usually peak in the later part of the second week

among stroke patients.²¹ The early occurrence of infection has been documented among other Asian populations. Hamidon noted that severe disability, large middle cerebral artery infarct and depressed levels of sensorium predicted the development of early infection, specifically pneumonia and urinary tract infection, among acute stroke patients in Malaysia.²² In general, the risk of developing pneumonia appears to be higher among older patients and among those with more severe strokes.^{6,23} There is evidence that nasogastric tubes may predispose patients to aspiration.^{24,25} Studies have shown the advantage of percutaneous endoscopic gastrostomy over the nasogastric tube feeding to decrease the risk of pulmonary complications.²⁶

The rate of complications was lower among patients admitted in an organized stroke unit compared to patients admitted in a general medical ward or a general neurology ward. This may be because of improved assessment procedures and early rehabilitation resulting from standardized evaluation and early management protocols that are employed in such settings.⁴

This paper is a prospective, multi-country study utilizing pre-defined complications to monitor the occurrence of complications during the two-week period of admission in the hospital. Numerous retrospective data on the occurrence of complications have already been published, coming mostly from single hospital surveys.^{7,9-11,13} Most of the papers that have been published were retrospective reviews of hospital records so that the biases inherent in a retrospective

Table 3: Occurrence of complications according to area of admission

Complications	Stroke unit	General neurology ward	General ward	Total
Recurrent stroke	7 (1.5%) n= 453	12(2.6%) N=456	29 (29%) N=100	48 (4.7%) N=1009
Seizure	0 N=461	12 (2.6%) N=457	2 (1.5%) N=128	14 (1.3%) N=1046
Urinary tract infection	8 (1.8%) N=453	38 (8.8%) N=430	9 (7.4%) N=121	55 (5.5%) N=1004
Chest infection	11 (1.5%) N=454	69 (16.9%) N=409	9 (7.4%) N=121	89 (9.0%) N=984
Falls	1 (0.2%) n=459	12 (2.6%) N=457	11 (9.2%) N=119	24 (2.3%) N=1035
Pressure sore	4 (0.9%) N=453	17 (3.8%) N=445	4 (3.1%) N=126	25 (2.4%) N=1024
Deep vein thrombosis	1 (0.2%) N=458	1 (0.2%) N=467	2 (1.5%) N=128	4 (0.3%) N=1053
Pulmonary embolism	0 N=460	1 (0.2%) N=467	0 N=130	1 (0.1%) N=1057
Depression	5 (1.1%) N=454	10 (2.2%) N=449	25 (23%) N=105	40 (4.0%) N=1008
Upper gastrointestinal bleeding	2 (0.4%) N=453	13 (2.9%) N=445	1 (0.77%) N=129	16 (1.6%) N=1027
Congestive heart failure	0 N=461	1 (0.2%) N=464	1 (0.77%) N=129	2 (0.2%) N=1054
Constipation	20 (4.6%) N=435	25 (0.1%) N=405	19 (17%) N=111	64 (6.7%) N=951
Heart arrhythmia	2 (0.4%) N=459	14 (3.2%) N=432	1 (0.78%) N=128	17 (1.7%) n=1019
Arthritis	1 (0.2%) N=457	4 (0.9%) N=462	1 (0.72%) N=129	6 (0.6%) N=1048
Urinary retention	13 (3.0%) N=431	24 (6.0%) N=417	18 (16%) N=112	55 (5.7%) N=960
Aspiration	8 (1.8%) N=451	10 (2.4%) N=450	5 (4%) N=125	23 (2.2%) N=1026

study are unavoidable. There are only a few prospective studies that have been published on the complication of stroke.^{6,14}

There are some limitations encountered in the course of this study. Monitoring for the development of the above complications was limited to the first two weeks of admission. This is in keeping with the study objectives of determining the time of onset of complications

during the acute phase of the illness. In addition, although an attempt was made to reduce inter-observer variability in evaluating the subjects by using a standard form, this could not always be ensured because of the inherent differences in the evaluation and management of patients across various countries and social strata. Monitoring in the above time frame has also made direct comparisons with previous prospective studies

difficult. Previous studies followed up their study cohorts for up to 30 months and it is likely that this may have accounted for a higher rate of complications.

On the other hand, our study cohort consisted of the largest sample size in the literature to date, supporting strongly the spectrum of complications in Asian stroke patients within diverse settings.

In summary, this study has shown that a multi-country collaboration could be carried out among Asian countries. While the basic pathophysiology of stroke may be the same across races, regional and ethnic variations do exist with regard to the

complications that develop. The recognition of these complications as well as their expected time of occurrence would enable physicians to address these problems in an anticipatory manner, which could well hasten the process of recovery and contribute towards improved outcome. Further research into this aspect of management of stroke patients is therefore essential, with emphasis on the role of various interventions designed to address the various complications encountered in the care of such patients.

Appendix No.1 Modified predefined complications

Complications	Follow-up in hospital
<p><i>1. Neurological</i></p> <p>Recurrent Stroke</p> <p>Epileptic Seizure</p> <p>Unexplained events</p>	<p>Clinical features lasting more than 24 hours consistent with World Health Organization definition of stroke.</p> <p>Clinical diagnosis of focal and/or generalized seizure in a previously non-epileptic patient</p>
<p><i>2. Infection</i></p> <p>Urinary tract infection</p> <p>Chest infection</p> <p>Other infection</p>	<p>Clinical symptoms of urinary tract infection or positive urine culture</p> <p>Auscultatory respiratory crackles and fever or radiographic evidence, or new purulent sputum.</p> <p>Any pyrexial illness lasting more than 24 hours</p>
<p><i>3. Immobility</i></p> <p>Falls</p> <p>Pressure sore/skin break</p>	<p>Any documented falls regardless of cause (fall with serious injury was defined as one that resulted in fracture, radiological investigation, neurological investigation, or suturing of wound).</p> <p>Any skin break or necrosis resulting from either pressure or trivial trauma (skin trauma directly resulting from falls was not included)</p>
<p><i>4. Thromboembolism</i></p> <p>Deep vein thrombosis</p> <p>Pulmonary embolism</p>	<p>Clinical diagnosis of deep vein thrombosis</p> <p>Clinical diagnosis of pulmonary embolism</p>
<p><i>5. Psychological</i></p> <p>Depression</p>	<p>Low mood considered to interfere with daily activities or require pharmacological or psychiatric intervention</p>
<p><i>6. Miscellaneous</i></p>	<p>Any documented complication resulting in a specific medical or surgical intervention (e.g. Gastrointestinal hemorrhage, constipation, episodes of cardiac failure, cardiac arrhythmias and arthritis).</p>

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