

CHAPTER 4

Limited efficacy of a long-term secondary prevention program in ischemic stroke and transient ischemic attack patients

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A B S T R A C T

Background

Few studies have focused on the quality of care with regard to long-term secondary prevention after ischemic stroke or transient ischemic attack (TIA). The aim of this study was 2-fold: **(1)** to determine if ischemic stroke and TIA patients are motivated for a long-term secondary prevention program after hospital discharge and **(2)** to study the effect of this program on the attainment of guideline-recommended secondary prevention targets.

Methods

A single-centre, cohort study of ischemic stroke and TIA patients. The number of visits to the long-term secondary prevention program and the number of patients whom achieved the composite endpoint of optimal medical therapy at their last visit to our outpatient clinic were assessed.

Results

Of the 237 included ischemic stroke and TIA patients, only 164 (69%) visited the long-term secondary prevention program at least once. Of these patients, 37% reached the primary endpoint of optimal medical therapy at their last visit to our outpatient clinic. We found a significant increase in secondary prevention target attainment for the primary outcome of optimal medical therapy and its individual components.

Conclusions

Despite our systematic approach to care for patients after ischemic stroke or TIA, we observed that 31% of our patients did not visit our outpatient clinic for the long-term secondary prevention program at all. In addition, the long-term secondary prevention program alone, consisting of regular follow-up visits and a medication treatment algorithm, was not sufficient to reach guideline-recommended treatment targets in most of our ischemic stroke and TIA patients.

Introduction

Stroke is a major cause of death and disability worldwide. Ischemic stroke and transient ischemic attack (TIA) patients have a high risk of recurrent stroke, myocardial infarction, and death from vascular causes.^{1,2} Management of ischemic stroke and TIA patients should therefore not only aim to reduce future stroke but cardiovascular disease in general. Evidence for the effectiveness of secondary prevention strategies after ischemic stroke and TIA is overwhelming. A combination of antithrombotic therapy, such as the combination of aspirin and dipyridamol or clopidogrel, blood pressure control, statins, dietary modification, and exercise, lowers the risk of recurrent stroke and other future cardiovascular events.³⁻⁶ The combination of these strategies applied to survivors of an ischemic stroke is estimated to result in a cumulative relative risk reduction of recurrent vascular events of approximately 80%, with a number needed to treat of 5.⁷ Because of this compelling evidence, national and international guidelines emphasize the importance of adequate risk factor assessment and management in ischemic stroke and TIA patients.^{8,9} However, these guidelines lack additional information on who should provide long-term secondary prevention in these patients and on how to reach treatment targets in routine clinical practice. Few studies have focused on the quality of care with regard to long-term secondary prevention after TIA or ischemic stroke. The limited data available indicate that despite advances in treatment, patients after ischemic stroke or TIA often do not receive the recommended interventions.¹⁰⁻¹³ In our clinic, a secondary care hospital in Amsterdam, it was common practice that ischemic stroke and TIA patients were invited to visit a long-term secondary prevention program. The aim of this study was 2-fold: **(1)** to determine if ischemic stroke and TIA patients were motivated for a long-term secondary prevention

program after hospital discharge and **(2)** to study the effect of this program on the attainment of guideline-recommended secondary prevention targets.

Methods

In our hospital, it was a common practice that all ischemic stroke and TIA patients were offered a 1-year long-term secondary prevention program after initial hospitalization. We conducted a retrospective cohort study by identifying all ischemic stroke or TIA patients admitted to the Sint Lucas Andreas Hospital in Amsterdam from April 2008 to April 2009. Patient's demographic and clinical data, cardiovascular risk factors, and follow-up duration were collected through medical record review. In addition, we collected data on medication use, blood pressure, and low-density lipoprotein cholesterol (LDL-C) from baseline (at discharge after initial hospitalization) and from the last visit to our outpatient based long-term secondary prevention program. Patients were excluded in the case of death during the initial hospitalization. Patients were also excluded when baseline data could not be retrieved (ie, missing values for cardiovascular risk factors, medication use, blood pressure, or LDL-C).

Long-term Secondary Prevention Program

This 1-year program consisted of follow-up visits to our outpatient clinic at 4 weeks, 3 months, 6 months, 9 months, and 12 months after the index event. During these sessions, modifiable vascular risk factors were identified, and tailored advice was given regarding the treatment of these risk factors. For this purpose, participating nurses, neurology residents, and neurologists used a medication treatment algorithm to lower blood pressure and LDL-C levels with pharmacologic therapy. This medication treatment algorithm was documented in a protocol and distributed to all participating physicians and nurses.

Outcome Measures

To determine if ischemic stroke and TIA patients were motivated for a long-term secondary prevention program and to study the effect of this program on the attainment of guideline-recommended secondary prevention targets, we chose the number of visits to the long-term secondary prevention program and the number of patients who achieved the composite endpoint of optimal medical therapy at their last visit to this program as primary outcomes. Optimal medical therapy was defined as the combination of the use of prescribed antithrombotic therapy (antiplatelet agents or oral anticoagulants) and achievement of both blood pressure (<140/90 mm Hg) and LDL-C (<2.5 mmol/l, <100 mg/dl) targets. Secondary outcome measures were the three individual components of the composite endpoint of optimal medical therapy, the percentage of patients using cholesterol-lowering medication, and the percentage of patients using antihypertensive medication at their last visit to the long-term secondary prevention program.

Statistical Analysis

All statistical analyses were carried out using IBM SPSS statistics (IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp). Dichotomous data are described as numbers and percentages, and continuous data are presented as means with standard deviations. For non-normal distributed outcomes, we reverted to median values and interquartile range (IQR). For continuous data, the paired sample t-test was used to evaluate the difference between baseline data and data from the last visit to the long-term secondary prevention program. The McNemar test was used for the outcome measures with a dichotomous outcome. For the comparison of groups at baseline, we performed the independent-sample t-test for continuous data and chi-square analyses for categorical data. A probability p-value of less than 0.05 was considered significant.

Results

Patients

Between April 2008 and April 2009, we identified 318 ischemic stroke and TIA patients. Of these, 15 patients died during initial hospitalization and were therefore not included in this study. Another 66 patients were excluded from analysis because of incomplete baseline data.

Compared with the 237 patients who were included in the final analysis, in this group of excluded patients, the percentage of TIA patients was significantly higher (51/66 [77%] versus 83/237 [35%], $p < 0.001$). All other retrievable patient characteristics, including age and reported cardiovascular risk factors, were similar between these both groups.

The remaining 237 patients (127 men and 110 women) were included in this analysis. The mean (SD) age in this group was 69 (+/-13.8) years, 65% presented with ischemic stroke and 35% with TIA. Table 1 summarizes the baseline characteristics of all patients. In total, 68% of the included patients had a history of hypertension at baseline. In addition, we found that a high number of our patients were current smokers (31%) or had a history cardiovascular disease (31%).

Long-term Secondary Prevention Program Participation

Of the 237 included ischemic stroke and TIA patients, 164 (69%) patients visited the long-term secondary prevention program at least once. The 73 (31%) ischemic stroke and TIA patients who did not visit the long-term secondary prevention program were significantly more often transferred to other hospitals, rehabilitation units, and nursing homes, compared with the cohort who returned for at least one follow-up visit (38 of 73 [52%] versus 16 of 164 [9.8%] patients, $p < 0.05$). In addition, these 73 patients were younger and were significantly more often diagnosed with ischemic stroke than with TIA ($p < 0.05$; Table 1). Of the 164 patients who visited the long-term secondary prevention program at least once, the median (IQR) follow-up was 8.5 (4-12)

TABLE 1 Baseline characteristics

Variables	At least 1 visit to the long-term secondary prevention program n=164	No visits to the long-term secondary prevention program n=73	p-value
Male, n (%)	87 (53)	40 (55)	NS#
Age, mean (SD)	80.0 (12.6)	65.7 (15.7)	0.006*
TIA, n (%)	66 (40)	17 (23)	0.012#
BP, mean (SD), mm Hg	-	-	-
Systolic	159.9 (29.1)	155.3 (29.2)	NS*
Diastolic	82.8 (18.2)	79.9 (17.2)	NS*
LDL-C, mean (SD), mmol/l	3.22 (1.21)	3.00 (1.14)	NS*
Risk factors	-	-	-
Hypertension, n (%)	105 (64)	56 (77)	NS#
Diabetes, n (%)	27 (16.5)	14 (19.2)	NS#
Current smoker, n (%)	52 (32)	21 (29)	NS#
AF, n (%)	13 (7.9)	12 (16.4)	NS#
History of CVD, n(%)	48 (29)	25 (34)	NS#
Hypercholesterolemia, n (%)	30 (18.3)	7 (9.6)	NS#

TIA = transient ischemic attack; BP = blood pressure; LDL-C = LDL-cholesterol; AF = atrial fibrillation; CVD = cardiovascular disease; NS = non significant; SD = standard deviation.

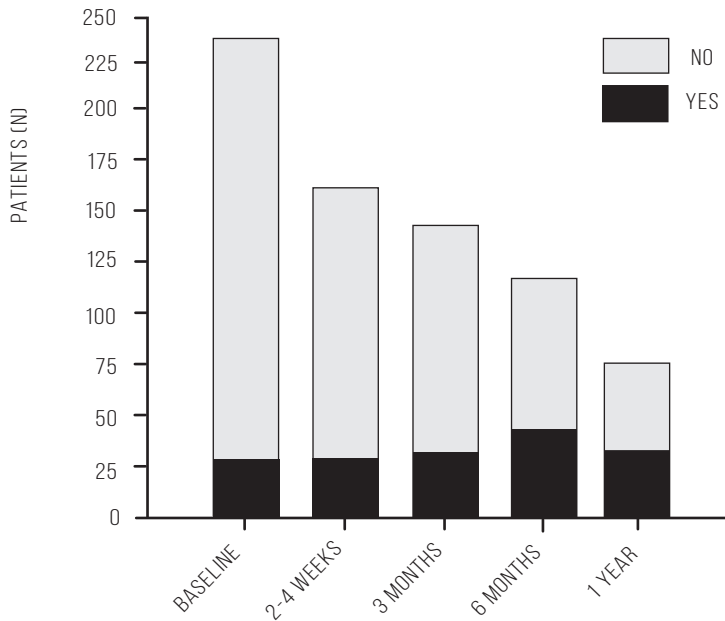
* Determined by use of the independent sample t-test.

Determined by use of the chi-squared test.

months; the median (IQR) number of visits was 3 (2-3); and only 76 patients (46%) completed the full follow-up period of 1 year (Figure 1).

Secondary Prevention Targets

Overall, we obtained follow-up data on 164 ischemic stroke and TIA patients (87 men and 77 women), and these patients were included in the final analysis on the effect of the long-term secondary prevention program on the attainment of guideline-recommended secondary prevention

FIGURE 1 Results on follow-up and the primary outcome

Patients whom achieved the combined targets for use of antithrombotics, blood pressure <140/90 mm Hg, and LDL-cholesterol <2.5 mmol/l.

targets. A total of 61 patients (37%) reached the primary endpoint of optimal medical therapy at their last visit to the long-term secondary prevention program (Figure 1, Table 2). In addition, we found that 157 patients (96%) used antithrombotic therapy, 90 patients (55%) reached the target of a blood pressure of 140/90 mm Hg or lower, and 95 patients (58%) reached the target of an LDL-C less than 2.5 mmol/l at their last visit to the long-term secondary prevention program. Compared with baseline data, we found a significant increase in secondary prevention target attainment for the primary outcome of optimal medical therapy and its individual components (all p-values <0.05; Table 2). Furthermore, we found a significant reduction in the absolute values of both systolic blood pressure and LDL-C (p<0.05; Table 2). At the last visit to the long-term secondary prevention

TABLE 2 Baseline and follow up secondary prevention targets (n=164)

Outcomes	Baseline	Last clinic visit	p-value
Optimal medical care, n (%)	17 (10.4)	61 (37)	<0.001#
Use of antithrombotics, n (%)	145 (88)	157 (96)	0.031#
BP <140/90 mm Hg, n (%)	50 (31)	90 (55)	<0.001#
Systolic BP, mm Hg (SD)	159 (29.1)	140 (22.9)	<0.001*
Diastolic BP, mm Hg (SD)	82 (18.2)	80 (12.6)	NS*
LDL-C <2.5 mmol/l, n (%)	52 (32)	95 (58)	<0.001#
LDL-C, mmol/l (SD)	3.22 (1.21)	2.53 (1.01)	<0.001*

BP = blood pressure; LDL-C = LDL-cholesterol; NS = non significant; SD = standard deviation.

Determined by use of the McNemar test.

* Determined by use of the paired sample t-test.

program, significantly more patients used a lipid-lowering agent (68% versus 79%, $p < 0.05$) and an antihypertensive agent (57% versus 82%, $p < 0.05$) compared with baseline data. Nonetheless, 12 patients (7.3%) with raised blood pressure and 16 patients (9.8%) with an LDL-C more than 2.5 mmol/l remained untreated.

Discussion

Despite our systematic approach to care for patients after ischemic stroke or TIA, we observed that a substantial part (31%) of our patients included in the study did not visit the long-term secondary prevention program at all. Those who did not visit the long-term secondary prevention program were significantly more often transferred to other hospitals, rehabilitation units, and nursing homes, compared with the cohort who returned for at least one follow-up visit. In addition, they were younger and had more often been diagnosed with ischemic

stroke than with TIA. Furthermore, less than half of the remaining 164 patients completed the follow-up period of 1 year. Possible reasons for this remarkable and unexpected short follow-up duration are unclear in most patients. We presume that these findings can be linked to patient characteristics (eg, poststroke cognitive dysfunction, lack of motivation, functional limitations, and socioeconomic status), health care provider issues, and health care delivery processes. In our long-term secondary prevention program there were no structured interventions used to facilitate behaviour change or to increase knowledge of stroke and stroke risk factors.^{14,15} The use of these interventions may increase the willingness of ischemic stroke and TIA patients to engage in a long-term secondary prevention program.

In contrast to cardiac rehabilitation programs for patients with coronary artery disease, a specific rehabilitation program after TIA or ischemic stroke to improve cardiorespiratory fitness, to influence secondary prevention targets, and to systematically address cardiovascular lifestyle targets has not been implemented. Although there are significant differences in signs and symptoms between patients with coronary artery disease and patients with stroke, both conditions share risk factors and pathologic mechanisms. A previous report by Saposnik et al demonstrated a difference in treatment guideline attainment between patients with coronary artery disease and patients with stroke, with the latter group being less likely to achieve the recommended treatment targets.¹⁰ A more recent study by Heeley et al confirmed these results. They related these results to the misperception in both doctors and patients that patients with a stroke or TIA are at a lower risk of vascular disease compared with those with coronary artery disease.¹⁶ Improving adherence to guidelines and cardiovascular lifestyle changes by standardizing poststroke care including behaviour change interventions, mirroring practice in cardiac rehabilitation programs, could be a promising method for increasing the effectiveness of secondary stroke prevention.

Among the 164 patients who returned for at least 1 follow-up visit to

the long-term secondary prevention program, we found a significant increase in secondary prevention target attainment. After a median follow-up of 8.5 months, 37% of these patients reached the composite endpoint for use of antithrombotics, a blood pressure less than 140/90 mm Hg, and LDL-C less than 2.5 mmol/l as recommended by guidelines. These results compare favourably with those reported in literature,^{10-12, 17} but one has to be careful in interpreting these results because this analysis only concerns the subgroup of patients (69%) who returned for at least 1 follow-up visit to our outpatient clinic. This study adds to the evidence that the quality of secondary prevention in routine clinical practice is suboptimal.

Several limitations of our study deserve comment. First, because of incomplete baseline data, 66 patients were excluded from analyses. Compared with the 237 patients who were included in the final analysis, these 66 excluded patients were significantly more often diagnosed with TIA than with ischemic stroke. Second, we have no information on lifestyle modifications. Because of the retrospective nature of our study, reliable information on the different lifestyle factors could not be retrieved. Third, reasons for the unexpected short follow-up duration are unclear in most of our patients.

In conclusion, the results of our analysis indicate that there is a need for effective strategies to improve the quality of long-term secondary prevention after ischemic stroke or TIA. In this retrospective study, we were not able to motivate all patients to fulfil a complete year of follow-up. In addition, the long-term secondary prevention program alone, consisting of regular follow-up visits and a medication treatment algorithm, was not sufficient to reach guideline-recommended treatment targets in most of our ischemic stroke and TIA patients.

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