Factors associated with favorable outcomes in acute severe stroke patients: A real-world, national database study

NARONGRIT KASEMSAP, NISA VORASOOT, KANNIKAR KONGBUNKIAT, SOMSAK TIAMKAO, WATCHARA BOONSAWAT and KITTISAK SAWANYAWISUTH

Department of Medicine and North-Eastern Stroke Research Group, Faculty of Medicine, Khon Kaen University, Khon Kaen 40002, Thailand

Received March 14, 2022; Accepted June 22, 2022

DOI: 10.3892/br.2022.1557

Abstract. Thrombolytic therapy is useful in severe stroke, but it increases the risk of intracerebral hemorrhage. In addition, it may have limited use in resource-limited due to a lack of trained neurologists and equipment to perform CT scans. There are limited data available from studies of national databases on stroke outcomes and predictors of severe stroke. This study, therefore, aimed to evaluate acute severe ischemic stroke outcomes in a real-world setting. Additionally, predictors of favorable stroke outcomes were explored using a retrospective cohort. Data were extracted from the National Health Security Office (NHSO) in Thailand. The inclusion criteria were: Aged ≥18 years or older, diagnosis of acute severe ischemic stroke (defined by an admission National Institutes of Health Stroke Scale score of 15-24), and available data on stroke outcomes. Outcomes were evaluated at discharge using a modified Rankin score at discharge. Factors associated with good outcomes were determined using multivariate logistic regression analysis. During the study period, 268 severe stroke patients met the inclusion criteria. Of those, 38 (14.18%) had good outcomes at discharge. A total of 223 patients received intravenous recombinant tissue plasminogen activator (83.21%). Of those, 38 (17.04%) had favorable outcomes. A predictive model for good outcomes revealed two independent factors: Male sex and atrial fibrillation with adjusted odds ratios (95% confidence interval) of 2.30 (1.10-4.82) and 0.38 (0.16-0.91), respectively. Predictors for good stroke outcomes in severe stroke patients included rtPA treatment, atrial fibrillation, and male sex.

Correspondence to: Professor Kittisak Sawanyawisuth, Department of Medicine and North-Eastern Stroke Research Group, Faculty of Medicine, Khon Kaen University, 123 Mitraparp Road, Khon Kaen 40002, Thailand
E-mail: kittisak@kku.ac.th

Key words: acute ischemic stroke, predictor, outcome, atrial fibrillation, thrombolysis

Introduction

Acute severe ischemic stroke, defined as a baseline National Institutes of Health Stroke Scale (NIHSS) score >15 (1), accounts for ~12.7% of stroke cases (2). Patients with this condition suffer from high rates of morbidity, severe complications, and mortality (2). A previous study found that the NIHSS scores of severe stroke patients at 7 days after treatment were significantly higher than those with non-severe stroke (22 vs. 2; P<0.01). The rate of favorable outcomes in these patients has been reported to be only 28%, and they have a mortality rate of 80% (2,3).

A meta-analysis found that alteplase therapy significantly improved outcomes in patients with acute severe ischemic stroke with NIHSS scores of 16-21 with an odds ratio of 1.50 [95% confidence interval (CI), 1.03-2.17] (4). However, the meta-analysis included only randomized clinical trials, suggesting that it may not reflect real-world results. Additionally, alteplase may increase intracerebral hemorrhage by up to 6.4%. (5) Thus, it is important to determine the predictors of good outcomes of alteplase or thrombolytic therapy.

In Thailand, the rate of thrombolytic therapy in acute ischemic stroke patients since the practice was implemented in 2008 has increased from 0.38 to 4.78% in 2016 (10). Due to the lack of availability of neurologists and the country's stroke fast-track program, thrombolytic therapy may have limited use in Thailand (6). A previous study conducted at a university hospital found that severe stroke treated with thrombolytic therapy was associated with a poorer outcome at 3 months compared with non-severe stroke patients (7). However, there are limited data available on outcomes and predictors of patients with severe stroke in Thailand. This study, therefore, aimed to evaluate stroke outcomes in acute severe ischemic stroke in a real-world setting. Additionally, predictors of good stroke outcomes were explored.

Patients and methods

Study design. This was a retrospective cohort study. Data were extracted from medical admission records submitted to the National Health Security Office (NHSO). The NHSO oversees the reimbursement of medical costs for Thailand's universal health coverage scheme, which covers ~75% of the Thai

population. Data used in this study was obtained from between October 2015 and September 2018. The inclusion criteria were: >18 years or older, diagnosed with acute severe ischemic stroke (defined by an admission NIHSS score of 15-24), and available stroke outcome data. Patients with incomplete data were excluded.

Studied variables and outcomes. The admission record of each patient was reviewed to evaluate their eligibility. Data were retrospectively retrieved from the medical records including baseline characteristics, co-morbidities, NIHSS score, modified Rankin score (mRS), Barthel index, complications, cost of treatment, and length of stay at the time of stroke diagnosis (8,9). Outcomes were evaluated at discharge using the mRS. An mRS score of 0-2 was defined as a good outcome and 3-6 as a poor outcome.

Statistical analysis. The patients were divided into two groups based on outcomes (good and poor). Clinical data at baseline were compared between the two groups using descriptive statistics. Factors associated with good outcomes were determined using univariate and multivariate logistic regression analysis. Univariate logistic regression analysis was used to determine the P-value of each factor to predict good outcomes. Factors with a P-value <0.20 by univariate logistic regression analysis were entered into the multivariate logistic regression analysis. The final multivariate logistic regression analysis model was calculated using a stepwise method. Factors retained in the final model of multivariate logistic regression analysis were those with a P-value <0.20. The best model was defined based on the lowest Akaike information criterion (AIC). Factors in the final model for good outcomes in severe stroke were tested for interaction with other factors using multivariate logistic regression analysis. A P-value <0.10 of interaction was considered statistically significant. The predictive model was also applied to patients who underwent thrombolysis treatment. All statistical analyses were performed using R software version 3.6.1. (R Foundation for Statistical Computing, Vienna, Austria) (10).

Results

Baseline characteristics. During the study period, there were 268 severe stroke patients who met the study criteria. Of those, 38 (14.18%) had good outcomes at discharge. There were four factors that differed significantly between the good and poor outcome groups (Table I). The good outcome group had a higher proportion of male patients (65.8 vs. 45.2%) and patients who underwent thrombolysis treatment (100 vs. 80.4%) but a lower proportion who underwent atrial fibrillation (18.4 vs. 39.1%) and shorter admission duration (4 vs. 6 days). Additionally, scores on the three stroke outcome indexes (mRS, Barthel index, and NIHSS) were significantly better at discharge in the good outcome group. The total cost of admission did not differ significantly between the groups (~1,760 vs. ~1,730 USD).

Outcomes. There were 223 patients who received rtPA (83.21%). Of those, 38 (17.04%) had good outcomes (Table II). A predictive model for good outcomes revealed two independent factors: Male sex and atrial fibrillation, with adjusted odds ratios (95% CI) of 2.30 (1.10-4.82) and 0.38 (0.16-0.91), respectively (Table III). Neither stroke nor atrial fibrillation was found to have significant interactions in the final model (Table IV). In patients who received rtPA treatment (n=223), only atrial fibrillation was negatively and independently associated with good outcomes; the adjusted odds ratio (95% CI) was 0.36 (0.15-0.88), as shown in Table V.

Discussion

The percentage of patients with good stroke outcomes in this study was somewhat lower than in previous reports (17.04% vs. 28-47%) (2,7,11). There are several possible explanations for this. The first is that few of the patients were able to undergo advanced treatment modalities such as endovascular treatment. In addition, thrombolytic therapy may not have been available in all health care facilities (6). Finally, the median onset-to-needle time in our study was higher than in a previous study of patients undergoing thrombolytic therapy (150-155 vs. 140 min) (12).

However, rtPA treatment perfectly predicted good outcomes in acute severe ischemic stroke according to multivariate logistic regression analysis. The patients who did not receive rtPA treatment did not have favorable outcomes. This implies that acute severe ischemic stroke patients have a 17.04% chance of improvement with rtPA treatment, but none if thrombolysis is not administered. Note that patients in the good outcome group had shorter hospital stays but comparable hospital costs, likely due to the rtPA treatment (13).

Previous studies have found atrial fibrillation to be a predictor of severe stroke (2,14). Here, it was found that atrial fibrillation was negatively associated with good outcomes in severe stroke. However, it was a poor predictor of outcomes in cases of severe stroke, both overall and in patients receiving rtPA treatment (Tables III and IV). These findings may be due to the larger infarct size from atrial fibrillation. Stroke patients who undergo atrial fibrillation have significantly larger infarct sizes compared with those who do not (48.1 vs. 36.4 mm; P<0.001), leading to a higher risk of hemorrhagic transformation and a 1.7x higher mortality rate (15). Additionally, patients with atrial fibrillation have a higher risk of thrombogenicity associated with larger thrombus formation (16), diminished cerebral autoregulation resulting in cerebral dysfunction after stroke (17), poor collateral circulation due to chronic hypoperfusion from cervical atherosclerosis (18,19), and no recanalization after thrombolytic therapy, as old and large thrombi in the left atrium are more resistant to thrombolysis (20). However, the Danish Stroke Registry found atrial fibrillation was associated with a higher rate of mortality, which is primarily driven by worse stroke severity and not atrial fibrillation itself (21). On the other hand, the present study found atrial fibrillation was still associated with higher odds of worse outcomes after adjustment for severity of stroke.

Previous reports have also shown that women tend to have more severe strokes than men (44 vs. 36%), which may account for the better stroke outcomes in men in this study (Table III) (22,23). Sex was an independent predictor for stroke outcome overall, but narrowly failed to reach statistical significance in those treated with rtPA (P=0.054). Note that there was no association between sex and outcome in patients who underwent atrial fibrillation (24).

Table I. Baseline characteristics of patients with severe stroke (NIHSS 15-24) by stroke outcome (mRS 0-2) at discharge.

Factor	Poor outcome, n=230	Good outcome, n=38	P-value
Age, years, median (IQR)	67.90 (59.00-76.88)	63.50 (58.25-70.00)	0.119
Male sex, n (%)	104 (45.2)	25 (65.8)	0.030[a]
Thrombolysis use, n (%)	185 (80.4)	38 (100.0)	0.006[b]
Systolic blood pressure, mmHg, median (IQR)	148.00 (130.00-167.00)	156.50 (137.25-170.00)	0.327
Diastolic blood pressure, mmHg, median (IQR)	84.00 (73.00-97.00)	90.00 (78.00-98.75)	0.163
Mean arterial pressure, mmHg, median (IQR)	106.17 (93.33-118.58)	112.50 (100.00-122.58)	0.174
Body weight, kg, median (IQR)[d]	57.30 (50.00-65.00)	59.00 (51.40-67.00)	0.192
NIHSS admit, median, IQR	18.00 (16.00-21.00)	17.00 (15.00-20.00)	0.064
Hypertension, n (%)	138 (60.0)	24 (63.2)	0.850
Diabetes, n (%)	51 (22.2)	5 (13.2)	0.293
Dyslipidemia, n (%)	91 (39.6)	22 (57.9)	0.052
Atrial fibrillation, n (%)	90 (39.1)	7 (18.4)	0.023[a]
Coronary artery disease, n (%)	21 (9.1)	3 (7.9)	0.999
Valvular heart disease, n (%)	12 (5.2)	1 (2.6)	0.780
Previous stroke or TIA, n (%)	30 (13.0)	7 (18.4)	0.525
Smoking, n (%)	50 (21.7)	10 (26.3)	0.677
Chronic kidney disease, n (%)	14 (6.1)	6 (15.8)	0.076
Hyperthyroidism, n (%)	5 (2.2)	1 (2.6)	0.999
Onset to needle time, min, mean (SD)	155.43 (49.83)	150.77 (47.25)	0.612
mRS at discharge, n (%)			<0.001[c]
1	0 (0.0)	21 (55.3)	
2	0 (0.0)	17 (44.7)	
3	23 (10.0)	0 (0.0)	
4	65 (28.3)	0 (0.0)	
5	99 (43.0)	0 (0.0)	
6	43 (18.7)	0 (0.0)	
Barthel index at discharge, median (IQR)[d]	20.00 (10.00-35.00)	82.50 (70.00-100.00)	<0.001[c]
NIHSS at discharge, median (IQR)	15.00 (10.00-19.00)	3.00 (1.00-6.75)	<0.001[c]
Cost, USD, median (IQR)[e]	1,727.44 (1163.30-2,270.14)	1,755.64 (1,482.69-2,000.85)	0.807
Length of hospital stay, days, median (IQR)	6.00 (4.00-10.00)	4.00 (3.00-6.00)	0.001[c]

[a]P<0.05, [b]P<0.01, [c]P<0.001. [d]Percentage missing data for Barthel index at discharge in 8.6%, 14.4%, and 8.6%, respectively. [e]United States Dollar = 35.49 Thai Baht on June 23, 2021. TIA, transient ischemic attack.

Table II. rtPA treatment of patients with severe stroke (NIHSS 15-24) by stroke outcome (mRS 0-2) at discharge.

rtPA use, n (%)	mRS >2, (poor outcome) n=230 (%)	mRS 0-2 (good outcome) n=38 (%)
No	45 (19.57)	0 (0)
Yes	185 (80.43)	38 (100)

rtPA, recombinant tissue plasminogen activator; mRS, modified Rankin scale; NIHSS, National Institutes of Health Stroke Scale.

Predictors for good stroke outcomes in this study differed slightly from those found in a previous study conducted in Switzerland, despite comparable population sizes (223 and 243, respectively) (2). The predictors for good stroke outcomes in the previous study were age, physical signs, lab test results, and endovascular treatment. Here, atrial fibrillation and sex were predictors of a good outcome, neither of which were included in the Swiss study. In this study, age was included in the initial model but not in the final model. In addition, treatment with rtPA was an independent predictor for good stroke outcome, while there was no endovascular treatment in this study. Finally, there were differences in the ethnicity of the study populations, which may account for some of the differences observed.

There were some limitations in this study. First, a predictive model for those who did not receive rtPA treatment was not created, as no patient in this group had good outcomes. Second, only those patients whose stroke severity scores were available were included, which limited the available sample size. However, there were still independent predictors for good outcomes. Third, the outcomes were evaluated only at discharge and not over a longer term. Fourth, some factors

Table III. Factors related with good outcomes in patients with severe stroke (NIHSS 15-24) (n=268) using univariate and multivariate logistic regression analysis.

Factor	Univariate OR (CI)	P-value	Multivariate OR (CI)	P-value
Male sex	2.33 (1.14-4.78)	0.021[a]	2.30 (1.10-4.82)	0.027[a]
Dyslipidemia	2.10 (1.05-4.21)	0.037[a]	2.01 (0.98-4.12)	0.056
Atrial fibrillation	0.35 (0.15-0.83)	0.017[a]	0.38 (0.16-0.91)	0.029[a]
Chronic kidney disease	2.89 (1.04-8.07)	0.042[a]	2.77 (0.95-8.08)	0.062

[a]P<0.05. OR, odds ratio; CI, confidence interval; NIHSS, National Institutes of Health Stroke Scale.

Table IV. Interactions tested for factors in the final model for good outcomes in patients with severe stroke (NIHSS 15-24) using multivariate logistic regression analysis.

Interactions	Adjusted odds ratio (95% confidence interval)	P-value
Sex:AF	2.61 (0, Inf)	0.989
CKD:AF	1.71 (0, Inf)	0.998
Dyslipidemia:AF	5.47 (0, Inf)	0.989
Sex:CKD	9.14 (0, Inf)	0.996
CKD:Dyslipidemia	4.38 (0, Inf)	0.998
Sex:Dyslipidemia	1.51 (0.25, 9.18)	0.652
Sex:AF:CKD	3.31 (0, Inf)	0.997
Sex:AF:Dyslipidemia	1.50 (0, Inf)	0.988
Sex:Dyslipidemia:CKD	4.28 (0, Inf)	0.998
CKD:AF:Dyslipidemia	3.26 (0, Inf)	0.996
Sex:AF:CKD:Dyslipidemia	NA	NA

AF, atrial fibrillation; CKD, chronic kidney disease; Inf, infinity; NA, no univariate odds ratio is available for interactions; NIHSS, National Institutes of Health Stroke Scale.

Table V. Factors related to good outcomes in patients with severe stroke (NIHSS 15-24) who received rtPA treatment (n=223) using univariate and multivariate logistic regression analysis.

Factor	Univariate OR (CI)	P-value	Multivariate OR (CI)	P-value
Male sex	2.12 (1.02-4.40)	0.044	2.10 (0.99-4.45)	0.054
Dyslipidemia	1.97 (0.97-4.00)	0.060	1.86 (0.90-3.87)	0.095
Atrial fibrillation	0.33 (0.14-0.79)	0.013	0.36 (0.15-0.88)	0.024[a]
Chronic kidney disease	2.70 (0.95-7.73)	0.063	2.46 (0.83-7.34)	0.106

[a]P<0.05. OR, odds ratio; CI, confidence interval; rtPA, recombinant tissue plasminogen activator; NIHSS, National Institutes of Health Stroke Scale.

possibly related to both stroke and atrial fibrillation were not examined such as laboratory tests and obstructive sleep apnea (25-33). Finally, authorization to access the database was only for the mentioned study period (2015-2017). Thus, data may not be up-to-date. Further studies are required to validate the results of this study.

In conclusion, predictors for good stroke outcomes in severe stroke patients included rtPA treatment, atrial fibrillation, and male sex.

Acknowledgements

We would like to thank Dr Dylan Southard (Khon Kaen University, Thailand) for his kind review of the final manuscript.

Funding

No funding was received.

Availability of data and materials

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Authors' contributions

NK designed the study, analyzed and interpretated the data, and wrote the manuscript. NV, KK, ST, and WB interpretated the data. KS participated in data analysis and interpretation and prepared the manuscript. All authors read and approved the final manuscript. NK and NV confirm the authenticity of all the raw data.

Ethics approval and consent to participate

The study protocol was approved by the Khon Kaen University Ethics Committee for Human Research (approval no. HE611014).

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

References

1. Wu S, Yuan R, Xiong Y, Zhang S, Wu B and Liu M: Clinical features, management and outcomes of severe ischaemic stroke in tertiary hospitals in China: Protocol for a prospective multicentre registry-based observational study. BMJ Open 8: e024900, 2018.
2. Bill O, Zufferey P, Faouzi M and Michel P: Severe stroke: Patient profile and predictors of favorable outcome. J Thromb Haemost 11: 92-99, 2013.
3. Huttner HB and Schwab S: Malignant middle cerebral artery infarction: Clinical characteristics, treatment strategies, and future perspectives. Lancet Neurol 8: 949-958, 2009.
4. Emberson J, Lees KR, Lyden P, Blackwell L, Albers G, Bluhmki E, Brott T, Cohen G, Davis S, Donnan G, *et al*: Effect of treatment delay, age, and stroke severity on the effects of intravenous thrombolysis with alteplase for acute ischaemic stroke: A meta-analysis of individual patient data from randomised trials. Lancet 384: 1929-1935, 2014.
5. National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group: Tissue plasminogen activator for acute ischemic stroke. N Engl J Med 333: 1581-1587, 1995.
6. Suwanwela NC, Chutinet A and Kijpaisalratana N: Thrombolytic treatment in Thailand. J Stroke Med 1: 41-44, 2018.
7. Dharmasaroja PA, Dharmasaroja P and Muengtaweepongsa S: Outcomes of Thai patients with acute ischemic stroke after intravenous thrombolysis. J Neurol Sci 300: 74-77, 2011.
8. Banks JL and Marotta CA: Outcomes validity and reliability of the modified Rankin scale: Implications for stroke clinical trials: A literature review and synthesis. Stroke 38: 1091-1096, 2007.
9. Quinn TJ, Langhorne P and Stott DJ: Barthel index for stroke trials: Development, properties, and application. Stroke 42: 1146-1151, 2011.
10. R Core Team (R Foundation for Statistical Computing): R: A Language and Environment for Statistical Computing. Vienna, 2021.
11. Mazya MV, Lees KR, Collas D, Rand VM, Mikulik R, Toni D, Wahlgren N and Ahmed N: IV thrombolysis in very severe and severe ischemic stroke: Results from the SITS-ISTR Registry. Neurology 85: 2098-2106, 2015.
12. Sharma S, Mazya MV, Wahlgren N and Ahmed N: IV thrombolysis in very severe and severe ischemic stroke: Results from the SITS-ISTR Registry. Neurology 86: 2115, 2016.
13. Kongbunkiat K, Kasemsap N, Thepsuthammarat K, Tiamkao S and Sawanyawisuth K: National data on stroke outcomes in Thailand. J Clin Neurosci 22: 493-497, 2015.
14. Appelros P, Nydevik I, Seiger A and Terént A: Predictors of severe stroke: Influence of preexisting dementia and cardiac disorders. Stroke 33: 2357-2362, 2002.
15. Jørgensen HS, Nakayama H, Reith J, Raaschou HO and Olsen TS: Acute stroke with atrial fibrillation. The Copenhagen stroke study. Stroke 27: 1765-1769, 1996.
16. Yoo J, Song D, Baek JH, Kim YD, Nam HS, Hong GR, Kim J, Lee HS and Heo JH: Poor outcome of stroke patients with atrial fibrillation in the presence of coexisting spontaneous echo contrast. Stroke 47: 1920-1922, 2016.
17. Junejo RT, Braz ID, Lucas SJ, van Lieshout JJ, Phillips AA, Lip GY and Fisher JP: Neurovascular coupling and cerebral autoregulation in atrial fibrillation. J Cereb Blood Flow Metab 40: 1647-1657, 2020.
18. Liebeskind DS: Collateral circulation. Stroke 34: 2279-2284, 2003.
19. Guglielmi V, LeCouffe NE, Zinkstok SM, Compagne KC, Eker R, Treurniet KM, Tolhuisen ML, van der Worp HB, Jansen IG, van Oostenbrugge RJ, *et al*: Collateral circulation and outcome in atherosclerotic versus cardioembolic cerebral large vessel occlusion. Stroke 50: 3360-3368, 2019.
20. Kimura K, Iguchi Y, Yamashita S, Shibazaki K, Kobayashi K and Inoue T: Atrial fibrillation as an independent predictor for no early recanalization after IV-t-PA in acute ischemic stroke. J Neurol Sci 267: 57-61, 2008.
21. Vinding NE, Kristensen SL, Rørth R, Butt JH, Østergaard L, Olesen JB, Torp-Pedersen C, Gislason GH, Køber L, Kruuse C, *et al*: Ischemic stroke severity and mortality in patients with and without atrial fibrillation. J Am Heart Assoc 11: e022638, 2022.
22. Girijala RL, Sohrabji F and Bush RL: Sex differences in stroke: Review of current knowledge and evidence. Vasc Med 22: 135-145, 2017.
23. Gall SL, Donnan G, Dewey HM, Macdonel R, Sturm J, Gilligan A, Srikanth V and Thrift AG: Sex differences in presentation, severity, and management of stroke in a population-based study. Neurology 74: 975-981, 2010.
24. Andrade JG, Deyell MW, Lee AY and Macle L: Sex differences in atrial fibrillation. Can J Cardiol 34: 429-436, 2018.
25. Sawunyavisuth B: What are predictors for a continuous positive airway pressure machine purchasing in obstructive sleep apnea patients? Asia Pac J Sci Technol 23: APST-23-03-10, 2018.
26. Jeerasuwannakul B, Sawunyavisuth B, Khamsai S and Sawanyawisuth K: Prevalence and risk factors of proteinuria in patients with type 2 diabetes mellitus. Asia Pac J Sci Technol 26: APST-26-04-02, 2021.
27. Khamsai S, Chootrakool A, Limpawattana P, Chindaprasirt J, Sukeepaisarnjaroen W, Chotmongkol V, Silaruks S, Senthong V, Sittichanbuncha Y, Sawunyavisuth B and Sawanyawisuth K: Hypertensive crisis in patients with obstructive sleep apnea-induced hypertension. BMC Cardiovasc Disord 21: 310, 2021.
28. Khamsai S, Mahawarakorn P, Limpawattana P, Chindaprasirt J, Sukeepaisarnjaroen W, Silaruks S, Senthong V, Sawunyavisuth B and Sawanyawisuth K: Prevalence and factors correlated with hypertension secondary from obstructive sleep apnea. Multidiscip Respir Med 16: 777, 2021.
29. Soontornrungsun B, Khamsai S, Sawunyavisuth B, Limpawattana P, Chindaprasirt J, Senthong V, Chotmongkol V and Sawanyawisuth K: Obstructive sleep apnea in patients with diabetes less than 40 years of age. Diabetes Metab Syndr 14: 1859-1863, 2020.
30. Yaranov DM, Smyrlis A, Usatii N, Butler A, Petrini JR, Mendez J and Warshofsky MK: Effect of obstructive sleep apnea on frequency of stroke in patients with atrial fibrillation. Am J Cardiol 115: 461-465, 2015.
31. Kaewkes C, Sawanyawisuth K and Sawunyavisuth B: Are symptoms of obstructive sleep apnoea related to good continuous positive airway pressure compliance? ERJ Open Res 6: 00169-02019, 2020.
32. Manasirisuk P, Chainirun N, Tiamkao S, Lertsinudom S, Phunikhom K, Sawunyavisuth B and Sawanyawisuth K: Efficacy of generic atorvastatin in a real-world setting. Clin Pharmacol 13: 45-51, 2021.
33. Sawunyavisuth B, Ngamjarus C and Sawanyawisuth K: Any effective intervention to improve CPAP adherence in children with obstructive sleep apnea: A systematic review. Glob Pediatr Health: 8: 2333794X211019884, 2021.