# Incidence and Association of 30-day Recurrent Stroke in Ischemic Stroke Patients Who Received DAPT (dual antiplatelet therapy) in Rajavithi Hospital

Tunwarat Kongsawat,
Sirikanlaya Poonphol

## ABSTRACT

**Introduction**: Ischemic stroke ranking as the third leading cause of death in Thailand. It contributes to social and economic burdens and disability due to recurrent hospitalizations. The treatment of choice for patients with minor strokes or transient ischemic attacks is dual antiplatelet within the first 21 days then switch to single antiplatelet.

**Objectives**:

1. To investigate the incidence of recurrent acute ischemic stroke within 30 days whom treated with dual antiplatelet therapy.

2. To find association for the incidence of recurrent ischemic stroke within 30 days whom treated with dual antiplatelet therapy.

**Materials and Methods**: Retrospective cross-sectional study used collected data from patients who received dual antiplatelet with recurrent ischemic stroke in 30 days in Rajavithi Hospital during June 1,2021 - June 30,2023

**Results**: From 406 patients, the incidence of recurrent stroke is 8.4% and LDL is the only associated factor of 30-day recurrent stroke in ischemic stroke patients who received DAPT (p=0.045). There is no statistic significant association of incidence for risk recurrent stroke in gender, age, smoking, any inclusion underlying diseases, hormonal usage, DTX, HbA1c, SBP, brain parenchymal study, vascular study stroke protocol or TOAST classification.

**Conclusion:** The study result shows that 8.4% got recurrent stroke and the only significant risk factors is LDL. Further factors might be significant if the number of the populations and duration of the study increased.

**Keyword:** Acute ischemic stroke, Transient Ischemic Attack, Diabetes mellitus, Hypertension, Dyslipidemia

**Tunwarat Kongsawat, MD**
**Sirikanlaya Poonphol, MD**
Neurology unit, Department of Medicine, Rajavithi Hospital

**Corresponding author:**
**Tunwarat Kongsawat, MD**
Neurology unit, Department of Medicine, Rajavithi Hospital
2 Ratchawithi Road, Khwaeng Thung Phaya thai,
Khet Ratchathewi, Bangkok, Thailand 10400
E-mail emityenergy@gmail.com
Tel. 02-2062900 Fax. 02-3548179

*รับต้นฉบับ 24 กุมภาพันธ์ 2567, ปรับปรุงต้นฉบับ 4 สิงหาคม 2567, ตอบรับต้นฉบับตีพิมพ์ 31 สิงหาคม 2567*

## Introduction

Ischemic stroke is a significant public health issue, ranking as the third leading cause of death in Thailand with an incidence of 206 per 100,000 population. The trend is expected to rise continuously in the future[1]. The mortality rate for this disease is approximately 10%, with 50-60% of survivors experiencing disabilities[1]. Ischemic stroke poses a critical global health concern, especially in countries entering an aging society, such as Thailand. It contributes to social and economic burdens and disability due to recurrent hospitalizations.

Currently, the treatment involves using two antiplatelet medications, Aspirin and Clopidogrel, within the first 21 days for patients in minor strokes and transient ischemic attacks. This treatment has shown benefits in managing and preventing recurrent cerebral infarctions, as acknowledged in current academic literature and clinical practices[2-4]. The aim of this study is to investigate the occurrence of recurrent ischemic stroke within 30 days among patients recently treated in the hospital. The focus is on those who received the dual antiplatelet therapy to assess relevant risk factors and contribute to effective treatment decision-making for patients.

## Objective

1. To investigate the incidence of recurrent acute ischemic stroke within 30 days among patients with acute ischemic stroke treated with dual antiplatelet therapy at Rajavithi Hospital.

2. To find the association with the incidence of recurrent ischemic stroke within 30 days among patients with acute ischemic stroke treated with dual antiplatelet therapy at Rajavithi Hospital.

## Materials and Methods

### Study design

A retrospective cross-sectional study used collected data from patients who received dual antiplatelet with recurrent ischemic stroke in 30 days in Rajavithi Hospital during June 1, 2021 - June 30, 2023.

### Characteristics of study samples

The sample group was 406 ischemic stroke patients who received dual antiplatelet therapy at Rajavithi Hospital between June 1, 2021, - June 30, 2023.

*Inclusion criteria*

- Age 18 and over.
- Ischemic stroke was diagnosed from the signs and symptoms of permanent and acute neurological loss suggestive of ischemic stroke and/or brain CT scan results.
- Have information about smoking, oral contraceptive pill usage, underlying diseases such as diabetes mellitus, hypertension, dyslipidemia, cardiovascular diseases
- Have blood test results for FBS, HbA1C, LDL

*Exclusion criteria*

- Incomplete or missing treatment history information in the medical record.
- Misdiagnosed of acute ischemic stroke
- Loss follow up within 30 days after collecting data of prior event of acute ischemic stroke

*Sample Size*

Sample size calculating for descriptive to estimate single proportion (categorical data)

$$n = \frac{Z^2_{\alpha/2} p(1-p)}{d^2}$$

n = number of sample size

p = incidence of 30-day recurrent ischemic stroke using dual antiplatelet is 4.2% estimated from a study by Lovett JK et al., p = 0.042

d = 20% acceptable margin of error of p value, d = 0.2 x 0.042 = 0.01

$\alpha$ = margin of error in estimating = $Z_{\alpha/2} = Z_{0.05}$ = 1.96

$$n = \frac{(1.96)^2 \times 0.042 \times (1-0.042)}{(0.01)^2}$$

n = 1,546 + Missing data 10%

= 1,700

Total patients estimate for this study is 1,700.

The researcher collected data from patients who received dual antiplatelet in Rajavithi Hospital during June 1, 2021 - June 30, 2023 approximately 406 patients.

## Methodology

Patients with a history of diagnosed acute ischemic stroke and receiving dual antiplatelet therapy at Rajavithi Hospital fitted in inclusion criteria, who sought treatment between June 1, 2021, - June 30, 2023, were eligible based on the inclusion criteria and provided informed consent to participate in the research project. Some patients who had incomplete or missing treatment history information in the medical record, misdiagnosed of acute ischemic stroke or loss follow up within 30 days after collecting data of prior event of acute ischemic stroke would be excluded. Data collection using the match cross-sectional method and analyzed by using SPSS version 22 (SPSS Inc, Chicago, Illinois, U.S.A).

## Statistical analysis

### Descriptive statistics

The categorical data is reported by percentage. Continuous data with normal distribution is reported as means and standard deviation. If the data is not a normal distribution data, it is reported with median, minimum, maximum, and interquartile range and percentile Rank.

### Inferential statistics

Categorical data were compared using the Chi-square test or Fisher's exact test or McNemar test. The uncorrelated data is compared with Student t-test for normal distribution data and Mann-Whitney U-test was used for non-normal distribution data. Binary logistic regression was used for correlation factor analysis and risk was reported by OR (95% CI). Determination of the cut-off point for screening or diagnosis using the curve (ROC curve) and presented by AUC (Area under the curve). All tests were assigned a level of statistical significance at a p-value < 0.05.

## Results

Table 1: The demographic data of acute ischemic stroke receiving dual antiplatelet. Among individuals in the protocol, patient with acute ischemic stroke who received dual antiplatelet 57.6% are male, the mean age is 62 years (SD 13.40), 53.7% are smoking, 67% of the patients got underlying diseases; 84.6% are Hypertension, 50.7% are Diabetes mellitus, 94.1% are non-hormonal usage.

**Table 1.** Demographic data of acute ischemic stroke receiving dual antiplatelet (n = 406)

| Demographic data | | Value |
|---|---|---|
| Sex | | |
| | Male | 234 (57.6) |
| | Female | 172 (42.4) |
| Age (year) | | 62.00 ± 13.40 |
| Smoking | | |
| | Smoking | 218 (53.7) |
| | Non-smoking | 188 (46.3) |
| Underlying | | |
| | No underlying disease | 134 (33.0) |
| | Underlying diseases | 272 (67.0) |
| | HT | 230 (84.6) |
| | DM | 138 (50.7) |
| | DLP | 129 (31.8) |
| | CAD | 49 (12.1) |
| Hormonal | | |
| | Non-hormonal usage | 382 (94.1) |
| | Hormonal usage | 24 (5.9) |

Table 2: The laboratory data of acute ischemic stroke receiving dual antiplatelet. Among individuals in the protocol, patient with acute ischemic stroke who received dual antiplatelet the mean DTX is 134.86 (SD 68.85), 75.9% are HbA1c<7.0, 85.2% are LDL ≥ 70 and the mean SBP is 158.07 (SD 29.67).

**Table 2.** Laboratory data of acute ischemic stroke receiving dual antiplatelet (n = 406)

| Laboratory data | | Value |
|---|---|---|
| DTX (mean) mg/dL | | 134.86 ± 68.85 |
| HbA1c (mg%) | | |
| | < 7.0 | 308 (75.9) |
| | ≥7.0 | 98 (24.1) |
| LDL (mg/dL) | | |
| | < 70 | 60 (14.8) |
| | ≥ 70 | 346 (85.2) |
| SBP (mmHg) | | 158.07 ± 29.67 |

Table 3: The severity of brain imaging of primary stroke event. 60.9% have small lacune, 21.5% cannot seen significant hypodensity lesion in brain parenchymal imaging. 23.9% have large vessel stenosis > 50%, 18.2% have fewer stenosis of large vessel in vascular study stroke protocol. 54.9% are small vessel disease and 30.8% are large vessel atherosclerosis classified by TOAST classification.

**Table 3.** Severity of brain imaging of primary stroke event (n = 406)

| | Imaging data | n% |
|---|---|---|
| Brain parenchymal imaging | | |
| | Small lacune | 247 (60.9) |
| | Not seen | 88 (21.5) |
| | Giant lacune | 71 (17.6) |
| Vascular study stroke protocol | | |
| | Not done | 235 (57.9) |
| | Large vessel stenosis >50% | 97 (23.9) |
| | Large vessel stenosis ≤50% | 50 (12.3) |
| | No stenosis | 24 (5.9) |
| TOAST classification | | |
| | Small vessel disease | 223 (54.9) |
| | Large vessel atherosclerosis | 125 (30.8) |
| | Undetermined cause | 42 (10.3) |
| | Cardioembolic | 10 (2.5) |
| | Determined cause | 6 (1.5) |

Table 4: The clinical outcome of event recurrent stroke and severity. Among individuals in the protocol, most of the patients with 91.6% do not get recurrent stroke event. Meanwhile 8.4% of them did with the majority 41.2% presented with ischemic stroke NIHSS <4, 32.4% presented with NIHSS ≥ 4.

**Table 4.** Clinical 30-day Outcome of event recurrent stroke and severity (n = 406)

| Clinical Outcome | | n (%) |
|---|---|---|
| Recurrent stroke | | |
| | Not occurred | 372 (91.6) |
| | Occurred | 34 (8.4) |
| Severity | | |
| | TIA | 6 (17.6) |
| | NIHSS <4 | 14 (41.2) |
| | NIHSS ≥ 4 | 11 (32.4) |
| | Hemorrhagic stroke | 3 (8.8) |

Table 5: There is no statistically significant difference between gender (p-value 0.611), age (p-value 0.385), smoking (p-value 0.418), underlying disease (p-value 0.290), hormonal usage (p-value 1.000), DTX (p-value 0.355), HbA1c (p-value 0.613), SBP (p-value 0.800) or any type of brain parenchymal imaging (p-value 0.368), vascular study stroke protocol (p-value 0.053) or etiology (p-value 0.192) among the groups. The only statistically significant association for 30-day recurrent stroke in ischemic stroke patients who received DAPT is LDL (p-value 0.045).

**Table 5.** Risk factors of 30-day recurrent stroke in ischemic stroke patients receiving DAPT (n = 406)

| Demographic data | | Recurrent ischemic stroke | | p-value |
|---|---|---|---|---|
| | | Recurrent (n=34) | Not recurrent (n=372) | |
| Sex | | | | 0.611 |
| | Male | 21 (61.8) | 213 (57.3) | |
| | Female | 13 (38.2) | 159 (42.7) | |
| Age (year) | | 60.09 ± 13.96 | 62.17 ± 13.35 | 0.385 |
| Smoking | | | | 0.418 |
| | Smoking | 16 (47.1) | 202 (54.3) | |
| | Non-smoking | 18 (52.9) | 170 (45.7) | |
| Underlying | | | | 0.290 |
| | No underlying disease | 14 (41.2) | 120 (32.3) | |
| | Underlying diseases | 20 (58.8) | 252 (67.7) | |
| | HT | 18 (52.9) | 212 (57.0) | |
| | DM | 13 (38.2) | 125 (33.6) | |
| | DLP | 13 (38.2) | 116 (31.2) | |
| | CAD | 7 (20.6) | 42 (11.3) | |
| Hormonal | | | | 1.000 |
| | Non-hormonal usage | 32 (94.1) | 350 (94.1) | |
| | Hormonal usage | 2 (5.9) | 22 (5.9) | |
| Laboratory data | | | | |
| DTX (mg/dL) | | 124.38 ± 45.35 | 135.80 ± 70.58 | 0.355 |
| HbA1c (mg%) | | | | 0.613 |
| | < 7.0 | 27 (79.4) | 281 (75.5) | |
| | ≥7.0 | 7 (20.6) | 91 (24.5) | |
| LDL (mg/dL) | | | | 0.045 |
| | < 70 | 9 (26.5) | 51 (13.7) | |
| | ≥ 70 | 25 (73.5) | 321 (86.3) | |
| SBP (mmHg) | | 156.82 ± 31.37 | 158.19 ± 29.88 | 0.800 |

| Demographic data | | Recurrent ischemic stroke | | p-value |
|---|---|---|---|---|
| | | Recurrent (n=34) | Not recurrent (n=372) | |
| Brain parenchymal imaging | | | | 0.368 |
| | Small lacune | 17 (50.0) | 230 (61.8) | |
| | Not seen | 10 (29.4) | 77 (20.7) | |
| | Giant lacune | 7 (20.6) | 64 (17.2) | |
| Vascular study stroke protocol | | | | 0.053 |
| | Not done | 13 (38.2) | 222 (59.7) | |
| | Stenosis >50% | 12 (35.3) | 85 (22.8) | |
| | Stenosis ≤50% | 5 (14.7) | 45 (12.1) | |
| | No stenosis | 4 (11.8) | 20 (5.4) | |
| TOAST classification | | | | 0.192 |
| | Small vessel disease | 14 (41.2) | 209 (56.2) | |
| | Large vessel atherosclerosis | 13(38.2) | 112 (30.1) | |
| | Undetermined cause | 4 (11.8) | 38 (10.2) | |
| | Cardioembolic | 2 (5.9) | 8 (2.2) | |
| | Determined cause | 1 (2.9) | 5 (1.3) | |

## Discussion

According to CHANCE trial; Aspirin and Clopidogrel within the first 21 days for patients with minor strokes and transient ischemic attacks is the treatment of choice which shown benefits in managing and preventing recurrent cerebral infarctions[2-4].

This CHANCE trial shows the incidence of recurrent acute ischemic stroke from 5170 patients at any onset is 8.2% which may assume to be relevant to the incidence recurrent acute ischemic stroke within 30 days among 406 patients with acute ischemic stroke treated with dual antiplatelet therapy at Rajavithi Hospital from this study which is 8.4% (34 patients).

Further, the results show that there is no statistically significant difference in risk factor of 30-day recurrent stroke in ischemic stroke patients who received DAPT between the gender, age, smoking, underlying disease, hormonal usage, DTX, HbA1c, SBP or any type of brain parenchymal imaging, vascular study stroke protocol or etiology among the groups. The only statistically significant risk factors of 30-day recurrent stroke in ischemic stroke patients who received DAPT is LDL (p-value 0.045).

Limitations which may lead to statistically insignificant of this study included 1) the under power available collectable small size of the study group (N= 406) compared to calculating sample size (N=1700) due to incomplete data records or decrease in number of patients during COVID-19 during 2021-2022 2) the short period of observation due to the overwhelming of patients made this study to be just a pilot study which could be further collecting more data to develop more valuable study aim to prevent the incidence of recurrent stroke in the future.

## Conclusion

This study shows only 8.4% who received DAPT occurred recurrent stroke minor type. The only significant association of 30-day recurrent stroke is LDL. Further factors might be significant if the number of study populations increased and increased the duration of observation and follow up.

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