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Quality of Life in Stroke Survivors after Local Intra-Arterial Thrombolysis

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Key Words
Stroke · Quality of life · Intra-arterial thrombolysis · Outcome research

Abstract
Background: We aimed to assess quality of life (QOL) and its predictors in stroke survivors after local intra-arterial thrombolysis (IAT) as well as to measure QOL according to the site of pretreatment vessel occlusion. ***Methods:*** From January 2000 to April 2004, 175 consecutive patients underwent IAT for acute ischemic stroke. Clinical and radiological data were collected prospectively. We contacted 135 stroke survivors after a mean of 923 (±431) days, 132 responded. QOL, assessed with EuroQol (EQ-5D), and functional abilities, measured with the modified Rankin Scale (mRS) and the Barthel Index, were compared, and predictors of QOL were analyzed. ***Results:*** Measured with EQ-5D, 56% of the patients reported a good QOL (EQ-5D Index ≥70). Low mRS and high Barthel Index scores at follow-up were associated with better overall QOL (Kendall's tau >0.5). Nevertheless, 25% of the functionally independent patients (mRS 0–2) indicated a markedly impaired QOL (EQ-5D Index <70) and 10% of disabled patients indicated good QOL. QOL was significantly lower in patients with occlusion of the internal carotid artery compared to patients with occlusion of the basilar artery or the M1, M2 or M3/4 segment of the middle cerebral artery (EQ-5D Index: p = 0.005). A high National Institute of Health Stroke Scale score on admission and occlusion of the internal carotid artery were independent predictors of impaired QOL ($p < 0.05$). ***Conclusion:*** More than half of the stroke survivors treated with IAT reported a good QOL, mostly survivors with mild disabilities. QOL assessment gives information that is not provided by traditional outcome scores. Our results support guidelines to measure QOL in stroke research.

Introduction

Little is known about the quality of life (QOL) and social status of stroke survivors after intra-arterial thrombolysis (IAT). All major thrombolysis trials analyzed the outcome 3 months after treatment using the modified Rankin Scale (mRS) and the Barthel Index (BI). mRS and BI capture the gross physical aspects of disability but are insensitive to mild changes after stroke [1–5]. Furthermore, they assess functions like memory, emotion, thinking, communication and social role only marginally, whereas patient-centered outcomes such as QOL are at least as important as functional measures [6]. Guidelines such as the 'Trial Design and Reporting Standards for Intra-Arterial Cerebral Thrombolysis for Acute Ischemic Stroke' of the American Society of Interven-

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tional and Therapeutic Neuroradiology suggest to measure disability and handicap with a QOL scale [7]. Therefore, we measured QOL, functional dependency and social status in stroke survivors after IAT. We analyzed whether QOL differs in patients with different vessel occlusions. In addition, we investigated whether baseline data at hospital admission of stroke predict QOL at long-term follow-up.

Methods

This study is based on the Bernese Stroke Data Bank, which is a systematic prospective registry of consecutive patients with ischemic stroke admitted to a university-hospital-based tertiary stroke center. All patients who underwent IAT from January 2000 to March 2004 were included in this study. IAT was considered in the carotid territory up to 6 h after stroke onset and in basilar artery (BA) occlusion up to 12 h. Some aspects of these patients, inclusion and exclusion criteria for IAT, have been published previously [8–12]. In brief, IAT was performed if: (1) diagnosis of ischemic stroke was established; (2) the baseline National Institutes of Health Stroke Scale (NIHSS) score was ≥4 points or isolated hemianopia or aphasia were present; (3) the time of symptom onset was clearly defined; (4) treatment could be initiated within 6 h from symptom onset, and (5) the patient or his/her family consented to arteriography and potential thrombolysis. The neurological deficit on admission was graded in all patients using the NIHSS score [13].

Pre-existing comorbidities were assessed with the Charlson Comorbidity Index, and vascular risk factors such as hypertension, diabetes, cigarette smoking, hypercholesterolemia, a history of transient monocular blindness, retinal infarction, transient ischemic attack or ischemic stroke were recorded [14, 15]. The Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification was used to categorize stroke subtypes [16]. Arteriograms served to group patients according to the location of their arterial occlusion: (1) internal carotid artery (ICA); (2) main stem of the middle cerebral artery (MCA) (M1); (3) main branch of the MCA (M2); (4) branches of the MCA (M3/4); (5) anterior cerebral artery (ACA); (6) posterior cerebral artery (PCA), and (7) BA. All patients with an ICA occlusion had a concomitant brain infarction, either of the MCA, ACA or both. Collaterals and vessel recanalization were assessed by a neuroradiologist using published criteria [10, 17]. Primary and secondary prevention was performed according to the 'European Stroke Initiative Recommendations for Stroke Management' [18]. Functional outcome was measured using the mRS [4]. Favorable outcome was defined as mRS score ≤2, unfavorable outcome as mRS score ≥3. The BI was used to indicate functional dependency in activities of daily life [5]. A BI score ≥70 was considered as mild to moderate impairment in daily activities, and a BI score <70 meant functional dependency.

QOL was assessed using EuroQol [19]. EuroQol provides a simple profile of health status in several ways. There are questions to assess status in 5 domains (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) with 3 possible categories of response in each domain (no problems, moderate problems, extreme problems) (http://www.euroqol.org/). The resulting health state can be defined by a 5-digit number by combining 1 level from each of the 5 dimensions. According to this classification 243 potential health states can be defined, each of which has been assigned a utility. The 5-digit number can be converted into a single overall score. The single summary index (EQ-5D Index) was obtained according to the EQ-5D visual analogue scale valuation set (range: 3.5–97.7) [20]. The EuroQol also includes a visual analogue scale (EQ VAS, range: 0–100) on which patients rate their own health between 0 (worst imaginable health state) and 100 (best imaginable health state). An EQ-5D Index score ≥70 and an EQ VAS score ≥70 were considered to indicate good QOL, <70 as an impaired QOL. The validity of EuroQol for stroke patients and proxies and for postal follow-up has been shown previously [21, 22]. EuroQol has also been used in randomized controlled trials to assess the impact of a new drug on QOL [23]. Functional outcome and QOL were assessed from July to September 2004 in a cross-sectional survey. If a patient was not able to communicate by phone, e.g. because of aphasia, a caregiver was contacted. In a structured phone interview mRS, BI, residential status, occupation and marital status were assessed [24]. Telephone interviews were performed by a physician, who was experienced in the use of mRS and BI. QOL was assessed with a postal questionnaire (EuroQol) after the phone contact. In addition, we asked whether the patient needed help by their proxies to answer the questions.

Demographic data are given as mean values. The NIHSS score is given as a median value. Correlation between functional outcome and QOL was measured with nonparametric correlations (Kendall's tau). Continuous variables were compared with the t test for normally or the Mann-Whitney U test for not normally distributed variables. Categorical variables were compared with χ^2 and Fisher's exact test, as appropriate. Forward stepwise logistic regression was used to determine the predictors of an impaired QOL. The dependent variable was QOL and dichotomized as mentioned above. A 2-sided p value <0.05 was considered statistically significant.

Results

Baseline Data and Functional Outcome

From January 2000 to March 2004, 175 patients (84 women and 91 men) were treated with IAT using urokinase in our stroke unit. Twenty of the 175 patients (11%) showed an occlusion of the ICA, 74 (42%) of the M1 segment, 33 (19%) of the M2 segment and 18 (10%) of the M3/4 segment of the MCA, 24 (14%) of the BA, 3 (2%) of the ACA and 3 (2%) of the PCA. At follow-up, 135 patients (77%) were alive (mean follow-up: 924 days, standard deviation: 431, range: 159–1,642). The baseline characteristics of the survivors and radiographic findings on admission are given in tables 1 and 2.

Of the 135 survivors, 132 (98%) could be contacted by phone. At follow-up, 117 patients were living at their home, 14 at a nursing home and 1 had been admitted to

a hospital after hip fracture. Nineteen survivors had severe aphasia and were not able to communicate by phone. Before the stroke, 61 patients had been working full-time, 11 part-time, 57 were retired and 3 had been disabled. After the stroke, 18 survivors had resumed full-time employment, 17 part-time, 64 were retired and 33 were disabled. The outcome at follow-up, measured with the mRS is given in figure 1. The BI showed a ceiling effect: 100 of 130 survivors (76.9%) had a score between 90 and 100.

Quality of Life

The EQ-5D was completed by 123 of the 132 survivors (93%), the EQ VAS by 120 (91%). Eighty-two survivors were able to complete the questionnaires without help of their proxies. Assessed with the EQ-5D Index, 69 of 123 patients (56%) showed a good QOL, measured with the

Table 1. Baseline characteristics and radiological findings of survivors (n = 135)

Variable	
Mean age at stroke, years	61 (SD = 13; range = 19–87)
Female	68 (50.3)
Median baseline NIHSS score	14 (range = 3–38)
Vascular risk factors	
Previous TIA/stroke	17 (13)
Elevated cholesterol	50 (37)
Current smoker	23 (17)
Diabetes	15 (11)
Hypertension	73 (54)
Family history of stroke	25 (20)
Mean Charlson Comorbidity Index	0.68 (SD = 1.1)
Etiology (TOAST)	
Cardioembolic	74 (55)
Large-artery disease	15 (11)
Small-artery disease	1 (0.7)
Others	10 (7)
Unknown	35 (26)

Figures are numbers of patients with percentages in parentheses unless otherwise indicated. SD = Standard deviation; TIA = transitory ischemic attack.

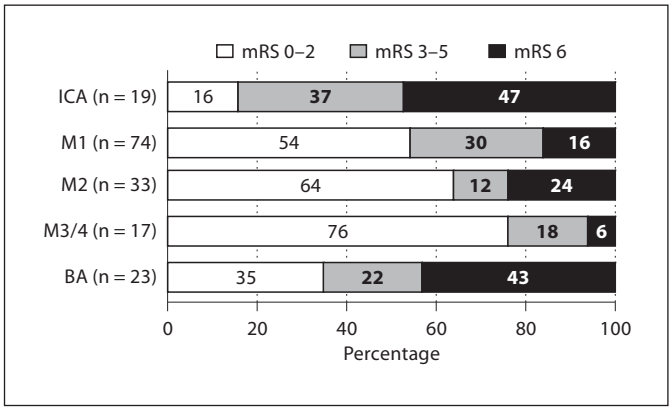

Fig. 1. mRS scores at follow-up in 166 patients after IAT. Three patients were lost to follow-up (1 patient with an occlusion of the BA, 1 with an occlusion of the ICA and 1 with an occlusion of the M3/4 segment of the MCA). The outcome of 3 patients with an occlusion of the PCA and of 3 patients with an occlusion of the ACA is not given because of the small numbers. MCA = Middle cerebral artery; M1 = M1 segment of the MCA; M2 = M2 segment of the MCA; M3/4 = M3/4 segment of the MCA.

Table 2. Radiological findings of survivors (n = 135)

Occluded vessel	Patients	NIHSS		Minutes (mean)	TIMI		Collaterals		ICH	CE
		median	range		0–1	2–3	good	poor		
ICA	11	17	12–25	277	4	7	5	6	0	1
M1	62	15.5	5–24	244	12	50	15	47	3	3
M2	25	14	6–24	261	8	17	11	14	0	0
M3/4	17	10	3–14	254	7	10	8	9	0	0
BA	14	15	6–38	330	4	10	3[a]	10[a]	0	0
ACA	3	12		233	0	3	0	3	0	0
PCA	3	9		314	0	3	1	2	0	0

SD = Standard deviation; minutes = minutes to thrombolysis; TIMI = thrombolysis in myocardial infarction; ICH = symptomatic intracerebral hemorrhage; CE = craniectomy.

[a] Data of 1 patient are missing.

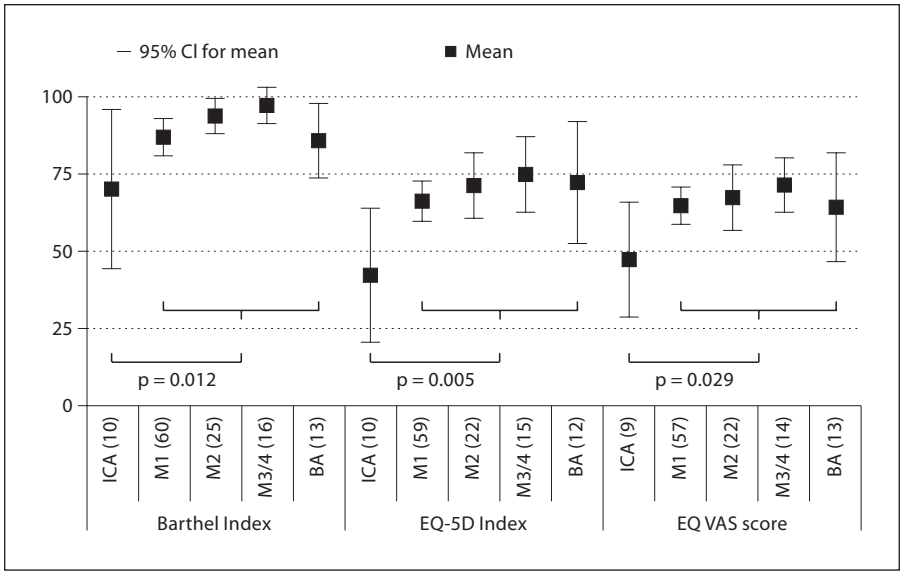

Fig. 2. BI and EuroQol (EQ-5D and EQ VAS) scores in stroke survivors after IAT according to the occluded vessel. BI and EQ VAS score range from 0 to 100, EQ-5D Index from 3.5 to 97.7. A 2-sided p value <0.05 was considered statistically significant. Figures in parentheses are numbers of patients. CI = Confidence interval.

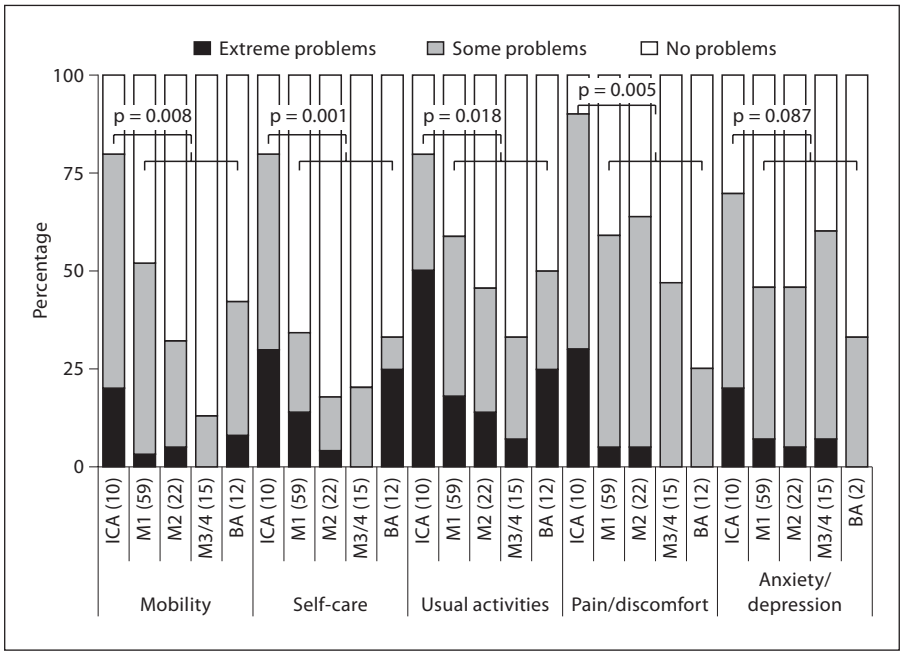

Fig. 3. Subitems of the EuroQol (EQ-5D) according to the occluded vessel. A 2-sided p value <0.05 was considered statistically significant. Figures in parentheses are numbers of patients.

EQ VAS score, 67 of 120 (56%). There was an overall correlation of handicap and QOL ($p < 0.001$): patients with a high mRS score and a low BI score had, measured with both scales, an impaired QOL (Kendall's tau >0.5). Nevertheless, impaired QOL was observed in some patients with a favorable outcome (mRS 0–2): assessed with the EQ-5D Index 22 of 87 (25%), measured with the EQ VAS score 25 of 86 (29%). On the other hand, good QOL was also observed in patients with an unfavorable outcome (mRS 3–5): measured with the EQ-5D Index, 4 of 36 patients (11%) had a good QOL, assessed with the EQ VAS score 6 of 34 (18%).

QOL, measured with the EQ-5D Index and the EQ VAS score, and functional outcome, assessed with the BI, differed among patients with different vessel occlusions (fig. 2). QOL and functional outcome were significantly lower in patients with an occlusion of the ICA compared to patients with an occlusion of the BA or the M1, M2 or M3/4 segment of the MCA (EQ-5D Index: $p = 0.05$, EQ VAS score: $p = 0.029$, BI: $p = 0.012$). QOL was best in pa-

Table 3. Predictors of QOL (multivariate analysis)

Variable	Odds ratio	95% CI	p value
Demographic variables			
EQ-5D Index			
NIHSS on admission	0.904	0.843–0.968	0.004
EQ VAS score			
NIHSS on admission	0.858	0.790–0.933	<0.001
Diabetes	0.242	0.064–0.907	0.035
Radiological findings			
EQ-5D Index			
ICA occlusion	0.190	0.038–0.962	0.045
EQ VAS score			
ICA occlusion	0.205	0.041–1.034	0.055

Demographic variables: variables not in the equation: EQ-5D Index: previous cerebrovascular event, hypercholesterolemia, diabetes, TOAST, marital status; EQ VAS score: Charlson Comorbidity Index, hypercholesterolemia, diabetes, TOAST, marital status, formation, time interval to thrombolysis. Radiological findings: variables not in the equation: EQ-5D Index: collaterals, hyperdense artery sign; EQ VAS score: M3/4 occlusion. EQ-5D Index = EuroQol index; SD = standard deviation; CI = confidence interval.

tients with occlusions of the M3/4 segments of the MCA, intermediate after M2, M1 and BA occlusions and worst after ICA occlusions. Patients with different vessel occlusions did not differ regarding age, sex, comorbidities, vascular risk factors, time to follow-up or proxy assessment ($p > 0.05$). The only significant difference among the 5 groups was the NIHSS score on admission, ICA occlusions having the highest scores. Figure 3 shows the 5 dimensions of the EQ-5D Index. In all items – except for mobility and anxiety/depression – QOL was significantly lower in patients with an ICA occlusion compared to patients with an occlusion of the BA or the M1, M2 or M3/4 segment of the MCA (mobility: $p = 0.08$, self-care: $p = 0.001$, usual activities $p = 0.017$, pain/discomfort: $p = 0.005$, anxiety/depression: 0.087). Patients with more peripherally located occlusions (M3/4) were only slightly affected in the domains mobility, self-care and usual activities but up to 50% of these patients were affected in the domains pain/discomfort and anxiety/depression. The results of multivariate logistic regression analysis are given in table 3. A high NIHSS score on admission and an occlusion of the ICA were independent predictors of an impaired QOL. Diabetes was an independent predictor of an unfavorable outcome, measured with the EQ VAS score but not when measured with the EQ-5D Index.

Discussion

This study analyzes QOL and long-term functional outcome in 132 consecutive stroke survivors, who had been treated with IAT after occlusion of the ICA, MCA, ACA, PCA or BA. Their median NIHSS score on admission was 14, indicating fairly severe strokes. At follow-up more than half of the survivors reported a good overall QOL, mostly survivors with mild disabilities. Two thirds of the survivors were living at their home without assistance.

The results show that the majority of the stroke survivors are coping well with stroke-related impairments and that functional outcome and QOL are not synonymous. The mRS and the BI emphasize functional outcome but do not record the patients' perception. Measured with EQ-5D Index, one fourth of the patients with no, minimal or mild disabilities (mRS 0–2) complained of impaired QOL, whereas >10% of the disabled patients (mRS 3–5) reported a good QOL. Nevertheless, there was an overall correlation of handicap and QOL ($p < 0.001$). Patients with mild disabilities reported a better overall QOL, whereas patients with moderate to severe disability had a lower QOL.

Unlike other QOL studies after stroke this study included only patients who had been treated with IAT. Therefore, the location of arterial occlusion causing the stroke was known in all the patients. QOL and functional outcome differed among survivors with different vessel occlusions, a finding not reported previously: QOL and functional outcome were worst in patients with ICA occlusions and best in patients with M3/4 segment occlusions of the MCA. While patients with more peripheral occlusions (M3/4) complained about 'pain and discomfort' and 'anxiety and depression' in up to 50%, the QOL of the other patients was more likely impaired because of reduced mobility. Functional outcome and QOL in patients with occlusion of the BA were similar to those in patients after IVT thrombolysis [25]. A high NIHSS score on admission and occlusion of the ICA were independent predictors of impaired QOL. This finding is consistent with the NEMESIS study that found a correlation between high NIHSS on admission and impaired QOL as well [26].

Comparisons of our results with other QOL studies in stroke are limited because of the large number of different modes of QOL measurements, inhomogeneous populations and different social and cultural environments. However, the finding of high QOL in the majority of our patients is consistent with other reports indicating that

52–82% of long-term stroke survivors were satisfied with their lives [27].

Furthermore, our results indicate that QOL assessment gives information that is not provided by functional outcome scales such as mRS and BI, though there is an overall correlation between handicap and QOL. A quarter of the survivors with minimal or mild disabilities experienced poor QOL, and 10% of the disabled patients indicated good QOL. The results support statements of current guidelines which suggest to measure QOL in stroke research. In addition, some standardization on how to assess QOL is needed.

A potential limitation of our study is that only two thirds of the survivors were able to complete the questionnaire without help. One third needed help by caregivers. Patients' perception of QOL and caregivers' perception may disagree because proxies tend to report more dysfunction in multiple aspects of QOL than stroke patients themselves [22]. Therefore, the QOL in our patients might be better than assessed. Another limitation is the wide range of follow-up from 5 months to 923 days. However, because most of the changes after stroke occur within a few months and changes after 3 months are mostly small, it is unlikely that this might have biased our results [28, 29]. Because of the wide range of time to follow-up, new and/or other diseases might have influenced QOL in our patients. However, time to follow-up did not differ significantly in patients with different vessel occlusions. Therefore, it seems unlikely that this might have influenced the results.

In conclusion more than half of the stroke survivors after IAT reported a good QOL, mostly survivors with mild disabilities. Nevertheless, some stroke patients with minimal or mild disabilities experienced poor and a few disabled survivors good QOL. NIHSS score on admission and occlusion of the ICA were independent predictors of impaired QOL. Our results indicate that QOL assessment should be incorporated in future trials, which will compare IAT with other treatment modalities.

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