Health-Related Quality of Life Among Young Adults With Ischemic Stroke on Long-Term Follow-Up

Halvor Naess, MD, PhD; Ulrike Waje-Andreassen, MD; Lars Thomassen, MD, PhD; Harald Nyland, MD, PhD; Kjell-Morten Myhr, MD, PhD

Background and Purpose—We sought to compare health-related quality of life (HRQoL) in young adults with ischemic stroke on long-term follow-up with controls and to evaluate HRQoL in clinically relevant patient subgroups.

Methods—HRQoL was determined with the use of the 8 subscales of the Short-Form General Health Survey (SF-36). Subgroups of patients were defined by sex, age, functional status (modified Rankin Scale), marital status, education, depression (Montgomery-Åsberg Depression Rating Scale), and fatigue (Fatigue Severity Scale). SF-36 scores among patients were compared with SF-36 scores among age- and sex-matched controls and SF-36 scores available from the general Norwegian population.

Results—SF-36 scores were obtained after a mean follow-up of 6.0 years among 190 young adults with ischemic stroke during 1988–1997 and among 215 responding controls (55%). The difference in HRQoL between patients, controls, and the general Norwegian population was restricted mainly to the 3 subscales physical functioning, general health, and social functioning (P<0.001). Subgroup analysis showed significantly reduced scores for all SF-36 items among patients who were depressed, suffered from fatigue, or unemployed. Linear regression analysis showed that fatigue and depression were major independent variables correlated with low HRQoL.

Conclusions—Compared with controls and the general Norwegian population, low level of HRQoL among young adults with ischemic stroke was most pronounced in regard to physical functioning. Early identification and treatment of depression, fatigue, and physical disability may potentially improve HRQoL among stroke patients. (Stroke. 2006;37:1232-1236.)

Key Words: case-control studies ■ cerebral infarction ■ quality of life ■ young adults

The outcome of ischemic stroke is more favorable among young than older patients, but morbidity is still significant.1 Follow-up studies have focused on the mortality from and recurrence of ischemic stroke, whereas there are few studies on health-related quality of life (HRQoL) among young adults with ischemic stroke. Young patients with stroke need information on prognosis, including factors related to HRQoL, to make informed choices about vocation and employment. HRQoL should assess at least physical, functional, mental, and social health.2 Furthermore, HRQoL registration should be included to evaluate the effectiveness of healthcare and medical treatment intended to improve HRQoL.3

The primary objective of this study was to evaluate HRQoL among young adults with ischemic stroke on long-term follow-up and to compare the results with those of age- and sex-matched controls and the general Norwegian population. The second objective was to evaluate the HRQoL in clinically relevant subgroups of patients by means of well-established instruments (rating scales). We hypothesized that depression and fatigue are important conditions associated with low HRQoL in young adults with ischemic stroke. Furthermore, we sought to evaluate the possible association between important factors such as stroke location, causation, functional state, education, marital state, and low HRQoL. This study was part of a population-based study of young adults with ischemic stroke in western Norway.

Subject and Methods

Patients

All surviving patients aged 15 to 49 years with first-ever cerebral infarction during 1988–1997 (10 years) living in Hordaland County, western Norway, were invited to a follow-up interview in person. Cases were found by computer search from hospital registries at each of the 5 acute care hospitals in the county. The searching criteria were patients aged 15 to 49 years admitted to either an inpatient or an outpatient department of one of the hospitals during 1988–1997 and discharged with a diagnosis of primary or secondary stroke: categories 430 to 438 of the International Classification of Diseases, Ninth Revision. Cerebral infarction was defined in accordance with the Baltimore-Washington Cooperative Young Stroke Study. The criteria comprised neurological deficits lasting >24 hours because of ischemic lesions or transient ischemic attacks in which CT or MRI showed infarctions related to the clinical findings.4 We excluded...
patients with cerebral infarction associated with other intracranial diseases such as subarachnoid hemorrhage, sinus venous thrombosis, and severe head trauma. The total population comprised 232 patients, 136 men (59%) and 96 women (41%), giving an incidence rate of 11.4 per 100 000 population.6 Twenty-three patients had died at the time of analysis. Haukeland University Hospital is responsible for neurological services in the county, and 95% of the patients were admitted to this hospital (on average, 22 patients per year).

Neurological deficits on admission for the index stroke were classified as none, minor, moderate, and severe.6 Hypertension was defined as treatment with antihypertensive drugs before stroke onset or the introduction of antihypertensive treatment before discharge. Diabetes mellitus was considered present if it was diagnosed before stroke onset (patient on glucose-lowering diet or medication) or during the hospital stay (fasting plasma glucose >7.7 mmol/L). Current smoking at stroke onset was defined as smoking at least 1 cigarette per day. Causation was based on the Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria.7 Stroke location was based on the intracranial artery involved as revealed by the neurological deficit and CT or MRI findings. Information was obtained on recurrent ischemic strokes, education, employment, and marital status. Functional state was assessed with the use of the modified Rankin Scale. Depression was assessed with the use of the Montgomery-Åsberg Depression Rating Scale, which is well validated among patients with stroke,8 and defined as a score >6.9 Fatigue was measured with the Fatigue Severity Scale10 and defined as a score >4.11

Health-Related Quality of Life
HRQoL was measured with the Short-Form General Health Survey (SF-36) at a follow-up visit. The SF-36 consists of 8 subscales: physical functioning, role limitations due to physical problems, bodily pain, general health perceptions, vitality, social functioning, role limitations due to emotional problems, and emotional well-being. Subscales scores range from 0 to 100, with higher values representing better function. The SF-36 has been validated previously in a Norwegian population.12

Controls
Two age- and sex-matched controls were selected randomly from the official population registry in Hordaland County by computer search. Controls born outside Norway were excluded. SF-36 scores were obtained by postal questionnaire. Comparison was also made with the published norms for the SF-36 in a random sample, representative of the general Norwegian population.13

Statistical Analysis
Independent-samples t test was performed for comparison of the mean SF-36 subscale scores between patients and controls. Linear regression analysis was used to investigate the partial correlations between clinically important variables and the subscales of the SF-36 treated as dependent variables. The analysis was performed with the Statistical Package for the Social Science 11.0.1 for Windows.

Results
The mean time to follow-up was 6.0 years (range, 1.4 to 12.3). HRQoL was measured for 190 patients and 215 controls. Of 464 randomly selected controls, 72 were excluded because they were dead, they were born outside of Norway, or their address was unknown. The response rate of controls was 55%, and that of surviving patients was 91%. Table 1 shows demographic data for the patients and the controls. The mean age of the patients on follow-up was 47.8 years and of the controls was 51.5 years.

The patients had significantly lower SF-36 scores on physical functioning (P<0.001), role limitations due to physical health (P<0.001), and social functioning (P<0.001) compared with the controls and the general Norwegian population (Table 2). The differences were <1 SD.

Patients who were depressed, fatigued (Figure), or unemployed had significantly lower scores for all SF-36 subscales. Unmarried patients reported significantly lower scores for all SF-36 subscales except pain (P=0.08). Patients with recurrent ischemic stroke had reduced scores restricted to role limitation due to physical health (P=0.03).

Except vital functioning, which was significantly lower among women (P=0.04), SF-36 subscale scores did not differ by sex. Patients older and younger than 40 years did not differ except for lower scores on physical functioning among patients with cerebral infarction associated with other intracranial diseases such as subarachnoid hemorrhage, sinus venous thrombosis, and severe head trauma. The total population comprised 232 patients, 136 men (59%) and 96 women (41%), giving an incidence rate of 11.4 per 100 000 population.6 Twenty-three patients had died at the time of analysis. Haukeland University Hospital is responsible for neurological services in the county, and 95% of the patients were admitted to this hospital (on average, 22 patients per year).

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### Table 1. Demographic and Clinical Data Among 190 Young Adults With Ischemic Stroke and 215 Controls

<table>
<thead>
<tr>
<th></th>
<th>Patients, %</th>
<th>Controls, %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Women</strong></td>
<td>43</td>
<td>47</td>
</tr>
<tr>
<td><strong>Age &lt;40 y at stroke onset</strong></td>
<td>29</td>
<td>...</td>
</tr>
<tr>
<td><strong>Anterior circulation</strong></td>
<td>62</td>
<td>...</td>
</tr>
<tr>
<td><strong>Cause</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac embolism</td>
<td>7</td>
<td>...</td>
</tr>
<tr>
<td>Small-vessel disease</td>
<td>14</td>
<td>...</td>
</tr>
<tr>
<td>Atherosclerosis</td>
<td>14</td>
<td>...</td>
</tr>
<tr>
<td>Dissection</td>
<td>7</td>
<td>...</td>
</tr>
<tr>
<td>Prothrombotic state</td>
<td>8</td>
<td>...</td>
</tr>
<tr>
<td><strong>Risk factors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>11</td>
<td>3</td>
</tr>
<tr>
<td>Hypertension</td>
<td>36</td>
<td>18</td>
</tr>
<tr>
<td>Ever smoked</td>
<td>74</td>
<td>59</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>Angina pectoris</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Intermittent claudication</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td><strong>Follow-up</strong></td>
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<td></td>
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<tr>
<td>Employed</td>
<td>58</td>
<td>87</td>
</tr>
<tr>
<td>Modified Rankin Scale score ≤2</td>
<td>87</td>
<td>...</td>
</tr>
<tr>
<td>Depression</td>
<td>28</td>
<td>...</td>
</tr>
<tr>
<td>Fatigue</td>
<td>52</td>
<td>...</td>
</tr>
<tr>
<td>Recurrent ischemic stroke</td>
<td>9</td>
<td>...</td>
</tr>
</tbody>
</table>

### Table 2. SF-36 Subscores in Young Adults With Ischemic Stroke and 215 Controls

<table>
<thead>
<tr>
<th></th>
<th>Patients</th>
<th>Controls</th>
<th>General Population</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, y</strong></td>
<td>47.8 (mean)</td>
<td>51.5 (mean)</td>
<td>40–49</td>
</tr>
<tr>
<td>Physical functioning</td>
<td>78</td>
<td>89‡</td>
<td>90‡</td>
</tr>
<tr>
<td>Role–physical</td>
<td>62</td>
<td>78‡</td>
<td>85‡</td>
</tr>
<tr>
<td>Bodily pain</td>
<td>75</td>
<td>78</td>
<td>77</td>
</tr>
<tr>
<td>General health</td>
<td>67</td>
<td>73‡</td>
<td>79‡</td>
</tr>
<tr>
<td>Vitality</td>
<td>57</td>
<td>61*</td>
<td>62†</td>
</tr>
<tr>
<td>Social functioning</td>
<td>79</td>
<td>87‡</td>
<td>87‡</td>
</tr>
<tr>
<td>Role–emotional</td>
<td>80</td>
<td>82</td>
<td>87*</td>
</tr>
<tr>
<td>Mental health</td>
<td>80</td>
<td>80</td>
<td>79</td>
</tr>
</tbody>
</table>

*P<.05; †P<.01; ‡P<.001.
SF-36 subscale scores among young adults with ischemic stroke at long-term follow-up vs controls and divided into subgroups defined by depression, functional state, and fatigue. pf indicates physical functioning; rp, role–physical; bp, bodily pain; gh, general health; vt, vitality; sf, social functioning; re, role–emotional; mh, mental health; mRS, modified Rankin Scale; and FSS, Fatigue Severity Scale. *P<0.05; **P<0.01; ***P<0.001.
those older than 40 years ($P = 0.02$). Except physical functioning, which was reduced among patients with less education ($P = 0.01$), educational level did not influence SF-36 subscale scores.

Table 3 shows the results of linear regression analysis, with scores on the SF-36 subscales as the dependent variables. Fatigue was independently associated with scores on all SF-36 subscales except for role limitation due to emotional problems ($P = 0.09$). Depression was independently associated with all SF-36 subscales except physical functioning ($P = 0.16$), role limitation due to physical problems ($P = 0.49$), and bodily pain ($P = 0.28$). The SF-36 scores were not influenced by stroke causation or stroke location.

**Discussion**

The differences between patients and controls or the general Norwegian population were <1 SD in all subscale scores, indicating that ischemic stroke has only moderate effects on self-reported HRQoL among young adults with ischemic stroke as a group. The largest differences were related to physical functioning and thus related to physical disability from the stroke. This indicates that intensive physical therapy has a potential for important improvement of HRQoL after ischemic stroke. Smaller but significant differences were also found in general health and social functioning. There were no differences in pain and emotional well-being, but a small difference in role limitations due to emotional problems was found only between patients and the general Norwegian population. There was a trend toward slightly reduced energy among the patients.

Subgroup analysis showed differential impact on HRQoL among the patients. Clinically significant reduction of HRQoL was associated with functional dependence, unemployment, being unmarried, depression, and fatigue.

Linear regression showed that fatigue was independently associated with low scores on all SF-36 subscales except role limitation due to emotional problems. Fatigue was especially associated with low scores on the physical health items of SF-36. Fatigue was more strongly correlated with low HRQoL than the functional score (modified Rankin Scale score). This demonstrates the impact of fatigue on stroke, in accordance with other studies$^{14}$ that have shown fatigue to be associated with stroke independent of depression. We have previously shown that fatigue is more frequent among stroke patients than controls.$^{15}$ Thus, more research is needed to shed light on the mechanisms causing fatigue in order to treat this important condition.

Depression was independently associated with low HRQoL in all dimensions except those related to physical function and pain. Because depression is treatable, early diagnosis is important. Our finding shows that successfully treating depression has the potential to greatly improve HRQoL among depressed young adults with ischemic stroke. Other studies$^{16–18}$ have reported a close association between depression and low HRQoL among older patients with stroke. Treating depression has been reported to improve outcome after stroke.$^{19}$

Unmarried patients had lower HRQoL than married patients. This result contrasts with another study including older patients with stroke in which being married was associated with lower HRQoL.$^{17}$

The SF-36 subscale scores did not differ by age or sex on linear regression. This differs from results in older patients, among whom a study showed lower scores among women for all subscales.$^{20}$

HRQoL has been little studied in young adults with ischemic stroke. In accordance with our findings, a previous study showed that low HRQoL at a mean of 32 months after stroke onset was independently associated with neurological deficits, depression, and unemployment.$^{21}$ Another study showed that HRQoL was not associated with stroke subtypes,$^{1}$ which is also compatible with the present study.

A potential bias is that only 55% of the controls responded. However, this response rate is similar to other studies using comparable designs.$^{22–24}$ It might be speculated that the healthiest controls did not respond, thus reducing the differences between patients and controls. However, the distribution of diseases such as diabetes mellitus, hypertension, and migraine corresponded to the frequencies in the general population, suggesting that the controls were representative.$^{25,26}$ The SF-36 subscore differences between the controls and the general Norwegian population were minor, indicating that the controls were representative.
A limitation of our study was that we had no data on the time course of HRQoL in our patients. Future studies should compare HRQoL in the early poststroke phase and at long-term follow-up to disclose factors associated with persistent low HRQoL. It is possible that the subscale scores of the SF-36 are differentially dependent on the time course.

The SF-36 is a generic scale. The advantages of generic scales are that they are applicable to patients with different conditions and the general population. Thus, it is possible to make comparisons and evaluate clinical relevance. However, stroke-specific measures such as the Stroke-Specific Quality of Life Scale and the Impact Stroke Scale may add important information, for example, on the impact of time course on HRQoL, and should be included in future studies.

### Summary

Young adults with ischemic stroke differed only moderately from controls and the general Norwegian population in HRQoL. However, subgroup analysis showed marked reduction in HRQoL among the patients who were functionally dependent, depressed, unmarried, or unemployed. Furthermore, fatigue seems to be an important independent predictor of low HRQoL. Thus, early identification and improved therapy for conditions such as depression, fatigue, and physical disability may improve HRQoL among young adults with ischemic stroke.

### Acknowledgments

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### References

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