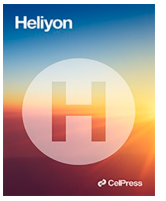
Heliyon 9 (2023) e21988

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon



The impact of antiplatelet drugs on recurrent stroke in patients with intracerebral hemorrhage

Yi-Sin Wong [a,b], Ching-Fang Tsai [c], Cheung-Ter Ong [d,*]

[a] Department of Family Medicine, Ditmanson Medical Foundation Chiayi Christian Hospital, Chiayi City, Taiwan
[b] Department of Nursing, Min-Hwei Junior College of Health Care Management, Tainan, Taiwan
[c] Department of Medical Research, Ditmanson Medical Foundation Chiayi Christian Hospital, Chiayi City, Taiwan
[d] Department of Neurology, Ditmanson Medical Foundation Chiayi Christian Hospital, Chiayi City, Taiwan

ARTICLE INFO

Keywords:
Stroke
Intracerebral hemorrhage
Ischemic stroke
Hemorrhagic stroke
Antiplatelet
Outcome
Risk factors
Diabetes mellitus
Hypertension

ABSTRACT

Background: The influence of antiplatelet drugs on the risk of hemorrhagic stroke and the reduction of ischemic stroke in patients with intracerebral hemorrhage (ICH) remains unclear. This study aimed to elucidate the impact of antiplatelet therapy on the risk of recurrent stroke in ICH patients.

Methods: The study encompassed ICH survivors discharged from a central Taiwanese teaching hospital between January 1, 2013, and December 31, 2019. Patient hospitalization and treatment data were retrieved from electronic medical records. The primary endpoint was re-hospitalization due to ischemic or hemorrhagic stroke. Patients who continued antiplatelet drug use for over a month prior to stroke recurrence constituted the antiplatelet drug use group. Risk factors for recurrent hemorrhagic and ischemic strokes were evaluated using binary logistic regression.

Results: The study incorporated 407 ICH patients, each monitored for 4 years post-stroke. Recurrent stroke incidence showed no significant disparity between hemorrhagic and ischemic strokes. Hemorrhagic stroke recurrence stood at 5.16 % (21/407), and ischemic stroke recurrence was 4.42 % (18/407). In the non-antiplatelet group, hemorrhagic and ischemic stroke rates were 5.48 % (20/365) and 3.56 % (13/365) respectively. In the antiplatelet group, the rates were 2.38 % (1/42) for hemorrhagic and 11.9 % (5/42) for ischemic stroke, with a significantly higher ischemic stroke rate ($p = 0.03$). Hypertension emerged as a risk factor for recurrent hemorrhagic stroke, while diabetes mellitus was identified as a risk factor for ischemic stroke. Antiplatelet drug use did not escalate the risk of recurrent ICH.

Conclusion: Diabetes mellitus and hypertension are risk factors for recurrent ischemic and hemorrhagic strokes respectively in ICH patients. Antiplatelet therapy does not appear to elevate the risk of recurrent hemorrhagic stroke in these patients.

1. Introduction

Hemorrhagic stroke represents 10%–20 % of stroke cases and 60%–70 % of hemorrhagic strokes are caused by ICH [1–3]Its global burden is on the rise, due to a decline in the mortality rate from intracranial hemorrhage, and an increase in survivors post hemorrhagic stroke [4]. Hypertension, a personal history of ischemic stroke, a family history of ICH, low cholesterol level, and the use of

* Corresponding author. Department of Neurology, Chia-Yi Christian Hospital, 539 Chung-Shao Road, Chiayi City, Taiwan.
E-mail address: 01288@cych.org.tw (C.-T. Ong).

https://doi.org/10.1016/j.heliyon.2023.e21988
Received 4 May 2023; Received in revised form 30 August 2023; Accepted 1 November 2023
Available online 3 November 2023

warfarin have been identified as risk factors for intracranial hemorrhage [5–8]. Post hemorrhagic stroke outcomes include mortality, functional impairment, diminished quality of life, recurrent ICH, ischemic stroke, cognitive impairment, psychiatric diseases, and epilepsy [9,10]. The annual stroke recurrence rate following Intracerebral Hemorrhage (ICH) is estimated at 3%–10 % [11–13]. Notably, patients with ICH exhibit a 3.1 hazard ratio, indicating a heightened risk of ischemic stroke, compared to individuals without stroke [14].

The types of recurrent stroke in ICH patients have been the subject of inconsistent reports. Studies have indicated that ICH patients face a higher risk of subsequent hemorrhage stroke compared to those with ischemic stroke [15,16]. Prior research has shown that patients with deep ICH are more prone to subsequent ischemic stroke than those with hemorrhagic stroke, while patients with lobar hemorrhage have an increased risk of recurrent hemorrhagic stroke [13]. However, certain studies have reported no significant difference in the type of recurrent stroke between patients with lobar hemorrhage and deep hemorrhage stroke [11,17].

Blood pressure management in ICH patients is vital in preventing recurrent hemorrhagic strokes. Hypertension is a recognized risk factor for recurrent ICH [18]. Effective blood pressure control in intracranial hemorrhage patients is essential for preventing recurrent cerebral hemorrhage, with improper control increasing the likelihood of ICH recurrence [19]. As per the ICH management guidelines, blood pressure control is recommended immediately post ICH onset for all patients, to prevent recurrence [20].

ICH patients often present with risk factors for ischemic stroke or cardiovascular disease and may have been on antiplatelet drugs prior to intracranial hemorrhage. Some studies have shown no increased risk in ICH recurrence, bleeding volume, or major vascular events in ICH patients treated with antiplatelet agents [21–24]. Conversely, other studies have suggested that antiplatelet drugs may heighten the risk of ICH recurrence and influence patient prognosis, particularly in those with lobar hemorrhage [19,25,26]. Given that subsequent ischemic stroke and myocardial infarction are more prevalent in hemorrhagic stroke patients, antiplatelet therapy is

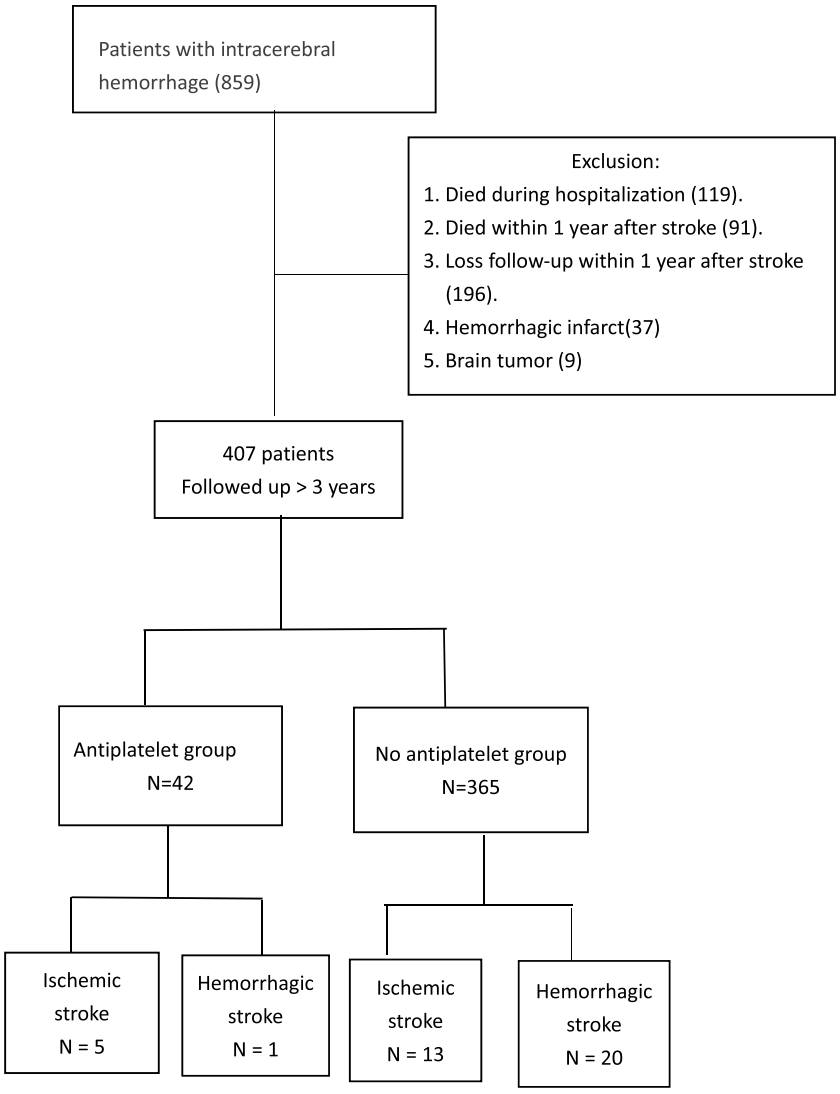


Fig. 1. Flowchart of patient enrollment, follow-up, and outcomes.

advised [27].

Recurrent strokes can amplify mortality rates and impede daily activities and function. The risk factors for recurrence of both ischemic and hemorrhagic stroke remain contentious. Similarly, the efficacy of antiplatelet agents in preventing stroke recurrence is yet to be definitively proven. As such, this study aims to ascertain the role of antiplatelet agents in stroke prevention and explore the risk factors for recurrent ischemic or hemorrhagic stroke in ICH patients.

2. Methods

2.1. Data sources and ethical approval

This study enrolled patients admitted with Intracerebral Hemorrhage (ICH) between January 1, 2013, and December 31, 2019, from a teaching hospital in central Taiwan. We conducted a comprehensive review of patients' medical records, including demographics, vascular risk factors, and care from stroke onset to 4 years post-stroke based on electronic medical records. A brain Computed Tomography scan was performed on each patient. Exclusions were patients without stroke recurrence and those lost to follow-up within 1 year after onset.

The study received approval from the Institutional Review Board (IRB) of Ditmanson Medical Foundation Chiayi Christian Hospital, Taiwan (CYCH-IRB: 2020131). The IRB waived the requirement for informed consent, given the study's retrospective nature.

2.2. Study participants and definitions

Hemorrhagic stroke is characterized as a swift development of neurological deficit attributable to a focal collection of blood within the brain parenchyma or ventricular system (ICH) or subarachnoid bleeding (subarachnoid hemorrhage) of non-traumatic origin [24]. All hospitalized patients diagnosed with ICH were considered for the study. The antiplatelet drug use group comprised patients who consistently used antiplatelet drugs for over 1 month before stroke recurrence and maintained their use throughout the study period. Patients who were tracked for over 3 years without subsequent hospitalization were deemed as having no stroke recurrence. The exclusion criteria include: 1) Patients under the age of 20; 2) Those with a history of hemorrhagic stroke; 3) Patients who died within 1 month post-stroke onset; 4) Patient loss to follow-up within 1 year post-stroke onset; 5) Ischemic stroke with hemorrhagic transformation; 6) Brain tumor hemorrhage (Fig. 1).

2.3. Outcome measures

The primary endpoint of this study was the onset of a new hemorrhagic or ischemic stroke.

2.4. Statistical analysis

The study compared stroke recurrence rates in patients receiving antiplatelet drugs with those not on such treatment. Baseline characteristics of patients as categorical variables (age, sex, diabetes mellitus, hypertension, atrial fibrillation, stroke history, cortex involvement, operation, smoking, and antiplatelet use) were presented as percentages and examined using the chi-square test or Fisher's exact test. Continuous variables were expressed as (mean $\pm$ standard deviation) and compared using the *t*-test. To assess potential risk factors linked with recurrent ischemic or hemorrhagic strokes, binary logistic regression was employed, with $p \leq 0.05$

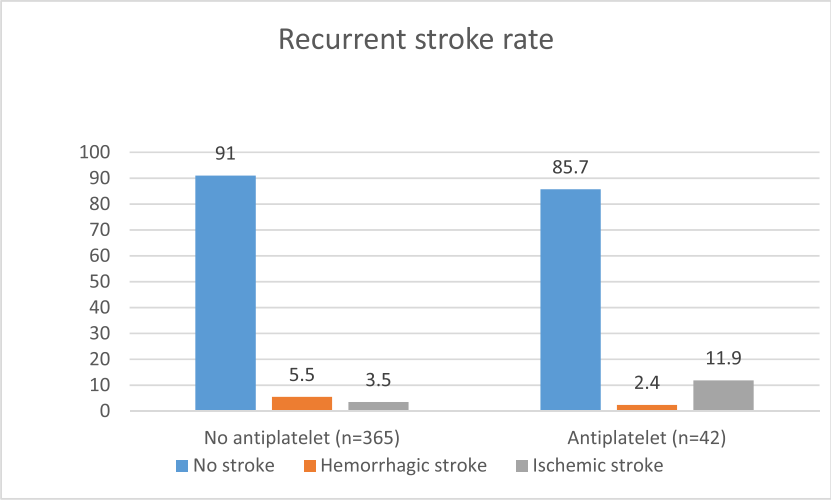


Fig. 2. Rates of recurrent strokes in patients who were (n = 42), and were not (n = 365), administered antiplatelet drugs.

regarded as significant. After adjusting for confounding factors (age, sex, diabetes mellitus, hypertension, atrial fibrillation, stroke history, cortex involvement, and antiplatelet use), the odds ratios, 95 % CIs, and p-values for recurrent stroke risk factors were calculated using logistic regression analysis. All statistical analyses were conducted using SPSS statistical software (version 28.0; IBM Corporation, Somers, NY, USA).

3. Results

Between 2013 and 2019, 407 patients were eligible for inclusion in this study. The process of patient enrollment is outlined in Fig. 1.

Throughout the 4-year follow-up period, stroke recurrence was observed in 39 patients, resulting in an overall stroke recurrence rate of 9.58 % (39/407). This included hemorrhagic stroke at 5.16 % (21/407) and ischemic stroke at 4.42 % (18/407). There was no significant difference in the recurrence rates between hemorrhagic and ischemic strokes. Among patients not receiving antiplatelet therapy, the rates of hemorrhagic and ischemic stroke were 5.48 % (20/365) and 3.56 % (13/365), respectively. In contrast, for those on antiplatelet therapy, the rates of hemorrhagic and ischemic stroke were 2.38 % (1/42) and 11.9 % (5/42), respectively. Notably, the ischemic stroke rate was significantly higher in the antiplatelet group ($p = 0.03$) (Fig. 2).

Patient characteristics are detailed in Table 1. Patients above the age of 60, with a history of diabetes and ischemic stroke, were more likely to be prescribed antiplatelet therapy. Conversely, patients who underwent craniotomy or had a hematoma volume greater than 30 cc were less likely to receive antiplatelet agents (Table 2). Univariate analysis demonstrated a correlation between cortex involvement and a heightened risk of stroke recurrence. Multivariate logistic regression analysis revealed that diabetes was linked to an elevated risk of subsequent ischemic stroke, while antiplatelet drugs did not elevate the risk of recurrent ischemic or hemorrhagic strokes (Table 3). Interestingly, hypertension was correlated with an increased risk of recurrent hemorrhagic strokes (Table 4).

4. Discussion

The primary findings of this study are: 1) in patients with ICH, diabetes might heighten the risk of recurrent ischemic stroke; 2) hypertension could elevate the risk of recurrent hemorrhagic stroke in patients with ICH; and 3) antiplatelet therapy does not seem to influence the risk of recurrent ischemic or hemorrhagic stroke.

Previous studies have reported that the recurrence rate of hemorrhagic stroke in patients with ICH, followed for less than 3–5 years, ranges between 6 % and 12 %, with an annual recurrence rate of 2–4 per person-year [13,15,16,28]. Our study, with a follow-up period less than 5 years, observed a hemorrhagic stroke recurrence rate of 4.65 %, lower than rates reported by Hanger et al. and Vermeer et al. These discrepancies could be attributed to variations in stroke type, hemorrhage location, and patient condition. Notably, studies have shown that patients with lobar hemorrhages are at a higher risk of hemorrhage recurrence than those with deep hemorrhage [9,12,13]. Vermeer's study, which reported a higher rate of hemorrhagic stroke recurrence, had a larger proportion (55 %) of patients with lobar hemorrhage [28].

In our study, the recurrence rate of ischemic stroke in patients not receiving antiplatelet drugs was 9.04 % (33/365), a rate higher than that reported by Murthy et al. [13]. In a 5-year follow-up study, the cumulative recurrence rate of ischemic stroke was 9.8 % [17]. This discrepancy may be attributed to our study's population being younger on average than those in Casolla et al.'s study (mean ages of 62.2 years and 70 years, respectively). Additionally, our study found that patients with a history of hemorrhagic stroke faced a higher risk of recurrent ischemic stroke. The Hazard Ratio for these patients was 3.1 [14].

Antiplatelet therapy is generally considered to decrease the risk of ischemic stroke and increase the risk of hemorrhagic stroke. Nevertheless, many ICH patients possess risk factors for ischemic stroke or cardiovascular disease, necessitating the use of antiplatelet drugs to prevent ischemic strokes or cardiac events. In our study, we found that antiplatelet therapy in patients with intracranial

Table 1
Characteristics of patients with intracerebral hemorrhage (n = 407).

Variables	No recurrent stroke (n = 368)	Recurrent stroke (n = 39)	*P#*	95 % CI
Age				
>60	210 (57.1 %)	27 (69.2 %)		
≤60	158 (42.9 %)	12 (30.8 %)	0.17	0.29–1.20
Sex (men)	245 (66.6 %)	25 (64.1 %)	0.85	0.45–1.78
Diabetes mellitus	115 (31.3 %)	18 (46.2 %)	0.07	0.96–3.67
Hypertension	329 (89.4 %)	32 (82.1 %)	0.18	0.22–1.31
Atrial fibrillation	14 (3.80 %)	4 (10.3 %)	0.08	0.92–9.25
Stroke history				
Hemorrhage	49 (13.3 %)	8 (20.5 %)		
Infarct	30 (8.2 %)	6 (15.4 %)		
No	289 (78.5 %)	25 (64.1 %)	0.06	
Cortex involvement	99 (26.9 %)	17 (43.6 %)	0.04	1.07–4.11
Operation	127 (34.5 %)	12 (30.8 %)	0.72	0.58–2.41
Smoking	113 (30.7 %)	13 (33.3 %)	0.71	0.55–2.27
Antiplatelet	36 (9.78 %)	6 (15.4 %)	0.27	0.65–4.27

CI: confidence interval, #. Chi-square or Fisher's exact test.

Table 2
Characteristics of patients who were (n = 42), and were not (n = 365), administered antiplatelet drugs.

Variables	Without antiplatelet (n = 365)	Antiplatelet (n = 42)	P#	95 % CI
Age				
>60	206 (56.4 %)	31 (73.8 %)		
≤60	159 (43.6 %)	11 (26.2 %)	0.03	0.22–0.94
Sex (men)	240 (65.8 %)	30 (71.4 %)	0.49	0.64–2.63
Diabetes mellitus	113 (30.9 %)	20 (47.6 %)	0.03	1.06–3.86
Hypertension	324 (88.8 %)	37 (88.1 %)	0.80	0.34–2.51
Atrial fibrillation	15 (4.10 %)	3 (7.14 %)	0.41	0.49–6.47
Stroke history				
Hemorrhage	34 (9.31 %)	2 (4.8 %)		
Infarct	37 (10.1 %)	20 (47.69 %)		
No	294 (80.6 %)	20 (47.67 %)	<0.01	
Cortex involvement	104 (28.5 %)	12 (28.6 %)	1.0	0.49–2.03
Operation	131 (35.9 %)	8 (19.0 %)	0.04	1.07–5.29
Smoking	114 (31.2 %)	12 (28.6 %)	0.86	0.43–1.78
Alcohol	85 (23.3 %)	9 (21.4 %)	1.0	0.41–1.95
Volume				
>30 cc	63 (17.3 %)	3 (7.14 %)		
≤30 cc	302 (82.7 %)	39 (92.9 %)	0.12	0.11–1.23

CI: confidence interval, #. Chi-square of Fisher's exact test.

Table 3
Binary logistic regression results for patients who sustained recurrent ischemic stroke.

Variable	Odds ratio	95 % CI	P
Age <60	1.02	0.36–2.91	0.98
Sex M	3.57	0.96–13.33	0.06
Diabetes mellitus	3.76	1.39–10.21	0.009
Hypertension	2.08	0.24–18.03	0.51
Atrial fibrillation	4.15	0.97–17.78	0.06
Stroke history			
Hemorrhage	2.95	0.94–9.21	0.06
Infarct	1.92	0.38–9.60	0.43
Cortex	1.28	0.47–3.50	0.64
Antiplatelet	1.51	0.43–5.26	0.53

CI: confidence interval.

Table 4
Binary logistic regression results for patients who sustained recurrent hemorrhagic strokes.

Variable	Odds ratio	95 % CI	P
Age <60	0.43	0.14–1.33	0.14
Sex M	0.42	0.16–1.11	0.08
Diabetes mellitus	0.76	0.25–2.32	0.63
Hypertension	0.3	0.10–0.92	0.03
Atrial fibrillation	0.67	0.07–6.53	0.73
Stroke history			
Hemorrhage	0.43	0.05–3.65	0.44
Infarct	2.42	0.70–8.32	0.16
Cortex	2.52	1.00–0.03	0.06
Antiplatelet	0.65	0.08–5.61	0.70

CI: confidence interval.

hemorrhage did not escalate the risk of hemorrhagic stroke or affect the recurrence of ischemic stroke. This observation aligns with previous studies, such as AL-Shahi et al., who found that the history of ischemic stroke, the site of cerebral hemorrhage, and the number of cerebral microbleeds did not influence ICH recurrence [29]. Similarly, our study discovered that a prior history of ischemic stroke and cortex involvement in hemorrhage did not affect the recurrence of hemorrhagic stroke.

Following ICH, recurrent ischemic and hemorrhagic strokes are common events, often leading to poorer outcomes and increased mortality [9]. Preventing hemorrhagic stroke recurrence is essential, and blood pressure control can significantly mitigate the risk of recurrent intracranial hemorrhage [30]. Given that recurrent ischemic strokes are more common than hemorrhagic strokes in patients post intracerebral hemorrhage [9], preventing recurrent ischemic stroke is crucial for improving long-term outcomes. The decision to prescribe antiplatelet or anticoagulant agents should consider the patient's vascular risk factors, such as atrial fibrillation, dyslipidemia, diabetes, heart condition, etiology, and location of intracranial hemorrhage. While some studies have indicated that

antiplatelet drugs might increase the risk of death, hematoma expansion, and surgery in patients with intracranial hemorrhage [31], others like Spiegel et al. found that antiplatelet drugs did not impact the characteristics and prognosis of intracranial hemorrhage in patients with primary ICH. However, when combined with anticoagulants, antiplatelet drugs could lead to an increase in intracranial hemorrhage volume and poor functional prognosis [25]. Several studies have found that restarting antiplatelet therapy does not influence functional outcome in patients with ICH [27,29]. Similarly, our study discovered that antiplatelet drugs did not elevate the risk of recurrent hemorrhagic stroke or affect ischemic stroke recurrence.

We found hypertension to be associated with an increased risk of recurrent hemorrhagic stroke, a finding that appears to be particularly relevant for the small proportion of ICH patients without hypertension, as most patients with hemorrhagic stroke have hypertension. Therefore, aggressive measures to control blood pressure should be encouraged to minimize recurrent hemorrhagic strokes.

Our study was conducted at a teaching hospital, and we included data regarding stroke location, hemorrhage volume, and surgical history. Our results indicate that hypertension is a risk factor for recurrent intracranial hemorrhage, and diabetes mellitus is a risk factor for recurrent ischemic stroke. Antiplatelet drugs did not increase the risk of intracranial hemorrhage and did not affect ischemic stroke recurrence. Despite these strengths, our study also had several limitations: 1) This was a retrospective study rather than a randomized one. 2) The pathophysiology of intracranial hemorrhage is not entirely clear. 3) Most patients receiving antiplatelet therapy had small hematoma volumes. 4) This was a single-center study with a relatively small sample size. 5) We do not have patient blood pressure and blood sugar data. Therefore, further investigation is warranted to confirm whether antiplatelet therapy does not increase the risk of hemorrhagic stroke in patients with ICH due to the small number of patients in our study.

In conclusion, hypertension is a risk factor for the recurrence of hemorrhagic stroke, and diabetes augments the risk of ischemic stroke recurrence in patients with intracranial hemorrhage. Antiplatelet drugs do not appear to increase the risk of recurrent hemorrhagic strokes in ICH patients.

Author contribution statement

Yi-Sin Wong: Contributed reagents, materials, analysis tools or data; Wrote the paper.
Ching-Fang Tsai: Analyzed and interpreted the data.
Cheung-Ter Ong: Conceived and designed the experiments; analyzed and interpreted the data.

Data availability statement

Data included in article/supp. material/referenced in article.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgment

This study was supported by a research grant from Ditmanson Medical Foundation Chiayi Christian Hospital, Taiwan (R111-13).

References

[1] S.J. An, T.J. Kim, B.W. Yoon, Epidemiology, risk factors, and clinical features of intracerebral hemorrhage: an update, J stroke 19 (1) (2017) 3–10, https://doi.org/10.5853/jos.2016.00864.
[2] V.L. Feigin, C.M. Lawes, D.A. Bennett, et al., Worldwide stroke incidence and early case fatality reported in 56 population-based studies: a systematic review, Lancet Neurol. 8 (4) (2009) 355–369.
[3] R.A. Grysiewicz, K. Thomas, D.K. Pandey, Epidemiology of ischemic and hemorrhagic stroke: incidence, prevalence, mortality, and risk factors, Neurol. Clin. 26 (4) (2008) 871–895.
[4] A.J. DeLago, H. Singh, C. Jani, A. Rupal, J. Shalhoub, R. Goodall, et al., An observational epidemiological study to analyze intracerebral hemorrhage across the United States: incidence and mortality trends from 1990 to 2017, J. Stroke Cerebrovasc. Dis. 31 (4) (2022) 1–11.
[5] C.-Y. Chen, P.-T. Lin, Y.-H. Wang, et al., Etiology and risk factors of intracranial hemorrhage and ischemic stroke in young adults, J. Chin. Med. Assoc. 84 (10) (2021) 930–936.
[6] V.A. Lioutas, A.S. Beiser, H.J. Aparicio, J.J. Himali, M.H. Selim, J.R. Romero, et al., Assessment of incidence and risk factors of intracerebral hemorrhage among participants in the Framingham Heart Study between 1948 and 2016, JAMA Neurol. 77 (10) (2020) 1252–1260.
[7] H. Sallinen, A. Pietilä, V. Salomaa, D. Strbian, Risk factors of intracerebral hemorrhage: a case-control study, J. Stroke Cerebrovasc. Dis. 29 (4) (2020), https://doi.org/10.1016/j.jstrokecerebrovasdis.2019.104630.
[8] Y.-W. Chen, C.-H. Li, C.-D. Yang, et al., Low cholesterol level associated with severity and outcome of spontaneous intracerebral hemorrhage: results from Taiwan Stroke Registry, PLoS One 12 (4) (2017).
[9] P. Daverat, J.P. Castel, J.F. Dartigues, J.M. Orgogozo, Death and functional outcome after spontaneous intracerebral hemorrhage. A prospective study of 166 cases using multivariate analysis, Stroke 22 (1991) 1–6.
[10] M.T.C. Poon, A.F. Fonville, R.S. Salman, Long-term prognosis after intracerebral haemorrhage: systematic review and meta-analysis, JNNP 85 (6) (2014) 660–667.
[11] L. Li, R. Luengo-Fernandez, S.M. Zuurbier, N.C. Beddows, P.S. Lavallee, E. Louise, eet al, Ten-year risks of recurrent stroke, disability, dementia and cost in relation to site of primary intracerebral haemorrhage: population-based study, J. Neurol. Neurosurg. Psychiatry 91 (2020) 580–585.
[12] Y.-S. Wong, C.-F. Tsai, C.-T. Ong, Risk factors for stroke recurrence in patients with hemorrhagic stroke, Sci. Rep. 12 (1) (2022) 1–10.

[13] H.C. Hanger, T.J. Wilkinson, N. Fayzer-Iskander, R. Sainsbury, The risk of recurrent stroke after intracerebral haemorrhage, JNNP 78 (8) (2007) 836–840.
[14] S.B. Murthy, I. Diaz, X. Wu, et al., Risk of arterial ischemic events after intracerebral hemorrhage, Stroke 51 (1) (2020) 137–142.
[15] G. Banerjee, D. Wilson, G. Ambler, I.C. Hostettle, C. Shakeshaft, H. Cohen, et al., Longer term stroke risk in intracerebral haemorrhage survivors, JNNP 91 (8) (2020) 840–845.
[16] K.M.V. Nieuwenhuizen, I. Vaartjes, J. Verhoven, G.J. Rinkel, J. Kappelle, F.H.M.B. Schreuder, et al., Long-Term prognosis after intracerebral hemorrhage, European stroke Journal 5 (4) (2020) 336–344.
[17] E. Zia, G. Engström, P.J. Svensson, B. Norrving, H. Pessah-Rasmussen, Three-year survival and stroke recurrence rates in patients with primary intracerebral hemorrhage, Stroke 40 (11) (2009) 3567–3573.
[18] K.N. Sheth, Spontaneous intracerebral hemorrhage, N. Engl. J. Med. 387 (2022) 1589–1596.
[19] L. Li, S.M. Zuurbier, W. Kuker, C.P. Warlow, P.M. Rothwell, Blood pressure control and recurrent stroke after intracerebral hemorrhage in 2002 to 2018 versus 1981 to 1986 population-based study, Stroke 52 (2021) 3243–3248, https://doi.org/10.1161/STROKEAHA.121.034432.
[20] J.C. Hemphill III, S.M. Greenberg, C.S. Anderson, et al., Guidelines for the management of spontaneous intracerebral hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association, Stroke 46 (7) (2015) 2032–2060.
[21] V. Caso, M. Paciaroni, M. Venti, A. Alberti, F. Palmerini, P. Milia, et al., Effect of On-Admission antiplatelet treatment on patients with cerebral hemorrhage, Cerebrovasc. Dis. 24 (2–3) (2007) 215–218.
[22] L. Sansing, S. Messe, B. Cucchiara, S. Cohen, P. Lyden, S. Kasner, Prior antiplatelet use does not affect hemorrhage growth or outcome after ICH, Neurology 72 (16) (2009) 1397–1402.
[23] B.B.M. Thompson, Y.M. Bejot, V.M. Caso, et al., Prior antiplatelet therapy and outcome following intracerebral hemorrhage: a systematic review (e-Pub ahead of print), Neurology 75 (15) (2010) 1333–1342.
[24] R. Al-Shahi Salman, M.S. Dennis, P.A.G. Sandercock, et al., Effects of antiplatelet therapy after stroke caused by intracerebral hemorrhage: extended follow-up of the RESTART randomized clinical trial, JAMA Neurol. 78 (10) (2021) 1179–1186.
[25] M.I. Sprugel, Md, J.B. Kuramatsu, et al., Antiplatelet therapy in primary spontaneous and oral anticoagulation-associated intracerebral hemorrhage. [Article], Stroke 49 (11) (2018) 2621–2629.
[26] S. Rustam Al-Shahi, D.P. Minks, D. Mitra, et al., Effects of antiplatelet therapy on stroke risk by brain imaging features of intracerebral haemorrhage and cerebral small vessel diseases: subgroup analyses of the RESTART randomised, open-label trial, Lancet Neurol. 18 (7) (2019) 643–652.
[27] C.-J.M. Chen, D.M. Ding, T.J. Buell, et al., Restarting antiplatelet therapy after spontaneous intracerebral hemorrhage: functional outcomes. [Article], Neurology 03 91 (1) (2018) e26–e36.
[28] S. Vermeer, A. Algra, C. Franke, P. Koudstaal, G. Rinkel, Long-term prognosis after recovery from primary intracerebral hemorrhage, Neurology 59 (2) (2002) 205–209.
[29] R. Al-Shahi Salman, D.P. Minks, D. Mitra, et al., Effects of antiplatelet therapy on stroke risk by brain imaging features of intracerebral haemorrhage and cerebral small vessel diseases: subgroup analyses of the RESTART randomised, open-label trial, Lancet Neurol. 18 (7) (2019) 643–652.
[30] M.M. Rymer, Hemorrhagic stroke: intracerebral hemorrhage, Mo. Med. 108 (1) (2011) 50.
[31] J. Roquer, C. Ana Rodríguez, M. Gomis, A. Ois, V. Puente, E. Munteis, Previous antiplatelet therapy is an independent predictor of 30-day mortality after spontaneous supratentorial intracerebral hemorrhage, J. Neurol. 252 (4) (2005) 412–416.