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Infective endocarditis is associated with worse outcomes in stroke: A Thailand National Database Study

Running title: Stroke prognosis in infective endocarditis

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Abstract

Background: There is lack of data on the association between infective endocarditis (IE) and outcomes of mortality and complications is stroke. We aimed to compare characteristics and outcomes of stroke patients with and without IE.

Methods: We retrospectively examined the above association using data obtained from an insurance database which covers ~75% of the Thai population. All hospitalized strokes between 8th January 2003 and 31st December 2013 were included in the current study. Characteristics and outcomes were compared between stroke patients with or without IE, and then between two main stroke types. Multiple logistic regression models including propensity score matched analyses were constructed to assess study outcomes controlling for age, sex, stroke type and co-morbidities.

Results: A total of 590,115 stroke patients (mean (SD) age = 64.2±13.7 years) (ischemic = 51.7%; hemorrhagic=32.6%; undetermined=15.7%) were included, of whom 2,129(0.36%) had stroke associated with IE. After adjustment, we found that IE was significantly associated with the following complications: arrhythmias (adjusted odds ratio (95% CI) 6.94(6.29-7.66)), sepsis (1.24(1.01-1.52)), pneumonia (1.34(1.17-1.53)), respiratory failure (1.43(1.24-1.66)) and in-hospital mortality (1.29(1.13-1.47)) (p for all<0.001). Patients with hemorrhagic stroke with IE had poorer outcomes for in-hospital mortality and respiratory failure compared to their counterparts with ischemic stroke. Propensity score matched analysis showed similar results.

Conclusions: Our results suggest that stroke patients with infective endocarditis differ from that of the general stroke population and these patients have worse outcomes. Future studies are needed to determine the best treatment strategies for stroke patients with infective endocarditis.

What is known about the topic?

- Infective endocarditis (IE) remains a significant burden in low and middle income countries with high incidence of rheumatic heart disease and stroke is a recognized serious complication of IE.

- Due to the fact IE is a relatively uncommon cause of stroke in western countries, there is a lack of understanding regarding the prognosis of stroke in people with IE.

What does the study add?

- Our analysis of 590,115 stroke patients in the Thailand National Insurance Database found that 0.36% (n=2,129) had stroke associated with IE.

- We found that IE was significantly associated with arrhythmias (OR 6.94(6.29-7.66)), sepsis (OR 1.24(1.01-1.52)), pneumonia (OR 1.34(1.17-1.53)), respiratory failure (OR 1.43(1.24-1.66)) and in-hospital mortality (OR 1.29(1.13-1.47)).

- Patients with hemorrhagic stroke with IE had poorer outcomes for in-hospital mortality and respiratory failure compared to their counterparts with ischemic stroke.

Introduction

Infective endocarditis (IE) remains a significant burden in low and middle income countries, particularly in regions with high incidence of rheumatic heart disease. Though relatively uncommon in developed countries, IE is of importance due to the high mortality rate associated with the condition - up to 40% of patients will die within 5 years of diagnosis [1-6]. Furthermore, IE has become a condition that affects all ages; trends in incidence show an increase in the age of patients developing IE over the last five decades [7].

Stroke is a recognized serious complication of infective endocarditis [8]; typically due to dissemination of multiple emboli from an endocardial vegetation. Studies have reported that stroke accounts for as much as 16.9% of the complications of IE [9,10]. While variations in the prevalence of stroke in IE have been identified across different regions in the world (as well as between different regions of the same country) [11], studies have found that moderate strokes are associated with poorer prognosis and higher mortality in patients with IE [12].

To the best of our knowledge, there has been no literature specifically regarding clinical characteristics and outcomes (including common stroke complications) in stroke patients with IE. Due to the fact IE is a relatively uncommon cause of stroke in western countries, there is a lack of understanding regarding the prognosis of stroke in people with IE.

Using the Thailand National Insurance Database of the Universal Coverage Scheme, our study aims were: (1) to compare characteristics of stroke patients with and without IE; (2) to compare acute stroke outcomes (in-hospital mortality, long length of stay (>14 days), cardiac and non-cardiac complications following stroke in patients with and without IE; and (3) to compare the outcomes of patients with IE between ischemic and hemorrhagic stroke admitted to secondary care in Thailand.

Methods

Study Design

We used data from the Universal Coverage Health Security Insurance Scheme Database which includes routinely collected consecutive admission data representative of all hospital admissions of stroke in Thailand. The Thai population is covered by 3 insurance schemes. The Civil Servant Benefit System covers government employees and their dependents (≈7% of the population). The Social Security scheme covers private sector employees (≈13% of the population). The Universal Coverage Health Security Scheme is a basic health insurance scheme covering the remaining ~75% of the population.[13]

The study participants comprised of a cohort of adult Thai patients admitted to provincial and large community hospitals in Thailand between January 2003-December 2013. We excluded those who are over 100 years as they only constitute 0.00016% of the sample and are also most likely to be an error of data entry in most cases. Diagnosis of stroke and infective endocarditis were identified from ICD coding on reimbursement forms (ICD10; I60-I64 for stroke and I38 for Infective endocarditis). In Thailand diagnosis of stroke is made by attending clinical teams based on clinical features and investigation findings including brain imaging (since 2009 all received a head CT scan in line with National Guidelines). Demographic and clinical data were obtained from reimbursement forms using ICD codes on an annual basis. Stroke types were categorized as hemorrhagic (I61, I62), ischemic (I63) or stroke of undetermined pathology (I64). Our study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a prior approval by the Ethics Committee in Human Research, Khon Kaen University, Khon Kaen, Thailand." The description of the cohort has also been described previously.[14,15]*Outcome Measures*

Serious common post-stroke complications were examined as primary outcomes in this study with their relationship with in-hospital mortality and length of in-hospital stay. Data on post stroke complications and co-morbid conditions were obtained from the ICD codes (Supplementary Table 1). Outcomes of interest such as cardiac complications, in-hospital mortality and length of stay were pre-selected and other complications were chosen based on their common occurrence.

Statistical Analysis

Statistical analyses were performed using SPSS for Mac version 24.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were compared by IE status and stroke type. Logistic regression models were constructed to examine the association between infective endocarditis and selected

outcomes following stroke. The selected outcomes of interest were cardiac complications; MI, cardiac arrest, arrhythmias, and non-cardiac complications of sepsis, pneumonia, respiratory failure and convulsions. We also examined the in-hospital mortality and likelihood of long length of stay (>14 days). The reference category for these regression models was stroke patients with no IE. Unadjusted and three adjusted models with incremental adjustments (models A-C) were carried out to examine the associations for complications (see Table 3 footnotes). For the outcome of long length of stay, to gain deeper insight and better understanding of the relationships, analyses were carried out for those who died as an in-patient and those who were discharged alive. Matched propensity score analyses based on factors in Model C of logistic regression were carried out to attempt to eliminate the possibility that the differences observed were due to inadequately controlled co-variates.

To better understand the impact of some selected major prognostic factors, the likelihood of aforementioned outcomes were examined using logistic regression models stratified according to age group (18-64 and 65 -100), stroke type (ischemic, hemorrhagic and undetermined stroke type) and sex. We also performed sub-group analysis comparing two major stroke sub-types (using ischemic stroke as reference) in those with IE only.

Results

A total of 590,115 stroke patients admitted to secondary care under Universal Coverage scheme in Thailand between 8th January 2003 and 31st January 2013 were included. Sample mean age (SD) was 64.2(±13.7) years and the prevalence of infective endocarditis was 0.36% (N=2,129). Males constituted 55% of the sample and ischemic strokes were the most common stroke subtype (51.7%). Hemorrhagic stroke and undetermined stroke types made up 32.6% and 15.7% of the sample, respectively. Characteristics comparison according to presence or absence of infective endocarditis is presented in Table 1. On average, patients with infective endocarditis were slightly younger (4.4 years) and a greater proportion was female (p<0.0001). The most common type of stroke in both groups was ischemic stroke (8% higher in IE), however hemorrhagic stroke was 1.55 times more common in stroke patients without infective endocarditis (p<0.0001). The prevalence of heart failure was almost 5 times greater in the IE group and other coagulation defects were almost 10 times as common (p<0.0001). Stroke patients without infective endocarditis were almost twice as likely to have cardiovascular risk factors such as

dyslipidemia and type II diabetes mellitus (p<0.0001). The characteristics according to stroke subtype is shown in Supplementary Table 2.

Common complications of stroke in this cohort were MI, cardiac arrest, arrhythmias, sepsis, pneumonia, respiratory failure and convulsions, and were therefore selected as outcomes of interest (Table 2). Overall, stroke complications were more prevalent in the infective endocarditis patients, although there was no statistically significant difference in the rates of convulsions between two groups (p=0.35). Arrhythmias were 5.5 times more common in the infective endocarditis patients. MI was twice as common in the IE group. Cardiac arrest, sepsis, pneumonia and respiratory failure were all more prevalent in the IE patients. In- hospital mortality was marginally greater in the infective endocarditis group. There was no statistically significant difference in length of inpatient stay (p=0.56).

Table 3 displays odds ratios and corresponding 95% confidence intervals for outcomes of stroke in patients with infective endocarditis compared to those without. After full adjustment, infective endocarditis was significantly associated with greater odds of arrhythmias, sepsis, pneumonia, respiratory failure and in-hospital mortality. Infective endocarditis was less likely to be associated with convulsions (OR 0.72;0.52-0.99). Arrhythmias were almost 7 times greater in odds of occurring in the stroke patients with infective endocarditis (OR 6.94;6.29-7.66). IE was not significantly associated with having a long length of stay.

Propensity score matched analyses showed similar results. It also showed that IE was associated with ~4folds greater odds of in-hospital mortality (OR 4.80;3.70-6.24) and arrhythmias (OR 4.06 (3.37-4.75)) as well as significantly increased odds of MI and cardiac arrest (P<0.0001) and of having a long length of stay.

Supplementary Table 3 stratifies the analysis presented in Table 3 according to key characteristics (age, stroke type and sex) to compare the impact of these variables on the likelihood of in-hospital mortality and having a long length of stay. In ischemic stroke, being a patient with IE was associated with the greatest increase in odds of in-hospital mortality. It was also associated with increased odds of having a long length of stay. Being a female stroke patient with IE had greatest increased odds of in-hospital mortality when compared to stroke patients without IE (OR 1.57(1.34-1.85)).

Supplementary Table 4 stratifies as in Supplementary Table 3 comparing the impact of the specific patient characteristics on the likelihood of the development of certain common stroke complications in the stroke patients with infective endocarditis compared to those without IE. IE

was associated with increased odds of developing arrhythmias across all stroke subtypes but particularly high odds were in association with hemorrhagic stroke. Ischemic stroke in association with IE was associated with the greatest increase in odds of development of respiratory failure. Female patients who also had IE had greatest increased odds in the development of pneumonia (1.52;1.28-1.80) and respiratory failure (1.90;1.59-2.27) when compared to stroke patients without IE. Male patients who also had IE had greatest increased odds in the development of arrhythmias (8.87;7.60-10.35).

Table 4 shows frequency distribution of complications by IE status and fully adjusted results of regression analyses that compare the odds of outcomes in hemorrhagic stroke patients with IE compared to their counterparts with ischemic stroke. Arrhythmias were almost double as common in ischemic stroke, whereas in-hospital mortality was over twice as common (2.55;1.90-3.43) in the hemorrhagic strokes (P<0.0001 for both). Patients with hemorrhagic stroke also had increased odds of developing respiratory failure (1.60;1.13-2.27).

Discussion

There are several key findings to this national study of IE and stroke from a non-Western country. First, IE in the context of stroke is pro-arrhythmic as it is associated with a 7-fold increase in odds of arrhythmias compared to non-IE patients. Secondly, not only does it increase in-hospital mortality but IE also increases non-cardiac pathology such as sepsis, pneumonia and respiratory failure compared to patients without IE. Third, among stroke patients, patients with IE are younger, more likely to be female with ischemic stroke type and have rheumatic mitral valve disease, coronary artery disease, heart failure, anaemia and coagulation defects. Fourth, patients with haemorrhagic stroke and IE had poorer outcomes for in-hospital mortality and respiratory failure compared to their counterparts without ischemic stroke. These findings suggest that IE as associated with worse prognosis among stroke patients and this high-risk group may require early identification within the general stroke cohort, escalation to high dependency or critical care areas if they are found to be at risk of deterioration and urgent management.

To date, most literature surrounding IE and stroke largely focusses on neurological outcomes of IE and does not address the more specific question of the prognosis in stroke in patients with IE. They report that neurological complications, particularly when they are symptomatic, are associated with poorer outcomes such as higher rates of in-hospital mortality. Consequently, other literature on the topic concerns examining appropriate indications for and

timing of cardiac surgery to improve prognosis in IE patients, in part to avoid further cerebral events [12,16,17]. To our knowledge, this study provides the first analyses to date specifically on the clinical characteristics and outcomes (including common stroke complications) in stroke patients with IE. This may help allow for better insight into identifying stroke patients at greatest risk of severe complications. The strengths of our analyses include the national, unselected large sample size that is representative of a country where rates of infective endocarditis are significant with prospective identification of participants.

In line with previous literature on the characteristics of patients with IE, the stroke patients with IE were younger than those without IE. However, contrary to these reports, our study found a greater proportion of stroke patients with IE were female [18,19]. Consistent with the morbidity profile of older individuals in Asia, traditional stroke risk factors such as diabetes mellitus and hypertension were more common in the patients without infective endocarditis [20-22]. We demonstrate a higher rate of post stroke complications in patients with IE and, to our knowledge, are the first group to specifically report this. IE had a large impact on the likelihood of developing arrhythmias and was associated with greater prevalence of serious complications such as sepsis, pneumonia and in-hospital mortality.

In line with current statistics on common stroke types in Asia, patients with IE also had a higher proportion of ischemic stroke and they had higher proportion of cardiac comorbidities. There are several plausible mechanisms by which ischemic stroke is commoner in patients with infective endocarditis; embolization of infective or platelet thrombi from a cardiac vegetation or underlying socioeconomic and cardiovascular risk factors such as smoking, excessive alcohol consumption and poor diet all increase the risk of ischemic stroke in the population and so may influence the prevalence of stroke sub-type [23-25].

Interestingly, among the stroke patients with infective endocarditis, a lower prevalence of hemorrhagic stroke than would be expected of an Asian population was observed [26-28]. We postulate that this may be due to the fact that infective endocarditis patients are younger and that increased rates of hemorrhagic stroke in the Asian population tends to be linked to high salt diet with resultant hypertension which is common with older age [22,29-32].

There was a greater proportion of stroke patients with infective endocarditis who developed cardiac arrest and had a MI compared to stroke patients who did not have infective endocarditis. Acute coronary syndromes have previously been reported as being complications of infective endocarditis, and may relate to embolic phenomena, particularly from aortic valve endocarditis

[33]. The results from the Propensity Score Matched analyses mirror the results from the regression analysis, further strengthening the evidence suggesting that infective endocarditis is associated with worse outcomes in stroke. There was no significant result associated with length of inpatient stay. Several factors are involved in predictors of length of inpatient stay in stroke patients including severity of stroke, co-morbid conditions and nutritional status [34-36] and so the findings observed may be explained by unmeasured confounders which are important for this specific outcome. Furthermore, the association between increased in-hospital mortality in stroke patients and the female sex has previously been described [37-38]. This paper serves to further emphasize the importance in sex-specific differences in the outcomes of stroke related to certain co-morbidities – in this instance, infective endocarditis.

Due to the large sample, we could examine the impact of IE in stroke patients comparing the characteristics and outcomes of two main stroke sub-types. In keeping with literature on stroke prognosis, patients with IE and hemorrhagic stroke had worse in-hospital mortality. We also identified that they had higher odds of respiratory failure compared to those with ischemic stroke. The reason is unclear and beyond the remit of the current study although this may be related to stroke severity.

To date, most literature surrounding IE and stroke largely focusses on neurological outcomes of IE and does not address the more specific question of the prognosis in stroke in patients with IE. They report that neurological complications, particularly when they are symptomatic, are associated with poorer outcomes such as higher rates of in-hospital mortality. One study did suggest that IE-related stroke had a favourable prognosis with regard to long-term survival and neurological recovery [39].

Our study has some limitations. Firstly, we relied on ICD coding for diagnosis of stroke, comorbidity and complication data, including infective endocarditis. Secondly, we did not have data on the medical therapies used, which may affect stroke outcome. However, there is evidence to suggest that pre-existing anticoagulation does not have effect on stroke, cerebrovascular haemorrhage or mortality in patients with left-sided infective endocarditis at 10 weeks [40]. Thirdly, we were unable to study mild strokes that were not admitted to hospital or very severe strokes where the patient died before being admitted. Nevertheless, truncation of distribution would only be likely to attenuate the results. Due to the nature of large scale epidemiological data, detailed information on heart valve lesions (size, location and infecting organism), cardiac surgery, stroke severity (as classified by the NIH Stroke Score) and whether the patients had

active infective endocarditis at the time of the stroke or were diagnosed thereafter, has not been included. These factors have important implications on outcomes in stroke patients and would be valuable to examine in any future study specifically regarding outcomes in stroke patients with infective endocarditis [12]. Another limitation is that we lack data on microbiological investigations, cardiology investigations and cardiac surgery which may be relevant to infective endocarditis. Finally, we did not have information on the temporal relationship between infective endocarditis and stroke. It has been suggested that the association between IE and stroke are made close together in time but the period of heightened stroke risk becomes apparent several months before diagnosis of IE and lasts several months after [41].

However, despite these limitations this study provides important insights into the prognosis of stroke patients with infective endocarditis for the first time in literature. We describe detailed information on the rates of common stroke complications and important outcomes such as in-hospital mortality and length of stay in IE patients who developed stroke. The use of large data based on unselected patient population through record linkage allows us to robustly control case-mix with a particular focus on a comprehensive list of co-morbidities. Indeed, this approach has formed the basis of better understanding of epidemiology and outcomes in relatively rare conditions. It overcomes selection bias which is the major limitation of small scale clinical studies and randomized trials.

In conclusion, the findings confirm that the characteristics of stroke patients with infective endocarditis are different from those in the general stroke population and that the prevalence, and in some cases, risk of certain concomitant comorbidities and post-stroke complications are greater. Though certain findings may seem self-explanatory that having one serious condition (infective endocarditis) would make the prognosis in another serious condition (stroke) worse, this study nevertheless contributes vital information, important in evidence based medicine, to help clinicians in ensuring extra-care that should be given to patients with IE who have stroke. Although infective endocarditis is a rare condition, it is associated with high morbidity and mortality and as such is important for the clinician to recognize and effectively manage what is a challenging condition with poor prognosis. Future work should focus on fully establishing risk factors and mechanisms of stroke in infective endocarditis, and developing the best treatment strategies for stroke patients with infective endocarditis.

Author contributions

PKM conceived the study. ST co-ordinated the data acquisition and obtained ethical approval. ABC and JHBS cleaned the data. PKM and KAR formulated the analysis plan. KAR analyzed the data and drafted the paper. All authors contributed in the writing of the paper. PKM is the guarantor.

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Table 1: Characteristic comparison between 590,115 stroke patients with and without infective endocarditis admitted to secondary care in Thailand (2003-2013).

	Infective endocarditis (%)	No infective endocarditis (%)	
Total N	2,129 (0.4)	587,986 (99.6)	
Mean Age (SD)*	59.8 (15.6)	64.2 (13.7)	<0.0001
Sex			
Male	866 (40.7)	323,551 (55.0)	
Female	1,263 (59.3)	264,435 (45.0)	
Stroke Type			
Ischemic	1,268 (59.6)	303,543 (51.6)	
Hemorrhagic	449 (21.1)	192,063 (32.7)	
Undetermined	412 (19.4)	92,380 (15.7)	<0.0001
Comorbidities			
RMVD*	55 (2.6)	5,394 (0.9)	<0.0001
CAD*	98 (4.6)	16,652 (2.8)	<0.0001
Hypertension	515 (24.2)	264,393 (45)	<0.0001
Heart Failure	153 (7.2)	8,660 (1.5)	<0.0001
Dyslipidemia	210 (9.9)	117,145 (19.9)	<0.0001
Anemia	179 (8.4)	31,428 (5.3)	<0.0001
Other Coagulation Defects	146 (6.9)	4,386 (0.7)	<0.0001

Type II Diabetes Mellitus	180 (8.5)	99,116 (16.9)	<0.0001
CKD*	62 (2.9)	18,894 (3.2)	0.431
Alcohol Related Disorders	11 (0.5)	9,185 (1.6)	<0.0001
Age-related Physical Debility	7 (0.3)	3,476 (0.6)	0.115
COPD*	42 (2.0)	11,441 (1.9)	0.928

*SD = standard deviation, RMVD = Rheumatic Mitral Valve Disease, CAD = Coronary Artery Disease, CKD= Chronic Kidney Disease, COPD= Chronic Obstructive Pulmonary Disease

Table 2: Comparison of outcomes following stroke in 590,115 patients (all ages) with and without infective endocarditis admitted to secondary care in Thailand (2003-2013).

Outcome	Infective endocarditis (%)	No infective endocarditis (%)	p*
Total N	2,129 (0.4)	587,986 (99.6)	
Serious Complications			
MI	26 (1.2)	3,383 (0.6)	<0.0001
Cardiac Arrest	36 (1.7)	6,112 (1.0)	0.0030
Arrhythmias	764 (35.9)	38,293 (6.5)	<0.0001
Sepsis	101 (4.7)	18,908 (3.2)	<0.0001
Pneumonia	272 (12.8)	56,086 (9.5)	<0.0001
Respiratory Failure	231 (10.9)	41,965 (7.1)	<0.0001
Convulsions	33 (1.6)	10,720 (1.8)	0.3470
In-hospital mortality	314 (14.7)	69,287 (11.8)	<0.0001
Length of Inpatient Stay			0.5560
<=14 days	1,941 (91.2)	533,891 (90.8)	
>14 days	188 (8.8)	54,095 (9.2)	

*Data are presented as median (IQR) for continuous data (length of stay) and number (%) for categorical data (in-hospital mortality and complications). MI= Myocardial Infarction

Table 3: Odds ratios and corresponding 95% confidence intervals from binary logistic regression analyses to examine outcomes in stroke in 2,129 patients with infective endocarditis using 587,986 patients without infective endocarditis as the reference category in Thailand (2003-2013).

Odds Ratio (95% Confidence Interval)

Outcome	Unadjusted*	Model A†	Model B§	Model C‖	Propensity Score Matched Analyses*****
MI	2.14 (1.45-3.15)	2.25 (1.53-3.32)	2.20 (1.49-3.24)	1.46 (0.98-2.17)	2.01 (1.03-3.93)
Cardiac Arrest	1.64 (1.18-2.28)	1.57 (1.13-2.18)	1.78 (1.28-2.48)	1.34 (0.96-1.87)	2.27 (1.26-4.11)
Arrhythmias	8.04 (7.35-8.79)	8.91 (8.13-9.77)	8.53 (7.77-9.37)	6.94 (6.29-7.66)	4.06 (3.47-4.75)
Sepsis	1.50 (1.23-1.83)	1.54 (1.26-1.88)	1.61 (1.31-1.97)	1.24 (1.01-1.52)	1.99 (1.42-2.79)
Pneumonia	1.39 (1.22-1.58)	1.54 (1.36-1.75)	1.68 (1.47-1.91)	1.34 (1.17-1.53)	1.74 (1.42-2.14)
Respiratory Failure	1.59 (1.38-1.82)	1.60 (1.39-1.84)	1.90 (1.65-2.20)	1.43 (1.24-1.66)	2.23 (1.77-2.83)
Convulsions	0.86 (0.63-1.19)	0.85 (0.62-1.18)	0.85 (0.62-1.17)	0.72 (0.52-0.99)	0.80 (0.50-1.27)
In-hospital mortality	1.30 (1.15-1.46)	1.29 (1.14-1.45)	1.69 (1.49-1.92)	1.29 (1.13-1.47)	4.80 (3.70-6.24)
Long Length of Stay (>14 days)	0.96 (0.82-1.11)	0.97 (0.84-1.13)	1.14 (0.98-1.32)	0.95 (0.81-1.11)	1.25 (1.00-1.56)
Living Patients Long Length of Stay (>14 days)	0.97 (0.82-1.14)	0.96 (0.81-1.14)	1.17 (0.99-1.39)	0.96 (0.81-1.14)	

Deceased Patients Long Length of Stay (>14 days)	0.83 (0.59-1.17)	0.94 (0.67-1.32)	0.84 (0.60-1.19)	0.84 (0.59-1.20)

*Unadjusted

†Model A= adjusted for age, sex and year of secondary care admission

‡Model B= adjusted for age, sex, year of secondary care admission and stroke type

§Model C= adjusted for age, sex, year of secondary care admission, stroke type and comorbidities

| |Propensity Score Matched Analyses=based on factors in Model C

Table 4: Comparison of outcomes in stroke in 1,717 people with infective endocarditis with ischemic stroke or hemorrhagic stroke admitted to secondary care in Thailand (2003-2013).

Outcome	Ischemic Stroke n (%)	Hemorrhagic Stroke n (%)	P	OR(CI)†
Total N	1268(73.8)	449(26.2)		
Serious Complications				
MI	15(1.2)	6(1.3)	0.799	1.07(0.37-3.16)
Cardiac Arrest	22 (1.7)	10(2.2)	0.508	0.91(0.36-2.32)
Arrhythmias	524(41.3)	105(23.4)	<0.0001	0.46(0.35-0.61)
Sepsis	68(5.4)	24(5.3)	0.989	0.75(0.43-1.31)
Pneumonia	187(14.7)	53(11.8)	0.122	0.74(0.51-1.06)
Respiratory Failure	136(10.7)	78 (17.4)	<0.0001	1.60(1.13-2.27)
Convulsions	28(2.2)	6(1.3)	0.254	0.50(0.18-1.41)
In-hospital mortality	157(12.4)	133(29.6)	<0.0001	2.55(1.90-3.43)
Length of In-patient Stay			0.026	
>14 days	117(9.2)	58(12.9)		1.21(0.83-1.78)

∗Data are presented as median (IQR) for continuous data (length of stay) and number (%) for categorical data (in-hospital mortality and complications). MI= Myocardial Infarction

†Odds ratios and corresponding 95% confidence intervals from binary logistic regression analyses to examine outcomes in 449 hemorrhagic stroke patients with infective endocarditis using 1268 ischemic stroke patients as a reference category in Thailand (2003-2013). Adjusted for age, sex, year of hospital admission and co-morbidities.