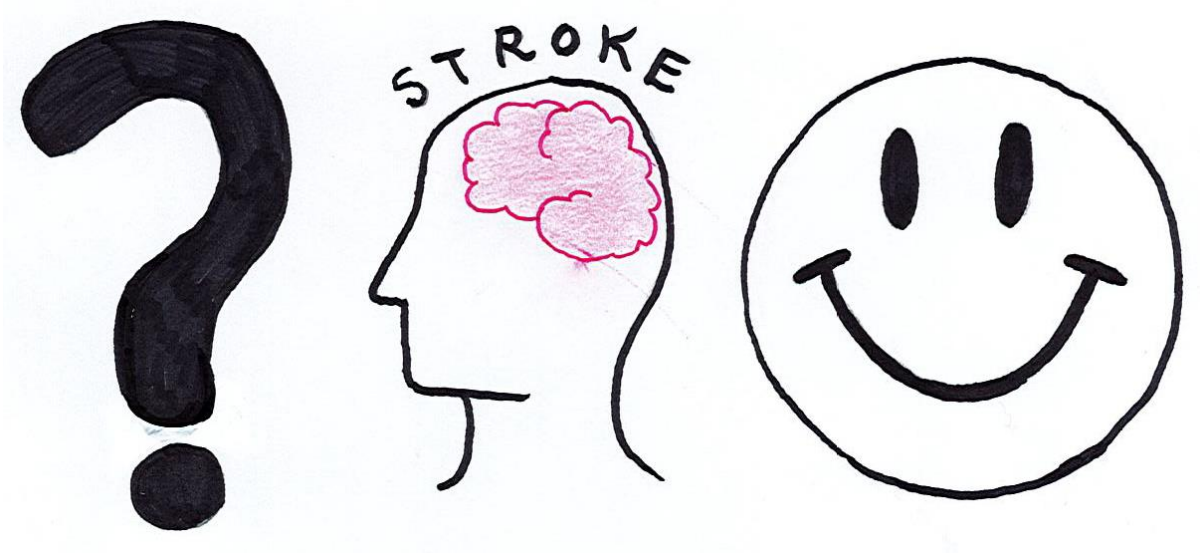
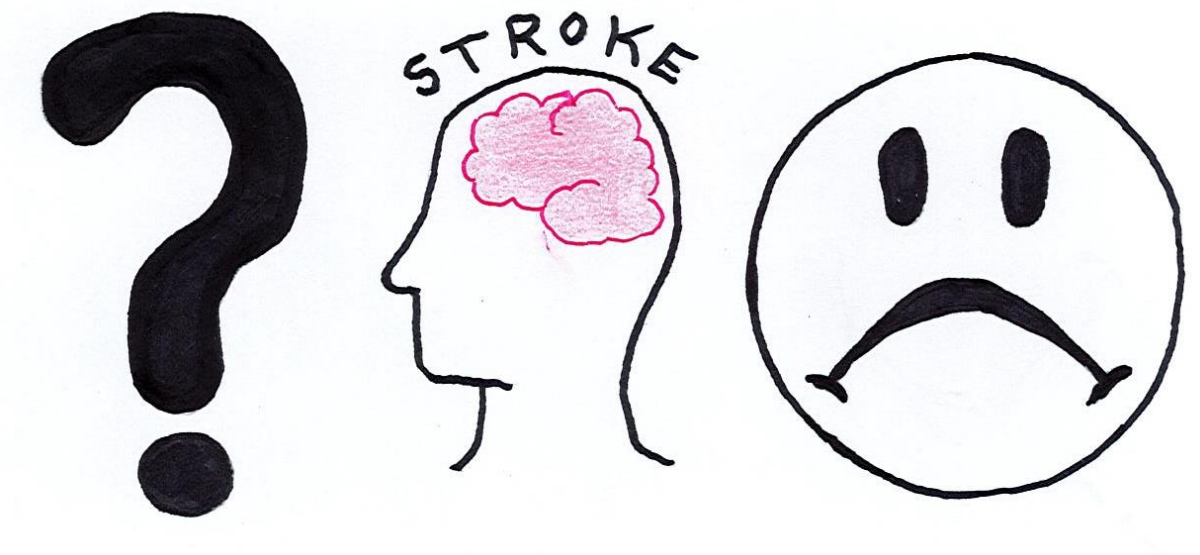


Health-Related Quality of Life Three Months After Stroke



Degree Project in Medicine

Lisa Söderblom

Programme in Medicine

UNIVERSITY OF GOTHENBURG

THE SAHLGRENSKA ACADEMY

Health-Related Quality of Life Three Months After Stroke

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Gothenburg, Sweden 2018

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Abbreviations

B - B coefficient

Barthel index - a measure of performance in activities of daily living

CI - confidence interval

EQ VAS - EuroQoL visual analogue scale, a measure of perceived general health

EQ5D - EuroQoL 5 Dimensions, a measure of health-related quality of life

EQ5D3L - EuroQoL 5 Dimensions 3 Levels, a measure of health-related quality of life

EQ5D5L - EuroQoL 5 Dimensions 5 Levels, a measure of health-related quality of life

HRQoL - health-related quality of life

MOCA - Montreal Cognitive Assessment, a measure of cognitive function

mRS - modified Rankin Scale, a measure of disability

n - number of patients

NIHSS - National Institutes of Health Stroke Scale, a measure of stroke severity

OR - odds ratio

QoL - quality of life

SD - standard deviation

SPSS - Statistical Package for the Social Sciences

TIA - transient ischemic attack

WHO - World Health Organization

Abstract

Degree project. Programme in medicine. *Health-Related Quality of Life Three Months After Stroke*. Lisa Söderblom. 2018. Institute of Neuroscience and Physiology, Department of Clinical Neuroscience. Gothenburg. Sweden.

Introduction and Background

Stroke is a common and severe disorder with several possible sequelae and with significant impact on the single individual and on the whole society. Health-related quality of life (HRQoL), is an important aspect of stroke outcome. Knowledge of HRQoL enables patient-centred health care with satisfactory quality. Previously, large variations in HRQoL after stroke between European countries have been presented.

Aims

To examine HRQoL after stroke, using the EuroQoL 5 Dimensions 5 Levels (EQ5D5L) questionnaire, including the EuroQoL visual analogue scale (EQ VAS), in survivors three months after an acute stroke cared for at the stroke units at the Sahlgrenska University Hospital. Additionally, to identify factors at acute stroke that are associated with poor HRQoL after stroke.

Methods

Data was obtained from Väststroke, a local quality register for stroke. In the study, 3 495 consecutive patients with acute stroke, admitted to stroke units at the Sahlgrenska University Hospital, were included. Multivariate analyses of factors associated with EQ5D5L index and EQ VAS were performed.

Results

Mean EQ5D5L index was 0.68 (95% confidence interval, CI: 0.66 - 0.69). Mean EQ VAS was 63.8 (95% CI: 62.7 - 64.9). Increased age, female sex, low physical activity before stroke and increased stroke severity were predictors of poor EQ5D5L index. Anxiety/depression showed the strongest correlation with the EQ VAS, followed by everyday activities ability, pain/discomfort, mobility and self-care ability.

Conclusions and Implications

Survivors after stroke reported poorer mean EQ5D5L index and EQ VAS compared to normative data. The identified risk groups may represent possible target groups for intervention in order to improve HRQoL after stroke. Moreover, some of the identified associated factors are modifiable, pointing to potential targets for intervention.

Keywords

Stroke, Quality of Life, Patient Outcome Assessment, Risk Factors and Surveys and Questionnaires.

Background

Introduction

Stroke is a common and severe disorder with several possible sequelae and with significant impact on the single individual and on the whole society. Health-related quality of life, HRQoL, is an important aspect of stroke outcome. Knowledge of HRQoL enables patient-centred health care with satisfactory quality. This study will examine HRQoL after stroke and which factors predict HRQoL after stroke.

Stroke

Stroke is the common name for three cerebrovascular disorders: brain infarction, intracerebral haemorrhage and subarachnoid haemorrhage (1). According to the World Health Organization, WHO: *"A stroke is caused by the interruption of the blood supply to the brain, usually because a blood vessel bursts or is blocked by a clot. This cuts off the supply of oxygen and nutrients, causing damage to the brain tissue."* (2).

In Sweden, the incidence of first-ever stroke is 200-300 per 100 000 per year (1) and the prevalence of surviving patients in Sweden that have been hospitalized with ischemic stroke is 1 990 per 100 000 (3). Stroke incidence increases with age (1). Amongst younger and middle-aged people, stroke is more common in males (4). Amongst the elderly, stroke is more common in females (4). Mean age at stroke onset is 73 years in males and 77 years in females (1). Additionally, the risk of stroke depends on the occurrence of atrial fibrillation, hypertension and diabetes, smoking habits, alcohol use, physical activity, blood lipids and diet (1).

Consequences of stroke are major. Amongst adults, stroke is the third most common cause of death (1, 5). Additionally, it is the most common cause of acquired neurologic disability in Sweden (1). Paresis (1, 6) is the most obvious stroke sequelae (1). Additional long time sequelae of stroke include aphasia (1, 7), epilepsy (8), swallowing disorders (9, 10), aspiration (9) and spasticity (1, 11). Depression after stroke (1, 12, 13) occurs in more than a third of the patients (1). Cognitive impairment is also common (1, 14), with more than a fourth of patients developing severe cognitive failure or dementia, beyond mild cognitive impairment (1). Fatigue after stroke (13, 15, 16) has been shown to occur in 53% of patients (16), and pain (11, 13, 16) in 48 % of patients (13). Additionally, comorbidity in stroke patients is common (17), explained partly by old age (18). Common comorbidity includes dementia (19), cardiovascular diseases, heart failure and diabetes (20). Health care requirements due to stroke are major, requiring considerable resources from the health care. For example, stroke is the most hospital day requiring somatic disease in Sweden (1, 5) and the social cost of stroke is estimated to 14 billion per year (1).

Health-Related Quality of Life

There are several definitions of quality of life, QoL (21). The WHO defines it as *"an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns"* (22). Felce et al (1995) describe QoL as comprising of "*five dimensions: physical wellbeing, material wellbeing, social wellbeing, emotional wellbeing, and development and activity*" (21). Health is defined by the Constitution of the WHO as *"A state of complete physical, mental, and social well-being not merely the absence of disease . . ."* (22).

Likely, disease has influence on QoL. However, the correlation between symptoms and perceived QoL is not absolute. Patients with severe disease do not necessarily report poor

QoL (23). Likely, QoL depends on the combination of personal attributes, cognitive mechanisms and social environment (23).

Although QoL depends on several aspects, the health care´s task is to focus on the health-related aspects. HRQoL is a major objective in health care efforts (23). Whereas health care personnel may focus on objective measures in evaluating treatment outcome, HRQoL outcome may be a measure more relevant in the patients´ perspectives (23). In chronic diseases, perhaps the HRQoL aspect is even more important than in acute conditions, since the cure of the disease is not in question (23). HRQoL is clearly an important aspect of medicine, and knowledge about HRQoL is sought in research where HRQoL is used as an outcome measurement (24).

HRQoL measures are either general or disease-specific (23, 24). General measures cover several aspects of HRQoL relevant to the general population. (23). Disease-specific measures cover specific aspects of the disease in question, and are well suited for detecting changes within patient groups or individuals (23).

In some HRQoL measures, including the EQ5D (EuroQoL 5 Dimensions), HRQoL worse than death exists (25). This state of being cannot be reliably identified, but still exists in the measures, since people apparently identify states of being as worse than death in the making of the measures (23).

The EQ5D Instrument

The EQ5D instrument is considered a general measure (23) of health state and HRQoL (26). The instrument evaluates mobility, self-care ability, everyday activities ability, pain/discomfort and anxiety/depression, in addition to general health (27). In the first five questions, patients tick a box, grading their problems between 1-5 (27). These answers can be

converted into index values, which are based on the general population´s perception of the possible health states (24). The individuals´ own perception of general health is evaluated by marking an X on a scale between 0 and 100, named EQ VAS (EuroQoL visual analogue scale) (27).

Previous Studies on Stroke and Quality of Life

Validity of EQ5D5L

Validity of the EQ5D5L (EuroQoL 5 Dimensions 5 Levels) in stroke has been supported in comparison to the earlier EQ5D version, EQ5D3L (EuroQoL 5 Dimensions 3 Levels). The EQ5D5L has fewer missing values, better discriminatory power and less of a ceiling effect (28). Additionally, the EQ5D5L index has proven to correlate well with the EQ VAS, and objective scales measuring disability and neurological deficits after stroke such as the mRS (modified Rankin Scale, a measure of disability) (28), the Barthel Index (a measure of performance in activities of daily living) (28, 29) and the NIHSS (National Institutes of Health Stroke Scale) score (a measure of stroke severity) (29).

Normative Data

Normative EQ5D index and EQ VAS for the general population of several countries have been reported. Swedish, Danish, Spanish and Polish normative data are presented in table 1 (30-32). For the index, -0.624 is the poorest and 1 is the highest possible HRQoL. In the EQ VAS, 0 is the poorest and 100 is the best possible general health. As shown in table 1, the EQ5D index differ somewhat between countries and both the EQ5D index and the EQ VAS tend to decrease with age.

Table 1. *EQ5D3L and EQ5D5L index and mean EQ VAS normative data from different countries in different age groups*

	18-24 y	25-34 y	35-44 y	45-54 y	55-64 y	65-74 y	75+ y	Total
Sweden, EQ5D3L[a] (30)	0.888	0.893	0.868	0.835	0.813	0.836	0.701	0.851
Denmark, EQ5D3L[a] (30)	0.914	0.914	0.881	0.861	0.845	0.818	0.753	0.866
Spain, EQ5D3L[a] (30)	0.968	0.963	0.939	0.911	0.884	0.870	0.773	0.915
Spain, EQ5D5L[a] (32)								0.897
Poland, EQ5D5L[a] (31)	0.963	0.953	0.938	0.898	0.856	0.813	0.723	0.888
Sweden, EQ VAS[b] (30)	81.7	81.5	80.7	79.2	78.1	75.9	68.5	78.7

Abbreviations: y = years, EQ5D3L = EuroQoL 5 Dimensions 3 Levels, EQ5D5L = EuroQoL 5 Dimensions 5 Levels, EQ VAS = EuroQoL visual analogue scale. [a] For the EQ5D3L and EQ5D5L index, -0.624 is the poorest and 1 is the highest possible HRQoL. [b] For the EQ VAS, 0 is the poorest and 100 is the best possible health.

EQ5D Index

There are no published studies exploring HRQoL after stroke as measured by EQ5D5L in unselected stroke populations. However, there are five population-based studies and one cross-sectional study using the EQ5D3L.

The first study, exploring EQ5D3L index three months and six months after stroke in France, Lithuania, Great Britain, Poland and Italy, presents large variations between the European countries (33). Exact EQ5D3L index values are not given, but means vary between approximately 0.55 and 0.75 (33). Mean EQ5D3L index values reported by four other studies are presented in table 2 (13, 25, 34, 35). These four studies are hospital-based or population-based, and the patients are unselected (13, 25, 34, 35). In a cross-sectional Korean study, mean EQ5D3L index is 0.67 in patients who previously (not specified when) have suffered from stroke, compared to 0.87 in controls (36). Additionally, EQ5D3L index at three months

Table 2. *Mean EQ5D3L index values* [a]

	1 mo	2 mo	6 mo	12 mo	24 mo	66 mo
Norway (13)			0.70 [b]			
Great Britain (25)	0.64		0.70	0.70	0.66	0.68
The Netherlands (34)		0.73	0.74	0.74		
Korea (35)			0.82, 0.83 [c]			

Abbreviations: EQ5D3L = EuroQoL 5 Dimensions 3 Levels, mo = month/months. [a] *For the EQ5D3L index, -0.624 is the poorest and 1 is the highest possible HRQoL.* [b] *The Norwegian study only include ischemic stroke patients. Median EQ5D3L index is 0.74.* [c] *In the Korean study, index in ischemic stroke patients is 0.82 and in haemorrhagic stroke patients 0.83.*

after stroke has been found as a predictor of one-year survival (33), indicating the importance and relevance of HRQoL as a measure of prognosis.

EQ VAS

The EQ VAS is barely used in studies of HRQoL after stroke. The only study using the EQ VAS is a hospital-based Norwegian study which presents 70 as median EQ VAS and 66 as mean EQ VAS, six months after stroke (13).

Predictors of Health-Related Quality of Life

Previous studies using the EQ5D3L have suggested some predictors for poor HRQoL: female sex (25, 34), increased age (13, 25, 34, 35), education level, unmarried status, living alone (25), smoking, prior depression (13), event severity, recurrent strokes (25), number of stroke deficits (hemiplegia in particular) (36), functional level at discharge (13, 35), duration of hospitalization (35) and not being sent home after discharge (34).

A previous study using the EQ VAS has suggested some predictors for poor general health: increased age, prior depression, Barthel index seven days after stroke and smoking (13). Suggested factors at follow-up which correlate with poor EQ VAS are anxiety/depression, fatigue and Barthel Index (13).

Taken together, with an aging population and a well-advanced healthcare, more patients are expected to live with the effects of stroke, creating a major health concern (1). An important purpose of stroke care is to improve health and HRQoL in people affected by stroke (37). Despite this, studies of outcomes following stroke measuring the patient's own perception of their HRQoL are still scarce. Given the limited literature on HRQoL following stroke, especially with respect to large unselected, up-to-date stroke populations, further studies are needed to identify groups at risk for poor HRQoL, and to search for possible modifiable factors associated with HRQoL after stroke. EQ5D assessment in Swedish stroke patients has not been reported at all, leaving the Swedish health care without this knowledge of HRQoL.

Aims

The aim of this study is to examine HRQoL in survivors three months after hospital discharge in a large contemporary unselected population treated at a stroke unit for an acute stroke in Sweden. Specifically, we will:

A) describe the HRQoL according to the EQ5D5L index and the EQ VAS, three months after stroke and compare with normative data and previous studies of stroke from other countries
B) identify factors at acute stroke that are predictive of a poor outcome with respect to HRQoL as measured by the EQ5D5L index
C) investigate the relation between HRQoL as measured by the EQ5D5L index and the EQ VAS after stroke and determine to what extent the pre-specified items in the EQ5D5L are associated with the subjective perception of general health after stroke, as measured by the EQ VAS

Material and Methods

Design of the Study

In figure 1, the time relationships between the examination of HRQoL and perceived general health and the predictors in research question B) and the determinants in research question C) are explained.

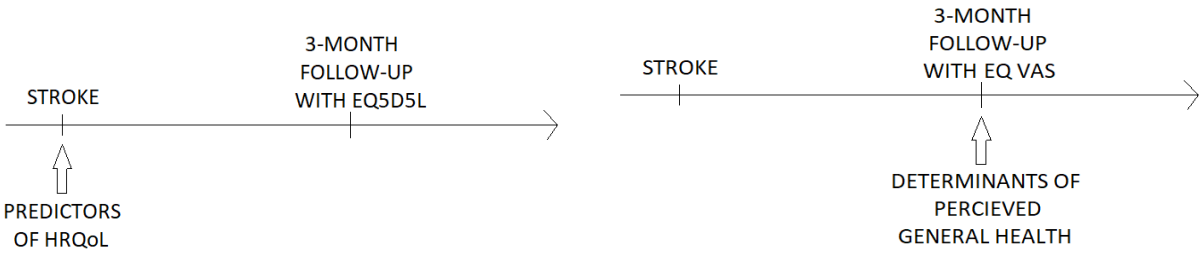

Figure 1. *The Time Relationships between Follow-Up with Health-Related Quality of Life and Perceived General Health and Investigated Variables*

Abbreviations: HRQoL = Health-Related Quality of Life, EQ5D5L = EuroQoL 5 Dimensions 5 Levels, EQ VAS = EuroQoL visual analogue scale. EQ5D5L measures quality of life and EQ VAS measures general health. The timeline to the left refers to research question B) and the timeline to the right refers to research question C).

Study Population

Data for the study was obtained from the Väststroke registry (38), which is a local quality register for stroke care in the Swedish region Västra Götaland. All patients treated for stroke or TIA (transient ischemic attack) at the stroke units at the Sahlgrenska University Hospital are entered into the registry since April 2012. The registry also comprises all stroke and TIA patients who received prehospital care in the region of Västra Götaland between 2013 and 2015. To date, the registry contains 17 134 unique episodes for care.

The Väststroke registry complements the national quality registry Riksstroke with variables not included in Riksstroke. These variables cover the prehospital chain of care and aspects of nursing, physiotherapy, occupational therapy and speech therapy during the acute care at the

stroke unit. The Väststroke register also comprises a follow-up, three to six months after stroke, when recurrent vascular events, medication and HRQoL are registered.

Inclusion criteria for the study were acute stroke, admission to a stroke unit at the Sahlgrenska University Hospital between October 1, 2014 and February 28, 2017. Consequently, patients with TIA and patients who were treated at any other hospitals in the region of Västra Götaland during the hospitalization were excluded. Additionally, two patients with obvious incorrect data were excluded. Of the 17 134 patients in the Väststroke registry, 3 495 patients fulfilled the inclusion criteria.

Clinical Variables

Clinical variables obtained from the Väststroke registry were date of hospitalization, year of birth, sex, postal code, physical activity before stroke, diagnosis, stroke severity (as measured by NIHSS), cognitive function at discharge (as measured by MOCA, Montreal Cognitive Assessment), independence walking ten meters at discharge, independence in personal care at discharge, degree of disability (as measured by mRS, modified Rankin Scale) at follow-up and recurrent strokes.

Data regarding socioeconomic status was collected from a previous master thesis by Amanda Niklasson (2017) (39). In that thesis, Niklasson analysed the stroke patients of the Väststroke registry with respect to socioeconomic status (39). Socioeconomic status was estimated by mean salary and mean education level of people in the different post code areas of Gothenburg (39). Analyses resulted in the dividing of patients into three groups (1, 2 and 3), with 1 as the lowest socioeconomic status and 3 as the highest socioeconomic status (39). Here the same socioeconomic index, based on the individual patient´s residence post code, was applied.

Outcome Variables, EQ5D5L and EQ VAS

The EQ5D5L and EQ VAS questionnaires were posted three months after stroke onset. The patients were instructed that the questionnaires were to be filled in by the patients themselves, not by care personnel or by relatives. If the responses were not returned within a month, a nurse tried to contact the patients by telephone during the coming months, at average two to four times. If the questionnaires were not returned within six months, the attempts of contacting the patients ended.

The five answers to the EQ5D5L questions were transformed into an index using a calculation programme in Excel. Each unique combination of EQ5D5L answers was assigned an index value between -0.624 and 1, with -0.624 as poorest possible HRQoL, 0 as HRQoL equal to being dead and 1 as highest possible HRQoL. Currently, there is no EQ5D5L calculation programme based on the Swedish population. Instead, a Danish version was used.

Data Analysis

Excel files from the Väststroke registry and an IBM SPSS (Statistical Package for the Social Sciences) STATISTICS 25 file from Niklasson (2017) (39) were merged into a single SPSS file. This file was organized based on episode of care at the hospital.

Management of Incomplete and Incorrect Data in the Baseline Population

Follow-up date did not always occur precisely at three months after enrolment at hospital. In this study, only those patients with follow-up between 2.5 and six months were considered having had a follow-up and were included in the analyses.

In the Väststroke registry, only mRS between 0 and 5 were stated. Patients who died within six months from enrolment without follow-up, were assigned mRS 6, which equals status at death.

In the Väststroke registry, a few patients had answered some, but not all parts of the MOCA assessment. Patients with incomplete answers were considered not to have answered the MOCA assessment.

In the electronical file for the EQ5D5L and EQ VAS questionnaire, “50” is pre-set in advance. In order to inform whether this response represented a true answer or not, the registering nurse must tick in a box if the EQ VAS was not answered by the patient. Consequently, answers where the nurse had ticked the box were excluded, regardless of whether the EQ VAS answers were “50” or otherwise. However, despite this, a quality check of the data revealed an unreasonable high number of “50” as EQ VAS answer. Therefore, patients who did not have any registered answer for any of the EQ5D5L questions were also considered not having answered the EQ VAS, regardless of whether the EQ VAS answers were “50” or otherwise.

Finally, one patient responded an invalid answer to the EQ VAS, specifically “550”. This patient was considered as having answered the EQ VAS, but was excluded from the statistical analyses of EQ VAS.

Statistics

All analyses were performed in IBM SPSS STATISTICS 25.

Comparison of Patients Answering EQ5D5L with Patients Not Answering EQ5D5L

When comparing patients who answered the EQ5D5L with patients who did not, p-values were calculated with Chi2 tests for categorical variables, Mann Whitney tests for non-parametric continuous variables and t-tests for normal distributed continuous data.

EQ5D5L Index

Mean and median EQ5D5L index were calculated.

Predictors of EQ5D5L Index

The variables studied as HRQoL predictors were age, sex, socioeconomic status, physical activity before stroke, stroke severity as measured by NIHSS score, independence walking ten meters at discharge and independence in personal care at discharge. These variables were chosen based on the variables that were used in previous studies and which variables that were available in the Väststroke registry. Physical activity before stroke was included in this study since it has proven to correlate to several aspects of health in previous studies. (40-44) Cognitive function, as measured by MOCA score, was not included due to substantial proportion of non-responders.

A univariate analysis of each possible predictor was performed. Mann Whitney tests were used when the variables were divided into two ordered groups, while Jonckheere-Terpstra tests were used when the variables were divided into more than two ordered groups. Variables with p-value < 0.1 were then included in a binary logistic regression multivariate analysis. However, variables concerning functionality at discharge were not included in this analysis, since they were assumed to interact with other variables, such as age, physical activity before stroke and stroke severity. In the multivariate analysis, the EQ5D5L index was dichotomized at the median, with those above the median considered as having “high” HRQoL and those below as having “poor” HRQoL. Bonferroni correction was performed to compensate for the

number of analyses. Consequently, the required p-value for statistical significance in the multivariate analysis was < 0.0083.

EQ VAS

Mean and median EQ VAS were calculated.

Correlation between EQ5D5L and EQ VAS

The correlation between the EQ5D5L index and the EQ VAS was evaluated by Spearman correlation. Then a univariate linear regression analysis was performed with each EQ5D5L question and the EQ VAS. Questions with p-value < 0.1 were included in a multivariate linear regression analysis. Bonferroni correction was performed to compensate for the number of analyses. Consequently, the required p-value for statistical significance in the multivariate analysis was < 0.01.

Ethics

The study has not been reviewed by any ethical board. The Väststroke registry data was collected and stored for quality assessment of stroke care (38). The present analysis of the registry data is partly defined as quality assessment of the health care. In addition, this is a student project, for which the approval by an ethical board is not regulated by the law (45).

Despite this, it is important to be aware that data analysis of the collected data may interfere with the patients' integrity as the patients have not actively been asked for their informed consent of the use of data for the present study. However, if patients express a reluctance to participate in quality registries, their wishes are obeyed. Also, the collected data is coded and presented anonymously so the patients´ privacy will be preserved. Therefore, it is not possible to recognize the patients' identities. This means that it is not possible to contact any participants reporting very poor HRQoL to offer assistance.

Results

A flowchart of the study population is presented in figure 2. Patients with acute stroke and admission to a stroke unit at the Sahlgrenska University Hospital between October 1, 2014 and February 28, 2017 were included in the baseline population. Baseline characteristics of the study population are presented in table 3.

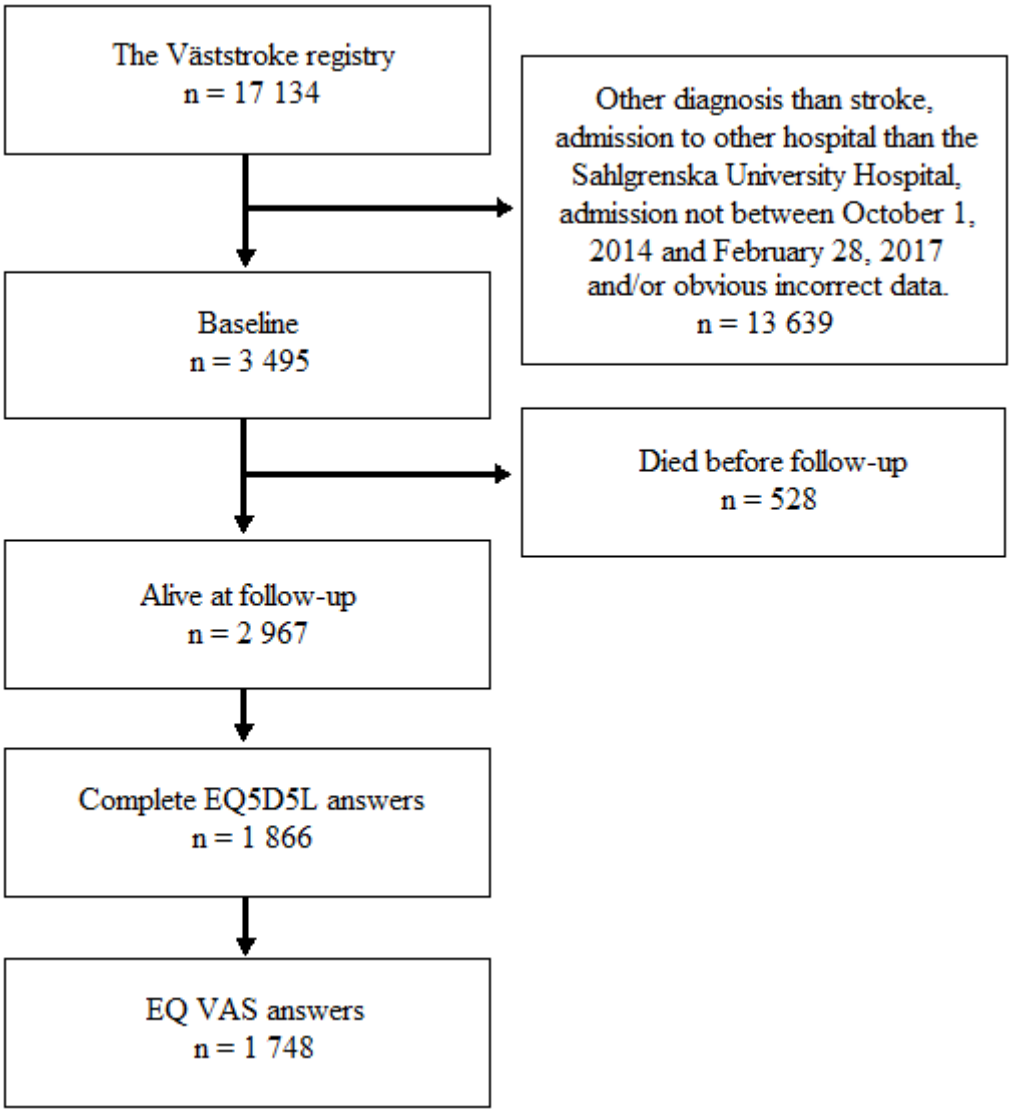

Figure 2. *Flowchart of the study population*

Abbreviations: n = number of patients, EQ5D5L = EuroQoL 5 Dimensions 5 Levels, EQ VAS = EuroQoL visual analogue scale. EQ5D5L measures quality of life and EQ VAS measures general health.

Table 3. *Baseline characteristics of the study population*

	n = 3 495
Age, years, mean (SD)	74.5 (13.9)
Males, n (%)	1 851 (53.0)
Females, n (%)	1 644 (47.0)
Socioeconomic status	n = 2 943 [a]
Socioeconomic status, median (IQR)	2 (1)
1, Low, n (%)	1 167 (39.7)
2, Middle, n (%)	1 061 (36.1)
3, High, n (%)	715 (24.3)
Physical activity before stroke	n = 2 674
Physical activity, median, (IQR)	1 (1)
1, Mostly sedentary leisure time, n (%)	1 539 (57.6)
2, Easy to moderate activity at least four times/week, n (%)	988 (36.9)
3, Heavier activity two-three hours/week, n (%)	143 (5.3)
4, Hard training or competitive sport, n (%)	4 (0.1)
Stroke type	
Ischemic, n (%)	3 085 (88.3)
Intracerebral haemorrhage, n (%)	401 (11.5)
Unknown ischemic or haemorrhagic, n (%)	9 (0.3)
Stroke severity at admission	n = 2 310
NIHSS score median (IQR)	2 (5)
Minor stroke (NIHSS score 0-3), n (%)	1 472 (63.7)
Moderate stroke (NIHSS score 4-10), n (%)	534 (23.1)
Severe stroke (NIHSS score >10), n (%)	304 (13.2)
Cognitive function at discharge [b]	n = 1 342
MOCA score median (IQR)	25 (6)
MOCA score 0-25, n (%)	630 (46.9)
MOCA score 26-30, n (%)	439 (32.7)
MOCA not performed due to severe cognitive impairment or dementia, n (%)	273 (20.3)
Independence walking ten meters at discharge	n = 2 655
Yes, n (%)	1 772 (66.7)
No, n (%)	883 (33.3)
Independence in personal care at discharge	n = 2 391
Yes, n (%)	1 291 (54.0)
No, n (%)	1 100 (46.0)
Recurrent stroke before follow-up	n = 2 197
Yes, n (%)	68 (3.1)
No, n (%)	2 129 (96.9)
Degree of disability at follow-up [c]	n = 2 108
mRS, median (IQR)	3 (5)
0, n (%)	309 (14.7)
1, n (%)	353 (16.7)
2, n (%)	310 (14.7)
3, n (%)	303 (14.4)
4, n (%)	178 (8.4)
5, n (%)	127 (6.0)
6, n (%)	528 (25.0)

Abbreviations: n = number of patients, SD = standard deviation, IQR = interquartile range, NIHSS = National Institutes of Health Stroke Scale, MOCA = Montreal Cognitive Assessment, mRS = modified Rankin Scale. [a] *Only patients living in the Gothenburg area were assigned a socioeconomic index in Niklasson´s thesis paper (39). The large non-response is explained by patients living in other areas.* [b] *Increasing MOCA score stands for increasing cognitive function.* [c] *Increasing mRS stands for increasing disability.*

Of the 2967 survivors, 63 % returned a complete answer to the EQ5D5L questions, and 59 % returned an EQ VAS answer. A comparison of the surviving patients who answered all

Table 4. *Comparison of patients who answered all 5 EQ5D5L [a] questions with patients who did not. Only living patients included.*

	Answered all 5 EQ5D5L questions n = 1 866	**Not answered all 5 EQ5D5L questions n = 1 101**	**Statistical significance, p-value**
Age, years, mean (SD)	73.7 (13.3)	71.7 (14.9)	< 0.001
Sex			0.270
Males, n (%)	1 000 (53.6)	613 (55.7)	
Females, n (%)	866 (46.4)	488 (44.3)	
Socioeconomic status	n = 1 715	n = 767	0.057
1, Low, n (%)	652 (38.0)	334 (43.5)	
2, Middle, n (%)	641 (37.4)	248 (32.3)	
3, High, n (%)	422 (24.6)	185 (24.1)	
Physical activity before stroke	n = 1 649	n = 795	< 0.001
Physical activity, median, (IQR)	1 (1)	1 (1)	
1, Mostly sedentary leisure time, n (%)	847 (51.4)	497 (62.5)	
2, Easy to moderate activity at least four times/ week, n (%)	692 (42.0)	262 (33.0)	
3, Heavier activity two-three hours/week, n (%)	108 (6.5)	34 (4.3)	
4, Hard training or competitive sport, n (%)	2 (0.1)	2 (0.3)	
Stroke type			< 0.001
Ischemic, n (%)	1 711 (91.7)	959 (87.1)	
Intracerebral haemorrhage, n (%)	153 (8.2)	138 (12.5)	
Unknown ischemic or haemorrhagic, n (%)	2 (0.1)	4 (0.4)	
Stroke severity at admission	n = 1 451	n = 664	< 0.001
NIHSS score median (IQR)	1 (5)	3 (6)	
Minor stroke (NIHSS score 0-3), n (%)	1 065 (73.4)	361 (54.4)	
Moderate stroke (NIHSS score 4-10), n (%)	285 (19.6)	185 (27.9)	
Severe stroke (NIHSS score >10), n (%)	101 (7.0)	118 (17.8)	
Cognitive function at discharge [b]	n = 932	n = 324	< 0.001
MOCA score median (IQR)	25 (5)	24 (7)	
MOCA score 0-25, n (%)	469 (50.3)	145 (44.8)	
MOCA score 26-30, n (%)	366 (39.3)	69 (21.3)	
MOCA not performed due to severe cognitive impairment or dementia, n (%)	97 (10.4)	110 (34.0)	
Independence walking ten meters at discharge	n = 1 593	n = 842	< 0.001
Yes, n (%)	1 272 (79.8)	457 (54.3)	
No, n (%)	321 (20.2)	385 (45.7)	
Independence in personal care at discharge	n = 1 460	n = 727	< 0.001
Yes, n (%)	961 (65.8)	305 (42.0)	
No, n (%)	499 (34.2)	422 (58.0)	
Recurrent stroke before follow-up	n = 1 695	n = 497	0.029
Yes, n (%)	43 (2.5)	22 (4.4)	
No, n (%)	1 652 (97.5)	475 (95.6)	
Degree of disability at follow-up [c]	n = 1 228	n = 352	< 0.001
mRS, median (IQR)	2 (2)	3 (2)	
0, n (%)	273 (22.2)	36 (10.2)	
1, n (%)	302 (24.6)	51 (14.5)	
2, n (%)	266 (21.7)	44 (12.5)	
3, n (%)	213 (17.3)	90 (25.6)	
4, n (%)	114 (9.3)	64 (18.2)	
5, n (%)	*60 (4.9)*	*67 (19.0)*	

Abbreviations: EQ5D5L = EuroQoL 5 Dimensions 5 Levels, n = number of patients, SD = standard deviation, IQR = interquartile range, NIHSS = National Institutes of Health Stroke Scale, MOCA = Montreal Cognitive Assessment, mRS = modified Rankin Scale. [a] EQ5D5L measures quality of life. [b] Increasing MOCA score stands for increasing cognitive function. [c] Increasing mRS stands for increasing disability.

five EQ5D5L questions with those who did not is presented in table 4. Patients who answered the EQ5D5L were older, more physically active before stroke, more likely to had had a less severe stroke, less cognitive dysfunction at discharge, more independent in walking and personal care at discharge, less likely to had had a recurrent stroke and less disabled at follow-up.

EQ5D5L Index

Mean EQ5D5L index was 0.68 (95% confidence interval (CI): 0.66 - 0.69, standard deviation (SD): 0.28). Median EQ5D5L index was 0.74 (IQR: 0.26). See box plot in figure 3.

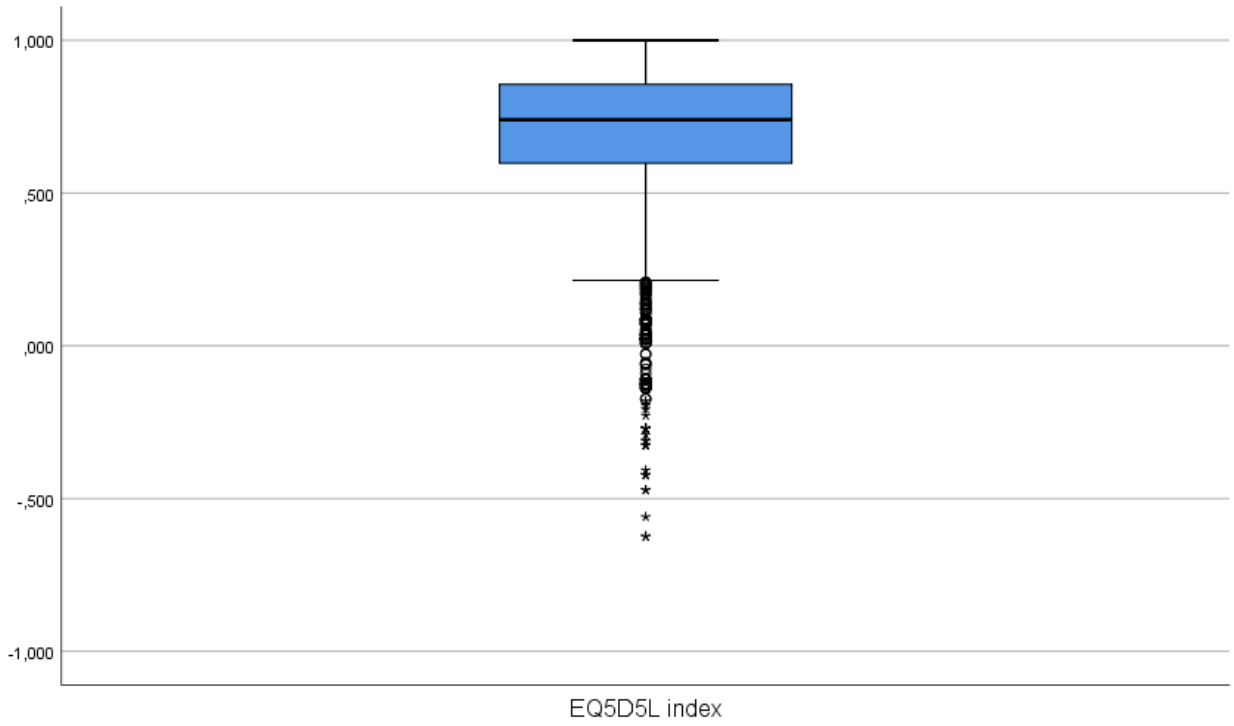

Figure 3. *Distribution of the EQ5D5L index[a] in the whole study population*

Abbreviations: EQ5D5L = EuroQoL 5 Dimensions 5 Levels. The figure presents the median EQ5D5L index as the line in the box, the box represents the interquartile ratio, the whiskers represent the highest and lowest values that are not deviating, circles and asterisks represent outliers and extreme values. [a] For the EQ5D5L index, -0.624 is the poorest and 1 is the highest possible HRQoL.

Predictors of EQ5D5L Index

Associations between the EQ5D5L index and the clinical variables registered at acute stroke are given in table 5. All the investigated clinical variables showed association to the EQ5D5L with a p-value < 0.1, and could therefore be included in the multivariate analysis.

Table 5. *Associations between clinical variables at acute stroke and the EQ5D5L index*

	Median EQ5D5L index [a]	**IQR**	**P - value**
Age			< 0.001
20-69 years	0.78	0.20	
70-80 years	0.75	0.24	
81-100 years	0.67	0.29	
Sex			< 0.001
Female sex	0.70	0.25	
Male sex	0.76	0.24	
Socioeconomic status			0.030
Low	0.73	0.26	
Middle	0.74	0.27	
High	0.74	0.25	
Physical activity before stroke			< 0.001
Mostly sedentary leisure time	0.68	0.31	
Easy to moderate activity at least four times/week	0.79	0.18	
Heavier activity two-three hours/week or hard training/competitive sport	0.86	0.26	
Stroke severity, measured by NIHSS			< 0.001
Minor stroke (NIHSS score 0-3)	0.76	0.20	
Moderate stroke (NIHSS score 4-10)	0.69	0.28	
Severe stroke (NIHSS score >10)	0.60	0.66	
Independence walking ten meters at discharge			< 0.001
Yes	0.77	0.18	
No	0.47	0.57	
Independence in personal care at discharge			< 0.001
Yes	0.79	0.17	
No	0.58	0.44	

Abbreviations: EQ5D5L = EuroQoL 5 Dimensions 5 Levels, IQR = interquartile range, NIHSS = National Institutes of Health Stroke Scale. There are 1 866 patients included in the analysis. [a] For the EQ5D5L index, -0.624 is the poorest and 1 is the highest possible HRQoL.

Multivariate analysis results are presented in table 6. After Bonferroni correction, required p-value for statistical significance was < 0.0083. Increased age, female sex, low physical activity before stroke and increased stroke severity were independent predictors of poor

HRQoL. The R square of the multivariate model was 0.21, meaning that 21 % of the EQ5D5L index variation were explained by the investigated clinical variables.

Table 6. *Multivariate analysis of EQ5D5L index [a] predictors*

	OR [b]	**95 % CI**	**P – value [c]**
Increasing age, per year	0.97	0.96-0.98	< 0.001
Sex:			
Female sex	1.00 (reference)		
Male sex	1.53	1.19-1.97	0.001
Increasing socioeconomic status, per tertile	1.01	0.86-1.19	0.897
Physical activity before stroke:			
Mostly sedentary leisure time	1.00 (reference)		
Easy to moderate activity at least four times/week	3.02	2.33-3.92	< 0.001
Heavier activity two-three hours/week or hard training/competitive sport	2.42	1.41-4.18	0.001
Increasing stroke severity, per NIHSS score	0.92	0.89-0.95	< 0.001

Abbreviations: EQ5D5L = EuroQoL 5 Dimensions 5 Levels, OR = odds ratio. CI = 95% confidence interval, NIHSS = National Institutes of Health Stroke Scale. There are 1 866 patients included in the analysis. [a] EQ5D5L index measures quality of life. [b] OR > 1 stands for increasing EQ5D5L index. [c] After Bonferroni correction, required p-value for statistical significance was < 0.0083.

EQ VAS

Mean EQ VAS was 63.8 (95% CI: 62.7 - 64.9, SD: 23.6). Median EQ VAS was 70 (IQR: 30).

Correlation between EQ5D5L and EQ VAS

There was a correlation between the EQ5D5L index and the EQ VAS, with a correlation coefficient of 0.741. In the univariate analyses, all 5 EQ5D5L questions had p-values < 0.1 and were therefore included in the multivariate analysis, see table 7. After Bonferroni correction, required p-value for statistical significance in the multivariate analysis was < 0.01. Anxiety/depression had the strongest correlation with the EQ VAS, followed by everyday

activities ability, pain/discomfort, mobility and self-care ability. The R square of the multivariate model was 0.57, meaning that 57 % of the EQ VAS variation were explained by the five EQ5D5L questions.

Table 7. *Associations between the EQ5D5L [a] questions and the EQ VAS [b]. Univariate and multivariate linear regression analyses.*

	Univariate analyses			**Multivariate analysis**		
Question	**B**	**95 % CI**	**P-value**	**B**	**95 % CI**	**P-value [c]**
1, mobility	-11.88	(-12.56) - (-11.20)	< 0.001	-3.20	(-4.25) - (-2.14)	< 0.001
2, self-care ability	-12.02	(-12.74) - (-11.29)	< 0.001	-2.37	(-3.46) - (-1.29)	< 0.001
3, usual activities ability	-11.41	(-12.01) - (-10.82)	< 0.001	-4.23	(-5.15) - (-3.30)	< 0.001
4, pain/ discomfort	-11.77	(-12.67) - (-10.88)	< 0.001	-3.73	(-4.57) - (-2.89)	< 0.001
5, anxiety/ depression	-13.41	(-14.37) - (-12.45)	< 0.001	-6.10	(-6.98) - (-5.22)	< 0.001

Abbreviations: EQ5D5L = EuroQoL 5 Dimensions 5 Levels, EQ VAS = EuroQoL visual analogue scale, B = B coefficient, CI = confidence interval. There are 1 747 patients included in the analysis. [a] EQ5D5L measures quality of life. [b] EQ VAS measures general health. [c] After Bonferroni correction, required p-value for statistical significance in the multivariate analysis was < 0.01.

Discussion

Key Findings

Compared to normative data from the general population, survivors three months after stroke reported poorer HRQoL, both as measured by the EQ5D5L index and the EQ VAS.

The main factors at acute stroke predicting poor HRQoL index after stroke were increasing age, female sex, physical inactivity before stroke and increasing stroke severity. Cross-sectional analyses three months after stroke showed a strong correlation between the subjects´

own perception of their general health state (EQ VAS) and the EQ5D5L index. The question about anxiety and depression contributed most to this correlation, followed by ability to perform usual everyday activities, pain/discomfort, mobility and self-care ability.

Health-Related Quality of Life Comparisons

The mean EQ5D5L index three months after stroke is poorer than the mean EQ5D3L values in all age groups from both the Swedish and the Danish general population (30).

Previous studies have not examined HRQoL at exactly three months after stroke. However, since there are no obvious trends and HRQoL seems to be stable over time (25, 34), comparison is possible. The EQ5DL index in this study seems to be closely similar to the EQ5D3L index in stroke survivors in Norway (13) and Great Britain (25) but poorer than the EQ5D3L index in stroke survivors in the Netherlands (34) and Korea (35). Differences between countries may be due to differences in health care quality, social networks and expectations on HRQoL. This, however, is not possible to determine from the results of this study.

Also, mean EQ VAS three months after stroke is poorer than the mean EQ VAS in all age groups in the Swedish general population (30), but closely similar to in Norwegian stroke survivors (13).

Both the decreased EQ5D5L index and the decreased EQ VAS show that the consequences of stroke are considerable, impacting on the patients´ perception of HRQoL and general health.

Predictors of EQ5D5L Index

Consistent with previous studies, increased age (25, 34, 35), female sex (25, 34) and stroke severity (25) were found as predictors of poor HRQoL after stroke. Physical activity before

stroke has however not been investigated before. Socioeconomic status did not prove to be an independent predictor of HRQoL, unlike in a previous study (25).

Previously, correlation between low socioeconomic status and less physical activity has been showed (46). Thus, the lack of independent association between socioeconomic status and HRQoL in this study might have been due to the inclusion of physical activity in the multivariable model.

The negative effect of physical inactivity before stroke on HRQoL after stroke might partly be explained by comorbidity before stroke, as the reason of physical inactivity might have been disease and/or disability, for example depression. Also, the physical inactivity might have led to disease and/or disability (for example a previous stroke), since a substantial number of studies have suggested positive effects of physical activity in several aspects of health (40-44), and physical inactivity is an identified risk factor for stroke (1). Also, physical activity can have a positive effect on depression (47), creating a possible confounder, since presence of depression is a part of the EQ5D5L instrument. However, it might also be that individuals who were physically active before stroke remained physically active to a larger extent than those who were inactive before stroke, thus had been able to benefit from the positive effects of physical activity also after the stroke.

The difference in HRQoL between female and male stroke patients might be explained by several causes. The females might had had more severe strokes, (females have been shown to suffer from more severe strokes in previous research (48)) been treated in a different manner than male patients and obtained other treatments and therefore had a poorer outcome of the stroke. The same questions can be asked concerned the elderly patients in relation to younger patients. However, some decreasing HRQoL with increasing age and decreased HRQoL in

females compared to males were expected, due to the same relations in the normative data, both in the EQ5D index and in the EQ VAS (30).

Determinants of EQ VAS

In this study, the main HRQoL measure is EQ5D5L index, which was chosen at the expense of EQ VAS. Previous studies have mainly used the EQ5D index, and to be able to compare this study´s results to previous results, the EQ5D5L index was chosen. However, while the EQ5D5L index covers several predetermined aspects, the EQ VAS provides the self-perceived general health, which is valuable information. This study therefore includes additional analyses with EQ VAS.

EQ5D5L index correlated well with the EQ VAS, suggesting that the EQ5D5L questions are relevant in deciding self-perceived HRQoL in people who have suffered from a stroke. A multivariate analysis with the EQ5D5L questions and the EQ VAS was performed to explore which questions determine the self-perceived health and HRQoL. Anxiety and depression (which have been presented as EQ VAS determinants previously (13)) were the most crucial factors, but all EQ5D5L questions correlated well to the EQ VAS. (Including independence in personal care, which has been presented as an EQ VAS determinant previously (13).) Thus, it can be assumed that the perception of general health may be improved by finding patients with these conditions and providing anxiety and depression treatment, tools to facilitate everyday activities, pain treatment and rehabilitation of mobility and personal care ability. Walking ability and personal care ability might be aspects that the health care usually invest in, but the other aspects should not be forgotten and might also be easier to affect.

Methodological Considerations

Previous validation of EQ5D5L index as a measure of HRQoL (26) after stroke (28, 29) makes it a relevant measure to use in this study. A general measure of HRQoL is preferred, since it allows comparisons with the general population. It also enables comparisons with other diseases, which can be valuable in future studies. That the questionnaires were to be filled in by the patients themselves is also considered a study strength, since the aim of the study was to investigate the patients` own perception of health. Another advantage is that the questionnaires are short and easy to fill in. However, a study weakness is that the only available language in the questionnaires was Swedish. Therefore, the results reflect the Swedish speaking population only, and not the whole stroke affected population.

The EQ5D5L index was chosen as the outcome variable at the expense of the EQ5D3L index, since advantages of the EQ5D5L have been presented in previous studies (28). However, the absence of Swedish and Danish normative EQ5D5L data is a weakness. Instead EQ5D3L data was used as a reference. However, differences between the editions are probably not large. In Spanish normative data, EQ5D3L index is slightly higher than EQ5D5L index (30, 32).

In the absence of a Swedish programme to calculate the EQ5D5L index, a Danish version was used. This version was chosen due to assumable similarities in genetics and culture between the countries. However, miss-match may exist in how the population in each country value the effect of health states on HRQoL, creating another study weakness.

A major strength of this study is the considerable number of patients. Previous population-based studies have had between 395 and 2 857 patients (25, 34-36). Also supporting the study strength is that the study population is unselected, all patients who sought health care and were diagnosed with acute stroke were included, preventing bias.

Multivariate analyses were performed in order to identify independent predictors. When analysing EQ5D5L index predictors, a multivariate linear regression analysis would have been preferred. Unfortunately, data was not normally distributed, even after attempt to exponentiate data. Instead, a multivariate logistic regression analysis was used, based on dichotomisation with the median as cut-off, making the outcome variable less nuanced.

The EQ5D5L index and the EQ VAS results were not age-standardized. However, the resulting values were poorer than in all age groups of the normative data, making the data easy to interpret anyway.

The response rate was relatively low despite repeated reminders. (63 % answered all EQ5D5L questions, and 59 % answered the EQ VAS.) Patients who answered the EQ5D5L were older, more physically active before stroke, more likely to have had a less severe stroke, had better cognitive function at discharge, more independent in walking and personal care at discharge, less likely to have had a recurrent stroke and less disabled at follow-up. Thus, with exception of age, the patients answering the EQ5D5L questionnaire can be expected to be healthier than all the unselected patients treated for acute stroke. Consequently, if all patients in the study would have responded, the HRQoL would have been even poorer compared to the general population.

This study included patients even though they had had a recurrent stroke before follow-up. It can be argued that this might have obscured the results, as a recurrent stroke may affect HRQoL. However, the purpose of this study was to provide knowledge about which patients were at risk of poor HRQoL, including those that will relapse in stroke. Therefore, individuals with a recurrent stroke was not excluded. Moreover, the proportion experiencing a recurrent stroke was very low.

There were a considerable amount of missing values concerning cognitive function. Consequently, MOCA score was excluded from the analysis, despite being a very interesting variable to investigate.

Clinical variables concerning functional level at discharge were not included in the multivariate analysis, since they were assumed to interact with other variables, such as age, physical activity before stroke and stroke severity.

There are other relevant and interesting variables which were not included in this study. Examples are comorbidity, previous stroke and risk factors for vascular disease. These are not included in the Väststroke registry. They would have been obtainable from the Riksstroke registry, but that process would have taken considerable time and was not possible in this master thesis.

The socioeconomic status variable was based on mean salary and mean education level in different post code areas. However, socioeconomic status involve more aspects than these two, and the socioeconomic status vary within the post code areas. With this in consideration, future studies may investigate socioeconomic status by other measures.

Future Studies

In addition to investigation of HRQoL after stroke in relation to an alternative socioeconomic status measure, there are other suggestions of future research questions. Further studies investigating the explanation for the associations between HRQoL and physical activity and gender are warranted. An important next step is also to investigate if interventions towards the modifiable predictors and determinants of HRQoL identified in this study would improve HRQoL in stroke survivors. Such a study would preferably be randomized.

Moreover, in this study, HRQoL three months after stroke was investigated. Future studies may focus on HRQoL in a more long-term perspective. The effect of cognitive function on HRQoL after stroke is still unexplored. It would also be interesting to explore the association between functional level and HRQoL, since this was not included in the multivariate analysis in this study. Lastly, there is also a need for Swedish EQ5D5L normative data.

Conclusions and Implications

Compared to the general population, stroke survivors experienced poorer HRQoL as measured by the EQ5D5L and the EQ VAS. Elderly, women, those who were physically inactive before stroke and those with severe strokes were at higher risk for a poor HRQoL after stroke, indicating that in these groups more active interventions for improvement of HRQoL may be warranted. Interventions may include treatment of anxiety, depression and pain as well as interventions aiming at increasing the ability of participation in everyday activities. However, further studies with a randomised design are needed to evaluate whether such interventions will improve HRQoL after stroke or not. Nevertheless, already now health care personnel may use this knowledge to identify individuals in substantial risk of poor HRQoL.

Additionally, in future studies, the EQ5D5L index data and the EQ VAS data presented in this study may be used as a reference, enabling comparisons and detection of development in the area.

Lastly, given the results in this study, this paper encourages physical activity. Physical activity may pay off in case of stroke and is worth prioritizing by the health care and the decision-makers.

Hälsorelaterad livskvalitet tre månader efter stroke - populärvetenskaplig sammanfattning på svenska

Denna studie har undersökt hur strokedrabbade personers livskvalitet är, tre månader efter insjuknande i stroke. Studien har genomförts på Sahlgrenska universitetssjukhuset i Göteborg.

Om stroke

Stroke är en vanlig och allvarlig sjukdom som innebär att man antingen får en propp i ett blodkärl i hjärnan eller en blödning i hjärnan. Detta gör att en del av hjärnan inte längre får någon blodcirkulation, vilket kan orsaka en skada på hjärnvävnaden. Detta kan i sin tur leda till kvarstående symptom, t.ex. förlamningar, talsvårigheter, epilepsi, depression, trötthet och smärta.

Studiens metod

Alla strokedrabbade personer som vårdades på Sahlgrenska universitetssjukhuset mellan oktober 2014 och februari 2017 var med i studien. Uppgifter om personerna registrerades under sjukhusvistelsen och vid uppföljning efter tre månader. Efter tre till sex månader fick de strokedrabbade även fylla i ett frågeformulär om livskvalitet.

Studiens resultat

Studien visade att livskvaliteten tre till sex månader efter en stroke är lägre än hos den generella befolkningen i Sverige. Livskvaliteten är ungefär på samma nivå som den hos strokedrabbade i Norge och Storbritannien, men sämre än hos strokedrabbade i Nederländerna och Korea.

Bland faktorer som registrerades i samband med det akuta insjuknandet i stroke visade sig ökad ålder, kvinnligt kön, låg mängd av fysisk aktivitet innan insjuknandet och högre svårighetsgrad av stroke öka risken för låg livskvalitet efter stroke.

Ångest och depression visade sig vara väldigt viktiga faktorer för hur strokedrabbade upplevde sin generella hälsa. Andra viktiga faktorer var förmåga att utföra vardagliga aktiviteter, smärta och obehag, förmåga att förflytta sig och förmåga att tvätta sig och klä på sig själv.

Resultatens användbarhet

Dessa resultat kan tänkas användas i sjukvården, för att hjälpa sjukvårdspersonal att identifiera patientgrupper som är i behov av åtgärder för att förbättra livskvalitet. Möjliga åtgärder som kan prövas är att behandla ångest, depression och smärta och att underlätta för de strokedrabbade att delta i olika vardagsaktiviteter.

Resultaten visar även på att fysiska aktivitetsvanor har betydelse för hur livet blir efter en stroke. Resultatet utgör ett exempel på hur viktigt fysisk aktivitet är för hälsan och innebär motivation för att uppmuntra enskilda individer att röra på sig, och att sjukvård och politiska beslutsfattare bör satsa på fysisk aktivitet som förebyggande friskvård.

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References

1. Fagius J, Nyholm D, Ansved T, Aquilonius SM, Borg J, Ekbom K, et al. Neurologi. 5 ed. Stockholm: Liber AB; 2013.

2. Stroke, Cerebrovascular accident: World Health Organization; 2017 [cited 2017 13 October]. Available from: http://www.who.int/topics/cerebrovascular_accident/en/.

3. Giang KW, Mandalenakis Z, Nielsen S, Bjorck L, Lappas G, Adiels M, et al. Long-term trends in the prevalence of patients hospitalized with ischemic stroke from 1995 to 2010 in Sweden. PloS one. 2017;12(6):e0179658.

4. Lofmark U, Hammarstrom A. Evidence for age-dependent education-related differences in men and women with first-ever stroke. Results from a community-based incidence study in northern Sweden. Neuroepidemiology. 2007;28(3):135-41.

5. Läkemedelsboken. 18 ed: Läkemedelsverket.

6. Page SJ, Sisto S, Levine P, McGrath RE. Efficacy of modified constraint-induced movement therapy in chronic stroke: a single-blinded randomized controlled trial. Archives of physical medicine and rehabilitation. 2004;85(1):14-8.

7. Behroozmand R, Phillip L, Johari K, Bonilha L, Rorden C, Hickok G, et al. Sensorimotor impairment of speech auditory feedback processing in aphasia. NeuroImage. 2017.

8. Olsen TS, Hogenhaven H, Thage O. Epilepsy after stroke. Neurology. 1987;37(7):1209-11.

9. Veis SL, Logemann JA. Swallowing disorders in persons with cerebrovascular accident. Archives of physical medicine and rehabilitation. 1985;66(6):372-5.

10. Gordon C, Hewer RL, Wade DT. Dysphagia in acute stroke. British medical journal (Clinical research ed). 1987;295(6595):411-4.

11. Poulin de Courval L, Barsauskas A, Berenbaum B, Dehaut F, Dussault R, Fontaine FS, et al. Painful shoulder in the hemiplegic and unilateral neglect. Archives of physical medicine and rehabilitation. 1990;71(9):673-6.

12. Burvill PW, Johnson GA, Jamrozik KD, Anderson CS, Stewart-Wynne EG, Chakera TM. Prevalence of depression after stroke: the Perth Community Stroke Study. The British journal of psychiatry : the journal of mental science. 1995;166(3):320-7.

13. Naess H, Lunde L, Brogger J. The effects of fatigue, pain, and depression on quality of life in ischemic stroke patients: the Bergen Stroke Study. Vascular health and risk management. 2012;8:407-13.

14. Jokinen H, Melkas S, Ylikoski R, Pohjasvaara T, Kaste M, Erkinjuntti T, et al. Post-stroke cognitive impairment is common even after successful clinical recovery. European journal of neurology. 2015;22(9):1288-94.

15. Ingles JL, Eskes GA, Phillips SJ. Fatigue after stroke. Archives of physical medicine and rehabilitation. 1999;80(2):173-8.

16. Appelros P. Prevalence and predictors of pain and fatigue after stroke: a population-based study. International journal of rehabilitation research Internationale Zeitschrift fur Rehabilitationsforschung Revue internationale de recherches de readaptation. 2006;29(4):329-33.

17. Karatepe AG, Gunaydin R, Kaya T, Turkmen G. Comorbidity in patients after stroke: impact on functional outcome. Journal of rehabilitation medicine. 2008;40(10):831-5.

18. Fillenbaum GG, Pieper CF, Cohen HJ, Cornoni-Huntley JC, Guralnik JM. Comorbidity of five chronic health conditions in elderly community residents: determinants and impact on mortality. The journals of gerontology Series A, Biological sciences and medical sciences. 2000;55(2):M84-9.

19. Schubert CC, Boustani M, Callahan CM, Perkins AJ, Carney CP, Fox C, et al. Comorbidity profile of dementia patients in primary care: are they sicker? Journal of the American Geriatrics Society. 2006;54(1):104-9.

20. Kesarwani M, Perez A, Lopez VA, Wong ND, Franklin SS. Cardiovascular comorbidities and blood pressure control in stroke survivors. Journal of hypertension. 2009;27(5):1056-63.

21. Felce D, Perry J. Quality of life: its definition and measurement. Research in developmental disabilities. 1995;16(1):51-74.

22. WHOQOL: Measuring Quality of Life [cited 2017 October 16]. Available from: http://www.who.int/healthinfo/survey/whoqol-qualityoflife/en/.

23. Quality of life. London: BMJ Books; 2003.

24. Henriksson M, Carlsson P. Att mäta hälsorelaterad livskvalitet : en beskrivning av instrumentet EQ-5D. Linköping: Centrum för utvärdering av medicinsk teknologi; 2002.

25. Luengo-Fernandez R, Gray AM, Bull L, Welch S, Cuthbertson F, Rothwell PM. Quality of life after TIA and stroke: ten-year results of the Oxford Vascular Study. Neurology. 2013;81(18):1588-95.

26. EuroQol--a new facility for the measurement of health-related quality of life. Health policy (Amsterdam, Netherlands). 1990;16(3):199-208.

27. EQ-5D-5L User Guide Basic information on how to use the EQ-5D-5L instrument [cited 2017 October 16]. Available from: https://euroqol.org/wp-content/uploads/2016/09/EQ-5D-5L_UserGuide_2015.pdf.

28. Golicki D, Niewada M, Buczek J, Karlinska A, Kobayashi A, Janssen MF, et al. Validity of EQ-5D-5L in stroke. Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation. 2015;24(4):845-50.

29. Pinto EB, Maso I, Vilela RN, Santos LC, Oliveira-Filho J. Validation of the EuroQol quality of life questionnaire on stroke victims. Arquivos de neuro-psiquiatria. 2011;69(2b):320-3.

30. Self-Reported Population Health: An International Perspective based on EQ-5D. 1 ed. Springer Dordrecht Heidelberg New York London: Springer Netherlands; 2014. 196 p.

31. Golicki D, Niewada M. EQ-5D-5L Polish population norms. Archives of medical science : AMS. 2017;13(1):191-200.

32. Garcia-Gordillo MA, Adsuar JC, Olivares PR. Normative values of EQ-5D-5L: in a Spanish representative population sample from Spanish Health Survey, 2011. Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation. 2016;25(5):1313-21.

33. Ayis S, Wellwood I, Rudd AG, McKevitt C, Parkin D, Wolfe CD. Variations in Health-Related Quality of Life (HRQoL) and survival 1 year after stroke: five European population-based registers. BMJ open. 2015;5(6):e007101.

34. van Eeden M, van Heugten C, van Mastrigt GA, van Mierlo M, Visser-Meily JM, Evers SM. The burden of stroke in the Netherlands: estimating quality of life and costs for 1 year poststroke. BMJ open. 2015;5(11):e008220.

35. Chang WH, Sohn MK, Lee J, Kim DY, Lee SG, Shin YI, et al. Predictors of functional level and quality of life at 6 months after a first-ever stroke: the KOSCO study. Journal of neurology. 2016;263(6):1166-77.

36. Min KB, Min JY. Health-related quality of life is associated with stroke deficits in older adults. Age and ageing. 2015;44(4):700-4.

37. Nationella riktlinjer för vård vid stroke 2017 [cited 2017 October 17]. Available from: https://roi.socialstyrelsen.se/riktlinjer/nationella-riktlinjer-for-vard-vid-stroke.

38. Verksamhetsplan Stroke Centrum Väst: Stroke Centrum Väst; [cited 2017 20 September]. Available from: http://strokecentrumvast.gu.se/digitalAssets/1524/1524155_verksamhetsplan-2012-stroke-centrum-vast.pdf.

39. Niklasson A. Associations between Socioeconomic Status and Prehospital Stroke Care [degree project]. Gothenburg: University of Gothenburg; 2017.

40. American College of Sports Medicine Position Stand. Exercise and physical activity for older adults. Medicine and science in sports and exercise. 1998;30(6):992-1008.

41. Blair SN, Kohl HW, 3rd, Paffenbarger RS, Jr., Clark DG, Cooper KH, Gibbons LW. Physical fitness and all-cause mortality. A prospective study of healthy men and women. Jama. 1989;262(17):2395-401.

42. Paffenbarger RS, Jr., Hyde RT, Hsieh CC, Wing AL. Physical activity, other life-style patterns, cardiovascular disease and longevity. Acta medica Scandinavica Supplementum. 1986;711:85-91.

43. Puett DW, Griffin MR. Published trials of nonmedicinal and noninvasive therapies for hip and knee osteoarthritis. Annals of internal medicine. 1994;121(2):133-40.

44. Dohrn IM, Sjostrom M, Kwak L, Oja P, Hagstromer M. Accelerometer-measured sedentary time and physical activity-A 15 year follow-up of mortality in a Swedish population-based cohort. Journal of science and medicine in sport. 2017.

45. Regionala etikprövningsnämnden i Göteborg. Etikprövning för studentarbeten och ST-arbeten. 2015 [cited 2017 November 15]. Available from: https://www.epn.se/goeteborg/anslagstavlan/etikproevning-under-st-utbildning/.

46. Lampinen EK, Eloranta AM, Haapala EA, Lindi V, Vaisto J, Lintu N, et al. Physical activity, sedentary behaviour, and socioeconomic status among Finnish girls and boys aged 6-8 years. European journal of sport science. 2017;17(4):462-72.

47. Cooney GM, Dwan K, Greig CA, Lawlor DA, Rimer J, Waugh FR, et al. Exercise for depression. The Cochrane database of systematic reviews. 2013(9):Cd004366.

48. Santalucia P, Pezzella FR, Sessa M, Monaco S, Torgano G, Anticoli S, et al. Sex differences in clinical presentation, severity and outcome of stroke: results from a hospital-based registry. European journal of internal medicine. 2013;24(2):167-71.

Appendices

The EQ5D5L Questionnaire

(English version for the UK)

Under each heading, please tick the ONE box that best describes your health TODAY

MOBILITY

I have no problems in walking about ❑
I have slight problems in walking about ❑
I have moderate problems in walking about ❑
I have severe problems in walking about ❑
I am unable to walk about ❑

SELF-CARE

I have no problems washing or dressing myself ❑
I have slight problems washing or dressing myself ❑
I have moderate problems washing or dressing myself ❑
I have severe problems washing or dressing myself ❑
I am unable to wash or dress myself ❑

USUAL ACTIVITIES *(e.g. work, study, housework, family or leisure activities)*

I have no problems doing my usual activities ❑
I have slight problems doing my usual activities ❑
I have moderate problems doing my usual activities ❑
I have severe problems doing my usual activities ❑
I am unable to do my usual activities ❑

PAIN / DISCOMFORT

I have no pain or discomfort ❑
I have slight pain or discomfort ❑
I have moderate pain or discomfort ❑
I have severe pain or discomfort ❑
I have extreme pain or discomfort ❑

ANXIETY / DEPRESSION

I am not anxious or depressed ❑
I am slightly anxious or depressed ❑
I am moderately anxious or depressed ❑
I am severely anxious or depressed ❑
I am extremely anxious or depressed ❑

- We would like to know how good or bad your health is TODAY.
- This scale is numbered from 0 to 100.
- 100 means the best health you can imagine.
  0 means the worst health you can imagine.
- Mark an X on the scale to indicate how your health is TODAY.
- Now, please write the number you marked on the scale in the box below.

YOUR HEALTH TODAY =