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Evaluation of Physicians' Compliance With Secondary Prevention Among Ischemic Stroke Patients: A Retrospective Study

Alaa Alhubaishi[a] , Maha A. Almutairi[b] , Malak A. Alasqah[b] , Shihanah H. Alharthi[b] ,
Abdulhadi M. Alqahtani[c] , Lina I. Alnajjar[a, d]

Abstract

Background: Stroke is a leading cause of disability and death worldwide. Globally, stroke affects 13.7 million individuals every year. Several studies have shown an increase in the rehospitalization rate among stroke patients caused by non-adherence to secondary prevention as recommended by the American Heart Association/American Stroke Association (AHA/ASA) guideline. The aim of this study was to evaluate physicians' compliance with secondary prevention of stroke upon patients' discharge.

Methods: A retrospective chart review study was conducted at King Fahad Medical City. The primary outcome of this study was the number of patients discharged with the recommended medications for the secondary prevention of ischemic stroke (IS). The data were collected from the patient's medical record files and analyzed using the Statistical Package for the Social Sciences (SPSS).

Results: Of the 675 patients who were screened for eligibility, 507 were included and 168 were excluded. The mean age of the patients was 59.5 ($\pm$ 15.6) years. Of the 507 patients, 181 (35.7%) had a history of previous stroke. Overall, 376 (74%) stroke patients were discharged with appropriate secondary prevention recommendation per AHA/ASA guideline.

Conclusions: This study stresses the importance of compliance with the AHA/ASA guideline for secondary stroke prevention and highlights the role of pharmacists in the stroke unit in which it is necessary to ensure that all stroke patients are discharged with the recommended medications to reduce recurrent stroke.

[a]Department of Pharmacy Practice, College of Pharmacy, Princess Nourah bint Abdulrahman University, Riyadh 11671, Saudi Arabia
[b]Collage of Pharmacy, Princess Nourah Bint Abdulrahman University, Riyadh, Saudi Arabia
[c]Clinical Research Department, Research Center, King Fahad Medical City, Riyadh, Saudi Arabia
[d]Corresponding Author: Lina I. Alnajjar, Department of Pharmacy Practice, College of Pharmacy, Princess Nourah bint Abdulrahman University, PO Box 84428, Riyadh 11671, Saudi Arabia. Email: lialnajjar@pnu.edu.sa

Introduction

Stroke affects 13.7 million individuals globally every year and is the cause of death for around 5.5 million individuals annually [1]. Stroke occurs in one out of every four people over the age of 25. While men have a higher risk of ischemic stroke (IS) than women at a younger age, women have a higher mortality rate. Locally, in Saudi Arabia, stroke is the second contributor to mortality, according to data reported by the World Health Organization (WHO) [2]. It occurs in 57.64 per 1,00,000 individuals every year and IS has the highest prevalence rate of 65.6% among other types of strokes [3].

The American Heart Association/American Stroke Association (AHA/ASA) defined stroke as an infraction in the spinal cord and brain, or retinal cell death due to ischemia, as indicated by the imaging, pathological, or objective evidence of central nervous system (CNS) infraction in a specified vascular distribution or the clinical evidence of CNS infraction as indicated by symptoms extending for $\geq$ 24 h or until death. Stroke can be categorized into three main categories: hemorrhagic, ischemic, or transient ischemic attack (TIA). IS defined as a neurological disorder affected by a CNS infraction [4], while TIA is a transient episode of neurological dysfunction induced by the spinal cord, focal brain, or retinal ischemia without acute infarction [4]. Risk factors for IS can be described as nonmodifiable, such as age and race, or modifiable, such as cigarette smoking, hypertension (HTN), diabetes mellitus (DM), dyslipidemia, atrial fibrillation (AF), and physical inactivity.

After IS managed urgently, AHA/ASA provides recommendations for secondary prevention, which includes pharmacological and non-pharmacological options (Table 1). Pharmacological options are mediation, such as β-hydroxy β-methyl glutaryl-CoA (HMG-CoA) reductase inhibitors known as statins and antiplatelet or anticoagulation therapy. This is recommended for all IS patients unless they are contraindicated. In addition, it is critical to control other comorbidities that can contribute to a new incidence of stroke, such as HTN, DM

Table 1. Recommended Secondary Prevention Medications for Ischemic Stroke per AHA/ASA Guideline

Class of medication	Recommendation
Antiplatelet	Aspirin or clopidogrel as alternative
Anticoagulation	Warfarin heparin or LMWH for: VAF, AV, LV, congenital heart disease
	DOACs for: NVAF
Statins	High-intensity statin

Manage other comorbidities that increase the risk of stroke if existing, such as HTN, DM, AF and smoking. AF: atrial fibrillation; AHA/ASA: American Heart Association/American Stroke Association; AV: aortic valve; DM: diabetes mellitus; DOACs: direct oral anticoagulants; HTN: hypertension; LMWH: low molecular weight heparin; LV: left atrial myopathy; NVAF: non-valvular atrial fibrillation; VAF: valvular atrial fibrillation.

and dyslipidemia. Non-pharmacological options can improve overall health and reduce the risk factors of stroke, including physical activity, a healthy lifestyle, weight reduction, and smoking cessation [5].

Several studies have shown an increase in the rehospitalization rate among IS patients caused by not adhering to the guideline recommendations for secondary stroke prevention. Studies have found a decline in the rehospitalization rate of stroke patients as they followed the guideline recommendations [6-10]. According to a retrospective cohort study, patients who were discharged after IS with secondary stroke prevention therapies in the short and long term will help reduce the risk of recurrent stroke [10].

The aim of this study was to evaluate the physician's adherence to secondary prevention of IS by determining the number of patients discharged from stroke units with appropriate secondary prevention medications recommended by AHA/ASA.

Materials and Methods

Study design and setting

A retrospective chart review study was conducted in one of the largest hospitals in the Riyadh region, which includes 460 beds. The targeted population was adult patients admitted to the stroke unit with a confirmed IS or TIA diagnosis. All patients were followed up from admission to discharge between January 2019 and December 2020.

Ethical issues and informed consent

The study was approved by the Institutional Review Board (IRB) at the King Fahad Medical City (KFMC) Research Center (IRB number 21-380), and the need for informed consent was waived. The study was conducted in accordance with the Declaration of Helsinki, and before the analysis, the patients' information was anonymized and de-identified.

Study participants

Patients older than 18 years and admitted to the stroke unit

with confirmed IS or TIA were eligible for inclusion. Patients were excluded if they were diagnosed with hemorrhagic stroke, pregnant, discharged against medical advice, or if the stroke was medically ruled out (Fig. 1).

Study variables

The study data were collected and managed using a Microsoft Excel sheet. All patient data were obtained from the stroke unit at KFMC. The data included the patients' demographics, medical history, date of admission and discharge, diagnosis type of stroke, number of prior strokes, laboratory results, and discharged medication. The primary outcome was the number of stroke patients discharged with appropriate secondary prevention. The medications of focus were the recommended secondary prevention medications based on the AHA/ASA guideline, which include antiplatelets or anticoagulants, statins, and other medications to manage high-risk comorbidities that can lead to stroke (Table 1). All patients' discharged medication lists were reviewed and compared with AHA/ASA guideline recommended medications.

Statistical analysis

All data analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 25. Since the study was a descriptive retrospective study, the data variables were expressed using descriptive statistics ether by percentage, mean ± standard deviation (SD), median, or average. The source data were validated using Pearson correlation, and the association was very strong (Pearson correlation = 1.0).

Results

A total of 675 patients were screened for eligibility, and 507 IS patients met our inclusion criteria in the final analysis sample. The exclusion criteria included patients who were diagnosed with hemorrhagic stroke (88, 52.3%), passed during hospitalization (16, 9.5%), were less than 18 years old (5, 2.9%), were pregnant (1, 0.5%), had no documentation in electronic medical records (EMR) (10, 5.9%), were discharged against medical advice (3, 1.7%), and were suspected to have IS or TIA, with no confirmed medical diagnosis (45, 26.7%) (Fig. 1).
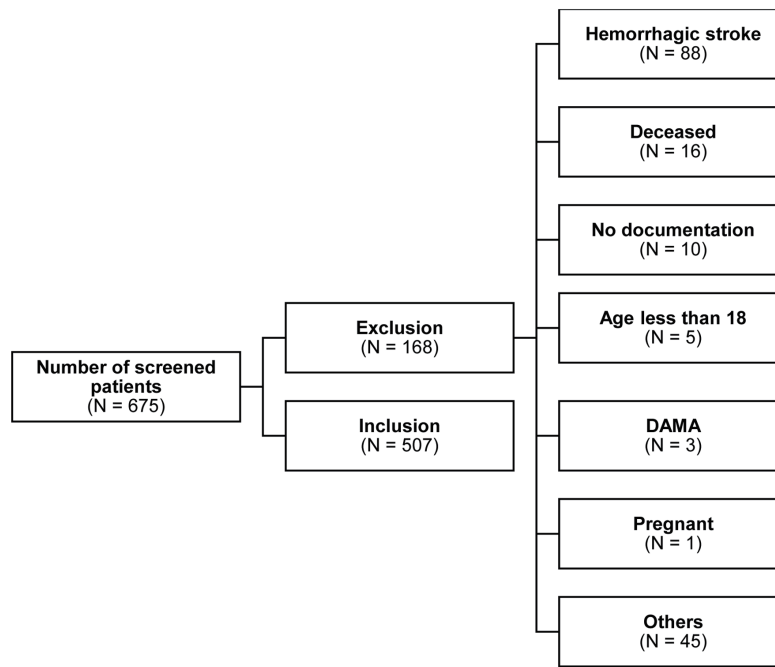
Figure 1. Flowchart of patients admitted to the stroke unit. Others were patients who were suspected of having IS or TIA but without any confirmed medical diagnosis. DAMA: discharged against medical advice; IS: ischemic stroke; N: number; TIA: transient ischemic attack.

Demographics and clinical characteristics

As demonstrated in Table 2, most patients were male (63% versus 37.2% female) with a mean age of 59.5 ± 15.6 years. HTN was the most common past medical history in IS patients (398, 76.7%), followed by DM (311, 61.3%), obesity (191, 37.7%), ischemic heart disease (129, 25.4%), dyslipidemia (124, 24.5%), AF (49, 9.7%), chronic kidney disease (42, 8.3%), and seizures (73, 14.5%). A total of 181 (35.7%) patients in this study had a history of stroke before study enrolment: about 150 patients had one previous stroke, 30 patients had 2 - 4 stroke incidences, and one patient had more than five stroke events in his life. About 20 (17.8%) patients were currently smokers, and 64 (12.6%) were former smokers.

Number of patients discharged with IS secondary prevention

Out of 507 IS patients, only 376 (74%) were discharged with complete recommended secondary prevention per guideline, which includes medications that prevent recurrent stroke and medications that manage other comorbidities that increase the risk of stroke. Moreover, 131 (26%) patients missed complete appropriate recommendations.

During admission, about 13 patients (2.5%) developed AF, which was the most prevalent new diagnosis comorbidity, followed by HTN (12, 2.3%), then DM (8, 1.5%). The majority of patients diagnosed with new comorbidities that increase the risk of recurrent stroke were discharged on appropriate

Table 2. Patients' Demographic Characteristics

Characteristics	n (%)
Age, years	
Mean ± SD	59.5 ± 15.6
Median (IQR)	60 (19 - 107)
Gender	
Male	318 (62.1)
Female	189 (37.9)
Body mass index (mean), kg/m^2	30.3
Smoker	90 (17.8)
Former smoker	64 (12.6)
Obesity	191 (37.7)
Chronic kidney disease	42 (8.3)
Past medical history	
Hypertension	389 (76.7)
Diabetes mellitus	311 (61.3)
Dyslipidemia	124 (24.5)
Atrial fibrillation	49 (9.7)
Seizure patient	73 (14.4)
Ischemic heart disease	129 (25.4)
Stroke	181[a] (35.7)

[a]One stroke event: 150 patients; 2 - 4 stroke events: 30 patients; more than five stroke events: one patient. IQR: interquartile range; SD: standard deviation.

Table 3. Number of Patients Discharged on Medications to Manage Comorbidities (Diagnosed During Admission)

Comorbidities	HTN	DM	AF
Number of patients newly diagnosed comorbidities during admission	12	8	13
Number of patients discharged with appropriate medication	11 (91.6%)	8 (100%)	10 (80%)

AF: atrial fibrillation; DM: diabetes mellitus; HTN: hypertension.

Table 4. Number of Patients Discharged on Medications to Manage Comorbidities (Past Medical History)

Comorbidities	HTN	DM	Dyslipidemia	AF	Smokers
Number of patients with past medical history (a)	398	311	124	49	90
Number of patients discharged with appropriate medication (b)	367	275	124	41	20

Number of patients with history of comorbidities who did not discharge on appropriate medications = a - b. AF: atrial fibrillation; DM: diabetes mellitus; HTN: hypertension.

medications (Table 3). However, not all patients with past medical history of comorbidities other than stroke have been discharged on their medications (Table 3). A high number of patients (469, 92.5%) were discharged on statin, 409 (80.6%) were discharged on antiplatelet, and 146 (28.7%) were discharged on anticoagulant. The types of antiplatelet or anticoagulation are detailed in Table 4. Nicotine replacement therapy was prescribed only for 20 out of 90 smokers in the study, and there were no documented recommendations for weight loss in obese patients.

Discussion

According to the AHA/ASA guideline, all IS or TIA patients should be discharged with antiplatelet therapy, either single or dual antiplatelet therapy (DAPT), depending on the patients' case, high-intensity statin to prevent secondary vascular events, including stroke, and anticoagulant medication depending on the conditions associated with the embolic IS. Antiplatelet therapy is recommended for all IS patients un-

less contraindicated. This study showed a high number of patients discharged on antiplatelets (409, 80.7%) (Table 5) and 98 (19.3%) did not. The reason may be due to medical contraindication, such as severe bleeding or high sensitivity to antiplatelet medication. However, there was no documentation behind not recommending antiplatelets for the rest of the patients. A similar study found that 32 out of 275 stroke patients were discharged with no antiplatelet therapy [9]. In addition, the guideline recommended that DAPT should not exceed 90 days and should not be combined with anticoagulant medication, as recent trials have shown that there is no benefit over single antiplatelet therapy to reduce recurrent stroke, in addition to increasing the risk of major bleeding and intracerebral hemorrhagic stroke [11, 12]. Accordingly, in this study, about 46 patients had DAPT for longer than 90 days and six patients had a combination of DAPT and an anticoagulant without a clear indication of which was against the AHA/ASA guideline.

Individuals with AF have a 3 - 5 times greater risk of IS. Direct oral anticoagulant (DOAC) is recommended for nonvalvular AF and warfarin for valvular AF as lifetime management for the secondary prevention of IS unless contraindicated.

Table 5. Total Number of All Patients Discharged on Complete Ischemic Stroke Secondary Prevention

Antiplatelet therapy	409 (80.7%)
Aspirin	178 (43.7%)
Clopidogrel	49 (12.04%)
DAPT	182 (44.7%)
Anticoagulant (for AF)	146 (28.8%)
Warfarin, heparin or LMWH	67 (45.9%)
DOAC	79 (54.1)
Statins	469 (92.5%)
Antihypertensive medication	378
Antidiabetic medication	283
Atrial fibrillation medication	51
Nicotine replacement therapy	20
Number of patients discharged with all secondary prevention medication when appropriate	376 (74%)

AF: atrial fibrillation; DAPT: dual antiplatelet therapy; DOAC: direct oral anticoagulant; LMWH: low molecular weight heparin.

A total of 49 patients had a history of AF, and 13 patients were newly diagnosed during admission. Moreover, 11 patients were not discharged on anticoagulants, probably which might be due to contraindication as high-risk hemorrhage, but this was not documented. However, this study had a lower percentage of physician noncompliance compared to another study, which mentioned that 1,756 out of 6,273 IS patients with a history of AF were discharged without anticoagulant therapy [13].

As for high-intensity statin, about 469 (92.5%) statins were prescribed upon discharge, while 38 (7.5%) IS patients were not discharged with any kind of statin. Although this study saw a higher rate of statin prescription, a retrospective, cross-sectional study found that only five patients out of 105 IS patients were not discharged with a statin [7]. On the other hand, a population-based survey study reported that 321 out of 931 IS patients were discharged with a statin, which was significantly low compared to this study [14]. Some patients found that the side effect of statin as rhabdomyolysis was unbearable. Here comes the importance of pharmacists, as they will suggest some strategies to manage the side effects of statins while using them.

In addition to the above medications, AHA/ASA guidelines recommend managing other comorbidities that increase the risk of stroke, such as HTN, diabetes, and AF. Lifestyle modifications, including physical activity, healthy diet, weight reduction in the case of obesity, and smoking cessation, are highly recommended by the guideline [15].

We found that across all patients who were admitted for stroke or TIA, cases were better managed when a new comorbidity was diagnosed during admission which indicate better practice at this cite. About 31 patients developed new comorbidities in which the majority were discharged on medications (Table 3). Incomplete secondary prevention medication on discharge was higher in patients with a past medical history of health conditions that increase the risk of stroke. However, vital signs confirmed uncontrolled HTN in 31 patients, and laboratory results showed A1C more than 7% in 36 diabetic patients and AF in eight patients (Table 4). Moreover, patients were not prescribed the necessary medications on discharge. This could be related to the physicians' perception that the primary care physician would take the lead in prescribing the needed medications. If so, this practice exposes these patients to a higher risk of recurrent stroke sooner than expected. About 181 IS patients had a history of stroke (Table 2), which may be the result of not adhering to the guideline recommendation previously or of the patient not complying with their medication. Either way, there was no clear document about recurrent stroke history because some patients did not have the electronic record for their first-time stroke, as they had a stroke around 10 years ago, which was most likely managed in a different hospital.

HTN is the most critical risk factor for the development of stroke [15]. Therefore, ensuring that all patients with HTN are discharged with hypertensive medication is important to prevent recurrent IS. Overall, 378 out of 398 HTN patients were discharged with antihypertensive medications (Table 5). This study had higher patient compliance rates with antihypertensive medications compared with a similar study that found

that 23 out of 116 IS patients with HTN were not prescribed antihypertensive medication at discharge [16].

Diabetic patients are twice more at risk of stroke than non-diabetic patients. About 283 out of 311 patients were discharged with antidiabetic medication, which leaves about 28 patients who were discharged with no medications although their A1C was higher than 7%, which indicates the need to manage medication according to the guideline to reduce the recurrence of IS. This might be due to the lack of pharmacists in the stroke unit since we could not find any documentation on why antidiabetic patients were not prescribed on discharge.

Regarding lifestyle modification, in this study, there were 191 (37.7%) obese patients with an average body mass index (BMI) of 30.3 kg/m^2. Unfortunately, there was no mention of a weight loss plan for those patients in their records. Regarding smoking, continuing to smoke after a stroke is associated with a higher risk of stroke recurrence and other cardiovascular events [17]. In this study, there were 90 (17.8%) smokers. However, only 20 (22.2%) patients had a prescription for nicotine replacement therapy. This also emphasizes the role of a pharmacist in the stroke unit, as a meta-analysis concluded that stroke patients who smoked had an increased risk of recurrent stroke, with a pooled odds ratio (OR) of 1.61 (95% confidence interval (CI): 1.34 - 1.93, $P < 0.001$) [18].

This study demonstrated that about 376 (74%) IS or TIA patients were discharged with complete secondary prevention, while 131 (26%) patients were not discharged with the recommended medication for secondary stroke prevention.

Our study emphasizes the crucial role of pharmacists in stroke units. A systematic review concluded that pharmacist involvement in a stroke unit positively impacts stroke patient outcomes [17]. Another study found that clinical pharmacists in a stroke unit were able to identify 22.6% of 796 patients with untreated indications and 21% of patients with noncompliance [19].

For these purposes, it is recommended that pharmacists should be included in the stroke unit team for better outcomes.

There were some limitations to our study. First was the nature of the retrospective design in which data were based on patient records only. Second, some patients with past medical history were treated in other hospitals, and there was an obstacle in understanding the reasons behind the lack of management of comorbidities before admission that might have contributed to the cause of their current stroke.

Conclusions

Physician adherence to the guideline recommendations for secondary stroke prevention must be optimized. Comorbidity management, such as prescribing HTN, DM, and AF medications, is vital to reducing stroke recurrence. The presence of a pharmacist in a stroke unit is essential to ensure that stroke patients are discharged with the recommended medication according to recent guidelines that help reduce stroke recurrence. Future studies need to assess the impact of pharmacists' role in reducing the number of recurrent IS and recommending appropriate secondary prevention.

Conflict of Interest

The authors declare that they have no conflict of interest.

Informed Consent

Not applicable. IRB clearance was provided for this study.

Author Contributions

AA has conceived of the presented idea, involved in planning, and reviewed the manuscript. AMA has verified the analytical methods, involved in planning, and supervised the research. MAA, MAA, and SHA have contributed to the design and implementation of the research, to the analysis of the results and to the writing of the manuscript. LIA has contributed to the writing of the manuscript, to the final editing and review. All authors were involved in writing, reviewing, and revising the article prior to submission.

Data Availability

The authors declare that data supporting the findings of this study are available within the article.

Abbreviations

AF: arterial fibrillation; AHA/ASA: American Heart Association/American Stroke Association; BMI: body mass index; CNS: central nervous system; DAPT: dual antiplatelet therapy; DM: diabetes mellitus; DOAC: direct oral anticoagulant; HTN: hypertension; IQR: interquartile range; IRB: Institutional Review Board; KFMC: King Fahad Medical City; SD: standard deviation; SPSS: Statistical Package for the Social Sciences; TIA: transient ischemic attack; WHO: World Health Organization

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