One-year outcome after first-ever stroke according to stroke subtype, severity, risk factors and pre-stroke treatment. A population-based study from Tartu, Estonia

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The aim of the current study was to evaluate the outcome at 1 year following a first-ever stroke based on a population-based registry from 2001 to 2003 in Tartu, Estonia. The outcome of first-ever stroke was assessed in 433 patients by stroke risk factors, demographic data and stroke severity at onset using the Barthel Index (BI) score and the modified Rankin Score (mRS) at seventh day, 6 months and 1 year. Female sex, older age, blood glucose value >10 mmol/l on admission and more severe stroke on admission were the best predictors of dependency 1 year following the first-ever stroke. At 1 year, the percentage of functionally dependent patients was 20% and the survival rate was 56%. The use of antihypertensive/antithrombotic medication prior to stroke did not significantly affect the outcome. The survival rate of stroke patients in Tartu is lower compared with other studied populations. The outcome of stroke was mainly determined by the initial severity of stroke and by elevated blood glucose value on admission. Patients with untreated hypertension had more severe stroke and trend for unfavourable outcome compared with those who were on treatment.

Introduction

Stroke is a disease, which often has serious consequences and affects the life of the patient in many different ways. While doctors concentrate mainly on the medical aspects of a disease, the outcome remains the most important issue for the patient. Impairments are defined as organic dysfunctions, disabilities a patient’s difficulty with activities of daily living (ADL) and handicap as limitations in the fulfilment of a role that is normal for that individual [1]. The most frequently used scales of disability and handicap, used in clinical trials, are the Barthel Index (BI) and the modified Rankin Scale (mRS) respectively [2–4]. These scales are easy to complete and they have shown good inter-observer agreement.

The case-fatality rate at 1 month shown by the two previous population-based studies in Tartu, Estonia, has been high (49% and 30% respectively) [5]. The hypothesis for the current study was that stroke may be more severe in Estonia compared with other countries resulting in a worse outcome. The aim of the study was to evaluate the outcome during 1 year following the first-ever stroke, to analyse its relation to different stroke subtypes, severity of stroke and determine the factors predicting outcome after a stroke using a population-based design.

Subjects and methods

The data from the Third Stroke Registry in Tartu, Estonia (from 01.12.2001 to 30.11.2003), were used [6,7]. Tartu is the second largest town in Estonia with a population of 101 122 inhabitants [8]. The study area is served by the Department of Neurology and Neurosurgery of the University Clinics of Tartu. The proportion of people ≥65 years of age amongst the study population is 14%. All patients living in Tartu, who received the diagnosis of first-ever stroke, were registered. Out-of hospital cases were prospectively registered using information from general practitioners, emergency department, death certificates and autopsy protocols. The diagnosis of stroke was based on clinical evaluation, using the WHO criteria, as ‘rapidly developing clinical signs of focal (or global) disturbance of cerebral function of presumed vascular origin, lasting more than 24 h or leading to death’. Cases of subarachnoid haemorrhage (SAH) were excluded from the current analysis. The detailed overview of case ascertainment and other used methods have been described previously [6,7].

Stroke was divided into brain infarction and intracerebral haemorrhage (ICH), according to computerized tomography (CT) findings. If the CT scan was not done, the stroke subtype was considered as ‘not classified’ (NC). Stroke risk factors (hypertension, atrial...
fibrillation, ischaemic heart disease, diabetes mellitus and smoking) were registered according to pre-stroke medical documents or case-history and/or clinical evaluations at the hospital. In addition, a risk factor was documented when the patient was known to be on treatment due to the comorbidity. The cut-off point of hypertension was \( >140/90 \text{mmHg} \). In addition, hypertension was diagnosed when the elevated blood pressure was stable at three measurements during the first post-stroke week. Atrial fibrillation was confirmed by electrocardiogram on admission. The diagnosis of diabetes was based on patient’s medical documentation or if the blood glucose values remained \( >10 \text{mmol/l} \) after a week following the stroke. Smoking was considered as a risk factor only in current smokers. The pre-stroke use of antithrombotic and/or anticoagulant treatment was also registered.

Outcome was assessed using BI score 0–20 [3] on the seventh day in hospital, 6 and 12 months after stroke. At 6 and 12 months following the stroke, the BI was sent by mail to the surviving patient’s home as a questionnaire. Severity of disability was determined by classification of patients as very severely disabled (BI = 0–4), severely disabled (BI = 5–9), moderately disabled (BI = 10–14) or mildly disabled (BI = 15–19) [3]. If the patient did not respond to the first mailed questionnaire, a second letter was sent.

The pre-stroke handicap was measured with the mRS score 0–5. The data were collected from patients, their relatives and/or medical documentation. Handicapped patients were defined as the mRS 3–5. The mRS scores were also evaluated on the seventh day in hospital, 6 and 12 months after stroke. All mRS assessments were made by the study physician, and at 6 and 12 months following the stroke, the scores were set according to the BI reported by the patients. The Scandinavian Stroke Scale (SSS) [9] was used to assess neurological deficit on admission (SSS0) and on the seventh day in hospital (SSS7).

The 1-year survival was analysed using outcome data provided by the patients and by the National Population Registry. In the acute phase of stroke, BI, mRS and SSS were registered only for the hospitalized patients. The study is approved by the Ethics Review Committee on Human Research of the University of Tartu.

### Statistical methods
Confidence intervals (CI) for the probability of death within 6 months and 1 year after the stroke were calculated assuming binomial distribution. The influence of prognostic factors, on the probability of death within 6 months (or year) after the stroke, was assessed by means of logistic regression. A stepwise selection procedure was used to obtain a most parsimonious model. The chi-squared test, or Wilcoxon rank sum test, was used when analysing the difference between subgroups. The survival of patients 1 year following stroke was analysed using the Kaplan–Meier survival analysis method. Mean values presented are followed by standard deviation (SD) in parentheses. Analysis was done with S-Plus 6.2 [10] and R [11].

### Results
Of a total of 451 patients in the registry, 18 patients with the diagnosis of SAH were excluded and thus the data of 433 patients were used in the outcome analysis. The basic characteristics of patients included are shown in Table 1. Three hundred and seventy-seven (87%) patients were hospitalized. Hypertension was diagnosed in 61% of patients, whereas 42% of them had not used antihypertensive treatment prior to stroke. Eighty-five (20%) patients used antithrombotic treatment before stroke, and none of the patients was on anticoagulant treatment.

The SSS0 score for the patients with ICH was significantly lower compared with the patients having brain infarction \( (\chi^2 = 14.3; P < 0.001) \). The SSS0 score for the patients with hypertension not using antihypertensive medication prior to stroke was significantly lower compared with those who had used antihypertensive medication \( (27.9 \text{ vs. } 34.9 \text{ points respectively}; P < 0.001) \). Patients who had used antithrombotic treatment prior to stroke had higher SSS0 values, but the difference compared with non-users was not statistically significant \( (P = 0.09) \). Other registered risk factors were non-significantly related with stroke severity. The mean length of hospital stay was 8.6 days. Fifty per cent of patients were discharged

### Table 1 Basic characteristics of patients included in the stroke outcome study in Tartu, Estonia in 2001–2003

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>n (%)</th>
</tr>
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<tbody>
<tr>
<td>Patients included</td>
<td>433</td>
</tr>
<tr>
<td>Men, n (%)</td>
<td>176 (41)</td>
</tr>
<tr>
<td>Women, n (%)</td>
<td>257 (59)</td>
</tr>
<tr>
<td>Mean age (all patients), y ± SD</td>
<td>72 ± 12.1</td>
</tr>
<tr>
<td>Brain infarction, n (%)</td>
<td>332 (77)</td>
</tr>
<tr>
<td>ICH, n (%)</td>
<td>57 (13)</td>
</tr>
<tr>
<td>NC, n (%)</td>
<td>44 (10)</td>
</tr>
<tr>
<td>Stroke risk factors, n (%)</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>264 (61)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>130 (30)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>61 (14)</td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>160 (37)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>30 (7)</td>
</tr>
</tbody>
</table>

ICH, intracerebral haemorrhage; NC, not classified.
home from the hospital, 29% were transferred to rehabilitation departments and/or long-care departments, 5% moved to other departments of the same hospital and 16% died in the hospital.

**Outcome**

The 267 patients, surviving the first 6 months, and 246 patients, surviving 1 year after stroke, were followed up using a BI questionnaire. The proportion of patients who responded to the questionnaire was 82% at 6 months and 80% at 1 year following stroke. The mean age, sex and the severity of stroke of responders and non-responders were not significantly different. The non-responders were more frequently (30% vs. 6%) patients with NC type of stroke (i.e. non-hospitalized patients).

**Functional ability (BI)**

Functional dependency of the patients according to the BI score at different time-points is shown on Fig. 1 (survivors and non-survivors). Logistic regression models were used to determine the risk of dependency (BI score < 20) at 1 year after the stroke. The final multivariate model included female sex (OR = 2.47; 95% CI 1.12–5.44), older age (OR = 3.53; 95% CI 1.56–7.96), blood glucose value > 10 mmol/l on admission (OR = 2.1; 95% CI 1.1–4.6; P = 0.02) and lower SSS (OR = 0.92; 95% CI 0.86–0.98) as the best predictors of dependency 1 year following the first-ever stroke. Other risk factors (atrial fibrillation, diabetes, hypertension, smoking, previous transient ischaemic attack) and stroke subtypes did not have significant influence on post-stroke disability. The chi-squared test showed that disability was more profound amongst the patients ≥ 65 years for both follow-up periods (P < 0.001).

**Handicap (mRS)**

The proportion of patients with favourable outcome (mRS 0–2) at 1 year according to different stroke subtypes is shown in Table 2. The mRS score 3–5 before stroke significantly increased the odds of higher mRS score 6 months after the stroke (OR = 11.9; 95% CI 1.4–98.8). Also, the patients in the mRS group 3–5 before stroke had higher probability of death compared with the patients in the group of 0–2 (OR = 3.7; 95% CI 1.6–8.5). The level of handicap of patients, according to the mRS score at different time-points, is shown on Fig. 2 (survivors and non-survivors).

**Survival**

Sixty-five men and 120 women had died at 1 year after stroke occurrence and the overall probability of death was 0.44 (95% CI 0.39–0.48). The survival rates at 1 year (according to stroke subtypes) following stroke are shown in Table 2.
are shown in Table 2. The survival rates for different stroke subtypes were not statistically significant. The odds for death were 1.38 times higher for patients with hypertension not using antihypertensive medication prior to stroke, but the finding did not reach statistical significance ($P = 0.23$). The odds for death for patients using antithrombotic treatment prior to stroke was also not significant ($OR = 0.92; P = 0.8$).

**Discussion**

We have analysed the factors determining the outcome and 1-year survival rates of first-ever stroke. The strength of our study is a population-based design, prospective stroke subtyping according to CT findings, assessment of stroke severity and use of well-defined outcome measures. The outcome of first-ever stroke in Estonia has also been evaluated earlier for the period of 1991–1993 [5].

The survival data are analysed including all 433 patients. The proportion of responders to the follow-up questionnaire was 82% at 6 months and 80% at 1 year. Unfortunately, the incomplete response rate is not very rare in population-based studies [12,13], but these studies characterize the outcome of all stroke patients from a community rather than only a certain group of hospitalized patients. No differences were found between responders and non-responders in our study and thus, we suppose that the results represent the whole sample of the patients.

Our registry consists of somewhat younger patients compared with other community-based stroke populations studied [14–17], but still the percentage of atrial fibrillation, which is usually known to have more prevalent amongst the elderly, was 30%. The rest of the risk factor profile was comparable with other population-based studies evaluating the outcome of stroke [12,15,16,18]. A recent study from USA has shown that pre-stroke use of antiplatelet agents results in less severe incident stroke [19]. This trend was also confirmed in our study, but it did not reach statistical significance. However, we found that patients with hypertension using antihypertensive medication prior to stroke had significantly less severe stroke and a trend for more favourable outcome was observed. To our knowledge, we are the first reporting this association.

It could be expected that a higher number of risk factors in individual patients should influence stroke outcome, but this was not confirmed in our sample. We have used the modified version of BI [3]. The same method has been used in the previous study [5]. It has been shown that evaluating ADL is reliable either by telephone interview or by postal questionnaire [20].

Favourable outcome (BI score 20) at 6 months amongst those who responded to the questionnaire was found for 25% of patients in our study, 38% in the previous study from Tartu (1991–1993) [5] and 49% in the Australian registry [12]. The lower proportion of patients with favourable outcome in Tartu (both in 1991–1993 and 2001–2003) and lower survival rates at 1 year compared with Australian registry (54%, 56% and 63% respectively) could be associated with more severe stroke in Estonia.

The proportion of survived patients with favourable outcome according to mRS score in our study was 69% compared with 70% in the Greek registry [16] and 74% in the UK study [15]. However, the percentage of handicapped patients is somewhat lower compared with others [15,17]. We speculate that more severe stroke patients just die because of insufficient rehabilitation possibilities, while those who survive are not so dependent of outside care.

The predictors of dependency following stroke were older age, female sex, higher blood glucose levels on admission and more severe stroke. Similar results have been reported in some other studies [5,16–17]. The probability of death at 1 year is comparable with the previous study from Tartu [5], but is somewhat higher than in other centres [12,16–18,21]. The higher death rate at 1 year can partially be explained by more fatal stroke cases at acute stage [7].

The 1-year survival rates for first-ever stroke patients range from 63% [16,22] to 86% [18]. Both the mean age of patients in our study and the median 1-year survival rate is lower (56%) compared with other studies [16,18,22]. In addition, the outcome of younger patients is also worse compared with other studies. A Norwegian study [23] of young ischaemic stroke patients aged 15–49 years reported that long-term (mean time 5.7 years) favourable outcome (mRS ≤2) was 79%. The authors conclude, that although the majority had favourable functional outcome, cerebral infarction had major long-term impact on young adults as evaluated by mortality, recurrence and employment status. The corresponding mRS rate in our sample at 1 year was only 58%.

Recent studies from China [18], also Greece [16] and Swedish [17] registries, have shown significant differences in 1-year survival of different stroke subtypes. This trend was also seen in our sample, but the differences did not reach statistical significance, probably due to the small number of cases (Table 2).

Although there are no comparative data, we still suggest, that stroke is more severe in Estonia (lower proportion of independent patients and lower survival rate at 1 year). It can be speculated that according to our results, intensive treatment of blood pressure and
anticoagulant use for patients with atrial fibrillation before stroke not only can decrease the incidence, but can also reduce the stroke severity and thereby improve the outcome of stroke. The fact that none of our 451 patients in the registry was on anticoagulants is surprising, but shows clearly that this might be the main shortage in the primary prevention of stroke in Tartu. The use of anticoagulation can increase the number of ICHs with bad prognosis, but the improvement of overall outcome of stroke should probably overweight this risk. Moreover, cardioembolic strokes are usually severe and have worse outcome compared with other subtypes of stroke [24]. The functional independency after stroke is achieved with qualified acute therapy and especially with an adequate rehabilitation programme. However, the goal is to prevent stroke from happening, and therefore it is necessary to intensify the primary prevention of stroke.

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