Acknowledgement

First, we would like to express our gratitude to our thesis promotor Prof. Dr. Peter Feys and our co-promotor Dr. Ilse Lamers for their critical and constructive guidance during the two-year process of writing our Master's Thesis. Furthermore, we would like to thank the direction and personnel of Ziekenhuis Oost-Limburg (ZOL) for the availability of their accomodation during our testing moments. We would especially like to thank Dr. Van Cauter, Dr. Mesotten, Dr. Wibail, Elly Vandermeulen and Leen Dreesen for their help and advice during the second part of our Master's Thesis. Finally, we would like to express our gratitude to all participants who participated in our master thesis.

Geel, 5/06/2018 Y.D.
Lommel, 5/06/2018 W.M.

Research context

The topic of this thesis can be categorized in the research domain of neurological rehabilitation and more specifically stroke rehabilitation. The onset of stroke is sudden, leaving the patient and his environment unprepared. Patients suffering from stroke are confronted with various physical, mental and social disabilities. Motor and sensory impairments, cognitive deterioration, reduced social well-being and psychological problems such as fear of a new stroke incident lead to different degrees of disability and a possible deterioration in quality of life (QoL). Therefore, a rapid diagnosis followed by an adequate treatment and specific rehabilitation program is essential for these individuals.

The first part of the Master's Thesis was completed last year. In this literature research, we evaluated the evolution of QoL in patients with neurological disorders (stroke, multiple sclerosis, spinal cord injury, Parkinson's disease and traumatic brain injury) on the long-term (> 3 years). Additionally, we identified the most important factors influencing this QoL in these patients. In stroke, we found that the QoL improved up to six months post-stroke. This level of QoL remained stable in the following five years. However, the QoL in stroke patients always remained significantly lower compared to healthy matched controls. The factors significantly influencing this course of QoL were: disease severity, anxiety, depression, fatigue, comorbidities, age, level of education and marital status. During the construction of the research protocol of the second part of our thesis, we kept these findings in mind.

The second part of this Master's Thesis consists of evaluating the effect of different treatment methods (conservative, thrombolysis, thrombectomy or a combination of both) on different outcome measures. At this moment, it's unclear what the long-term effects of these innovative treatments are on the patient's health situation in its totality, i.e. on the different levels of the International Classification of Functioning Disability and Health (ICF).

During the construction of the second part of our Master's Thesis, the included number of patients appeared to be lower than expected. The distribution of these patients among four intervention groups did not allow us to apply statistical analyses in the between-group comparison. Therefore, descriptive statistics were used for the major parts of this study.

This Master's Thesis was a duo thesis by Douwen Yannick and Moelans Wim. Both students contributed equally to the research. The writing of this Master's Thesis was supervised by Prof. Dr. Feys and Dr. Lamers.

Abstract

Background: 2015 was a critical year in the field of treatment of acute stroke. Multiple scientific studies showed the added value of 'mechanical thrombectomy' as an adjuvant treatment for thrombolysis.

Objectives: to evaluate the multidisciplinary care-pathway of Ziekenhuis Oost-Limburg (ZOL) and to investigate the long-term effects in four different intervention groups (conservative treatment, thrombolysis, thrombectomy, the combination of thrombolysis and thrombectomy) on different levels of the International Classification of Functioning, Disability and health (ICF) model.

Participants: Adults who have been diagnosed with an acute ischemic stroke by a neurologist were invited to participate in the study.

Measurements: Various outcome measures on different levels of the ICF-model were used to evaluate different aspects of the patient's quality of life and his/her functioning during daily activities. The primary outcome measures were: National Institute of Health Stroke Scale (NIHSS), Modified Rankin Scale (mRS), EuroQol-5Dimensions-5Levels (EQ-5D-5L) and Stroke Specific Quality of Life Scale (SSQoL). Specific outcome measures were examined on specific points in time. For the prospective part, the measurement points over time were: baseline, day five to seven (D5-7), three months (D90), one year to 18 months (12-18M). For the retrospective part data collection occurred at baseline and after one year to 18 months (12-18M).

Results: Retrospective part: in the total sample, the primary outcome measures 12-18 months post-stroke showed a good overall health status. The thrombectomy subgroup showed worse NIHSS- and mRS-scores, compared to the other intervention groups. This tendency was also found in the EQ-5D-5L scores. The SSQoL however, was comparable in all subgroups. Prospective part: at three months the lowest mean scores of the NIHSS and mRS were found in the thrombectomy subgroup. Concerning the QoL, the combination (thrombolysis and thrombectomy) subgroup had the best scores.

Conclusion: Due to the small sample size in combination with the disproportional distribution among subgroups, we could not make any conclusions concerning the differences between intervention groups.

Introduction

In Belgium, acute stroke is the fourth most common cause of death and the most important cause leading to persistent disability and reduced quality of life. Annually, 10.400 people are being diagnosed with acute stroke, leading to 9500 deaths each year. The surviving population often remain care-dependent, this causes an enormous economic impact. The healthcare cost of stroke in Belgium was estimated at 393.7 million euro in 2015. These findings were shown by the Stroke Alliance for Europe in a report on the burden of stroke in Europe (SAFE, 2017) and illustrate the importance of a rapid diagnosis followed by immediate intervention, as well as the early identification and treatment of risk-factors.

There are two types of acute stroke, being ischemic stroke and hemorrhagic stroke. Acute ischemic stroke is caused by an arterial occlusion in the cervical or cranial region causing deprivation of oxygenated blood, which leads to progressive brain cell death. Early reversal of vascular occlusion limits the volume of damaged tissue and correlates positively with the outcome (Ueda, Sakaki, Kumon, & Ohta, 1999). Reperfusion can be attained by a medicamentous venous treatment: intravenous thrombolysis (IVT), or by a mechanical treatment variant: thrombectomy. A hemorrhagic stroke occurs when a weakened blood vessel ruptures and bleeds in the surrounding brain tissue. The blood accumulates and compresses the surrounding tissue. Hemorrhagic strokes were excluded in this study because these interventions are not applicable in hemorrhagic strokes.

In intravenous thrombolysis (IVT) thrombolytic agents are injected in the veins to chemically dissolve clots. This treatment has been proven effective for patients with acute ischemic stroke when treatment is possible within 4.5 hours after stroke onset. In approximately 33% of the patients with acute anterior circulation ischemic stroke, symptoms are caused by a proximal occlusion of one of the major intracranial arteries. In these patients the effect of this treatment is limited. A history of previous intracranial or gastro-intestinal bleedings is an absolute contra-indication for IVT (Hacke et al., 2008; Lees et al., 2010; Wardlaw et al., 2012).

Since 2015 however, thrombectomy has been accepted as an additional treatment in acute ischemic stroke. In this treatment variant, the clot is fragmented or completely retrieved using mechanical devices. The time window for treatment is 6 hours post-stroke. With this

intervention, patients who don't respond to or have contra-indications for IVT, can still be treated. In addition, it is possible to remove emboli consisting of insoluble materials. These advantages lead to better outcomes in the field of stroke severity (NIHSS) and degree of disability (mRS). (Berkhemer et al., 2015; B. C. Campbell et al., 2015; B. C. V. Campbell et al., 2015; Goyal et al., 2016; Jovin et al., 2015; Powers et al., 2015; J. L. Saver et al., 2015). Berkhemer et al. (2015) also found that the QoL (using the EQ-5D-5L) was better in patients who received thrombectomy, compared to other treatment variants. The time window in these studies were limited to three months or less post-stroke.

Following these scientific findings in 2015, Ziekenhuis Oost-Limburg (ZOL) Genk has developed a multidisciplinary care-pathway for patients diagnosed with acute stroke. The primary objective of this study is to evaluate the multidisciplinary care-pathway of ZOL and to investigate the long-term effects in four different intervention groups (conservative treatment, IVT, thrombectomy, the combination of IVT with thrombectomy) on different levels of the International Classification of Functioning, Disability and health (ICF) model.

The study includes a retrospective and prospective data. The aims of the two parts of this study are: 1) to analyze and describe the patient's health situation in the total sample and in the different intervention groups, using a holistic approach, 2) to describe the changes of the NIHSS and MRS in the different intervention groups. Primary outcome measures were NIHSS, mRS, EQ-5D-5L and SSQoL. The secondary outcome measures were various functional scales in the field of bodily functions and activities. The difference between the two parts lies in the different measurement points in time.

The hypothesis is that patients with acute stroke who received intervention (or thrombolysis, or thrombectomy, or a combination of both) will show more positive outcomes concerning function, disabilities, QoL and re-integration in society, compared to a conservative treatment patient group.

Methods

Study design

A real life interventional study was executed in ZOL, Genk. All patients diagnosed with acute stroke were invited to participate in the study. After consent, patients were included and screened. Written informed consent was given by the patient or by his/her legally designated representative when the patient was not mentally competent to give his/her consent. An extensive explanation of the study procedures was given by one of the researchers.

Selection and description of participants

All patients who were older than 18 years and who had been diagnosed with an acute stroke by a neurologist, were selected for the study. As mentioned above, this study was divided in two parts according to the admission date in ZOL.

Retrospective: clinical data of patients admitted to the ZOL acute stroke care-pathway between 01/08/2016 and 01/10/2017 were extracted from the medical records. A follow-up meeting only took place in the time window of 12-18 months after onset of the event.

Prospective: clinical data of patients admitted to the ZOL acute stroke care-pathway after 01/10/2017 were extracted from the medical records. These patients completed the entire study procedure, as described below.

Procedures

The acute stroke care-pathway starts in the Emergency Care Unit (ECU). After an initial clinical evaluation, the stroke patient is transferred to the medical imaging department of the ECU. These patients are given absolute priority in the radiology department by means of a specific 'acute stroke' electronic formulary. The acute stroke CT protocol exists of two parts. First a CT scan of the head without contrast is important to determine if the acute stroke is of an ischemic or a haemorrhagic origin. After ruling out haemorrhage, further investigation of the (ischemic) stroke is done by a CT-angiography (CTA) of the blood vessels of the neck and brain.

Based on the CT images, the most appropriate treatment for the patient is chosen by the neurologist, in agreement with the radiologist. If there is no haemorrhage, if the onset of the stroke is within the time window for thrombolysis (4h) and if there are no contra-indications,

rt-PA is administered. The eligibility criteria for thrombectomy (based on CT) are described in table 1 in the appendix.

There are four possible treatment groups:

- the classic conservative treatment: anti-aggregation (aspirin, clopidogrel,…)
- thrombolysis
- thrombolysis in combination with thrombectomy
- thrombectomy solely

After a thrombectomy treatment, patients are transferred to the Intensive Care Unit (ICU). Once hemodynamically stable, these patients are transferred to medium care department and eventually to the neurology department, where additional examinations are performed (MRI, EEG, ECG,…). Patients who received IVT or conservative treatment, are directly transferred to medium care and subsequently to the neurology department.

Outcome measures

In this study, diverse **outcome measures on all levels of the ICF model** were investigated, as shown in the appendix (table 2). The aspect of **body functions and structures** was measured by a neuroradiological examination on the one hand: the NIHSS is a 15-item neurologic examination stroke scale used to evaluate the effect of acute stroke on the levels of consciousness, language, neglect, visual-field loss, motor strength, ataxia, dysarthria, sensory functions and pain. The NIHSS score ranges from 0 to 42, where a higher score indicates a higher stroke severity (Taylor-Rowan, Wilson, Dawson, & Quinn, 2018). On the other hand, we included specific outcome measures on the body functions level, such as the Motricity Index (MI) and the finger extension test of the Fugl-Meyer (FM) (Gor-Garcia-Fogeda et al., 2014). The MI is a test for maximal muscle strength of the arms and legs. A hemiplegia score is calculated and ranges from 0-100, with a higher score indicating better muscle activity. The finger extension item of the Fugl-Meyer test is rated by an ordinal scale (0 = no extension occurs, 1 = release of massive active flexion grasp, 2 = full active extension). The **activity related** outcome measures also consisted of a general scale assessed by the neurologist: the modified rankin scale (mRS) (Taylor-Rowan et al., 2018) assesses neurological disability using an ordinal scale ranging from 0 to 6 (0 = no symptoms, 3 = moderate disability 6 = dead). Furthermore, functional tests were included. The Trunk Control Test (TCT) evaluates the trunk

stability with possible scores from 0 to 100, a higher score indicates more trunk stability (Franchignoni, 2003). The Frenchay Arm Test (FAT) (Heller et al., 1987) is scored using an ordinal range from 0 to 5, where a higher score indicates a better dexterity of the paretic arm and hand. The 10-meter walk test (10-MWT) is a performance measure used to assess walking speed (Scrivener, Schurr, & Sherrington, 2014). The mean walking speed was calculated based on three attempts. Functional Ambulation Categories (FAC) assess the degree of independence during walking, it's an ordinal 6-point scale. A score of 0 indicates a full dependence on others, a score of 5 indicates independency in walking (Mehrholz, Wagner, Rutte, Meissner, & Pohl, 2007). The Barthel index (BI) (Taylor-Rowan et al., 2018) assesses the amount of help needed during 10 activities of daily living. The total score ranges from 0 to 20, where 20 indicates a total independence in activities of daily living. At the follow-up visit **personal factors** such as anxiety and depression were measured by the Hospital Anxiety and Depression Scale (HADS) (Burton & Tyson, 2015). The HADS assesses the presence of an anxiety/depression disorder, it ranges from 0 to 21. A score of 0 to 7 indicates the absence of such a disorder, a score from 8 to 10 indicates a possible disorder and with a score from 10 to 21 a disorder is presumably present. The level of education and the current living conditions were also evaluated. The QoL was measured by two specific questionnaires: the EQ-5D-5L (Golicki et al., 2015) and the SSQoL (Ewert & Stucki, 2007). The EQ-5D-5L assesses five dimensions of the patient's health (mobility, self-care, daily activities, pain/discomfort, anxiety/depression) which are scored on an ordinal 5 point-scale (1-5). A higher score indicates a worse condition. The total score is a 5-letter code (for example: 14321). The SSQoL is a specific QoL scale for stroke patients. 49 items are being scored by a 5-point ordinal scale (1-5) in 12 domains. A mean score of these domains is calculated to receive a total score that ranges from 1 to 5. Five indicates the best possible QoL. As an **external factor**, we asked patients if they have participated in a rehabilitation programme post-stroke (setting, frequency, disciplines) as this could potentially impact the outcomes.

These specific outcome measures were examined on specific points in time. The overview of these measurement points is shown in figure 1 and 2 of the appendix. For the prospective part, the measurement points over time were: baseline, day five to seven (D5-7), three months (D90), one year to 18 months (12-18M). The prospective part was still in its early phase, in this study the included patients did not reach the one-year post-stroke time window yet. For the

retrospective part data collection occurred at baseline and after one year to 18 months (12-18M). Additionally, we collected relevant patient characteristics from the medical records.

Statistics

SAS JUMP software was used for the analyses. Significance level was set at $p<0,05$. Normality of data distribution was investigated for each parameter applying the Shapiro-Wilk test. Despite the sample size, normality requirements were not fulfilled.

Retrospective part

Due to the substantial extent of missing data at baseline (NIHSS- and mRS-scores) we were not able to assess changes over time in the total group (n=23). The distribution of these 23 patients among four intervention groups did not allow us to apply statistical analyses. Therefore, descriptive statistics were used for the retrospective part of this study.

Prospective part

In the outcomes of the total sample (n=43) we used the Wilcoxon signed rank test to determine changes over time because of the absence of a normal distribution.

Because of the disproportional distribution of patients among the different intervention groups, it was decided not to apply statistics between-group comparison. Descriptive statistics were used to evaluate the differences among intervention groups.

Results

Retrospective part of the study

Participants

Between 1 December 2017 and 30 April 2018, 23 patients were included in the study. These patients were seen 12-18 months after the event. The mean age of these patients was 69 years; 16 (70%) of these patients were male. The majority of these patients received a conservative treatment approach (n=10) or a thrombolysis (n=8). Three patients received a thrombectomy and two received a combination of both (thrombolysis and thrombectomy). The most common risk factors in the stroke patients were hypercholesteremia (65%), hypertension (61%), diabetes (22%) and a history of stroke or cardiovascular diseases in the family (22%). We were not able to retrieve sufficient information on the baseline-NIHSS and the mRS pre-stroke. Data on the baseline NIHSS of 10 patients were missing and only two pre-stroke mRS scores were available.

Table 1: baseline characteristics

	Thrombolysis (n=8)	Thrombectomy (n=3)	Thrombolysis + Thrombectomy (n=2)	Conservative (n=10)	Total (n=23)
Baseline characteristics					
Age in years – $\bar{x}$ (SD)	72 (9)	65 (11)	52 (3)	71 (10)	69 (11)
Gender, male – n (%)	6 (75)	1 (33)	1 (50)	8 (80)	16 (70)
Risk factors					
Smokers – n (%)	0 (0)	1 (33)	0 (0)	2 (20)	3 (13)
Alcohol – n (%)	0 (0)	0 (0)	0 (0)	1 (10)	1 (4)
Hypertension – n (%)	6 (75)	2 (67)	2 (100)	4 (40)	14 (61)
Diabetes – n (%)	1 (13)	0 (0)	1 (50)	3 (30)	5 (22)
Hypercholesterolemia – n (%)	5 (63)	2 (67)	2 (100)	6 (60)	15 (65)
Family history – n (%)	1 (13)	1 (33)	1 (50)	2 (20)	5 (22)
ASPECT*, – $\bar{x}$ (SD)	9.5 (0.76)	10 (0)	9.5 (0.71)	9 (2)	9.33 (1.39)

**Alberta Stroke Program Early CT score (0-10): 10 = normal CT, 0 = diffuse involvement*

Primary outcome measures

In the total sample, the primary outcome measures 12-18 months post-stroke showed a good overall health status. The neurological symptoms and their effect on the daily activities of the patient were mild (mean NIHSS and mRS scores of 1). Regarding the QoL of the patients, the same status was found. The mean EQ-5D-5L scores ranged between one and two, with one being the best possible score. The mean SSQoL score of 4.43 also indicated a very good health-related QoL in stroke patients 12-18 months after the event.

The thrombectomy subgroup showed worse NIHSS- and mRS-scores, compared to the other intervention groups. This tendency was also found in the EQ-5D-5L scores, except in the anxiety sub scale where the thrombolysis and conservative intervention groups had a higher score. The SSQoL was comparable in all subgroups.

Table 2: primary outcome measures 12-18 months post-stroke

Outcome measures $\bar{x}$ (SD)	Thrombolysis (n=8)	Thrombectomy (n=3)	Thrombolysis + Thrombectomy (n=2)	Conservative (n=10)	Total (n=23)
NIHSS ↓	1 (1)	2.33 (2.31)	0 (0)	0.9 (1.60)	1.05 (1.5)
MRS ↓	0.71 (0.76)	1.67 (1.15)	0.5 (0.71)	1.1 (1.20)	1 (1.02)
EQ-5D mobility ↑	1.25 (0.71)	2.33 (0.58)	1 (0)	1.44 (1.01)	1.46 (0.86)
EQ-5D self-care ↑	1.38 (0.74)	2.33 (1.15)	1 (0)	1.44 (1.33)	1.5 (1.06)
EQ-5D activities ↑	1.63 (1.06)	2 (1)	1 (0)	1.44 (1.01)	1.55 (0.96)
EQ-5D pain ↑	1.63 (1.06)	2 (1)	1.5 (0.71)	1.44 (1.01)	1.59 (0.96)
EQ-5D anxiety ↑	2.13 (1.13)	1 (0)	1 (0)	1.78 (0.97)	1.73 (0.98)
SSQoL ↑	4.25 (0.71)	4.33 (1.15)	5 (0)	4.5 (0.53)	4.43 (0.66)

- National Institute of Health Stroke Scale (0-42): higher score indicates worse severity, modified Rankin Scale (0-6): higher score indicates higher degree of disability
- EuroQoL-5Dimensions (1-5): a higher score indicates worse QoL, Stroke Specific Quality of Life scale (1-5): higher score indicates better QoL

Secondary outcome measures

As shown in table 3, the total group results showed that the mean scores were close to these of the healthy population. in the ICF-levels of body functions (MI, FM) and activities (FAT, FAC, CT, BI). Furthermore, no indications for anxiety or depression disorders were present. The overall health condition of the included patients 12-18 months post-stroke was shown to be excellent in this study.

In general, the different intervention groups showed comparable scores. However, the thrombectomy subgroup walked slower (10MWT) and scored worse in the field of muscle activity on the hemiplegic side (MI). Anxiety and depression scores (HADS) were higher in the thrombolysis and conservative subgroups. However, no real indications for anxiety- or depression disorders were present (scores below 7).

Table 3: secondary outcome measures 12-18 months post-stroke

Outcome measures x̄ (SD)	Thrombolysis (n=8)	Thrombectomy (n=3)	Thrombolysis + Thrombectomy (n=2)	Conservative (n=10)	Total (n=23)
MI (0-100): ↑	96.38 (5.55)	81 (18.08)	93.57 (11.05)	94.65 (11.65)	93.57 (11.05)
FM (0-2): ↑	2 (0)	2 (0)	2 (0)	1.9 (0.32)	1.95 (0.21)
FAT (0-5): ↑	4.88 (0.35)	4 (1)	5 (0)	4.6 (1.26)	4.65 (0.93)
FAC (0-5): ↑	4.75 (0.71)	4.67 (0.58)	5 (0)	4.33 (1.41)	4.57 (1.03)
10 MWT: ↓	9.09 (2.95)	15.85 (0.64)	8.91 (0.58)	13.22 (7.39)	10.62 (4.01)
TCT (0-100): ↑	100 (0)	100 (0)	100 (0)	96.1 (12.33)	98.30 (8.13)
BI (0-20): ↑	18.86 (3.02)	17 (3.61)	20 (0)	17.89 (5.25)	18.29 (3.98)
HADS (0-21): ↓	6.57 (6.60)	3.5 (4.95)	3.5 (4.95)	6.3 (4.42)	5.86 (5.07)

- ↑: a higher score indicates a better outcome, ↓: a lower score indicates a better outcome
- MI (Motricity Index), FM (Fugl-Meyer), FAT (Frenchay Arm Test), FAC (Functional Ambulation Categories), 10MWT (10 Meter Walk Test), TCT (Trunk Control Test), HADS (Hospital Anxiety and Depression Scale), BI (Barthel Index)

The mortality in the retrospective part of the study was very high. We included 23 patients who survived the 12 to 18-month period post-stroke. However, in the medical records of ZOL we found that another 36 patients, who were eligible for our study, died in this period. As shown in table 4, the mortality was the highest in the conservative treatment group and the lowest in the intervention group which received a combination of thrombolysis and thrombectomy.

Table 4: mortality in the different intervention groups, 12-18 months post-stroke

	Thrombolysis	Thrombectomy	Thrombolysis + Thrombectomy	Conservative	Total
Deaths – no (%)	5 (14)	10 (28)	1 (3)	20 (55)	36 (100)

Prospective part of the study

Participants

Between 1 December 2017 and 30 April 2018, 43 patients were included in the study. The mean age of these patients was 70 years; 26 (60%) of these patients were male. The majority of these patients received a conservative treatment approach (n=30), three patients received a thrombectomy, five patients received thrombolysis and five received a combination of both (thrombolysis and thrombectomy). The risk factors are also described in table 5. The most common risk factors in the stroke patients were hypertension (65%), hypercholesteremia (35%) and smoking (19%). We were not able to retrieve information on the location of the stroke from the medical records. The mean baseline NIHSS score of the total sample was 10. The mean score was the lowest in the conservative treatment group (8) and the highest in the thrombectomy group (19).

Table 5: baseline characteristics

	Thrombolysis (n=5)	Thrombectomy (n=3)	Thrombolysis + Thrombectomy (n=5)	Conservative (n=30)	Total (n=43)
Age in years – x̄ (SD)	70 (14)	79 (10)	69 (12)	69 (16)	70 (15)
Gender, male – no (%)	2 (40)	1 (33)	2 (40)	21 (70)	26 (60)
Previous events	2 (40)	0 (0)	1 (20)	4 (13)	7 (16)
Risk factors					
Smokers – no (%)	1 (20)	1 (33)	0 (0)	6 (20)	8 (19)
Alcohol – no (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Hypertension – no (%)	5 (100)	1 (33)	4 (80)	18 (60)	28 (65)
Diabetes – no (%)	0 (0)	1 (33)	1 (20)	4 (13)	6 (14)
Hypercholesterolemia – no (%)	3 (60)	0 (0)	2 (40)	10 (33)	15 (35)
Obesity – no (%)	1 (20)	0 (0)	0 (0)	4 (13)	5 (12)
Severity of stroke					
NIHSS*-baseline – x̄ (SD)	10 (3)	19 (5)	15 (5)	8 (7)	10 (7)
Pre-stroke handicap					
MRS*-baseline – x̄ (SD)	1.75 (1.30)	2 (1)	0.50 (0.50)	0.96 (1.27)	1.06 (1.26)
ASPECT*, – x̄ (SD)	10 (0)	9.67 (0.47)	9.20 (1.17)	9.33 (1.28)	9.38 (1.19)

**National Institute of Health Stroke Scale (0-42): higher score indicates worse severity*
**Modified Rankin Scale (0-6): higher score indicates higher degree of disability*
**Alberta Stroke Program Early CT score (0-10): 10 = normal CT, 0 = diffuse involvement*

Primary outcome measures

The NIHSS improved significantly over three months ($p<0.001$). The degree of disability was still significantly ($p<0.01$) higher at D90 compared to the pre-stroke period. The EQ-5D scores improved as well, but not significantly. The high sum score of the SSQoL at D90 indicates a high level of overall QoL in stroke patients.

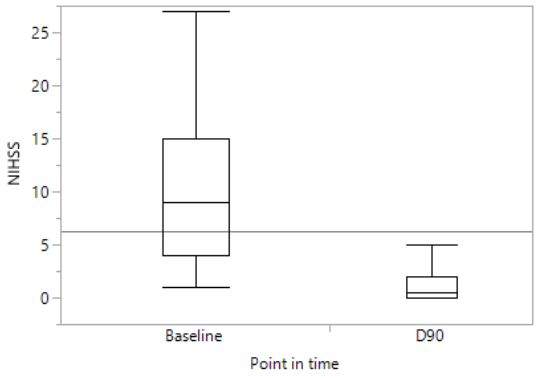

Figure 1: analysis of NIHSS-scores in the total sample over a 3-month time window

In the between group comparison of the NIHSS at baseline (emergency care unit), the mean scores were by far the highest in the thrombectomy subgroups. At D90, the NIHSS was the highest in the conservative treatment group. The mean MRS score was the highest in the thrombolysis subgroup. The lowest mean scores of the NIHSS and MRS were found in the thrombectomy subgroup. Concerning the QoL, the combination (thrombolysis and thrombectomy) subgroup had the best scores.

Table 6: the evolution of primary outcome measures in the total sample and in the different intervention groups

Outcome measures x̄ (SD)	Thrombolysis (n=5)	Thrombectomy (n=3)	Thrombolysis + Thrombectomy (n=5)	Conservative (n=30)	Total (n=43)	p-value*
NIHSS ↓						
- E.U.	9.75 (0.94)	19.33 (1.15)	15.20 (0.78)	7.96 (1.02)	9.9 (1.23)	
- D90	0.66 (0.86)	0 (0)	0.80 (0.68)	1.52 (0.86)	1.27 (0.89)	**< 0.001**
MRS ↓						
- PRE	2.33 (0.98)	2.00 (1.06)	0.50 (1.03)	0.96 (0.85)	1.06 (0.97)	
- D90	2.25 (0.87)	0 (0)	1.00 (0.82)	1.29 (1.20)	1.32 (1.02)	**< 0.0122**
EQ-5D mobility ↑						
- D5	1.33 (1.15)	(3)	1 (0.71)	1.79 (1.55)	1.68 (1.47)	< 0.1212
- D90	0.5 (0.71)	1 (0)	1 (1.41)	0.81 (1.25)	1 (1.26)	
EQ-5D self-care ↑						
- D5	0 (0)	2 (0)	0.6 (0.89)	1.90 (1.76)	1.55 (1.66)	< 0.3840
- D90	1 (1)	2 (0)	0.6 (1.34)	0.77 (1.23)	0.81 (1.119)	
EQ-5D activities ↑						
- D5	1.5 (2.12)	3 (0)	1 (1)	2.1 (1.65)	1.89 (1.57)	< 0.1259
- D90	2 (1)	2 (0)	0.8 (1.79)	1 (1.15)	1.10 (1.25)	
EQ-5D pain ↑						
- D5	0 (0)	3 (0)	0 (0)	0.5 (0.92)	0.46 (0.95)	< 0.7947
- D90	0.67 (1.15)	2 (0)	0 (0)	0.55 (0.91)	0.52 (0.89)	
EQ-5D anxiety ↑						
- D5	0.5 (0.71)	3 (0)	0.8 (1.30)	1.25 (1.12)	1.15 (1.12)	< 0.1991
- D90	2 (1)	0 (0)	0 (0)	0.77 (0.92)	0.74 (0.96)	
SSQoL, ↑						
- D90	3.99 (0.89)	3.80 (0)	4.62 (1.02)	4.18 (0.76)	4.21 (0.91)	

** p-values lower than 0.05 indicate a significant difference between the 2 scores over time*

- National Institute of Health Stroke Scale (0-42): higher score indicates worse severity, modified Rankin Scale (0-6): higher score indicates higher degree of disability

- EuroQoL-5Dimensions (1-5): a higher score indicates worse QoL, *Stroke Specific Quality of Life scale (1-5): higher score indicates better QoL*

Secondary outcome measures

Over the time window of three months, only the FM and the FAC improved significantly ($p<0.037$ and $p<0.001$ respectively) in the total sample (figure 2: FAC). The scores of the other functional test all improved, but the changes were not significant. The thrombolysis intervention was the only subgroup where a score of a functional test (MI) deteriorated over time.

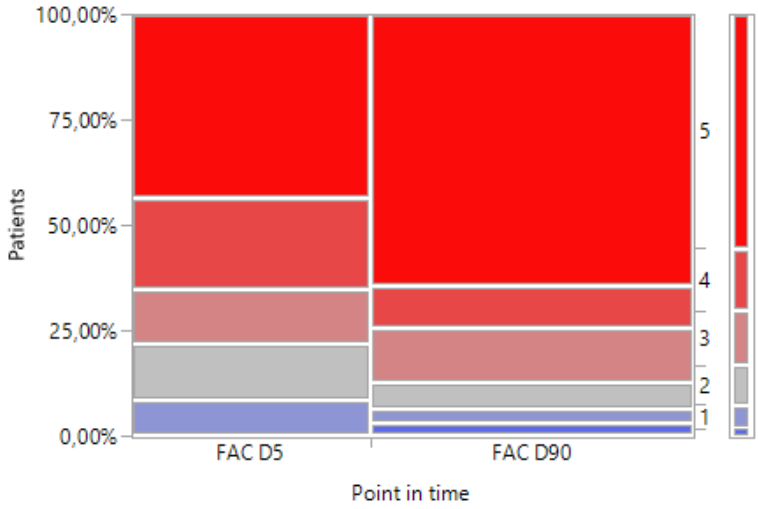

Figure 2: evolution of FAC scores in the total sample: a score of 5 indicates full independence in walking

In the comparison between groups at D90, we found comparable scores in all subgroups for the FM and the FAT. The MI was the highest in the thrombectomy group and the lowest in the thrombolysis subgroup. Furthermore, the FAC was equal in all groups (score of 4) except the thrombectomy subgroup (score of 3). The patients who received thrombolysis walked slower compared to the other groups with a mean 10MWT of 13.75. The TCT scores were also comparable in all groups except the combination subgroup, which scored worse. According to the mean scores of the HADS, anxiety and depression disorders were presumably present in the thrombolysis subgroup and probably present the conservative subgroup. The Barthel scores indicate a functional independence level of 'reasonable to good' in all groups. During the 90-day period, a mortality of 23% was found in the total sample, 10 people died. The highest number of deaths was recorded in the conservative group (7 deaths). The percentage of deaths was the highest in the thrombectomy group (67%). Two of the three patients in this subgroup died during the first days after surgery.

Table 7: the evolution of secondary outcome measures in the total sample and in the different intervention groups

Outcome measures x̄ (SD)	Thrombolysis (n=5)	Thrombectomy (n=3)	Thrombolysis + Thrombectomy (n=5)	Conservative (n=30)	Total (n=43)	p-value
MI (0-100): ↑ - D5 - D90	99 (0) 79.33 (4.01)	79.5 (0) 95 (0)	88.2 (9.21) 90.05 (9.80)	70.09 (32.63) 85.02 (19.26)	75.53 (29.38) 85.7 (16.79)	< 0.173
FM (0-2): ↑ - D5 - D90	2 (0) 2 (0)	1 (0) 2 (0)	1.8 (0.45) 2 (0)	1.26 (0.96) 1.86 (0.47)	1.39 (0.88) 1.90 (0.40)	**< 0.037**
FAT (0-5): ↑ - D5 - D90	5 (0) 5 (0)	5 (0) 5 (0)	4.6 (0.55) 5 (0)	3.09 (2.39) 4.18 (1.65)	3.52 (2.19) 4.42 (1.43)	< 0.168
FAC (0-5): ↑ - D5 - D90	3 (0) 4.33 (1.15)	4 (0) 3 (0)	3.8 (1.30) 4.4 (1.34)	3.05 (2.01) 4.14 (1.46)	3.22 (1.87) 4.16 (1.37)	**< 0.001**
10 MWT: ↓ - D5 - D90	11.35 (0) 13.75 (1.40)	18 (0) /	11.90 (4.06) 11.24 (3.20)	13.03 (6.18) 10.64 (2.69)	12.95 (5.39) 11.11 (2.78)	< 0.309
TCT (0-100): ↑ - D5 - D90	100 (0) 87 (22.52)	87 (0) 87 (0)	90.25 (19.5) 77.4 (31.29)	69.24 (37.74) 87.86 (26.25)	75.07 (34.77) 86.06 (25.75)	< 0.354
HADS (0-21): ↓ - D90	13 (3.56)	1 (0)	2.25 (3.34)	7.38 (8.63)	7.29 (8.09)	/
BI (0-20): ↑ - D90	18 (2.83)	14 (0)	18.40 (3.20)	17.55 (4.92)	17.61 (4.49)	/
Deaths – no (%)	1 (20)	2 (67)	0 (0)	7 (23)	10 (23)	/

** p-values lower than 0.05 indicate a significant difference between the 2 scores over time*

↑: a higher score indicates a better outcome, ↓: a lower score indicates a better outcome

MI (Motricity Index), FM (Fugl-Meyer), FAT (Frenchay Arm Test), FAC (Functional Ambulation Categories), 10MWT (10 Meter Walk Test), TCT (Trunk Control Test), HADS (Hospital Anxiety and Depression Scale), BI (Barthel Index)

Discussion

General considerations

The general aim of this study was to evaluate the multidisciplinary care-pathway of ZOL and to investigate the long-term effects in four different intervention groups: conservative, thrombolysis, thrombectomy and a combination of thrombolysis and thrombectomy. The novelty in this study, compared to previous research, was the addition of several outcome measures related to the concept of 'functioning' as defined by WHO's international classification. As a result of this addition, we received a more complete view on the patient's health situation and we can interpret the need for complementary rehabilitation services.

In the discussion section below, we compared the results of the intervention groups in a descriptive manner. However, it is important to emphasize that due to the small sample size in combination with the disproportional distribution among subgroups, we could not make any conclusions concerning the differences between intervention groups.

- **Retrospective part**

Reflection on the findings in function of the research question

One of the most important findings of the retrospective part was that the overall health situation of the total sample was very good at 12-18 months post-stroke. However, we can't exclude a selection bias given that perhaps only the healthier patients agreed to come to the follow-up appointment. It's possible that more disabled patients or their caregivers did not have the energy or were simply not capable to come to ZOL without specialized transport support. Furthermore, the retrospective nature of the study combined with the long time-window between event and follow-up, resulted in a large number of deceased patients. These patients were not included in the analysis and this might have resulted in a selection bias, leading to an overestimation of the health situation 12-18 months post-stroke. Another finding was the worse scores of the thrombectomy subgroup in almost all the primary outcome measures, the MI and the 10MWT. Due to the low number of patients among the different intervention groups and the missing NIHSS data at baseline, we were not able to explain these outcomes.

Reflection on the weaknesses and strengths of the retrospective study part

The retrospective part of our study had several limitations. First, the small sample of 23 patients had to be divided among four intervention groups. This (disproportional) distribution led to the fact that we could not apply statistics to analyse the differences between intervention groups. Subsequently, we could not confirm or reject the hypothesis that an intervention with thrombectomy led to a better outcome 12-18 months post-stroke. Second, there was a large amount of missing data at baseline. The missing NIHSS and mRS scores led to an inability to assess the change over time in stroke severity and stroke-related disability, respectively. Third, there was a high probability for a selection bias in this study. As mentioned above, the high mortality, combined with the retrospective nature and long time window for follow-up resulted in this probability. Last, the location of the stroke could not be taken into account because of missing data.

One of the strengths of the retrospective study was the comprehensive assessment of the patient's health situation. Various outcome measures on different levels of the ICF-model were used to evaluate different aspects of the patient's quality of life and his/her functioning during daily activities. Furthermore, the time window of 12 to 18 months can definitely be considered a strength. The majority of previous research in this field was limited to the comparison of the mRS between intervention groups at three months post-stroke (A. et al., 2015; Demchuk et al., 2015; J. Saver et al., 2015). Only the MR CLEAN study from van den Berg et al. (2017) investigated the mRS and the EQ-5D-3L after two years. Furthermore, the questionnaires were always scored in the presence of a researcher. No questionnaires were given with patients to fill in at home, nor administered by phone. In this manner, possible questions or uncertainties could always be immediately clarified.

- **Prospective part**

Reflection on the findings in function of the research question

In the prospective part of the study we were able to identify some important findings when comparing the outcome measures at different time points. As expected, the NIHSS- and mRS-scores at 3 months were significantly better than at baseline. After 3 months, the neurological status of the included patients returned to a level close to the healthy population (mean score of 1.27). When we compare the different intervention groups, the stroke severity (NIHSS) after

three months was worse in the conservative group compared to the groups receiving an early treatment. Similar findings were found in previous studies where thrombolysis and/or thrombectomy were compared to a conservative treatment at three months (Berkhemer et al., 2015; Jiang et al.; Rodrigues et al., 2016). All studies showed the effectiveness and safety of endovascular/intra-arterial treatment in stroke patients. Specifically, a better clinical outcome (mRS and/or NIHSS) was found at D90. This might be an indication to confirm our hypothesis that the outcome of patients who received an intervention would be better compared to these the conservative treatment group. However, we can't confirm this indication in this study due to the low number of patients in the different intervention groups. The mRS score at three months was still significantly lower, compared to the pre-stroke period. Ischemic stroke patients still experience a certain degree of disability three months after the event. Another interesting finding is the lack of significant improvement in the EQ-5D QoL scales over the three-month follow-up. This might be explained by the fact that the level of QoL in stroke patients keeps improving over a longer period of time (up to six months). This was shown by several studies in our literature search (Luengo-Fernandez et al., 2013; Patel, McKevitt, Lawrence, Rudd, & Wolfe, 2007). The functioning-oriented outcome measures all increased, only the FAC and the FM increased significantly. Thus, the general functionality of stroke patients increased in the first three months after stroke. According to the findings, the presence of anxiety and depression was low in the total sample. However, after the assessments and the contact with the patients, we believe that the presence of these conditions might be higher than demonstrated by the HADS scores. This was in line with previous research, where post-stroke depression was shown to be present in 36.2% of the included stroke patients at one year follow-up (Bour et al., 2010). The low scores might be explained by a possible social desirability bias. The presence of the researcher and/or family members during the assessment might have influenced the patient to give the 'desirable' answer. The patient might have been ashamed to admit certain feelings of depression or anxiety. Finally, the mortality in the prospective part (23%) was in line with recent comparable studies, where the mortality varied between 9% and 24% (Campbell et al., 2014; Demchuk et al., 2015; Powers et al., 2015; J. Saver et al., 2015). The highest mortality was noted in the thrombectomy subgroup, two out of three patients died in this group (67%). However, this is probably by chance given the low number in this group. An explanation for this finding is the higher NIHSS score at baseline. The patients in this group had an average NIHSS-score of 19.33

in the ECU. Thus, the possibility of death in the first days/weeks was higher in this subgroup. Moreover, the mortality in recent research that compared thrombectomy to other treatment variants (thrombolysis and/or conservative) differed among studies. Some studies reported a higher number of deaths in the thrombectomy subgroup (A. et al., 2015; Ciccone, Valvassori, & Nichelatti, 2011), other research indicated a lower mortality rate in patients who received thrombectomy (Demchuk et al., 2015; J. Saver et al., 2015; van den Berg et al., 2017).

Reflection on the weaknesses and strengths of the prospective study part

As in the retrospective part, the (disproportional) distribution of patients among four different treatment groups led to the impossibility to analyse the between-group comparison. The limited number of patients was related to the short period of time in which patients could be included in the framework of this Master's Thesis. Second, the time window of 3 months can be considered a limitation in this thesis since most patients are still rehabilitating from their stroke. Therefore, a time window of at least 12 to 18 months is recommended. Third, the location of stroke was not included in the analysis given that precise data were not available, even though we acknowledge its great importance for the degree of recovery and ultimately the quality of life in patients after stroke. Last, the assessment was performed by several (four) researchers of which not all had a medical or an allied health professional background. Despite a detailed written instruction booklet, a difference in feedback and instructions could have occurred. These individual differences might have had an impact on the results.

In contrast to the retrospective part, a comprehensive test battery of the patient's health situation was used during the baseline measurements in the prospective part of the study. This baseline measurement allowed us to assess whether or not patients were progressing over time. Second, only validated measurement tools were used of which the psychometric properties were extensively examined and were found to be satisfactory to very good. Last, we used a disease-specific questionnaire (SSQoL) in combination with a generic QoL assessment (EQ-5D-5L). The disease specific items insure an assessment of the QoL, taking into account specific characteristics of the disease. At the same time, the possibility of comparison to healthy individuals or to other diseases is preserved by the generic assessment.

Recommendation for future research

To reject or confirm the hypothesis that an intervention leads to a beneficial outcome compared to the conservative treatment, future research should focus on the inclusion of a larger number of stroke patients. In this manner, the statistical power will increase and an adequate between group comparison is possible. Furthermore, the effects of other factors such as the type and intensity of rehabilitation or the marital status (or caregiver support) can be added in the statistical analysis.

Conclusion

Stroke is an acute neurological event with a significant impact on the general health status of the patient. Over time, this health status gradually recovers, but not to the level of the pre-stroke period. A certain degree of disability remains, compared to the healthy population.

Due to the small sample size in combination with the disproportional distribution among subgroups, we could not make any conclusions concerning the differences between intervention groups.

References

A., M. C., Angel, C., Àlex, R., Angeles, M., Joaquin, S., San, R. L., . . . Erik, C. (2015). REVASCAT: a randomized trial of revascularization with SOLITAIRE FR® device vs. best medical therapy in the treatment of acute stroke due to anterior circulation large vessel occlusion presenting within eight-hours of symptom onset. *International Journal of Stroke, 10*(4), 619-626. doi:doi:10.1111/ijs.12157

Berkhemer, O. A., Fransen, P. S., Beumer, D., van den Berg, L. A., Lingsma, H. F., Yoo, A. J., . . . Dippel, D. W. (2015). A randomized trial of intraarterial treatment for acute ischemic stroke. *N Engl J Med, 372*(1), 11-20. doi:10.1056/NEJMoa1411587

Bour, A., Rasquin, S., Aben, I., Boreas, A., Limburg, M., & Verhey, F. (2010). A one-year follow-up study into the course of depression after stroke. *The journal of nutrition, health & aging, 14*(6), 488-493. doi:10.1007/s12603-010-0033-x

Burton, L. J., & Tyson, S. (2015). Screening for mood disorders after stroke: a systematic review of psychometric properties and clinical utility. *Psychol Med, 45*(1), 29-49. doi:10.1017/s0033291714000336

Campbell, B., Mitchell, P., Yan, B., Churilov, L., Ma, H., Parsons, M., . . . Davis, S. (2014). *Extending the Time for Thrombolysis in Emergency Neurological Deficits - Intra-Arterial: The EXTEND-IA Trial* (Vol. 38).

Campbell, B. C., Mitchell, P. J., Kleinig, T. J., Dewey, H. M., Churilov, L., Yassi, N., . . . Davis, S. M. (2015). Endovascular therapy for ischemic stroke with perfusion-imaging selection. *N Engl J Med, 372*(11), 1009-1018. doi:10.1056/NEJMoa1414792

Campbell, B. C. V., Donnan, G. A., Lees, K. R., Hacke, W., Khatri, P., Hill, M. D., . . . Davis, S. M. (2015). Endovascular stent thrombectomy: the new standard of care for large vessel ischaemic stroke. *Lancet Neurol, 14*(8), 846-854. doi:10.1016/s1474-4422(15)00140-4

Ciccone, A., Valvassori, L., & Nichelatti, M. (2011). SYNTHESIS expansion: design of a nonprofit, pragmatic, randomized, controlled trial on the best fast-track endovascular treatment vs. standard intravenous alteplase for acute ischemic stroke. *Int J Stroke, 6*(3), 259-265. doi:10.1111/j.1747-4949.2011.00587.x

Demchuk, A. M., Goyal, M., Menon, B. K., Eesa, M., Ryckborst, K. J., Kamal, N., . . . Hill, M. D. (2015). Endovascular treatment for Small Core and Anterior circulation Proximal occlusion with Emphasis on minimizing CT to recanalization times (ESCAPE) trial: methodology. *Int J Stroke, 10*(3), 429-438. doi:10.1111/ijs.12424

Ewert, T., & Stucki, G. (2007). Validity of the SS-QOL in Germany and in survivors of hemorrhagic or ischemic stroke. *Neurorehabil Neural Repair, 21*(2), 161-168. doi:10.1177/1545968306292255

Franchignoni, F. (2003). *Psychometric properties and practical attributes of the trunk control test in stroke patients* (Vol. 35).

Golicki, D., Niewada, M., Buczek, J., Karlińska, A., Kobayashi, A., Janssen, M. F., & Pickard, A. S. (2015). Validity of EQ-5D-5L in stroke. *Quality of Life Research, 24*(4), 845-850. doi:10.1007/s11136-014-0834-1

Gor-Garcia-Fogeda, M. D., Molina-Rueda, F., Cuesta-Gomez, A., Carratala-Tejada, M., Alguacil-Diego, I. M., & Miangolarra-Page, J. C. (2014). Scales to assess gross motor function in stroke patients: a systematic review. *Arch Phys Med Rehabil, 95*(6), 1174-1183. doi:10.1016/j.apmr.2014.02.013

Goyal, M., Menon, B. K., van Zwam, W. H., Dippel, D. W., Mitchell, P. J., Demchuk, A. M., . . . Jovin, T. G. (2016). Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. *Lancet, 387*(10029), 1723-1731. doi:10.1016/s0140-6736(16)00163-x

Hacke, W., Kaste, M., Bluhmki, E., Brozman, M., Davalos, A., Guidetti, D., . . . Toni, D. (2008). Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. *N Engl J Med, 359*(13), 1317-1329. doi:10.1056/NEJMoa0804656

Heller, A., Wade, D. T., Wood, V. A., Sunderland, A., Hewer, R. L., & Ward, E. (1987). Arm function after stroke: measurement and recovery over the first three months. *J Neurol Neurosurg Psychiatry, 50*(6), 714-719.

Jiang, S., Peng, Y., Jing, C.-h., Fei, A.-h., Wang, H.-r., Gao, C.-j., . . . Pan, S. Endovascular thrombectomy can be beneficial to acute ischemic stroke patients with large infarcts. *Journal of Neurosurgery, 0*(0), 1-8. doi:10.3171/2017.11.jns171297

Jovin, T. G., Chamorro, A., Cobo, E., de Miquel, M. A., Molina, C. A., Rovira, A., . . . Davalos, A. (2015). Thrombectomy within 8 hours after symptom onset in ischemic stroke. *N Engl J Med, 372*(24), 2296-2306. doi:10.1056/NEJMoa1503780

Lees, K. R., Bluhmki, E., von Kummer, R., Brott, T. G., Toni, D., Grotta, J. C., . . . Byrnes, G. (2010). Time to treatment with intravenous alteplase and outcome in stroke: an updated pooled analysis of ECASS, ATLANTIS, NINDS, and EPITHET trials. *Lancet, 375*(9727), 1695-1703. doi:10.1016/s0140-6736(10)60491-6

Luengo-Fernandez, R., Gray, A. M., Bull, L., Welch, S., Cuthbertson, F., & Rothwell, P. M. (2013). Quality of life after TIA and stroke: ten-year results of the Oxford Vascular Study. *Neurology, 81*(18), 1588-1595. doi:10.1212/WNL.0b013e3182a9f45f

Mehrholz, J., Wagner, K., Rutte, K., Meissner, D., & Pohl, M. (2007). Predictive validity and responsiveness of the functional ambulation category in hemiparetic patients after stroke. *Arch Phys Med Rehabil, 88*(10), 1314-1319. doi:10.1016/j.apmr.2007.06.764

Patel, M. D., McKevitt, C., Lawrence, E., Rudd, A. G., & Wolfe, C. D. (2007). Clinical determinants of long-term quality of life after stroke. *Age Ageing, 36*(3), 316-322. doi:10.1093/ageing/afm014

Powers, W. J., Derdeyn, C. P., Biller, J., Coffey, C. S., Hoh, B. L., Jauch, E. C., . . . Yavagal, D. R. (2015). 2015 American Heart Association/American Stroke Association Focused Update of the 2013 Guidelines for the Early Management of Patients With Acute Ischemic Stroke Regarding Endovascular Treatment: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. *Stroke, 46*(10), 3020-3035. doi:10.1161/str.0000000000000074

Rodrigues, F. B., Neves, J. B., Caldeira, D., Ferro, J. M., Ferreira, J. J., & Costa, J. (2016). Endovascular treatment versus medical care alone for ischaemic stroke: systematic review and meta-analysis. *BMJ, 353*. doi:10.1136/bmj.i1754

SAFE. (2017). *The burden of stroke in Europe*. Retrieved from

Saver, J., Goyal, M., Bonafé, A., Diener, H.-C., I Levy, E., Pereira, V., . . . Jahan, R. (2015). *Solitaire™ with the Intention for Thrombectomy as Primary Endovascular Treatment for Acute Ischemic Stroke (SWIFT PRIME) trial: protocol for a randomized, controlled, multicenter study comparing the Solitaire revascularization device with IV tPA with IV t* (Vol. 10).

Saver, J. L., Goyal, M., Bonafe, A., Diener, H. C., Levy, E. I., Pereira, V. M., . . . Jahan, R. (2015). Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke. *N Engl J Med, 372*(24), 2285-2295. doi:10.1056/NEJMoa1415061

Scrivener, K., Schurr, K., & Sherrington, C. (2014). Responsiveness of the ten-metre walk test, Step Test and Motor Assessment Scale in inpatient care after stroke. *BMC Neurol, 14*, 129-129. doi:10.1186/1471-2377-14-129

Taylor-Rowan, M., Wilson, A., Dawson, J., & Quinn, T. J. (2018). Functional Assessment for Acute Stroke Trials: Properties, Analysis, and Application. *Front Neurol, 9*, 191. doi:10.3389/fneur.2018.00191

Ueda, T., Sakaki, S., Kumon, Y., & Ohta, S. (1999). Multivariable analysis of predictive factors related to outcome at 6 months after intra-arterial thrombolysis for acute ischemic stroke. *Stroke, 30*(11), 2360-2365.

van den Berg, L. A., Dijkgraaf, M. G. W., Berkhemer, O. A., Fransen, P. S. S., Beumer, D., Lingsma, H. F., . . . Roos, Y. B. W. E. M. (2017). Two-Year Outcome after Endovascular Treatment for Acute Ischemic Stroke. *New England Journal of Medicine, 376*(14), 1341-1349. doi:10.1056/NEJMoa1612136

Wardlaw, J. M., Murray, V., Berge, E., del Zoppo, G., Sandercock, P., Lindley, R. L., & Cohen, G. (2012). Recombinant tissue plasminogen activator for acute ischaemic stroke: an updated systematic review and meta-analysis. *Lancet, 379*(9834), 2364-2372. doi:10.1016/S0140-6736(12)60738-7

Appendices

- Table 1: eligibility criteria for thrombectomy (based on CT-scan)
- Table 2: ICF classification of outcome measures
- Figure 1: measurement points of the retrospective part
- Figure 2: measurement points of the prospective part
- Table 3: overview of the total clinical follow-up after stroke in ZOL
- Score sheets of the neurological scales used during the study (Dutch)
    - Modified Rankin Scale (mRS)
    - National Institute of Health Stroke Scale (NIHSS)
- Progress report of Master's Thesis

Table 1: Eligibility criteria thrombectomy (based on CT-scan)

Candidate	Ideal	Good	Bad
Time window (time post-stroke)	<6 h	<6h	>6h
Ischemic core volume	ASPECTS 8-10	ASPECTS 5-7	ASPECTS 0-4
Clot (thrombus)	Proximal/Large	Distal/Small	Not visible
Collateral score	Good	Reasonable	No/insufficient

Table 2: ICF classification of outcome measures

Body function (impairments)	**Activities (disabilities)**	**Participation (handicap)**
The National Institute of Health Stroke Scale (NIHSS)	Modified Rankin Scale (MRS)	EuroQoL- 5 Dimensions (EQ-5D-5L)
Motricity Index (MI)	Functional ambulation categories (FAC)	Stroke-Specific Quality of Life scale (SSQOL)
Finger extension (Fugl Meyer)	10-meter walk test (10-MWT)	**Personal factors**
	Trunk Control Test (TCT)	The Hospital Anxiety and Depression Scale (HADS)
	Frenchay Arm Test (FAT)	
	Barthel-Index (BI)	

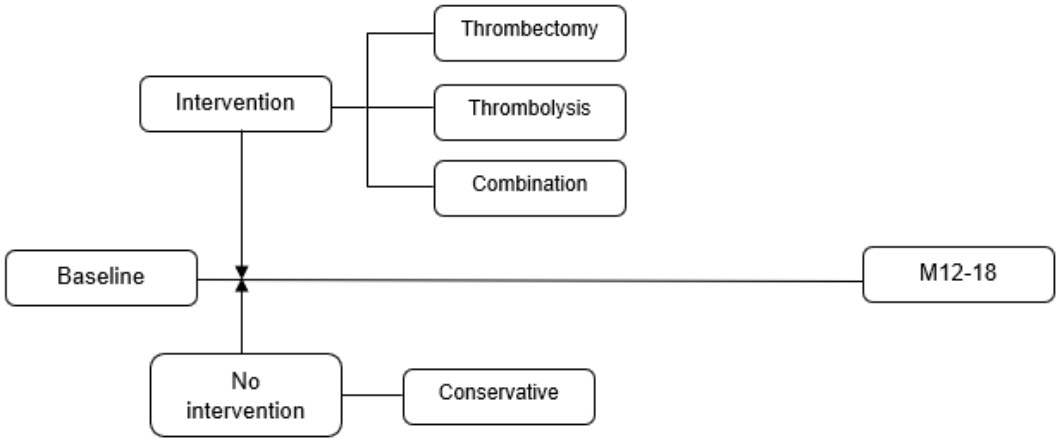

Figure 1: measurement points of the retrospective part

Baseline (neurologist, neuro-radiologist)

- Patient demographics (age, gender)
- Risk factors (family history, hypertension, smoking habit, diabetes mellitus, alcohol and drug abuse)
- Type of stroke (hemorrhagic, ischemic), location of stroke, ASPECT and collateral score (radiologist)
- MRS and NIHSS (neurologist)

M12-18

- Body functions: NIHSS (neurologist), FM, MI
- Activities: mRS (neurologist), BI, FAT, TCT, FAC, 10MWT
- Participation: EQ-5D-5L, SSQOL
- Personal factors: HADS
- Participation in a rehabilitation program post-stroke (setting, frequency, disciplines), education level, marital status

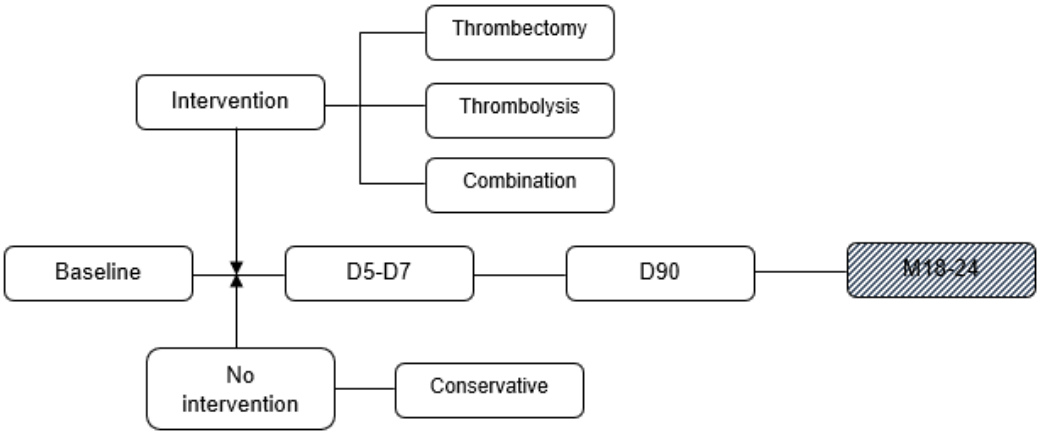

Figure 2: measurement points of the prospective part

Baseline (neurologist, neuro-radiologist)

- Patient demographics (age, gender)
- Risk factors (family history, hypertension, smoking habit, diabetes mellitus, alcohol and drug abuse)
- Type of stroke (hemorrhagic, ischemic), location of stroke, ASPECT and collateral score (radiologist)
- MRS and NIHSS

D5–7

- Body functions: FM, MI
- Activities: FAT, TCT, FAC, 10MWT
- Participation: EQ-5D-5L

D ± 90

- Body functions: NIHSS (neurologist), FM, MI
- Activities: mRS (neurologist), BI, FAT, TCT, FAC, 10MWT
- Participation: EQ-5D-5L, SSQOL
- Personal factors: HADS
- Participation in a rehabilitation program post-stroke (setting, frequency, disciplines), education level, marital status

(M12-18)

- Body functions: NIHSS (neurologist), FM, MI
- Activities: mRS (neurologist), BI, FAT, TCT, FAC, 10MWT
- Participation: EQ-5D-5L, SSQOL
- Personal factors: HADS
- Participation in a rehabilitation program post-stroke (setting, frequency, disciplines), education level, marital status

Table 3: overview of the total clinical follow-up after stroke in ZOL

	Diagnosis stroke	Treatment stroke	After treatment of stroke			
	Baseline	D0	D1-D3	D5-D7	D90	M12-18
Neurologist/neuro-radiologist						
- National institutes of health stroke scale (NIHSS)	X		X		X	X
- Assessment type of stroke (hemorrhagic or ischemic) and location of occlusion	X					
- Treatment of stroke (conservative, thrombolysis and/or thrombectomy)		X				
- Effectiveness of therapy: TICI score			X			
- Infarct volume	X		X			
- Modified Rankin Scale (mRS)	X		X		X	X
Level of body functions						
- Motricity Index (MI) – evaluation strength hemiplegic arm and leg				X	X	X
- Fugl-Meyer (FM) – evaluation finger extension				X	X	X
Level of activities						
- Functional Ambulation Categories (FAC) – evaluation of walking capacity				X	X	X
- Trunk Control Test (TCT) – evaluation trunk stability				X	X	X
- Frenchay Arm Test (FAT) – evaluation arm and hand dexterity				X	X	X
- Barthel Index (BI) – evaluation Activitites of Daily Living (ADL)					X	X
- 10 Meter Walk Test (10MWT) – evaluation of walking speed				X	X	X
Level of participation (evaluation QoL)						
- EuroQol 5 Dimensions 5 Levels (EQ-5D-5L)				X	X	X
- Stroke Specific Quality of Life scale (SSQol)					X	X
Personal factors						
- Hospital Anxiety and Depression Scale (HADS) – evaluation anxiety and depression					X	X
- Education level					X	X
- Living situation (single – living together – care home)				X	X	X
External factors						
- Rehabilitation (setting, frequency, disciplines)					X	X

Modified Rankin Scale (mRS)

- **0** geen symptomen
- **1** geen significante handicap, ondanks aanwezigheid van symptomen; kan alle dagelijks activiteiten en taken uitvoeren
- **2** lichte handicap; niet in staat om alle voorgaande activiteiten uit te voeren, maar kan eigen zaken regelen zonder hulp
- **3** matige handicap; behoeft enige hulp, maar is in staat om zonder hulp te lopen
- **4** matig zware handicap; niet in staat om zonder hulp te lopen en te voorzien in de eigen lichamelijk verzorging zonder hulp
- **5** ernstige handicap; bed gebonden, incontinent en behoeft constante verzorging en aandacht
- **6** Dood

National Institute of Health Stroke Scale (NIHSS)

NIHSS		
Naam patiënt: Geboortedatum: Patiëntnummer:		Datum Tijd Arts
Item	Omschrijving:	Score:
1a Bewustzijn	0 Alert. 1 Niet alert, maar wekbaar met een geringe stimulus. 2 Niet alert, moet herhaaldelijk gestimuleerd worden. 3 Coma (niet wekbaar).	
1b Vraag naar maand en leeftijd	0 Beantwoordt beide correct. 1 Beantwoordt één van beide correct. 2 Beantwoordt niet of beide incorrect.	
1c Vraag de ogen te sluiten en vuist te maken	0 Voert beide opdrachten correct uit. 1 Voert één van beide opdrachten correct uit. 2 Voert geen van beide opdrachten correct uit.	
2 Blikrichting/Oogbewegingen	0 Normaal. 1 Kijkt bij voorkeur naar één kant. 2 Dwangstand	
3 Gezichtsvelden	0 Lijken intact. 1 Gedeeltelijke gezichtsveld uitval/extinctie. 2 Complete halfzijdige gezichtsveld uitval. 3 Blind (bilaterale hemianopsie/corticale blindheid).	
4 Aangezichtsverlamming (vraag wenkbrauwen op te trekken, ogen te sluiten en tanden te laten zien)	0 Normaal/symmetrisch. 1 Lichte asymmetrie, verstreken nasolabiaal-plooi. 2 Totale of subtotale verlamming onderste gelaatshelft. 3 Complete verlamming van oog en mondspieren (een of beide zijden).	

5a Motorische functie - Rechterarm	0 Kan normaal arm uitstrekken (gedurende 10 sec). 1 Arm zakt uit (“drift”). 2 Enige beweging tegen de zwaartekracht. 3 Geen beweging tegen de zwaartekracht (wel aanspanning spieren). 4 Geen beweging. 9 Niet te testen (geef oorzaak aan; b.v. amputatie)	
5b Motorische functie - Linkerarm	0 Kan normaal arm uitstrekken (gedurende 10 sec). 1 Arm zakt uit (“drift”). 2 Enige beweging tegen de zwaartekracht. 3 Geen beweging tegen de zwaartekracht (wel aanspanning spieren). 4 Geen beweging. 9 Niet te testen (geef oorzaak aan; b.v. amputatie)	
6a Motorische functie - Rechterbeen	0 Kan normaal been optillen (30° gedurende 5 sec). 1 Been zakt uit (“drift”). 2 Enige beweging tegen de zwaartekracht. 3 Geen beweging tegen de zwaartekracht (wel aanspanning spieren). 4 Geen beweging. 9 Niet te testen (geef oorzaak aan; b.v. amputatie).	
6b Motorische functie - Linkerbeen	0 Kan normaal been optillen (30° gedurende 5 sec). 1 Been zakt uit (“drift”). 2 Enige beweging tegen de zwaartekracht. 3 Geen beweging tegen de zwaartekracht (wel aanspanning spieren). 4Geen beweging. 9 Niet te testen (geef oorzaak aan; b.v. amputatie).	
7 Ataxie	0 Niet aanwezig. 1 Aanwezig in één arm of één been . 2 Aanwezig in twee of meer ledematen	

8 Sensibiliteit (pijnzin links en rechts vergelijken)	0 Normaal. 1 Verminderd 2 Afwezig.	
9 Taal (laat een plaatje beschrijven en voorwerpen benoemen, zinnen nazeggen)	0 Geen afasie. 1 Lichte tot matig ernstige afasie. 2 Ernstige afasie. 3 Mutistisch of globale afasie	
10 Spraakstoornis/Dysarthrie (woorden laten oplezen)	0 Normale articulatie. 1 Onduidelijke spraak. 2 Ernstige dysarthrie/anarthrie. 9 Niet te testen (tube).	
11 Extinctie en inattentie (visuele en tactiele prikkels tegelijk links en rechts aanbieden)	0 Normaal (niet aanwezig). 1 Inattentie of extinctie voor één soort prikkel. 2 Ernstige hemi-inattentie voor beide prikkels.	
	Totaalscore	

Progress report

UHASSELT

VOORTGANGSFORMULIER WETENSCHAPPELIJKE STAGE DEEL 2

DATUM	INHOUD OVERLEG	HANDTEKENINGEN
5/10	Planning opvolgstudie stroke : ZOL	Promotor: Copromotor: Student(e): Student(e):
23/10	Aanpassingen / tips : instructie - en invulboek stroke studie	Promotor: Copromotor: Student(e): Student(e):
30/01	Vergadering : inclusie prospectieve patiënten te ZOL	Promotor: Copromotor: Student(e): Student(e):
27/02	Feedback : inleiding, methodes.	Promotor: Copromotor: Student(e): Student(e):
16/05	Feedback : a methodes (statistics) & resultaten	Promotor: Copromotor: Student(e): Student(e):
25/05	Feedback : resultaten & discussie.	Promotor: Copromotor: Student(e): Student(e):
		Promotor: Copromotor: Student(e): Student(e):
		Promotor: Copromotor: Student(e): Student(e):
		Promotor: Copromotor: Student(e): Student(e):
		Promotor: Copromotor: Student(e): Student(e):

Auteursrechtelijke overeenkomst

Ik/wij verlenen het wereldwijde auteursrecht voor de ingediende eindverhandeling:
The care of acute stroke: functional outcome and quality of life after different treatment procedures

Richting: **master in de revalidatiewetenschappen en de kinesitherapie-revalidatiewetenschappen en kinesitherapie bij musculoskeletale aandoeningen**
Jaar: **2018**

in alle mogelijke mediaformaten, - bestaande en in de toekomst te ontwikkelen - , aan de Universiteit Hasselt.

Niet tegenstaand deze toekenning van het auteursrecht aan de Universiteit Hasselt behoud ik als auteur het recht om de eindverhandeling, - in zijn geheel of gedeeltelijk -, vrij te reproduceren, (her)publiceren of distribueren zonder de toelating te moeten verkrijgen van de Universiteit Hasselt.

Ik bevestig dat de eindverhandeling mijn origineel werk is, en dat ik het recht heb om de rechten te verlenen die in deze overeenkomst worden beschreven. Ik verklaar tevens dat de eindverhandeling, naar mijn weten, het auteursrecht van anderen niet overtreedt.

Ik verklaar tevens dat ik voor het materiaal in de eindverhandeling dat beschermd wordt door het auteursrecht, de nodige toelatingen heb verkregen zodat ik deze ook aan de Universiteit Hasselt kan overdragen en dat dit duidelijk in de tekst en inhoud van de eindverhandeling werd genotificeerd.

Universiteit Hasselt zal mij als auteur(s) van de eindverhandeling identificeren en zal geen wijzigingen aanbrengen aan de eindverhandeling, uitgezonderd deze toegelaten door deze overeenkomst.

Voor akkoord,

Douwen, Yannick **Moelans, Wim**