

CHAPTER 8

Practice variation in long-term secondary stroke prevention in the Netherlands

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A B S T R A C T

Background

Stroke guidelines emphasize the importance of adequate vascular risk factor assessment and management in transient ischemic attack (TIA) and ischemic stroke patients, but it is not clear how these guidelines are applied in routine clinical practice. The limited data that are available indicate that TIA and ischemic stroke patients often do not receive the recommended interventions. The aim of this study was to investigate practice variations in long-term secondary stroke prevention in the Netherlands.

Methods

Between June and December 2013, an invitation for a web-based survey was sent to 90 Dutch neurologists with a special interest in stroke neurology. This web-based survey contained questions regarding the organization of outpatient care for TIA and ischemic stroke patients after initial hospital assessment, pharmacologic treatment, and nonpharmacologic strategies for long-term secondary prevention.

Results

In total, 84 (93%) neurologists completed the survey. Although nearly all respondents reported that they follow-up TIA and ischemic stroke patients after initial hospital assessment, the number of follow-up visits and the follow-up duration were variable. A similar variation was found in treatment targets levels for both blood pressure and low-density lipoprotein cholesterol. Regarding nonpharmacologic strategies for long-term secondary stroke prevention, most respondents inform their TIA and ischemic stroke patients about the importance of smoking cessation. There is considerably less attention for the other lifestyle risk factors.

Conclusions

We found considerable practice variation in long-term secondary stroke prevention. These variations may have an impact on the risk for stroke recurrence and cardiovascular disease in general.

Introduction

Stroke is a major cause of death and disability world-wide. Evidence from randomized trials and meta-analyses for the effectiveness of long-term secondary prevention strategies after transient ischemic attack (TIA) and ischemic stroke is compelling. A combination of antithrombotic therapy, blood pressure control, statins, dietary modification, and exercise lowers the risk of recurrent stroke and other future cardiovascular events.¹⁻⁵ The combination of these strategies could result in a cumulative relative risk reduction of 80%.⁶ Therefore, national and international guidelines emphasize the importance of adequate risk factor assessment and management in TIA and ischemic stroke patients, but it is not clear how these guidelines are applied in routine clinical practice.⁷⁻¹⁰ Few studies have focused on the quality of care regarding long-term secondary stroke prevention. The limited data that are available indicate that despite advances in treatment, TIA and ischemic stroke patients often do not receive the recommended interventions.¹¹⁻¹⁴

We hypothesized that considerable variations in long-term secondary stroke prevention may exist among neurologists in the Netherlands. We used an online survey to seek the opinion of Dutch neurologists about long-term secondary stroke prevention. The results of this survey can be used to improve future quality of care for these patients.

Methods

We analyzed national and international TIA and ischemic stroke guidelines to identify topics and situations where practice variation, regarding long-term secondary prevention for TIA and ischemic stroke patients, could be expected. An online survey creator (<http://>

www.enqueteviainternet.nl) was used to develop a web-based survey, which included multiple choice questions, multi-answer multiple choice questions, and free-text fields for additional comments. This survey was divided into 3 parts. The first part contained questions on how outpatient care for TIA and ischemic stroke patients is organized after initial hospital assessment (Table 1). The second part of the survey consisted of questions about pharmacologic treatment regarding long-term secondary stroke prevention (Table 2). The third part contained questions regarding nonpharmacologic strategies for long-term secondary stroke prevention (Table 3). Between June and December 2013, an e-mail invitation for an anonymous web-based survey was sent to 90 Dutch neurologists with a special interest in stroke neurology, working in 90 different hospitals. Most of them participated in an earlier online survey on variation in clinical practice of intravenous thrombolysis in stroke in the Netherlands.¹⁵ To increase the response rate, a monthly reinvitation was sent.

Results

Ninety neurologists were invited to participate, of whom 84 (93%) completed the survey. Most of the respondents (92%) worked in nonacademic hospitals.

The Organization of Outpatient Care for TIA and Ischemic Stroke Patients

Almost all respondents (98%) reported that they follow-up TIA and ischemic stroke patients after initial hospital assessment. The average number of follow-up visits were variable, ranging from 1 visit in 34 (40%) respondents to 4 visits or more in 2 (2.4%) respondents. The follow-up duration ranged from 0-3 months (62%) to 12 months or more (4.8%). Respondents reported that during follow-up patients are managed by neurologists (76%), neurology residents (15%), physician

TABLE 1 Questions regarding the organisation of long-term secondary prevention after TIA and ischemic stroke

Questions	n (%)
Do you follow-up TIA and ischemic stroke patients after initial hospital assessment?	
Yes	82 (98)
No	2 (2.4)
What is the average number of follow-up visits?	
1 visit	34 (40)
2 visits	37 (44)
3 visits	9 (11)
4 visits ore more	2 (2.4)
Did not specify	2 (2.4)
What is the average follow-up duration?	
0-3 months	52 (62)
4-6 months	18 (21)
7-12 months	8 (9.5)
>12 months	4 (4.8)
Did not specify	2 (2.4)
Who does manage your patients after TIA and ischemic stroke with regard to long-term secondary prevention? (more than one answer allowed)	
Neurologist	64 (76)
Neurology resident*	13 (15)
Physician assistant	26 (31)
Stroke nurse	27 (32)
Other	9 (11)
Did not specify	2 (2.4)
Who is primarily responsible for your patients after TIA and ischemic stroke with regard to long-term secondary prevention?	
Neurologist	22 (26)
General practitioner	36 (43)
Physician assistant	6 (7.1)
The stroke nurse	3 (3.6)
The internist	1 (1.2)
Other	12 (14)
No one is primarily responsible	4 (4.8)
Who, in your opinion, should ideally be responsible for patients after TIA and ischemic stroke with regard to long-term secondary prevention?	
Neurologist	21 (25)
General practitioner	42 (50)
Physician assistant	6 (7.1)
The stroke nurse	7 (8.3)
The internist	2 (2.4)
Other	6 (7.1)

* neurology residency training programs are not limited to academic centers in the Netherlands.

TABLE 2 Questions regarding pharmacological treatment for patients after TIA or ischemic stroke

	n (%)
Do you use clopidogrel monotherapy as first-line antiplatelet agent in long-term secondary stroke prevention, instead of the combination aspirin/dipyridamol?	
Always	10 (12)
Usually	11 (13)
Sometimes	57 (68)
Never	6 (7.1)
Have you prescribed a NOAC in the past year?	
Yes	21 (25)
No	63 (75)
Do you initiate antihypertensive therapy for long-term secondary stroke prevention?	
Always	9 (11)
Usually	28 (33)
Sometimes	37 (44)
Never	10 (12)
Which blood pressure target level do you aim for?	
The lower, the better	12 (14)
≤140/90 mm Hg for all	22 (26)
≤140/90 mm Hg, ≤130/80 mmHg for patients with diabetes	15 (18)
≤130/80 mm Hg for all	19 (23)
Other	8 (9.5)
Did not specify	10 (12)
Do you prescribe antihypertensive therapy in normotensive patients?	
Always	1 (1.2)
Usually	10 (12)
Sometimes	29 (35)
Never	34 (40)
Did not specify	10 (12)
Do you initiate lipid-lowering therapy for long-term secondary stroke prevention?	
Always	53 (63)
Usually	25 (30)
Sometimes	5 (6.0)
Never	1 (1.2)
Do you routinely assess LDL cholesterol levels after initiating statin therapy?	
Yes	34 (40)
No	49 (58)
Did not specify	1 (1.2)
Which LDL-cholesterol target level do you aim for?	
No target	17 (20)
<100 mg/dl	51 (61)
<70 mg/dl	8 (9.5)
Depending on stroke subtype	2 (2.4)
Other	5 (6.0)
Did not specify	1 (1.2)

NOAC = New oral anticoagulant

TABLE 3 Questions regarding non-pharmacological strategies for patients after TIA or ischemic stroke: Do you systematically discuss the following lifestyle risk factors with patients after TIA or ischemic stroke?

	Always	Usually	Sometimes	Never
Tobacco use	74 (88%)	10 (11%)	0	0
Heavy alcohol use	45 (53%)	22 (26%)	16 (19%)	1 (1.2%)
Physical inactivity	35 (41%)	34 (40%)	14 (16%)	1 (1.2%)
Unhealthy diet	30 (35%)	29 (34%)	20 (23%)	5 (6.0%)
Non-adherence to medication	35 (41%)	25 (29%)	21 (25%)	3 (3.6%)

assistants (31%), and stroke nurses (32%). Table 1 details responses to questions regarding the organization of outpatient care for TIA and ischemic stroke patients.

Twenty-two (26%) respondents stated that the neurologist is primarily responsible for long-term secondary prevention for TIA and ischemic stroke patients after initial hospital assessment, 36 (43%) reported that the general practitioner is primarily responsible, 6 (7.1%) the physician assistant, 3 (3.6%) the stroke nurse, 1 (1.2%) the internist, and 4 (4.8%) reported that no one is primarily responsible. Regarding who ideally should be responsible for long-term secondary prevention after TIA and ischemic stroke, 42 (50%) respondents answered the general practitioner, 21 (25%) the neurologist, 7 (8.3%) the stroke nurse, 6 (7.1%) the physician assistant, 2 (2.4%) the internist, and 6 (7.1%) preferred a combination of either the neurologist and the general practitioner or the latter and the stroke nurse.

Pharmacological Treatment for Long-term Secondary Stroke Prevention

Overall, 75 (89%) respondents reported that the pharmacologic treatment for TIA and ischemic stroke patients is described in a local protocol. Ten (12%) respondents use clopidogrel monotherapy as first-line antiplatelet agent in secondary stroke prevention, instead of the in the Netherlands–recommended combination of acetylsalicylic acid and dipyridamole (Table 2). Among those respondents who did usually (13%) or sometimes (68%) use clopidogrel in secondary

stroke prevention, the most common reason cited were side effects of acetylsalicylic acid or dipyridamole (66%). Other reported reasons included recurrent TIA or ischemic stroke while on acetylsalicylic acid and dipyridamole (20%), acetylsalicylic acid resistance (13%), similarity in efficacy to aspirin and dipyridamole (9.5%), ease of administration (9.5%), and low costs (7.1%). When asked whether they used new oral anticoagulants as long-term secondary stroke prevention for patients with atrial fibrillation during the last year, 21 (25%) respondents reported that they did. Most respondents (83%) stated that they are planning to prescribe new oral anticoagulants in the near future.

Eleven percent of respondents reported that they always initiate antihypertensive therapy for secondary stroke prevention in patients with high blood pressure. On the contrary, 10 (12%) respondents never initiate anti-hypertensive therapy for secondary stroke prevention. Most respondents usually (33%) or sometimes (44%) initiate antihypertensive therapy for secondary stroke prevention in patients with high blood pressure. The most frequently prescribed antihypertensive agents were angiotensin-converting enzyme inhibitors (71%) and diuretics (63%). Less commonly used antihypertensive agents were calcium channel blockers (26%), angiotensin receptor blockers (17%), and beta blockers (13%). More than one third (38%) of the respondents use 2 antihypertensive agents in fixed dose combinations if indicated. The blood pressure targets reported were variable, 22 (26%) respondents use a target of 140/90 mm Hg or less for all patients, 19 (23%) respondents use a target of 130/80 mm Hg or less for all patients, and 15 (18%) respondents use a target of 140/90 mm Hg or less or 130/80 mm Hg or less for patients with diabetes mellitus. Only the minority of the respondents always (1.2%) or usually (12%) prescribe antihypertensive agents in normotensive stroke patients. Fifty-five (66%) of the respondents take patient age into account when prescribing antihypertensive agents.

In total, 53 (63%) of respondents stated that they always start a statin for secondary stroke prevention. A total of 34 (40%) respondents

reported that they check their patients' low-density lipoprotein cholesterol (LDL-C) levels routinely. Most (70%) respondents use a "treat to target" strategy, 51 (61%) use an LDL-C target level of less than 100 mg/dl (< 2.5 mmol/l), and 8 (9.5%) use a level of less than 70 mg/dl (< 1.8 mmol/l). Seventeen (20%) respondents do not use a specific LDL-C target, and 2 (2.4%) respondents use an LDL-C target depending on the ischemic stroke subtype. More than half of the respondents take patient age into account when deciding whether statin prescription is indicated.

Nonpharmacologic Strategies for Long-term Secondary Stroke Prevention

Overall, 42 (50%) of the respondents stated that the nonpharmacologic treatment for long-term secondary stroke prevention, regarding lifestyle risk factors, is described in a local protocol. The assessment and documentation of the lifestyle risk factors are variable. Nearly all respondents systematically ask for and document tobacco use (99%) and alcohol use (98%), if applicable. Less systematically body weight (68%), body mass index (42%), physical inactivity (42%), unhealthy diet (23%), and waist circumference (6.0%) are asked for and documented. Forty-four (52%) respondents always deliver lifestyle modification advice to TIA and ischemic stroke patients. Overall, 74 (88%) respondents always and 10 (12%) respondents usually discuss the importance of smoking cessation in secondary stroke prevention. The other lifestyle risk factors are less systematically addressed (Table 3).

Discussion

As hypothesized, we found considerable practice variation in long-term secondary stroke prevention among Dutch neurologists. We found considerable variation in the organization of outpatient care after initial hospital assessment, pharmacologic treatments, and

nonpharmacologic strategies. To our knowledge, this is the first study investigating practice variations in long-term secondary stroke prevention.

Although nearly all respondents reported that they follow-up TIA and ischemic stroke patients after initial hospital assessment, the type of health care workers who delivered the care, the number of follow-up visits, and follow-up duration were highly variable. There was also considerable disagreement among the respondents on who ideally should be responsible for long-term secondary prevention after TIA and ischemic stroke. Half of the respondents stated that the general practitioner should primarily be responsible for long-term secondary stroke prevention, whereas the other half of the respondents favored a hospital-based strategy. To date, it is unclear who is best suited to coordinate cardiovascular risk management for TIA and ischemic stroke patients, and further studies are needed on this topic. Irrespectively of who is or should be responsible for long-term secondary prevention after TIA and ischemic stroke, all involved health-care professionals should in our opinion work in a coordinated manner and attempt to reach a targeted standard of care. Therefore, a close collaboration between primary and secondary care is of paramount importance.

Since the results of the Profess trial, which showed similar rates of stroke recurrence with the combination of acetylsalicylic acid and dipyridamole compared with clopidogrel, the latter is a convenient alternative for antithrombotic therapy.¹⁶ This is in accordance with daily practice as in our survey 12% of respondents always and 13% usually prescribe clopidogrel monotherapy. Most of the (remaining) respondents answered that they sometimes prescribe clopidogrel in secondary stroke prevention. It seems that, although the combination of acetylsalicylic acid and dipyridamole still is the first-line antithrombotic therapy for secondary stroke prevention in the Netherlands, the use of clopidogrel monotherapy is increasing. Together with the use of antihypertensive agents in fixed dose combinations, this will improve medication adherence in TIA and ischemic stroke patients.¹⁷

This survey shows there is considerable variation in blood pressure treatment targets. Most respondents use a blood pressure target of 140/90 mm Hg or less or 130/80 mm Hg or less for all patients. This variation could possibly be explained by the lack of an absolute target blood pressure level in international ischemic stroke guidelines, although the Dutch guideline for cardiovascular risk management advises a blood pressure target of 140/90 mm Hg or less for patients with cardiovascular disease. In addition, it is remarkable that although national and international guidelines recommend starting blood pressure lowering therapy regardless the initial blood pressure, only 1 (1.2%) respondent always and 10 (12%) respondents usually commence blood pressure lowering therapy in normotensive TIA or ischemic stroke patients.⁷⁻¹⁰

A similar variation in treatment targets was found regarding lipid-lowering therapy for secondary stroke prevention. Although 53 (63%) respondents always and 25 (30%) respondents usually commence lipid-lowering therapy, only 51 (61%) respondents use the national guideline recommended LDL-C target of less than 100 mg/dl.⁷⁻¹⁰ A possible explanation for this variation could be the unclear association between LDL-C levels and stroke risk in TIA and ischemic stroke patients. Until now, studies comparing normal versus intensive LDL-C lowering strategies in patients after TIA or ischemic stroke are lacking. This may have resulted in the fact that a substantial part of the neurologists prescribe statins to ischemic stroke patients without aiming for a specific LDL-C level.

Half of the respondents reported that treatment regarding lifestyle modification advice is described in a local protocol. Most respondents always inform their TIA and ischemic stroke patients about the importance of smoking cessation. There is considerably less attention for the other lifestyle risk factors. Again, these results are in contrast with the targeted standard of care in national and international guidelines.⁷⁻¹⁰ Thus, regarding lifestyle modification, there is still much to be gained. To improve health behavior (ie, physical activity,

medication adherence, cessation of smoking, moderate alcohol intake, and healthy eating), we find that effective behavior change interventions, for example, motivational interviewing, need to be incorporated in routine clinical practice for TIA and ischemic stroke patients.¹⁸ Comprehensive cardiac rehabilitation programs, including a physical exercise program, reduce mortality in patients after myocardial infarction.¹⁹ Although TIA, ischemic stroke, and myocardial infarction share risk factors and pathologic mechanisms, a specific rehabilitation program to improve cardiorespiratory fitness, to influence secondary prevention targets, and to systematically address cardiovascular lifestyle targets has not been implemented for TIA or ischemic stroke patients. Improving adherence to guidelines and cardiovascular lifestyle changes by standardizing poststroke care, mirroring practice in cardiac rehabilitation programs, could be a promising method for increasing effectiveness of secondary stroke prevention.

The strength of this study lies in the high response rate (93%) and the fact that it was a relatively large sample of Dutch neurologists, covering nearly all Dutch Hospitals. Our study has some limitations. First, a problem inherent to an online survey is that management as reported in a questionnaire does not always reflect actual practice. Despite the high response rate of our online survey, participating stroke neurologists were not necessarily representative for the local policy. Second, because this survey does not measure the quality of care, it is not possible to determine which approach to long-term secondary prevention reduces recurrent stroke and other cardiovascular disease most. Third, because all Dutch inhabitants have an assigned general practitioner who treats chronic illnesses, including cardiovascular diseases, quality of stroke care may be better than what is perceived in this survey. Because of these factors, care must be taken into extrapolating the results. In the Netherlands, currently

a national database, developed by a national knowledge-based network for stroke professionals “Kennisnetwerk CVA Nederland” has been developed and is being implemented in collaboration with the Dutch Institute for Clinical Auditing, in which baseline variables and functional outcome at 3 months after stroke will be prospectively assessed, enabling evaluation and prognostification of stroke care in the future.

In conclusion, our survey shows considerable variation in long-term secondary stroke prevention among Dutch neurologists. These variations may have an impact on the risk for stroke recurrence and cardiovascular disease in general. Further studies are needed to address this issue and to detect possible causes for the gap between guideline recommendations and routine clinical practice, to eventually improve quality of care for TIA and ischemic stroke patients.

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REFERENCES

1. Zhang H, Thijs L, Staessen JA. Blood pressure lowering for primary and secondary prevention of stroke. *Hypertension* 2006;48:187–195.
2. Hankey GJ, Eikelboom JW. Antithrombotic drugs for patients with ischaemic stroke and transient ischaemic attack to prevent recurrent major vascular events. *Lancet Neurol* 2010;9:273–284.
3. Rothwell PM, Algra A, Amarenco P. Medical treatment in acute and long-term secondary prevention after transient ischaemic attack and ischaemic stroke. *Lancet* 2011;377:1681–1692.
4. Manktelow BN, Potter JF. Interventions in the management of serum lipids for preventing stroke recurrence. *Cochrane Database Syst Rev* 2009:CD002091.
5. Hankey GJ. Secondary stroke prevention. *Lancet Neurol* 2014;13:178–194.
6. Hackam DG, Spence JD. Combining multiple approaches for the secondary prevention of vascular events after stroke: a quantitative modeling study. *Stroke* 2007;38:1881–1885.
7. Furie KL, Kasner SE, Adams RJ, et al. Guidelines for the prevention of stroke in patients with stroke or transient ischemic attack: a guideline for healthcare professionals from the American heart association/American stroke association. *Stroke* 2011;42:227–276.
8. Perk J, de Backer G, Gohlke H, et al. European Guidelines on cardiovascular disease prevention in clinical practice (version 2012). The Fifth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of nine societies and by invited experts). *Eur Heart J* 2012;33:1635–1701.
9. The European Stroke Organisation (ESO) Executive Committee and the ESO Writing Committee. Guidelines for Management of Ischaemic Stroke and Transient Ischaemic Attack 2008. *Cerebrovasc Dis* 2008;25:457–507.
10. Multidisciplinaire richtlijn cardiovasculair risicomangement, herziening 2011. Bohn Stafleu van Loghum, ISBN 978-90-313-91769.
11. Saposnik G, Goodman SG, Leiter LA, et al. Applying the Evidence: Do Patients With Stroke, Coronary Artery Disease, or Both Achieve Similar Treatment Goals? *Stroke* 2009;40:1417–1424.
12. Chwojnicky K, Yagensky A, Wierucki L, et al. Assessment of the quality of secondary ischemic stroke prevention in selected urban areas of Poland and Ukraine: the ASCEP study results. *Eur Neurol* 2011;65:323–331.
13. Hornnes N, Larsen K, Boysen G. Little change of modifiable risk factors 1 year after stroke: a pilot study. *Int J Stroke* 2010;5:157–162.
14. Li C, Engstrom G, Janzon L, et al. Long-term stroke prognosis in relation to medical prevention and lifestyle factors. A prospective population-based study. *Cerebrovasc Dis* 2008;25:526–532.
15. Bauer A, Limburg M, Visser MC. Variation in Clinical Practice of Intravenous Thrombolysis in Stroke in the Netherlands. *Cerebrovasc Dis Extra* 2013;3:74–77.
16. Sacco RL, Diener H-C, Yusuf S, et al. Aspirin and Extended-Release Dipyridamole versus Clopidogrel for Recurrent Stroke. *N Engl J Med* 2008;359:1238–1251.
17. Thom S, Poulter N, Field J, et al. Effects of a fixed-dose combination strategy on adherence and risk factors in patients with or at high risk of CVD: the UMPIRE randomized clinical trial. *JAMA* 2013;310:918–929.

18. Taylor RS, Brown A, Ebrahim S, et al. Exercise-based rehabilitation for patients with coronary heart disease: systematic review and meta-analysis of randomized controlled trials. *Am J Med* 2004;116:682–692.