

Incidence and Characteristics of In-hospital Ischemic Strokes

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Incidence and Characteristics of In-hospital Ischemic Strokes

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Abstract

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The incidence and characteristics of in-hospital ischemic stroke are not clear yet. The purpose of this study was to provide the incidence, relationship with specific procedures, risk factors, stroke mechanism and discharge status of in-hospital ischemic strokes in a large general hospital of Korea. We retrospectively analyzed 111 consecutive in-hospital ischemic stroke patients (in-hospital group) from January 2002 to December 2006 and compared 1907 out-of-hospital ischemic stroke events (out-of-hospital group) during the same period. A total of 111 patients of in-hospital ischemic stroke comprised 0.04% of the 282,202 hospitalized patients during the study period. More than a half of the in-hospital ischemic events (60%) were associated with procedures. Almost all of them occurred during the first days of hospitalization or early in

the postoperative time period. The in-hospital group had more risk factors for stroke including; acute myocardial infarction, coronary artery occlusive disease, peripheral artery occlusive disease, atrial fibrillation, sick sinus syndrome, congestive heart failure, dilated cardiomyopathy, bacterial endocarditis and leukocytosis than the out-of-hospital group. In terms of stroke mechanisms, the in-hospital group showed a significantly higher incidence of cardioembolic stroke and other determined etiologies, and a greater tendency for an incomplete evaluation than the out-of-hospital group. The in-hospital group had up to a 10-fold higher mortality and 30-day fatality rate than the out-of-hospital group. Sepsis was the most common cause of death in the in-hospital group. We should be concerned with the careful screening of stroke risks in surgical candidates, especially candidates for cardiac procedures. Prevention and the control of infection may be important to reduce the mortality of in-hospital stroke patients.

Key Words: in-hospital stroke, incidence, risk factor, mortality

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I. Introduction

Stroke is the second leading cause of death in Korea.¹ Hospitalized patients due to various diseases commonly have stroke risk factors and are often exposed to procedures which may bear a risk of stroke. Therefore, patients who are being admitted to a hospital due to diseases other than stroke may have a stroke during their hospitalization (in-hospital stroke). It has been known that in-hospital strokes account for about 6.5-8.7% of the total number of strokes in previous reports, and that certain surgical procedures are frequently associated with strokes.²⁻⁴ However, the characteristics of in-hospital ischemic stroke, particularly in comparison with stroke that occurs out of a hospital have not been well known. We retrospectively analyzed in-hospital ischemic stroke patients in Severance hospital, one of the major general hospitals in Korea, and investigated the incidence, relationship with

specific procedures, risk factors, stroke mechanisms, and mortality associated with in-hospital ischemic strokes.

II. Materials and methods

Subjects for this study were patients who developed ischemic stroke during their admission to Severance hospital in Korea from January 2002 to December 2006. For patient selection, patients who fulfilled the following two conditions were identified from the medical record; (1) patients who were diagnosed with ischemic stroke based on the *International classification of Diseases, 10th rev.* (ICD-10) codes for cerebral infarction or unspecified stroke (I63 and I64) at the time of discharge, (2) patients who were discharged from the departments other than Neurology or who were transferred to the Neurology department from other departments. By these criteria, 1154 patients were selected. Then, patients with the following were excluded after review of their medical records; (1) old cerebral infarction, (2) no medical records or neuroimaging studies, (3) hemorrhagic stroke, (4) ischemic stroke after surgery for a cerebral aneurysm. Finally, 111 patients were enrolled for this study. For comparison, the out-of-hospital group was selected from the Yonsei Stroke registry⁵. The out-of-hospital group included 1907 patients who developed ischemic stroke at a site other than the hospital and were admitted to our hospital during the same study period. In the in-hospital group, we investigated the incidence of ischemic stroke, the association of stroke with medical or surgical procedures (defined as a cerebral infarction within 30 days after the procedure or surgery according to previous reports⁶), the classic

vascular risk factors, the vascular territory of cerebral infarction, the stroke mechanisms based on a trial of Org 10172 in acute stroke treatment (TOAST) classification⁷, the status of the patients at discharge and their mortality.

Statistical Analysis.

The χ^2 test was used to compare discrete variables, and independent t-tests to compare the means of the two samples for continuous variables. Differences were considered statistically significant at $p < 0.05$.

III. Results

1. Incidence of in-hospital ischemic stroke

During the study period, there were a total of 282,202 admissions in our hospital. Therefore, the incidence rate of in-hospital ischemic stroke was 0.04% (Table 1). Ischemic stroke frequently developed when a patient was being admitted to the departments of cardiology/cardiovascular surgery and emergency medicine. Ischemic stroke that developed in cardiology and cardiovascular surgery comprised 46% of the total in-hospital ischemic strokes. More than half of the in-hospital strokes (60%) occurred within seven days of admission.

Table 1. Incidence rate of in-hospital ischemic strokes in each department

Clinical Department	No. of in-hospital ischemic strokes	Total No. of admitted patients	Incidence (%)
Family medicine	1	1,829	0.05
Infectious medicine	1	2,124	0.05
Urology	4	11,443	0.04
Obstetrics and gynecology	1	24,902	< 0.01
Pediatrics	1	24,011	0.00
Pediatric cardiology	2	3,387	0.06
Gastroenterology	7	33,349	0.02
Neurosurgery	6	13,083	0.05
Nephrology	4	4,784	0.08
Cardiology + Cardiovascular surgery	51	21,667	0.24
General surgery	8	21,049	0.04
Emergency medicine	1	85	1.17
Transplant surgery	1	4,067	0.03
Psychiatry	1	2,772	0.04
Orthopedic surgery	7	15,258	0.05
Oncology	8	23,457	0.03
Hematology	3	3,372	0.09
Pulmonology	2	8,117	0.03
Chest surgery	2	3,010	0.07
Total	111	282,202	0.04

2. Relationship between medical or surgical procedures and in-hospital strokes

A total of 67 events were found to be associated with surgical or medical procedures (45 events in surgical procedures and 22 events in medical procedures, Table 2). In addition, four events occurred during or after cerebral angiography, two events during esophagogastro-duodenoscopy and one event each in association with electrophysiologic study, cardioversion, pericardiocentesis, external pacemaker implantation, abdominal aorta stent insertion and liver biopsy. After the procedures, 37 events (55%) occurred within one day and a total of 59 events (88 %) occurred within seven days. Among the procedures, strokes developed most frequently in association with coronary artery bypass graft (CABG) surgery, followed by percutaneous transfemoral coronary angioplasty/stent (PTCA) and cardiac surgery other than CABG (Table 2).

When compared with the non-cardiovascular group, the cardiovascular group (patients who were admitted to the department of cardiology or cardiovascular surgery) showed a significantly higher association with the medical or surgical procedures (38/51,75% vs 29/60,48%, $p=0.005$) and had more peripheral artery occlusive disease (PAOD, 12/58,24% vs 5/60,8%, $p=0.012$), coronary artery occlusive disease (CAOD, 22/51,43% vs 7/60,12%, $p<0.001$), acute myocardial infarctions (15/51,29% vs 4/60,7%, $p=0.002$), and cardiac arrhythmias (24/51,47% vs 9/60,16%, $p<0.001$).

Table 2. Incidence of ischemic stroke associated with surgical procedures and coronary studies

	No. of in-hospital ischemic strokes	Total cases	Incidence (%)
Surgery by general anesthesia	44	99,774	0.04
Surgery by local anesthesia	1	52,401	<0.01
Coronary artery bypass graft surgery	8	1,279	0.63
Surgery in cardiovascular department	18	11,147	0.16
Coronary angiography	3	9,579	0.03
PTCA	7	4,715	0.15

* PTCA: Percutaneous transfemoral coronary angioplasty

3. Comparison between the cases of in-hospital and out-of-hospital attacks

The mean age of the in-hospital group was slightly younger than that of the out-of-hospital group (in-hospital group; 60.8 years, the out-of-hospital group; 63.9 years, $p=0.052$). There was a tendency for a higher proportion of women in the in-hospital group (48%) when compared with the out-of-hospital group (39%, $p=0.059$).

A. Risk factors for in-hospital ischemic stroke

Patients with in-hospital ischemic strokes more frequently had a history of acute myocardial infarction, CAOD, PAOD, atrial fibrillation, sick sinus syndrome, congestive heart failure, dilated cardiomyopathy (DCMP), and

bacterial endocarditis than those with out-of-hospital ischemic strokes. In contrast, hypertension and current smoking were more frequently noted in the out-of-hospital group. (Table 3).

Table 3. Comparison of the risk factors between the in-hospital group and the out-of-hospital group

Risk factors	In-hospital group (n=111)	Out-of-hospital group (n=1907)	p-value
Hypertension	64(57.7)	1,404(73.6)	<0.001
Diabetes mellitus	44(39.6)	617(32.4)	0.111
Acute myocardial infarction	18(16.2)	11(0.6)	<0.001
History of stroke	22(19.8)	420(22.0)	0.580
Current smoking	19(17.1)	828(43.4)	<0.001
CAOD	27(24.3)	126(6.6)	<0.001
PAOD	16(14.4)	52(2.7)	<0.001
Atrial fibrillation	29(26.1)	346(18.1)	0.036
Sick sinus syndrome	4(3.6)	11(0.6)	0.007
Congestive heart failure	16(14.0)	32(1.7)	<0.001
Patent foramen ovale	2(1.8)	32(1.7)	0.922
Dilated cardiomyopathy	4(3.6)	6(0.3)	<0.001
Thrombus in left atrium	2(1.8)	5(0.3)	0.053
Mitral valve sclerosis	2(1.8)	22(1.2)	0.384
Mitral valve replacement	3(2.7)	23(1.3)	0.177
Bacterial endocarditis	2(1.8)	4(0.2)	0.039

* CAOD: coronary artery occlusive disease, PAOD: peripheral artery occlusive disease

* Numbers in parentheses are percentages.

Patients who had an out-of-hospital stroke showed significantly higher systolic and diastolic blood pressures, and higher blood lipid levels (Table 4). In contrast, white blood cell counts were significantly higher in the in-hospital group.

Table 4. Comparison of the laboratory findings between the in-hospital group and the out-of-hospital group

	In-hospital		Out-of-hospital		p-value
	group		group		
	Mean	SD	Mean	SD	
Hemoglobin (g/dL)	11	2	15	39	0.269
White blood cell counts (μL)	11,540	11,342	8,486	3,825	0.006
Systolic BP (mmHg)	133	27	159	30	<0.001
Diastolic BP (mmHg)	80	15	89	17	<0.001
Total cholesterol (mg/dL)	153	46	178	41	<0.001
HDL-cholesterol* (mg/dL)	39	11	45	13	<0.001
Triglyceride (mg/dL)	112	43	133	83	<0.001
LDL-cholesterol† (mg/dL)	98	34	106	36	0.096

* BP: Blood pressure, HDL-cholesterol: High density lipoprotein cholesterol, LDL-cholesterol: Low density lipoprotein cholesterol

B. The vascular territory of cerebral infarction involved

The in-hospital group more frequently had multiple infarctions over the territories of both the anterior and posterior circulations and less frequently had infarctions in the territory of posterior circulation when compared with the out-of-hospital group (Table 5).

Table 5. The vascular territory of the cerebral infarction

Vascular territory	In-hospital group (n=111)	Out-of-hospital group (n=1907)	p-value
Anterior circulation	73 (66)	1183 (62)	0.431
Posterior circulation	21 (19)	691 (36)	<0.001
Both anterior and posterior circulation	15 (14)	24 (1)	<0.001
Negative evaluation	2 (2)	9 (0)	0.119

* Numbers in parentheses are percentages.

C. Stroke mechanism based on the TOAST classification

Stroke mechanisms were different between the groups. Cardioembolism, other determined etiologies and an incomplete evaluation were more common in the in-hospital group while large artery atherosclerosis was more frequent in the out-of-hospital group. Small vessel occlusion was rare in the in-hospital group (Table 6).

Table 6. The stroke mechanisms of the in-hospital group and the out-of-hospital group

Stroke mechanism	In-hospital group (n=111)	Out-of-hospital group (n=1907)	p-value
Large artery atherosclerosis	13 (12)	459 (23)	0.003
Cardioembolism	46 (41)	395 (21)	<0.001
Small vessel occlusion	2 (2)	266 (14)	<0.001
Stroke of other determined etiology	8 (7)	51 (3)	0.006
More than two causes	8 (7)	204 (11)	0.224
Negative evaluation	20 (18)	479 (25)	0.092
Incomplete evaluation	14 (13)	53 (3)	<0.001

* Numbers in parentheses are percentages.

D. Status of the patients at discharge

At the time of discharge, 63 patients (57%) went home on foot, 12 patients (11%) by wheel chair, 16 patients (14%) by ambulance, and 21 patients (19%) expired. Patients with in-hospital ischemic strokes had up to a 10-fold higher mortality rate and 30 day fatality rate compared with the out-of-hospital group (21/111, 19% vs 35/1907, 2%, $p<0.001$ for total mortality; 14/111, 12% vs 30/1907, 2%, $p<0.001$ for 30 day case fatality). Sepsis was the most frequent cause of death in the in-hospital group, whereas brain herniation was most common in the out-of-hospital group ($p<0.001$ for sepsis, $p<0.001$ for brain herniation). (Figure 1)

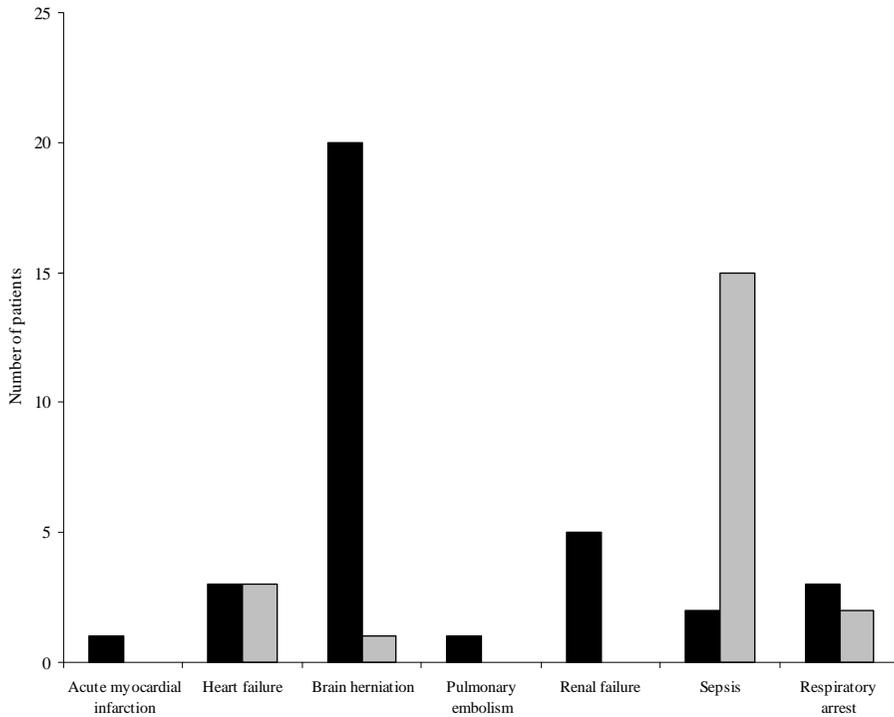


Figure 1. The cause of death associated with in-hospital and out-of-hospital cerebral ischemia. Black bars and gray bars represent the out-of-hospital group and in-hospital group, respectively. Mortalities in the out-of-hospital group were frequently caused by brain herniation and those in the in-hospital group were frequently associated with sepsis.

IV. Discussion

Although many studies assessed the risk of stroke in specific disease conditions or procedures, few reported the incidence of in-hospital ischemic stroke.^{8,9} One report demonstrated that the incidence rate of in-hospital stroke was 0.058%.¹⁰ However, no study has shown the incidence rate of in-hospital ischemic stroke in each department. The present study demonstrates that in-hospital ischemic stroke is rare and that patients who were being admitted to the departments of cardiology and cardiovascular surgery more frequently suffered from ischemic stroke than those admitted to other departments. The high incidence of ischemic stroke for the patients in cardiology and cardiovascular surgery is expected because those patients are more likely to have underlying potential cardiac sources of embolism and are subjected to cardiac procedures or surgery, which are known to carry a high risk of stroke.^{9,11}

Among medical and surgical procedures, in-hospital ischemic stroke was most common in patients who underwent CABG or cardiac catheterization in this study. Cardiovascular procedures for the heart and main arteries themselves are known to be associated with a higher incidence of ischemic stroke.^{6,11-17} However, the incidence was lower than those of previous studies.¹¹⁻¹⁵ Because we analyzed only symptomatic cases with brain imaging studies retrospectively, not only patients with clinically silent or minor strokes

but also patients with unstable vital sign could not be included. Therefore, the incidence of in-hospital stroke related to those cardiac procedures in this study might be underestimated. In this study, while 55% of the events that were procedure-associated stroke developed within one day after the procedure, many events occurred thereafter, usually within seven days of the procedure. These delayed procedure-associated strokes might be partially related to atrial fibrillation that developed during the postoperative period. Postoperative atrial fibrillation occurs in 30 to 50% of patients who have undergone cardiac surgery and it has a peak incidence between the second and fourth postoperative days.^{11,16-18}

A comparison between the in-hospital and out-of-hospital strokes demonstrated that patients with in-hospital strokes have distinct characteristics, including vascular risk factors, stroke mechanisms and causes of death, from those with out-of-hospital strokes. The patients with in-hospital ischemic strokes had more cardioembolic sources while hypertension and dyslipidemia were less commonly noted. In addition, the in-hospital group had a significantly higher incidence of multiple territorial infarctions. These seemed to attribute to the higher prevalence of cardioembolism as a stroke mechanism in the in-hospital group. This is similar to a previous report.¹⁹

Leukocytosis was also a significant parameter of in-hospital ischemic strokes in our study. Recent infection is one of the risk factors for stroke.²⁰⁻²² Inflammation contributes to the progression and acute rupture of

atherosclerotic plaques with subsequent thrombus formation.²¹ Leukocytosis is one of several inflammatory markers and an independent risk factor for acute ischemic stroke.²⁴⁻²⁷ The prevalence of infection is much more frequent in hospitalized patients than in the general population because many patients are admitted to hospitals due to various infections, and nosocomial infections are also common. These patients with infections may have underlying atherosclerosis of the cerebral arteries, which is prone to rupture when aggravated by systemic infectious and inflammatory conditions.

When comparing with out-of-hospital group, stroke of other determined etiology was common in in-hospital group. This is also expected because stroke is one of presenting symptoms in many diseases with etiologies differing from the classic etiologies of stroke such as atherosclerosis, cardioembolism, and small artery disease. Other etiologies in this study, which included moyamoya disease, graft interposition of the ascending aorta, and other medical or surgical procedures, are rare, but well known causes of cerebral infarction. Of note, small vessel occlusion (lacunar infarction) was rare in the in-hospital group in this study. This might be due to the relatively high incidence of cardioembolism and other determined etiologies that are affected by the underlying systemic conditions of admitted patients while the development of lacunar infarctions is less affected by them.

It appeared that assessments for determining stroke etiologies are incomplete in more patients with in-hospital ischemic strokes than those with

out-of-hospital strokes. Whereas patients with out-of-hospital stroke are typically admitted to the neurology department and are evaluated by standardized imaging protocols, those with in-hospital attacks may not have complete evaluations because of their underlying medical and surgical conditions.

Mortality was much higher in the in-hospital group, which might be ascribed to their serious co-morbid diseases and high incidence of cardioembolic infarctions. Among stroke subtypes, neurologic deficits and mortality are most severe with cardioembolisms.^{28,29} Their causes of death were also quite different from the out-of-hospital group. Brain swelling is the most common cause of death following cerebral infarction.³⁰ Brain herniation was the most common cause of death in the out-of-hospital group as was expected. However, in the in-hospital group, sepsis and renal failure were most common, which suggests an aggravation of their primary diseases. The development of stroke and the resulting immobilization might contribute to their aggravations.

This study has limitations to address. Because this was a retrospective study based on medical records, minor strokes might be unrecognized in patients who were under serious medical or surgical conditions due to their primary diseases. Therefore, the incidence of in-hospital ischemic stroke in this study might be under-estimated. In-hospital ischemic stroke seemed to be more severe than out-of-hospital ischemic stroke as the mortality rate was higher.

However, we could not compare the neurologic severity between them by using a standardized stroke scale such as the National Institute of Health Stroke Scale because the data was lacking for many patients with in-hospital strokes.

V. Conclusion

Our study revealed the incidence of in-hospital ischemic strokes and their characteristics. In-hospital ischemic stroke was frequently associated with specific procedures including CABG and PTA. Cardioembolism related with cardiovascular procedures and arrhythmia was the most common etiologic mechanism. Sepsis was the most common cause of death in these patients and a higher mortality rate was observed when compared with patients with out-of-hospital strokes. To reduce the incidence and mortality of in-hospital strokes, we should be concerned with the careful screening of high-risk candidates for stroke, particularly those who are undergoing cardiovascular procedures. Effective prevention of infection is also warranted to reduce mortality after in-hospital strokes.

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Abstract (in Korean)

원내 뇌경색의 유병률과 특성

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원내 뇌경색의 유병률과 특성에 대한 보고는 아직 부족하다. 본 저자들은 국내 단일기관을 토대로 원내 뇌경색의 유병률, 특정시술과의 연관성, 위험요인, 발생기전, 사망률에 관한 연구를 진행하였다. 2002년 1월부터 2006년 12월까지 세브란스병원에서 입원 치료받았던 환자들을 대상으로 신경과를 제외한 타과에서 입원치료를 받던 중 뇌경색이 생겼던 111명의 원내 뇌경색환자와 원외에서 뇌경색이 생겨서 신경과로 직접 입원하였던 1907명의 원외 뇌경색환자에 대하여 후향적 연구방법으로 조사하였다. 원내 뇌경색환자 발생률은 총 입원환자 대비 0.04%였다. 임상 각 분과 별로 살펴볼 때 심장내과와 심장혈관외과에서 입원치료 받던 환자들 중에서 가장 빈번하게 있었고, 외과적 또는 내과적 시술과 연관되어 나타나는 뇌경색이 전체 원내 뇌경색의 60%를 차지하였다. 시간적으로 보면 원내 뇌경색의 60%가 병원 입원 7일 이내에 나타났고 시술과 연관된 원내 뇌경색은 55%에서 시술로부터 하루 이내에 관찰할 수 있었다. 원내 뇌경색환자들이 갖고 있던 위험인자를 살펴보면 원외 뇌경색

이 있던 환자들에 비해 급성 심근경색, 관상동맥 폐쇄성 질환, 말초 동맥 폐쇄성 질환, 심방세동, 동기능부전증후군, 울혈성 심부전증, 확장성 심근병증, 심내막염, 백혈구증다증이 유의하게 높은 빈도로 갖고 있음을 확인하였다. 원내 뇌경색환자의 뇌경색기전은 원외 뇌경색환자에 비해서 심장인성(cardioembolism), 기타 원인에 의한 경색증(stroke of other determined etiology), 뇌경색에 대한 검사가 충분하지 못한 경우가 유의하게 많았으나 심장인성이 41%로 가장 흔한 유형이었다. 원내 뇌경색환자의 사망률은 원외 뇌경색환자에 비해 10배 이상 높았고, 사인으로는 원외 뇌경색환자에서는 뇌탈출이 빈번했던 반면 원내 뇌경색환자에서는 폐혈증이 많았다. 원내 뇌경색의 유병률과 이로 인한 사망률을 줄이기 위해서는 입원환자들 중 심장내과나 심장혈관외과로 입원한 환자들과 내과적 또는 외과적 시술을 받게 될 환자들에서 특히 입원초기나 시술직후에 주의할 해야 하고, 이들 환자에 대한 감염 예방과 뇌경색 진단 시 빠르고 적극적인 치료가 필요할 것으로 생각된다.

핵심 되는 말: 원내 뇌경색, 유병률, 위험요인, 치사율