Improving Stroke Care

Quality of care and health education in patients with a stroke or transient ischemic attack

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Het verbeteren van zorg voor patiënten met een beroerte

Kwaliteit van zorg en gezondheidsvoorlichting aan patiënten met een herseninfarct of een transient ischemic attack

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By three methods we may learn wisdom:
first, by reflection, which is noblest;
second, by imitation, which is easiest;
and third, by experience, which is the bitterest.
Confucius (Chinese philosopher & reformer)

Voor mijn mannen

CONTENTS

Chapter 1

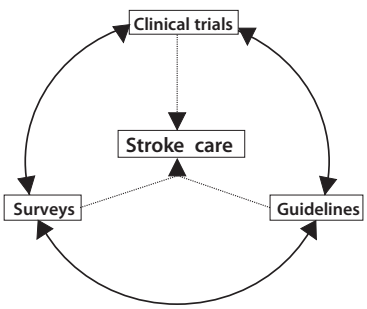
General Introduction

From scientific evidence to high quality stroke care

Medical care for patients with stroke or TIA constitutes a challenge in more than one way. Stroke is a major health problem; it is the second cause of death and the leading cause of disability in the Western world. Therefore, efficient, high quality stroke care is important to reduce this enormous burden of stroke. The past two decades, there have been many improvements in acute stroke treatment modalities, including new medications, surgical procedures and improvements in the organization of care, e.g multidisciplinary stroke units.[1] In order to assist neurologists in everyday clinical decision-making aiming to deliver adequate stroke care, evidence-based guidelines are developed for appropriate use and selection of the management options. In these guidelines, (overviews of) randomized controlled trials (RCTs) are valued as the highest level of evidence and the most reliable method of determining the effect of a treatment (Figure 1).

One of the limitations of RCTs is that they often have strict enrolment criteria, which mainly serve to limit the risk of complications. For example, multiple exclusion criteria were present in the RCTs investigating antiplatelets in stroke and TIA patients the last two decades.[2] Consequently, the question rises whether patients who participate in those RCTs are not a selected group and so only partly representative group of patients seen in routine clinical practice.

Figure 1. *Relation of clinical trials, guidelines and surveys to stroke care*



Clinical trials are the basis of guidelines, surveys will analyse whether guidelines are adhered to in practice. All these 3 elements are important in developing and improving stroke care.

Guidelines can be regarded as an important tool for improving the quality of care. Although physicians are encouraged to apply national guidelines, those guidelines cannot be applied to all individual patients. Treating patients is more complex than simply following the guidelines. Numerous factors could influence decisions made by the practicing physician, like lack of awareness and incentives, lack of time or facilities and lack of agreement with peers. Therefore, surveys are developed to evaluate the adherence to the recommended management. Surveys give feedback to clinicians about the quality of the clinical practice. In this way, variations in stroke care may be reduced and improvements can be promoted. The Netherlands Stroke Survey, an nationally integrated part of the Euro Heart Survey

Programme, provides adequate insight in stroke patient management in the Netherlands. The survey was conducted in 2002-2003 in 10 centers in the Netherlands.

In surveys, quality of care can be measured by means of performance indicators. Donabedian has argued that quality of care can be viewed as a function of three components: structure, process and outcome.[3] This framework leads to a set of performance indicators in the three different domains, based on the existing guidelines. Outcome indicators, like mortality rate, are important because they give a global impression of quality of care. Therefore, quality of care in stroke is still often evaluated by use of outcome measures, usually (standardized) mortality rates on hospital level.[4] Assessment of outcome is generally easier than assessment of process. Process indicators are indicators that reflect decision making, policies and/or clinical practices.[3] Process indicators often have a high face-validity, and inadequate performance may provide direct opportunities for intervention and improvement. Because of the potential benefits, the question raises, whether process indicators are valid and useful indicators of quality of stroke care, instead of outcome indicators.

Health education is an essential, but underexposed aspect of stroke care. Most of the RCTs that form the basis for guidelines for stroke prevention focus primarily at pharmacological intervention of vascular risk factors. Nevertheless, health behavior is regarded as an important part of primary and secondary prevention; for example physical activity has specific beneficial effects on hypertension, hyperlipidemia and obesity.[5,6] The goal of health education is to improve the patient's awareness of vascular risk factors and induces changes in behavior toward controlling risk factors and risk behavior. However, health education is not an integral part of secondary preventive stroke care in clinical practice. Some international guidelines on secondary prevention do not even have recommendations about health education in stroke and TIA patients.[1,7] Considering the trend to develop guidelines aimed at reducing cardiovascular risks by education and behavioral change, one needs evidence of RCTs focused at health education of stroke and TIA patients.

The challenges of stroke care, translating trial results adequately into clinical practice, maintaining and monitoring a high level of quality and combining medical treatment with health education in an efficient way, have in common that they are all concerned with processing evidence-based medicine, and are all meant to reduce the burden of stroke. Meeting those challenges is the objective of my thesis.

Aim and outline of this thesis

This thesis focuses on the applicability of results of clinical trials of stroke and TIA patients in everyday practice and on measurement of quality of stroke care. A third aim is to further expand an underexposed aspect of stroke care, namely health education in stroke patients.

Chapter 2.1 describes which proportion of patients in a stroke population fulfils the enrolment criteria of recently performed randomized controlled trials investigating antiplatelets in stroke patients. Chapter 2.2 focuses on the question whether the combination of low dose aspirin and dipyridamole is more effective than aspirin alone in reducing the risk of recurrent stroke and other major cardiovascular events in patients with a disabling stroke. Chapter 3.1 focuses on the measurement of quality of stroke care by

process-of-care indicators. Chapter 4.1 covers the rationale, background and design of the computer-supported individualized health education for TIA and minor stroke patients (COSTA) study. Chapter 4.2 describes the knowledge of stroke and TIA patients about this disease and accessory risk factors and treatment. The main results of the COSTA study are presented in chapter 4.3. Chapter 4.4 provides a review of the literature on health education in stroke and TIA patients. Finally, chapter 5 and 6 provide a general discussion and summary of the results of the studies presented in this thesis.

References

1. The European Stroke Organisation (ESO) Executive Committee and theESO Writing Committee. Guidelines for management of ischaemic stroke and transient ischaemic attack 2008. Cerebrovasc Dis 2008;25:457-507.
2. Rothwell PM. External validity of randomised controlled trials: "to whom do the results of this trial apply?". Lancet 2005;365:82-93.
3. Donabedian A. The quality of care. How can it be assessed? JAMA 1988;260:1743-1748.
4. Mant J. Process versus outcome indicators in the assessment of quality of health care. Int J Qual Health Care 2001;13:475-480.
5. Mora S, Cook N, Buring JE, Ridker PM, Lee IM. Physical Activity and Reduced Risk of Cardiovascular Events: Potential Mediating Mechanisms. Circulation 2007;116:2110-2118.
6. Manson JE, Greenland P, LaCroix AZ et al. Walking compared with vigorous exercise for the prevention of cardiovascular events in women. N Engl J Med 2002;347:716-725.
7. Sacco RL, Adams R, Albers G et al. Guidelines for prevention of stroke in patients with ischemic stroke or transient ischemic attack: a statement for healthcare professionals from the American Heart Association/American Stroke Association Council on Stroke: co-sponsored by the Council on Cardiovascular Radiology and Intervention: the American Academy of Neurology affirms the value of this guideline. Stroke 2006;37:577-617.

Chapter 2

Generalizability of trial results

Chapter 2.1

Patients enrolled in large randomized clinical trials of antiplatelet treatment for prevention after TIA or ischemic stroke are not representative of patients in clinical practice

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Abstract

Background: Many randomized clinical trials (RCT) have evaluated the benefit of long-term use of antiplatelet drugs in reducing the risk of new vascular events in patients with a recent TIA or ischemic stroke. Evidence from these trials forms the basis for national and international guidelines for the management of nearly all such patients in clinical practice. However, abundant and strict enrolment criteria may limit the validity and the applicability of results of RCTs to clinical practice. We estimated the eligibility for participation in landmark trials of antiplatelet drugs of an unselected group of patients with stroke or TIA from a national stroke survey.

Methods: 972 patients with TIA or ischemic stroke were prospectively and consecutively enrolled in the Netherlands Stroke Survey. We applied 7 large antiplatelet trials' enrolment criteria.

Results: In total, 886 patients were discharged alive and available for secondary prevention. Mean follow-up was 2.5 years. The annual rate of TIA, stroke or non-fatal myocardial infarction was 6.7%. The proportions of patients fulfilling the trial enrolment criteria ranged from 25% to 67%. Mortality was significantly higher in ineligible patients (27-41%) than in patients fulfilling enrolment criteria (16-20%). Rates of vascular events were not higher in trial-eligible patients than in ineligible patients.

Conclusions: Our data confirm that TIA and stroke patients enrolled in RCTs are only partially representative of patients in clinical practice. Use of less strict enrolment criteria could enhance generalizibility and result in more efficient selection of patients for randomized clinical trials.

Introduction

Stroke and coronary heart disease are the leading causes of death and disability among adults.[1] Among those who survive ischemic stroke, the long term risk of major vascular events is at least 5% annually.[2] In the last decades several treatments for the prevention of recurrent stroke and other vascular events have been proven safe and effective. Randomized clinical trials (RCTs) indicated that aspirin alone reduces the relative risk of stroke and other major vascular events by 13%.[3] The addition of extended release dipyridamole (400 mg/d) to aspirin contributes a further 18% (9% to 26%) reduction in relative risk of serious vascular events.[4-6]

Well-designed and well-conducted RCTs are the best method to estimate the effect of an intervention. Evidence from RCTs forms the basis for many general clinical guidelines. RCTs often have strict enrolment criteria, which mainly serve to limit the risk of complications. Moreover, stroke prevention trials often require additional risk factors or symptoms beyond the presenting clinical syndrome in order to select patients who are at a higher risk for an outcome event and to increase homogeneity and statistical power. One study[7] found that additional enrolment criteria in datasets from trials conducted between 1976 and 1994, increased the risk of outcome events only slightly. The authors also suggested that these additional enrolment criteria would make recruitment more difficult, and might limit external validity.

The aim of our study was to estimate the eligibility for participation in landmark trials of antiplatelet drugs of an unselected group of patients with stroke or TIA from a national stroke survey. We assessed the effect of additional enrolment criteria by comparing baseline characteristics, cardiovascular events and mortality rates between trial-eligible and trial-ineligible patients.

Methods

Study population

The Netherlands Stroke Survey was conducted in 10 centres in the Netherlands. The participating sites included 2 small centres (< 400 beds), 5 of intermediate size (400 to 800 beds) and 4 large centres (>800 beds). Two centres were university hospitals. All centres had a neurology department, a neurologist with expertise in stroke and a multidisciplinary stroke team. All but one hospital had a stroke unit, 8 were participating in a regional stroke service, and 9 were equipped for thrombolytic therapy. These institutions deliver care to approximately 10% of all acute stroke patients in The Netherlands, and their size and stroke expertise can be considered representative of stroke care in the Netherlands.[8,9] All patients who were admitted to the neurology department or seen in the outpatient clinic with suspected acute stroke or TIA between October 2002 and May 2003 were screened. Patients were enrolled consecutively and prospectively if the initial diagnosis of first or recurrent acute brain ischemia was confirmed by the neurologist's assessment and if symptom onset was less than 6 months ago. All patients were admitted to the neurology department and were followed throughout their hospital stay. All patients or their proxies provided informed consent and the Medical Ethics Committees and Review Boards of the

participating hospitals approved the study. Centers were allowed to enrol patients until a local target, proportional to hospital size and compatible with an overall target of 900 patients was reached.

Data collection

Trained research assistants collected all data from the patients' hospital charts, within 5 days after discharge. Research assistants worked independently of the hospital team. All data were entered into the electronic case record form and transferred regularly to a central database via Internet. The overall proportion of missing values was 0.2%. At 1 and 3 years, survival status was obtained through the Civil Registries. In all survivors a telephone interview was conducted by trained research assistants based on a structured questionnaire, which was sent to the patient in advance. The data collectors confirmed the diagnosis by information obtained from general practitioners and hospital discharge letters. An experienced vascular neurologist checked all collected information and the subsequent diagnosis. Follow-up of the last patients was completed in December, 2006. Follow-up information at 3 years, including vital status was complete in 86% of the patients. More details on the study population and methods of data collection can be found in earlier publications.[8,9]

Trial selection

We compared patients in the RCTs with those enrolled in the Netherlands Stroke Survey. Therefore we selected trials that focused only on antiplatelet therapy for secondary prevention after a recent ischemic stroke or transient ischemic attack.Trials that reported a subgroup analysis of patients with recent TIA or ischemic stroke were included as well. Registers (Cochrane database, Current Controlled trials, Pubmed (Medline) and EMBASE) were systematically searched. We included multicenter international, randomized controlled trials which investigated or are still investigating antiplatelet therapy for secondary prevention. Enrolment had to be started after 1990. We included 6 trials: ESPS-2, CAPRIE, TACIP, MATCH, ESPRIT, PRoFESS.[10-16] The first 3 trials assessed the effectiveness and safety of antiplatelet agents compared with aspirin or placebo and were published before the start of this survey.[10,13,16] The results of MATCH (aspirin + clopidogrel versus clopidogrel alone)[17] and ESPRIT (a three-armed trial comparing anticoagulation with coumarines, or aspirin with dipyridamole with aspirin alone) were published during the follow-up of our survey.[4] Results of the PRoFESS study (dipyridamole + aspirin versus clopidogrel alone) were published in 2008.[18]

Identifying trial-eligible survey patients

We excluded patients from the Stroke Survey who did not survive up to hospital discharge, because those patients are ineligible for secondary prevention. Major enrolment criteria for the 6 RCTs were extracted from the published trial protocols,[10-16] and summarized in Table 1.

Table 1. *Major in- and exclusion criteria of selected randomized clinical trials*

Year of publication	ESPS 2 1996	CAPRIE 1996	TACIP 2003	MATCH 2004	ESPRIT 2006	PRoFESS 2008
Drug comparison	ASA, DP or both vs placebo	Clopidogrel vs. ASA	Triflusal vs. ASA	ASA vs. placebo on top of clopidogrel	ASA vs.ASA and DP	ASA and DP vs. clopidogrel
Number of participants	6602	6431	2113	7599	2739	20333
Major inclusion criteria						
Age (years)	>18	>21	=>40	>40	No age limit	>55 or 50-54*
Diagnosis	Stroke or TIA	Stroke	Stroke or TIA	Stroke or TIA	Stroke or TIA	Stroke
Additional criteria	none	none	None	1 or more RF	mRS <4	2 or more RF*
Inclusion time window	3 months	>1 week <6 months	6 months	3 months	6 months	3/3-4 months*
Exclusion criteria						
Related to diagnosis						
Cerebral or subarachnoid haemorrhage	Excluded	Excluded	Excluded	Excluded	Excluded	Excluded
Cardiac source of embolism	Excluded	-	-	Excluded	Excluded	-
Stroke cause other than atherosclerosis	-	Excluded	Excluded	-	Excluded	Excluded
Related to bleeding risk						
Gastrointestinal bleeding/peptic ulcer	Excluded	-	Excluded	Excluded	-	Excluded
Bleeding disturbances	Excluded	Excluded	-	Excluded	-	-
(History of) Thrombocytopenia, neutropenia	-	Excluded	-	-	Excluded	Excluded
Anaemia	-	-	-	-	Excluded	-
History of intracranial haemorrhage	-	-	-	-	-	Excluded
Major surgery or trauma < 6 weeks	Excluded	-	-	-	-	-
Related to prognosis						
Uncontrolled hypertension	Excluded	Excluded	-	-	Excluded	Excluded†
Systolic BP <= 120 mmHg	-	-	-	-	-	Excluded
Uncontrolled diabetes	Excluded	-	-	-	-	-
Severe renal dysfunction ‡	Excluded	Excluded	Excluded	-	-	Excluded
(Acute) hepatic dysfunction §	-	Excluded	Excluded	Excluded	-	Excluded
Hyperkaliemia	-	-	-	-	-	Excluded
Unstable AP or MI < 3 months	-	-	Excluded	-	-	Excluded
Endarterectomy < 1 month	Excluded	Excluded	Excluded	Excluded	Excluded	Excluded

Table 1 (continued). *Major in- and exclusion criteria of selected randomized clinical trials*

Year of publication	ESPS 2 1996	CAPRIE 1996	TACIP 2003	MATCH 2004	ESPRIT 2006	PRoFESS 2008
Related to current medical conditions						
Life – threatening disease	Excluded	Excluded	Excluded	Excluded	Excluded	Excluded
Dementia	Excluded	Excluded	-	Excluded	-	Excluded
Unconsciousness	Excluded	-	-	-	-	Excluded
Dysphagia	Excluded	-	-	-	-	-
Pregnancy	Excluded	Excluded	-	-	-	Excluded
Severe disability	-					Excluded
Related to concomitant therapy						-
Anticoagulants	Excluded	Excluded	Excluded	Excluded	Excluded	Excluded
NSAIDS	Excluded	Excluded	Excluded	-	-	-
Angiotensin II receptor blocker	-	-	-	-	-	Excluded

ASA=Aspirin, DP=dipyridamole, RF=risk factor
**2 additional risk factors and 50 to 54 years or those with strokes within 3-4 months*
† systolic >180 mmHg or diastolic > 95 mmHg
‡ creatinine clearance <30 ml/min according to the Cockcroft formula
§ ASAT/ALAT > 3 upper limit

We then distinguished 5 categories of exclusion criteria: related to diagnosis, prognosis, bleeding risk, current medical condition and to concomitant therapy. Exclusion criteria related to diagnosis and prognosis form the criteria aimed at selection of patients at high risk for (recurrent) vascular events. Exclusion criteria related to bleeding risk, current medical condition and concomitant therapy represent safety criteria. We considered patients who were severely disabled and therefore not eligible for participating in a secondary prevention trial if they had a score on the modified Rankin scale (mRS) of more than 4 at discharge, when they were living in a nursing home before hospital admission, conducted to a nursing home for permanent residence after discharge, or when patients had a severely disabling recurrent ischemic stroke, intra-cerebral hemorrhage, or a hip fracture during hospital stay.

End points

The end point was the first occurrence of non-fatal myocardial infarction, stroke or TIA, or death, during the follow-up period, which extended from hospital discharge until the three-year follow-up visit. Endpoints were patient-reported; confirmation was sought from general practitioners and hospital discharge letters. Cause of death was not registered in our survey.

Statistical analyses

Dichotomous data are described as numbers and percentages, and continuous data are presented as means with standard deviations. Comparison between trial-eligible and trial-ineligible patients were analysed by Chi-square test.

We estimated the number of patient-years-at-risk and combined this with the number of first non-fatal vascular events to compute an event rate. Data on patients who did not reach an endpoint were censored on the date of the patients' last assessment. Non-fatal event rates and mortality rates were calculated and compared with Chi-square tests. STATA10 statistical software was used for all analyses.

Results

The Stroke Survey population consisted of 972 patients who were evaluated because of ischemic stroke or TIA. Of all patients, 86 (8.8%) died before discharge, leaving 886 patients suitable for secondary prevention. In our survey, 238 (61%) of the 393 outpatients had a TIA and 60 (10%) of the 579 admitted patients had a TIA. In total, 38% of all patients had a TIA (Table 2). Mean follow-up was 2.4 years (SD 1.2). In our study 2% of the patients were lost to follow-up at 1 year, and 13% at three years. There were no significant differences in age, risk profile, trial-eligibility, mortality and non-fatal event rate at 1 year between patients lost and patients with a complete follow-up at 3 years. The demographic and clinical characteristics of the survey population are presented in Table 2. The patients were more often male (56%) than female, and had a mean age of 68.6 (SD 13) years (range 21-95) (Table 2).

Table 2. *Characteristics of patients enrolled in randomized trials as compared to trial-eligible and trial-ineligible patients in the Netherlands Stroke Survey*

	Stroke Survey	**ESPS 2 1996**	**ESPS 2 eligible**	**ESPS 2 ineligible**	**CAPRIE 1996**	**CAPRIE eligible**	**CAPRIE ineligible**	**TACIP 2003**	**TACIP eligible**	**TACIP ineligible**	**MATCH 2006**	**MATCH eligible**	**MATCH ineligible**
N	*886*	6602	556 (63%)	330 (37%)	6431	286 (32%)	600 (68%)	2107	592 (67%)	174 (33%)	7599	224 (25%)	662 (75%)
Mean age, yr	*68.6*	66.7	**66.0**	**72.9**	64.6	**67.5**	**69.1**	64.5	**67.2**	**70.7**	66.3	69.6	68.2
Male gender	*56%*	58%	59%	53%	64%	58%	56%	66%	**60%**	**52%**	63%	**65%**	**54%**
History													
Cerebrovascular disease	*19%*	-	**17%**	**24%**	19%	18%	20%	22%	18%	22%	27%	**42%**	**11%**
Hypertension	*58%*	61%	58%	61%	65%	**66%**	**55%**	62%	60%	57%	78%	63%	58%
Hyperlipidemia	*40%*	23%	36%	42%	38%	41%	39%	39%	43%	34%	56%	45%	38%
Diabetes	*17%*	15%	***15%***	***21%***	26%	18%	17%	24%	15%	22%	68%	**38%**	**10%**
Current smoker	*33%*	24%	35%	30%	22%	37%	32%	31%	34%	33%	48%	33%	34%
Ischemic heart disease	*10%*	35%	**9%**	**12%**	12%	9%	10%	2%	10%	10%	5%	**23%**	**6%**
Qualifying event													
Stroke	*62%*	76%	**50%**	**81%**	100%	**100%**	**44%**	74%	**48%**	**83%**	79%	55%	64%
TIA	*38%*	23%	**50%**	**19%**	0%	**0%**	**56%**	26%	**52%**	**17%**	21%	46%	33%
Stroke severity													
mRS 0-1-2	*77%*	69%	**92%**	**51%**		**84%**	**73%**	82%	**91%**	**48%**	74%	**88%**	**73%**
mRS 3-5	*23%*	31%	**8%**	**49%**		**16%**	**27%**	18%	**9%**	**52%**	26%	**12%**	**27%**

Bold=significant difference $p < 0.05$
mRS=modified Rankin Scale

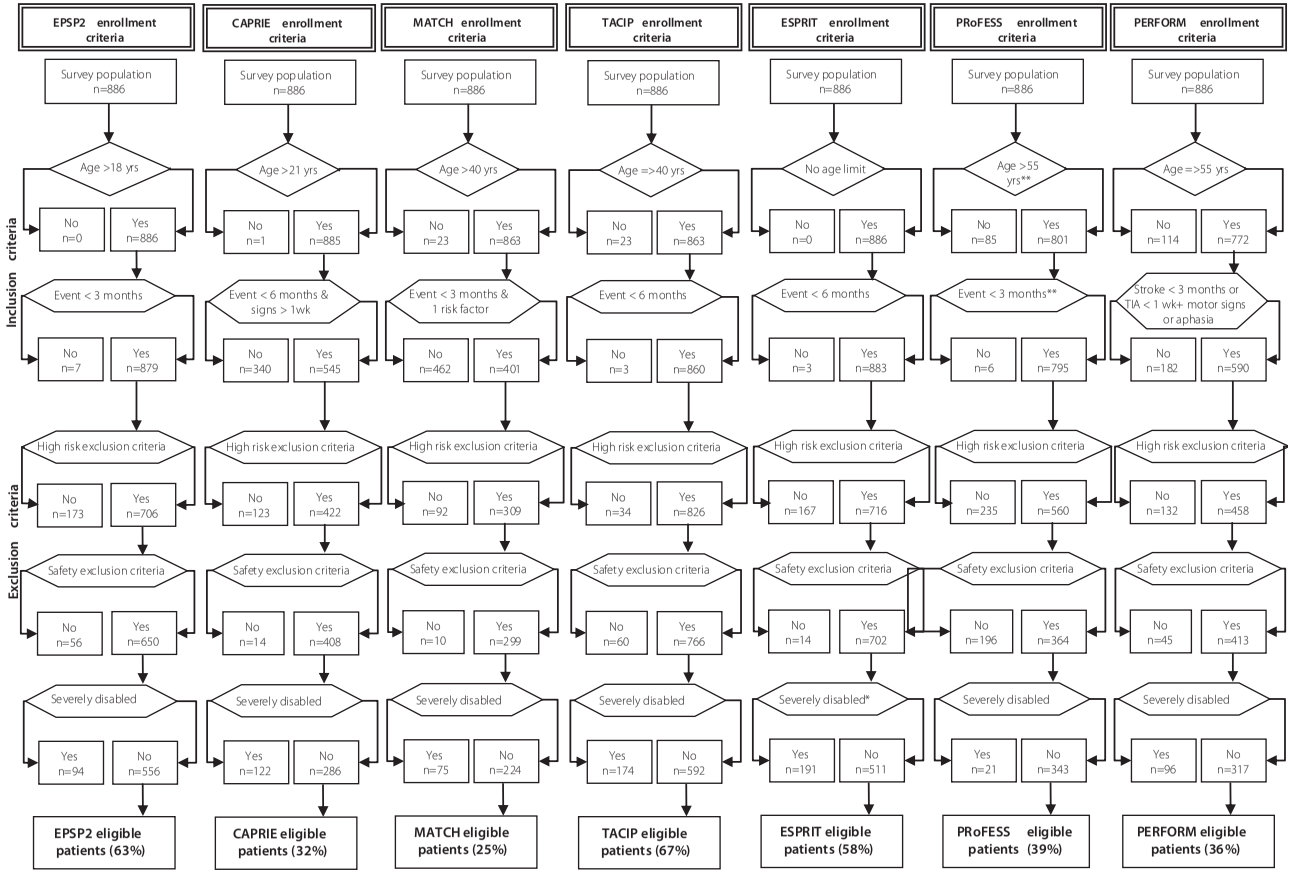
Table 2 (continued). *Characteristics of patients enrolled in randomized trials as compared to trial-eligible and trial-ineligible patients in the Netherlands Stroke Survey*

	Stroke Survey	**ESPRIT 2006**	**ESPRIT eligible**	**ESPRIT ineligible**	**PRoFESS 2008**	**PRoFESS eligible**	**PRoFESS ineligible**
N	*886*	2739	511 (58%)	375 (42%)	20333	343 (39%)	543 (61%)
Mean age, yr	*68.6*	63	**65.5**	**72.8**	66	68.9	68.4
Male gender	*56%*	66%	**59%**	**52%**	64%	59%	55%
History							
Cerebrovascular disease	*19%*	12%	**15%**	**25%**	24%	**15%**	**25%**
Hypertension	*58%*	60%	57%	61%	74%	**65%**	**55%**
Hyperlipidemia	*40%*	47%	**44%**	**34%**	47%	**48%**	**35%**
Diabetes	*17%*	19%	**14%**	**22%**	28%	16%	18%
Current smoker	*33%*	37%	35%	31%	21%	32%	35%
Ischemic heart disease	*10%*	7%	9%	11%	23%	21%	17%
Qualifying event							
Stroke	*62%*	67%	**46%**	**83%**	100%	**52%**	**68%**
TIA	*38%*	33%	**54%**	**17%**	0%	**48%**	**32%**
Stroke severity							
mRS 0-1-2	*77%*	94%	**95%**	**52%**	76%	**93%**	**66%**
mRS 3-5	*23%*	6%	**5%**	**48%**	24%	**7%**	**34%**

Bold=significant difference $p < 0.05$
mRS=modified Rankin Scale

As Figure 1 indicates, varying proportions of patients enrolled in the Stroke Survey would have qualified for participating in the MATCH (25%), CAPRIE (32%), PROFESS (39%), ESPRIT (58%), ESPS-2 (63%) and TACIP (67%). Exclusion criteria aimed at selection of high-risk patients of an outcome event and being severely disabled were the most important reasons for disqualification of patients as trial-eligible. If severely disabled patients in our Stroke Survey would have been considered as trial-eligible, the proportion of trial-eligible patients would increase by 10 to 20%. Trial-eligible patients differed from those who did not qualify for inclusion in a trial. Patients who did not qualify for participation in a trial were significantly older, except for the MATCH and PRoFESS trial. Trial-eligible patients had significantly better scores on the mRS at the time of assessment for inclusion (Table 2). Consistent with the results of the selected trials, more trial-eligible patients were male. There were no consistent significant differences in the cardiovascular risk profile between patients who participated in trials and those who were trial-ineligible. Mortality rates of hospital survivors during the 3 years follow-up period differed between study eligible and study ineligible patients (Table 3).

Figure 1: *The influence of in- and exclusion criteria of trials investigating antiplatelet drugs for secondary prevention on the proportion of eligible patients in the Netherlands Stroke Survey.*



*Severely disabled in ESPRIT study is Rankin > 3

** or 50-54 yrs or stroke 3-4 months with 2 additional risk factors

Table 3. *Mortality rates and vascular event rates of non-fatal myocardial infarction, stroke or TIA in trial-eligible (E) and trial-ineligible (IE) patients per trial.*

	N at risk		Mortality rate (%/yr)		Rate difference (CI 95%)	Event rate (%/yr)		Rate difference (CI 95%)
	E	IE	E	IE		E	IE	
ESPS2	556	330	9.6	12.1	2.5 (-0.7-5.7)	6.3	7.7	1.4 (-1.1-4.0)
CAPRIE	286	600	7.4	12.0	4.6 (1.7–7.4)	6.4	6.9	0.5 (-1.9–3.0)
TACIP	592	294	7.0	18.6	11.6 (7.8–15.5)	6.5	7.4	0.9 (-1.7–3.6)
MATCH	224	662	7.6	11.4	3.8 (0.7-6.8)	8.0	6.3	-1.7 (-4.6-1.1)
ESPRIT	511	375	5.4	18.7	13.3 (9.6–16.7)	6.1	7.8	1.7 (-0.8–4.2)
PRoFESS	343	543	5.9	13.8	7.9 (5.1–10.7)	5.3	7.8	2.5 (0.1-4.8)

Trial-ineligible patients had a significantly higher mortality rate, 11.4-18.7 %/yr versus 5.4-9.6%/yr in trial-eligible patients. The annual rate of TIA, stroke or non-fatal myocardial infarction was 6.7% for all 886 patients. The rates of a first non-fatal vascular event (myocardial infarction, stroke or TIA) were not increased in trial-eligible patients of all studies, except for the MATCH trial where the trial-eligible patients had a tendency to have a vascular event more often.

Discussion

Our study showed that patients enrolled in international, multicenter randomized clinical trials of antiplatelet treatment for secondary prevention after TIA and stroke are not fully representative of patients treated in daily practice. After applying the trials' in- and exclusion criteria to the Stroke Survey population, 33% to 75% of all patients in our Stroke Survey were not eligible for participation. We also show that trial-eligible patients were younger and had a better clinical outcome than those who did not fulfil enrolment criteria. As only a small proportion of patients in clinical practice is trial-eligible, the question should be raised whether it is justified to extrapolate the results of the RCTs to the clinical practice. For example, Mant et al.[19] found important differences between the characteristics of patients with cerebrovascular disease in primary care with those of the participants in the PROGRESS trial.[20] This so-called lack of external validity or generalizability of RCT results may be one explanation for the widespread underuse in clinical practice of treatments that were beneficial in trials and that have been recommended in guidelines.[21]

Our results are consistent with findings of other studies in different clinical domains. In a review of 41 US National Institutes of Health RCTs an average exclusion rate of 73% was reported.[22] Another study showed that of the candidates for thrombolysis in the Copenhagen stroke study, 96% were ineligible based on the various criteria of the relevant RCTs.[23]

The strength of our survey was the inclusion of a large number of unselected and consecutively enrolled patients from multiple hospitals in the Netherlands with a confirmed diagnosis of TIA or stroke, leading to a cohort that is representative of clinical stroke care in the Netherlands.

A limitation of our study is that its scope is national. Most of the RCTs we studied, enrol patients worldwide. Because of differences between countries in methods of diagnosis and management, our Stroke Survey is not completely representative for stroke care worldwide. There was a lack of information on several minor exclusion criteria employed in the RCTs we studied. When these data would have been available, the proportion of patients fulfilling the enrolment criteria would have been smaller. In our study we aimed to distinguish between trial-eligible and trial-ineligible patients in our Stroke Survey population. We considered patients trial-eligible if they fulfilled the inclusion criteria and had no major exclusion criteria. We excluded patients who were severely disabled at discharge, as they probably would not have participated in a RCT. If we had not done this, but strictly applied the enrolment criteria to all our Stroke Survey patients 10-20% more patients would have been eligible, but in our opinion this would not have been realistic. Another limitation is that endpoints in the register were self-reported by patients; a telephone interview was conducted by trained research assistants based on a structured questionnaire. One could argue that especially the endpoint TIA is not a reliable outcome with the method of outcome ascertainment as used. However, we do not think that the use of this not so robust outcome measure does distract importantly from the findings of the study.

Our results may provide an optimistic view of the representativeness of clinical trials. Our survey involved voluntarily participating hospitals, and therefore the results may be biased towards better than average practice, with lower rates of recurrent vascular events. The possibility of early inclusion of hospitalized patients with recent ischemic stroke, as was done in the PRoFESS trial [18], may have biased the comparison with our cohort. However, patients were required to be "stable" and mortality within the first few days after stroke is mostly caused by the index event, not by recurrent vascular events. Therefore, we consider the risk of bias small.

In our study we have focused on randomized clinical trials of antiplatelet treatment for secondary prevention in TIA and stroke patients. This included trials that primarily included TIA or stroke patients, or reported a subgroup of patients with recent TIA or ischemic stroke. We chose this approach in order to directly compare our results of stroke patients with those of stroke patients in the trials. The CHARISMA[24] and BRAVO trials[25,26], which also investigated antiplatelets in stroke and TIA patients, did not report subgroup analyses of stroke patients.

A last limitation is that we could only study non-fatal cardiovascular and cerebrovascular events, as cause of death was not available in our dataset. As it concerns a systematic difference, the comparison between trial related in- and exclusion criteria will not be affected.

Enrolment criteria aimed at selecting patients at high risk of vascular events event were ineffective in our survey population. For example the MATCH trial, which required additional risk factors for eligibility[7, 27] had the lowest proportion of study eligible patients (25%) in our Stroke Survey. MATCH-eligible patients did not have a significantly increased risk of vascular events compared to MATCH-ineligible patients (Table 3), but there is a trend towards more vascular events in MATCH-eligible patients, in contrast to the other trials.

Howard et al.[7] analyzed the consequences of requiring additional risk factors in trials, as in the MATCH trial. They found that additional eligibility criteria undermine generalizability. Our data indicate that ineligible patients are older, more often female or suffered a more severe stroke. To our knowledge, no clinical trials have reported follow-up in excluded patients. Subgroup analyses in trials are not often reported, and individual patient meta analyses of antiplatelet therapy in stroke are scarce. But so far, subgroup analyses in trials and individual patient meta-analyses do not raise a concern for a differential treatment effect of antiplatelets among these subgroups.[28] This provides further arguments for using wide inclusion criteria and for limiting exclusion criteria as much as possible in phase III RCT.

Our results confirm that RCTs investigating antiplatelets enrol patients that are only partially representative of the entire spectrum of patients with TIA or stroke in clinical practice. Furthermore, we demonstrated that currently employed enrolment criteria were not successful in selecting patients at a high risk of a vascular event. However, the enrolment criteria were successful in selecting patients on safety criteria. Use of less strict enrolment criteria could result in easier, more efficient and valid selection of patients for randomized clinical trials.

References

1. Truelsen T, Mahonen M, Tolonen H, Asplund K, Bonita R, Vanuzzo D. Trends in stroke and coronary heart disease in the WHO MONICA Project. Stroke 2003;34:1346-1352.
2. van Wijk I, Kappelle LJ, van GJ et al. Long-term survival and vascular event risk after transient ischaemic attack or minor ischaemic stroke: a cohort study. Lancet 2005;365:2098-2104.
3. Algra A, van Gijn J. Cumulative meta-analysis of aspirin efficacy after cerebral ischaemia of arterial origin. J Neurol Neurosurg Psychiatry 1999;66:255.
4. ESPRIT Study Group. Aspirin plus dipyridamole versus aspirin alone after cerebral ischaemia of arterial origin (ESPRIT): randomised controlled trial. Lancet 2006;367:1665-1673.
5. O'Donnell MJ, Hankey GJ, Eikelboom JW. Antiplatelet therapy for secondary prevention of noncardioembolic ischemic stroke: a critical review. Stroke 2008;39:1638-1646.
6. Verro P, Gorelick PB, Nguyen D. Aspirin plus dipyridamole versus aspirin for prevention of vascular events after stroke or TIA: a meta-analysis. Stroke 2008;39:1358-1363.
7. Howard SC, Algra A, Warlow CP, Rothwell PM. Potential consequences for recruitment, power, and external validity of requirements for additional risk factors for eligibility in randomized controlled trials in secondary prevention of stroke. Stroke 2006;37:209-215.
8. Scholte Op Reimer WJ, Dippel DW, Franke CL et al. Quality of hospital and outpatient care after stroke or transient ischemic attack: insights from a stroke survey in the Netherlands. Stroke 2006;37:1844-1849.
9. Lingsma HF, Dippel DW, Hoeks S et al. Variation between hospitals in patient outcome after stroke is only partly explained by differences in quality of care. Data from the Netherlands Stroke Survey. J Neurol Neurosurg Psychiatry 2008;79:888-894.
10. CAPRIE Study Group. A randomised, blinded, trial of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE). Lancet 1996;348:1329-1339.
11. De Schryver EL. Design of ESPRIT: an international randomized trial for secondary prevention after non-disabling cerebral ischaemia of arterial origin. European/Australian Stroke Prevention in Reversible Ischaemia Trial (ESPRIT) group. Cerebrovasc Dis 2000;10:147-150.
12. De Schryver EL. ESPRIT: protocol change. Cerebrovasc Dis 2001;11:286.
13. Diener HC, Cunha L, Forbes C, Sivenius J, Smets P, Lowenthal A. European Stroke Prevention Study. 2. Dipyridamole and acetylsalicylic acid in the secondary prevention of stroke. J Neurol Sci 1996;143:1-13.
14. Diener HC, Bogousslavsky J, Brass LM et al. Management of atherothrombosis with clopidogrel in high-risk patients with recent transient ischaemic attack or ischaemic stroke (MATCH): study design and baseline data. Cerebrovasc Dis 2004;17:253-261.
15. Diener HC, Sacco R, Yusuf S. Rationale, design and baseline data of a randomized, double-blind, controlled trial comparing two antithrombotic regimens (a fixed-dose combination of extended-release dipyridamole plus ASA with clopidogrel) and telmisartan versus placebo in patients with strokes: the Prevention Regimen for Effectively Avoiding Second Strokes Trial (PRoFESS). Cerebrovasc Dis 2007;23:368-380.
16. Matias-Guiu J, Ferro JM, varez-Sabin J et al. Comparison of triflusal and aspirin for prevention of vascular events in patients after cerebral infarction: the TACIP Study: a randomized, double-blind, multicenter trial. Stroke 2003;34:840-848.
17. Diener HC, Bogousslavsky J, Brass LM et al. Aspirin and clopidogrel compared with clopidogrel alone after recent ischaemic stroke or transient ischaemic attack in high-risk patients (MATCH): randomised, double-blind, placebo-controlled trial. Lancet 2004;364:331-337.
18. Sacco RL, Diener HC, Yusuf S et al. Aspirin and extended-release dipyridamole versus clopidogrel for recurrent stroke. N Engl J Med 2008;359:1238-1251.
19. Mant J, McManus RJ, Hare R. Applicability to primary care of national clinical guidelines on blood pressure lowering for people with stroke: cross sectional study. BMJ 2006;332:635-637.
20. Randomised trial of a perindopril-based blood-pressure-lowering regimen among 6,105 individuals with previous stroke or transient ischaemic attack. Lancet 2001;358:1033-41.
21. Rothwell PM. External validity of randomised controlled trials: "to whom do the results of this trial apply?". Lancet 2005;365:82-93.

22. Charlson ME, Horwitz RI. Applying results of randomised trials to clinical practice: impact of losses before randomisation. Br Med J (Clin Res Ed) 1984;289:1281-1284.
23. Tissue plasminogen activator for acute ischemic stroke. The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. N Engl J Med 1995;333:1581-1587.
24. Bhatt DL, Fox KA, Hacke W et al. Clopidogrel and aspirin versus aspirin alone for the prevention of atherothrombotic events. N Engl J Med 2006;354:1706-1717.
25. Topol EJ, Easton JD, Amarenco P et al. Design of the blockade of the glycoprotein IIb/IIIa receptor to avoid vascular occlusion (BRAVO) trial. Am Heart J 2000;139:927-933.
26. Topol EJ, Easton D, Harrington RA et al. Randomized, double-blind, placebo-controlled, international trial of the oral IIb/IIIa antagonist lotrafiban in coronary and cerebrovascular disease. Circulation 2003;108:399-406.
27. Rothwell PM. Lessons from MATCH for future randomised trials in secondary prevention of stroke. Lancet 2004;364:305-307.
28. Halkes PH, Gray LJ, Bath PM et al. Dipyridamole plus aspirin versus aspirin alone in secondary prevention after TIA or stroke: a meta-analysis by risk. J Neurol Neurosurg Psychiatry 2008;79:1218-1223.

Chapter 2.2

Prevention with low dose aspirin plus dipyridamole in patients with disabling stroke

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Abstract

Background: The combination of low dose aspirin and dipyridamole is more effective than aspirin alone in reducing the risk of recurrent stroke and other major cardiovascular events in patients with a recent transient ischemic attack or minor stroke. It is unknown whether this also applies to patients with a disabling stroke.

Methods: We reanalyzed the data of 5700 patients from ESPRIT and ESPS-2 to study the effect of aspirin and dipyridamole according to mRS at baseline. Primary outcome was vascular events (stroke, myocardial infarction or vascular death). We used proportional hazards regression to estimate the treatment effect across modified Rankin Scale (mRS) strata at baseline, and we tested for interactions with treatment.

Results: In total, 426 patients (7.5%) had an mRS score of 4 or 5 at baseline. The risk of an outcome event increased with mRS. The relative risk associated with the combination of aspirin and dipyridamole compared to aspirin alone in patients with mRS 0 to 5 was 0.79 (95% CI: 0.69 to 0.91). The relative risk according to mRS subcategory 0 to 4 at baseline varied between 0.73 and 0.96 for vascular events and between 0.62 and 0.96 for stroke. The number of patients with mRS 5 was too small for reliable estimates, but the data suggest a beneficial effect. There was no evidence of interaction between treatment effect and mRS at baseline.

Conclusion: The beneficial effect of the combination of low dose aspirin and dipyridamole was present in all subcategories of the mRS.

Introduction

Two large randomized clinical trials have shown that the combination of aspirin and dipyridamole is more effective than aspirin alone in reducing the risk of stroke and other major vascular events in patients with a recent transient ischemic attack (TIA) or minor ischemic stroke.[1,2] Patients who participated in these trials may not have been representative of patients with a recent TIA or ischemic stroke in general. We and others showed that patients in antiplatelet trials are generally younger, have less comorbidity and less severe strokes than patients in hospitals and population surveys.[3-5] This may raise concerns about extrapolation of trial results to all patients with a recent TIA or minor ischemic stroke.

Of particular interest is stroke severity. Patients with disabling stroke may have a high risk of recurrent vascular events, including ischemic stroke in other vascular territories. However, more severely disabled patients may benefit less because of a limited lifespan and susceptibility to other than vascular complications. We reanalyzed the data of ESPRIT and ESPS-2 to study the effect of the combination aspirin and dipyridamole in relation to subcategories of the modified Rankin Scale (mRS) at baseline.

Methods

We pooled the data concerning patients treated with aspirin plus dipyridamole and aspirin alone, from two multicenter randomized clinical trials (mRCT). ESPRIT was an open label mRCT in which the effect of low dose aspirin (30-325 mg daily) and dipyridamole (200 mg, twice daily) was compared with low dose aspirin alone. Patients with a TIA or minor ischemic stroke (mRS grade ≤3) in the previous 6 months were eligible for the trial.[1] The mean follow-up was 3.5 years. ESPS-2 was a double blind mRCT with a 2x2 factorial design, that compared low dose aspirin (25 mg twice daily), and dipyridamole (200 mg, twice daily) in combination or alone, with placebo.[2] Patients with a TIA or stroke that occurred in the preceding 3 months were included. All patients were followed for 2 years, or until death.

The primary outcome was defined as vascular event, i.e. the composite of non-fatal stroke, non-fatal myocardial infarction (MI), or vascular death. We used Cox proportional hazards regression to estimate the effect of aspirin and dipyridamole versus aspirin alone, for each outcome, across mRS strata at baseline, and we tested for interaction between treatment and mRS.

Results

Information on the mRS at baseline was missing in 338 patients (5.6%) of 6038 patients included in the trials, leaving 5700 patients with complete baseline data for evaluation. In total, 426 patients (7.5%) had mRS>3 at baseline. The risk of an outcome event increased with higher scores on the mRS (Table 1).

The overall hazard ratio for vascular events associated with the combination of aspirin and dipyridamole compared to aspirin alone was 79% (RRR: 20.6% (95% CI: 8.9% to 30.8%)).

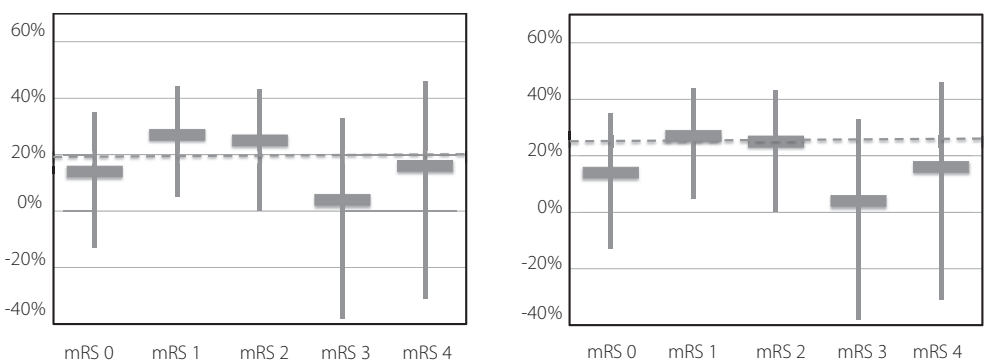
The hazard ratio for vascular events in mRS categories 0 to 4 ranged from 73% to 96% (Table 1). The hazard ratio for stroke in mRS categories 0-4 ranged from 62% to 96%.

Table 1. *Effect of aspirin (ASA) and dipyridamole (DIP) compared with aspirin alone, according to handicap at baseline (modified Rankin score (mRS)), on the occurrence of fatal or non-fatal vascular events (upper table), and fatal or non-fatal stroke (lower table). Data are expressed as events/patient-years at risk. Effects are expressed as hazard ratios with 95% confidence intervals (CI), adjusted for study.*

	ASA+DIP N=2839	ASA N=2861	HR (95% CI)
Vascular events			
All patients	366/7122 (5.1%)	460/7091 (6.5%)	0.80 (0.69 – 0.91)
mRS=0	94/2593 (3.6%)	107/2519 (4.2%)	0.86 (0.65 – 1.13)
mRS=1	95/2275 (4.2%)	128/2239 (5.7%)	0.73 (0.56 – 0.95)
mRS=2	83/1352 (6.1%)	117/1430 (8.1%)	0.75 (0.57 – 1.00)
mRS=3	59/567(10.4%)	61/557 (10.9%)	0.96 (0.67 – 1.38)
mRS=4	34/316 (10.8%)	45/334 (13.2%)	0.84 (0.54 – 1.31)
mRS=5	1/19.5 (5.1%)	4/11.8 (34%)	0.18 (0.02 – 1.59)
			p-interaction = 0.99
Stroke			
Overall	255/7181 (3.6%)	334/7161 (4.7%)	0.76 (0.65 – 0.90)
mRS=0	66/2609 (2.5%)	67/2550 (2.6%)	0.96 (0.69 – 1.35)
mRS=1	76/2289 (3.3%)	93/2258 (4.1%)	0.80 (0.59 – 1.08)
mRS=2	56/1375 (4.1%)	90/1446 (6.2%)	0.65 (0.46 – 0.90)
mRS=3	37/571 (6.5%)	49/560 (8.8%)	0.75 (0.49 – 1.15)
mRS=4	19/317 (6.0%)	33/334 (9.9%)	0.62 (0.35 – 1.09)
mRS=5	1/19.6 (5.1%)	2/11.8 (16.9%)	0.34 (0.03 – 3.74)
			p-interaction = 0.12

The number of patients in mRS 5 was too small for precise estimates, but the data suggest a beneficial effect in this category as well. The relative risk reductions with 95% confidence interval corresponding to the hazard ratios are displayed in Figure 1.

Figure 1. *Relative risk reduction (RRR) with 95% confidence intervals, for categories of the modified Rankin score at baseline, by the combination of aspirin and dipyridamole compared with aspirin alone in a pooled analysis of data from ESPS-2 and ESPRIT.[1,2] Left graph: RRR for vascular events, right graph: RRR for stroke. The dashed line indicates the point estimate for the effect of aspirin and dipyridamole. Both estimates were adjusted for study.*



There was no evidence of interaction between the treatment effect and baseline mRS. More precisely, it could be estimated from the regression models that the probability of an interaction effect that would at least annihilate the effect of treatment on the occurrence of vascular events among patients with mRS 4 would be 13% and the probability of a similarly sized interaction effect on stroke events would be 2.3%.

Discussion

Previous publications on the effect of dipyridamole and aspirin did not report on a differential effect according to disability at baseline. In most trials of antiplatelet treatment, the proportion of patients with severe stroke (mRS>3) was small. This can be explained by active exclusion of severely disabled patients, by a lower likelihood of being asked to participate and by clustering of exclusion criteria. Also, analyses of effects and adverse events were not specifically reported for this subgroup.[5]

In the present study, we found that the beneficial effect of the combination of low dose aspirin and dipyridamole compared with aspirin alone applied to all subcategories of the mRS. Therefore, optimal prevention in patients with disabling stroke should include the combination of aspirin and dipyridamole instead of aspirin alone.

References

1 The ESPRIT Study Group. Aspirin plus dipyridamole versus aspirin alone after cerebral ischaemia of arterial origin (ESPRIT): randomised controlled trial. Lancet 2006;367:1665-73.

2 Diener HC, Cunha L, Forbes C, Sivenius J, Smets P, Lowenthal A. European Stroke Prevention Study 2. Dipyridamole and acetylsalicylic acid in the secondary prevention of stroke. J Neurol Sci 1996;143:1-13.

3 Howard SC, Algra A, Warlow CP, Rothwell PM. Potential consequences for recruitment, power, and external validity of requirements for additional risk factors for eligibility in randomized controlled trials in secondary prevention of stroke. Stroke 2006;37:209-15.

4 O'Donnell MJ, Hankey GJ, Eikelboom JW. Antiplatelet therapy for secondary prevention of noncardioembolic ischemic stroke: a critical review. Stroke 2008;39:1638-46.

5 Maasland L, van Oostenbrugge RJ, Franke CF, Scholte Op Reimer WJ, Koudstaal PJ, Dippel DWJ. Patients enrolled in large randomized clinical trials of antiplatelet treatment for prevention after transient ischemic attack or ischemic stroke are not representative of patients in clinical practice: the Netherlands Stroke Survey. Stroke 2009;40:2662-8.

Chapter 3

Quality of care

Chapter 3.1

Validity of process indicators of quality of in-hospital stroke care

Insights from The Netherlands Stroke Survey

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Submitted

Abstract

Background: The use of process indicators to assess the quality of in-hospital stroke care has been advocated because they offer high face-validity, and provide direct opportunities for intervention. However, single process indicators may not be representative of overall quality of stroke care. We used data from a multicenter survey of in-hospital stroke care of patients with ischemic stroke to assess the validity of different process indicators across domains and areas.

Methods: In total, 579 admitted patients with acute stroke were prospectively enrolled in 10 centers. We selected 29 process-of-care indicators and categorized them along 2 axes: the domains of diagnostic, cure and care procedures (3 elements) and the areas of acute or preventive management procedures (2 elements), resulting in a matrix containing 6 fields. We attributed a score of 1 to an indicator when the procedure was indicated and carried out in a single patient. We calculated standardized mean subscores for each field in the matrix. We then derived subtotals per domain and area, and a total score by adding up subscores. Linear regression analyses with adjustment for clustering per hospital were performed to relate process indicators with domain, area and total scores.

Results: In acute management, scores for swallowing test, physical therapy on day 1, speech therapy or occupational therapy, CT/MRI, laboratory investigation on admission and antiplatelet therapy had a statistically significant association with scores in the relevant area and domain, and with the total score. In preventive management, carotid imaging, laboratory tests including total and LDL cholesterol, glucose, consultation by a rehabilitation physician, antiplatelet treatment within 48 hours and temperature lowering drugs on indication, were associated with significantly higher domain scores, area scores and total score.

Conclusions: Fourteen of the 29 process indicators in our study were not a valid indicator of the overall quality. This implies that the overall quality of stroke care should be measured by means of carefully selected sets of indicators across all domains of clinical stroke care.

Introduction

Quantifying and improving the quality of stroke care is increasingly recognized as important in health care. In the Helsingborg conference one stated that the goal to be achieved in 2015 of quality assessment is that all countries aim to establish a system for the routine collection of data needed to evaluate the quality of stroke management, including patient safety issues.[1]

According to Donabedian's concept, assessments of health care quality should distinguish structure, process and outcome.[2] Quality performance measures have been proposed for these three domains in a Scientific Forum.[3] Outcome indicators are important because they may give a global impression of quality of care. In assessing overall quality of a service their interpretation is difficult, because of differences in case-mix,[4] and because global outcome measures may cover differences in quality of care in separate domains. Process-of-care indicators or performance indicators often have a high face-validity, and inadequate performance may provide direct opportunities for intervention and improvement.[5] A serious drawback is the requirement to routinely collect data on many aspects of the care process from many different sources, because hospital-based stroke care has a broad spectrum with different care aspects in the acute and chronic phase. Whether high performance in one domain implies good quality of care in another is unknown. The aim of this study was therefore to assess the validity of various process-of-care indicators by comparing them across several domains of in-hospital stroke care. Secondary, we aimed to determine which process-of-care indicators best represent the total spectrum of quality of stroke care.

Methods

Definitions

Quality indicators are explicit standards of care against which actual clinical practice is judged. Process refers to the use of appropriate diagnostic and therapeutic modalities for individual patients.

Study population

The Netherlands Stroke Survey was conducted in 10 centres in the Netherlands. The participating sites included 2 small centres (< 400 beds), 5 of intermediate size (400 to 800 beds) and 4 large centres (>800 beds). All centres had a neurology department, a neurologist with expertise in stroke and a multidisciplinary stroke team. All but one hospital had a stroke unit. These institutions together deliver care to approximately 10% of all acute stroke patients in The Netherlands, and their size and stroke expertise can be considered representative of stroke care in the Netherlands.[4,6]

In the Netherlands, all stroke patients are admitted to a neurology ward, not to departments of internal medicine or geriatrics. All acute stroke patients who were admitted to the neurology department between October 2002 and May 2003 were screened. Patients were enrolled consecutively and prospectively if the initial diagnosis of first or recurrent acute brain ischemia was confirmed by the neurologist. All patients were followed throughout their hospital stay. They or their proxies provided

informed consent and the Medical Ethics Committees and Review Boards of the participating hospitals approved the study. Centers were allowed to enrol patients until a local target of at least 30 patients, proportional to hospital size and compatible with an overall target of 900 patients. In total, 972 patients were enrolled in The Netherlands Stroke Survey; 393 visited an outpatient clinic and 579 were admitted.

Data collection

Trained research assistants collected data from the patients' hospital charts, within 5 days after discharge. Research assistants worked independently of the hospital team. All data were entered into the electronic Case Record Form and were transferred regularly to a central database via Internet. The overall proportion of missing values was 0.2%. More details on the study population and methods of data collection can be found in earlier publications.[4,6]

Selection of quality process-of-care indicators

We used the recommendations of national and international guidelines, the Helsingborg conference and the First Scientific Forum of assessment of Quality of Care and Outcomes Research in Cardiovascular Disease and Stroke as the basis of the selection for process-of-care quality indicators.[1, 3, 7, 8] We selected 29 process-of-care indicators and categorized them along 2 axes: the domains of diagnostic, cure and care procedures (3 elements) versus the areas of acute or preventive management (2 elements), resulting in a matrix of 6 fields (Table 1). We computed subscores for the three domains and for the two areas. Each indicator was considered present in a patient when the diagnostic or therapeutic procedure was considered indicated according to national guidelines, and was carried out. For example, the indicator for percutaneous endoscopic gastrostomy (PEG) tube was scored 1 when carried out in patients with swallowing difficulty that was present for more than 2 weeks. Otherwise the indicator scored 0.

Statistical analyses

To measure differences between the hospitals within the different process-of-care fields, we gave a binary score to every indicator, see Table 1. We calculated a mean subscore per field and rescaled to a range of 0-1 to make comparisons between fields possible. Furthermore, we computed weighted subscores per domain and area and a total score by adding up subscores of the 6 fields. Both the subscores of the areas acute and preventive care, along the horizontal axis of our matrix, had a maximum of 3 points, subscores of the domains (vertical axis) of diagnosis, care and cure a maximum of 2 points and the maximum total score varied from 0-6 points. We calculated the weighted average of the domains, areas and total scores per hospital. Student's *t* was used to assess the association of the average score on a single process indicator with the weighted averages on a domain subscore, or the total score (after leaving out the contribution of the particular process indicator). Linear regression analyses with adjustment for clustering per hospital were performed to relate process indicators with area, domain and total scores. We thereby took into account that indicator scores of patients in each hospital were likely correlated. This measure of quality assessment was not validated externally.

Table 1. *Matrix of process-of-care indicators (N=579).*

Area	Acute management		Preventive management	
Domain				
Diagnostic	CT/MRI	567 (98)	Carotid Imaging in patients with indication*	89/115 (77)
	ECG	555 (96)	Laboratory tests	560 (97)
	Laboratory test	564 (98)	Total cholesterol	430 (74)
			LDL cholesterol	323 (56)
			Glucose	545 (94)
			Cardiologist	210 (37)
Care	Swallowing test *	203 (65)	Rehabilitation consultant*	246 (49)
	Indwelling bladder catheter*	108 (21)	PEG tube insertion in patients with swallowing problems > 2 weeks	7 (22)
	Intravenous fluid *in patients without parental feeding	198 (39)		
	Mobilisation on day 1 after admission*	121 (24)		
	Physical therapy on day 1 after admission *	106 (21)		
	Compression stockings†	1 (20)		
	Speech therapy*	244 (49)		
	Occupational therapy*	223 (44)		
Cure	Thrombolysis	40 (7)	Carotid endarterectomy within 6 months in patients with carotid stenosis >70%‡	9/52 (17)
	Acetylsalicyclic acid < 48 hours after stroke onset	479 (83)	Antiplatelet therapy in patients without AF	448/480 (93)
	Acetylsalicyclic acid in patients without OAC arriving < 48 hours	393/431 (91)	Oral anticoagulants in patients with AF	59/99 (60)
			Antihypertensive therapy in hypertensive patients	258/346 (75)
			Cholesterol lowering therapy in patients with hypercholesterolemia	134/188 (71)
			Antibiotics in patients with pneumonia or urinary tract infection	74/84 (88)
			Temperature lowering drug in patients with fever >38 °C	55/126 (44)

OAC=oral anticoagulations
PEG=percutaneous endoscopic gastrostomy
**in patients with brain infarction , N=510*
† in patients with intracerebral hemorrhage
‡Barthel Index>18 and no brainstem or cerebelllar symptoms or isolated hemianopsia

Results

Baseline

The study population consisted of 579 patients who were admitted to the hospital because of stroke. The remaining 393 of the total 972 patients in the Netherlands Stroke Survey visited the outpatient clinic. Mean age was 70.4 (+/-13.2), 311 patients were male (54%). The majority of patients (510, 88%) had a brain infarction and 536 (93%) had one or more vascular risk factors (Table 2).

Table 2. *Patient characteristics*

	N (%)
Male gender	311 (54)
Mean age, year	70.4
Vascular risk factors	
Hypertension	346 (60)
Hyperlipidemia	335 (58)
Diabetes Mellitus	119 (21)
Atrial fibrillation	99 (17)
Peripheral vascular disease	57 (10)
Ischemic heart disease	116 (20)
Previous stroke/TIA	144 (25)
Thrombolysis	40 (7)
Stroke subtype	
Brain infarction	510 (88)
TIA	60 (10)
Amaurosis fugax	3 (1)
Hemorrhagic infarction	6 (1)

Performance of indicators

Most patients received the recommended diagnostic investigations in the acute and prevention phase, with the exception of consultation by a cardiologist and performance of echocardiography (Table 1). Cure indicators, mostly concerning medical treatment, were present in the majority of patients, except for thrombolytic therapy (40 patients, 7%), temperature lowering drug treatment in patients with fever (55/126, 44%) and carotid endarterectomy in patients with symptomatic carotid stenosis of more than 70% (9/52, 17%) (Table 1). Procedures involving care were less often performed than advocated in national guidelines, with the exception of intravenous fluid in patients without enteral feeding (48%), speech therapy (49%), consultation of a rehabilitation consultant (49%) and occupational therapy (44%). The mean score of the all process indicators across the different hospitals was 2.80 (SD 0.61) (Table 3)

out of maximal 6 points. All hospitals performed better on process indicators for acute care than for preventive care. This is illustrated by the difference between the subscores of 0.41 (95%CI:0.37-0.45) in favor of the acute score. In general, hospitals performed better on diagnostic process indicators than on indicators in the cure and care domains.

Table 3. *Mean total and subscores of process-of-care indicators per domain or area per hospital*

Hospital	N	Total*	Acute management**	Preventive management**	Diagnosis†	Care†	Cure†
1	37	3.02	1.58	1.44	1.75	0.69	0.59
2	85	2.88	1.70	1.18	1.63	0.54	0.72
3	104	2.87	1.65	1.21	1.72	0.53	0.62
4	118	2.81	1.64	1.17	1.70	0.46	0.65
5	25	2.78	1.62	1.16	1.58	0.53	0.68
6	42	2.77	1.57	1.21	1.67	0.50	0.60
7	58	2.70	1.53	1.17	1.76	0.32	0.61
8	43	2.63	1.63	1.00	1.57	0.43	0.63
9	43	2.58	1.47	1.10	1.72	0.18	0.68
10	24	2.53	1.50	1.02	1.60	0.40	0.53
Mean	**579**	**2.80**	**1.60**	**1.19**	**1.67**	**0.50**	**0.63**

** maximum = 6 points*
***maximum =3 points*
†maximum= 2 points

The association of process indicators with quality scores

In the area of acute management of patients with cerebral infarction, a higher score on the domain, area and total score was associated with a swallowing test, physiotherapy from day after admission, speech or occupational therapy, CT/MRI or laboratory investigation on admission and treatment with acetylsalicylic acid within 48 hrs after admission in the absence of a contra-indication (Table 4a). Intravenous thrombolysis was only strongly associated with the acute management domain score and total score.

In preventive management, carotid imaging, laboratory tests, including total and LDL cholesterol, glucose, consultation of a rehabilitation consultant, and antiplatelets or temperature lowering drugs if indicated, were significantly associated with a higher score at the domain, area and total score (Table 4b).

Table 4a. *Effect of the performance of the acute process-of-care indicators on the total score, relevant domain and area (acute) scores.*

Process-of-care indicators	Relevant domain	Prevalence % (Range hospitals)	Increase in total score* (95% CI)	Increase in acute score* (95% CI)	Increase in relevant domain score* (95% CI)
CT/MRI	diagnosis	98 (95-100)	**0.81** (0.47-1.15)	**0.30 (**0.14-0.47)	**0.33** (0.12-0.54)
ECG	diagnosis	96 (88-100)	**0.50** (0.21-0.78)	0.16 (-0.01-0.33)	**0.35** (0.22-0.48)
Laboratory test	diagnosis	98 (96-100)	**0.94** (0.64-1.24)	**0.52** (0.39-0.66)	**0.45** (0.27-0.63)
Swallowing test	care	65 (28-100)	**0.25** (0.16-0.39)	**0.15** (0.07-0.22)	**0.15** (0.07-0.23)
Intravenous fluid	care	39 (14-66)	0.07(-0.03-0.17)	**0.07** (0.00-0.12)	0.05 (-0.01-0.11)
Mobilisation on day 1	care	24 (3-44)	**0.20** (0.07-0.33)	**0.08** (0.00-0.15)	0.04 (-0.04-0.11)
Physiotherapy on day 1	care	21 (2-38)	**0.41** (0.28-0.54)	**0.21** (0.13-0.29)	**0.21** (0.17-0.29)
Compression stockings	care	20 (0-100)	**	**	**
Speech therapy	care	49 (3-71)	**0.32** (0.21-0.43)	**0.15** (0.08-0.21)	**0.23** (0.17-0.30)
Occupational therapy	care	44 (0-57)	**0.46** (0.35-0.57)	**0.12** (0.05-0.19)	**0.33** (0.28-0.39)
Indwelling bladder catheter	care	21 (14-35)	NC	NC	NC
Thrombolysis	cure	7 (0-24)	**0.21** (0.00-0.44)	**0.37** (0.22-0.51)	0.02 (-0.06-0.02)
Antiplatelets < 48 hours after admission	cure	83 (63-97)	**0.41** (0.31-0.50)	**0.43** (0.44-0.52)	0.02 (-0.01-0.04)
Antiplatelets in patients without OAC < 48 hours after admission	cure	91 (71-100)	**0.48** (0.27-0.70)	**0.31** (0.19-0.43)	**0.29** (0.20-0.38)

Table 4b. *Effect of the performance of the preventive process-of-care indicators on the total score, relevant domain and area (preventive) scores*

Process-of-care indicators	Relevant domain	Prevalence % (Range hospitals)	Increase in total score* (95% CI)	Increase in preventive score* (95% CI)	Increase in relevant domain score* (95% CI)
Carotid Imaging	diagnosis	77 (11-92)	**0.31** (0.20-0.41)	**0.28** (0.21-0.34)	**0.18** (0.14-0.23)
Laboratory tests	diagnosis	97 (58-100)	**0.95** (0.68-1.21)	**0.62** (0.44-0.80)	**0.71** (0.60-0.82)
Total cholesterol	diagnosis	74 (54-94)	**0.51** (0.40-0.63)	**0.43** (0.35-0.50)	**0.32** (0.27-0.37)
LDL cholesterol	diagnosis	56 (3-84)	**0.40** (0.30-0.51)	**0.38** (0.31-0.46)	**0.31** (0.28-0.35)
Glucose	diagnosis	94 (91-100)	**0.33** (0.05-0.61)	**0.24** (0.04-0.43)	**0.32** (0.19-0.45)
Cardiologist	diagnosis	37 (13-49)	0.02 (-0.08-012)	0.04 (-0.03-0.10)	0.02 (-0.02-0.05)
PEG tube insertion	care	22 (0-50)	NC	NC	NC
Rehabilitation consultant	care	49 (27-85)	**0.23** (0.13-0.32)	**0.11** (0.05-0.17)	**0.08** (0.03-0.12)
Carotid endarterectomy	cure	17 (0-75)	NC	NC	NC
Antiplatelet therapy	cure	88 (74-100)	**0.77** (0.56-0.98)	**0.25** (0.10-0.40)	**0.41** (0.31-0.51)
Oral anticoagulants	cure	60 (20-100)	NC	NC	NC
Antihypertensive therapy	cure	75 (48-86)	NC	0.02 (-0.07-0.11)	0.02 (-0.05-0.10)
Cholesterol lowering therapy	cure	71 (60-89)	0.12 (-0.05-0.31)	0.08 (0.03-0.19)	0.03(-0.06-0.11)
Antibiotics	cure	88 (50-100)	0.09 (-0.29-0.47)	0.20(-0.47-0.45)	NC
Temperature lowering drug	cure	44 (0-100)	**0.35** (0.14-0.56)	**0.21** (0.07-0.31)	**0.19** (0.07-0.35)

**in the absence of the indicator, **number too small for statistic analysis, NC = negative coefficient; decrease in score in the absence of the indicator, OAC = oral anticoagulation, PEG = percutaneous endoscopic gastrostomy*

Discussion

Our study shows that only fifteen of the 29 process indicators used in our study were a valid indicator of the overall quality of in-hospital stroke care in patients with ischemic stroke. Most process indicators in our study measure one aspect of care or at an isolated moment. For example, in the Netherlands, the percentage of patients receiving intravenous thrombolysis is frequently used as standard indicator for the total quality of process-of-care. This indicator comprises, however, only one aspect of stroke care, namely acute management. Our data suggest that this indicator by itself is not representative for the total in-hospital stroke care. In other words, a single process indicator will not suffice to measure total quality of stroke care of patients with an ischemic stroke. This suggests that the overall quality of stroke care should be measured by means of a carefully selected set of process indicators. The strength of measuring process is to indicate in which patients process-of-care is incomplete and where improvements can be made.

In different countries national registers have been developed with the aim to set benchmarks for high quality stroke care and to monitor performance of hospitals against a national standard for stroke care, like the Swedish RIKS-Stroke[9,10] and the Scottish Stroke Care Audit (SSCA).[11,12] From 2009, in the SSCA,[11,12] 6 indicators for inpatients quality stroke care have been validated; admission to a stroke unit within one day, brain CT or MRI on day of admission, treatment with aspirin within 1 day of admission, swallow screen within 1 day of admission, carotid endarterectomy within 2 weeks of the most recent event and for thrombolysis to treat to at least five patients per 100 000 population each year and 80% of patients receive the bolus within one hour of arrival. The audit reports from SSCA gives also data on use of antiplatelet drugs, blood pressure lowering, cholesterol lowering and warfarin use in those with ischaemic stroke and AF. The Get With The Guidelines (GWTG)-Stroke program[13] is a quality improvement program to stimulate adherence to stroke guidelines. In this study with data of more than 300.000 patients in 790 hospitals, 7 performance measures were used:thrombolysis in patients who arrive < 2 hr after symptom onset; antithrombotic medication within 2 days of admission; deep venous thrombosis (DVT) prophylaxis during hospitalization; discharge use of antithrombotic medication; discharge use of anticoagulation for atrial fibrillation; treatment for LDL >100 mg/dL; and counseling or medication for smoking cessation. The program was associated with substantial percentage improvements in all the performance measures over more than 4 years. The RIKS-Stroke[9,10], a Swedish national quality register for stroke care evaluate stroke units in routine clinical care. Is it an extended register, in which in the acute phase the use of CT/MRI, carotid ultrasound, swallow screen, NIHHS score and level of consciousness are measured. Furthermore they used pharmaceutical treatment, including thrombolysis as performance indicators.

In the mentioned studies above, as in our survey, process-of-care indicators were selected on the basis of the combination of strength of evidence, clinical relevance and feasibility. In our survey we assessed all the indicators mentioned in the studies of the SSCA en GWTG[13], except the percentage patients admitted to a stroke unit within one day, smoking cessation and DVT prophylaxis, because those data were not available. The indicators in the Scottish Stroke Care Audit focused on those parameters which

have the best evidence for having an effect on patient outcomes e.g. stroke unit care, swallowing assessments, brain scanning, acute aspirin use, delays to assessments in neurovascular clinics and use of secondary prevention drugs. In the GWTG[13] predominantly concern medical management of acute stroke, i.e. acute cure management in our matrix, except for smoking cessation counseling. In our survey we focused both on acute and preventive stroke care and on medical and non-medical process-of-care indicators. The indicators used in the Scottish Stroke Care Audit were valid process-of-care indicators of the overall quality in our Survey, except for the new indicators thrombolysis and carotid endartectomy. Only the indicators antithrombotic medication within 2 days of admission and discharge use of antiplatelets in the GWTG[13] project had a statistically significant higher score on the relevant domain, area and total score; i.e. were representative of overall stroke care quality in our study.

In a review of process indicators used to evaluate stroke care it was concluded that many indicators have been published, but a quarter did not conform with current guidelines.[14] The authors advised a set of indicators, including rehabilitation interventions. In our study we used process indicators recommended by (inter)national guidelines. We remark that is difficult to align process indicators with all international guidelines because of the marked variation international in stroke care.

The strength of our survey was the inclusion of unselected and consecutively enrolled patients from multiple hospitals in the Netherlands with a confirmed diagnosis of TIA or stroke, leading to a cohort that is representative of clinical stroke care in the Netherlands.

Several limitations of the present study deserve consideration. First, the scope of our study was national and the numbers per hospital are small in comparison with other studies and surveys, like the GWTG project.[13] Because of differences between countries in methods of diagnosis and management, our Stroke Survey may not be entirely representative for stroke care worldwide. However, stroke care in the Netherlands has a high standard and conforms to international guidelines and the collected data per patient were detailed and extensive. The second limitation is that the survey was performed in 2002-2003. Quality of stroke care may have improved hereafter, but not substantially. Third, no data were available in our Stroke Survey about risk factor and lifestyle modification and patient education. Both may comprise relevant process indicators, but they are not easy to measure; moreover, the evidence is less strong than for medical treatment. Fourth, in the Netherlands Stroke Survey we did not acquire data on timeliness of investigations and interventions. Such data may indicate efficiency of logistics, and therefore good quality of care.

Our data showed that single process indicators will not suffice to measure quality of care. Therefore we recommend to use a package of different process indicators that represents the total spectrum of stroke care, i.e. acute, preventive, medical and non medical care (Table 5).

Table 5. *Process-of-care indicators associated with significant higher total score and relevant area and domain scores*

Area	Acute management	Preventive management
Domain		
Diagnostic	CT/MRI Laboratory test	Carotid Imaging in patients with indication Laboratory tests Total cholesterol LDL cholesterol Glucose
Care	Swallowing test Physical therapy on day 1 after admission Speech therapy Occupational therapy	Rehabilitation consultant
Care	Antiplatelet therapy in patients without OAC arriving < 48 hours after admission	Antiplatelet therapy in patients without AF Temperature lowering drug in patients with fever > 38 ℃

OAC=oral anticoagulation
AF=atrial fibrillation

An ideal package should include indicators with level 1 evidence, but it is important to recognize that stroke care is complex. Many important care elements may never be tested in randomized controlled trials and therefore important process indicators with a lower level of evidence must inevitably be included in quality assessment. Furthermore, the ideal package of indicators must be easy to measure, likely influence outcome and be generally available in all hospitals. In addition, a set of indicators should reduce the variability in published process indicators and permit more accurate benchmarking and reliable comparisons between hospitals and countries. Moreover, indicators must not be performed in almost all patients, as for example CT scan of the brain, because in that case they will not discriminate anymore. Also process-of-care indicators need regular re-evaluation; carrying out a certain procedure may be indicative of high quality care today, but it may be part of standard routine in every hospital tomorrow. This also implies that a valid combination of quality indicators may change over time, but will also differ between countries, even within Western Europe.

References

1. Kjellström T, Norrving B, Shatchkute A. Helsingborg Declaration 2006 on European Stroke Strategies. Cerebrovascular Diseases 2007;23:229-241.
2. Donabedian A. The quality of care. How can it be assessed? JAMA 1988;260:1743-1748.
3. Measuring and Improving Quality of Care: A Report From the American Heart Association/American College of Cardiology First Scientific Forum on Assessment of Healthcare Quality in Cardiovascular Disease and Stroke. Stroke 2000;31:1002-1012.
4. Lingsma HF, Dippel DW, Hoeks S et al. Variation between hospitals in patient outcome after stroke is only partly explained by differences in quality of care. Data from the Netherlands Stroke Survey. J Neurol Neurosurg Psychiatry 2008;79:888-894.
5. Mant J. Process versus outcome indicators in the assessment of quality of health care. Int J Qual Health Care 2001;13:475-480.
6. Scholte Op Reimer WJ, Dippel DWJ, Franke CL et al. Quality of hospital and outpatient care after stroke or transient ischemic attack: insights from a stroke survey in the Netherlands. Stroke 2006;37:1844-1849.
7. Kwaliteitsinstituut voor de Gezondheidszorg CBO. Diagnostiek, behandeling en zorg voor patiënten met een beroerte .
8. Heuschmann PU, Biegler MK, Busse O et al. Development and implementation of evidence-based indicators for measuring quality of acute stroke care: the Quality Indicator Board of the German Stroke Registers Study Group (ADSR). Stroke 2006;37:2573-2578.
9. Asplund K, Hulter AK, Norrving B, Stegmayr B, Terent A, Wester PO. Riks-stroke - a Swedish national quality register for stroke care. Cerebrovasc Dis 2003;15 Suppl 1:5-7.
10. Birgitta Stegmayr, Eva-Lotta Glader. Five Years with Riks-Stroke. The Swedish National Registry for Quality. Assessment of Acute Stroke Care. http://www.riks-stroke.org/index.php?content=&lang=eng
11. Dennis M. Developing a National System to Monitor the Quality of Hospital-based Stroke Service. http://www.nhshealthquality.org/nhsqis/files/Hospital_Stroke_Services_Feb06.pdf
12. Scottish Stroke Care Audit 2009 national report. Stroke Services in Scottish Hospitals.Data relating to 2007-2008. http://www.strokeaudit.scot.nhs.uk/Downloads/files/SSCA_ExecutiveSummary_2008.pdf.
13. Schwamm LH, Fonarow GC, Reeves MJ et al. Get With the Guidelines-Stroke is associated with sustained improvement in care for patients hospitalized with acute stroke or transient ischemic attack. Circulation 2009;119:107-115.
14. Purvis T, Cadilhac D, Donnan G, Bernhardt J. Systematic review of process indicators: including early rehabilitation interventions used to measure quality of acute stroke care. Int J Stroke 2009;4:72-80.

Chapter 4

Health education in patients with a stroke or transient ischemic attack

Chapter 4.1

The COSTA study

The background of the COSTA study

The last 20 years, there have been many improvements in stroke treatment modalities, including new medications, like alteplase for intravenous thrombolysis, and organized multidisciplinary stroke units.[1] These treatment modalities aim to decrease stroke mortality and disability. Because of the age increase in western populations, the population risk of recurrent vascular events and vascular dementia after TIA and stroke is still considerable. Therefore, secondary prevention is an important part of stroke care. An important angle to improve secondary prevention may be patient awareness of stroke risk factors and changes in behavior toward controlling risk factors. This awareness can be enhanced by health education. At population level there is no proof that more knowledge about stroke and risk perception directly leads to healthy lifestyle behavior. More knowledge could lead to a better stage of motivation, which is a step in the cascade of changing lifestyle behavior.[2] The difference between prevention in population or patients is that patients had an event, so they know what they could prevent. Also there is a physician-patient relation which could help patients adhere to healthy behavior and medication regimens. Information provided by the treating physician or a stroke nurse has the advantage of being delivered personally, thereby generating emotional impact. Nevertheless, the information and the way health education is presented may be of varying quality between and within professionals, which may lead to deficient information transfer. Computerized health education could augment patient-physician interaction by being an extension of the face-to-face care. Computerized health education has the advantage of being delivered consistent and systematic. Computers could combine audio, video, text and graphics to communicate educational messages. Patients are allowed to study at their own pace, meaning that this type of education is suitable even for people with lower educational level. Interventions can be distinguished along a continuum, from generic, or one-size-fits-all to highly individualized, tailored approaches[3] (Figure 1).

Figure 1: *Intervention types continuum*

Personalized messages address the recipient of the information by name and or other characteristics. The content however, may not be adapted to the individual's diagnostic, behavioral or motivational characteristics. Targeted message content is customized to reach a specific subgroup of the population. Targeted interventions do not account for individual differences in needs among individuals.

Tailored interventions are messages based on specific individual's characteristics. The message content is specific to the (unique) combination of relevant factors that may exist in an individual at a point in time. The material is not fixed and feedback is based on individual, not subgroup, characteristics. The information needed to tailor the message can be obtained through medical records and specific questionnaires. The technique which uses computers to generate materials attuned to the characteristics

of one person is called computerized tailoring.[4]

The last two decades computers are gaining popularity as a tool for providing information and health education. Studies of computerized health education across a number of health areas other than stroke have been carried out, like diabetes[5], cancer, arthritis[3,6,7], asthma[8], hypertension[9] and coronary heart disease.[10] Evidence for a beneficial effect on health outcome is not consistent, due to the heterogeneity of the disease, the target population and study designs. There is a trend that computerized health education improves knowledge, symptoms, satisfaction and reduce medical malpractice.[6] The effect on objective clinical outcomes is not consistent. Subject age did not appear to affect the acceptability of the computerized educational methods. Positive results were shown for patients of all ages, from children to eldery.[7] Literature indicated that tailored computer-generated health behavior interventions positively affect health behavior at short term than targeted, personalized or generic interventions.[3]

In our study we try to combine the advantages of the mentioned methods of health education; the individual approach of the professionals and the systematic and multimedia way of a computer. We created a computerized health education program in which the health education is standardized and categorized and we tailored the intervention; only the items relevant to a certain patient would be provided.

The aim of the study

The aim of the COSTA (**co**mputer-**s**upported individualized health education for **T**IA and minor stroke p**a**tients) study was to develop and to evaluate an individualized, intensive and structured method of health education to patients with a TIA or minor stroke by a multimedia computer program. We had the following questions:

1. Is it possible to develop health education by a multimedia computer program tailored to suit individual characteristics such as age, educational background, and risk profile of the patient?
2. Is health education by a multimedia computer program in combination with standard health education better than standard health education concerning the level of knowledge of causes, warning signs and risk factors and treatment of stroke and TIAs?
3. Does health education assisted by a computer program lead to better compliance with measures of secondary prevention in patients with TIA or minor stroke than standard health education by a physician?

The design of the study

COSTA is a phase II, open randomized clinical trial. Patients were consecutively recruited at our TIA outpatient clinic at the department of Neurology of the Erasmus MC between March and November 2004. The TIA outpatient clinic provides a rapid diagnostic work-up of patients with TIA or minor stroke in a single day. Patients were seen within 2 weeks after their event.

Inclusion and exclusion criteria

All patients were given verbal and written information about the study, and had to give written informed consent prior to inclusion. Patients with a TIA, including amaurosis fugax, or minor ischemic stroke within the preceding 3 months were enrolled. Patients had to be at least 18 years of age, had to speak and write Dutch fluently, and a modified Rankin score of less than 4. We excluded patients who were professionally engaged in cardiovascular health education and patients with aphasia or dementia or the absence of written informed consent. The diagnosis of dementia was based on the DSM-IV criteria.

Definitions and measurement

Transient ischemic attacks (TIAs) were defined as episodes of focal cerebral or retinal dysfunction of vascular origin, with sudden onset and of variable duration, with complete resolution of the symptoms within 24 h. Attacks with persistent symptoms were classified as stroke. At the TIA outpatient clinic the standard screening consists of a medical history, general physical and neurological examinations, ECG, CT scan and CT-angiography, carotid duplex ultrasound and laboratory tests. In all patients we collected detailed information about cardiovascular risk factors, such as previous cardiovascular events, smoking habits, hyperlipidemia, weight, hypertension, diabetes mellitus, and family history of cardiovascular events. We also collected the educational level and the number of alcoholic drinks a day. College and university was defined as high educational level. We used the modified Rankin scale to determine the functional status pre-stroke and 12 weeks after assessment. Blood pressure was measured twice by a calibrated noninvasive semi-continuous measurement with 5-min intervals for 30 min. Blood samples for the evaluation of total cholesterol, triglycerides (TG), high-density lipoprotein and low-density lipoprotein (LDL) and glucose were obtained after a fasting period of 12 h and again 12 weeks later. Hypertension was defined as a systolic blood pressure above 160 mmHg or a diastolic blood pressure above 90 mmHg, or the use of medication because of hypertension at inclusion. Hyperlipedemia was defined as fasting cholesterol above 5.0 mmol/l or the use of medication because of hyperlipedemia at inclusion. Diabetes mellitus was defined as the use of antidiabetic medication at assessment of glyco-Hb >6.5%. Ischemic changes on ECG or a history of angina pectoris combined with increasing level of CK was scored as myocardial infarction.

Procedures

The COSTA trial consisted of three stages. First, we made a selection and summary in modules of the information needed for the health education about stroke and TIAs. Therefore we did a literature search and mainly used information from meta-analysis about vascular risk factors, TIA and minor stroke.[11-26] The information in the modules was classified, when possible, into pathogenesis, lifestyle advice and compliance. Secondly, we developed a questionnaire which was meant to test the knowledge of our study population. We developed 20 questions concerning general vascular knowledge, the pathophysiology of TIA or stroke, medication and risk factors. The questionnaire was tested on 42 partners of patients visiting our TIA outpatient clinic. We developed our individualized multimedia

computer program (IMCP) tailored to individual characteristics like age, level of education, diagnosis and risk factors by using the information from the modules in stage 1. The third stage consisted of a phase I evaluation of the IMCP in TIA patients and partners. Aspects like comprehensibility, instructions and usability were tested and improved afterwards. Finally, we performed the phase II clinical trial. In this trial all patients underwent the diagnostic investigations described above, which took about 120 minutes. At the end of the day, after all diagnostic investigations were carried out, patients consulted one of the 3 senior vascular neurologists and the vascular neurologist in training to discuss the results of the investigations and receive the standard health education. The standard health education comprised information on stroke in general, major vascular risk factors and lifestyle recommendations. Flyers containing information on stroke, TIA and risk factors were provided. Patients could read the flyers at home. Those who were allocated to receive the IMCP, received the IMCP information directly after the standard health education.

Tailoring information content

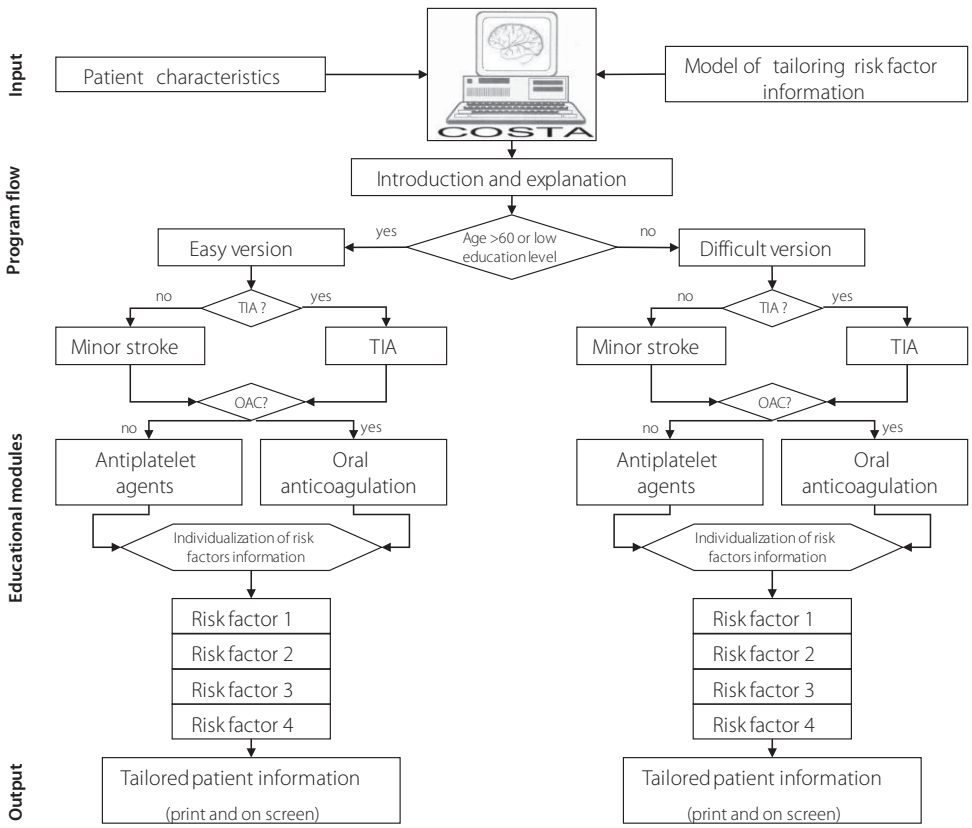
For eight modifiable risk factors (i.e., hypertension, cholesterol, atrial fibrillation, diabetes mellitus, weight, smoking, alcohol intake, and level of exercise) a module containing lay information was created for the IMCP. Each module, except for atrial fibrillation and diabetes mellitus, had a version for patients with no, moderate or large deviations from the desirable level of that risk factor, and a version for those who were already treated for that specific risk factor. Other modules contained general information on symptoms of TIA and stroke, and on treatment with antiplatelet agents or anticoagulants. All modules were highly structured, and contained combinations of slide shows, background voice and a personal address by one of us (PJK). All modules were available in an easy and a difficult version. Both versions carried the same information, but the easy version used less difficult words, had a restriction of words with more than 4 syllables, short sentences and used more repetitions. The difficult version of health education by the IMCP took totally 25 minutes, the easy version 20 minutes. Modules on risk factors were ranked for each individual patient, according to a newly developed algorithm. This algorithm was based on the strength (risk ratio) of each risk factor with respect to the occurrence of vascular complications, the expected effect of modification of the risk factor, and the effect of health education on compliance with risk factor modifying interventions.[11-26] The maximum number of modules of risk factors shown was 4. If a patient has less than four risk factors, he or she was presented general information about another frequent vascular risk factor. Finally, both the individual patient characteristics and the ranking of the modules determined the content of health information (Figure 1).

The individualized multimedia computer program

The IMCP is a very simple computer program; it runs automatically. Patients do not need any skills in computer operation. The program is written in Visual Basic, and runs under Windows 2000 or Windows XP. When applying, we made an update of the information about stroke risk factors and interventions in stroke care, because those can become outdated after some time. Age and educational level determine

the level of the health education; easy or difficult. We showed the patients aged 60 years and older the easy version, because they tire more easily. The IMCP starts with a brief introduction and explanation (Figure 1).

Figure 1: *Systematic representation of the IMCP*



Secondly, the patients receive general background information on their personal condition, i.e. TIA, minor stroke, or amaurosis fugax. Thirdly, they receive an explanation of the medication they will be using including antiplatelet agents, or coumarines. Fourth, each patient is shown four risk factor modules. At last patients receive a printed summary of the information. They also have the possibility to repeat the modules.

Outcome measurement: questionnaire

We developed a questionnaire which was meant to test the knowledge of our study population. We developed 20 questions concerning general vascular knowledge, the pathophysiology of TIA or stroke,

medication and risk factors. The questionnaire was developed and validated in 42 elderly persons. Validation was assessed by an interview done by an investigator blinded of the scores of the questionnaire. The final version consisted (Appendix II) of 14 questions instead of the 20 in the validation phase; six general vascular questions, one simple question about the pathophysiology of TIA or stroke, three about medication and four about risk factors. Each patient received the six general vascular questions, but the individual diagnosis (TIA or stroke), medication use (antiplatelet agents or coumarines), and vascular risk factors determined the content of the other eight questions. The questions corresponded to the information modules of the IMCP. Multiple choice questions contained 5–7 possible answers, half of which were right. Open questions were prestructured; answers should contain 3 predefined items. For every right answer or item, 1 point was added, and for every wrong answer or item, 1 point was subtracted. The highest possible score was 47 points in total for the questions on general knowledge, pathophysiology and medication, and 24 points for the questions concerning risk factors, for a total score of 71 points. Patients received the first questionnaire at home 1 week after their visit to the outpatient clinic. The second questionnaire was filled in at the 12-week follow-up visit. This contained the same questions as the first questionnaire, but the questions and answers had a different sequence.

Randomization and blinding

Intervention allocation was random, and based on computer-generated random numbers. The randomization was blocked in lots of ten; block size was unknown to the investigators at the time of the trial. All patients consulted the vascular neurologist (in training) at the end of the day, to discuss the results of the investigations and receive the standard health education. The physician who educated the patient was blinded to the randomization code.

Outcomes

The primary outcome was the score on the questionnaire at 1 week after intervention. The secondary outcome was the score on the questionnaire after 12 weeks. Tertiary outcomes were functional outcome at 12 weeks (modified Rankin Score) and changes in cholesterol levels, weight, cigarette and alcohol consumption, and physical activity.

Sample size

The sample size estimation was based on a prototype questionnaire that was tested in 42 partners of TIA patients. The mean total score in this questionnaire was 24.8 (SD 6.8); the highest attainable score was 48. With a maximal score of 71 in the recent questionnaire the estimated mean total score and SD would be 36.7 and 10.1, respectively (factor 1.5). With a sample size of 2 x 25 we would be able to detect a difference of 8 points (11% of the total score or 1 SD) with a significance level of alpha=0.05 and power 1-beta=0.8, assuming that the mean score and SD would be 37 and 10.

Statistical methods

The main results of this study are presented as the mean difference in scores between the two treatment groups at 1 and 12 weeks after assessment. The precision of these estimates was expressed with 95% confidence intervals, based on Student's *t* distribution. Student's *t* and χ^2 were used to compare the distribution of baseline parameters over the two treatment strata. We used multiple linear regression to adjust for the effect of unequal distributions of possible confounders, such as age and education.

Follow-up

Patients were seen 12 weeks after their first visit. Blood pressure, cholesterol levels, BMI, Rankin score, number of cigarettes, alcoholic drinks and medication use were assessed. Afterwards, the second questionnaire was filled in.

References

1. The European Stroke Organisation (ESO) Executive Committee and theESO Writing Committee. Guidelines for management of ischaemic stroke and transient ischaemic attack 2008. Cerebrovasc Dis 2008;25:457-507.
2. Damoiseaux V, van der Molen HT, Kok GJ. Gezondheidsvoorlichting en gedragsverandering. 1998.
3. Revere D, Dunbar PJ. Review of computer-generated outpatient health behavior interventions: clinical encounters "in absentia". J Am Med Inform Assoc 2001;8:62-79.
4. de Vries H, Brug J. Computer-tailored interventions motivating people to adopt health promoting behaviours: introduction to a new approach. Patient Educ Couns 1999;36:99-105.
5. Turnin MC, Beddok RH, Clottes JP et al. Telematic expert system Diabeto. New tool for diet self-monitoring for diabetic patients. Diabetes Care 1992;15:204-212.
6. Lewis D. Computer-based approaches to patient education: a review of the literature. J Am Med Inform Assoc 1999;6:272-282.
7. Krishna S, Balas EA, Spencer DC, Griffin JZ, Boren SA. Clinical trials of interactive computerized patient education: implications for family practice. J Fam Pract 1997;45:25-33.
8. Bussey-Smith KL, Rossen RD. A systematic review of randomized control trials evaluating the effectiveness of interactive computerized asthma patient education programs. Ann Allergy Asthma Immunol 2007;98:507-516.
9. Ben Said M, Consoli S, Jean J. A comparative study between a computer-aided education (ISIS) and habitual education techniques for hypertensive patients. Proc Annu Symp Comput Appl Med Care 1994;10-14.
10. Beranova E, Sykes C. A systematic review of computer-based softwares for educating patients with coronary heart disease. Patient Educ Couns 2007;66:21-28.
11. The Dutch TIA Trial Study Group. Predictors of major vascular events in patients with a transient ischemic attack or nondisabling stroke. Stroke 1993;24:527-531.
12. Cholesterol, diastolic blood pressure, and stroke: 13,000 strokes in 450 000 people in 45 prospective cohorts. Lancet 1995;1647-1653.
13. Abbott RD, Behrens GR, Sharp DS et al. Body mass index and thromboembolic stroke in nonsmoking men in older middle age. The Honolulu Heart Program. Stroke 1994;25:2370-2376.
14. Burn J, Dennis M, Bamford J, Sandercock P, Wade D, Warlow C. Long-term risk of recurrent stroke after a first-ever stroke. The Oxfordshire Community Stroke Project. Stroke 1994;25:333-337.
15. Camargo C. Moderate alcohol consumption and stroke. Stroke 1989;20:1611-1626.
16. Gill JS, Zezulka AV, Shipley MJ, Gill SK, Beevers GD. Stroke and alcohol consumption. N Engl J Med 1986;315:1041-1046.
17. Hankey GJ, Jamrozik K, Broadhurst RJ et al. Long-term risk of first recurrent stroke in the Perth Community Stroke Study. Stroke 1998;29:2491-500.
18. Jamrozik K, Broadhurst RJ, Anderson CS, Stewart-Wynne EG. The role of lifestyle factors in the etiology of stroke. A population-based case-control study in Perth, Western Australia. Stroke 1994;25:51-59.
19. Jamrozik K, Broadhurst RJ, Forbes S, Hankey GJ, Anderson CS. Predictors of death and vascular events in the elderly : the Perth Community Stroke Study. Stroke 2000;31:863-868.
20. Lai SM, Alter M, Friday G, Sobel E. A multifactorial analysis of risk factors for recurrence of ischemic stroke. Stroke 1994;25:958-962.
21. Njolstad I, Arnesen E, Lund-Larsen PG. Body height, cardiovascular risk factors, and risk of stroke in middle-aged men and women. A 14-year follow-up of the Finnmark Study. Circulation 1996;94:2877-2882.
22. Rexrode KM, Hennekens CH, Willett WC et al. A prospective study of body mass index, weight change, and risk of stroke in women. Jama 1997;277:1539-1545.
23. Rodgers A, MacMahon S, Gamble G, Slattery J, Sandercock P, Warlow C. Blood pressure and risk of stroke in patients with cerebrovascular disease. The United Kingdom Transient Ischaemic Attack Collaborative Group. Bmj 1996;313:147.
24. Wolf PA, D'Agostino RB, Kannel WB, Bonita R, Belanger AJ. Cigarette smoking as a risk factor for stroke. The Framingham Study. Jama 1988;259:1025-1029.
25. Wolf PA, D'Agostino RB, Belanger AJ, Kannel WB. Probability of stroke: a risk profile from the Framingham Study. Stroke 1991;22:312-318.
26. Blauw GJ, Lagaay AM, Smelt AH, Westendorp RG. Stroke, statins, and cholesterol. A meta-analysis of randomized, placebo-controlled, double-blind trials with HMG-CoA reductase inhibitors. Stroke 1997;28:946-950.

Chapter 4.2

Knowledge and understanding of disease process, risk factors and treatment modalities in patients with a recent transient ischemic attack or minor ischemic stroke

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Abstract

Background: Patients with acute stroke often have a striking lack of knowledge of causes, warning signs, and risk factors. Lack of knowledge may lead to inappropriate secondary prevention behaviour. We investigated the knowledge of patients with a transient ischemic attack (TIA) or minor stroke about specific aspects of their disease 3 months after the event.

Methods: Patients with a TIA or minor stroke who participated in a randomized controlled trial of the effect of health education by an individualized multimedia computer program (IMCP) were included. All patients received information about their disease from their treating neurologist and half of the patients received extra information through the IMCP. The patients' knowledge was tested after 3 months by means of a questionnaire that contained items on pathogenesis, warning signs, vascular diseases, risk factors, life style and treatment. The highest possible score was 71 points.

Results: The 57 patients had a mean total score of 41.2 points (SD 10.4) of the maximum 71. Only 15 (26%) correctly identified the brain as the affected organ in stroke and TIA, and only 21 (37%) could give a correct description of a TIA or stroke. In contrast, 80% to 90% of the patients identified hypertension and/or obesity as vascular risk factors. Knowledge of various treatment modalities of hypertension, hypercholesterolemia and obesity was moderate to high (40-91% adequate responses).

Conclusion: The vast majority of patients with TIA or stroke lack specific knowledge about their disease, but they do have a reasonable knowledge of general vascular risk factors and treatment. This suggests that counselling by neurologists of patients with a TIA or stroke can be improved.

Introduction

Knowledge about stroke is poor both among the general public and among stroke patients.[1,3] Lack of knowledge may lead to misconceptions, anxiety, fear, inappropriate behavior with regard to seeking medical attention[4,5] and to suboptimal secondary prevention.[6]

Patients do have a desire for further knowledge about causes and consequences of stroke.[7] They and their caregivers regard their family physician or neurologist as the most important sources of information.[8] However, the information provided by the treating physician in routine care may be inadequate.[7] Previous studies assessed level of knowledge in stroke patients within 48-72 hours after hospital admission.[1,4,9] Patients with acute stroke may have difficulties in capturing, retaining and reproducing information in the acute phase. Only one recent study evaluated the knowledge and awareness of cerebrovascular risk factors at 3 months after the stroke. Awareness was relatively poor in patients with stroke; less than 50% of cerebrovascular risk factors were recognized as relevant, poor awareness was correlated to suboptimal control of high blood pressure.[6] These studies assessed only a few aspects of stroke knowledge, i.e. warning signs and risk factors. The aim of this single center prospective study was to assess the conceptions and ideas of patients with minor stroke or TIA concerning their own disease. This included pathogenesis, warning signs, vascular diseases in general, risk factors, life style and treatment. The assessment was carried out 3 months after inclusion of patients with a minor stroke or TIA in our trial.

Methods

Participants

All patients were included in the COSTA study, a randomized controlled trial that evaluated the effect of health education by an individualized multimedia computer program (IMCP) on the level of knowledge and compliance with measures of secondary prevention in patients with TIA or minor stroke. The design of the study has been extensively described in chapter 4.1 of this thesis. Patients with a TIA, including amaurosis fugax, or minor ischemic stroke within the preceding 3 months were enrolled. Patients had to be at least 18 years of age, had to speak and write Dutch fluently, and had to have a modified Rankin score of less than 4. We excluded patients who were professionally engaged in cardiovascular health education and patients with aphasia or dementia. The diagnosis of dementia was based on the DSM-IV criteria. All patients were given verbal and written information about the study, and had to give consent in writing prior to inclusion. We obtained the approval of our local medical ethics committee and review board.

Definitions

Transient ischemic attacks (TIAs) were defined as episodes of focal cerebral or retinal dysfunction of vascular origin, with sudden onset and of variable duration, with complete resolution of the symptoms

within 24 hours. Attacks with persistent symptoms were classified as stroke.
All patients visited our TIA service that provides a rapid diagnostic work-up of patients with TIA or minor stroke in a single day. Patients were seen within 2 weeks after their event at our TIA service. The work-up consists of a medical history, general physical and neurological examinations, ECG, CT scan and CT-angiography, carotid duplex ultrasound and laboratory tests. At the end of the day, all patients consulted one of the 3 senior vascular neurologists and the vascular neurologist in training, to discuss the results of the investigations and receive the standard health education. The standard health education comprised information on strokes in general, major vascular risk factors and life style recommendations. Flyers containing information on stroke, TIA and risk factors were provided. Patients could read the flyers at home. In the COSTA trial half of the patients were allocated to receive the individualized multimedia computer program (IMCP). The IMCP consisted of modules containing information on TIA and stroke, treatment with antiplatelet agents or anticoagulants, and information on modifiable risk factors. Only the patients allocated to the ICMP received a printed summary of the information.[10]

Outcome measurement: questionnaire

The questionnaire was developed and validated in 42 partners of TIA patients. After minor changes in the text, the final version consisted of 14 questions (Appendix II). We divided the questionnaire in two parts. One general part consisting 10 questions including 6 general vascular questions, 1 simple open question about the pathophysiology of TIA or stroke and 3 question about medication. The other part consisted of 4 multiple-choice questions about risk factors. Each patient received the same 6 general vascular questions, but the individual diagnosis (TIA, including amaurosis fugax or stroke), medication use (antiplatelet agents or coumarines), and vascular risk factors determined the content of the 8 other questions. Each question consisted of 5, 6 or 7 answers for the multiple-choice questions, and 3 items for the open questions. Every good answer was worth 1 point. A wrong answer in a multiple-choice answer gave a 1 point reduction. The highest possible score was 47 points total for the 10 questions in the general part and 24 points for the 4 risk factors questions, for a total score of 71 points. The questionnaire was filled in at the 3-months follow-up visit.

Outcomes

The primary outcome was the score on the separate questions of the questionnaire at 3 months after inclusion in our trial.

Statistical methods

Frequency distributions of scores for each item were assessed and compared using standard methods. We used Chi-squared tests to assess the relation between clinical characteristics and components of stroke knowledge, and linear regression analysis to test for trends.
We assessed the ability of each question to discriminate between patients with high and low overall scores. For this purpose, we divided the study population according to quartiles of the total score,

yielding groups with low, low average, high average and high scores. We then used contingency table analysis to relate scores on separate questions with the total score. Chi-squared tests and Fisher's exact tests were used to assess statistical significance (p<.05), where appropriate.

Results

Patient flow

Seventy-seven consecutive patients who visited the TIA outpatient clinic between March and November 2004 were considered eligible. Of these, 12 were not included, because they had a diagnosis other than TIA or stroke (8 pts) or refused to participate (4 pts). Sixty-five patients were included in the study. Seven patients were lost to follow-up; 2 withdrew their consent, 3 had left their home without leaving an address. One patient was unable to complete the questionnaire because of a major depression and another because of chemotherapeutic treatment for cancer. Fifty-eight patients completed the 3-month questionnaire. We excluded one patient from the analysis because she later appeared to be a professional health education worker. The patients were mostly male (60%) and had a mean age of 64 (SD 16) years (range 34-84 years) with a representative distribution of the vascular risk factors. Sixty percent of the patients completed primary or secondary school, 40% college or university. The mean assessment time was 14 weeks (SD 5). The mean total score on the questionnaire was 41.2 (SD 10.4) out of a total of 71. Level of education was associated with the total score (p=0.05) (Table 1).

Table 1. *Association of clinical characteristics with total score on questionnaire at 3 months.*

Characteristic	Increase of total score	95 % CI	P-value
Age (per year)	0.0	-0.2 - 0.2	0.99
Male Sex	-0.8	-6.5 - 5.0	0.28
TIA instead of stroke	-6.0	-11.4 - -0.6	0.03
Educational level			
primary school	Ref		
secondary school	5.9	-1.5 - 13.2	0.12
College	8.1	-0.1 - 16.3	0.06
University	9.0	0.2 - 17.8	0.05

Patients with the diagnosis TIA instead of stroke had a lower total score of 6.0 points (p=0.03). Scores of patients who had suffered from previous TIA or stroke did not have higher or lower scores than those without (p=0.8) Health education by IMCP was not associated with an improvement in the 3-months score. Mean three-month scores did not differ significantly between the two groups (40.6 versus 41.8 points, p=0.67).

General knowledge; the pathogenesis of TIA or stroke

Fifteen patients (26%) could mention the brain as affected organ in stroke or TIA. The eyes (n=7;12%) and the heart (n=3;5%) were also put forward. Many patients mentioned body-parts as affected organ: extremities (n=11; 19%), face (n=2; 4%) (Table 2).

Subsequently, patients were asked to give a brief description of a TIA or stroke, depending on their own diagnosis. They could obtain the maximum score when their description included the following 3 items or synonyms in their description: brain, a problem in the blood circulation, permanent for stroke and transient for TIA. Only 13 (23%) could describe a TIA or stroke completely and correctly. Twenty-seven percent could not mention even one item. A "local disturbance of the blood circulation" was the most frequently mentioned item, by 36 (63%) patients. A total of 28 (49%) participants mentioned the brain or head in their description. The question "What is a stroke/TIA?" discriminated well between patients with a high or low total score (p=0.03), but the question "which organ was affected" did not (p=0.28).

General knowledge; warning signs, vascular disease and risk factors

Unilateral weakness (n=35; 61%) and speech difficulties (n=14; 25%) were most often mentioned as warning signs for stroke (Table 2). Seventeen patients (30%) did not know a single warning sign. Patients identified on average 1.5 (SD 1.3) warning signs.

The presenting symptoms of the patients, stroke type, nor age and sex were related to the number of recognized warning signs. There was however, an association between level of education and the number of warning signs that were brought up ($p<0.01$).

The patients often identified TIA and stroke (79%-88%) as vascular diseases (Table 2). Intermittent claudication and heart failure were less often identified. Migraine (9%), epilepsy (9%), and diabetes mellitus (7%) were also identified as vascular diseases.

Knowledge of risk factors was better than knowledge of warning signs. Answers such as high blood pressure (91%), high cholesterol level (86%), smoking (86%) and obesity (88%) were frequently given (Table 2). Only one patient (2%) did not recognize a single risk factor and one individual named just 1 risk factor. Two participants (4%) knew 2 risk factors. The other 53 patients (93%) identified 3 or more risk factors. The average number of risk factors listed was 4.8 (SD 1.5). There was no relationship between identification of a risk factor and the fact that the patient received medical treatment for that risk factor.

Table 2. *Frequencies of answers to specific questions from the questionnaire. Wrong answers are indicated by †.*

General knowledge	
What could be presenting signs of a TIA or stroke?‡	N=57
Speech difficulties	14 (25%)
Visual disturbances	10 (18%)
Unilateral weakness	35 (61%)
Unilateral numbness	5 (9%)
Facial weakness	3 (5%)
Which organ is primarily affected when you have a TIA or stroke?	N=57
Brain	15 (26%)
Eyes†	7 (12%)
Extremities†	11 (19%)
Heart†	3 (5%)
What is a stroke or TIA? (Description)?	N=57
Brain or head	31 (54%)
Blood clot	37 (65%)
Permanent or temporary deficit	17 (30%)
Which of the following do you consider manifestations of vascular diseases?	N=57
Intermittent claudication	30 (53%)
TIA	50 (88%)
Stroke	50 (88%)
Myocardial infarction	50 (88%)
Heart failure	9 (16%)
Intracranial bleeding	45 (79%)
Migraine†	5 (9%)
Epilepsy†	5 (9%)
Diabetes mellitus†	4 (7%)
Which of these items do you consider risk factors for vascular diseases?	N=57
Obesity	50 (88%)
Diabetes Mellitus	17 (30%)
High cholesterol level	49 (86%)
High blood pressure	52 (91%)
Excessive alcohol intake	40 (70%)
Smoking	49 (86%)
Lack of physical exercise	42 (74%)

Knowledge of medication	
How do aspirin or acetyl-salicylic acid work?	N=48
Platelet inhibition	14 (29%)
Risk reduction: myocardial infarction	32 (67%)
Risk reduction: TIA	40 (83%)
Risk reduction: stroke	37 (77%)
Reduction blood clotting	39 (81%)
Reduction palpitations†	6 (13%)
Lowering blood pressure†	8 (17%)
Knowledge of vascular risk factors	
How does one lower high cholesterol?	N=55
Reduction of saturated fatty acids	45 (82%)
Weight reduction	29 (53%)
Use of medication	45 (82%)
Reduction of unsaturated fatty acids†	35 (63%)
How does one treat hypertension?	N=50
Sufficient physical exercise	40 (80%)
Blood pressure control	40 (80%)
Limit salt intake	45 (90%)
Limit alcohol intake	36 (72%)
Reduce weight	42 (84%)
Use of medication	33 (66%)
More garlic†	6 (12%)
More vegetables and fruit†	23 (46%)
How does one prevent obesity?	N=35
Consult dietician	28 (80%)
Eat more fruit and vegetables	25 (71%)
Increase fiber intake	14 (40%)
Reduce fat intake	29 (83%)
Limit sugar intake	25 (71%)
Increase physical exercise	32 (91%)

* Answers reported by fewer than 5% of the patients are not listed

‡ The questions stated in this table are a short variant of the original questions (see Appendix II)

Knowledge of medication and vascular risk factors

Many participants knew that antiplatelet agents reduce the risk of myocardial infarction (67%), TIA (83%) and stroke (77%). Eighty-one percent knew that antiplatelet agents influence the blood clotting process, and 14 patients (29%) exactly mentioned the mechanism of inhibition of platelet aggregation. Reductions of palpitations (13%) or lowering of blood pressure (17%) were incorrectly presumed effects of antiplatelet agents (Table 2).

Patients frequently recognized a limited salt intake (90%), a limited alcohol intake (72%), sufficient exercise (80%) and weight reduction (84%) as treatment modalities for high blood pressure (Table 2)

The question on treatment modalities of high cholesterol levels was more difficult. Patients quite often gave the answer of "reduction of unsaturated fatty acids" (63%) (Table 2).

The vast majority of patients knew that visiting a dietician (80%), limiting fat (83%) and sugar intake (71%), eating more fruit and vegetables (71%) and more physical activity (91%) are methods to prevent and to treat obesity.

Discussion

Our study shows that patients with TIA or minor stroke have a moderate to good knowledge of the most common vascular diseases, risk factors and general treatment options of vascular risk factors. However, the knowledge of stroke and TIA-specific items such as the awareness of the affected organ and warning symptoms is disappointing.

All patients had received standard information and health education from their treating neurologist at the time of the diagnosis and half of the patients had received extra information by the IMCP. Before we explore the causes of limited knowledge of stroke and TIA patients, several limitations of this study have to be discussed. A partial explanation for the difference in knowledge between common vascular and stroke specific items could be the format and nature of our questions. The stroke-specific questions were more often open-ended, and therefore required an active recalling mechanism whereas the items on common vascular risk factors were more often multiple-choice questions and depended therefore more on recognition. For example, only 26% mentioned the brain as affected organ in stroke or TIA. The term "organ" in the question "Which organ is primarily affected when you have a TIA or stroke?" may have generated confusion and could be ambiguous, because in the question that asked for a description of TIA or stroke, 49% of the patients spontaneously mentioned brain or head.

Our study population consisted of a representative group of patients with TIA or minor stroke, collected at a TIA outpatient clinic. The intensity and content of the stroke specific and general health information provided by the neurologists in this study was representative for usual care in the Netherlands. The neurologists themselves provided the information, during two or three follow-up visits of 15 minutes each. Flyers containing information on stroke, TIA and risk factors were provided at the discretion of the treating neurologist. However, selection bias may have influenced our results.

A limitation of our study is its small size with a relatively high percentage of dropouts (10%). The patients

who were lost to follow-up were younger (mean 55 yrs) and higher educated. An explanation could be that these patients probably needed the relatively simple information provided by the computer program less than others. This may have contributed to the limited knowledge of TIA and stroke in our study-population. On the other hand, patients willing to participate in a study like ours are probably more interested in getting information and improving their knowledge of stroke and vascular disease.

Also, the ability to retrieve information after 3 months could be influenced by cognitive impairment, which we did not formally assess in our population. In hospital-based studies, the incidence of post-stroke dementia after 3 months ranges from 6 to 27%.[11] The prevalence is likely much lower in our study, because our patients were not hospitalized, had only a TIA or minor stroke and were on average, younger than hospitalized stroke patients.

Patients in the acute phase of their disease may have difficulties in capturing and retaining information. In our COSTA trial we evaluated knowledge at 1 week and 3 months. The goal of the study was particularly to evaluate the knowledge in a later phase, because this may be more strongly related to compliance with secondary prevention and lifestyle measures to be taken.[6] We did not access the baseline knowledge in the 2 groups, because we wanted to avoid learning effects and to limit the burden of the study.

Despite the assessment of the knowledge after 3 months in contrast to the acute phase of the other studies[1-3], our results confirm that knowledge of warning signs remains poor. However, in a hospital based population in Ohio USA, 43% did not know a single risk factor[1], whereas in our study only 2% did not know one vascular risk factor.

An explanation for the striking difference of knowledge between common vascular and stroke specific items could be that the present population and patients have easy and rapid access to health education on common vascular knowledge by television, magazines and Internet. Besides, the last few years media attention for cardiovascular risk factors has been increasing, but specific information on stroke has been relatively underrepresented. A second explanation may be that patients with ischemic heart disease are on average younger than patients with stroke. Finally, the notion that stroke may occur at any age, and that stroke is a preventable disease may not be as familiar in the population as knowledge about ischemic heart disease. Ferris confirmed that awareness of stroke symptoms in a population of 1024 women aged 25 years and older, is less than knowledge of symptoms of myocardial infarction: 37% recognized weakness or numbness as a warning sign of stroke and 62% chest pain of a heart attack.[12]

Our study indicates deficient information provision by the neurologist, considering the lack of stroke specific knowledge among the patients in this study. A TIA outpatient clinic provides a rapid work-up, diagnosis and treatment of patients suspected of a TIA or minor stroke. In the past five years TIA services have been set up in many hospitals in the Netherlands. For neurologists in a TIA outpatient clinic, health education concerning TIA and stroke is daily work, but it still is a difficult task. Information needs of stroke patients and carers differ in content, frequency and method of presentation.[8] Moreover, perspectives on stroke education differ among doctors and patients. For example, in a Korean stroke population patients were more interested in post-stroke diet management and medical knowledge.[13]

In conclusion, our study shows that TIA and minor stroke patients do have a reasonable knowledge

of general vascular risk factors, but poor knowledge of stroke specific aspects. This emphasizes the importance of continued efforts to improve the information provision to stroke and TIA patients, but also on a public level. Future studies should investigate whether health education by the neurologist could be supported by interactive, repetitive, and tailored methods, by providing written information, through computer programs, stroke education programs and perhaps with the help of specialized nurse practitioners.

References

1. Kothari R, Sauerbeck L, Jauch E et al. Patients' awareness of stroke signs, symptoms, and risk factors. Stroke 1997;28:1871-1875.
2. Pancioli AM, Broderick J, Kothari R et al. Public perception of stroke warning signs and knowledge of potential risk factors. Jama 1998;279:1288-1292.
3. Parahoo K, Thompson K, Cooper M, Stringer M, Ennis E, McCollam P. Stroke: awareness of the signs, symptoms and risk factors-a population-based survey. Cerebrovasc Dis 2003;16:134-140.
4. Williams LS, Bruno A, Rouch D, Marriott DJ. Stroke patients' knowledge of stroke. Influence on time to presentation. Stroke 1997;28:912-915.
5. Sappok T, Faulstich A, Stuckert E, Kruck H, Marx P, Koennecke HC. Compliance with secondary prevention of ischemic stroke: a prospective evaluation. Stroke 2001;32:1884-1889.
6. Croquelois A, Bogousslavsky J. Risk awareness and knowledge of patients with stroke: results of a questionnaire survey 3 months after stroke. J Neurol Neurosurg Psychiatry 2006;77:726-728.
7. Rodgers H, Bond S, Curless R. Inadequacies in the provision of information to stroke patients and their families. Age Ageing 2001;30:129-133.
8. Wachters-Kaufmann C, Schuling J, The H, Meyboom-de Jong B. Actual and desired information provision after a stroke. Patient Educ Couns 2005;56:211-217.
9. Carroll C, Hobart J, Fox C, Teare L, Gibson J. Stroke in Devon: knowledge was good, but action was poor. J Neurol Neurosurg Psychiatry 2004;75:567-571.
10. Maasland E, Koudstaal PJ, Habbema JDF, Dippel DWJ. Effects of an individualized multimedia computer program for health education in patients with a recent minor stroke or transient ischemic attack; a randomized controlled trial. Acta Neurol Scand 2007;115:41-48
11. Leys D, Henon H, kowiak-Cordoliani MA, Pasquier F. Poststroke dementia. Lancet Neurol 2005;4:752-759.
12. Ferris A, Robertson RM, Fabunmi R, Mosca L. American Heart Association and American Stroke Association national survey of stroke risk awareness among women. Circulation 2005;111:1321-1326.
13. Kim JS, Yoon SS. Perspectives of stroke in persons living in Seoul, South Korea. A survey of 1000 subjects. Stroke 1997;28:1165-1169.

Chapter 4.3

Effects of an individualized multimedia computer program for health education in patients with a recent minor stroke or transient ischemic attack; a randomized controlled trial

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Abstract

Background: TIA and stroke patients often show a striking lack of knowledge about their disease. We developed a computer program that provided health education fitting the educational level, risk profile and symptoms of patients and evaluated it in a randomized controlled trial.

Methods: TIA or minor stroke patients were allocated to health education by a physician (n=32) or to a combination of education by a physician and the computer program (n=33). Knowledge was tested by means of a questionnaire at 1 and 12 weeks after inclusion. The maximal possible score was 71 points.

Results: Overall knowledge was low: mean score was 43.6 at 1 week and 42.0 points at 12 weeks for both groups. The intervention group had slightly better scores at 1 week after using the computer program, 45.4 versus 41.5 (p=0.09), with the difference increasing to 4.3 points after (post-hoc) adjustment for age and level of education (p=0.06). After 12 weeks, the score in the intervention group dropped significantly to 42.0 points (p=0.05), and was no longer different from the standard group

Conclusion: This study did not show a lasting effect of health education by an individualized computer program on the knowledge of TIA and minor stroke patients.

Introduction

Previous studies have shown a striking lack of knowledge about stroke, its warning signs, symptoms and of vascular risk factors among the general public, [1-5] but also among patients with a TIA or stroke.[6, 7] By providing information to their patients, physicians aim to improve the knowledge of the patients and try to change their behaviour in order to modify the risk of a recurrent stroke or other vascular events. However, stroke patients have reported dissatisfaction with the information and advice about their disease.[8,9] Lack of knowledge may be partially responsible for delays in seeking medical attention[10], and lack of compliance with preventive measures.[11] Organisations and physicians have made several efforts to improve public and stroke patients knowledge such as health education campaigns[12], television advertising[13], printed materials[14,15] and family education programs.[16-20] The general effectiveness of structured stroke information provision has not been conclusively demonstrated.[21] Randomized controlled trials of computerized health education for diseases other than stroke have been carried out.[22-28] Some of these studies, a few with simple, single interventions, showed improvement of knowledge and/or health behaviour.[23-26] ISIS, a randomized study in patients with hypertension assessed the effect of multimedia health education on top of standard education. The intervention led to a significant increase in knowledge among users of the multimedia program.[24] Information provided by the treating physician or a stroke nurse has the advantage of being delivered personally, thereby generating emotional impact. Nevertheless, the information and the way it is presented may be of varying quality, which may lead to deficient information transfer. Computerized health education has the advantage of being delivered in a consistent and systematic way. We tried to combine the best of both methods; we created a computerized health education program in which the health education is standardized and categorized. Only the items relevant to a certain patient will be provided, tailored to individual characteristics such as age, educational background, symptoms, and risk profile. In this study, computer-supported individualized health education for TIA and minor stroke patients (COSTA), we aimed to evaluate the effect of health education by an individualized multimedia computer program (IMCP) on the level of knowledge and compliance with measures of secondary prevention in patients with a TIA or minor stroke.

Methods

Participants

The design of this study has been extensively described in chapter 4.1. We included patients, aged 18 years and older, who had had a TIA or minor ischemic stroke within the preceding 3 months. All patients had to speak and write Dutch fluently, and had to have a modified Rankin score less than 4. Excluded were patients who were professionally engaged in cardiovascular health education, patients with aphasia or dementia. We excluded also patients with a visual impairment of a degree that would interfere with the delivery of health education. All patients were given verbal and written information about the study, and had to give consent in writing prior to randomization.

Individualization of information content

For eight modifiable risk factors (i.e. hypertension, cholesterol, atrial fibrillation, diabetes mellitus, weight, smoking, alcohol intake, and level of exercise) a module containing lay information was created for the IMCP. Each module, except for atrial fibrillation and diabetes mellitus, had a version for patients with no, moderate and large deviations from the desirable level of that risk factor, and a version for those who were already treated for that specific risk factor. Other modules contained general information on symptoms of a TIA and stroke, and on treatment with antiplatelet agents or anticoagulants. All modules were highly structured, and contained combinations of slide shows, background voice and a personal address by one of us (PJK).

Individualization: choice of modules

Modules on risk factors were individually ranked according to a newly developed algorithm. This algorithm was based on the strength (risk ratio) of each risk factor with respect to the occurrence of vascular complications [30-45], the expected effect of modification of the risk factor and the effect of health education on compliance with risk factor modifying interventions. The individual patient characteristics and the ranking of the modules determined the content of the individual general and risk factor health information.

The individualized multimedia computer program (IMCP)

The IMCP starts with a brief introduction and explanation (Figure 1, chapter 4.1) The IMCP is a continuous and very simple computer program; patients do not need any skills in computer operation. The program is written in Visual Basic, and runs under Windows 2000 or Windows XP. Age and educational level determine the level of the health education; easy or difficult. The difficult version takes 25 minutes, and the easy version takes 20 minutes, but this has more repetitive elements. We showed the patients aged 60 years and older the easy version, because they tire more easily.[46]

First, patients receive a general introduction of their personal diagnosis, TIA, minor stroke or amaurosis fugax. Next, they receive an explanation of the used or prescribed medication; antiplatelet agents or coumarines. Third, each patient is shown 4 risk factor modules. If a patient has less than 4 risk factors, he

or she is presented general information about another frequent vascular risk factor.
After the patients underwent the diagnostic procedures and their final consultation with their physician, they were shown the IMCP. Finally, patients received a printed summary of the information.

Outcome measurement: questionnaire

The questionnaire was developed and validated in 42 partners of TIA patients. The final version consisted of 14 questions (Appendix II), consisting of 6 general vascular questions, 1 simple question about the pathophysiology of TIA or stroke, 3 about medication and 4 about risk factors. Each patient received the 6 general vascular questions, but the individual diagnosis (TIA or stroke), medication use (antiplatelet agents or coumarines), and vascular risk factors determined the content of the 8 other questions. The questions corresponded to the information modules of the IMCP. The highest possible score was 47 points in total for the questions on general knowledge, pathophysiology and medication, and 24 points for the questions concerning risk factors, for a total score of 71 points.
Patients received the first questionnaire at home 1 week after they had used the ICMP during their visit to the TIA service. The second questionnaire was filled in at the 12-weeks follow-up visit.

Outcomes

The primary outcome was the score on the questionnaire at 1 week after intervention. Secondary outcome was the score at 12 weeks after assessment. Tertiary outcomes were functional outcome at 12 weeks (modified Rankin Score) and changes in cholesterol level, weight, cigarette and alcohol consumption, and physical activity.

Statistical methods

The main results of this study are presented as the mean difference in scores between the two treatment groups at 1 and 12 weeks after assessment. The precision of these estimates was expressed with 95% confidence intervals, based on Student's *t* distribution. Student's t and χ^2 was used to test compare the distribution of baseline parameters over the two treatment strata. We used multiple linear regression to adjust for the effect unequal distributions of possible confounders, such as age and education.

Sample size

The sample size estimation was based on a prototype questionnaire that was tested in 42 partners of TIA patients. The mean total score in this questionnaire was 24.8 (SD 6.8); the highest attainable score was 48. With a maximal score of 71 in the recent questionnaire the estimated mean total score and SD would be 36.7 and 10.1, respectively (factor 1.5). With a sample size of 2 x 25 we would be able to detect a difference of 8 points (11% of the total score, or 1 SD) with a significance level of alpha=0.05 and power 1-beta=0.8, assuming that the mean score and SD would be 37 and 10.

Randomization and blinding

Treatment allocation was random, and based on computer-generated random numbers. The randomization was blocked in lots of ten; block size was unknown to the investigators at the time of the trial. All patients consulted the neurologist (in training) at the end of the day, to discuss the results of the investigations and receive the standard health education. The physician who educated the patient was blinded to the randomization code.

Results

We assessed 77 consecutive patients between March and November 2004; 12 were not included, because they had a diagnosis other than TIA or stroke (8 pts) or chose not to participate (4 pts). Sixty-five patients were randomized and included. Clinical characteristics and factors possibly related to differences in the scores of the questionnaires were evenly distributed among the two treatment groups (Table 1).

Table 1: *Vascular risk factors and clinical characteristics of the study population (N (%) or mean, (SD))*

		Standard health education (n=27)	IMCP health education (n=30)
Demographics			
Age in years		63 (SD 13)	65 (SD 12)
Male sex		17 (63%)	17(57%)
Educational level	primary school	4 (15%)	8 (27%)
	secondary school	11 (41%)	11 (37%)
	college	7 (26%)	6 (20%)
	university	5 (9%)	5 (7%)
Risk factors			
Hypertension		13 (48%)	12 (41%)
Diabetes mellitus		3 (11%)	2 (7%)
Hypercholesterolemia		7 (25%)	10 (35%
Current smoker		5 (18%)	7 (23%)
Atrial fibrillation		2 (7%)	1 (3%)
Myocardial infarction/ angina pectoris		6 (21%)	8 (27%)
Previous stroke/TIA		4 (15%)	6 (20%)
TIA/stroke characteristics			
Minor stroke		13 (48%)	13 (43%)
TIA		14 (52%)	17 (57%)
Modified Rankin score	0	18 (67%)	20 (67%)
	1	5 (19%)	2 (7%)
	2	4 (15%)	6 (20%)
	3	0	2 (7%)
Clinical characteristics			
Systolic blood pressure (mmHg)		140 (SD 16)	144 (SD 23)
Diastolic blood pressure (mmHg)		86 (SD 8)	84 (SD 10)
Serum cholesterol (mmol/l)		5.6 (SD 1.5)	5.5 (SD 1.1)
Serum triglycerides (mmol/l)		1.7 (SD 0.9)	2.0 (SD 1.6)
Serum LDL (mmol/l)		3.8 (SD 1.4)	3.6 (SD 1.4)
Body mass index (kg/m^2)		25.7 (SD 3.8)	26.7 (SD 3.8)
Number of cigarettes/smoker		15.6 (SD 11.4)	27.6 (SD 17.7)
Number of alcoholic drinks/drinker		1.9 (SD 1.0)	1.7 (SD 1.0)

Patient flow

All 65 patients received and completed their allocated treatment. Four 1-week questionnaires were missing because they were lost in the regular mail or the patient had moved, and we did not have the right address. We sent reminders, but at the time we received the questionnaires back it was too close to the 12 weeks-follow-up in four patients. These four patients did attend the 12-weeks follow-up visit. Seven patients were lost to follow-up; 2 withdrew their consent, 3 had left their homes without leaving an address. One patient was unable to complete the questionnaire because he developed a depression during follow-up. We discovered asymptomatic lung cancer by a CT-angiography in one patient. He was subsequently treated with chemotherapeutics and could not return the questionnaire. Fifty-eight patients completed the 12-weeks assessment. We excluded one patient from the analysis because after she completed the questionnaires, she appeared to be a professional health education worker. Results will therefore be reported for 57 patients.

Outcomes and effect of the intervention

The mean total score of both groups combined was 43,6 (SD 8.5) at 1 week and 42.0 (SD 10.2) points at 12 weeks. At 1 week, the mean total score of the questionnaires in the 2 groups differed 3.9 points in favor of the intervention group (95% CI:-0.7-8.5, p=0.09) (Table 2).

Table 2: *Scores and subscores on the questionnaire at one week, and after 12 weeks*

	Standard health education (n=25)	IMCP health education (n=28)	Intervention effect* (95%CI)
Scores at 1 week			
Total score (mean, SD)	41.5 (8.3)**	45.4 (8.3)**	3.9 (-0.7-8.5)
General section score	27.7 (5.7)	31.0 (6.2)	3.3 (-0.3-6.6)
Risk factor section score	13.8 (4.1.)	14.4 (3.8)	0.6 (-1.6-2.7)
Scores at 12 weeks			
Total score	42.0 (10.4)**	42.0 (10.1)**	0.0(-5.6-5.7)
General section score	27.5 (6.9)	28.8 (7.1)	1.3(-2.6-5.2)
Risk factor section score	14.5 (5.0)	13.1 (4.1)	-1.4 (-1.2-3.9)

*Two-sample test with equal variances

**Total score=general section (including medication score) score and risk factor section. Maximal possible score: total 71, general section 47, and risk factor section 24. Higher scores mean a better knowledge.

Younger and high-educated people had higher scores at both assessments. In a post-hoc analysis after adjustment for educational level, and age, the difference between the two groups was 4.3 points (95% CI -0.1-8.9, p=0.06) in favour of the intervention group.

After 12 weeks the mean total scores of the two groups were virtually similar, because the score of the IMCP group dropped 3.4 (95% CI: -6.1 to -0.7) points to 42.0 points at 12 weeks (p=0.01). After 12 weeks, the mean systolic and diastolic blood pressure had decreased considerably (Table 3) in both groups,

with no difference between the two groups. Serum cholesterol, 1.63 versus 1.14 mmol/l, triglycerides, 0.62 versus 0,65 mmol/l and LDL 1.43. versus 1.17 mmol/l, levels dropped significantly in both groups, with no difference between the groups. Patients in neither group reduced their weight. Those who regularly used tobacco or alcohol reduced their intake more in the IMCP group, but these differences were not significant. No statistically significant differences in functional outcome were observed. The compliance with medication intake was high: 100% took their platelet inhibitors or anticoagulants, 93% took their lipid lowering medication and 92% their antihypertensive medication after 12 weeks. The significant decrease in blood pressure and cholesterol level reflects the high compliance rate. There were no differences in medication use between the 2 groups.

Table 3: *Differences between clinical parameters at 12 weeks and baseline assessment* *

	Standard health education (n=27)	IMCP health education (n=30)	Intervention effect † (95%CI)
Systolic blood pressure (mmHg)	-6.9	-8.4**	1.5 (-7.7-10.8)
Diastolic blood pressure (mmHg)	-6.2**	-5.4**	-0.8 (-6.1-4.5)
Serum cholesterol (mmol/l)	-1.6**	-1.1**	-0.5 (-1.2-0.2)
Serum triglyceride (mmol/l)	-0.6**	-0.6**	0.0 (-0.7-0.7)
Serum LDL (mmol/l)	-1.4**	-1.2**	-0.2 (-1.0-0.5)
Body mass index (kg/m2)	0.3	0.0	0.3 (-0.3-0.8)
Number of cigarettes/smoker	-13.2	-20.1	6.9 (-16.2-30.1)
Number of alcoholic drinks/drinker	-0.6	-0.8	0.2 (-0.6-1.0)

*See Table 1 for baseline data
†Two-sample *t* test
**Significant decline compared to baseline data, paired *t test*.

Discussion

This study did not show a lasting effect of health education by an individualized multimedia computer program on the knowledge of TIA and minor stroke patients. Our results suggest that a short-lasting increase in knowledge has occurred in the IMCP group. The overall knowledge of patients about TIA, stroke and vascular risk factors was quite moderate, in both treatment groups.

Our study consisted of a representative population of TIA and minor stroke patients. Clinical characteristics and factors possible related to differences at the scores of the questionnaires were evenly distributed among the two treatment groups. A limitation of our study is the relatively high proportion of dropouts (10%). Unexpectedly, the patients lost to follow-up were younger (mean 55 years) and more highly educated. This is difficult to explain, but it could be that this particular group of patients were poorly motivated and probably needed the relatively simple information provided by the IMCP less than others. Another limitation of our study is its small size, which may have led to unequal distributions of some confounding factors; the patients in the IMCP group were indeed slightly older and less well educated. The relatively small size of our study was based on the assumption that the intervention might improve

the score on the questionnaire by 11%, or 1 SD. This was an intermediary outcome, and therefore the effect had to be large in order to be clinically relevant by itself, and to influence more clinically relevant long-term outcomes in further studies. Moreover, the low level of knowledge at baseline suggested that a large effect would indeed be possible.

Selection bias may have influenced our results. Patients willing to participate in a study are probably more motivated to improve their knowledge and to change their life styles. This is reflected in the high compliance with medication. Patients received the IMCP at the end of the TIA service day, after the health education by the physician. Many patients, especially the elderly, were tired by that time after having received a lot of information and having discussed the results of investigations. This could have influenced their capacity to learn. Also, the ability to retrieve information after 3 months could be influenced by cognitive impairment, which we did not formally assess in our population. In hospital-based studies, the prevalence of post-stroke dementia after 3 months ranges from 6 to 27%.[47] The prevalence is probably much lower in our study, because our patients were not hospitalized, had only a TIA or minor stroke and were on average younger than a typical hospitalized cohort of stroke patients.

Furthermore we only once showed the IMCP to the patients; repeating the IMCP could have reinforced the health message. We did not access the baseline knowledge in the 2 groups before randomization, because we wanted to avoid learning effects and to limit the burden of the study. In our opinion, the difference in the score at 1 week (Table 2) is not a baseline difference between the groups, because the score in the IMCP group dropped significantly to the consistent 42 points of the non-intervention group

A striking observation was the short-lasting effect of our computerized health education program, despite the repetitive manner of education during the day. All patients who watched the IMCP were given the usual information by their neurologist, just as the control patients, within an hour before the start of the IMCP. This suggests that a single intensive visual educational course of 20-30 minutes is insufficient to achieve a long-lasting effect. Therefore we suggest that the program should be repeated during a control visit or by means of a DVD/CD-ROM, suitable for the computer at home. In our study, the compliance with lifestyle recommendations was disappointing. Non-compliance with life style advice is a well-known problem. Knowledge is a necessary factor for induction of changes in life style behaviour, but it is quite likely not sufficient by itself. One also needs motivation and the capacity to change. The process of behaviour change is a multi-stage process. We did not assess the levels of motivation of our patients. People in different stages of acceptance and motivation use tailored interventions in different ways.[48] This should be investigated in future studies of health education in patients with cerebrovascular disease.

Other studies

Published randomized computer based approaches to patient education show a significant heterogeneity that makes comparison difficult. Most programs have focused on symptomatic chronic diseases, like asthma, cancer and diabetes.[22,27] To our knowledge, COSTA is the only randomized trial with an individualized multimedia program for patients with TIA or minor stroke. These patients are relatively

old and do not have a disease with daily symptoms in contrast to children with asthma.[25,26] In studies aimed at these patients a multimedia education program improved knowledge of both patients and caregivers compared with standard education, although with a high percentage of dropouts of 20 to 45%. A study quite comparable to ours in design and target population was ISIS.[24] In this randomized study, 158 hypertensive patients received a one-time standard education or a non-tailored multimedia education. The intervention led to a significant increase in knowledge among users of the multimedia program 2 months later. The subjects' younger age, which means a greater capacity to capture and retain information, could be an explanation for the improvement of knowledge after 2 months, which was in sharp contrast to our findings. In conclusion, this study shows no lasting benefit of individualized health education by a multimedia program on the level of knowledge of patients with a TIA or minor stroke. However, the temporary increase in knowledge in the IMCP group suggests that further research should focus on more intensive and more interactive interventions in larger samples of patients with a longer follow-up period, with special attention to the elderly in order to find a lasting effect.

References

1. Pancioli AM, Broderick J, Kothari R et al. Public perception of stroke warning signs and knowledge of potential risk factors. Jama 1998;279:1288-1292.
2. Sug Yoon S, Heller RF, Levi C, Wiggers J, Fitzgerald PE. Knowledge of stroke risk factors, warning symptoms, and treatment among an Australian urban population. Stroke 2001;32:1926-1930.
3. Schneider AT, Pancioli AM, Khoury JC et al. Trends in community knowledge of the warning signs and risk factors for stroke. Jama 2003;289:343-346.
4. Pandian JD, Jaison A, Deepak SS et al. Public Awareness of Warning Symptoms, Risk Factors, and Treatment of Stroke in Northwest India. Stroke 2005;36.:644-648.
5. Reeves MJ, Hogan JG, Rafferty AP. Knowledge of stroke risk factors and warning signs among Michigan adults. Neurology 2002;59:1547-1552.
6. Samsa GP, Cohen SJ, Goldstein LB et al. Knowledge of risk among patients at increased risk for stroke. Stroke 1997;28:916-921.
7. Kothari R, Sauerbeck L, Jauch E et al. Patients' awareness of stroke signs, symptoms, and risk factors. Stroke 1997;28:1871-1875.
8. Rodgers H, Bond S, Curless R. Inadequacies in the provision of information to stroke patients and their families. Age Ageing 2001;30:129-133.
9. Wellwood I, Dennis MS, Warlow CP. Perceptions and knowledge of stroke among surviving patients with stroke and their carers. Age Ageing 1994;23:293-298.
10. Williams LS, Bruno A, Rouch D, Marriott DJ. Stroke patients' knowledge of stroke. Influence on time to presentation. Stroke 1997;28:912-915.
11. Hanger HC, Wilkinson TJ. Stroke education: can we rise to the challenge? Age Ageing 2001;30:113-114.
12. Stern EB, Berman M, Thomas JJ, Klassen AC. Community education for stroke awareness: An efficacy study. Stroke 1999;30:720-3.
13. Silver FL, Rubini F, Black D, Hodgson CS. Advertising strategies to increase public knowledge of the warning signs of stroke. Stroke 2003;34:1965-1968.
14. Mazor KM, Billings-Gagliardi S. Does reading about stroke increase stroke knowledge?. The impact of different print materials. Patient Educ Couns 2003;51:207-215.
15. Mant J, Carter J, Wade DT, Winner S. The impact of an information pack on patients with stroke and their carers: a randomized controlled trial. Clin Rehabil 1998;12:465-476.
16. Lincoln NB, Francis VM, Lilley SA, Sharma JC, Summerfield M. Evaluation of a stroke family support organiser: a randomized controlled trial. Stroke 2003;34:116-121.
17. Mant J, Carter J, Wade DT, Winner S. Family support for stroke: a randomised controlled trial. Lancet 2000;356:808-813.
18. Evans RL, Matlock AL, Bishop DS, Stranahan S, Pederson C. Family intervention after stroke: does counseling or education help? Stroke 1988;19:1243-1249.
19. Smith J, Forster A, Young J. A randomized trial to evaluate an education programme for patients and carers after stroke. Clin Rehabil 2004;18:726-736.
20. Rodgers H, Atkinson C, Bond S, Suddes M, Dobson R, Curless R. Randomized controlled trial of a comprehensive stroke education program for patients and caregivers. Stroke 1999;30:2585-2591.
21. Forster A, Smith J, Young J, Knapp P, House A, Wright J. Information provision for stroke patients and their caregivers. Cochrane Database Syst Rev 2001;CD001919.
22. Krishna S, Balas EA, Spencer DC, Griffin JZ, Boren SA. Clinical trials of interactive computerized patient education: implications for family practice. J Fam Pract 1997;45:25-33.
23. Shaw MJ, Beebe TJ, Tomshine PA, Adlis SA, Cass OW. A randomized, controlled trial of interactive, multimedia software for patient colonoscopy education. J Clin Gastroenterol 2001;32:142-147.
24. Ben Said M, Consoli S, Jean J. A comparative study between a computer-aided education (ISIS) and habitual education techniques for hypertensive patients. Proc Annu Symp Comput Appl Med Care 1994;10-14.
25. Krishna S, Francisco BD, Balas EA, Konig P, Graff GR, Madsen RW. Internet-enabled interactive multimedia asthma education program: a randomized trial. Pediatrics 2003;111:503-510.

26. Homer C, Susskind O, Alpert HR et al. An evaluation of an innovative multimedia educational software program for asthma management: report of a randomized, controlled trial. Pediatrics 2000;106:210-215.
27. Lewis D. Computer-based approaches to patient education: a review of the literature. J Am Med Inform Assoc 1999;6:272-82.
28. Revere D, Dunbar PJ. Review of computer-generated outpatient health behavior interventions: clinical encounters "in absentia". J Am Med Inform Assoc 2001;8:62-79.
29. van Swieten JC, Koudstaal PJ, Visser MC, Schouten HJ, van Gijn J. Interobserver agreement for the assessment of handicap in stroke patients. Stroke 1988;19:604-607.
30. Blauw GJ, Lagaay AM, Smelt AH, Westendorp RG. Stroke, statins, and cholesterol. A meta-analysis of randomized, placebo-controlled, double-blind trials with HMG-CoA reductase inhibitors. Stroke 1997;28:946-950.
31. Wolf PA, D'Agostino RB, Kannel WB, Bonita R, Belanger AJ. Cigarette smoking as a risk factor for stroke. The Framingham Study. Jama 1988;259:1025-1029.
32. Wolf PA, D'Agostino RB, Belanger AJ, Kannel WB. Probability of stroke: a risk profile from the Framingham Study. Stroke 1991;22:312-318.
33. Rodgers A, MacMahon S, Gamble G, Slattery J, Sandercock P, Warlow C. Blood pressure and risk of stroke in patients with cerebrovascular disease. The United Kingdom Transient Ischaemic Attack Collaborative Group. Bmj 1996;313:147.
34. Rexrode KM, Hennekens CH, Willett WC et al. A prospective study of body mass index, weight change, and risk of stroke in women. Jama 1997;277:1539-1545.
35. Njolstad I, Arnesen E, Lund-Larsen PG. Body height, cardiovascular risk factors, and risk of stroke in middle-aged men and women. A 14-year follow-up of the Finnmark Study. Circulation 1996;94:2877-2882.
36. Lai SM, Alter M, Friday G, Sobel E. A multifactorial analysis of risk factors for recurrence of ischemic stroke. Stroke 1994;25:958-962.
37. Jamrozik K, Broadhurst RJ, Anderson CS, Stewart-Wynne EG. The role of lifestyle factors in the etiology of stroke. A population-based case-control study in Perth, Western Australia. Stroke 1994;25:51-59.
38. Jamrozik K, Broadhurst RJ, Forbes S, Hankey GJ, Anderson CS. Predictors of death and vascular events in the elderly : the Perth Community Stroke Study. Stroke 2000;31:863-868.
39. Hankey GJ, Jamrozik K, Broadhurst RJ et al. Long-term risk of first recurrent stroke in the Perth Community Stroke Study. Stroke 1998;29:2491-2500.
40. Gill JS, Zezulka AV, Shipley MJ, Gill SK, Beevers GD. Stroke and alcohol consumption. N Engl J Med 1986;315:1041-1046.
41. Camargo C. Moderate alcohol consumption and stroke. Stroke 1989;20:1611-1626.
42. Burn J, Dennis M, Bamford J, Sandercock P, Wade D, Warlow C. Long-term risk of recurrent stroke after a first-ever stroke. The Oxfordshire Community Stroke Project. Stroke 1994;25:333-337.
43. Abbott RD, Behrens GR, Sharp DS et al. Body mass index and thromboembolic stroke in nonsmoking men in older middle age. The Honolulu Heart Program. Stroke 1994;25:2370-2376.
44. Cholesterol, diastolic blood pressure, and stroke: 13,000 strokes in 450 000 people in 45 prospective cohorts. Lancet 1995;1647-1653.
45. Predictors of major vascular events in patients with a transient ischemic. Stroke 1993;24:527-531.
46. Joyce CA, Paller KA, McIsaac HK, Kutas M. Memory changes with normal aging: behavioral and electrophysiological measures. Psychophysiology 1998;35:669-678.
47. Leys D, Henon H, kowiak-Cordoliani MA, Pasquier F. Poststroke dementia. Lancet Neurol 2005;4:752-759.
48. Brug J, van Assema P. Differences in use and impact of computer-tailored dietary fat-feedback according to stage of change and education. Appetite 2000;34:285-293.

Chapter 4.4

Health education in patients with a recent stroke or transient ischemic attack; a comprehensive review

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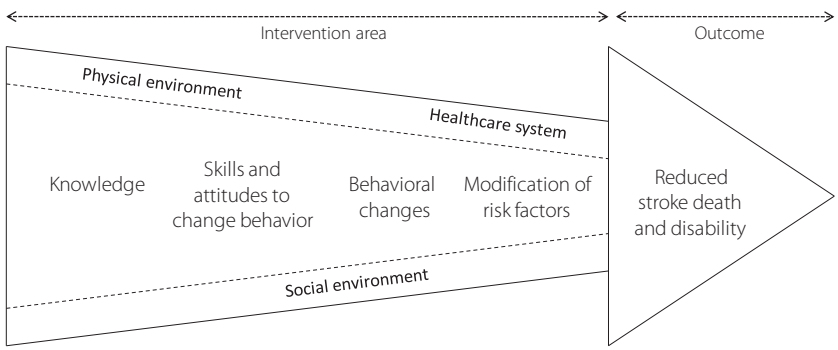
Introduction

Implementation of preventive treatments and reduction of risk factor exposure at population level has contributed to a significant reduction of the worldwide age and sex-specific stroke incidence over the past four decades.[1,2] In the last 20 years we have seen many improvements in acute stroke treatment modalities as well, including new medications, such as alteplase for intravenous thrombolysis[3] and organized multidisciplinary stroke units.[4] These treatment modalities aim to decrease stroke case fatality and disability. Despite these efforts and achievements, the absolute number of patients with stroke increases, because of the age-increase in western populations. As a consequence, the population risk of recurrent vascular events and vascular dementia after TIA and stroke is increasing considerably, despite successful efforts to decrease the risk of individual patients with stroke, through preventive treatment.[5] Therefore, secondary prevention is an important part of stroke care. An important target for improvement of secondary prevention may be patient awareness of risk factors for stroke and behavior toward modification of risk factors.

Health education (HE) is aimed at acquisition of skills and attitudes to change behaviors that influence health, and lead to a modification of risk factors, and to a decrease in disability and case fatality from stroke (Figure 1). The effect of HE on the desired outcome is influenced by many factors that may be related to the individual patients, their knowledge and skills, their social environment, i.e. family and friends, and the accessibility and quality of the healthcare system.

Figure 1. *The steps and influences in the process of health education(HE) aiming at reduction of case fatality and disability from stroke.*



Based on Carleton, R. A. et al. Circulation 1996;93:1768-1772; changed and adapted

The Helsingborg Declaration of 2006 stated that one of the core indicators for the assessment of quality of care is the proportion of patients given adequate advice about a healthy lifestyle.[6] However, HE is still an underdeveloped aspect of stroke care. It is not an accepted part of the secondary prevention program in clinical practice. Although presently only a few international guidelines provide recommendations for HE in stroke and TIA patients,[4] the number of guidelines that focus on reduction of vascular risk by

education and behavioral change is increasing.[7]

In many patients, risk factors are not reduced to an optimal level by standard treatment. This is caused by lack of compliance with medical regimes[8] and by suboptimal health behavior with regard to diet and physical activity. We estimated the effect of changes in modifiable risk factors from typical to optimal, on the risk of new vascular events in patients with a recent TIA or stroke (Table 1).

Table 1. *The estimated relative risk reduction of modifiable risk factors by health education for major vascular events in patients with a TIA or ischemic stroke. Data from cohort studies or RCT in patients with recent TIA or ischemic stroke.*

Risk factor	Typical value in a stroke or TIA patient	Optimal value	Difference	Estimated Relative Risk Reduction*	Source
BMI (kg/m2)	28	22	6	30%	Cohort studies[8, 9]
Smoking behavior (nr/day)	10	0	10	22%	Cohort studies[8, 9]
Cholesterol (mmol/l)	5.9	4.5	1.4	25-33%**	RCT[10, 11]
LDL cholesterol (mmol/l)	3.4	2.5	1.0	25-33%**	RCT[10, 11]
Blood pressure (mmHg)	130/80	120/75	10/5	25%	RCT[12]
Physical activity (minutes/day)	<10	> 30	>20	21%	Cohort studies[8, 9]

RCT= Randomized Controlled Trials
*Not adjusted for the other risk factors
** if the compliance for statins is optimal

The estimated relative risk reduction which can be achieved by adequate health education on top of the standard medical treatment ranges from 21%-30% per separate risk factor. One has to take into account that this is a theoretical maximal effect. Moreover, there will be interaction between the risk factors; for example, reducing weight by increasing physical activity will also reduce the blood pressure. However, the effect of adequate HE can still be considerable.

HE is important for a number of reasons.[9] First, with the current regime of medication, like antiplatelet drugs, antidiabetica, lipid-lowering and anti-hypertensive drugs, physicians try to reduce the risk of a recurrent vascular event in stroke and TIA patients. Compliance with the pharmacological therapy is essential for the effectiveness of secondary prevention, but this is not optimal in stroke and TIA patients.[10] HE could improve risk reduction by promoting compliance and healthy behavior. Second, it aims to improve patients' and caregivers' understanding of their health status and treatment options. Third, HE should facilitate interactive communication between health provider and patient, and enhance patient participation in continuing care. Fourth, HE is considered necessary for prevention, because it is assumed that the more people know about their disease and associated risk factors, the more they could be willing to change behavior in order to reduce the risk of future events. However, although patients with stroke and TIA already have had at least one vascular event, this does not automatically result in changes in health behavior to reduce their risk of a recurrent vascular event.

HE in stroke and TIA patients needs special consideration, because these patients have a few disadvantages in comparison with other vascular patients. They are generally older; patients with stroke are on average 5-10 years older than patients with acute coronary syndrome at the time of their

event.[11,12] Disability or handicaps after stroke often result in increased needs of personal care and training at home or in a rehabilitation facility. Physical handicaps like even a mild paresis or language disorder as a consequence of stroke, make it difficult to induce physical behavioral changes. Moreover, cognitive impairment after stroke may reduce the patient's ability to understand, retain and apply information provided through HE.

Stroke and TIA patients and their partners generally wish to be informed about all aspects of their disease. Although information is provided to patients in hospitals or after discharge, the patients' quest for information often cannot be met. A review indicated that patients and family are often dissatisfied with the content and quality of the provided stroke information about the causes, consequences and secondary preventive measures of stroke.[13] HE for patients with stroke and TIA may fulfil information needs at least at three different levels. On the first level, patients wish to be informed about the manifestations and nature of their disease. On the second, patients need information about short- and long-term prognosis, including rehabilitation options. On the third level comes the need for information focused on risk factor management and prevention of recurrent vascular events, which is often more a doctor's concern than a patient's need. During their disease, stroke and TIA patients experience different phases. The coping strategies are often aimed at actively adjusting circumstances to personal preferences and thus striving to maintain life as it was before the stroke (assimilative coping). Once the options of changing one's situation have been exhausted, coping changes into attempting to accept the consequences of the stroke by adjusting personal preferences and goals (accommodative coping).[14] In these different phases, different information is needed. It is likely that information concerning long term risk and related health behavior will only meet fertile grounds when patients are in the phase of accommodative coping.

We have reviewed the status and effect of HE in patients with stroke and TIA on different targets as indicated in Figure 1. We will first focus on studies of HE in stroke and TIA patients, aiming at feasibility, and effectiveness at the level of knowledge, attitude and skills, health behavior changes, and stroke outcome. Progress in affiliated health domains, such as coronary artery disease, may help and inspire the development of HE in stroke and TIA patients. Second, we will describe the current status of HE for patients with recent coronary artery disease and we will summarize what is known about effective and feasible approaches to public HE in stroke.

Health education in stroke and TIA patients

Knowledge

Many studies evaluated TIA and stroke patients' knowledge about etiology, warning signs and risk factors of their own disease.[15-19] The proportion of patients who are able to mention at least one warning sign varied between 39-93%.[15,16,18,19] Hemiparesis was the most commonly cited warning sign.[15,16] A variable proportion of stroke patients, 38-98%, was able to name at least one major risk factor.[15,16,18]

This proportion depended on the type of question: open-ended or multiple choice. The latter resulted in the highest proportions. The most commonly mentioned vascular risk factors were hypertension, hypercholesterolemia and smoking.[15,18,20] Only a quarter to half of the stroke patients could mention the brain as affected organ.[15-17] Most studies investigated the knowledge of stroke patients in the acute phase. In this stage, patients may not have received an appreciable amount of information yet. Therefore, the knowledge of stroke and TIA patients in the acute phase would be limited and not be very different of knowledge in the general population.

HE to stroke patients can be provided by different persons; a general practitioner, a stroke nurse specialist or a neurologist. No studies have compared the quality and effect of HE provided by different persons. There are many ways by which HE can be provided, both actively and passively. Examples of passive methods are booklets, a computer program and computer-generated individualized written information. Active methods are information presented to a group or individual by, for example, a multidisciplinary team including a specialist stroke nurse, by means of presentations and interactive sessions. Few randomized controlled trials investigated the effect of an intervention on knowledge of stroke and TIA patients compared with standard care only. In a Cochrane review[21], data were available for 536 of 770 participants from 6 trials.[22-27] Knowledge assessment of warning signs and risk factors varied between 1 week and 6 months. Overall, patients in the intervention groups had significantly more knowledge of stroke than those in the control groups. The magnitude of effect between passive and active information and the effect of individual tailored information was not different between the groups.

Attitude and skills

Patients with acute stroke often experience a significant delay in reaching the hospital. This delay has three components: appraisal delay, the time from noticing a symptom to deciding one is ill; illness delay, the time from onset of symptoms to seeking professional help; and utilization delay, time from seeking professional care to arrival at the hospital.[28] Especially the appraisal and illness delay are patient-dependent. Data about appraisal delay in stroke patients are limited, but studies showed that a history of stroke contributes to heightened awareness and recognition of stroke symptoms.[19,29] Data about the illness delay, the time from onset of symptoms to seeking help, are conflicting. Some studies showed that patients who knew they had a stroke did not promptly seek medical attention. Even when stroke symptoms were correctly recognized, most patients who delayed their call for help, interpreted their symptoms as "not serious".[19,30] Other observational studies suggest that if patients realize that they are having a stroke or have symptoms comparable to previous experience, they seek medical treatment sooner.[18,29]

Studies reporting interventions aimed at changes in attitudes towards risk factors for stroke and TIA are not available. Studies have focused on risk factor changes and compliance with lifestyle advice, the next step in the process of health education aiming to reduce stroke death and disability (Figure 1).

Health behavior and risk factor modification

A well-known problem at behavioral level is the non-compliance with lifestyle advice. Vascular risk factors are negatively influenced by unhealthy lifestyles leading to obesity and an increased risk of hypertension, hypercholesterolemia and diabetes mellitus. Studies investigating the effect of HE on behavioral changes and risk factor modification in stroke and TIA patients are limited. We performed a small randomized controlled study with passive information provision to TIA and stroke patients provided by physicians versus a combination of an individualized multimedia computer program with physician support. We found no statistically significant differences between the two groups at 3 months with regard to compliance with lifestyle recommendations.[22]

Two trials showed there was no evidence of an effect of active information on the modification of health behaviors or risk reduction.[25,31] The first trial investigated a 1-hour small group educational session followed by six 1-hour sessions after discharge.[25] A second study, with 205 stroke and TIA patients, evaluated the effect of additional input from the stroke nurse versus advice provided by medical staff. The stroke nurse reviewed patients at monthly-intervals for approximately 3 months.[31]

Another randomized controlled trial assessed whether extra care of a stroke nurse specialist could be beneficial in terms of the cardiovascular risk profile.[32] In addition to a vascular screening and prevention program, self-management of risk factors was promoted by the stroke nurse specialist in an outpatient clinic. Self-management refers to the individual's ability to manage both physical and psychosocial consequences including lifestyle changes inherent to living with a chronic condition. In self-management, attention can be given to what is important and motivational to the individual patient.[33] Two hundred and thirty-six patients with manifestations of a vascular disease and with two or more modifiable vascular risk factors were pre-randomized according to the Zelen design to receive treatment by a nurse practitioner plus usual care or usual care alone. In the Zelen design participants are randomly allocated prior to seeking consent.[34] Participants allocated to the intervention group are then approached and offered the intervention, which they can decline or accept. Sixty-one patients (25%) refused to participate. This may have led to selection of more motivated patients in the intervention group, and therefore, larger effects. After 1 year, risk factors were assessed again. The primary endpoint was achievement of treatment goals for blood pressure, lipid, glucose and homocysteine levels, body mass index, and smoking. Treatment delivered by nurse practitioners resulted in a significantly better management of blood pressure, cholesterol and BMI than usual care alone after 1-year.[32] The PROTECT cohort study systematically implemented, at the time of TIA or ischemic stroke, 8 medication/behavioral secondary prevention measures known to improve outcome.[35] Medication goals were initiation of an antithrombotic, a statin, an angiotensin-converting enzyme inhibitor and a thiazide diuretic. The four behavioral interventions were smoking cessation counseling, exercise counseling, diet counseling and education about personal stroke risk factors, and the need to call 911 if new stroke symptoms would occur. Endpoints were the proportion of individuals compliant with medical and lifestyle modification interventions after 3 months and the frequency of recurrent vascular events. Adherence rates in patients were 100% for antithrombotics, 99% for statins, 92% for angiotensin-converting enzyme inhibitors, and

80% for thiazide diuretics. Adherence to diet and exercise guidelines were 78% and 70%, respectively. Of the 24 smokers, 20 permanently stopped (83%). The authors from this uncontrolled study concluded that the increase in treatment adherence was associated with a favorable clinical event rate, with substantially fewer recurrent vascular events within the PROTECT cohort of individuals compared with results from other 3-month hospitalization cohort studies.[36]

Outcome

If information about stroke is not adequately provided to or received by stroke patients this is likely to affect their compliance with secondary prevention and long-term outcome.[37]

The direct effect of HE on compliance of lifestyle recommendations and consequently on outcome is not easy to measure. The chain of events leading from HE through changes in attitude and behavior to outcome is long, and the effect of interventions is dampened because of the many links in this chain. Outcome is a broadly defined item, which includes case fatality, recurrent vascular events, disability, anxiety or depression and quality of life. Moreover, outcome is influenced by many other factors, like healthcare system, social and physical environment (Figure 1). Only a few trials are available of the effect of HE on outcome. In a Cochrane review,[21] interventions to deliver HE did not reduce lethality in patients with a recent TIA or stroke, compared to standard management (OR 0.82, 95% CI 0.56 to 1.21). The intervention consisted of group sessions, educational programs, stroke nurse, booklets or individualized information delivered by computers. The review showed that HE did not affect the occurrence of anxiety (data from 681 participants in 6 trials), and depression (data from 956 participants in 8 trials).[21] Three studies investigated the effect of a nurse-led support or education programme for stroke patients and their caregivers or spouses. No effects were found on quality of life, well-being[38] or depression,[39] and small effects (in subgroup analyses) on social activities[40]. In one trial in which patients were visited at home, perception of health increased and emotional reactions and social isolation decreased significantly.[39]

Public stroke knowledge and education

Knowledge

It is well known that there are deficiencies in public knowledge of risk factors for stroke and of stroke warning signs. Moreover, in many countries the public awareness of acute stroke as a disabling, life threatening disease, requiring prompt treatment, is far from optimal.[16,41-56] The proportion of individuals able to mention a single warning sign for stroke varied from 40-70%.[57] In studies investigating knowledge of risk factors, at least 20% of the people could not correctly mention at least one risk factor.[18,43,45,51,58] The proportion of those who identified at least two risk factors was low, and ranged from 25% to 62%.[57] Hypertension was the most frequently recalled risk factor, followed by smoking. The most frequently noted sources of stroke knowledge were friends, family and mass-media. Less commonly, physicians and hospital personnel were cited as sources.[42,43,51,58] There is some evidence that those who are most at risk, the elderly, are the ones with the lowest level of knowledge. The effect of public educational

campaigns aimed at improvement of stroke knowledge is variable.[52,56,59,60] Producing long-term change in public knowledge and behavior is possible[61], but difficult.[38,61,62] A study performed in the US found that public knowledge of stroke risk factors did not substantially improve between 2000 and 2005 despite numerous national stroke public awareness campaigns.[63] An explanation for the failure of some public campaigns could be that they not have been targeted to the proper audience nor tested for efficacy before widespread implementation.

However, the mass-media campaign in the Netherlands, consisting of television and radio advertisements, combined with flyers distributed personally by volunteers at every household door, which started in 2005 with repeated advertisements till 2008, has improved knowledge about warning signs, i.e. the Face-Arm-Speech-Time (FAST) test and care-seeking intention.[64] The number of respondents who could name at least one correct warning sign of stroke increased from 70% at baseline to 89% in 2008.

Attitude and skills

Studies indicated that recognition of stroke is not sufficient to prompt stroke victims in the general population to call the national emergency number.[52,65] One study found[66] that people who knew that stroke was a serious and treatable disease, were about twice as likely to call the emergency number. Calling the national emergency number was not driven by knowledge of risk factors and warning signs. Previous studies found that delay in seeking medical attention after stroke onset is the most frequent reason for low rates of thrombolysis for acute ischemic stroke.[67]

Health behavior and risk factor modification

There are no studies available on the effect of HE on the public and the effect of risk factor modification concerning stroke.

Health education in patients with coronary artery disease

Coronary artery disease (CAD) is a significant public health problem in the developed world with high case fatality. CAD caused about 1 of every 5 deaths in the United States in 2005.[60,68] CAD and stroke share many aspects such as the need of risk factor management and lifestyle change, of acute treatment and of treatment with antiplatelets or other preventive treatment. Given these similarities, the state of the art of HE for cardiovascular patients is of great interest.

Knowledge

In contrast to studies in stroke, only a few studies assessed knowledge of disease, symptoms and risk factors in patients with a acute coronary syndrome.[69-71] All studies indicated low levels of knowledge of the participants. Short individual teaching by a nurse and counseling intervention resulted in improved knowledge of CAD.[72,73] A review of 5 studies investigating computer-software for education of patients with coronary heart disease demonstrated their effectiveness in increasing knowledge. The increased knowledge was demonstrated in patients who used the educational software immediately after the

procedure. Only two of the five studies reported knowledge after 6 months, with a large effect, using Cohen's delta as effect size measure.[74] Loss to follow-up varied from 12% to 33%.[75]

Attitude and skills

Similar to stroke patients, it is important for patients to have knowledge of warning signs, so that they can quickly identify symptoms of acute coronary syndrome and take prompt action to seek care. Reperfusion therapy with either percutaneous coronary intervention or fibrinolytic drugs leads to lower case fatality and fewer complications. The case-fatality of acute myocardial infarction is largely dependent on the time between symptom onset and reperfusion.[76] The main reasons for delay were the patients' perception that the symptoms might pass, because the symptoms were either not severe, or because the patient thought that the symptoms were caused by a different illness.[77] Some studies found that better awareness of CAD symptoms was associated with shorter pre-hospital delay times[72,73] but others did not.[78,79] The Rapid Early Action Coronary Treatment (REACT) trial, in which members of the community received education through the mass media and one-on-one approach from their local health care providers, showed limited success.[78] Despite an 18-month exposure to the intervention, time from symptom onset to hospital arrival for patients with chest pain did not change significantly, although appropriate use of medical emergency facilities was more frequently observed in the intervention communities. In one other trial, participants (n=3522) with documented CAD were randomized to experimental (n=1777) or control (n=1745) groups. Patients in the experimental groups received education and counseling about CAD symptoms and required actions. The education and counseling intervention did not lead to reduced pre-hospital delay or increased ambulance use.[79] However, short individual teaching and counseling intervention by a nurse resulted in improved knowledge of CAD and also in more appropriate responses to symptoms in people with a myocardial infarction sustained to 12 months.[72,73]

Health behavior and risk factor modification

The EUROASPIRE III survey showed that large numbers of CAD patients do not achieve the desired lifestyle, risk factor modification and therapeutic targets for cardiovascular disease prevention.[80] Therefore, intervention trials with integrated HE are designed to achieve targets as defined in the prevention guidelines in routine clinical practice. In one trial, 3241 patients with recent myocardial infarction were randomized to a 3-year multifactorial educational and behavioral program or usual care.[81] Comprehensive cardiac rehabilitation sessions with one-to-one support were held monthly from month 1 to month 6, then every 6 months for 3 years. Each session consisted of 30 minutes of supervised aerobic exercise, plus lifestyle and risk factor counseling lasting at least 1 hour and reinforcement of preventive interventions lasting approximately 30 minutes. In this way every patient received in total 15 hours counseling in 3 years. To improve adherence to lifestyle modification and help patients adopt a positive role in the care of their own health, a booklet explaining how to deal with exercise, diet, smoking cessation, and stress management was distributed. The mutual support of family members was

encouraged in ad hoc meetings together with the patients to make correct lifestyle habits more likely to be maintained in the long run. Compared with usual care, the intensive intervention did not decrease the primary combined end point of fatal and nonfatal vascular events significantly, but intervention decreased several secondary end points like cardiovascular mortality plus nonfatal MI and stroke and induced a considerable improvement in lifestyle habits.

In the EUROACTION study[82], a cluster-randomized, controlled trial in eight European countries, a nurse-coordinated multidisciplinary, family-based preventive cardiology program versus standard care was investigated. More than 3000 patients with CAD and their partners were encouraged to achieve a healthy lifestyle with support from their families, other people attending the program, and the health professionals—i.e., hospital nurses, dietitians, and physiotherapists—who used stages of change and motivational interviews. Nurses coordinated a program of eight workshops—one a week—for coronary heart disease; cardiovascular risks—ie, lifestyle and risk factor control; cardioprotective treatments; and return to work and leisure. After completion of the 16-week hospital program, patients and their partners were reassessed for lifestyle, risk factors, and therapeutic management, and results were sent to each individual's own family doctor. All patients and their partners were invited back for reassessment at 1 year. Endpoints were smoking cessation, blood pressure <140/90 mmHg, LDL < 3mmol/l, BMI < 25 kg/m^2 , physical activity ≥30 min more than 4 times per week, intake of more than 400 gram a day of fruit and vegetables, and <10% of total energy supplied by saturated fat. This study did not include vascular events as endpoints. The intervention group had significantly lower blood pressures, made significantly healthier food choices and became physically more active. This effect was mainly attributed to lifestyle change supported by families.

Improving health education in stroke and TIA patients

Basic knowledge of stroke and TIA patients of their disease and associated risk factors is not sufficient. This is observed in patients with CAD and in the general population as well.

The preventive effect on the occurrence of major vascular events of interventions focusing on improvement of stroke knowledge has not been conclusively demonstrated, but a tendency toward a positive effect on knowledge of warning signs and vascular risk factors in public and patients can be observed. No specific method of HE is superior, although the individual and repetitive, active methods seem more successful. There is no conclusive effect of active information aimed at stroke patients on the modification of health behavior, risk reduction or outcome measurements. Trials in patients with coronary artery disease have provided promising results.[81,82] Two randomized trials showed considerable improvement in lifestyle. Compared to trials in stroke patients, these trials included more patients, involved partners more actively and used intensive and repetitive ways of health education with active participation of the patients. Moreover, they had a longer follow-up period than trials in stroke patients. Knowledge is a necessary factor for inducing change, but the process of modification of risk factors is a multi-staged and complex one, requiring the right attitude, motivation and capacity to change behavior. HE provides a different approach to reduction of stroke death and disability. Moreover, HE may

be used to improve medication compliance.

The first step in modification of risk factor behaviour is improvement of the quality of the provided information. HE provided by physicians is often based upon what health professionals think patients should know. Reports have demonstrated that patients are dissatisfied with the content of stroke information.[13] The question is whether this is only due to quality of the information or to the mental and emotional status of the patient, who may have difficulty in retaining information. Three levels should be discerned when one provides HE to stroke patients, HE about nature and manifestations of stroke, about prognosis and rehabilitation and about risk factor management and prevention. It is likely that patients are generally more interested in their prognosis and rehabilitation possibilities, and physicians in risk factor modulation and lifestyle advices. Many educational programs are hospital-based, the time when patients are least able to retain information. HE about stroke should start during the acute phase, and should be continued after discharge, and should preferably be provided by the same persons.

Interactive stroke-specific software may offer an opportunity, with possibility of accessibility, repetition, but with the disadvantage of missing personal information. Stroke specialist nurses or nurse practitioners may play an important role in providing information in HE to TIA and stroke patients.

In conclusion, the information should address the patients' issues, needs and concerns. The information should be patient-centered, interactive, personalized, flexible and repetitive. It should create opportunities to apply the new knowledge that leads to attitude changes. HE is a time consuming way of preventive medicine for stroke physicians. Studies showed that extra care of a stroke nurse specialist could be beneficial in terms of the cardiovascular risk profile.[32,82] These studies showed a positive effect of a nurse practitioners who used stages of change or self-management techniques as part of vascular preventive program.[32, 82] Stroke nurse specialists could combine vascular care coordination with promoting self-management or another cognitive behavioral approaches to induce healthy lifestyle. They could also pay attention to patients' relatives, who play an important role in inducing and promoting healthy lifestyle behaviors in patients.[82]

HE is a time-consuming, but potentially effective way of preventing vascular events after TIA or stroke. HE should offer more than telling patients general facts on vascular disease. It should not only focus on improving knowledge, but also on attitude and risk factor behavior, should take the stage of motivation or willingness to change lifestyle into account, and demand active participation of patients. A stroke nurse specialist could play an important role in HE. The experience of cardiologists, who have shown that HE results in a change of lifestyle, is important also for neurologists.

Nevertheless, the effect of HE on the incidence of vascular events or on outcome after stroke remains to be demonstrated. Future trials investigating the effect of HE in stroke and TIA patients should be large, have a longer follow-up period, should use an intensive and repetitive manner of HE and involve patients' relatives to induce and maintain a healthy lifestyle.

References

1. Rothwell PM, Coull AJ, Giles MF et al. Change in stroke incidence, mortality, case-fatality, severity, and risk factors in Oxfordshire, UK from 1981 to 2004 (Oxford Vascular Study). The Lancet 2004;363:1925-1933.
2. Feigin VL, Lawes CM, Bennett DA, Barker-Collo SL, Parag V. Worldwide stroke incidence and early case fatality reported in 56 population-based studies: a systematic review. Lancet Neurol 2009;8:355-369.
3. Wardlaw JM, Murray V, Berge E, Del Zoppo GJ. Thrombolysis for acute ischaemic stroke. Cochrane Database Syst Rev 2009;CD000213.
4. The European Stroke Organisation (ESO) Executive Committee and theESO Writing Committee. Guidelines for management of ischaemic stroke and transient ischaemic attack 2008. Cerebrovasc Dis 2008;25:457-507.
5. Pendlebury ST, Rothwell PM. Risk of recurrent stroke, other vascular events and dementia after transient ischaemic attack and stroke. Cerebrovasc Dis 2009;27 Suppl 3:1-11.
6. Kjellström T, Norrving B, Shatchkute A. Helsingborg Declaration 2006 on European Stroke Strategies. Cerebrovascular Diseases 2007;23:229-241.
7. Guidelines for management of ischaemic stroke and transient ischaemic attack 2008. Cerebrovascular Diseases 2008;25:457-507.
8. Cutler DM, Everett W. Thinking Outside the Pillbox—Medication Adherence as a Priority for Health Care Reform. N Engl J Med 2010;362:1553-1555.
9. Rankin SH, Stalling KD. Patient education; principles and practise. Lippincott; 2001.
10. Sappok T, Faulstich A, Stuckert E, Kruck H, Marx P, Koennecke HC. Compliance with secondary prevention of ischemic stroke: a prospective evaluation. Stroke 2001;32:1884-1889.
11. Mandelzweig L, Battler A, Boyko V et al. The second Euro Heart Survey on acute coronary syndromes: characteristics, treatment, and outcome of patients with ACS in Europe and the Mediterranean Basin in 2004. Eur Heart J 2006;27:2285-2293.
12. Scholte Op Reimer WJ, Dippel DW, Franke CL et al. Quality of hospital and outpatient care after stroke or transient ischemic attack: insights from a stroke survey in the Netherlands. Stroke 2006;37:1844-1849.
13. Rodgers H, Bond S, Curless R. Inadequacies in the provision of information to stroke patients and their families. Age Ageing 2001;30:129-133.
14. Darlington AS, Dippel DW, Ribbers GM, van Balen R, Passchier J, Busschbach JJ. Coping strategies as determinants of quality of life in stroke patients: a longitudinal study. Cerebrovascular Diseases 2007;23:401-407.
15. Maasland L, Koudstaal PJ, Habbema JD, Dippel DWJ. Knowledge and understanding of disease process, risk factors and treatment modalities in patients with a recent TIA or minor ischemic stroke. Cerebrovasc Dis 2007;23:435-440.
16. Kothari R, Sauerbeck L, Jauch E et al. Patients' awareness of stroke signs, symptoms, and risk factors. Stroke 1997;28:1871-5.
17. Wellwood I, Dennis MS, Warlow CP. Perceptions and knowledge of stroke among surviving patients with stroke and their carers. Age Ageing 1994;23:293-298.
18. Carroll C, Hobart J, Fox C, Teare L, Gibson J. Stroke in Devon: knowledge was good, but action was poor. J Neurol Neurosurg Psychiatry 2004;75:567-571.
19. Williams LS, Bruno A, Rouch D, Marriott DJ. Stroke patients' knowledge of stroke. Influence on time to presentation. Stroke 1997;28:912-915.
20. Tissue plasminogen activator for acute ischemic stroke. The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. N Engl J Med 1995;333:1581-1587.
21. Smith J, Forster A, Young J, On behalf of the Cochrane Group for information provision after stroke. Cochrane review: information provision for stroke patients and their caregivers. Clinical Rehabilitation 2009;23:195-206.
22. Maasland E, Koudstaal PJ, Habbema JD, Dippel DW. Effects of an individualized multimedia computer program for health education in patients with a recent minor stroke or transient ischemic attack - a randomized controlled trial. Acta Neurol Scand 2007;115:41-48.
23. Lowe DB, Sharma AK, Leathley MJ. The CareFile Project: a feasibility study to examine the effects of an individualised information booklet on patients after stroke. Age Ageing 2007;36:83-89.
24. Hoffmann T, McKenna K, Worrall L, Read SJ. Randomised trial of a computer-generated tailored written education package for patients following stroke. Age Ageing 2007;36:280-286.

25. Rodgers H, Atkinson C, Bond S, Suddes M, Dobson R, Curless R. Randomized controlled trial of a comprehensive stroke education program for patients and caregivers. Stroke 1999;30:2585-2591.
26. Mant J, Carter J, Wade DT, Winner S. The impact of an information pack on patients with stroke and their carers: a randomized controlled trial. Clin Rehabil 1998;12:465-476.
27. Smith J, Forster A, Young J. A randomized trial to evaluate an education programme for patients and carers after stroke. Clin Rehabil 2004;18:726-736.
28. Safer MA, Tharps QJ, Jackson TC, Leventhal H. Determinants of three stages of delay in seeking care at a medical clinic. Med Care 1979;17:11-29.
29. Lacy CR, Suh DC, Bueno M, Kostis JB. Delay in Presentation and Evaluation for Acute Stroke : Stroke Time Registry for Outcomes Knowledge and Epidemiology (S.T.R.O.K.E.). Stroke 2001;32:63-69.
30. Derex L, Adeleine P, Nighoghossian N, Honnorat J, Trouillas P. Factors Influencing Early Admission in a French Stroke Unit. Stroke 2002;33:153-159.
31. Ellis G, Rodger J, McAlpine C, Langhorne P. The impact of stroke nurse specialist input on risk factor modification: a randomised controlled trial. Age Ageing 2005;34:389-392.
32. Goessens BM, Visseren FL, Sol BG, de Man-van Ginkel JM, van der Graaf Y. A randomized, controlled trial for risk factor reduction in patients with symptomatic vascular disease: the multidisciplinary Vascular Prevention by Nurses Study (VENUS). Eur J Cardiovasc Prev Rehabil 2006;13:996-1003.
33. Barlow J, Wright C, Sheasby J, Turner A, Hainsworth J. Self-management approaches for people with chronic conditions: a review. Patient Educ Couns 2002;48:177-187.
34. Torgerson DJ, Roland M. What is Zelen's design? BMJ 1998;316:606.
35. Ovbiagele B, Saver JL, Fredieu A et al. In-Hospital Initiation of Secondary Stroke Prevention Therapies Yields High Rates of Adherence at Follow-up. Stroke 2004;35:2879-2883.
36. Johnston SC, Gress DR, Browner WS, Sidney S. Short-term prognosis after emergency department diagnosis of TIA. JAMA 2000;284:2901-2906.
37. O'Mahony PG, Rodgers H, Thomson RG, Dobson R, James OF. Satisfaction with information and advice received by stroke patients. Clin Rehabil 1997;11:68-72.
38. Larson J, Franzen-Dahlin A, Billing E, Arbin M, Murray V, Wredling R. The impact of a nurse-led support and education programme for spouses of stroke patients: a randomized controlled trial. J Clin Nurs 2005;14:995-1003.
39. Burton C, Gibbon B. Expanding the role of the stroke nurse: a pragmatic clinical trial. J Adv Nurs 2005;52:640-650.
40. Forster A, Young J. Specialist nurse support for patients with stroke in the community: a randomised controlled trial. BMJ 1996;312:1642-1646.
41. Yoon SS, Byles J. Perceptions of stroke in the general public and patients with stroke: a qualitative study. Bmj 2002;324:1065-1068.
42. Hux K, Rogers T, Mongar K. Common perceptions about strokes. J Community Health 2000;25:47-65.
43. Pancioli AM, Broderick J, Kothari R et al. Public perception of stroke warning signs and knowledge of potential risk factors. Jama 1998;279:1288-1292.
44. Mosca L, Jones WK, King KB, Ouyang P, Redberg RF, Hill MN. Awareness, perception, and knowledge of heart disease risk and prevention among women in the United States. American Heart Association Women's Heart Disease and Stroke Campaign Task Force. Arch Fam Med 2000;9:506-515.
45. Reeves MJ, Hogan JG, Rafferty AP. Knowledge of stroke risk factors and warning signs among Michigan adults. Neurology 2002;59:1547-1552.
46. Parahoo K, Thompson K, Cooper M, Stringer M, Ennis E, McCollam P. Stroke: awareness of the signs, symptoms and risk factors—a population-based survey. Cerebrovasc Dis 2003;16:134-140.
47. Pandian JD, Jaison A, Deepak SS et al. Public Awareness of Warning Symptoms, Risk Factors, and Treatment of Stroke in Northwest India. Stroke 2005;36:644-648.
48. Muller-Nordhorn J, Nolte CH, Rossnagel K et al. Knowledge about risk factors for stroke: a population-based survey with 28,090 participants. Stroke 2006;37:946-950.
49. Kim JS, Yoon SS. Perspectives of stroke in persons living in Seoul, South Korea. A survey of 1000 subjects. Stroke 1997;28:1165-1169.

50. Blades LL, Oser CS, Dietrich DW et al. Rural community knowledge of stroke warning signs and risk factors. Prev Chronic Dis 2005;2:A14.
51. Schneider AT, Pancioli AM, Khoury JC et al. Trends in community knowledge of the warning signs and risk factors for stroke. Jama 2003;289:343-346.
52. Becker K, Fruin M, Gooding T, Tirschwell D, Love P, Mankowski T. Community-based education improves stroke knowledge. Cerebrovasc Dis 2001;11:34-43.
53. Ferris A, Robertson RM, Fabunmi R, Mosca L. American Heart Association and American Stroke Association national survey of stroke risk awareness among women. Circulation 2005;111:1321-1326.
54. Pontes-Neto OM, Silva GS, Feitosa MR et al. Stroke Awareness in Brazil: Alarming Results in a Community-Based Study. Stroke 2008;39:292-296.
55. Vukovic V, Mikula I, Kesic MJ et al. Perception of stroke in Croatia - knowledge of stroke signs and risk factors amongst neurological outpatients. Eur J Neurol 2009;9:1060-1065.
56. Neau JP, Ingrand P, Godeneche G. Awareness within the French population concerning stroke signs, symptoms, and risk factors. Clinical Neurology and Neurosurgery 2009;111:659-664.
57. Nicol MB, Thrift AG. Knowledge of risk factors and warning signs of stroke. Vasc Health Risk Manag 2005;1:137-147.
58. Sug Yoon S, Heller RF, Levi C, Wiggers J, Fitzgerald PE. Knowledge of stroke risk factors, warning symptoms, and treatment among an Australian urban population. Stroke 2001;32:1926-1930.
59. Silver FL, Rubini F, Black D, Hodgson CS. Advertising strategies to increase public knowledge of the warning signs of stroke. Stroke 2003;34:1965-1968.
60. Stern EB, Berman M, Thomas JJ, Klassen AC. Community Education for Stroke Awareness : An Efficacy Study. Stroke 1999;30:720-723.
61. Marx JJ, Gube C, Faldum A et al. An educational multimedia campaign improves stroke knowledge and risk perception in different stroke risk groups. Eur J Neurol 2009;16:612-618.
62. Hodgson C, Lindsay P, Rubini F. Can Mass Media Influence Emergency Department Visits for Stroke? Stroke 2007;38:2115-2122.
63. Kleindorfer D, Khoury J, Broderick JP et al. Temporal Trends in Public Awareness of Stroke. Warning Signs, Risk Factors, and Treatment. Stroke 2009;40:2502-2506.
64. van Leijden AJ, Wimmers RH, Hinlopen CH, Franke CL. Public stroke knowledge and care-seeking intention 2004-2008. The long term impact of an educational mass media campaign in the Netherlands. Cerebrovascular Diseases 2009; 27(supp 6):68.
65. Marx JJ, Nedelmann M, Haertle B, Dieterich M, Eicke BM. An educational multimedia campaign has differential effects on public stroke knowledge and care-seeking behavior. J Neurol 2008;255:378-384.
66. Mikulik R, Bunt L, Hrdlicka D, Dusek L, Vaclavik D, Kryza J. Calling 911 in response to stroke: a nationwide study assessing definitive individual behavior. Stroke 2008;39:1844-1849.
67. Anderson BE, Rafferty AP, Lyon-Callo S, Fussman C, Reeves MJ. Knowledge of Tissue Plasminogen Activator for Acute Stroke Among Michigan Adults. Stroke 2009;40:2564-2567.
68. Lloyd-Jones D, Adams R et al. Heart Disease and Stroke Statistics 2009 Update: A Report From the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation 2009;119:e21-181.
69. Kayaniyil S, Ardern CI, Winstanley J et al. Degree and correlates of cardiac knowledge and awareness among cardiac inpatients. Patient Education and Counseling 2009;75:99-107.
70. Dracup K, McKinley S, Doering LV et al. Acute Coronary Syndrome: What Do Patients Know? Arch Intern Med 2008;168:1049-1054.
71. Zerwic JJ, King KB, Wlasowicz GS. Perceptions of patients with cardiovascular disease about the causes of coronary artery disease. Heart & Lung: The Journal of Acute and Critical Care 2003;26:92-98.
72. McKinley S, Dracup K, Moser DK et al. The effect of a short one-on-one nursing intervention on knowledge, attitudes and beliefs related to response to acute coronary syndrome in people with coronary heart disease: A randomized controlled trial. International Journal of Nursing Studies 2009;46:1037-1046.
73. Buckley T, McKinley S, Gallagher R, Dracup K, Moser DK, Aitken LM. The effect of education and counselling on knowledge, attitudes and beliefs about responses to acute myocardial infarction symptoms. Eur J Cardiovasc Nurs 2007;6:105-111.

74. Cohen J. A power primer. Psychol Bull 1992;112:155-159.
75. Beranova E, Sykes C. A systematic review of computer-based softwares for educating patients with coronary heart disease. Patient Educ Couns 2007;66:21-28.
76. Simoons ML, Serruys PW, Van den Brand M et al. Early thrombolysis in acute myocardial infarction: limitation of infarct size and improved survival. J Am Coll Cardiol 1986;7:717-728.
77. Meischke H, Ho MT, Eisenberg MS, Schaeffer SM, Larsen MP. Reasons Patients With Chest Pain Delay or Do Not Call 911. Annals of Emergency Medicine 1995;25:193-197.
78. Luepker RV, Raczynski JM, Osganian S et al. Effect of a Community Intervention on Patient Delay and Emergency Medical Service Use in Acute Coronary Heart Disease: The Rapid Early Action for Coronary Treatment (REACT) Trial. JAMA 2000;284:60-67.
79. Dracup K, McKinley S, Riegel B et al. A Randomized Clinical Trial to Reduce Patient Prehospital Delay to Treatment in Acute Coronary Syndrome. Circ Cardiovasc Qual Outcomes 2009;2:524-532.
80. Kotseva K, Wood D, De Backer G et al. EUROASPIRE III: a survey on the lifestyle, risk factors and use of cardioprotective drug therapies in coronary patients from 22 European countries. [Article]. European Journal of Cardiovascular Prevention & Rehabilitation 2009;16:121-137.
81. Giannuzzi P, Temporelli PL, Marchioli R et al. Global Secondary Prevention Strategies to Limit Event Recurrence After Myocardial Infarction: Results of the GOSPEL Study, a Multicenter, Randomized Controlled Trial From the Italian Cardiac Rehabilitation Network. Arch Intern Med 2008;168:2194-2204.
82. Wood DA, Kotseva K, Connolly S et al. Nurse-coordinated multidisciplinary, family-based cardiovascular disease prevention programme (EUROACTION) for patients with coronary heart disease and asymptomatic individuals at high risk of cardiovascular disease: a paired, cluster-randomised controlled trial. The Lancet 2008;371:1999-2012.
83. Harmsen P, Lappas G, Rosengren A, Wilhelmsen L. Long-term risk factors for stroke: twenty-eight years of follow-up of 7457 middle-aged men in Goteborg, Sweden. Stroke 2006;37:1663-1667.
84. van Wijk I, Kappelle LJ, van Gijn J et al. Long-term survival and vascular event risk after transient ischaemic attack or minor ischaemic stroke: a cohort study. Lancet 2005;365:2098-2104.
85. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. Lancet 2002;360:7-22.
86. Amarenco P, Goldstein LB, Szarek M et al. Effects of Intense Low-Density Lipoprotein Cholesterol Reduction in Patients With Stroke or Transient Ischemic Attack: The Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) Trial. Stroke 2007;38:3198-3204.
87. Randomised trial of a perindopril-based blood-pressure-lowering regimen among 6,105 individuals with previous stroke or transient ischaemic attack. Lancet 2001;358:1033-41.

Chapter 5

General discussion

The burden of disease caused by stroke in terms of suffering and costs is enormous. Each year approximately 600,000 people in the US and 41,000 in the Netherlands experience a first stroke. [1, 2] The estimated direct and indirect costs of stroke in the US for 2009 are 68.9 billion dollars.[1] There is ample evidence that stroke care in clinical practice often falls short of the ideal care set in official guidelines. The aim of this thesis is to make a contribution to the improvement of the quality of stroke care.

I focused on three interrelated subjects: the assessment of the quality of stroke care, health education (HE) in patients with TIA or ischemic stroke, and the applicability of results of clinical trials of stroke and TIA patients in everyday practice. Besides their focus on improvement of clinical practice, these topics have one more aspect in common; they constitute new and relatively unexplored areas of stroke research. In this chapter, I will summarize my main findings and discuss some of the methodological issues. After that, I will discuss the clinical implications and provide suggestions for future research.

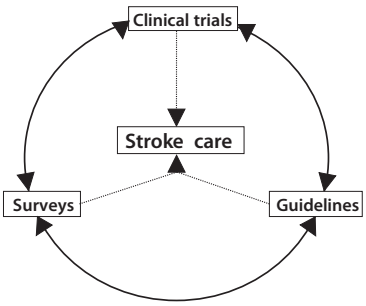
Main findings

All over the world results of medical trials are published, which creates an overflow of information from which knowledge can be distilled. This knowledge has to reach the physician who makes a decision concerning the medical management of a unique patient at a specific place with locally available treatment modalities. Because of this overflow of information, physicians have sometimes difficulties in separating the "good from the bad" i.e. useful information from useless, and proven effective treatments versus unproven interventions. They use the double-blinded randomized controlled trials (RCTs) as a gold standard. However, patients treated by a physician are not completely comparable to the average patient included in randomized clinical trials, due to the many and strict enrolment criteria used in RCTs. To assist physicians in decision making, evidence-based guidelines have been developed in which results of the RCTs are valued as the highest level of evidence. Therefore, guidelines can be regarded as an important tool for improving the quality of stroke care. However guidelines are not always adhered to in all patients. This has numerous reasons, ranging from lack of awareness, time or facilities to lack of agreement with peers.

Surveys constitute an approach to collect quantitative information about unselected patients in a hospital setting, their clinical characteristics, and outcome, but also about the medical and nursing care they received. Surveys have been used to evaluate the adherence to guidelines and to give feedback to clinicians about the quality of stroke care. (Figure 1).

Results of RCT are the basis of the development of guidelines in clinical practice. The fact that RCTs have strict enrolment criteria, which mainly serve to limit the risk of complications, may limit the generalizability and applicability of the results of RCTs. Stroke prevention trials often require additional risk factors or symptoms beyond the presenting clinical syndrome in order to select patients who are at a higher risk for an outcome event and to increase homogeneity and statistical power. This thesis showed that the applicability of RCTs investigating antiplatelet treatment may be limited. Patients enrolled in international, multicenter randomized clinical trials of antiplatelet treatment for secondary prevention

Figure 1. *Relation of clinical trials, guidelines and surveys to stroke care*



after TIA and stroke are not fully representative of patients treated in daily practice. After applying the trials' in- and exclusion criteria to the Netherlands Stroke Survey population, 33% to 70% of all patients in the survey did not fulfil enrolment criteria and were therefore not eligible for inclusion in the trial. We also showed that trial-eligible patients were younger and had a better clinical outcome than those who did not fulfil enrolment criteria (Chapter 2.1). This raised concerns about extrapolation of the trial results to elderly patients and to those with a severe stroke (score on the modified Rankin scale (mRS) of 4 or 5).These concerns gave us a reason to reanalyze the data from the ESPRIT[3] and ESPS-2[4] to study the preventive effect of aspirin and dipyridamole according to mRS at baseline. We showed that the beneficial effect of the combination of low dose aspirin and dipyridamole fortunately applied to patients in all subcategories of the mRS (Chapter 2.2).

Another important aspect of accurate stroke care and prevention is that general and scientific knowledge about stroke has to be available to the right person at a specific moment in time. This is particularly difficult for stroke patients, who are frequently not in a position to judge what is of value because they lack the necessary education and resources. In addition, if patients do not know that special conditions or lifestyle put them at higher risk of vascular events, they are less likely to pay attention to health education (HE), because they miss the relevance. We found that the vast majority of patients with TIA or minor stroke lacks specific knowledge about their disease, but do have a reasonable knowledge of general vascular risk factors and treatment (Chapter 4.2). Health education by an individualized computer program did not show a lasting effect on the knowledge of TIA and minor stroke patients of their own disease (Chapter 4.3). Our review of health education in stroke and TIA patients showed that basic knowledge of their own disease and associated risk factors is not sufficient (Chapter 4.4). Data are limited, but there is no conclusive evidence of an effect of active information in stroke and TIA patients on attitude of lifestyle behaviour, health behaviour, risk reduction or outcome measurements like vascular events. However, there are promising data from trials in patients with coronary artery disease (CAD),[5,6] in whom randomized trials showed considerable long lasting improvement in lifestyle habits after a multidisciplinary health education program. Compared with trials in patients with ischemic stroke, these

studies were performed in a large number of patients and used more intensive and repetitive ways of HE. Also, family members were involved to make correct lifestyle habits more likely to be maintained in the long run.

One way to improve the quality of stroke care is to provide effective and adequate HE. Another way is quality measurement of delivered stroke care using indicators. An indicator is not a direct measure of quality, but points to an aspect of stroke care which deserves further investigation aimed at improving quality of care. According to Donabedian's concept, assessment of health care quality can be separated into structure, process and outcome.[7] We focused on quality measurement of stroke care by process indicators, they have a high face-validity, can often be collected over a shorter period of time and inadequate performance may provide direct opportunities for intervention and improvement.[8] We showed that one process indicator by itself is not representative for the total in-hospital stroke care. In other words, a single process indicator will not suffice to measure total quality of stroke care of patients with an ischemic stroke. This implies that the overall quality of stroke care should be measured by means of carefully selected sets of indicators across all domains of clinical stroke care (Chapter 3.1).

Limitations

Results of surveys can be used to give feedback to clinicians about the quality of their clinical practice. We used data from the Netherlands Stroke Survey to obtain insight in stroke management in the Netherlands (Chapter 3.1). Although surveys by design include all patients in a given time period, selection bias could still play a role at hospital level: hospitals participated voluntarily in the survey, and the participating hospitals were not evenly distributed over all of the Netherlands. Therefore results in the survey are biased towards better than average practice.

In the Netherlands Stroke Survey, we observed high-quality acute stroke care in admitted patients with ischemic stroke. Arguments to withhold recommended treatment were plausible for the majority of admitted patients, whereas reasons for withholding procedures in outpatients were often not clear. Secondary preventive measures and procedures, however, were too often withheld in both admitted patients and outpatients [7, 9] For example, in 7% of the outpatients a CT scan or MRI was not performed. A reason for withholding brain imaging was not documented. Therefore reasons for non-adherence to guidelines, which might have given more insight in quality of stroke care, were not available.

The survey was performed in 2002-2003. Stroke care is moving forward and treatment modalities and quality of care nowadays are different than 8 years ago. In the Netherlands Stroke Survey[9], in which 10 selected hospitals collected patients, the percentage of patients with ischemic stroke receiving thrombolysis was 7%. In 2008, this percentage in the 10 participating hospitals in the Netherlands Stroke Survey was 12%[10] and the overall percentage of thrombolysis in all hospitals in the Netherlands 7%.[11,12] It seems that the hospitals which participated in the Netherlands Stroke Survey, are a positive selection

of all hospitals in the Netherlands, given the higher percentage of thrombolysis.

The 2002-2003 guidelines do not mention timing as an important aspect of stroke care, except for thrombolysis. Rapid assessment and intervention is emerging as the new standard for TIA care. This development is not driven by proof from RCTs that rapid assessment can reduce stroke risk, but by evidence from population-based cohort studies that indicate that patients with TIA are particularly at high risk of recurrent stroke during the first few days after the index event, and from intervention studies of rapid assessment for TIA that made use of historical controls or score charts to assess risk without rapid assessment.[13,14]

Benchmarking is a way to compare care in different stroke services by predetermined indicators and targets and provides an overview of the quality of care . In the Netherlands Stroke Survey data on all current stroke benchmarks indicators were not available; the percentage of ischemic stroke patients receiving thrombolysis, and the modified Rankin score after 3 months were assessed, but not the door-to-needle time, the percentage of patients with a TIA or minor stroke who received the standard diagnostic procedures within 72 hours and the interval between start of diagnostic procedures and carotid endarterectomy. These last three indicators are all related to speed and efficiency. They were not available in the Netherlands Stroke Survey, as they were not included in guidelines around that time. The awareness that in stroke as well as in TIA patients time since onset is both a very important modifiable risk factor for poor outcome and also an interesting quality parameter, has gained recognition through the last years. Timeliness has therefore become an important aspect of stroke care.[13,14]

Another limitation of our study is that the survey is national. Most of the RCTs investigating antiplatelet treatment enrol patients worldwide. In our national survey we used indicators recommended by national guidelines. Because of differences between countries in methods of diagnosis and management, leading to difference in indicators, our Stroke Survey is not completely representative for stroke care worldwide.

In the second part of my thesis I reported the COSTA trial (chapter 4.1), one of the few published controlled clinical studies in health knowledge and education for patients with stroke or TIA. A limitation of this trial is the small size of 65 patients with a relatively high proportion of lost to follow-up (10%), which may have led to unequal distributions of some confounding factors. The patients who were lost to follow-up were younger and had a higher level of education. An explanation could be that these patients probably needed less the relatively simple information provided by the computer program. This may have contributed to the limited knowledge of our study population. On the other hand, patients willing to participate in a study like ours are probably more interested in improving their knowledge and changing their lifestyle. The patients' knowledge was tested after 3 months by means of a questionnaire. The ability to retain information until 3 months could have been influenced by cognitive impairment, which we did not formally assess in our population. In hospital-based studies, the incidence of post-stroke dementia after 3 months ranges from 6 to 27%.[15] The prevalence is likely much lower in our study, because our patients were not hospitalized, had only a TIA or minor stroke and were, on average, younger than hospitalized stroke patients.

Clinical implications

Translating trial results into clinical practice

RCTs are valued as highest in the hierarchy of clinical evidence. As only a small proportion of patients in clinical practice is eligible for a RCT, the question should be raised whether it is always justified to extrapolate the results of the RCTs to the clinical setting. Simulation studies suggest that additional eligibility criteria undermine generalizability and prolong recruitment.[16,17] When broader enrolment criteria are used it is to be expected that the external validity increases.

Recent pooled analyses of individual patient data do not indicate different effects among younger and older patients using dipyridamole and aspirin.[18] We showed a beneficial effect of the combination of low dose aspirin and dipyridamole in all subcategories of the modified Rankin score, including score of 4 and 5. Therefore, one could argue that there should be not too much concern about the extrapolation of trials findings to very elderly patients or patients with a severe stroke who were not recruited in the trials. However both patient groups, old and with a disabling stroke, are still underrepresented in these RCTs' due to exclusion criteria that are more prevalent or by a lower likelihood of being asked to participate, leaving the frail elderly out of the study. This implies that physicians using guidelines with results of RCTs incorporated, have to take into account the generalizability of those results; they have to weigh to which extent their patients are comparable to the patients who participated in the RCTs, regarding age, comorbidity, severity of stroke and risk factors.

Monitoring a high level of quality

In chapter 3.1 we discuss the validity of different process indicators assessing quality of stroke care. We recommend the use a standard set of process indicators that represents the total spectrum of stroke care are, i.e. acute, preventive, medical and non medical care, because a single process indicator is not representative of the total spectrum of stroke care. A standard set of process indicators can facilitate a common language that promotes benchmarking, sharing of best practice and reliable comparisons between settings and if possible between countries. The best set of indicators may be a flexible one; fitted to the development of new treatment modalities and adapted to the needs of a clinician, stroke team, organization or country. The set should preferably reflect care based on level I evidence, but many process indicators currently in use for assessing quality of acute stroke care were not based on high levels of evidence.

Improving health education

We showed that patients with a recent TIA or minor stroke lack stroke-specific knowledge. "Simple" one-stage HE does not have a lasting positive effect on TIA patients' knowledge of their own disease. Still, HE has to be an integral part of a secondary prevention program; the goal of HE is acquisition of skills and attitudes to change behaviors that lead to a modification of risk factors, and finally to a decrease in disability and death from stroke. This is a multi-stage and complex process that requires adequate

knowledge of the patients. The first step is to improve the quality of the provided information. HE provided by physicians is often based upon what health professionals think patients want to know. HE for patients with stroke and TIA can be divided into at least three different levels, that is, HE about nature and manifestations of stroke, about prognosis and rehabilitation and about risk factor management and prevention. People providing health information should pay attention to these different levels, which is depending of the phase of the disease: acute, rehabilitation or adaptation. One may assume that patients are generally more interested in their prognosis and rehabilitation possibilities and physicians in risk factor modulation and life style advices. Our review of results of more extensive HE approaches in cardiovascular disease suggests that the individualized, repetitive, active methods of HE may be more successful, especially when relatives are involved.[5,6]

Adequate knowledge is not enough; just telling facts to patients does not lead to altered behaviors or diminished outcomes. The second step is to realize that patients need a perception of the threat of a health problem, a readiness and capacity to change with adequate motivation patterns.[19,20] Studies assessing compliance with cardiovascular prevention reveal that interventions became more effective with active participation or self-management of patients.[21] Stroke physicians, with the aid of stroke nurse specialists, should focus on the motivational levels of patients, and make use of self management techniques.

Future research

Stroke care should be evidence-based, safe, timely, fairly distributed, patient-oriented and cost-effective. Development of new treatment modalities could prompt redefinitions of process indicators for of quality measurement and adaptation of HE. Future research in quality measurement should focus on all elements of stroke care which are believed to be important, even procedures or treatments with lower level of evidence, for example rehabilitation therapy.

The evaluation of quality of stroke care could be improved by automatic data capturing from electronic patient records. This could be a time-efficient, reliable and reproducible approach to data management. This would allow data from one center to be contrasted at an aggregated level with those of similar centers. The challenge will be to assess if this improvement at process level will lead to improvements at the outcome level.

Future surveys should incorporate current benchmark indicators aiming to compare stroke care within national and international stroke services. Timeliness, an important part of stroke care, should be incorporated in benchmarks.

Nowadays, most of the process indicators measure the quality of a stroke care at hospital level. Another way to assess quality of care is to use benchmarks that measure quality at population level. In the Scottish Stroke Care Audit[22] a benchmark is that acute stroke care should deliver thrombolysis to at least 5 per 100,000 population per year and that 80% of treated patients should start treatment within 60 minutes of arrival at hospital. This benchmark implies that a hospital is considered to have a responsibility for

adequate care in the adherence area and not only for stroke care of patients in the hospital. Future work should therefore develop benchmarks that include care in the adherence area, in hospital and timeliness.

Future work in HE should address the needs and motivation of an individual patient and seek to identify appropriate teaching strategies which can be successfully implemented within clinical practice. Given the promising data of cardiovascular trials investigating the effect of HE, randomized trials in stroke and TIA patients should be developed, focused at lifestyle and risk factor counseling and with cardiovascular events as endpoint. These trials should be sufficiently powered, use an intensive and repetitive approach and involve patients' families in the trial to induce and maintain healthy lifestyle behaviors.

References

1. Lloyd-Jones D, Adams R et al. Heart Disease and Stroke Statistics--2009 Update: A Report From the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation 2009;119:e21-181.
2. Vaartjes I, Reitsma JB, de BA et al. Nationwide incidence of first stroke and TIA in the Netherlands. Eur J Neurol 2008;15:1315-1323.
3. Esprit Study Group, Halkes PH, Van Gijn J., Kappelle LJ, Koudstaal PJ, Algra A. Aspirin plus dipyridamole versus aspirin alone after cerebral ischaemia of arterial origin (ESPRIT): randomised controlled trial. Lancet 2006;367:1665-1673.
4. Diener HC, Cunha L, Forbes C, Sivenius J, Smets P, Lowenthal A. European Stroke Prevention Study. 2. Dipyridamole and acetylsalicylic acid in the secondary prevention of stroke. J Neurol Sci 1996;143:1-13.
5. Giannuzzi P, Temporelli PL, Marchioli R et al. Global Secondary Prevention Strategies to Limit Event Recurrence After Myocardial Infarction: Results of the GOSPEL Study, a Multicenter, Randomized Controlled Trial From the Italian Cardiac Rehabilitation Network. Arch Intern Med 2008;168:2194-2204.
6. Wood DA, Kotseva K, Connolly S et al. Nurse-coordinated multidisciplinary, family-based cardiovascular disease prevention programme (EUROACTION) for patients with coronary heart disease and asymptomatic individuals at high risk of cardiovascular disease: a paired, cluster-randomised controlled trial. The Lancet 2008;371:1999-2012.
7. Donabedian A. The quality of care. How can it be assessed? JAMA 1988;260:1743-1748.
8. Schwamm LH, Fonarow GC, Reeves MJ et al. Get With the Guidelines-Stroke is associated with sustained improvement in care for patients hospitalized with acute stroke or transient ischemic attack. Circulation 2009;119:107-115.
9. Scholte Op Reimer WJ, Dippel DW, Franke CL et al. Quality of hospital and outpatient care after stroke or transient ischemic attack: insights from a stroke survey in the Netherlands. Stroke 2006;37:1844-1849.
10. www.ziekenhuizentransparant.nl
11. Vaartjes I. Hart-en vaatziekten in Nederland 2008. Nederlandse Hartstichting 2009.
12. Inspectie van de gezondheidszorg. Het resultaat telt 2008. Kwaliteitsindicatoren als onafhankelijke graadmeter voor de kwaliteit van in ziekenhuizen verleende zorg.
13. Lavallee PC, Meseguer E, Abboud H et al. A transient ischaemic attack clinic with round-the-clock access (SOS-TIA): feasibility and effects. Lancet Neurol 2007;6:953-960.
14. Rothwell PM, Giles MF, Chandratheva A et al. Effect of urgent treatment of transient ischaemic attack and minor stroke on early recurrent stroke (EXPRESS study): a prospective population-based sequential comparison. Lancet 2007;370:1432-1442.
15. Leys D, Henon H, kowiak-Cordoliani MA, Pasquier F. Poststroke dementia. Lancet Neurol 2005;4:752-759.
16. Howard SC, Algra A, Warlow CP, Rothwell PM. Potential consequences for recruitment, power, and external validity of requirements for additional risk factors for eligibility in randomized controlled trials in secondary prevention of stroke. Stroke 2006;37:209-215.
17. Roozenbeek B, Maas AI, Marmarou A et al. The influence of enrollment criteria on recruitment and outcome distribution in traumatic brain injury studies: results from the impact study. J Neurotrauma 2009;26:1069-1075.
18. Halkes PH, Gray LJ, Bath PM et al. Dipyridamole plus aspirin versus aspirin alone in secondary prevention after TIA or stroke: a meta-analysis by risk. J Neurol Neurosurg Psychiatry 2008;79:1218-1223.
19. Brug J, van Assema P. Differences in use and impact of computer-tailored dietary fat-feedback according to stage of change and education. Appetite 2000;34:285-293.
20. Revere D, Dunbar PJ. Review of computer-generated outpatient health behavior interventions: clinical encounters "in absentia". J Am Med Inform Assoc 2001;8:62-79.
21. Burke LE, Dunbar-Jacob JM, Hill MN. Compliance with cardiovascular disease prevention strategies: a review of the research. Ann Behav Med 1997;19:239-263.
22. Scottish Stroke Care Audit 2009 national report. Stroke Services in Scottish Hospitals. Data relating to 2007-2008 .

Chapter 6

Summary/Samenvatting

Summary

Stroke is a major health problem; it is the second cause of death and the leading cause of disability in the Western world. Therefore, efficient, high quality stroke care is important to reduce this enormous burden of stroke. Stroke care is a challenging and dynamic area. A few challenges of stroke care are: translating trial results adequately into clinical practice, maintaining and monitoring a high level of quality and combining medical treatment with health education in an efficient way. These challenges have in common that they are concerned with processing evidence-based medicine, and are meant to reduce the burden of stroke.

In this thesis I focus on the applicability of results of clinical trials investigating antiplatelets of stroke and TIA patients in everyday practice, on measurement of quality of stroke care by process-of-care indicators and health education in stroke and TIA patients.

Chapter 1, the general introduction, describes the background and the rationale for the research and the contents of the other chapters.

Chapter 2 focuses on the generalizability of trial results. **Chapter 2.1** describes which proportion of patients in a stroke population fulfils the enrolment criteria of recently performed randomized controlled trials investigating antiplatelet treatment for secondary prevention after TIA and stroke. Patients enrolled in those randomized clinical trials of antiplatelet treatment are not fully representative of patients treated in daily practice. After applying the trials' in- and exclusion criteria to a Stroke Survey population, 33% to 75% of all patients in our Stroke Survey were not eligible for participation. We show also that trial-eligible patients were younger and less often had a disabling stroke than those who did not fulfil enrolment criteria.

The combination of low dose aspirin and dipyridamole is more effective than aspirin alone in reducing the risk of recurrent stroke and other major cardiovascular events in patients with a recent transient ischemic attack or minor stroke. It is unknown whether the effect of aspirin and dipyridamole also applies to patients with a disabling stroke. Our reanalysis of 2 randomized clinical trials, ESPRIT and ESPS-2, in **chapter 2.2** suggests a beneficial effect of the combination of low dose aspirin and dipyridamole for patients with a disabling stroke.

Chapter 3 concerns the measurement of quality of stroke care by process-of-care indicators. Process-of-care indicators reflect decision making, and/or clinical practices. Our data suggest that an indicator by itself is not representative for the total in-hospital stroke care. This implies that the overall quality of stroke care should be measured by means of carefully selected sets of indicators across all domains of clinical stroke care.

Health education in stroke and TIA patients is the focus of **chapter 4.**

Chapter 4.1 covers the rationale, background and design of the "computer-supported individualized health education for TIA and minor stroke patients" (COSTA) study. COSTA was a phase II, randomized clinical trial and included 65 minor stroke or TIA patients. In this study we compared the effect of health education by a multimedia computer program in combination with standard health education to standard health education by a physician concerning the level of knowledge of causes, warning signs,

risk factors and treatment of stroke and TIAs and also compliance of lifestyle advices. The results of the COSTA study are described in chapter 4.2 and 4.3.

Chapter 4.2 assesses the knowledge of patients with stroke or TIA who participated in COSTA of their disease, accessory risk factors and treatment. We found that the vast majority of patients with TIA or minor stroke lacks specific knowledge about stroke and TIA, but do have a reasonable knowledge of general vascular risk factors and treatment. **Chapter 4.3** shows no lasting benefit of individualized health education by a multimedia program on the level of knowledge and on the compliance with lifestyle recommendations of patients with a TIA or minor stroke. However, the temporary increase in knowledge in the patients with individualized health education by a multimedia program one week after the intervention suggests that further research should focus on more intensive and interactive methods.

In **chapter 4.4** we review the literature concerning health education in stroke and TIA patients and focus on feasibility, effectiveness at the level of knowledge, attitude and skills, health behavior changes, and stroke outcome. Progress in related health domains, such as coronary artery disease, may help and inspire the development of health education in stroke and TIA patients. Therefore, we describe also the current status of health education in patients with recent coronary artery disease and effective and feasible approaches to public health education in stroke. In general, basic knowledge of stroke and TIA patients of their disease and associated risk factors cannot be regarded as sufficient. This is observed in patients with coronary artery disease and in the general population as well. No specific method is superior, although the individual and repetitive, active methods of health education seem more successful. The effect of health education on the incidence of vascular events or on outcome after stroke remains to be demonstrated. However, randomized trials in patients with coronary artery disease showed considerable improvement in lifestyle.

In **chapter 5** our findings are discussed and placed in broader context and suggestions for further research are given.

Samenvatting

Een beroerte (TIA, herseninfarct of hersenbloeding) is de tweede doodsoorzaak en belangrijkste oorzaak van invaliditeit in de westerse wereld. Daarom is efficiënte en kwalitatief goede zorg aan patiënten met een beroerte belangrijk om de enorme impact van de beroerte te verminderen. Zorg voor patiënten met een beroerte is een uitdagend en dynamisch onderzoeksgebied. Een aantal uitdagingen, zoals vertalen van resultaten van klinische onderzoeken naar de dagelijkse praktijk, handhaven en monitoren van een hoog niveau van zorg en het combineren van behandeling met medicatie met gezondheidsvoorlichting op een efficiënte wijze voor patiënten met een beroerte, hebben gemeen dat ze "evidence-based" geneeskunde behelzen en als doel hebben de impact van de beroerte te verminderen.

In dit proefschrift beschrijf ik de toepasbaarheid van de resultaten van klinische onderzoeken, die zich richten op het effect van plaatjesremmers bij patiënten met een TIA of herseninfarct, in de dagelijkse praktijk. Ook beschrijf ik het meten van kwaliteit van zorg aan patiënten met herseninfarct door middel van procesindicatoren en tenslotte, het effect van gezondheidsvoorlichting aan patiënten met een TIA of herseninfarct.

Hoofdstuk 1, de algemene inleiding, beschrijft de achtergrond, achterliggende gedachtes voor mijn onderzoek en de inhoud van de andere hoofdstukken.

Hoofdstuk 2 richt zich op de generaliseerbaarheid van resultaten van klinische onderzoeken. **Hoofdstuk 2.1** laat zien welk deel van een ziekenhuispopulatie, bestaande uit patiënten met een beroerte, voldoet aan de inclusie criteria van recent uitgevoerde gerandomiseerde onderzoeken, die het effect van plaatjesremmers als secundair preventief middel na een TIA of herseninfarct onderzoeken. De patiënten die deelnemen aan deze gerandomiseerde onderzoeken zijn niet representatief voor patiënten in de dagelijkse praktijk. Na toepassing van de in- en exclusie criteria van de onderzoeken op onze ziekenhuispopulatie, blijkt dat 33% tot 75% van onze patiënten met een herseninfarct of TIA niet geschikt zou zijn voor deelname. We tonen ook aan dat patiënten die wel zouden kunnen deelnemen aan het onderzoek in het algemeen jonger zijn en minder vaak een herseninfarct met ernstige handicap hebben, dan patiënten die niet voldoen aan de in- en exclusiecriteria.

Het is bewezen dat de combinatie van een lage dosering aspirine met dipyridamol beter is dan aspirine alleen in het voorkómen van nieuwe herseninfarcten, hartinfarcten en overlijden door een vasculaire oorzaak bij patiënten met een TIA of een herseninfarct met een lichte handicap. Het is niet duidelijk of dit ook geldt voor patiënten met een ernstige handicap ten gevolge van een herseninfarct. Onze analyse van 2 gerandomiseerde trials, ESPRIT en de ESPS-2, in **hoofdstuk 2.2** suggereert een gunstig effect van de combinatie van een lage dosering aspirine en dipyridamol, óók voor patiënten met een ernstige handicap ten gevolge van een herseninfarct.

Hoofdstuk 3 betreft het meten van kwaliteit van zorg voor patiënten met een herseninfarct door middel van proces indicatoren. Proces indicatoren volgen een serie gebeurtenissen en beslissingen tijdens een onderzoek en/of behandeling van een patiënt in de dagelijkse praktijk. Onze data suggereren dat de kwaliteit van klinische zorg voor patiënten met een herseninfarct niet betrouwbaar kan worden vastgesteld op basis van één proces indicator. Dit houdt in dat kwaliteit van zorg voor patiënten met

een herseninfarct gemeten moet worden door middel van een zorgvuldig geselecteerde set van indicatoren, die alle domeinen van de zorg omvat.

Gezondheidsvoorlichting aan patiënten met een TIA of herseninfarct is het onderwerp van **hoofdstuk 4.** **Hoofdstuk 4.1** bevat de rationale, achtergrond en opzet van de "computer-supported individualized health education for TIA and minor stroke patients" (COSTA) studie. De COSTA studie was een fase II, gerandomiseerde studie waarin 65 patiënten met een herseninfarct met lichte uitval of een TIA geïncludeerd werden. We vergeleken het effect van gezondheidsvoorlichting door middel van een multimedia computer programma in combinatie met gewone voorlichting door een arts met standaard voorlichting door een arts. We hebben het niveau van kennis van oorzaken, waarschuwingssymptomen, risicofactoren, behandeling van een beroerte en de mate van opvolging van leefstijladviezen gemeten. De resultaten worden beschreven in hoofdstuk 4.2 en 4.3.

Hoofdstuk 4.2 beschrijft de kennis van patiënten met een herseninfarct of TIA die deelnamen aan de COSTA studie, over hun eigen ziekte, risicofactoren en behandelingsmogelijkheden. Het grootste deel van de patiënten mist specifieke kennis over de etiologie van hereninfarcten of TIAs, maar heeft een redelijk niveau van kennis over vasculaire risicofactoren en de behandelingsmogelijkheden.

Hoofdstuk 4.3 laat zien dat er geen langdurig effect optreedt bij patiënten met een herseninfarct of TIA op het niveau van kennis en opvolging van leefstijladviezen van een geïndividualiseerde gezondheidsvoorlichting door middel van een multimedia computer programma. Echter, de tijdelijke toename van kennis na een week in de groep van de geïndividualiseerde computervoorlichting suggereert dat verder onderzoek zich zal moeten richten op intensieve en interactieve methoden van gezondheidsvoorlichting.

In **hoofdstuk 4.4** geven we een samenvatting van de huidige literatuur over gezondheidsvoorlichting aan patiënten met een TIA of herseninfarct, gericht op haalbaarheid en effectiviteit op het niveau van kennis, attitude en vaardigheden, verandering van gezondheidsgedrag, zoals stoppen met roken of afvallen, en voorkomen van vasculaire gebeurtenissen, zoals een beroerte. Uitkomsten van onderzoeken in gerelateerde domeinen, zoals patiënten met een hartinfarct, kunnen de ontwikkeling van gezondheidsvoorlichting aan patiënten met een herseninfarct of TIA inspireren. We beschrijven daarom ook de huidige staat van gezondheidsvoorlichting aan patiënten met een hartinfarct en de effectieve, haalbare methodes van voorlichting over een beroerte aan de algemene populatie. In het algemeen geldt, dat de basis kennis van patiënten met een TIA of herseninfarct over hun eigen ziekte en risicofactoren niet voldoende is. Dit wordt ook geobserveerd bij patiënten met een hartinfarct over hun eigen ziekte en de algemene populatie. Geen enkele methode van voorlichting is superieur, maar de individuele, actieve en methodes, die herhaald worden, lijken meer succesvol. Het effect van gezondheidsvoorlichting op het voorkomen van vasculaire gebeurtenissen na een beroerte is nog niet bewezen. Echter gerandomiseerde onderzoeken bij patiënten met een hartinfarct laten een aanzienlijke verbetering van het gezondheidsgedrag zien.

In **hoofdstuk 5** worden onze bevindingen besproken en in een bredere context geplaatst. Verder geef ik suggesties voor verder onderzoek.

Appendices

Appendix I: The modified Rankin Scale

Grade	Description
0	No symptoms at all
1	No significant disability despite symptoms; able to carry out all usual duties and activities
2	Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance
3	Moderate disability; requiring some help, but able to walk without assistance
4	Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance
5	Severe disability; bedridden, incontinent and requiring constant nursing care and attention
6	Death

Appendix II: The questionnaire used in the COSTA trial

The questions below have been translated from the Dutch questionnaire.

General knowledge of TIAs or stroke

Open questions

- What could be presenting signs of a TIA or stroke?
- Which organ is primarily affected when you have a TIA or stroke?
- What is a TIA or stroke?

Multiple-choice questions

- Which of the following are consequences of atherosclerosis?
  (TIA, migraine, brain attack, diabetes mellitus, cancer, myocardial infarction, angina pectoris, anemia, intermittent claudication, stomach ulcer)
- Your best friend has extensive atherosclerosis of the arteries in his neck. What would you recommend him to prevent further progression?
  (Take vitamins, reduce alcohol intake, stop smoking, improve exercise, drink more milk, regular blood pressure control, drink more water, reduce fat intake, reduce pepper intake, reduce salt intake, eat more garlic)
- Which of the following conditions do you consider manifestations of cardiovascular or cerebrovascular disease?
  (Stroke, asthma, cancer, TIA, diabetes, intermittent claudication, migraine, myocardial infarction, epilepsy, heart failure, rheuma)
- Which of these items do you consider risk factors for cerebrovascular or cardiovascular disease?
  (High blood pressure, asthma, stress, reduced exercise, obesity, high cholesterol levels, muscle disease, renal stones, reduced vitamins, excessive alcohol intake, intensive exercise, smoking, diabetes, sex)

Knowledge of medication

Open questions

- How do you think that aspirin or acetyl-salicylic acid works?
- How many times a day should one take aspirin or acetyl-salicylic acid?
- At what time of the day should one take aspirin or acetylsalicylic acid?
- How do you think warfarin works?
- How many times a day should one take warfarin?
- How does one know if the right dose of warfarin has been taken?

Knowledge of vascular risk factors

Specific questions about risk factors (Multiple-choice questions)

Treatment of hypercholesterolemia

- Imagine your best friend has a high cholesterol level. What would be your advice?
  (Reduce unsaturated fatty acid intake, reduce overweight, eat more garlic, take statines, use more milk, reduce saturated fatty acids intake)

Treatment of hypertension

- Imagine your best friend has high blood pressure. What would be your advice?
  (Improve exercise, use more garlic, drink more water, regular blood pressure control, take blood pressure lowering medication, reduce salt intake, divide meal in small portions, eat more vegetables and fruit, use more sugar, reduce overweight, use more alcohol)

Weight reduction

- Imagine your best friend is heavily overweight. He wants to lose weight. What would be your advice?
  Visit a dietician, eat more vegetables, eat more fibers, eat less fat, take vitamins, improve exercise, visit a sauna twice a week, eat more bread and potatoes, use less fresh herbs, use less sugar, drink more coffee)

Smoking cessation

- Imagine your best friend is a heavy smoker. He really wants to stop, but he has not succeeded yet in doing so. What would be your advice?
  (Reduce inhalation, nicotine chewing gum, stop immediately, take medication, reduction, use a brand with less nicotine, follow a course)

Stroke and exercise

- Imagine your best friend had a stroke. He does not want to have a stroke again. He wonders about the relationship between exercise and the risk of cardiovascular disease. You explain to him that …
  (Too much is dangerous, half an hour a day is necessary, a quarter a day is necessary, frequent exercise reduces cholesterol, frequent exercise reduces high blood pressure)

Diabetes control management

- Imagine your best friend has diabetes mellitus. What is the best way to keep this under control?
  (Take more salt, use glucagon, reduce obesity, diet, take less coffee, frequent glucose control, take more sugar, take medication, use insulin, drink more water)

General risk factor questions **(***Multiple-choice questions)*

- Which items can be regarded in your view as an effective treatment for cardiovascular disease?
  (Garlic, aspirin, cholesterol lowering medication, vitamin E, antibiotics, blood pressure lowering medication, cardiac depressants)

- Imagine your best friend had a heart attack. She uses medication. She smokes 20 cigarettes per day, weighs 110 kg and her body length is 1.55m. What would you recommend her to prevent further heart attacks?
  (Take vitamins, reduce alcohol intake, stop smoking, stop working, improve exercise, reduce the amount of cigarettes, reduce fat intake, reduce saturated fatty acid intake, take more garlic, prevent obesity, take more salt)

- Imagine your neighbor, a man aged 57, has had a light stroke. He takes aspirin, smokes 10 cigarettes per day, and drinks 6 glasses of beer each day. He jogs every day, and afterwards he eats fish and chips. What would be your advice to him to prevent strokes?
  (Reduce alcohol intake, stop jogging, reduce fat, take more garlic, take medication, stop smoking, reduce the number of cigarettes)

Epilogue

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List of publications

1. **E.Maasland,** PJ.Koudstaal, JDF.Habbema, DWJ.Dippel. Effects of an individualized multimedia computer program for health education in patients with a recent minor stroke or transient ischemic attack; a randomized controlled trial. *Acta Neurologica Scandinavica 2007;115:41-48.*

2. **E.Maasland**, PJ.Koudstaal, JDF.Habbema, DWJ.Dippel.
Knowledge and understanding of disease process, risk factors and treatment modalities in patients with a recent TIA or minor ischemic stroke. *Cerebrovasc Dis 2007;23:435-440*

3. **E.Maasland**, RJ.van Oostenbrugge, CF.Franke, WJM.Scholte op Reimer, PJ.Koudstaal, DWJ.Dippel. Patients enrolled in large randomized clinical trials of antiplatelet treatment for prevention after TIA or ischemic stroke are not representative of patients in clinical practice. The Netherlands Stroke Survey. *Stroke 2009;40:2662-2668*

4. **E.Maasland**, RJ.van Oostenbrugge, CF.Franke, WJM.Scholte op Reimer, PJ.Koudstaal, DWJ.Dippel. Validity of process indicators to assess the quality of in-hospital stroke care. Insights from The Netherlands Stroke Survey. *Submitted*

5. **E.Maasland**, D.Brouwer-Goossensen, HM.den Hertog, PJ.Koudstaal, DWJ.Dippel. Health education in patients with recent stroke or transient ischemic attack; a comprehensive review. *Accepted for publication in International Journal of Stroke*

6. **E.Maasland**, DWJ.Dippel. Secundaire preventie na TIA of herseninfarct.
Farmaceutisch weekblad 2002;137:324-328

7. DWJ.Dippel, **E.Maasland**, P.Halkes, LJ.Kappelle, PJ.Koudstaal, A.Algra.
Prevention with low dose aspirin plus dipyridamole in patients with disabling stroke. *Stroke 2010;41: 2684-2686*

8. AD.Wijnhoud, **E.Maasland**, HF.Lingsma, EW.Steyerberg, PJ.Koudstaal, DWJ.Dippel Prediction of major vascular events in patients with a TIA or ischemic stroke. A comparison of 7 models. *Stroke 2010;41:2178-2185*

PhD portfolio

Research School:COEUR

1. PhD training	Year	Workload (ECTS)
General academic skills		
Biomedical English Writing and Communication	2005	2.0
In-depth courses		
PhD courses (4x) and seminars at COEUR (2 x), Rotterdam NL	2003-2004	6.6
Neurovascular meetings (3x), Utrecht NL	2008-2010	0.9
International conferences: participation and presentations		
European Stroke Conference, Genève, Switzerland, poster presentation	2002	1,5
European Stroke Conference, Brussels Belgium	2006	1
European Stroke Conference, Glasgow, UK , oral presentation	2007	2
European Stroke Conference, Nice France, oral presentation	2008	2
European Stroke Conference, Stockholm Sweden, poster presentation	2009	1,5
European Stroke Conference, Barcelona, Spain	2010	1
2. Teaching activities		
Supervising and teaching MSc students, Department of Neurology, Erasmus MC, NL	2003-2005	2.4
Total		**20.9**