Measurement of quality of life

in patients with ischemic disease of the heart or brain

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'Meten van kwaliteit van leven bij patienten
met ischemische ziekte van hart of hersenen':

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Chapter 3.2
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Chapter 3.3
Visser MC, Fletcher AE, Parr G, Simpson A, Bulpitt CJ. Comparison of three quality of life instruments in subjects with angina pectoris: the Sickness Impact Profile, the Nottingham Health Profile, and the Quality of Wellbeing Scale. J Clin Epidemiol 1994;47:157-63.

Chapter 4
Visser MC, Koudstaal PJ, Erdman RAM, Deckers JW, Passchier J, van Gijn J, Grobbee DE. Measuring quality of life in patients with myocardial infarction or stroke: a feasibility study of four questionnaires in the Netherlands. J Epidemiol Community Health 1995;49:513-7.

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Chapter 6
Visser MC, van Gijn J, Passchier J, van Gijn J, Grobbee DE, Koudstaal PJ. Quality of life in patients with ischemic stroke, submitted.

Contents

Chapter 1

Introduction

During this century average life expectancy at birth in the western world has increased considerably. In the United States, for example, about 28 years have been gained.[1] In the episode 1950-1990 life expectancy at birth in the Netherlands went up further, for men from 70.4 years to 73.8 years, and for women from 72.7 to 80.1 years. In the same period life expectancy at 65 years of age has increased as well: men gained 0.4 years, and women 4.4 years.[2] Future increase in life expectancy is expected to be minimal.[3]

With a clear reflection of overall improved health this increase of life expectancy may, however, have led to a paradoxical increase of morbid years. The general opinion is that health policy needs to be directed at compressing the average period between the onset of first major disease, infirmity, or disability, and the time of death.[4] In the elderly, the objective is not only to add years to life, but also to add 'life to years'.

To investigate the ways to achieve it is necessary to find means to describe these morbid years. Fries suggests to establish the point of first chronic morbidity, but this is difficult to define.[3]

At the same time, the importance of the quality of life in relation to disease is increasingly being recognized. This is particularly relevant for the growing number of elderly people in our society.[4] Treatment and prevention should not only prolong life but also improve - or at least not have a negative effect on - the quality of existence.

In the western world the impact of cardiovascular diseases on mortality and morbidity is considerable, and much research is focused at preventive and therapeutic interventions. Quality of life studies can provide important information concerning the value of such interventions. This thesis addresses measurement of quality of life in ischemic disease of the heart or brain.

In chapter 2 an overview is given of measurement of quality of life in patients with cardiovascular and cerebrovascular disease. Between November 1986 and April 1987 a pilot study on the measurement of the quality of life was carried out. The interobserver variation of the modified Rankin scale, a measure of handicap, was assessed in patients with ischemic stroke. The results of this study are presented in chapter 3.1. A similar investigation was performed in patients with a history of myocardial infarction and/or

angina pectoris in cooperation with the department of Cardiology of the Academic Hospital in Utrecht (chapter 3.2). Chapter 3.3 presents the results of the comparison of three quality of life instruments in subjects with angina pectoris, a study performed in the Epidemiology Research Unit of the department of Geriatrics of the Royal Postgraduate Medical School in London. The results of a pilot study assessing feasibility and reliability of selected quality of life instruments are presented in chapter 4.

These instruments, the Sickness Impact Profile, the Nottingham Health Profile, the Heart Patients Psychological Questionnaire and the Hospital Anxiety and Depression Scale, were used in 158 subjects with a history of a myocardial infarction. They participated in the Rotterdam Study, a study of the prevalence and risk factors of cardiovascular and other chronic diseases. 123 patients who had suffered an ischemic stroke and participated in the Rotterdam Stroke Databank were assessed as well. As a reference, 145 healthy Rotterdam Study participants matched for age and gender were tested. The results of these studies are presented in chapters 5 and 6. Finally the implications of the findings in this thesis are discussed.

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Chapter 2

Measurement of quality of life in patients with ischemic diseases of the heart and brain; an overview

Introduction

The impact of cardiovascular disease and the effectiveness of prevention and treatment can be expressed not only in terms of survival time or mortality rates but also in terms of morbidity. To an increasing extent, the importance of the quality of life in the presence of disease is being recognized.[1] This particularly applies to the growing number of elderly subjects in our society.[2] Treatment and prevention are expected not only to prolong life but also to improve - or at least not have a negative effect on - the quality of existence.

Over the years measurement of disease outcome has evolved. In 1980 the World Health Organisation initiated the International Classification of Impairments, Disabilities and Handicaps.[3] In this classification several levels of outcome measurement are defined. The lowest level of measurement is that of *impairment*, which means a disturbance of function at the level of the organ, for instance the elements of the neurological examination that make up stroke scales. At a higher level of measurement *disability* assesses the performance of specific tasks (scales for activities of daily living). In this classification the highest level of measurement is that of *handicap*. A person is handicapped when he or she is not able to fulfil the role that is normal (depending on age, social and cultural factors) for that individual.

From the 1970s more attention has been given to the concept of *quality of life* as a measure of outcome. Already in 1947 the WHO defined health as 'physical, mental and social well-being and not merely the absence of disease or infirmity', thus extending health to psychological, social and economic well-being. Inclusion of quality of life variables as measures of treatment results is a valid and necessary addition to the more traditional outcomes considered in medical care and research.[4]

Quality of life is not yet easily expressed in measures and quantities. This is not unusual in medicine since symptoms are often categorized according to nominal or ordinal scales based on observation and clinical experience.[5] On the other hand confusion still reigns about the definition of the concept "quality of life".[6] This has led to a multitude of

scales and scores that often measure similar elements in the quality of life but provide information about only a single detail as an ad hoc solution to this problem. For example, in studies on drugs, measures are often used that selectively register the occurrence of certain side effects whereas it is suggested that in this manner the quality of life is determined in a general sense. The other extreme is the opinion that measurement of the quality of life provides an indication of the "joy in life" in general. This latter concept would seem to be too broad as far as medical questions are concerned and therefore of little practical use.

A set of guidelines for measuring quality of life has been proposed by Spitzer.[6] Importantly, the quality of life in relation to the medical problem must be distinguished from other factors that determine the state of mind. At least three elements are distinguished that should be evaluated in combination with one another:

1. Physical disability
2. Independence and social functioning
3. Emotional and mental capacities.

A disease can affect one or more of these elements and thus can influence the objective and subjective health status of the patient. Any integrated profile of quality of life should consist at least of these elements. In addition it must be possible to extend or broaden one or more of these elements in the event of specific hypotheses, such as those encountered in therapeutic trials.

In the past few years there has been a flood of publications on quality of life instruments, all of which partially or completely meet this goal. Several of these instruments have been published in the international literature and are more or less accepted. The first attempts to include quality of life as an outcome measure were made in the field of oncology. The serious side-effects of cancer therapy raised the issue of the trade off between quantity and quality of life. The first instruments, the Karnofsky Performance Scale and the Spitzer Quality of Life index were designed for oncology patients.[6,7] The Karnofsky scale predominantly emphasizes physical invalidity, although there appears to be a good correlation between these scales and other aspects of the quality of life.[8,9]

In other fields scales attempt to express "handicap" in terms of the degree of independence of the patient, in order to give an impression of daily functioning. Examples of the latter are the Glasgow Outcome Scale, the (modified) Rankin scale and the scale proposed by the New York Heart Association as applied in neurology and cardiology, respectively.[10-15] The aim of this review is to select instruments for the measurement of quality of

life in patients who survived a myocardial infarction (MI) or a stroke. Most of these instruments have been reviewed previously.[16-24]

Different types of questionnaires are recognized, each with their own advantages and disadvantages. *Generic instruments* are comprehensive and non disease-specific. At least a physical, psychosocial and a social domain is recognised. This allows comparison across disease categories. *Disease-specific instruments* are developed for health status measurement in patients with a specific disease. This allows questioning about the burden of specific symptoms such as chest pain in angina. This might give useful additional information about a patient's response to a treatment but does not cover the multidimensional concept of quality of life. *Domain-specific instruments* measure the impact of disease on a specific domain of health status such as anxiety and depression.

As a rule we selected multidimensional instruments (which cover different facets of the effect of disease on the quality of life), with a large experience of use, and with demonstrated feasibility in a clinical setting. Some instruments which do not meet these criteria but which have been widely used to study outcome in cardiovascular research were included as well. We try to identify the areas of relevance for patients with heart disease and stroke patients, discuss methods for assessment of quality of life previously used in these patients and review the available instruments based on a number of predefined criteria, in which the views of previous authors are taken into account.

Methods

We searched MEDLINE using the key words "quality of life", "myocardial infarction", "stroke", "heart" and "cardiovascular" from 1980 up to May 1995. Furthermore, we interviewed some of the U.K. experts in the field of the assessment of quality of life (Dr Noreen Caine, Papworth Hospital, Cambridge; Dr Ann Bowling, St Bartholomew's Hospital, London; Dr Nadina Lincoln, General Hospital, Nottingham; Dr Sonja Hunt and Dr Stephen McKenna, Galen Research and Consultancy, Manchester). For the Dutch situation we used the information gathered by Essink-Bot and Rutten-van Mölken.[23] In addition we performed, as part of a pilot-study, a structured interview in 8 subjects with a history of MI, 12 subjects with a history of stroke, and in 17 subjects from a non-diseased reference group. Part of the results of this pilot study have been published recently.[25] As criteria for the assessment of the quality of life measures we used an adaptation of the framework proposed by Fletcher et al (table 2.1).[22] Key aspects in the assessment were development, description, scoring, validity, reliability, responsiveness, and experience of use. Additional aspects considered by us are the appropriateness of the

Table 2.1 *A framework for evaluation of quality of life measures (modified after Fletcher et al, 1992)*

Feature/dimension	*Example*
Development	
Conceptual basis	Characteristics of source population
Source of items	
Methods used	
Description	
Format	Open/closed questions
	Number of questions
	Can parts be used separately?
Content	
Modular	
Administration	Interview/self-filled
Method	
Time taken	
Acceptability	Expected response rates
Scoring	
How scored	Overall scores/subscales
Ceiling/floor effects	
Weighting?	
Norms available	
Validity	
Content	
Convergent/divergent	
Discriminative	
Statistical method used	
Responsiveness	
Type of study/trial	
Experience of use	
Previous studies/trials	Involving post-MI/-stroke patients?

instrument for the study and the acceptability of the instrument to the patients under study.[26]

Results

Aspects of quality of life proposed by previous authors as being relevant for patients with a history of MI are summarised in table 2.2. Aspects of quality of life proposed by previous authors as being relevant for patients with a history of stroke are summarised in table 2.3. The main results of the structured patient interview are summarised in table 2.4. Aspects mentioned by the participants as important for their quality of life included health in general, and items related to health: respiratory problems, walking difficulties, back pain, hip problems, memory problems, pain in shoulder and arm, impotence, shortness of breath, general condition, loss of sensation, speech problems and balance problems. Social activities were mentioned as well: meaning something to one's family, children and neighbours, or relearning to drive (after stroke). Living independently was considered an important aspect of quality of life, as were religion and enjoyment of life.

The instruments selected for review (table 2.5) were the Nottingham Health Profile (NHP), the Sickness Impact Profile (SIP), the Quality of Well-being Index (QWB), the Hospital Anxiety and Depression scale (HAD), and the General Health Questionnaire (GHQ). In addition the scales of the New York Heart Association and of the Canadian Cardiovascular Society (SAS), ADL-scales, and the Rankin-scale are discussed, because of their widespread use in cardiovascular disease, also in the context of "quality of life". Table 2.6 summarizes the results of the evaluation of the quality of life instruments according to the criteria proposed in table 2.1.

Summarised conclusions

I Quality of life: areas of interest

Quality of life in patients with heart diseases: areas of interest

Several factors have been reported to affect quality of life in patients with heart disease. Different aspects may be important in different episodes of the disease. In acute episodes concerns center around the effects of the intensive care experience and the resulting anxiety, denial, pain, disorientation and decrease in self-care. In a chronic phase the change in symptoms is the major concern. Ability to function physically and socially and maintenance of independence and self-esteem are important.[27]

Table 2.2 *Aspects of life most relevant for patients with heart disease*

	acute phase	*chronic phase*
Physical variables, symptoms:		
angina/chest pain	x (Wiklund 1989, Caine 1991)	x (Mayou 1991)
dyspnoea	x (Wiklund 1989)	x (Tandon 1989)
decreased self care	x (Matson 1984)	x (Matson 1989)
ability to function physically		x (Matson 1989)
maintenance of independence		x (Matson 1984, Mayou 1991)
sleeplessness		x (Croog 1982, Tandon 1989, Tandon 1991)
getting tired early/fatigued		x (Croog 1982, Tandon 1989, Tandon 1991)
energy		x (Wiklund 1989)
Psychological variables		
effect of intensive care experience	x (Mattson 1984)	
anxiety	x (Mattson 1984, Wiklund 1989)	
denial	x (Mattson 1984)	
disorientation	x (Mattson 1984)	
self-esteem/lack of confidence		x (Mattson 1984, Mayou 1991)
restlessness		x (Croog 1982)
nervousness		x (Croog 1982)
stress		x (Ruperman 1984)
Sexual variables		
libido	x (Bulpitt)	x (Wiklund 1989)
potency	x (Bulpitt)	
Social variables		
ability to function socially	x (Caine 1991)	x (Ruperman 1984)
participation in social and family groups	x (Ruperman 1984)	x (Mayou 1991)
work status		x (Paris 1993, Duitsman 1994)
limitation of activities	x (Caine 1991, Wiklund 1989)	
Satisfaction		
fulfilment of expectations		

A longitudinal study of 345 male heart patients, covering a period of eight years after their heart attack, revealed that, in the long term, the most prominently reported symptoms were "restlessness or nervousness", suggesting tension and anxiety, "sleeplessness", and "getting tired easily". These symptoms are reported more often than chest pain or breathlessness, even in patients with recent hospitalisation.[28] Long term survivors of coronary artery bypass surgery reported less angina and greater exercise capacity, reduction of anxiety and depression, improvement in general pleasure, job and family roles. Sexual adjustment improved the least.[29] Early social and psychological variables predicted later social and emotional conditions.[28]

In 539 patients 5 years after MI a decrease was noted in energy, sleep and mobility, and in sex life, leisure activities and holiday activity. Dyspnoea, angina pectoris and anxiety were closely associated with decreased quality of life.[30] Chest pain and limitation of activities were reported to be improved and general health to be better after coronary artery bypass grafting.[31] The importance of social contacts and psychological aspects is illustrated by a reported four-fold increase in the risk of death in 2320 male survivors of myocardial infarction with high levels of stress and social isolation.[32]

Quality of life in patients with a history of stroke: areas of interest

In a study in 70 stroke patients on factors affecting progress of patients in a stroke unit, incontinence turned out to be predictive of physical disabilities and Activities of Daily Living (ADL); perception, memory, reading and writing were important determinants of independence as assessed on an extended ADL-scale.[33] In 46 stroke survivors, assessed 4 years after a stroke, patients independent in ADL had as often a low quality of life as dependent patients, but when the severity of the deterioration was considered the positive influence of independence showed clearly. In the same study a marked deterioration in family relationships and leisure time activities was reported.[34]

Psychomotor slowing, general asthenia, fatigue, impaired memory, emotional instability, depression or anxiety and an increased need for sleep were common complaints in patients who experienced a stroke after a reversible ischemic attack.[35] In a study comparing five stroke scales with the Barthel Index, the Rankin Scale, and the Sickness Impact Profile arm and hand motor function, speech and hemianopsia were related to the patients' health status.[36]

Depression was reported in 30% of stroke patients attending a stroke outpatient clinic,[37] especially in patients with left anterior lesions[38] and in 25-30% of stroke survivors in the community.[39] Sexual function is decreased in the majority of patients, as

Table 2.3 *Aspects of quality of life most relevant for stroke patients*

Physical variables	
Performance:	
self care	(Niemi 1988, Lincoln 1989)
mobility	
Symptoms:	
headaches	
pain	
incontinence	
fatigue	
sleep disorders	(Soelberg Sørensen 1989)
Psychological variables	
emotional state	(Soelberg Sørensen 1989)
depression	(Soelberg Sørensen 1989)
anxiety	(Soelberg Sørensen 1989, Robinson 1982, Wade 1987)
cognitive performance: perception, memory, reading, writing	(Lincoln 1989, Soelberg Sørensen 1989)
Sexual variables	
libido	(Sjögren 1982, 1983)
potency	(Sjögren 1982, 1983)
Social variables	
participation in social and family groups	(Niemi 1988, Lehmann 1975, Evans 1987, Brocklehurst 1981, Wade 1986)
leisure time activities	(Niemi 1988, Gresham 1975, Sjögren 1982)
Satisfaction	
fulfilment of expectations	

(modified from Fletcher and Bulpitt 1987)

Table 2.4 *Main results of the structured interview n=37 (MI n=8, stroke n=12, controls n=7)*

* *Question* *Possible answers*	
* Do you need help with your daily activities?	
yes	4
no	29
missing	4
* Do you think you have fully recovered from your MI/stroke?	
yes	
no	8
missing	12
	17
* Have you heard of the concept "quality of life"	
yes	
no	24
missing	8
	5
* Is your quality of life different from the quality of life of other people?	
yes	23
no	11
better	11
worse	10
* Is health important for your quality of life?	
yes	37
no	0
missing	0
* Admitted to hospital in the last year?	
yes	15
no	22
missing	0
* Change of living conditions/financial situation because of change in health?	
yes	0
no	37
missing	0

illustrated by an abrupt and permanent cessation or at least a decrease in the frequency of intercourse in 72% of hemiplegic stroke patients; psychogenic aspects seemed to be important.[40-42] A positive correlation between family involvement and recovery was reported.[43,44] Effects on family life are illustrated by a reported increase of relatives being under medical care from 33% at the time of the stroke to 40% by the twelfth

month,[45] and by the presence of depression in 11-13% of the carers in the first two years following a stroke.[46] Living with a partner and a high frequency of social contact were reported, amongst other factors, as having a positive influence on outcome at one year with regard to independence.[47]

Families also report loneliness, boredom and maladjusted marital relationships.[48,49] On the other hand a majority of families reported a closer relationship. Socialization outside home was decreased in 62% of 119 stroke survivors.[50] Of 379 patients employed at the time of the stroke, 19% returned to some employment after the stroke. Leisure activities decreased in 79 of 110 subjects after a single stroke.[40]

Summarised conclusions

II Characteristics of the selected instruments

Instruments designed especially for patients with heart disease

The classification of the New York Heart Association[15]

This scale classifies patients according to the degree of limitation of physical activity as perceived by the physician. The measure is reported to have a high inter-observer variability, but in an interobserver-study only moderate agreement was observed (kappa between cardiologists (21 patients) of 0.26 (weighted kappa 0.55)).[51] There is a poor correlation with objective exercise testing because patients seem to adjust their activities to their symptoms.[52] The scale mainly classifies physical impairment and does not cover psychological and psychosocial aspects of quality of life.

Olsson et al used the NYHA-classification and presence or absence of side-effects or atherosclerotic-complications to create seven categories of health state in 301 post-MI-patients to study the effect of long term metoprolol on mortality and morbidity.[53] In a study in 58 angina patients a significant trend in quality of life scores of NHP, SIP and QWB was shown according to their classification with respect to the NYHA-classification.[54] The broad grouping of patients into four classes suggests that the NYHA classification is likely to be insensitive to change.[55]

Specific Activities Scale[56]

By naming specific activities this scale tries to circumvent the problem of 'improvement' due by adjustment of the patient to the situation. The activities should represent metabolic equivalents. Compared to NYHA it has a better inter-observer variability and a relation

with exercise testing, but its sensitivity to change may be poor since there are only four classes.

Instruments designed especially for stroke patients

ADL-scales

Especially in stroke patients Activities of Daily Living (ADL) scales have been used as an outcome measure.[57,58] ADL-scales have been developed to indicate the degree of domestic independence an individual can attain despite diseases or impairments.

The Katz Index of ADL is one of the best known and most carefully studied ADL tests.[18] The measure includes items on bathing, dressing, going to the toilet, transfer, continence and feeding. For each item dependency and independency is described and rated. The sum of all items is used to describe ADL activities.[59]

The Barthel index[60] consists of rating the ability to feed oneself, groom oneself, bathe, go to the toilet, walk (or propel a wheelchair), climb stairs, and bladder and bowel control. The score values are weighted and may be 15, 10, 5, or 0, or with a different scoring system 3, 2, 1, or 0. The average score at discharge is 17 out of 20, which leaves little room for improvement (ceiling effect).

In stroke research the Katz Index for ADL and the Barthel index are the most widely used instruments.[61,62] Gresham et al examined independence in activities of daily living in 148 Framingham Study stroke survivors using the Katz index of ADL, the Barthel Index, and the Kenny Self-Care Evaluation, and concluded each index adequately classified stroke survivors as dependent or independent.[63] There was a high degree of agreement between the scores. The authors see certain advantages in the use of the Barthel index, because of its completeness, sensitivity to change, amenability to statistical manipulation and more widespread use. In a trial of 167 stroke patients assessed shortly after admission and 5 weeks later, comparing six stroke outcome measures (mainly ADL-scales), the Barthel-Index was the most efficient, and required the fewest subjects to identify a significant effect.[64] In a review of clinical trials of stroke treatment summarising the elements that might be included in functional outcome scores the Barthel index is named as an alternative for some of these scores.[65]

In an interobserver-study with the Dutch version of the Barthel-Index this instrument was shown to be valid and reliable.[66] Following marital status, Barthel score was the most important predictor of living arrangement status, in 84 patients discharged from 8 different rehabilitation centres, especially in women.[67]

Extended ADL's have been developed to try and avoid the ceiling effect after discharge. Holbrook et al tried to measure lifestyle after stroke by constructing an extended ADL-scale including outdoor activities such as social outings and car maintenance.[68] In the Rivermead ADL-index ADL-items are organised hierarchically, and this index includes two household activities sections.[69]

After a stroke there is an early rapid phase of recovery within the first 3 months; this occurs for example in speech, arm function and ADL. After 6 months improvement has been shown less clearly. The measuring instruments may be too insensitive to detect small changes. In the Barthel score over 50% have achieved a score of 95 (=19) or more by 6 months, thus there is little chance of detecting further improvement. Even improvement between 3 to 6 months is only shown in the severely disabled.[62]

The Rankin-scale[11]

The Rankin-scale is a six-point handicap-scale. It was slightly modified by Warlow and associates for the UK-TIA study to accommodate language disorders and cognitive defects.[12] It was used in the European Carotid Surgery Trial, and in the Dutch TIA-trial.[70,71]. The interobserver agreement for stroke patients, and for heart patients was moderate to substantial.[14,53] Limitations are that the physician performs the assessment, and this does not necessarily correspond with the patient's point of view. Furthermore it is a six-point scale and thus not likely to be sensitive to change.

Generic Instruments

The Nottingham Health Profile[72,73]

The NHP is a general health profile, i.e. a single instrument covers a wide range of dimensions of quality of life with separate scores for these dimensions. The NHP consists of 38 items describing health related behaviour in six dimensions and seven yes/no questions concerning domains of daily life. No total sum score is derived, a high score indicates a poor quality of life. The NHP uses negative statements concerning health. Each statement is weighted and there has been some criticism about the method of weighting used. Scores are reported to be skewed to low or zero values, and therefore suggested not to be effective in discriminating health statuses.[74] However, in migraine and rheumatoid arthritis patients it was able to distinguish within and between illness groups.[75]

Table 2.5 *Quality of life instruments selected for review*

Nottingham Health Profile (NHP)	
Part I: 38 weighted statements describing behaviour	Six dimensions: pain, physical mobility, sleep, emotional reactions, energy, social isolation
Part II: 7 yes/no questions	work, home care, social life, home life, sex life, hobbies, holidays
Sickness Impact Profile (SIP)	
136 weighted statements describing behaviour related to health	12 Categories: ambulation, mobility, body care and movement, social interaction, communication, emotional behaviour, alertness behaviour, eating, work, sleep and rest, household management, recreation and pastimes
Quality of Well-Being Scale (QWB)	mobility, physical activity, social activities, report of symptoms
General Health Questionnaire-28 (GHQ)	
28 items	Four subscales: depression, anxiety, social functioning, physical symptoms
Hospital Anxiety and Depression Scale (HAD)	
14 items	Two subscales: anxiety, depression

Experience of use in patients with heart disease

The NHP has been used in several studies in cardiovascular patients. It has shown responsiveness to major interventions such as heart transplant and bypass surgery. [31,76] In 48 patients before and after heart lung transplantation it showed significant improvements in quality of life.[77] 62 patients were examined pre-and post heart transplant; there was some evidence of an increase in social isolation post transplant, but for all other dimensions, both before and after transplant, no significant change in NHP over time was observed.[78]

In 539 patients assessed 5 years after myocardial infarction the NHP showed an impaired quality of life in those suffering from angina pectoris, dyspnoea and emotional distress.[79] In the same population a relation between diuretics and a decreased quality of life was found.[80] In 185 patients six months after MI analysis of NHP scores by NYHA strata confirmed that higher NHP scores were associated with poorer cardiac functional status.[81] In a study in 50 angina patients the profile showed a significant association with the classification according to the New York Heart Association.[54] In a pilot study in 20 MI-patients it was shown to be feasible and reliable in patients with a history of MI, and even in small numbers it was able to make a distinction between MI patients and a reference group.[25]

In 1395 patients with suspected acute myocardial infarction 5 years after early intervention with metoprolol, no differences were observed in mortality, morbidity and quality of life according to the Nottingham Health Profile.[82] In a study of the effect of enoximone on mortality and quality of life in 151 patients with severe end stage heart failure an excess of mortality was observed in the enoximone group, but an improvement in the NHP physical mobility score.[83] Patients were in NYHA classification III and IV. It was not analyzed whether this improvement was an effect due to 'survival of the fittest'.

Experience of use in stroke patients

Ebrahim et al. assessed patients one and six months after a stroke. About 20% (11 and 28% at one and six months respectively) of the stroke survivors was not able to fill in the questionnaires but the scale was easy to use in the rest of the patients. A limitation was that results for the Physical Mobility dimension were not presented.[84] The NHP was also used in a study comparing patients treated with sensory stimulation and a control group. In this study it was able to demonstrate change over time and differences between the two study groups.[85]

In a trial of 44 stroke patients at least one year after a stroke no effect was shown with NHP and the General Health questionnaire of 16 weeks social work intervention.[86]

The advantages of the NHP are: its acceptability, the limited time needed for completion (10 minutes), subdivision of the scale into 6 scales measuring different quality of life dimensions, availability of data on different population groups, both in the community and patient groups. There is some evidence that it could be used as a screening instrument. A Dutch version has been validated.[87] The disadvantages of the NHP are the ceiling effects of the scores, and the lack of adequate trial data to show responsiveness to other than gross effects of medical interventions. Its potential as an evaluative instrument for a

whole spectrum of medical interventions has not been demonstrated yet, but it appears to be useful in certain specific conditions. At present the designers of the profile advise against using Part II as this does not reflect the impact of health related problems.

The Sickness Impact Profile[88,89]

The SIP was developed in the United States with a similar objective as the NHP. The SIP asks the respondent to make a judgement as to whether a problem is health related. It consists of 136 items describing the impact of ill health on behaviour in 12 dimensions. Scores are obtained for the overall profile, physical and psychosocial subtotals and separately for each of 12 categories. A high score indicates a poor quality of life. It has been used in a wide range of patients. In a comparative study in patients with renal insufficiency the NHP was found to be more feasible, and showed somewhat higher levels of internal consistency.[90]

Experience of use in patients with heart disease

In heart patients the instrument has been used for assessing outcome after a cardiac arrest; SIP scores for survivors of a cardiac arrest, 6 months later, were significantly higher than scores in a control group, consisting of persons enroling a panel health plan.[91] The SIP has also been applied in 96 cardiac transplant recipients,[92] Results suggested that the quality of life in cardiac transplant patients was worse than the quality of life in healthy people, but similar to cardiac-arrest survivors and post MI-patients. In another study a slightly lower quality of life was reported in cardiac arrest survivors, compared with MI-patients.[93]

In a trial of 111 patients with heart failure (67% NYHA Class III) over a 3 month period with two groups receiving standard therapy and placebo, no differences in quality of life were observed with SIP and the Quality of Wellbeing Index, but differences were observed with Spitzer's quality of life index.[94]

Experience of use in stroke patients

In a study of 21 stroke patients the SIP was able to predict the amount of help needed by another person.[95] In a study in 441 stroke patients six months after a stroke the SIP showed consistent pattern of disabilities in comparison with reference data with respect to body self-care, communication, eating as well as household management and recreation. Few relationships between hemispheral lesion sides and quality of life scores were found.[96]

In another group of neurological patients, head injured patients, the standard SIP turned out to perform well, and was also able to measure change over time in this group of patients. Modifications failed to make improvements sufficiently large to provide an advantage over the standard SIP.[97,98]

The SIP covers many relevant domains of health-related lifestyle. It might be suitable for monitoring outpatient progress. Its advantages are its extensive use in health care settings, and some evidence of its responsiveness to medical interventions. Its disadvantages are primarily its length and unsuitability in acute care.

Quality of Well-being Index (QWB)[99,100]

The QWB was developed for use within a model to analyze cost-effectiveness in the U.S. health care system. The QWB measures actual physical and social performance and symptoms over a 6 day period. It is divided in 4 separate sub-scales; the total score is on a continuum of health from 0 (death) to 1.

The questionnaire cannot be self-administered. The QWB has been previously used in a trial in rheumatoid arthritis where a significant benefit for the active treatment versus placebo was found, both by this instrument and through other clinical measures.[101] In patients with chronic obstructive pulmonary disease the QWB correlated with both performance and physiological variables.[100] The index is difficult to administer and a major drawback is that only the single most distressing symptom on a given day is taken into account. The weights attached to different handicaps also raises questions, e.g. wearing glasses or contact lenses is considered to be worse than being confined to a wheelchair. Furthermore psychological aspects are hardly taken into account (2 questions).

General Health Questionnaire[102]

This is a widely used screening questionnaire for detecting non-psychotic psychiatric illness. The GHQ-28 is a self-administered 28-item questionnaire with four sub-scales addressing depression, anxiety, social functioning and physical symptoms. The instrument was developed as a state measure, i. e. it assesses the present state in relation to the usual state. The GHQ has good reliability and has been validated against a structured clinical interview.[103] It also performs well against psychiatric screening tests. The instrument has been used in many different settings and in community studies. In stroke patients it was used in 44 patients to assess the contribution of social work to the alleviation of depression.[104] Its limitation is, that it primarily assesses physical functioning and psychological

status, so other quality of life dimensions would need to be determined by means of other questionnaires.[19,21]

Hospital Anxiety and Depression Scale[105]

Fourteen items divided in two subscales address anxiety and depression; the patient rates each item on a 4-point scale. Items relating to both emotional and physical disorder were excluded. This is considered to be an advantage since overlap with symptoms of physical illness, is less likely in this way.[19] The scale is derived from clinical experience. A high score indicates anxiety or depression. The severity ratings correlated with a structured clinical interview.[103] In cancer patients it was found to have 70% sensitivity and 75% specificity for screening for major depressive disorders.[106] The scale has been used to demonstrate the effect of in-hospital counselling for first ever myocardial infarction in men.[107] It also showed a statistically significant effect of the effect of counselling in 60 wives of first time myocardial infarction patients.[108] As a screening instrument in general practice it is reported to have too low a threshold for reporting possible cases.[109] It is easily understood and completed by patients.[21] It is reported to be a useful scale in everyday practice and sensitive to clinical improvement.[110,111]

Table 2.6 *Evaluation of the selected quality of life instruments*

QOL-instrument	*NHP*	*SIP*	*QWB*	*GHQ*	*HAD*
Development					
Conceptual basis	2000 statements, reduced to 38 statements, covering six dimensions	1000 statements reduced to 136 items covering 12 dimensions.	at least 14 items (depending on routing)	28 items, four sub-scales	14 items
Source of items	768 patients with a variety of chronic ailments	health professionals, carers, patient groups and healthy subjects		rating by nurses, graduate students and general population	developed for patients with physical disease
Description					
Format	38 yes/no questions	patient indicates health-related problems with respect to 136 items	flow-chart		14 questions, per question four possible answers
Administration	interviewer/selfassessed	inter-viewer/self-assessed	interviewer	interviewer/selfassessed	interviewer/selfassessed
Time taken	$\pm$ 10 minutes	20-40 minutes	18 minutes	minutes	5-10 minutes
Acceptability	response rates 68 (postal) to 90%.	good	good	good	good
Scoring					
How scored	scores for six dimensions, no total score	scores for 12 dimensions + total sum score	4 separate subscales, total score from 0 (death) to 1	30 items screening for non-psychotic psychiatric disturbances (0 = no change, 1 = change, max. score 30)	2 dimensions, 14 questions rated 1 to 4

Table 2.6 continued *Evaluation of the selected quality of life instruments*

QOL-instrument	*NHP*	*SIP*	*QWB*	*GHQ*	*HAD*
Ceiling/floor effects	floor effect	floor effect	ceiling effect		no
Weighting?	yes	yes	yes		yes
Norms available	yes	yes			
Validity					
Content	pain, physical mobility, sleep, emotional reactions, energy, social isolation, work, home care, social life, home life, sex life, hobbies, holidays.	Ambulation, Mobility, Body care & Movement, Soc. Interaction, Communication, Em. behaviour, Alertness behaviour, Eating, Work, Sleep & rest, Household management, Recreation and pastimes	symptoms, mobility, physical activity, social activities	anxiety, depression, social functioning, physical symptoms	anxiety, depression
Convergent/-divergent	moderate to high correlations with other health profiles (0.6-0.7)	correlations (0.5-0.7) subjective assessments, (0.4-0.8) clinical measures, 0.57 with mental health indicator	0.55 with SIP-total score, 0.33 with mental health indicator	correlates with structured clinical interview/psychiatric screening tests, and HAD	correlates with structured clinical interview/-psychiatric screening tests, and HAD
Discriminative	higher scores for migraine and rheumatoid arthritis (RA)-patients, no differences before and after minor surgery			higher scores for migraine patients/RA-patients	70% sensitivity and 75% specificity for major depressive disorders

Table 2.6 continued *Evaluation of the selected quality of life instruments*

QOL-instrument	*NHP*	*SIP*	*QWB*	*GHQ*	*HAD*
Statistical methods used	should be non-parametric	should be non-parametric			
Reliability					
Test/retest	correlation coefficients 0.77-0.88 for repeat administration after 4-8 weeks	reproducibility 97%, split half reliability 97% test-retest 0.75-0.92	0.90-0.93	good	0.89 Anxiety, 0.87 Depression
Interview/self-filled	self/interview	self/interview	interview	self	self
Between interviewers					
Responsiveness					
Type of study/trial	migraine patients, heart transplant patients patients with end stage heart failure, no change in minor surgery	measured effect in placebo controlled trials, change over time in head trauma patients		no effect measured of intervention by social work in depressed patients after stroke	measures change over time within different groups of cancer patients
Experience of use					
Previous studies/trials in cardiovascular patients	migraine, RA, heart transplant patients, post MI, minor surgery	cardiac arrest survivors, RA, angina, head trauma	RA	community, stroke patients, migraine patients, RA	first time acute myocardial infarction, RA, burning mouth, cancerpatients, psych out-patients, mothers of children with Down's syndrome

Discussion

From a health perspective a person with a good quality of life could be defined as someone who does not feel limited in his activities and role in society by physical or mental illness. By definition this implies that quality of life is a multi-dimensional concept. Gill and Feinstein defined quality of life as a reflection of the way that patients perceive and react to their health status and to other nonmedical aspects of their lives, rather than being the description of patient's health status.[112] The effect of a disease on a patient's quality of life could be defined as the impact of this disease on the patient's activities and social role. An ideal way to measure quality of life does not exist, and probably will never exist because of the personal interpretation an individual will have of his quality of life.

However, the assessment of quality of life is an issue of increasing importance in the evaluation of clinical trials of medical or surgical treatment in patients with cardiovascular diseases. From the initial reliance on measures of physical outcome, such as exercise tests there is a trend towards the inclusion of social and psychological aspects in the patient assessments. In a research setting there is a preference for self-assessed questionnaires above interviewer administered questionnaires. In other words, from the situation in which the doctor defines which aspects are important for the patient there is a change of emphasis towards asking patients what they feel is important. However, interviews with specific groups of patients about which aspects of quality of life they think important have so far hardly taken place.

Over the past twenty years several questionnaires have been developed to assess quality of life. None of these was developed especially for patients after a myocardial infarction or extensively tested in this group of patients. When measurement of quality of life is considered in a research setting the choice of (an) instrument(s) out of several instruments available should be made with special attention to its applicability to the group of patients under study. The development of a new instrument has disadvantages because of the initial lack of information with respect to validity, reliability and comparability with other studies.

In this chapter we set out to summarise the experience of use of several instruments for the measurement of quality of life in patients with ischemic diseases of the heart and brain. From this review and after the consultation of experts in the field, we conclude that three questionnaires appear attractive enough to be further investigated in patients with a history of a myocardial infarction; two generic instruments, the Nottingham Health Profile, the Sickness Impact Profile, and a domain specific instrument, the Hospital Anxiety and Depression scale. We recommend the NHP because of its value in earlier

studies with cardiovascular patients, its compact form and our recent and favourable experiences with its application in angina.[78] The SIP has been satisfactorily applied to several groups of patients, and might be more sensitive than other instruments to detect relatively small differences between categories of patients. Further investigation of the clinically derived and easy to use Hospital Anxiety and Depression Scale in patients with heart disease seems also worthwhile, since anxiety is a frequently reported complaint in these patients. Most areas of interest mentioned in the literature for the quality of life in patients with heart disease or a history of stroke are included in these questionnaires. Furthermore, aspects of quality of life mentioned by patients with a history of myocardial infarction or stroke are included in these questionnaires, the exception being religion.

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Chapter 3.1

Interobserver agreement for the assessment of handicap in stroke patients

Introduction

A reliable measure of deficits after a stroke is important in the analysis of a therapeutic trial. The purpose of the trial determines whether the measurement concerns a specific or more global function. In theory, the spectrum ranges from exact quantification of the force of one muscle to estimation of the quality of life.[1,2] Between these extremes, four different levels of measurement can be distinguished in practice. First, some clinical trials have limited the analysis to muscle strength and tendon jerks.[3] A slightly more complex level is represented by tests that have been developed for the assessment of partial functions, such as the use of the hemiplegic arm.[4] Tests for estimating the severity of aphasia are another example. However, such tests give no information about the function of the patient as a whole. The third level, formed by several disability indexes, of which the Barthel Index is one of the best known,[5] measures the activities of daily living (ADL). In several therapeutic trials such an assessment, with emphasis on motor functions, was used.[6,7] Other indexes, such as the activity index devised in Sweden, also take into account disorders of language and cognition.[8]

Finally, on the fourth level are scales that measure independence rather than performance of specific tasks and in this way incorporate mental as well as physical adaptation to the neurologic deficits. The score on such a scale gives a better impression of whether patients can look after themselves in daily life than ADL scores, and represents handicap rather than disability.[9] The Glasgow Outcome Scale was devised for head injury, but its general terms made it also suited for cerebrovascular disease.[12] The Rankin scale has been slightly modified by Warlow and associates for the UK-TIA study[13] to accommodate language disorders and cognitive defects (table 3.1.1). It is currently used in the European Carotid Surgery Trial and the Dutch TIA trial.[14] This modified Rankin scale not only measures the overall independence of stroke patients and allows comparison between patients with different kinds of neurologic deficits, but it also adds one further dimension by referring to previous activities. This is important because patients can be restricted in

their activities by complaints (arthritis, intermittent claudication) existing long before their stroke.

Clinical assessments are liable to disagreement between different observers.[15] Interobserver variation has been investigated for the performance of individual ADL items[16] but not for an overall handicap scale. The aim of our study was to determine the extent of interobserver agreement for the grading of stroke patients with the modified Rankin scale.

Subjects and Methods

Our aim was to imitate the circumstances of a multicentre clinical trial as closely as possible by involving many physician with different levels of clinical experience and by performing the study in two different hospitals (the University Hospital Utrecht and the University Hospital Dijkzigt, Rotterdam).

During the study period (March 1 to September 1, 1986) we tried to include all patients in whom cerebral infarction was diagnosed by the referring physician or by a resident in either department of neurology. One hundred patients were assessed, 50 in each centre; 67 were men. Patients were included only if the neurological deficit had lasted for >24 hours. Inpatients (86) were eligible within the first week after a brain infarct, outpatients (14) within 5 months after their stroke. In one centre six senior neurologists and 14 residents participated in the study, in the other four senior neurologists and 10 residents. In each canter the observers were randomly allocated into 50 pairs.

To record the degree of handicap, the modified Rankin scale was used (table 3.1.1); the terms were explained to the physicians in a training session. The assessment was carried out by questioning the patients on activities of daily living, including outdoor activities. Information about the patient's neurologic deficits on examination, including aphasia and intellectual deficits, was given beforehand. Results of computed tomography (CT scan) were also transmitted to the physicians. The nursing staff in the hospital or a relative could be interviewed about the degree of independence of the patient. All aspects of physical and mental performance and speech were combined in the choice of a single handicap grade. The two physicians graded the patient within 6 hours of each other to avoid disagreement caused by a change in the patient's condition.

The degree of agreement between the 100 pairs of observers was calculated with K (kappa) statistics.[17] If all degrees of disagreement are of equal importance, the coefficient of agreement is expressed as $K = (p_o - p_c)/(100 - p_c)$ where p_o is the percent agreement

Table 3.1.1 *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*: unable to walk without assistance, and unable to attend to own bodily needs 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

Original Rankin scale[11] did not contain Grade 0, defined Grade 1 as "No significant disability: able to carry out all usual duties," and defined Grade 2 as "Slight disability: unable to carry out some of the previous activities..."

observed and p_c is the percent agreement expected by chance. Weighted K (K_w)[18] is used when the degree of disagreement is taken into account. In our calculations four times as much weight was given to a difference of two grades as to a difference of one grade and nine times as much weight to a difference of three grades [quadratic disagreement weights $v_{ij}=(i-j)^2$ between Rankin grades i and j]. Perfect agreement was assigned 0 (diagonal in table 3.1.2). K_w is calculated as $K_w = 1 - (\Sigma v_{ij}p_{oij}/\Sigma v_{ij}p_{cij})$ where v_{ij} is the disagreement weight, p_{oij} is the observed percentage of a certain degree of disagreement between Rankin scores i and j, p_{cij} is the corresponding chance percentage of disagreement. K_w is 0 when there is only chance agreement and 1 when there is perfect agreement.

Results

The neurologic deficits consisted of only motor deficit in 58 patients, motor deficit with hemianopsia or aphasia in 33 patients, and only hemianopsia or aphasia in 9 patients. A CT scan of the brain was available on the day of assessment in 90 patients. Twenty-two patients had an infarct in the left and 26 patients in the right cerebral hemisphere, and in 42 patients abnormalities were not or not yet visible.

Table 3.1.2 *Agreement Between 100 Pairs of Observers for Degree of Disability Expressed Using Modified Rankin Scale*

Observer 2	*Observer 1*						
	0	1	2	3	4	5	Total
0	5						5
1		6	2				8
2	1	4	13	5	2		25
3			6	9	4		19
4				2	8	1	11
5					8	24	32
Total	6	10	21	16	22	25	100

Table 3.1.3 *Kappa According to Kind of Neurologic Deficit*

	Total number	*Number with disagreement*	*K*
Motor deficit only	58	25	0.47
Hemianopsia or aphasia only	9	3	0.59
Motor deficit with hemianopsia or aphasia	33	7	0.63

The 100 pairs of observers agreed about the degree of handicap in 65 of 100 patients (table 3.1.2). In 32 patients the assessments differed by one grade, and in three patients the difference was two grades. The corresponding K is 0.56, K_w is 0.91. Agreement for the different grades of the modified Rankin scale was best for Grades 0 and 5, which might be expected because disagreement is possible in only one direction, and worst for the Grades 2,3, and 4. The neurologic deficit in patients about whom the observers did not agree was motor deficit alone in 25 of 58 patients, motor deficit was hemianopsia or aphasia in 7 of 33 patients, and hemianopsia or aphasia alone in 3 of 9 patients. The agreement rates involving each kind of neurologic deficit are shown in table 3.1.3. Observers disagreed about 2 of the 15 outpatients and about 33 of 85 inpatients. K was 0.82 for outpatients and 0.51 for inpatients. This was a significant difference even though K_w was hardly different, 0.91 and 0.89, respectively.

The results from the two centres were not significantly different; for the University Hospital Rotterdam K was 0.50, K_w 0.90. For the University Hospital Utrecht, these values were 0.62 and 0.91, respectively.

Discussion

If a handicap scale is used for assessing outcome in a therapeutic trial of patients with cerebrovascular disease, the results of the trial might be influenced by variation in grading between physicians. In our study the interobserver agreement for the modified Rankin scale was satisfactory. The observers agreed on the extent of handicap in 65 of 100 patients. This corresponds with a true agreement rate, after correction for chance, of 0.56, which is substantial, The observers differed by one grade in 32 patients and by two grades in three patients, The latter cases concerned a difference in the assessment of the ability to perform previous activities in one patient and of the level of independence in the other two patients. If a difference of two grades is given four times as much weight as a difference of one grade, the weighted true agreement is excellent (0.91). These results are more convincing if the great number of observers, and particularly that of less experiences residents, is taken into account.

Because this is the first interobserver study of an overall handicap scale in stroke patients, our results cannot be compared with those of earlier studies. It is also difficult to find authoritative criteria on what represents a satisfactory K. Some have assumed that when K is >0.80, the agreement can be considered excellent, that K between 0.40 and 0.80 represents moderate to substantial agreement, K between 0.20 and 0.40 fair agreement, and K of <0.20 slight or poor agreement.[19] The same type of statistics is used for grading examination papers that consist of multiple choice questions, and then the limit is often set at 0.6. On the other hand, many common clinical signs and symptoms fail to attain this limit when subjected to an interobserver study. Interobserver agreement for symptoms and signs in stroke patients showed K between 0.40 and 0.70.[20,21] For the assessment of overall outcome following severe head injury with a five-category scale K was 0.77.[22] Interobserver agreement for individual ADL items (such as dressing, feeding, and walking) proved to be good, but this assessment did not take into account the degree of dependence.[16]

To further improve the agreement rate, it is necessary to unravel possible causes of variation. First, Grades 3 and 4 are defined in a way that assumes a constant relation between the ability to walk and the ability to lead an independent life. This assumption is not always correct and may lead to ambiguities. As overall handicap is clearly the main theme of the scale, walking should perhaps not be an explicit criterion. Such a modification is presently used in the Oxfordshire Community Stroke Project.[23] Furthermore, it may be difficult to assess restrictions of lifestyle in hospital inpatients, as was done for the most part in this study, and perhaps the handicap after stroke should not be graded until 6 months after the stroke. Second, uniformity might be improved if the observers

would use a checklist of activities of daily living as a guide in questioning the patient, as was found the case for he diagnosis of transient ischemic attacks (TIAs).[24] Third, discrepancies between observers are most striking for Grades 2, 3, and 4. This corresponds with the low K for the intermediate level (Grade 3) of the Hunt-Hess scale in the grading of patients with subarachnoid haemorrhage.[25] Reducing the modified Rankin scale to a four- or even a three- point scale would probably improve the interobserver variation. The Barthel Index has this advantage, with only two or three points for each item, although this scale is not very sensitive toward the upper end of the handicap range. On the other hand, modest but clinically relevant differences between patients can no longer be detected if the scale is contracted too much. Therefore, the modified Rankin scale is probably an acceptable compromise.

Fourth, variation might theoretically arise from a difficult in combining the impacts of different neurologic deficits such as hemiparesis, hemianopsia, or aphasia on the overall handicap of the patient. Nevertheless, the results were contrary to this hypothesis because patients with only motor deficit turned out to be the most difficult to assess. These patients were probably over represented among the middle parts of the scale, in which disagreement can go both ways. Finally, variation can perhaps also be reduced if the scale is thoroughly discussed with all participating physicians before the start of the study and if the observers practice the use of the scale, [26] but such training is hardly realistic in the context of a multicenter trial.

In conclusion, although we found a satisfactory interobserver agreement for the grading of stroke patients with the modified Rankin handicap scale, further improvement may be possible in two ways. The first is devising a simple pro forma with questions that are most useful in detecting restrictions of the patients' lifestyle. The second is the removal of walking from the scale, leaving overall handicap as the leading theme. It is important to include all causes of handicap in patients with TIA or minor stroke because they may suffer from other complications such as angina, myocardial infarction, intermittent claudication, or retinal infarction. Even nonvascular events may be side effects of the preventive treatment that is under study and ought to be included in the assessment.

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Chapter 3.2

Interobserver agreement for the application of two handicap scales in heart patients

Introduction

The impact of cardiovascular disease and the effect of prevention and treatment can not be expressed only in terms of survival and complications.[1] The importance of the measurement of quality of life is increasingly recognised. Quality of life, however, is difficult to express quantitatively. A large number of scales has been developed, more or less related to specific diseases.[2-7] Little is known regarding the reliability, validity, and reference values of these scales for patients with ischemic disease of the heart or brain.

From 1986 to 1990 a clinical drug trial was performed in patients with a 'transient ischemic attack' (TIA) or a minor, non disabling stroke.[8] In this trial a 6-point scale was used, the so-called modified Rankin scale; this scale concerns mainly capacity to get along independently (table 3.1.1).[9,10] In a study of interobserver-variation in stroke patients this scale turned out to be reliable.[11] Patients who have experienced a TIA are also at increased risk for myocardial infarction.[12,13]

The aim of the present study was to assess the reliability of the Rankin scale with respect to the assessment of handicap from heart disease. We wanted to make a comparison with the scale of the New York Heart Association (NYHA), applied frequently in cardiology.[14] This is a four-point scale with items related to severity of the disease itself and limitation of physical activities caused by the disease (table 3.2.1). This scale has been criticised several times, but is still widely applied in cardiology.[15]

Patients and Methods

From February to April 1987 fifty-two consecutive cardiac out-patients from the University Hospital in Utrecht were selected because of their history. They had angina (n=13), had suffered a myocardial infarction (n=14) or both (n=24). 13 of these patients had undergone coronary artery bypass grafting. 51 patients participated (36 men), one patient refused to participate. Mean age was 61.2 years (SEM 9.4).

Table 3.2.1 *Functional classification of the New York Heart Association*

Grading original criteria		*revised criteria*
I	patients with cardiac disease but without resulting limitations of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or anginal pain.	cardiac condition not restricted
II	patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain.	cardiac condition a little bit restricted
III	patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary physical activity causes fatigue, palpitation, dyspnea, or anginal pain.	cardiac condition moderately restricted
IV	patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of cardiac insufficiency or of the anginal syndrome may be present even at rest.If any physical activity is undertaken, discomfort is increased.	cardiac condition severely restricted

The observers were four cardiologists, two residents in cardiology, 6 neurologists, and 11 residents in neurology. In this way the circumstances were comparable to those of a clinical trial with different patients and different observers. The participating physicians were instructed by means of written instruction and through a departmental meeting. Ideally each of the patients was interviewed by four physicians: their own outclinic cardiologist or the resident in cardiology, 2 neurologists or residents in neurology, selected randomly, and finally by a second cardiologist.

The interviews were performed in succession, and the combination of observers was different for each patient. The ideal design -every patient interviewed by four observers- was not always realised. Twenty-one patients were interviewed by four physicians, 29 patients by three physicians, and one patient by only 2 physicians. This was caused by to practical problems, such as a too long delay for the patient or commitments elsewhere for the intended observer. In ten minutes the patients were questioned about their daily and social activities.

The results were subsequently graded on the two scales and analyzed with kappa-statistics.[16-19] Kappa-statistics corrects observed agreement for chance agreement. Kappa=$(P_o-P_e)/(1-P_e)$, i.e. proportion observed minus proportion expected, divided by one minus the proportion expected; the maximum value is 1.0. Kappa-values <0 indicate poor agreement, values between 0.00 and 0.20 slight agreement; 021-0.40: fair

agreement; 0.41-0.60 moderate agreement; 0.61-0.80: substantial agreement; 0.81-1.00: almost perfect agreement.[20]

Calculation of weighted kappa is preferred for hierarchical scales. This means that a difference between observers of several points is attributed a greater weight than a difference of a single point. We chose, a quadratic weight: a difference of two points was counted as a difference of four, while a difference of one point was counted only once.[17]

Results

In six of the 51 patients agreement between all observers was complete for both scales. In 10 patients agreement was complete for the Rankin scale and in 11 other patients agreement was complete for the NYHA scale.

Agreement for the Rankin-scale occurred between the cardiologists in seven of the 21 patients, and for the neurologists in 30 of the 50 patients; for the NYHA scale this occurred in nine out of 21, and in 28 out of 49 respectively. The number of grades on the two scales was sometimes enlarged by the observers, by ticking between two grades. In the calculations we took the grade that showed the biggest difference in score between the observers. The mean kappa-values are shown in table 3.2.2. For the total group of observers agreement was 0.21 for the Rankin scale and 0.24 for the NYHA scale. Weighted kappa was 0.56 for the Rankin scale and 0.47 for the NYHA scale. The agreement between neurologists was always somewhat higher than that between cardiologists.

Table 3.2.2 *Agreement between observers for the assessment of handicap on two scales, in 51 patients with heart disease*

observers	kappa	weighted kappa
modified Rankin-scale		
all observers (51 patients)	0.21	0.56
comparison between neurologists (50 patients)	0.36	0.70
comparison between cardiologists (21 patients)	0.08	0.48
scale of the New York Heart Association		
all observers (51 patients)	0.24	0.47
comparison between neurologists (49 patients)	0.28	0.70
comparison between cardiologists (21 patients)	0.26	0.55

Discussion

The Rankin scale primarily measures disability in daily life, and to a lesser extent handicaps in social activities.[1] Our study of this scale in patients with heart disease showed poor agreement between cardiologists, and a fair agreement between neurologists and in the total group of observers. Calculation of weighted kappa showed moderate, substantial and a moderate agreement, respectively. For the scale of the New York Heart Association we obtained fair agreement between cardiologists and neurologists, separately or together, and for weighted kappa we found a moderate agreement between cardiologists, and between neurologists a substantial agreement.

A study among neurologists to examine interobserver agreement for the Rankin scale in stroke patients showed a value for kappa of 0.56, and for weighted kappa of 0.91.[11] In the present study the results are less convincing for all groups of observers, but in the former study, patients were seen by only two observers.

The results for the two scales are comparable. The pairs of neurologists showed greater agreement than the pairs of cardiologists, even though the pool of neurologists was bigger than the pool of cardiologists. Because of the smaller number of observations by pairs of cardiologists chance may explain part of this difference.

Several factors may be responsible for the agreement being smaller than in the study of stroke patients. In the first place we might have chosen too complicated a design for the study, by using four observers. In the second place the assessment on one scale might have influenced the assessment on the other scale, with a different number of points on both scales. Furthermore the patient's "own" cardiologist or resident in cardiology might have had extra information, which could have influenced the assessment. Questions asked by neurologists and cardiologists to get an impression about the degree of independence of the patient might have been different, but this variation was not influenced to mimic the circumstances of a clinical trial in separate hospitals as much as possible.

The main finding in this study is that the modified Rankin scale, used in the past in neurological studies only, may be useful for the assessment of disability from heart disease, in particular in those with a neurological disease at the onset. Neurologists perform this assessment at least as accurate as cardiologists.

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Chapter 3.3

A comparison of three quality of life instruments in subjects with angina pectoris: the Sickness Impact Profile, the Nottingham Health Profile, and the Quality of Well Being Scale.

Introduction

Traditional measures of efficacy in therapeutic trials in angina have been the New York Heart Association (NYHA) and exercise tests.[1,2] An interest has developed in the use of Quality of Life instruments to provide a more comprehensive assessment of the impact of disease and treatments on patients' everyday lives.

The aim of this study was to assess the performance of three quality of life instruments in patients with angina using the NYHA classification to grade patients according to severity of disease. The study was undertaken in preparation for a clinical trial where the selected instrument must be responsive to the benefits or adverse effects of drug therapy in angina patients.

The quality of life instruments were the Quality of Well Being index (QWB), the Nottingham Health Profile (NHP), and the Sickness Impact Profile with minor adaptations to colloquial English (table 3.3.1).[3-8] We also included a measure of psychological state: the Symptom Rating Test (SRT).[9]

The NYHA categorizes patients into 4 classes ranging from normal (I) to severe (IV) expressing the limitation of activity due to cardiac disease. The QWB measures actual physical and social performance and symptoms over a 6 day period. It is scored in 4 separate sub-scales and a total score which lies on a continuum of health from 0 (death) to 1. In the 4 subscales a higher score indicates more impairment. The total score is derived by subtracting weighted scores in the subscales from 1, and a lower score indicates more impairment. The SIP and NHP are general health profiles, i.e. a single instrument covering a wide range of dimensions of quality of life with separate scores for these dimensions. In both profiles scores are weighted. A high score indicates a poorer quality of life. The SIP consists of 136 items describing the impact of ill health on behaviour in 12 dimensions. Scores are obtained for each of the 12 categories, and sum scores are

Table 3.3.1 *Content of the Quality of Life measurements*

Sickness Impact Profile (SIP)

12 categories	*Number of items*
Ambulation	12
Mobility	10
Body care and Movement	23
Social interaction	20
Communication	9
Emotional behaviour	9
Alertness behaviour	10
Eating	9
Work	9
Sleep and rest	7
Household management	10
Recreation and pastimes	8
	136

Nottingham Health Profile (NHP)

Six domains of experience:	
pain	8
physical mobility	8
sleep	5
emotional reactions	9
energy	3
social isolation	5
	38
Seven domains of daily life: employment, household work, relationships, personal life, sex, hobbies, vacations	7 yes/no questions

Quality of Well-being scale (QWB)

report of symptoms in the last six days	35 items
limitation of: mobility, physical activity, social activities	flowchart
health related/ not health related over four out of the past six days	

obtained for the overall profile, physical and psychosocial subtotals. The NHP consists of 38 items describing health related behaviour in six dimensions and seven yes/no questions concerning domains of daily life. No total sum score is derived for NHP. All three instruments have undergone field testing and shown to be valid measures of health related behaviour in the general population with high inter and intra reliability coefficients.[3-8] The ability of these instruments to discriminate patients according to severity of angina is not known.

The SRT is a self-assessed measure of psychological morbidity; it provides a total score, and separate anxiety, depression, somatic, cognitive and hostility scores. It was developed for use in a psychiatric context, and shown to be valid and reliable.[9] It has been shown to be sensitive to the effects of psychotropic drugs compared with placebo in double blind randomised controlled trials.[10,11] It has not been used in angina patients.

Methods

Patients aged 30-75 years attending their general practitioner for chronic stable angina were eligible for the study if they had been treated for at least the previous 3 months continuously, either with transdermal glyceryl trinitrate (GTN) or with oral long acting nitrates. The General Practitioner was asked to classify the patients' grade of angina using NYHA criteria. Nineteen general practitioners in 18 practices participated. Informed consent was obtained from all patients.

The questionnaires included, as stated above, the QWB, SIP, NHP and SRT. The QWB was administered by a trained interviewer; SIP, NHP, SRT and additional questions were combined in a self-administered questionnaire. Three interviewers were trained for a total of 7 days over a period of 1 month by one of the authors (AF). Agreement was calculated as the percentage of identical responses. The format of SIP was amended to provide a yes/no tick response instead of a tick only if there is a 'yes' response to produce compatibility with the NHP.

A non-parametric analysis of variance (Kruskal-Wallis) was used to test for difference in scores for each instrument classified by NYHA group. A total NHP score was established by calculating the average over the six dimensions. Spearman's correlation coefficients were calculated for comparison of total scores or similar dimension scores between instruments. Tests for trends to analyze part two of NHP (discrete variables) used X^2. The statistical package used was SAS.[12]

Table 3.3.2 *NHP-scores by NYHA Mean (SD)*

Dimension	NYHA-classification			
	I (n=10)	II (n=25)	III (n=21)	P
Part 1:				
Energy	12.0 (12.6)	37.3 (40.1)	44.1 (34.9)	0.05
Pain	4.5 (7.3)	11.4 (22.4)	20.7 (25.8)	0.05
Emotion	6.1 (10.5)	14.4 (22.9)	23.3 (27.3)	0.21
Sleep	33.8 (31.2)	22.7 (27.8)	31.6 (31.5)	0.41
Social Isolation	0.0 (0.0)	5.4 (14.6)	12.4 (16.9)	0.02
Physical Mobility	5.4 (10.5)	17.2 (18.1)	24.9 (21.3)	0.03
Part 2:				
%saying interference with				
Looking after home	0.0	12.0	33.3	0.05
Social life	20.0	16.0	23.8	0.80
Home life	0.0	12.0	14.3	0.47
Sex life	40.0	28.0	28.6	0.76
Hobbies	10.0	32.0	28.6	0.40
Holidays	30.0	12.0	38.1	0.12

Results

Fifty-nine patients participated in the study (43 men). The average age of patients was 65 years with a range from 46 to 79, 11 (19%) were still in full-time employment and 43 (73%) were retired. 27 (46%) of the patients were hypertensive and 33 (56%) had a history of a previous myocardial infarction, 6 patients (10%) suffered from cardiac failure. Angina had deteriorated over the last 3 months in 4 patients (7%), stayed the same in 40 patients (68%) and had improved in 15 patients (25%). Most patients were in NYHA Grade 2 (25=42%) or 3 (21=36%). Since very few (3=5%) were Grade 4, this group was excluded from the analysis. We excluded the Work Dimension of the SIP since most subjects were not working.

Both NHP and SIP showed increased impairment with higher NYHA class in most categories (tables 3.3.2 and 3.3.3). In QWB intra-observer variability over a 24 hour period was assessed for each of the three interviewers in three different patients and agreement ranged from 61.9% to 85.2%. Inter-observer variability between all three interviewers, also over a 24 hour period, was examined in three patients and agreement ranged from 62.3 to 73.9%. For QWB, the physical activity score was best for NYHA grade I ($p = 0.04$) and the symptoms scores differed between the groups ($p = 0.02$) increasing by 0.02 with each grade (table 3.3.4). For NHP significant differences across NYHA class were shown in four out of six categories. Chi-square tests in part II did not show an association with NYHA grade; the exception being 'looking after home'.

Nine out of eleven SIP dimensions showed increasing scores across NYHA class with significant differences found in six out of eleven. Only the dimensions Sleep and Rest, and Eating showed little change across NYHA class. Physical Score, Psychosocial Score and Total score showed highly significant increases with NYHA class. The SRT-scores tended to increase with NYHA class as well, particularly for depression and somatic scores ($p = 0.07$, and $p = 0.06$, respectively) (table 3.3.5).

The figure shows the total NHP scores against SIP total score. A very high correlation coefficient was observed of 0.82 ($p<0.001$). Both instruments tended to be skewed to lower scores. With QWB, in which higher scores indicate a better quality of life, negative correlations for NHP and SIP versus QWB were found; $r= -0.72$ ($p<0.01$), and -0.55 ($p<0.01$), respectively.

Correlation coefficients for corresponding categories of NHP and SIP showed in general a high level of agreement in similar dimensions with correlation coefficients significant at the 1% level and ranging from 0.84 (Emotional Behaviour SIP versus Emotional Reactions NHP), to 0.47 for Sleep and Rest (SIP) versus Sleep (NHP). Correlation coefficients between the total score of SRT and total SIP, the physical

sumscore of SIP, the social sumscore of SIP, and dimensions of NHP ranged from 0.53 (pain dimension of NHP) to 0.79 (emotional dimension of NHP) (all p-values < 0.01).

We calculated for different NYHA-classes the mean, the median, and coefficient of variation (CV=(Standard deviation/mean) x 100%) for three corresponding categories of NHP and SIP, namely social participation, emotional status and physical activity. The median values were zero for six out of nine results of the NHP and illustrate the tendency to skew to lower scores. For SIP the median was higher than zero in all corresponding categories. In eight out of the nine comparisons of CVs the values for CV were smaller for the SIP than for the NHP measures. This was particularly noticeable for the social dimensions of the two instruments.

Discussion

In angina traditional measures of outcome, such as the NYHA and exercise tests, have limitations.[13,14] The NYHA categorizes patients into 4 classes and is therefore likely to be insensitive to changes other than gross ones occurring during a trial. Furthermore the NYHA has a high interobserver variability and thus a lack of precision and in this way clinically important differences may be lost.[15,16] Besides NYHA class may improve if a patient stops doing stressful activities.[17] Exercise tests have been criticised, since patients' performance may not reflect lifestyle. Furthermore exercise tests are related to psychological factors and therefore are less objective then they appear.[14]

In some trials of angina treatment outcome measures included items such as angina severity, limitation of activity, return to work and medical treatment, and psychosocial items.[18-24] However, in these studies the outcome measures with respect to the quality of life of the patients were somewhat restricted and had not been formally validated.

The disadvantages and advantages of generic instruments, such as NHP and SIP have been considered in detail elsewhere.[25] All three instruments considered in this study have been used in a variety of diseases and treatments.[26-38] As no disease specific instrument is available for angina, the choice of a particular generic instrument is influenced by a variety of factors of which the most important is the validity of the instrument in the disease specific population and its responsiveness to effective drug therapy.

The results of this cross-sectional study suggests some evidence for the validity of NHP and SIP in the assessment of angina patients as indicated by their discriminative ability between NYHA class. The study may also allow physicians to become more familiar with these instruments because a comparison with a widely used clinical index is made. Evidence for the validity of the QWB in angina was unconvincing.

Table 3.3.3 *SIP-scores by NYHA Mean (SD)*

Dimension	NYHA-classification			
	I (n=10)	II (n=25)	III (n=21)	P
Body Care	4.6 (7.0)	10.7 (14.3)	15.8 (13.0)	0.04
Ambulation	5. 7 (6.9)	18.1 (15.9)	24.4 (11.8)	0.00
Mobility	6.8 (6.9)	10.6 (11.0)	21.4 (19.0)	0.05
Social Interaction	11.8 (10.3)	16.3 (13.2)	26.6 (18.9)	0.05
Alertness Behaviour	8.7 (15.6)	23.4 (33.3)	34.8 (31.7)	0.05
Emotional Behaviour	8.1 (11.6)	17.8 (24.4)	24.1 (26.1)	0.28
Home Maintenance	12.6 (18.3)	29.5 (30.0)	26.8 (22.9)	0.14
Recreation and Pastimes	20.2 (25.3)	34.9 (28.1)	42.3 (23.3)	0.13
Communication	0.7 (2.3)	5.2 (10.5)	13.1 (12.9)	0.01
Eating	3.7 (4.4)	5.1 (7.3)	5.5 (6.1)	0.74
Sleep and Rest	19.6 (28.4)	19.1 (17.5)	23.9 (20.5)	0.66
Physical Score	5.4 (6.8)	13.1 (12.8)	19.3 (11.8)	0.01
Psychosocial Score	8.1 (9.4)	15.8 (15.9)	25.1 (18.4)	0.02
Total Score	8.3 (9.7)	16.1 (13.5)	22.3 (12.6)	0.02

Table 3.3.4 *QWB-scores by NYHA Mean (SD)*

QWB score	NYHA-classification			
	I (n=10)	II (n=25)	III (n=21)	P
Mobility	0.01 (0.02)	0.02 (0.03)	0.02 (0.03)	0.46
Physical Activity	0.04 (0.03)	0.06 (0.02)	0.06 (0.02)	0.04
Social Activity	0.04 (0.03)	0.05 (0.03)	0.06 (0.02)	0.18
Symptoms	0.24 (0.06)	0.26 (0.05)	0.28 (0.04)	0.02
Total score*	0.68 (0.10)	0.62 (0.09)	0.62 (0.12)	0.26

*Total score = 1- (mobility score + physical activity score + social activity score + symptom score)

Table 3.3.5 *Psychiatric morbidity scores by NYHA Mean (SD)*

Scores	NYHA-classification			
	I (n=10)	II (n=25)	III (n=21)	P
Total	10.7 (12.4)	16.5 (14.0)	24.1 (19.2)	0.12
Anxiety	2.2 (2.5)	3.2 (3.6)	5.0 (4.2)	0.13
Depression	3.0 (3.5)	4.3 (3.4)	6.1 (4.1)	0.07
Somatic	1.9 (2.9)	3.4 (3.0)	4.5 (3.4)	0.06
Cognition	1.9 (2.0)	3.1 (2.9)	4.4 (4.3)	0.31
Hostility	1.9 (2.4)	2.7 (2.6)	4.7 (5.0)	0.45

A major drawback of the QWB is that the overall score is dominated by the symptom weightings. The symptom score does not however reflect all the patient's symptoms on a particular day but only the one rated as the most distressing. Fifty per cent of the patients in this study reported breathlessness as the most distressing symptom, rather than chest pain.

Another objection against the use of the QWB is that only two questions are included to cover psychological aspects. Furthermore the QWB was the instrument with the greatest practical problems in terms of length of administration and need for an interviewer. Nonetheless the use in angina trials of a health index may be useful, such as the index for hypertensive patients, derived from the work of Fanshel and Bush and successfully employed in studies of anti-hypertensive drugs.[39,40]

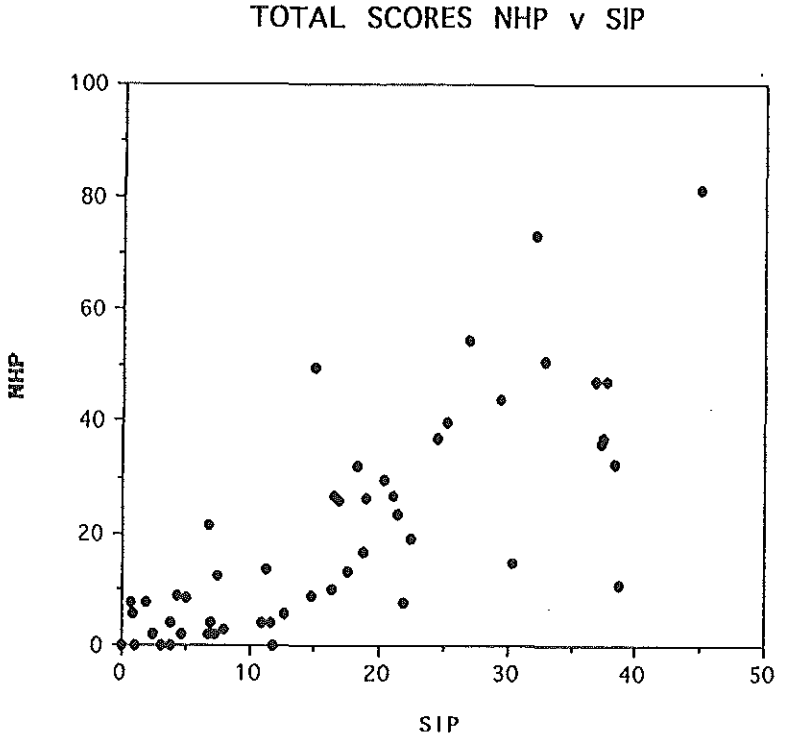
Responsiveness could not be measured directly in this study but the potential behaviour of an instrument can be assessed from its ability to discriminate between different health states. This indicates, that if during a clinical trial patients show improvement or deterioration, these instruments are likely to be responsive to this. An outcome measure with a continuous distribution such as the NHP and SIP is more likely to be a responsive measure than a categorical one such as the NYHA.

As a result of preliminary analysis of the data reported here, SIP plus diary cards of chest pain and GTN consumption were used to assess the effect of anginal treatment in a double blind randomised controlled trial.[26] No benefits from active treatment over placebo were found in any measures employed. However, the SIP detected an adverse treatment effect (probably due to headaches) in the active group shown by a deterioration in the psychosocial scores compared with placebo.

A further factor in evaluating the potential usefulness of these instruments in a trial is the distribution of scores. Published data for the SIP and NHP suggest that scores are skewed to low values.[37-38] In the present study both instruments tended to be skewed to lower values as well indicating that for less severe cases of angina these instruments might be less responsive since there is little room for improvement. This feature was more apparent in NHP than in SIP. Moreover the smallest CV's tended to be found in SIP. Although we did not observe a direct relationship between the number of items and coefficient of variation these results suggest, that in corresponding categories, the extra time required for the completion of the SIP compared with the NHP may be compensated by gains in the statistical properties of the instrument. In this study we introduced a yes/no option for SIP. We believe that this helped in obtaining a more complete ascertainment of the responses.

In conclusion, the present study indicates that differences in severity of angina patients, classified with NYHA-criteria are related to both NHP and SIP scores. The QWB index evaluated in this study showed greater administrative difficulties and less discrimination. The NHP and SIP both seem acceptable instruments. The SIP showed, in corresponding categories, less variability, but does take longer to complete.

Figure



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Chapter 4

Feasibility of measurement of quality of life in patients with a myocardial infarction or a stroke

Introduction

Measurement of disease outcome is an important issue in medical research, especially in treatment trials. In general, this assessment can be applied at several levels, of increasing complexity; 1) the biological process; 2) impairments (of separate functions); 3) disability; 4) handicap (in which social roles are included); and 5) quality of life.[1,2] Across the spectrum from disease process to quality of life, the measures become applicable to more than one disease, and usually also less sensitive and less objective, but closer to fulfilment of chosen roles and to well-being, and therefore more relevant from the patient's point of view.[3] Quality of life has rarely been measured in controlled trials of patients with cardiovascular disease, although the importance of this measure is widely recognized. Several instruments for measuring quality of life have been developed, but their applicability to these specific groups of patients has hardly been tested.[4-8]

For our feasibility study we selected multidimensional instruments, for which there is a large experience of use. According to previous recommendations, criteria used for the selection were concept, origin, format, content, scoring, validity, reliability and responsiveness.[9,10] Selected were two general purpose profiles designed for use in general populations, the Nottingham Health Profile (NHP), and the Sickness Impact Profile (SIP).[11-14] Both profiles have been applied in patient studies.[15-17] We also selected a heart disease specific measure developed in the Netherlands, the Heart Patients Psychological Questionnaire (HPPQ), because of the positive experience with this questionnaire in patients with heart disease in the Netherlands.[18,19] Since anxiety and depression are reported in both categories of patients and may influence their quality of life,[20-23] the Hospital Anxiety and Depression scale (HAD), derived from clinical practice and with a reported practicality of use, was included as an indicator of the presence of anxiety and or depression.[24,25]

The primary objective of the present study was to test the selected instruments for their feasibility in two groups of patients: a with a history of stroke within the previous five

Table 4.1 *Characteristics of the study groups Mean (SD)*

	Post-MI (n=20)	*Post-Stroke (n=16)*	*Controls (n=17)*	*Post-MI vs controls* p =*	*Post-Stroke vs controls* p =*
Age	72.7 (7.9)	66.0 (11.0)	72.8 (7.3)	0.96	0.05
Sex (no of men)	8	10	9	0.68	0.85
Time since event (months)	17.8 (9.3)	11.1 (5.1)	not applicable		

* T-test

years and another group of patients with a history of MI in the past five years. We studied assessment time and test-retest reliability. In addition we examined whether in spite of the limited size of the study NHP and SIP, as general purpose profiles, could distinguish between patient groups and control groups.

Patients and Methods

Since May 1990, all patients who are admitted to the University Hospital Rotterdam Dijkzigt with a stroke or a transient ischemic attack have been registered in the Rotterdam Stroke Data Bank, initiated by one of us (PJK). From the Data Bank we randomly selected 16 patients with an ischemic stroke more than 6 months before. One patient had experienced a transient ischemic attack, the other 15 patients had suffered a brain infarct, located in the right hemisphere in 7 patients, in the left hemisphere in six patients and in the posterior fossa in one patient; one patient had experienced multiple infarctions. All patients were functionally independent, none suffered from aphasia.

From the Rotterdam study we selected 20 patients with a history of MI and admission to hospital because of this MI in the past six to 24 months. The Rotterdam Study is a prospective follow-up study, which addresses determinants of progression of chronic disabling disease in the population of 55 years and over in the district of Ommoord in Rotterdam; 7983 participants (78% of those invited) were recruited between 1991 and 1993. The Rotterdam Study focuses on causally related determinants of major diseases in the elderly, especially conditions that interfere with the quality of life. There are four primary areas of research: cardiovascular diseases, neurogeriatric diseases, locomotor diseases and ophthalmologic diseases. After an

Table 4.2 *Content of the measurements*

Measurement	*Number of items*
Sickness Impact Profile (SIP)	
12 categories	
Sleep and rest	7
Emotional behaviour	9
Body care and Movement	23
Household management	10
Mobility	10
Social interaction	20
Ambulation	12
Alertness behaviour	10
Communication	9
Work	9
Recreation and pastimes	8
Eating	9
	136
Nottingham Health Profile (NHP)	
Six domains of experience	
pain	8
physical mobility	8
sleep	5
emotional reactions	9
energy	3
social isolation	5
	38
Seven domains of daily life	
occupation, jobs around the home, social life, personal life, sex, hobbies, vacations	7 yes/no questions
Heart Patients Psychological Questionnaire (HPPQ)	
Four dimensions	
Wellbeing	12
Feelings of being disabled	12
Displeasure	10
Social Inhibition	6
Dummy items (Answers: yes/?/no)	12
	52
Hospital Anxiety and Depression Scale	
Anxiety	7
Depression (four answers possible per item)	7
	14

initial home visit and interview subjects are physically examined and have several clinical measurements at a field centre. 2.5 years later, changes in health status and clinical measurements are reassessed.[26]

Also from the Rotterdam Study 17 controls were selected, matched for age and gender with the MI patients. Their medical history was negative for MI or stroke. The characteristics of the study groups are shown in table 4.1.

The questionnaires included the SIP, NHP, HPPQ and HAD (table 4.2). The SIP and NHP are general health profiles, i.e. single instruments covering a wide range of dimensions of quality of life with separate scores for each dimension. In both profiles a high score indicates a poor quality of life. The SIP consists of 136 items describing the impact of ill-health on behaviour in 12 dimensions. Weighted sum scores are obtained for the overall profile, physical and psychosocial subtotals, and separately for each of 12 categories. The NHP consists of 38 items describing health-related behaviour in six dimensions and seven yes/no questions concerning domains of daily life (part two). No sum score is derived for NHP. The number of positively answered questions within each dimension is given as no weighted scores are yet available for the Dutch version of NHP we used. For part two the total number of domains of daily life in which subjects experienced interference is mentioned to indicate differences in the total number of domains in which the subjects feel impaired. Both SIP and NHP have undergone field testing and were shown to be valid measures of health-related behaviour in the general population, with high inter- and intra-observer reliability coefficients.[11-14]

The Heart Patients Psychological Questionnaire was developed in the Netherlands as a measurement of well-being, feeling of being disabled, displeasure and social inhibition for patients with heart disease. The test consists of 52 items, with a yes/?/no response possibility. It has been validated in the Netherlands on a sample of 1,649 cardiac patients.[18] In addition the quality of life for patients with congestive heart failure has been studied.[19] Data on the reliability, validity and norms of this instrument are available for the Dutch population; a higher score in the well-being dimension indicates a greater degree of well-being, whereas a higher score in feelings of being disabled, displeasure, and social inhibition indicates a worse condition.[27]

The Hospital Anxiety and Depression Scale is derived from clinical experience.[20] Two subscales assess anxiety and depression; the patient rates each item on a 4-point scale. Items relating to both emotional and physical disorder are excluded. This is considered to be an advantage since overlap is less likely in this way.[28] A high score indicates anxiety and/or depression. The severity ratings correlate with a structured

clinical interview.[29] It is easily understood and completed by patients, but more work on its reliability and validity is required.

All four questionnaires were self-administered. We measured the time needed for completion of the questionnaires. For SIP and HPPQ a score was obtained by means of weights established for the Dutch population. The Mann-Whitney test was used for comparing differences in scores. To establish test-retest reliability all instruments were administered by the same person with an interval of 14 days and Spearman correlation coefficients were calculated. The statistical package used was BMDP.[30]

Table 4.3 *Assessment time instruments, minutes Mean (SD)*

	Post-MI (n=20)	*Post-Stroke (n=16)*	*Controls (n=17)*	*Post-MI vs controls* p =*	*Post-Stroke vs controls* p =*
NHP	8.6 (10.6)	8.6 (4.0)	6.1 (7.6)	0.04	0.06
HPPQ	10.4 (11.7)	11.9 (4.3)	9.0 (2.9)	0.36	0.05
SIP	22.1 (13.1)	23.5 (7.2)	17.3 (7.1)	0.27	0.05
HAD	5.8 (2.0)	6.5 (4.2)	5.2 (3.0)	0.09	0.19

* T-test

Results

Mean assessment time for the instruments in the different study groups varied between 5.2 minutes for HAD in the control group to 23.5 minutes for SIP in patients with a history of stroke (table 4.3). For the stroke patients the assessment time was longer for all instruments.

Median values for SIP total score, psychosocial and physical sum scores in the different study-groups are presented in table 4.4, with corresponding p-values. In tables 4.5, 4.6, and 4.7 the results are presented for different dimensions of NHP, HPPQ, and HAD. Most instruments were able to detect differences between the study groups. Statistically significant differences were found for SIP (total score) in the comparison between MI patients and controls (table 4.4). For separate dimensions of SIP statistically significant differences were found for Emotional Behaviour, both for post-stroke patients and post-MI patients in the comparison with controls; for

Table 4.4 *Sickness Impact Profile (SIP): total score, psychosocial and physical sumscores in the different studygroups. Median (Interquartile range)*

	Post-MI (n=20)	*Post-Stroke (n=16)*	*Controls (n=17)*	*Post-MI vs controls* p =*	*Post-Stroke vs controls* p =*
Sleep and rest	11.9 (0.0 - 30.4)	12.1 (0.0 - 22.0)	0.0 (0.0 - 12.1)	0.14	0.28
Emotional behaviour	3.3 (0.0 - 19.3)	0.0 (0.0 - 12.1)	0.0 (0.0 - 0.0)	0.01	0.02
Body care and movement	1.2 (0.0 - 7.3)	3.2 (0.0 - 8.1)	0.0 (0.0 - 3.2)	0.48	0.20
Household management	7.4 (0.0 - 28.2)	8.1 (6.1 - 21.3)	0.0 (0.0 - 10.4)	0.15	0.04
Mobility	0.0 (0.0 - 23.2)	0.0 (0.0 - 9.2)	0.0 (0.0 - 16.8)	0.58	0.82
Social interaction	10.1 (3.5 - 20.1)	9.6 (0.0 - 15.4)	4.6 (0.0 - 12.6)	0.09	0.38
Ambulation	11.5 (7.5 - 28.7)	4.2 (0.0 - 10.6)	0.0 (0.0 - 19.9)	0.03	0.90
Alertness behaviour	0.0 (0.0 - 26.5)	0.0 (0.0 - 47.0)	0.0 (0.0 - 10.2)	0.31	0.30
Communication	0.0 (0.0 - 0.0)	0.0 (0.0 - 9.7)	0.0 (0.0 - 9.5)	0.32	0.66
Recreation and pastimes	26.9 (18.7 - 51.5)	17.8 (0.0 - 41.9)	10.2 (0.0 - 33.0)	0.04	0.84
Eating	0.0 (0.0 - 6.1)	0.0 (0.0 - 0.0)	0.0 (0.0 - 6.1)	0.93	0.08
SIP-total	12.4 (7.0 - 19.1)	11.4 (5.9 - 15.4)	7.7 (3.7 - 11.3)	0.04	0.14
SIP-psychosocial	6.8 (2.3 - 17.2)	8.9 (1.4 - 20.8)	2.8 (0.0 - 8.8)	0.09	0.10
SIP-physical	5.8 (1.8 - 16.7)	5.1 (1.6 - 10.3)	3.3 (0.0 - 8.2)	0.10	0.30

* Mann-Whitney test

Household Management in the comparison between post-stroke patients and controls; for Mobility and Recreation and pastimes between the post-MI patients and controls.

For NHP there were statistically significant differences between both MI and stroke patients in the comparison with controls in the Energy dimension and in Part II, and in the Pain dimension in the comparison between MI patients and controls (table 4.5). For the HPPQ differences in scores were statistically significant in both comparisons in all dimensions except for the Social Inhibition dimension (table 4.6). The anxiety scores of HAD were significantly different in both comparisons, and the

depression score was significantly different between stroke patients and controls (table 4.7).

Test-retest reliability calculated with Spearman correlation coefficients is shown in table 4.8. 42 subjects (79.2%) agreed to participate in this part of the study. Correlation ranged from 0.31 (p=0.05) in the SIP sleep dimension to 0.95 for HPPQ in the 'Feelings of being disabled' dimension (p<0.01).

Table 4.5 *Nottingham Health Profile (NHP) scores for different dimensions in the groups Median (Interquartile range)*

Dimensions NHP	*Post-MI (n=20)*	*Post-Stroke (n=16)*	*Controls (n=17)*	*Post-MI vs controls* p =*	*Post-Stroke vs controls* p =*
Energy	0.0 (0.0 - 1.8)	0.0 (0.0 - 1.0)	0.0 (0.0 - 0.0)	0.01	0.01
Pain	1.0 (0.0 - 2.0)	0.0 (0.0 - 1.0)	0.0 (0.0 - 0.0)	< 0.01	0.18
Emotional reactions	1.0 (0.0 - 2.0)	0.5 (0.0 - 4.8)	1.0 (0.0 - 1.0)	0.14	0.40
Sleep	1.0 (0.0 - 3.0)	1.0 (0.0 - 2.8)	1.0 (0.0 - 2.0)	0.31	0.88
Social Isolation	0.0 (0.0 - 1.0)	0.0 (0.0 - 2.0)	0.0 (0.0 - 0.0)	0.23	0.17
Physical Mobility	1.0 (0.0 - 3.0)	1.0 (0.0 - 2.0)	0.0 (0.0 - 1.5)	0.23	0.58
Part II	1.0 (0.3 - 3.0)	1.5 (0.0 - 3.0)	0.0 (0.0 - 0.0)	< 0.01	0.01

* Mann-Whitney test

Table 4.6 *Heart Patients Psychological Questionnaire-scores in the different study-groups Median (Interquartile range)*

Dimension	*Post-MI (n=20)*	*Post-stroke (n=16)*	*Controls (n=17)*	*Post-MI vs Controls* p =*	*Post-stroke vs Controls *p =*
Well-being	23.5 (21.3 - 30.8)	26.5 (18.0 - 30.0)	33.0 (32.0 - 35.0)	< 0.001	< 0.001
Feelings of being disabled	29.0 (26.0 - 35.3)	28.5 (21.5 - 33.5)	20.0 (15.5 - 26.0)	< 0.01	0.02
Displeasure	16.0 (11.3 - 18.8)	14.5 (12.0 - 22.3)	11.0 (10.0 - 12.0)	0.01	< 0.01
Social Inhibition	12.0 (10.3 - 15.8)	13.0 (11.0 - 16.0)	11.0 (9.0 - 14.0)	0.44	0.33

* Mann-Whitney test

Discussion

This preliminary study indicates that measures of quality of life can be applied within reasonable time to patients who have suffered from myocardial infarction or stroke, and that these may distinguish even small numbers of patients from controls. Quality of life is an important aspect of health outcome, along with duration of life, and it is of interest as a determinant of outcome as well.[31] Inclusion of quality of life variables as measures of treatment effects is a valid and necessary addition to the more traditional outcomes considered in medical care, such as survival or the occurrence of specific events.[32]

When in a study of intervention or prognosis the choice is made to include the assessment of quality of life, one or several of the available instruments have to be selected, depending on a review of the literature and specific characteristics of the study. In general the use of an existing instrument is preferable to designing a new questionnaire because several characteristics such as reliability and validity of existing instruments may be known, although of course for a specific study the addition of extra items can be necessary.

After careful selection the next step is to test the feasibility and reliability of the selected instruments for the study population. The present study was set up to assess whether some of the instruments used would turn out to be less suitable than others and should be excluded from a planned main study with a larger number of participants.

Use of all instruments was feasible in the study groups as judged from an acceptable administration time and from the subjects' reactions. Since the time elapsed since MI or stroke was at least six months we expected the condition of the patients to remain relatively stable and the correlations between assessments with an interval of 14 days to be high. Test-retest reliability was satisfactory. In spite of the relatively limited number of patients included in the study the instruments were able to detect differences between the study groups, some of them statistically significant. These results seem promising with regard to the sensitivity of the instruments. That the average age of the post-stroke patients was 6 years lower than that of controls may have contributed to relatively low scores on SIP, but did not prevent the two HAD scores from being significantly higher than in controls.

The implications of some of the findings in the present study groups can be fully addressed only when based on a larger number of subjects. However, given the performance of the instruments in the present study, we believe that they deserve to be considered by other investigators in similar research.

Table 4.7 *Hospital Anxiety and Distress-scores in the different study groups Median (Interquartile range)*

Dimension HAD	*Post-MI (n=20)*	*Post-Stroke (n=16)*	*Controls (n=17)*	*Post-MI vs controls* p =*	*Post-Stroke vs controls* p =*
Anxiety	5.0 (2.0 - 7.5)	7.0 (3.0 - 10.3)	1.5 (0.0 - 3.0)	0.03	< 0.001
Depression	3.0 (1.0 - 8.0)	8.0 (2.0 - 10.8)	1.0 (0.0 - 2.8)	0.06	< 0.001

* Mann-Whitney test

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Chapter 5

Quality of life in patients with myocardial infarction

Introduction

The importance of measurement of disease outcome in medical research is increasingly recognized, especially in treatment trials. Traditional measures of physical performance, such as exercise tests, probably only have limited value as indicators of quality of life (QoL). Even though a therapy has no effect on exercise tolerance it may be considered successful, when it improves quality of life or survival.[1]

Quality of life has not been measured often in controlled trials of patients with cardiovascular disease, although the importance of this measure is widely recognized. A large number of questionnaires has been developed for the assessment of quality of life over the past twenty years. None of these was developed specifically for patients after a myocardial infarction or has been extensively tested in this group of patients.

The primary objective of the present study was to identify, by means of four questionnaires, differences in quality of life between patients with a history of myocardial infarction and population controls. Secondly, we set out to identify which factors determine quality of life within the group of MI-patients. Such possible factors are age and gender and interval since MI, as well as symptoms, health status, memory problems, depression, anxiety and social characteristics. To this aim we performed a cross-sectional study in a non-hospitalized population of subjects aged 55 years and over.

Patients and Methods

The Rotterdam Study is a prospective cohort study, which addresses determinants of progression of chronic disabling disease in the population of 55 years and over in the district of Ommoord in Rotterdam; 7983 participants (78% of those invited) were recruited between 1991 and 1993. Details of the study have been published previously.[2]

From this study we selected 206 patients with a history of hospital admission for MI; 158 patients participated (78%). A reference group was formed by 145 other participants of the Rotterdam study, without a history of myocardial infarction or stroke, and matched for age and sex. Within the setting of the Rotterdam Study, all patients were interviewed

and assessed by a research nurse on several issues including the Mini Mental State Examination (MMSE).[3]

Questionnaires included the Sickness Impact Profile (SIP), Nottingham Health Profile (NHP), the Heart Patients Psychological Questionnaire (HPPQ) and the Hospital Anxiety and Depression Scale (HAD).[4-12] They were tested in a pilot study and were shown to be feasible and reliable.[13] The SIP and NHP are general health profiles, i.e. single instruments covering a wide range of dimensions of quality of life with separate scores for each dimension. In both profiles a high score indicates a poor quality of life.

The SIP consists of 136 items describing the impact of ill-health on behaviour in 12 dimensions. Weighted sum scores are obtained for the overall profile, physical and psychosocial subtotals, and separately for each of 12 categories. Weights used were established for the Dutch population.[4]

The NHP consists of 38 items describing health-related behaviour in six dimensions (part I) and seven yes/no questions concerning domains of daily life (part II). No sum score is derived for NHP. The number of positively answered questions within each dimension is given, as no weighted scores are yet available for the Dutch version of NHP we used. For part II the total number of domains of daily life in which subjects experienced interference is indicated. These instruments have undergone field testing and were shown to provide valid measures of health-related behaviour in the general population, with high inter- and intra-observer reliability coefficients.[5-8] In a randomized double blind trial the NHP demonstrated an improvement in the physical mobility score after three months in 75 patients with severe heart failure treated with enoximone compared with 76 patients receiving placebo.[14]

The HPPQ was developed in the Netherlands as a measure of well-being, feeling of being disabled, displeasure and social inhibition for patients with heart disease. The test consists of 52 items, with a yes/?/no response possibility. It has been validated in the Netherlands on a sample of 1,649 cardiac patients.[9] In addition the quality of life of patients with congestive heart failure has been studied.[10] Data on the reliability, validity, norms, and weights of this instrument are available for the Dutch population, weights are established for the Dutch population; a higher score in the well-being dimension indicates a greater degree of well-being, whereas a higher score in feelings of being disabled, displeasure, and social inhibition indicates a worse condition.[11]

The HAD scale is derived from clinical experience.[12] Two subscales assess anxiety and depression; the patient rates each item on a 4-point scale. Items relating to both emotional and physical disorders are excluded. This is considered to be an advantage since overlap is less likely in this way.[15] A high score indicates anxiety and/or depression. The severity

ratings correlate with a structured clinical interview.[16] The instrument is easily understood and completed by patients, but more work on its reliability and validity is required.[17] All questionnaires apart from SIP were self-administered. Student's T-test and the Mann-Whitney test, and log transformed multiple linear regression analysis were used where appropriate. The statistical package used was BMDP.[18]

Results

The characteristics of the MI-patients and the reference group are shown in table 5.1. The patients and the reference group differed with respect to history of hypertension, coronary bypass, diabetes mellitus and depression. Also, as expected MI-patients more often used diuretics, beta-blockers and antihypertensive medication, as well as lipid lowering agents. A history of serious illness and/or hospital admission in the past twelve months was more frequent both in subjects with a history of MI and in their partners.

Table 5.2 gives the differences in scores for the quality of life instruments between patients with a history of MI and controls. All four instruments indicated an age-adjusted lower quality of life in subjects with a history of MI compared to controls. The SIP showed differences for Sleep and Rest, Emotional Behaviour, Household Management, Mobility, Ambulation, Recreation and Pastimes and all sum scores. The NHP showed statistically significant differences for Pain, Energy, and "Part II". Anxiety was more prominent in MI-patients as shown by higher HAD-Anxiety scores. The HPPQ showed statistically significant differences for Well-being, Feelings of being disabled and Displeasure.

To assess the effect of age and gender linear regression of the logarithm of the quality of life scores with age and gender as independent variables was performed. For SIP total scores no differences were present between men and women in either of the two groups. Within the group of MI-patients differences between men and women were observed with respect to SIP Mobility, Ambulation, and the SIP Physical sum score; for NHP differences were observed for Sleep, and for Social Isolation and part II; for HPPQ differences were observed for Social Inhibition, and for HAD differences were observed for both anxiety and depression scores. These differences indicated a worse quality of life for women.

Regression coefficients of SIP-total score on age were 0.002 ($p = 0.74$) for the MI-patients, and 0.03 ($p < 0.001$) for the reference group, thus indicating a worse quality of life with increasing age for the reference group, but not for the MI-patients. Within the group of MI-patients a worse quality of life with increasing age was observed however,

Table 5.1 *Characteristics of MI patients and controls Mean (SD)*

	Post-MI (n=158)	Controls (n=145)	p-value for the difference*
Age	71.2 (8.9)	70.4 (10.0)	0.45
Sex: no of men (%)	106 (67%)	97 (67%)	0.35
Comorbidity self-reported n (%)			
Ever hypertension	72 (48%)	44 (30%)	0.002
Coronary bypass	18 (12%)	1 (0.7%)	< 0.001
Diabetes	30 (20%)	7 (5%)	0.04
Rheumatoid arthritis	1 (1.8%)	2 (4%)	0.52
Osteoarthritis	14.8 (26 %)	19 (36%)	0.28
Memory complaints	36 (24%)	22 (15%)	0.07
Depression	54 (36%)	35 (25%)	0.03
Time since event (months)	28.6 (15.7)	not applicable	

* T-test

for SIP Body Care and Movement, SIP Household Management, SIP Mobility, SIP Ambulation, SIP Recreation and Leisure, and SIP Physical Sumscore, for NHP Physical Mobility, and for HPPQ Feelings of being disabled.

We performed a cross-sectional analysis to address the effect of the interval since MI on the quality of life. When patients who had experienced an MI six to 12 months or earlier, were compared to patients who had experienced an MI more than one year earlier, a significant difference was present for SIP Social interaction only, indicating a decrease in quality of life over time; median values for the early (n=24) and late group (n=117) were 6.0 (interquartile range 0.7-9.5) and 9.6 (interquartile range 3.5-18.6) respectively, p=0.02. This difference was not explained by a difference in age (69.1 SD 8.0, and 71.9 SD 8.8, respectively, p = 0.15).

We observed a strong relation with perceived quality of life and symptoms of heart disease; notably ankle oedema and shortness of breath. Cognitive impairment, as indicated by a lower Mini Mental State score and self reported memory problems, correlated with a worse quality of life as well. The same observation was made for

Table 5.2 *Sickness Impact Profile (SIP), Nottingham Health Profile (NHP), Hospital Anxiety and Depression scale (HAD), and Heart Patients Psychological Questionnaire (HPPQ).* Median (interquartile range)

	Post-MI (n=158)	Controls (n=145)	p value for the difference
SIP			
SIP-total	8.3 (4.8 - 14.4)	5.4 (2.5 - 10.5)	< 0.001
SIP-psychosocial	6.3 (2.3 - 12.5)	3.6 (1.4 - 8.7)	< 0.01
SIP-physical	5.1 (1.5 - 14.0)	2.9 (0.8 - 8.0)	< 0.05
Sleep and rest	9.8 (0.0 - 22.0)	9.8 (0.0 - 12.2)	< 0.05
Emotional Behaviour	6.5 (0.0 - 17.3)	0.0 (0.0 - 8.8)	0.001
Body care and movement			
Household management	1.5 (0.0 - 7.3)	1.5 (0.0 - 3.6)	0.10
Mobility			
Social Interaction	10.3 (0.0 - 29.0)	0.0 (0.0 - 14.7)	0.00
Ambulation	7.8 (0.0 - 23.0)	7.5 (0.0 - 17.5)	< 0.01
Alertness behaviour	9.5 (3.5 - 17.5)	5.9 (0.0 - 11.9)	0.06
Communication	10.6 (0.0 - 2.0)	0.0 (0.0 - 16.5)	< 0.01
Recreation and pastimes	0.0 (0.0 - 9.8)	0.0 (0.0 - 7.6)	0.16
Eating	0.0 (0.0 - 9.0)	0.0 (0.0 - 9.2)	0.46
	25.6 (7.8 - 39.1)	0.4 (0.0 - 1.3)	< 0.001
	1.3 (0.0 - 6.41	0.0 (0.0 - 6.1)	0.6
NHP			
Emotional reactions	0.0 (0.0 - 1.0)	0.0 (0.0 - 1.0)	0.06
Pain	0.0 (0.0 - 2.0)	0.0 (0.0 - 1.0)	0.006
Energy	0.0 (0.0 - 1.0)	0.0 (0.0 - 0.0)	0.001
Sleep	0.5 (0.0 - 2.0)	0.0 (0.0 - 1.0)	0.06
Social Isolation	0.0 (0.0 - 0.8)	0.0 (0.0 - 0.0)	0.13
Physical Mobility	1.0 (0.0 - 2.0)	0.0 (0.0 - 1.0)	0.05
Part II	0.0 (0.0 - 2.0)	0.0 (0.0 - 1.0)	< 0.001
HAD			
Anxiety	4.7 (2.0 - 7.0)	2.0 (1.0 - 5.0)	0.00
Depression	3.0 (1.0 - 5.0)	2.5 (1.0 - 5.0)	0.14
HPPQ			
Well-being	29.0 (23.0 - 34.0)	33.0 (29.0 - 35.5)	< 0.001
Feelings of being disabled	26.0 (21.0 - 31.0)	20.0 (16.0 - 26.0)	< 0.001
Displeasure	14.0 (12.0 - 18.0)	12.0 (10.0 - 14.0)	< 0.001
Social Inhibition	12.0 (9.0 - 14.0)	11.0 (9.0 - 14.0)	0.81

* Mann-Whitney test

patients who reported ever to have experienced a depressive period. In particular for dimensions indicating emotional behaviour and social interaction. Both HAD anxiety and depression scores were significantly different as well.

HAD Anxiety and Depression scores showed a Spearman correlation of 0.46 and 0.58 respectively with SIP-total score, showing a considerable impact of anxiety and depression on quality of life. In patients who had been admitted to the hospital over the last twelve months (for any reason) a negative influence on quality of life was not found for SIP, but was observed in NHP for all dimensions except Energy and Emotional reactions, in HPPQ for Wellbeing and Feelings of being disabled, and in HAD Anxiety. Determinants of reduced quality of life included change in living condition and change in financial situation. Quality of life was higher in patients with a higher income and in those with better education.

Discussion

The results of this study suggest that the perceived quality of life of subjects with a history of myocardial infarction is clearly reduced. This concerns physical aspects of quality of life, emotional aspects and social aspects.

Quality of life is associated with age, but the impact of age seems stronger in non-diseased subjects than in those with a history of MI, possibly because of the overriding impact of a history of MI on quality of life.

For women we observed, in general, a lower quality of life. An impact of gender, with women having a lower quality of life than men, was previously reported in patients 4 to 6 months after myocardial infarction, and five years after a MI.[19,20] In a study of 134 patients with advanced heart failure (nearly all NYHA class III and IV) age and gender did not account for differences in quality of life.[21] This again indicates that the effect of age and gender may decrease when patients have a worse condition.

A limitation of this study is its cross-sectional nature. Change in quality of life over time can only directly be investigated in a longitudinal study. However, we could obtain an indication of the change in quality of life over time. The time factor may be important; in a study in 122 male patients with severe effort induced angina pectoris (NYHA-classification II and III) patients with a history of angina pectoris of less than 8 years were more likely to show improvement than patients with a history of MI of more than 8 years[22]. In a trial of 111 patients with heart failure over a 3 month period SIP did not show differences between the two treatment groups.[23]

In a trial of three treatments in heart failure (xamoterol, digoxin, placebo) no significant differences with respect to exercise capacity or quality of life were shown[24].

When the whole group was taken into account, a marked improvement in quality of life was observed, as measured by the Profile of Mood State.[25] Cardiac symptoms, such as shortness of breath and ankle oedema had a considerable impact. These symptoms are distressing and limit daily and social activities. In a longitudinal study of 1000 middle-aged men dyspnea was shown to be one of the earliest signs of a deteriorating circulation.[26] In a study in the same population breathlessness was associated with feeling cold, cough, depression, general fatigue and chest pain, and a higher mortality.[27]

The quality of life in patients with cognitive defects, memory complaints and depression was considerably worse. Social factors were important as well; we observed a favourable effect of a higher income and level of education, and negative influence when the financial or living situation had changed because of health problems. We expect return to work also to have a considerable impact on quality of life, but this could not be investigated since the average age of the subjects was around 70.

The results of this study show, that the quality of life of MI-patients 6 to 60 months after the events differs considerably from the quality of life in a non diseased reference group. This is not only explained by physical impairment but also by mental and social factors.

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Chapter 6

Quality of life in patients with ischemic stroke

Introduction

The possibility to measure disease outcome is important in medical research, especially in treatment trials. Research on outcomes is important to determine the effectiveness of different interventions and may help increase the efficiency of existing systems by monitoring the quality of care.[1] Instruments aimed at quantifying subjective data from patients may provide important information that may not be evident from event rates and may be more valid than many of the clinical, biochemical, or physiologic indices on which doctors have traditionally relied.[2]

The first scales designed for this purpose, such as the Karnofsky scale and the ADL scales of Katz and Barthel, emphasized physical disability, although there appears to be a good correlation between these scales and other aspects of the quality of life.[3-6] Other scales attempt to express the "handicap" - the degree of social independence of the patient, in order to give an impression of daily functioning. Elements of handicap are included in the Glasgow Outcome Scale and the modified Rankin scale.[7-10]

Over the past twenty years there has been a development to extend the measurement of outcome to include quality of life. Quality of life is a multidimensional and individualized concept. Quality of life instruments should cover a wide range of aspects including physical, psychosocial and emotional dimensions.

Quality of life has so far received little attention in controlled trials of patients with ischemic stroke, although its importance is widely recognized. No treatment for ischemic stroke is known at this moment that in the acute stage improves the outcome.[11] However, the effect of different treatment strategies on quality of life in such trials deserves more attention. To be able to assess important differences in quality of life, more should be known about the validity of the available measures.

A number of instruments has been used to record various aspects of the quality of life in patients with cardiovascular diseases: for example, the Nottingham Health Profile (NHP), and the Sickness Impact Profile (SIP). Little is known about the characteristics of these specific quality of life instruments with respect to stroke patients.

The aim of this study was to assess the performance of the SIP, NHP and Barthel-ADL scale to identify differences in quality of life between stroke patients and controls in the general population. Furthermore, we investigated whether certain clinical and social variables may explain differences in quality of life among patients with ischemic stroke. Furthermore, in a cross-sectional approach the results were analyzed according to interval after stroke to obtain an estimate of changes in quality of life over time.

Patients and Methods

Since May 1990, all patients who are admitted to the University Hospital Rotterdam Dijkzigt with a stroke or a transient ischemic attack, are registered in the Rotterdam Stroke Data Bank, initiated by one of us (PJK). There are no selection criteria for the admission of stroke patients, but young stroke patients are referred relatively more often to this centre than to the nonacademic centres in the region.

All patients were investigated according to a strict protocol comprising a full neurological examination, standardized blood tests, chest x-ray, at least one and usually two computed tomographic scans of the brain, duplex scanning of the carotid arteries, and a cardiac workup including standard 12-lead electrocardiography, and if indicated, 24-hour electrocardiographic monitoring and echocardiography. Nature and time course of the symptoms were recorded by means of a detailed checklist.[12] Apart from the neurological history, the following vascular risk factors were recorded: smoking habits, hypertension, history of intermittent claudication, angina pectoris, prior myocardial infarction and previous vascular surgery. Stroke severity was assessed by means of the modified Rankin scale (the Oxford Handicap Scale).[8-10] The computed tomographic scans were reviewed by two neurologists, without knowledge of the clinical features or of any investigations.

From October 1992 to July 1993 all patients who had experienced an ischemic stroke at least six months earlier were eligible for the present study, amounting to 216 persons. 74 of them had deceased at the time of the study, 33 were untraceable, and 31 refused to participate. As a result 123 patients (77 men) were interviewed (67% of survivors). Mean age was 64.9 years (SD 15.3). A reference group was formed of 145 participants drawn from a population based cohort study, the Rotterdam Study, (97 men, age 70.4 years, (SD 15.9) consisting of subjects without a history of stroke or myocardial infarction[13]. The Rotterdam Study addresses determinants of progression of chronic, disabling disease in the population of 55 years and over in the district of Ommoord in Rotterdam; 7983 participants (78% of those invited) were recruited between 1991 and 1993.

Table 6.1 *Characteristics of stroke patients and controls* Mean (SD)

	Post-Stroke (n=123)	Controls (n=145)	p-value for the difference*
Age	64.9 (15.3)	70.4 (15.9)	0.05
No of men (%)	77 (62.6)	97 (66.9)	0.92
Time since event (months)	15.6 (9.5)	not applicable	

* T-test

The quality of life questionnaires used in the present study were Barthel-ADL, the Sickness Impact Profile, the Nottingham Health Profile, and the Hospital Anxiety and Depression Scale[14-21]. They were selected after a review of the literature. In a pilot study they showed an acceptable administration time and a good test-retest reliability. Furthermore they were able to distinguish between patient groups and the reference group even in small numbers[22].

The Nottingham Health Profile (NHP) and the Sickness Impact Profile (SIP) are general health profiles, single instruments covering a wide range of dimensions of quality of life, with separate scores for each of these dimensions. In both profiles scores are weighted. A high score indicates a poorer quality of life. The SIP consists of 136 items describing the impact of ill health on behaviour in 12 dimensions. Scores are obtained for each of the 12 categories, and sum scores are obtained for the overall profile, physical and psychosocial subtotals. The NHP consists of 38 items describing health related behaviour in six dimensions and seven yes/no questions concerning domains of daily life. No total sum score is derived for NHP. These three instruments have undergone field testing and were shown to be valid measures of health-related behaviour in the general population with high inter and intra reliability coefficients.[14-22]

The Hospital Anxiety and Depression Scale (HAD) is derived from clinical experience[23]. Two subscales address anxiety and depression; the patient rates each item on a 4-point scale. Items relating to both emotional and physical disorder are excluded. This is considered to be an advantage as overlap is less likely to occur in this way[24]. A high score indicates anxiety and/or depression. The severity ratings correlate with a structured clinical interview[25]. The HAD is easily understood and completed by patients.[24]

The use of the Barthel-ADL index (10 items concerning activities of daily living (ADL)) is recommended in clinical research involving stroke patients[5]. The maximum score is 20 (or 100 with a different scoring system), indicating that no help is needed in performing activities of daily life such as dressing, grooming and bathing.

Apart from the Barthel-index and the Sickness Impact Profile the questionnaires were filled in by subjects themselves, but assistance was offered if requested. Questions were asked concerning socioeconomic status, hospital admission and specific neurological complaints.The Mann-Whitney test, linear regression, Spearman correlation, and the pooled T-test were used to compare differences in scores, where appropriate. We analyzed the effect of age and gender by means of multiple linear regression with logtransformed outcome data. The statistical package used was BMDP.[26]

Results

Characteristics of stroke patients and controls are summarized in table 6.1. Thirty-five (28%) stroke patients had a history of myocardial infarction, 14 (11%) used anti-diabetic medication, 43 (36%) used beta-blockers and/or diuretics. Three patients were aphasic. Mean age in the stroke patients was 64.9 years (SD 15.3), and 70.4 (SD 15.9) in the controls ($p < 0.05$). Data about CT-scan findings were available for 110 patients (89%); in 84 ischemic lesions were shown. Of those 84 patients 70 had lesions relevant to the neurological signs and symptoms; 67 had supratentorial lesions; 35 had lesions in the left hemisphere, 32 had lesions in the right hemisphere, two patients had lesions in the cerebellum and one patient had a lesion in the cerebellum. Median Rankin score (data available for 80 patients) was 1 (interquartile range 1-2, range 0-4).

Table 6.2 shows differences in median scores for the three quality of life instruments and for Barthel ADL in patients with a history of stroke and controls. All instruments indicated a worse quality of life in stroke patients, with respect to the quality of life instruments in psychological, physical and social dimensions. The SIP showed differences for all dimensions except Eating, and the NHP showed statistically significant differences for all dimensions apart from Pain. HAD Depression scores were higher in strokes.

Correlations between corresponding NHP and SIP scores were 0.51 for NHP Energy and SIP Emotional Behaviour, and 0.34 for NHP Emotional Reactions and SIP Emotional Behaviour. Correlation between NHP Sleep and SIP Sleep and Rest was 0.28, whereas correlation between NHP Social Isolation and SIP Social

Table 6.2 *Sickness Impact Profile (SIP), Nottingham Health Profile (NHP), Hospital Anxiety and Depression scale (HAD), Barthel: results for separate dimensions and sum scores for stroke patients and controls.* Median (Interquartile range).

	Post-Stroke (n=123)	Controls (n=145)	p-value for the difference*
SIP-total	11.3 (5.9 - 21.6)	5.5 (2.5 - 10.5)	< 0.01
SIP-psychosocial	8.2 (3.3 - 16.6)	3.6 (1.4 - 8.7)	< 0.01
SIP-physical	8.4 (2.6 - 20.7)	2.9 (0.8 - 8.0)	< 0.01
SIP			
Sleep and rest	9.8 (0 - 22.0)	9.8 (0 - 12.2)	< 0.01
Emotional Behaviour	0.0 (0 - 17.6)	0.0 (0 - 8.8)	< 0.01
Body care and movement	4.7 (0 - 13.5)	1.5 (0 - 3.6)	< 0.01
Household management	14.7 (0 - 37.6)	0.0 (0 - 14.7)	< 0.01
Mobility	9.2 (0 - 25.4)	7.5 (0 - 17.5)	0.16
Social Interaction	9.5 (0 - 20.0)	5.9 (0 - 11.9)	0.06
Ambulation	10.7 (0 - 32.9)	0.0 (0 - 16.5)	< 0.01
Alertness behaviour	7.6 (0 - 18.4)	0.0 (0 - 7.6)	< 0.01
Communication	0.0 (0 - 21.1)	0.0 (0 - 9.2)	< 0.01
Recreation and pastimes	20.0 (7.8 - 44.6)	8.5 (0 - 30.8)	< 0.01
Eating	0.0 (0 - 9.3)	0.0 (0 - 6.1)	0.60
NHP			
Emotional reactions	1.0 (0 - 1.0)	0.0 (0 - 1.0)	0.02
Pain	0.0 (0 - 1.0)	0.0 (0 - 1.0)	0.60
Energy	0.0 (0 - 1.0)	0.0 (0 - 0.0)	< 0.01
Sleep	0.0 (0 - 2.0)	0.0 (0 - 1.0)	0.09
Social Isolation	0.0 (0 - 1.0)	0.0 (0 - 0.0)	< 0.01
Physical Mobility	1.0 (0 - 3.0)	0.0 (0 - 1.0)	< 0.01
Part II	1.0 (0 - 3.0)	0.0 (0 - 1.0)	0.01
HAD			
Anxiety	2.0 (1.0 - 5.0)	2.0 (1.0 - 5.0)	0.18
Depression	4.0 (1.0 - 7.0)	2.5 (1.0 - 5.0)	0.01
Barthel score	20.0 (18.0 - 20.0)	20.0 (20.0 - 20.0)	< 0.01

* Mann-Whitney test

Interaction was 0.35. NHP Physical Mobility score correlated highly with SIP Body Care and Movement (0.59) and Ambulation (0.64). HAD anxiety and depression scores were positively associated with quality of life scores, indicating a worse quality of life in patients with more feelings of anxiety and depression. For HAD Anxiety correlations ranged for NHP from 0.17 for Physical Mobility to 0.34 for Energy, and for SIP from 0.02 for Alertness Behaviour to 0.35 for Emotional Behaviour. For HAD Depression scores correlations ranged for NHP from 0.15 for Pain to 0.45 for Energy, and for SIP from 0.11 for Alertness Behaviour to 0.64 for Social Interaction.

The effect of age and gender was analyzed by linear regression of the logarithm of the SIP total sum score with age and gender as independent variables. Regression coefficients for stroke patients were - 0.32 ($p = 0.07$) for sex, and 0.003 ($p = 0.63$) for age, and for the reference group they were 0.08 ($p = 0.48$) and 0.03 ($p < 0.001$) respectively. This indicates a decrease in quality of life with increasing age in the reference group only. No differences were observed between men and women, except for the Barthel-index with better scores for men. Median Barthel scores for men and women were 20.0 (interquartile range 19.0 - 20.0) and 19.0 (15.5 - 20.0) respectively ($p = 0.01$). Scores for SIP tended to be higher in men, indicating a worse quality of life for men, but none of these differences was statistically significant.

Table 6.3 shows, within the group of stroke patients, a comparison according to the interval since ischemic stroke on the quality of life, expressed in SIP scores. The median interval of 1.3 years was chosen as a cut-off point and patients were divided in an early and a late group. Average age in the early ($N = 62$) and late group ($N = 61$) was 65.3 (SD 13.3) and 63.0 (SD 16.1) respectively ($p = 0.42$, pooled T-test). The Sickness Impact Profile showed differences for three of eleven dimensions, and for all sum scores. Scores were higher in the late group, indicating a deterioration of quality of life over time. The NHP showed a change in only one of its six dimensions (Social Isolation). HAD and Barthel scores showed no differences at different intervals.

Differences in quality of life scores were analyzed for 84 patients with and 26 patients without ischemic lesions shown on a computed tomography scan of the brain. Scores in the group with ischemic lesions tended to be higher, but a significant difference was observed only with the Nottingham Health Profile for Social Isolation. No differences in quality of life were found between 32 patients with clinically relevant cortical lesions in the right hemisphere and 35 patients with clinically relevant cortical lesions in the left hemisphere. In general higher scores were observed for patients with a motor deficit, but only the SIP Communication score was

Table 6.3 *Sickness Impact Profile (SIP): results for separate dimensions, total score, psychosocial and physical sumscores for early (elapsed time less than 1.3 years) and late (elapsed time more then 1.3 years) groups.* Median (Interquartile range)

	Early (n=62)	*Late (n=61)*	*p-value for the difference**
SIP-total	8.8 (4.6 - 15.8)	14.8 (6.1 - 25.2)	0.03
SIP-psychosocial	6.9 (1.9 - 13.8)	10.5 (5.0 - 24.7)	0.02
SIP-physical	5.7 (1.8 - 19.6)	10.7 (4.0 - 23.9)	< 0.05
Sleep and rest	9.8 (0.0 - 21.9)	9.8 (0.0 - 22.0)	0.34
Emotional Behaviour	0.0 (0.0 - 10.4)	8.8 (0.0 - 20.9)	0.03
Body care and movement	3.2 (0.0 - 10.7)	8.1 (0.0 - 14.3)	0.04
Household management	14.7 (0.7 - 23.9)	16.9 (0.0 - 45.1)	0.19
Mobility	9.2 (0.0 - 23.4)	9.2 (0.0 - 26.8)	0.19
Social Interaction	6.6 (0.0 - 18.2)	11.8 (3.5 - 22.5)	0.06
Ambulation	9.8 (0.0 - 27.5)	17.8 (2.1 - 35.4)	0.04
Alertness behaviour	0.0 (0.0 - 10.2)	9.6 (0.0 - 20.0)	0.13
Communication	0.0 (0.0 - 9.6)	8.8 (0.0 - 29.7)	0.07
Recreation and pastimes	18.3 (0.0 - 40.0)	22.3 (9.0 - 46.2)	0.23
Eating	0.0 (0.0 - 6.1)	1.3 (0.0 - 11.4)	0.11

* Mann-Whitney test

significantly different in them. We also observed a higher HAD depression score in this group. The number of aphasic patients was too small to allow a separate analysis.

Information on marital status was available for 117 stroke patients: 15 were unmarried, 80 were married, 3 lived together without being married, 12 were widow or widower and three were divorced. HAD Depression scores were reported more often in singles than in subjects with a partner; median values were 6.0 (interquartile range 1.0 - 11.0) and 3.0 (interquartile range 1.0 - 11.0) respectively ($p = 0.03$). Singles had a higher score in SIP Household Management compared with subjects with a partner, 23.8 (interquartile range 6.6 - 53.8), and 13.2 (interquartile range 0.0 - 31.6) ($p = 0.02$), respectively and in SIP Ambulation as well: 15.9 (interquartile range 0.6 - 35.3) and 9.2 (interquartile range 0.0 - 21.6), $p = 0.04$. The same applied to SIP

Recreation and pastimes, the value for singles was 29.2 (interquartile range 11.1 - 49.8), and for subjects with a partner 17.7 (interquartile range 0.0 - 40.5)($p = 0.05$). SIP Psychosocial score and Total sum score did not differ significantly, but SIP Physical sumscore was worse in singles (8.4, interquartile range 5.2 - 27.2) than in subjects with a partner (6.4, interquartile range 1.5 - 14.3) ($p = 0.03$). There were no differences between these groups with respect to age and gender.

Discussion

A stroke has a considerable impact on quality of life. This concerns physical, psychological as well as psychosocial dimensions. To appreciate these findings some aspects of the study need to be addressed. We studied the effect of a stroke by comparing a group of stroke patients with a reference group drawn from the general population. It would have been preferable to study the same patients before and after a stroke. This is difficult to carry out because of the relatively low incidence of stroke. We believe however, that the numbers in our study were large enough to neutralise random variations in perceived health before stroke, so that the comparison is valid. Another limitation is, that not all eligible subjects participated in the quality of life study. It is possible that the patients who did not participate differed from the participants in their quality of life. For example, in some patients relatives said that participation was impossible because of cognitive defects. This may also be the explanation for the relatively low number of aphasic patients participating. We believe however, that this will only have reduced the contrast between the patient group and the reference group. The same accounts for the younger age of the stroke patients.

Our cross-sectional data suggest that quality of life deteriorates after the first year. This should be confirmed in a true longitudinal study. At present no studies are available about changes in quality of life six months or more after a event. In one randomized study of 78 patients to evaluate the effect of sensory stimulation on functional outcome 3, 6, and 12 months following stroke the NHP showed differences in quality of life between stroke patients and controls, but changes over time were not analyzed separately.[27]

In our study, differences in quality of life among stroke patients were not related to gender, presence or absence of ischaemic lesions on CT, or location of the ischaemic lesions in the right or the left hemisphere. In an earlier study a trend was observed to less independence in patients with right hemisphere lesions. However, these differences were not formally analyzed, and differences in social activity were

not observed.[28] In another study of 296 young adults with ischemic stroke, no differences in quality of life were observed for different stroke subtypes.[29] In a study in 441 stroke patients six months after a stroke using the SIP for the assessment of quality of life few relationships between hemispheral lesion sides and quality of life scores were found.[30]

Both feelings of anxiety and depression seem important in determining quality of life, as both anxiety and depression scores correlate with quality of life scores. In comparison with the reference group feelings of depression were particularly more common. In other studies depressive feelings were reported in 23 to 63%.[31-38] Presence of depressive symptoms was found to have a negative impact on long-term outcome.[39,40] However, 16 weeks of social work intervention in forty-four depressed stroke patients, one year after stroke did not have a detectable effect on quality of life.[36]

Our findings suggest, that patients living singly report a lower quality of life. In a study by Henley et al. Living with a partner and frequent social contact was shown to positively affect outcome at one year with regard to independence, and conversely stroke patients without family support were shown to undergo more marked emotional deterioration[37]. Psychosocial factors influence rehabilitation.[40] The identification of these and other factors is important in the design and implementation of long term rehabilitation programs.

The observations in our study are, of course, dependent on the instruments we used. The choice of measurement instruments must be based on clearly established criteria for both the purpose of the instrument and criteria on which the measurement instrument can be evaluated.[41,42] The NHP and SIP were not developed specifically for stroke patients. Theoretical advantages of using these instruments instead of, or as a supplement to, more traditional outcome measures in stroke patients such as the Rankin scale or ADL-scales are that the outcome is determined not only by physical disabilities, but also by social functioning and emotional and mental aspects. Importantly, the patient's view of his or her well being is appreciated rather than the doctor's interpretation of the patient's well being, when generic instruments such as the NHP and SIP are applied.

New instruments developed especially for stroke patients, however, lack information with respect to validity, reliability and comparability with other studies. A problem with the inclusion of the questionnaires we used in clinical research is the effort needed to collect the data. A consistent collection of reliable data can only be achieved if those responsible for generating and collecting the data agree on its

relevance, and see a personally relevant reason for collecting it.[39] We believe, however, that if measurement of quality of life is an important goal of a study this investment has to be made. Use of an ADL-index such as the Barthel scale only, 6 months after the event is of limited value because of its ceiling effect. A large number of patients might not show any benefit from the investigational treatment when assessed by the Barthel index.[43]

In conclusion, our findings show clear reductions in quality of life in non-hospitalized survivors of a stroke. Quality of life seems to deteriorate after the first year. The Sickness Impact Profile and the Nottingham Health Profile are well suited for detecting these differences. We recommend the use of these instruments in intervention trials where the aim is to improve quality of life rather than to prevent specific events.

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General discussion

A 54-year-old lawyer woke up on a December morning with weakness of the left arm. In August of the same year he had had the same symptoms, but only briefly (three episodes of five or ten minutes). This time the weakness remained, and four days later his left leg was also weak, though he could still walk. Examination confirmed slight motor deficits of the left arm and leg, with a 'pyramidal' distribution and increased tendon jerks, and decreased superficial sensation of the left hand. CT scanning showed a row of small infarcts in the region of the left corona radiata, consistent with low flow. On cerebral angiography the left middle cerebral artery was completely occluded, in its terminal portion. Extracranial/intracranial bypass surgery was considered and was eventually performed with success. The deficits cleared within three months, and in the two years until the time of writing he remained in perfect health and working at full pace, in the Netherlands and abroad.

Mister A is 74 years of age. He has worked as an office worker until he was 63 when he was struck by his first myocardial infarction. Since then he has suffered two more myocardial infarctions. At present his cardiac condition is stable but he takes several drugs. He is severely impaired. He lives alone in a tower-block, accompanied by his little dog. When the wind is too strong he is not able to walk his dog himself. Two times a week he has domestic help, if necessary they do part of the shopping. His social activities have been severely reduced since he fell ill for the first time.

Suddenly someone is struck by a myocardial infarction or a stroke. Suddenly he or she has become a patient. Usually he or she is admitted to the hospital. First there is a phase of several investigations in which the degree of organ damage is established. At the same time acute therapy is started. As soon as possible rehabilitation is initiated. Then the patient is discharged from the hospital. The patient has survived, but the disease is not cured.

Why is it important to know the impact of a myocardial infarction or stroke?

As the two examples illustrate the consequences of a myocardial infarction or a stroke can be very diverse. Knowledge about the impact of a disease helps the clinician to explain to patients and peers what they can expect in the short term and in the long term. For example, is not unusual to suffer from anxiety after the experience of a myocardial infarction. It also helps the clinician to be receptive to certain signs and symptoms, such as those indicating anxiety and depression, and to act upon them. The varying severity of stroke or myocardial infarction underlines the importance of prevention and of therapy directed at limiting the damage produced by myocardial infarction or stroke, for example, by means of streptokinase in acute myocardial infarction.

Why is it important to measure this impact?

If we manage to quantify one way or another the effect of a MI or stroke we can accurately evaluate the effectiveness of preventive strategies, acute therapy and intervention programmes, not only with respect to survival or presence or absence of major complications, but also with respect to the quality of life. Also it enables us to monitor more precisely the degree of improvement or deterioration in individual patients.

How to measure?

Different levels of measurement of outcome are recognised. At one end of the spectrum there are measures of the biological disease process, such as the size of an infarct as indicated by the level of creatinine kinase in case of a MI, and by the size of the hypodense area on computed tomography in an ischemic stroke. Intermediate are specific signs and symptoms caused by a MI or stroke, and at the other end is the notion of quality of life. Presently at least three levels of outcome measurement are recognised and defined as such by the World Health Organisation. First, *impairment* is defined as disturbance of a specific function at the level of the organ, for instance the elements of the neurological examination that make up stroke scales. Next, *disability* assesses function at the level of the person and represents the extent of the remaining ability to perform tasks within the physical and social environment. Scales for activities of daily living, such as the Barthel-Index, and performance scales fall within this category. The next level is *handicap*, "a disadvantage for a given individual, resulting from an impairment or a disability, that limits or prevents the fulfilment of a role for that individual"; examples of instruments that at least incorporate some elements of social roles are the NYHA-classification and the Rankin-scale. Most scales designed to measure outcome have been

aimed at impairments at a disease specific level. Measures for disability and handicap can be applied to different diseases, but broader use is sometimes prevented by tradition within medical disciplines. In the range from impairment to handicap more factors are introduced and the measurement becomes more and more relevant to the patient. At the end of the spectrum quality of life can be defined as a reflection of the way that patients perceive and react to their health status and to other nonmedical aspects of their lives, rather than being the description of patient's health status.[1] A problem is that as more factors are introduced the less sensitive the measurement becomes. But an advantage may be that the generic character of instruments measuring quality of life enables application and potential comparison across different categories of disease. This also solves the problem of evaluating quality of life in patients who suffer from more than one disease. For example, it is not uncommon that stroke patients (will) suffer from heart disease as well.

How to select?

For each purpose the most optimal measurement instruments have to be chosen. This is guided by the question on which level(s) we want to measure. If the objective is to assess (differences in) quality of life several considerations may be made. First, the selected instrument has to include items that the patients under study consider important to their quality of life; do we measure what we want to measure? Second, the instrument has to be feasible and reliable for this group. If change over time has to be assessed an estimation has to be made on how big the changes might be that are expected, in other words how sensitive the instrument of choice has to be. The choice of existing instruments has advantages because of the information available with respect to validity, reliability and comparability with other studies. Finally the conditions for the quality of life study have to be defined. Who is responsible for the assessment and who checks whether the assessment is made at the planned time? Is there an opportunity for the patients to fill in the forms privately?

How to interpret?

The results of a descriptive study concerning quality of life in a population affected by a disease are best interpreted against the results in a reference group. Preferably this group should be assessed at the same time and preferably in the same setting as the 'cases', thus

[1] Gill TM, Feinstein AR. A critical appraisal of the quality of quality-of-life measurements. JAMA 1994;272:619-626.

avoiding misinterpretations of differences in the results because of incomparability of the reference group with the diseased subjects or due to differences in the test-situation. However, this reference group does not necessarily have to be a group of 'healthy' subjects. It can also consist of patients receiving another treatment or differing from the 'cases' with respect to certain predefined variables.

When quality of life measurements are incorporated in clinical trials new problems appear. Firstly because quality of life is conditional on survival. If the survival rate in two study-groups is not comparable a better quality of life in the group with the highest mortality might be the result of survival of the fittest. Thus differences at baseline between survivors and non-survivors have to be analyzed. When results for both mortality and quality of life are worse in one of the study-groups the interpretation is less difficult. Preferably an assessment should take place at every follow-up visit. In this way the most recent information about quality of life is available when a patient leaves the study. It also creates the possibility of analyzing initial changes in quality of life, for example, due to (initial) side-effects of the medication under study. For practical reasons, however, the assessments might be limited to the entry of the study and the end of the follow-up period. The quality of life assessment should be considered just as important as any other (clinical) investigation. To avoid misinterpretation of the results due to "lost to follow-up", every person who leaves the study should be urged to fill out the quality of life forms or to be interviewed at the moment they leave the study. However, the condition of a subject under study might worsen in the course of the study and at some stage filling in the quality of life forms or an interview with the same purpose might be too much of a burden. Thus the number of people not able to be assessed should be taken into account. Different classes may be defined within the quality of life scores and for the groups under study the time spent in each class is described, as suggested by Ollson et al.[2]

The thesis in perspective

This thesis concerns outcome measurement at the level of handicap and quality of life. Over time we shifted from the approach where the doctor assesses the condition of the patient by means of a handicap scale to the approach were the patient answers questions concerning different issues of quality of life. This thesis demonstrates that there are

[2] Ollson G, Lubsen J, van Es GJ, Rehnquist N. Quality of life after myocardial infarction: effect of long term metoprolol on mortality and morbidity. Br Med J 1986;292:1491-93.

important differences in quality of life between patients with a history of MI or stroke and a reference group.

It also shows that questionnaires are available that measure aspects of quality of life considered important by stroke and MI-patients. Several quality of life instruments are feasible and reliable for use in these patients. Differences in quality of life can be determined with the help of these instruments; the Nottingham Health Profile, the Sickness Impact Profile, the Heart Patients Psychological Questionnaire and the Hospital Anxiety and Depression scale. It shows that the presence of physical complaints is partly responsible for these differences in quality of life, but that psychosocial factors are important as well, including cognitive performance.

A limitation of our work is that we only performed a cross-sectional study and could not directly establish change over time. Thus the issue of responsiveness (i.e. can an instrument measure change over time?) is not directly addressed. Another limitation is that because of the limited number of stroke victims in the general population, we could not select the referents and the stroke patients from the same population.

Future research

More information should be gathered about the responsiveness of the selected instruments in patients with a myocardial infarction or a stroke. Although this topic is not addressed conclusively in this thesis we believe that our findings are promising enough to justify the incorporation of these instruments in clinical trials in patients with a history of stroke or MI. An ideal instrument for the measurement of quality of life does not exist. We have stressed the importance and advantages of collecting data about the characteristics of available instruments. But, with the increase of knowledge on the subject new instruments will be developed, hopefully incorporating the present experience. More research could be done to identify which factors determine quality of life conditional on damage at the organ level. The identification of certain factors as contributing to the quality of life might be a consideration in intervention therapy.

Summary

The importance of the quality of life in relation to disease is increasingly being recognized. Quality of life, however, is a heterogeneous entity that can be measured in several ways. Questionnaires have been developed with this aim for specific groups of patients, but their use in assessing patients with ischemic disease of the heart or brain is limited.

In *chapter 2* an overview is given of the literature with respect to those aspects of quality of life considered to be important by patients with heart disease and stroke. Several questionnaires developed for the measurement of quality of life in patients with cardiovascular and cerebrovascular disease are discussed. Three questionnaires appeared attractive enough to be further investigated in patients with a history of a myocardial infarction; the Nottingham Health Profile (NHP), the Sickness Impact Profile (SIP), and the Hospital Anxiety and Depression scale (HAD).

In a preparatory phase the interobserver variability was investigated of the Rankin scale, a six-point handicap scale. One hundred stroke patients were assessed by pairs of neurologists. The agreement was satisfactory, indicating that the Rankin scale is valid for the assessment of handicap in stroke patients. The results of this study are described in *chapter 3.1.*

In the next phase the agreement between neurologists and cardiologists was tested with respect to the Rankin scale and the four-point scale of the New York Heart Association (NYHA) in 51 patients with a history of a myocardial infarction (MI) or angina pectoris. The agreement among neurologists and cardiologists was similar. This study, described in *chapter 3.2*, indicated that the Rankin scale may be useful for the assessment of the degree of handicap from heart disease, also in patients with neurological disease.

Chapter 3.3 describes a quality of life study in 59 patients with angina pectoris. Quality of life was assessed with the Quality of Wellbeing index (QWB), the Nottingham Health Profile and the Sickness Impact Profile. NHP and SIP showed increased impairment with higher NYHA class as assessed by general practitioners. This indicated that NHP and SIP may be able to identify treatment effects in angina patients. There was a close relationship between SIP and NHP scores. The QWB showed greater administrative problems and less discrimination.

The study described in *chapters 4, 5, and 6* had several aims. In the first place instruments were selected for the measurement of quality of life in patients with ischemic disease of the heart or brain. The feasibility and reliability of SIP, NHP and the Heart Patient Psychological Questionnaire (HPPQ), developed in the Netherlands, and the Hospital Anxiety and Depression scale (HAD) were tested in patients with a history of MI or stroke. Furthermore reference values were assessed and possible factors with an impact on the quality of life were investigated.

Chapter 4 describes a pilot-study of 20 persons with a history of MI, 17 stroke patients and 16 controls. SIP, NHP, HPPQ and HAD were feasible in these patients, with an acceptable assessment time. The results after retesting, 14 days later, highly correlated with the first results. Participants were questioned with respect to which aspects they considered important for their quality of life. All aspects mentioned by the participants were included in the questionnaires, except religion. The HAD was included because it specifically addresses anxiety and depression. Heart patients are reported to suffer from anxiety, while depression is more common in stroke patients. In spite of the relatively limited number of patients included in the study the instruments were able to detect differences between the study groups, indicating a lower quality of life in the MI and stroke patients.

All questionnaires were incorporated in the main study. This study consisted of two parts; a study with respect to quality of life in MI patients, and a study concerning quality of life in stroke patients.

The Rotterdam study is a prospective cohort study, addressing determinants of progression of chronic disabling disease in a population of 55 years and over. 206 participants were approached who had experienced a myocardial infarction a half to five years earlier and were admitted to a hospital. 158 (78%) participated in the present study, described in *chapter 5*. Their results were compared with the results of a non-diseased reference group, matched for age and gender.

The SIP showed differences with respect to sleep, emotional behaviour, home management, walking, recreation and pastimes. The Nottingham Health Profile showed differences with respect to pain and energy. The Heart Patient Psychological Questionnaire showed differences with respect to well-being, feelings of being disabled, and displeasure. All results indicated a worse quality of life in the MI-patients. The HAD showed that feelings of anxiety were more common in MI-patients. This was not demonstrated for feelings of depression. The time elapsed since the MI did not seem to affect the quality of life. Age did have an impact on the quality of life, expressed in the SIP-total score in the reference group, but not in the group of heart disease patients.

However, within the group of heart patients a worse quality of life with increasing age was observed in several subdimensions, especially the physical mobility scores.

There were no differences in quality of life between men and women with respect to SIP total scores. In several sub-dimensions differences indicating a worse quality of life were observed in women, again in the physical mobility scores, but also in the dimensions indicating social isolation. For HAD differences were observed for both anxiety and depression scores. This was not explained by a difference in age.

We observed a strong relation with perceived quality of life and symptoms of heart disease. Cognitive impairment correlated with a worse quality of life as well. The same observation was made for patients who reported having experienced a depressive period, in particular for dimensions indicating emotional behaviour and social interaction. Both HAD anxiety and depression scores were significantly different as well. A higher income and a higher education seemed to have a positive effect on the quality of life.

In summary, important differences in quality of life were shown between patients with a history of MI and a reference-group matched in age and gender. These differences were partly explained by symptoms of heart disease. The impact of impairment of memory and depressive complaints as reported by the patients themselves is even bigger. Social factors seem to be important in modifying the effect of the disease.

In *chapter 6* a study is described of patients with a history of stroke. 266 patients were selected who had experienced an ischemic stroke six to twenty-four months earlier. They were registered in the Rotterdam Stroke Databank. At the time of the present study 192 patients were alive, and 123 of them (67%) participated. Quality of life, measured with SIP, NHP, HAD and the Barthel ADL-index was worse in nearly all subdimensions and sumscores in the stroke patients, compared with the quality of life in the reference group. Age, again, had a smaller effect in the patient group, compared with the effect in the reference group. No differences in quality of life were shown between men and women. Over time the quality of life seemed to deteriorate, and the SIP seemed most sensitive in detecting this change.

Within the group of stroke patients there were no clear differences in quality of life between patients with and without lesions detected with computed tomography, or between patients with lesions in the right or left hemisphere. Education did not have a clear influence. Quality of life scores were better in patients living with a partner, than in patients living singly.

In summary, considerable differences in quality of life were shown in patients with ischemic stroke, compared with a reference group. These differences were not explained

by the localisation of the stroke or the number of ischemic lesions. Social factors, such as the marital status, appeared to have a clear influence.

In conclusion the Sickness Impact Profile and the Nottingham Health Profile appear to provide feasible, valid and reliable instruments for the measurement of quality of life in Dutch patients with a history of MI or stroke. Important differences in quality of life in both groups of patients are shown in the comparison with a reference group. Physical impairments are partly responsible for these differences in quality of life. In the group of heart patients self-reported memory complaints and depression had a considerable impact. Social factors were very important. The SIP seemed most sensitive for the detection of change over time. The results of this study confirm the importance of the measurement of quality of life in clinical studies of patients with ischemic disease of the heart or brain.

Samenvatting

Het belang en de noodzaak om de gevolgen van ziekte voor de kwaliteit van leven te onderzoeken wordt steeds meer onderkend. Kwaliteit van leven is een heterogeen begrip, dat op diverse manieren kan worden gemeten. Meetinstrumenten zijn ontwikkeld voor verschillende groepen patiënten, maar de ervaring hiermee bij patiënten met ischemische aandoeningen van hart en hersenen is beperkt.

In *hoofdstuk 2* wordt een overzicht gegeven van de literatuur met betrekking tot aspecten van kwaliteit van leven die als belangrijk worden ervaren door patiënten met hartziekten en patiënten die een beroerte hebben doorgemaakt. Tevens worden diverse instrumenten voor het meten van kwaliteit van leven bij patiënten met ischemische aandoeningen van hart en hersenen besproken. Een aantal instrumenten kwam uit voorgaand onderzoek als veelbelovend naar voren: de Sickness Impact Profile (SIP), de Nottingham Health Profile (NHP) en de Hospital Anxiety and Depression scale (HAD).
In de voorbereidende fase van het onderzoek werd de variatie tussen waarnemers bepaald van twee handicap-schalen. In *hoofdstuk 3.1* worden de resultaten weergegeven van een interobserver-onderzoek met betrekking tot de classificatie op de Rankin-schaal, een handicap-schaal, door telkens verschillende paren neurologen; 100 patiënten die een beroerte hadden doorgemaakt werden hierbij onderzocht. De overeenstemming bleek redelijk tot goed en daarmee leek de Rankin-schaal bruikbaar voor het schatten van handicap bij patiënten met een herseninfarkt.

De overeenstemming tussen neurologen en cardiologen met betrekking tot de Rankin-schaal en de schaal van de New York Heart Association (NYHA) werd vervolgens nagegaan bij 51 patiënten die een hartinfarct hadden doorgemaakt of pijn op de borst (angina pectoris) hadden. De overeenstemming die nu werd gevonden met beide schalen was matig tot redelijk, waarbij de resultaten van neurologen en cardiologen vergelijkbaar waren. Hieruit valt op te maken dat neurologen met deze schaal ook de handicap veroorzaakt door hartziekten bij neurologische patiënten zouden kunnen inschatten. De resultaten van dit onderzoek zijn weergegeven in *hoofdstuk 3.2.*

Uit een analyse van de toepassing van de SIP, de NHP en de Quality of Wellbeing Index bij 53 patiënten met angina pectoris bleek een relatie te bestaan tussen de eerste

twee instrumenten en de inschatting van de handicap door de huisarts, volgens de NYHA-classificatie. Dit was een aanwijzing dat deze instrumenten in staat zijn relevante veranderingen in gezondheidstoestand te meten. Tevens bleek er een nauwe relatie te bestaan tussen de scores van SIP en NHP. De QWB bleek bij deze studie minder waardevol. Dit is beschreven in *hoofdstuk 3.3*.

Het in *hoofdstuk 4, 5 en 6* gepresenteerde onderzoek had meerdere doelen. In de eerste plaats betrof het de selektie van instrumenten voor het meten van kwaliteit van leven bij patiënten met ischemische aandoeningen van hart of hersenen. In de tweede plaats ging het om onderzoek naar de betrouwbaarheid en validiteit van deze instrumenten. In de derde plaats betrof het het verkrijgen van norm-gegevens voor deze instrumenten. Vervolgens werd onderzocht welke factoren een invloed zouden kunnen hebben op de kwaliteit van leven.

Hoofdstuk 4 beschrijft een voorstudie waarin de bruikbaarheid en betrouwbaarheid van SIP, NHP, de Medisch Psychologische Vragenlijst bij Hartpatiënten (MPVH) en de Hospital Anxiety and Depression Scale (HAD) werd getest bij 20 personen met een hartinfarct, 17 personen met een herseninfarct en 16 controle-personen. De MPVH is ontwikkeld in Nederland, speciaal voor hartpatiënten. De HAD werd toegevoegd omdat deze specifiek aandacht besteedt aan angst en depressie. Uit literatuuronderzoek was gebleken dat hartpatiënten vaak angstgevoelens kennen, terwijl bij herseninfarct-patiënten depressie meer op de voorgrond staat. Alle vragenlijsten bleken goed in te vullen voor de deelnemers en de benodigde tijd hiervoor was niet te lang. Bij herhaling van de vragenlijsten na 14 dagen bleken de resultaten goed overeen te komen. Aan de deelnemers werd tevens een aantal open vragen gesteld met betrekking tot de betekenis die zij hechtten aan het begrip 'kwaliteit van leven' en de aspecten die zij hiervoor van belang vonden. Met uitzondering van het begrip religie bleken al deze aspecten in de vragenlijsten naar voren te komen. Zelfs bij deze kleine aantallen bleken de instrumenten in staat patiënten-groepen te onderscheiden van controles; de scores wezen steeds in de richting van een slechtere kwaliteit van leven voor de patiënten-groepen.

Op grond van de resultaten van de voorstudie werd besloten alle vragenlijsten toe te passen in de hoofdstudie. De hoofdstudie valt uiteen in twee onderdelen: een onderzoek met betrekking tot kwaliteit van leven bij patiënten met een hartinfarct en een onderzoek met betrekking tot meten van kwaliteit van leven bij patiënten met een herseninfarct.

In het eerste onderzoek, beschreven in *hoofdstuk 5*, werden 206 deelnemers van het Erasmus Rotterdam Gezondheid en Ouderen onderzoek (ERGO) benaderd; 158 (78%)

hiervan namen aan het onderzoek deel. Een half tot vijf jaar tevoren hadden zij een hartinfarct doorgemaakt, waarvoor zij waren opgenomen in het ziekenhuis. Hun resultaten werden vergeleken met een groep van 145 controle-personen, eveneens deelnemers aan het ERGO onderzoek, vergelijkbaar in leeftijd en geslacht.

Met de SIP bleken verschillen in kwaliteit van leven aantoonbaar met betrekking tot slapen, emotioneel gedrag, huishouden, lopen en recreatie en vrije tijd, ten opzichte van de controle-groep. Uit scores van de NHP bleken ook verschillen met betrekking tot pijnbeleving en energie te bestaan. De MPVH toonde tevens verschillen aangetoond met betrekking tot welbevinden, handicapsbeleving en ontstemming. Steeds duidden deze resultaten op een minder goede kwaliteit van leven bij patiënten die een hartinfarct hadden doorgemaakt. Tevens bleek uit de scores van de HAD dat gevoelens van angst vaker voorkwamen bij patiënten met een hartinfarct; voor gevoelens van depressie was dit niet het geval. De tijd die verstreken was sinds het hartinfarct leek geen invloed te hebben op de kwaliteit van leven. Leeftijd had in de controle-groep wel een aantoonbare invloed op de SIP totaal-score, bij de patiënten-groep niet. Er bestonden verschillen in kwaliteit van leven tussen mannen en vrouwen met betrekking tot slapen (NHP), mobiliteit en intellectueel functioneren (SIP) en sociale geremdheid (MPVH). Deze verschillen wezen steeds op een minder goede kwaliteit van leven bij vrouwen. Dit werd niet verklaard door een verschil in leeftijd.

Patiënten met klachten gerelateerd aan hart- en vaatziekten zoals kortademigheid, enkeloedeem, pijn op de borst en pijn in de benen na lopen hadden een minder goede kwaliteit van leven. Dit kwam tot uiting in de dimensies die aandacht geven voor lichamelijk functioneren, maar ook in dimensies die aandacht geven aan het gevoel. Zowel geheugenproblemen als depressieve klachten werden door de hartpatiënten vaker gemeld dan door de controlegroep. De kwaliteit van leven bij hartpatiënten die zelf geheugenproblemen of depressieve klachten vermeldden was beduidend minder dan bij patiënten die dit niet deden. Een hoger inkomen en een hoge opleiding leken een gunstig effect te hebben op de kwaliteit van leven.

Samenvattend werden belangrijke verschillen in kwaliteit van leven aangetoond tussen patiënten die een hartinfarct hebben doorgemaakt en een controle-groep die vergelijkbaar was in leeftijd en geslacht. Gedeeltelijk werd dit verklaard door klachten toe te schrijven aan hart- en vaatziekten. De invloed van geheugenklachten en depressieve klachten, zoals die door de patiënten zelf beleefd worden zijn echter nog groter. Tevens blijken sociale factoren van belang te zijn.

In *hoofdstuk 6* wordt een onderzoek beschreven bij patiënten die een herseninfarct hadden doorgemaakt. Voor dit onderzoek werden 266 patiënten geselecteerd die 6 tot 24 maanden eerder een herseninfarct hadden doorgemaakt en die opgenomen waren in de zgn. Rotterdamse Stroke Databank. Ten tijde van het onderzoek waren nog 192 patiënten in leven, van wie 123 (67%) deelnamen. De kwaliteit van leven, zoals gemeten met behulp van SIP, NHP, HAD en de Barthel ADL index was op bijna alle gebieden minder groot bij de patiënten met een herseninfarct in vergelijking met de controle-groep. Ook bij herseninfarctpatiënten was de invloed van leeftijd minder groot dan bij controles. Verschillen tussen mannen en vrouwen waren niet aantoonbaar. Naarmate het herseninfarct langer geleden was leek de kwaliteit van leven te verslechteren. De SIP leek het meest gevoelig om deze verandering waar te nemen.

Binnen de groep van patiënten werd er geen duidelijk verschil in kwaliteit van leven gevonden bij personen met en zonder aantoonbare lesies bij computertomografie van de hersenen, of lesies in de linker of rechter hersenhelft. Opleiding leek geen duidelijke invloed te hebben. Bij patiënten met een partner werd een betere kwaliteit van leven gevonden dan bij patiënten die alleen woonden.

Samenvattend werden verschillen aangetoond in kwaliteit van leven tussen patiënten met en een controle-groep. Verschillen in kwaliteit van leven konden niet verklaard worden door de plaats van het herseninfarct of door het aantal aangetoonde lesies. Opnieuw bleken sociale factoren zoals gehuwde staat een modificerende rol te spelen.

Concluderend blijken de SIP en de NHP bruikbare en reproduceerbare instrumenten voor het meten van kwaliteit van leven bij Nederlandse patiënten die een hartinfarct of een herseninfarct hebben doorgemaakt. In vergelijking met een controle-groep bestaan belangrijke verschillen in kwaliteit van leven bij patiënten die een hartinfarct of een herseninfarct hebben doorgemaakt. Het bestaan van lichamelijke klachten vormde slechts een gedeeltelijke verklaring voor het bestaan van verschillen in kwaliteit van leven. Bij hartpatiënten had in het bijzonder het bestaan van geheugenklachten en depressiviteit een grote invloed. Sociale factoren bleken uitermate belangrijk. De SIP leek het meest gevoelig om verandering over tijd te meten. De resultaten van dit onderzoek bevestigen het belang van het meten van kwaliteit van leven bij onderzoek bij patiënten met een hartinfarct of herseninfarct.

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Curriculum Vitae

Marie Christine Visser was born on February 10, 1962 in Vlaardingen, The Netherlands. She graduated in 1980 at the 'Scholengemeenschap Spieringshoek' (secondary school) in Schiedam. Subsequently, she studied Biology at the State University in Utrecht for two years. In 1982 she started her medical training at the same university. As part of her medical training she studied factors determining rise of blood pressure in children (Department of Epidemiology & Biostatistics of the Erasmus University Rotterdam, supervision A. Hofman and D.E. Grobbee). She was a member of the Faculty board and participated for several years in the Faculty Educational Committee (Head Prof.dr. A Struyvenberg). She was a student member of the faculty board of the Dutch Association for Medical Education (Head Prof.dr L.N. Bouman). In 1990 she obtained her medical degree and started working as a junior doctor in the department of Neurology at the University Hospital Utrecht. From 1991 to 1994 she worked as a research associate at the department of Epidemiology & Biostatistics of the Erasmus University Rotterdam (head: prof. dr. A. Hofman) and the department of Neurology of the University Hospital Utrecht (head Prof.dr. J. van Gijn). She was supported by a grant of the Netherlands Heart Foundation. During this period she collaborated in the Rotterdam Study and received training as an epidemiologist. From September 1991 to December 1991 she worked at the Epidemiology Research Unit of the department of Geriatrics of the Royal Postgraduate Medical School in London, supervised by Prof C. Bulpitt and Dr A.E. Fletcher. In March 1994 she started her training as a neurologist at the University Hospital Utrecht.