Future Demographic Trends Decrease the Proportion of Ischemic Stroke Patients Receiving Thrombolytic Therapy
A Call to Set-Up Therapeutic Studies in the Very Old

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Background and Purpose—Thrombolytic therapy with tissue plasminogen activator (tPA) is rarely applied to ischemic stroke patients aged 80 years and above. As future demographic trends will increase the proportion of older stroke patients, the overall tPA treatment rate may decrease. The aim of the present analysis was to provide an estimate of the future number of ischemic stroke patients and the fraction thereof receiving tPA.

Methods—In 2005, n=12,906 hospitalized ischemic stroke patients were included into a large registry covering the Federal State of Hesse, Germany. Age- and gender-specific frequency rates for ischemic stroke and tPA therapy were calculated based on the registry and the respective population data. Population projections until 2050 were derived from the Hessian Bureau of Statistics.

Results—Assuming constant age- and gender-specific stroke incidence rates and treatment strategies, the total number of ischemic stroke patients will rise by approximately 68% until 2050, whereas the proportion of tPA-treated ischemic stroke patients will decrease from 4.5% to 3.8% in the same time frame (relative decrease 16%; \( \chi^2 P<0.001 \)).

Conclusions—Future demographic changes will reduce tPA treatment rates. Therapeutic studies focusing on very old stroke patients are necessary to counteract this trend. (Stroke. 2009;40:1900-1902.)

Key Words: cerebral infarct • thrombolysis • elderly • demographics

Future demographic trends will increase the proportion of seniors in many countries around the world. In the European Union, 30% of the population are estimated to age 65 years or more in 2050, compared to 16% in 2000.\(^1\) In particular, the proportion of very old individuals (≥80 years) is expected to grow. For Germany, an increase from 4% in 2000% to 15% in 2050 is projected for this age category.\(^2\) In parallel to these demographic changes, the number of very old stroke patients is likely to rise.

Thrombolysis with recombinant tissue plasminogen activator (tPA) is an effective acute treatment for patients with ischemic stroke.\(^3\) However, tPA-therapy is rarely applied to stroke patients older than 80 years.\(^4\) Based on data from a large stroke registry and the population projection for the Federal State of Hesse in Germany, this analysis aimed to provide an estimate for both the future number of ischemic stroke patients and the fraction thereof receiving thrombolytic treatment.

Methods

The Stroke Registry
Our analysis relies on a prospective quality assurance measure covering the entire Federal State of Hesse, Germany. All hospitalized patients with a final diagnosis of acute (ie, time span between symptom onset and admission ≤7 days) transient ischemic attack (TIA, ICD-10:G45), ischemic stroke (IS, I63), or intracerebral hemorrhage (ICH, I61) should be documented.\(^5,6\) For the present analysis, we chose datasets with a patient admission date between January 1 and December 31, 2005 and a diagnosis of ischemic stroke. Both patients with first-ever and recurrent strokes were included. Datasets with missing information on age and sex were excluded.

Statistical Analysis
For the year 2005, age- and gender-specific frequency rates for hospitalized ischemic stroke were calculated as ratios of the number of patients in the registry and the respective number of people in the general population. Similarly, frequency rates were calculated for patients receiving thrombolytic treatment. Based on these frequency rates and the population projection for Hesse provided by the Official Bureau of Statistics,\(^7\) we estimated both the total number of ischemic stroke patients and the proportion thereof receiving thrombolysis for the year 2050.

Results
In 2005, n=12,921 hospitalized patients with ischemic stroke were documented, and n=12,906 fulfilled the criteria for being included into the present analysis (for baseline charac-
teristics see Table 1). Assuming constant age- and gender-specific stroke incidence rates, the number of ischemic stroke patients per year will rise to around 22,000 until 2050 (68%, see Table 2). Within that time frame, the proportion of patients younger than 65 years will halve from 20% to 10%, whereas the proportion of patients above the age of 74 years will increase from 53% to 73% (see Figure).

In 2005, n=577 stroke patients were coded as having received thrombolysis. The proportion of tPA-treated patients on all ischemic stroke patients was high in the age group between 35 and 44 years (9.7%), but dropped with increasing age (65 to 74 years 4.9%, 75 to 84 years 4.5%, and 84 years 1.8%). According to our projection model, the number of patients receiving thrombolysis will rise to n=822 for the year 2050 (42%). Hence, the proportion of tPA-treated patients among all ischemic stroke patients will drop from 4.5% in 2005 to 3.8% in 2050 (relative decrease 16%; for comparing expected and observed frequencies: P<0.001).

### Discussion

Future demographic changes will increase the total number of ischemic stroke patients. If current treatment strategies according to age remain unchanged, a reduction of the proportion of tPA treated patients among all ischemic stroke patients has to be expected.

Why do very old stroke patients often not receive thrombolytic therapy? The large randomized tPA trials tended to disregard very old stroke patients. Both ECASS studies excluded patients above the age of 80 years. The NINDS stroke study did not define an upper age limit, but only 42 patients aged above 80 years were included. Thus, our knowledge about safety and efficacy of tPA therapy is limited for this age group. Some observational studies have tried to evaluate functional outcome and safety in very old stroke patients treated with tPA. However, the results are heterogeneous, and treatment recommendations cannot be derived from these investigations. In consequence, tPA therapy is not established for stroke patients over 80 years of age.

In the future, there will be an increasing divergence between the age span covered by the randomized tPA trials (eg, NINDS study, mean age 67±10 years) and the age distribution of real-life stroke populations. According to our projection, 90% of ischemic stroke patients will be 65 years or older in 2050, 73% will be above the age of 74 years, and 37% above the age of 84 years. Similar to primary and secondary prevention trials that have focused on the elderly, new therapeutic studies for very old stroke patients are needed. The currently ongoing Third International Stroke Trial (IST-3) may be considered as a first approach to fill this gap of knowledge. Based on age-related uncertainties whether to apply thrombolytic therapy or not, many very old stroke patients may qualify for study inclusion.

Our analysis has limitations. The prognostic model focused on evaluating the impact of demographic changes on the number of hospitalized ischemic stroke patients and tPA therapy. Thus, constant age-specific stroke incidence rates are assumed. If incidence rates decrease in the future, we may have overestimated the number of patients. Furthermore, despite being older on average, future stroke patients may present with a lesser degree of comorbidity, making them more likely to be considered eligible for tPA treatment. In this

### Table 1. Baseline Characteristics of the Study Population (n=12,906)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y (mean±SD)</td>
<td>74±12</td>
</tr>
<tr>
<td>Female, %</td>
<td>51</td>
</tr>
<tr>
<td>mRS, %</td>
<td></td>
</tr>
<tr>
<td>0–1</td>
<td>18</td>
</tr>
<tr>
<td>2–3</td>
<td>40</td>
</tr>
<tr>
<td>4–5</td>
<td>42</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>80</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>31</td>
</tr>
<tr>
<td>Admission &lt;3 hours, %</td>
<td>23</td>
</tr>
</tbody>
</table>

mRS indicates modified Rankin Scale (admission).

### Table 2. Female and Male Stroke Patients per Age Category in the Hessian Population (Pop) in 2005 and in 2050

<table>
<thead>
<tr>
<th>Age (y)</th>
<th>18–24</th>
<th>25–34</th>
<th>35–44</th>
<th>45–54</th>
<th>55–64</th>
<th>65–74</th>
<th>75–84</th>
<th>&gt;84</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>Females</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pop 2005</td>
<td>233 684</td>
<td>375 162</td>
<td>513 319</td>
<td>434 035</td>
<td>359 423</td>
<td>338 498</td>
<td>238 856</td>
<td>84 982</td>
<td>3 109 204</td>
</tr>
<tr>
<td>2050</td>
<td>158 500</td>
<td>260 600</td>
<td>267 100</td>
<td>309 300</td>
<td>356 400</td>
<td>348 200</td>
<td>352 600</td>
<td>258 800</td>
<td>2 641 300</td>
</tr>
<tr>
<td>IS 2005</td>
<td>3 37</td>
<td>145</td>
<td>438</td>
<td>1059</td>
<td>2101</td>
<td>1934</td>
<td>574</td>
<td>6291</td>
<td>11 214</td>
</tr>
<tr>
<td>2050</td>
<td>2 27</td>
<td>75</td>
<td>313</td>
<td>1032</td>
<td>2175</td>
<td>3806</td>
<td>3062</td>
<td>10 492</td>
<td>332</td>
</tr>
<tr>
<td>tPA 2005</td>
<td>0</td>
<td>1</td>
<td>13</td>
<td>26</td>
<td>65</td>
<td>102</td>
<td>112</td>
<td>13</td>
<td>332</td>
</tr>
<tr>
<td>2050</td>
<td>0</td>
<td>1</td>
<td>7</td>
<td>19</td>
<td>63</td>
<td>106</td>
<td>220</td>
<td>69</td>
<td>485</td>
</tr>
</tbody>
</table>

IS indicates ischemic stroke patients in 2005 and 2050; tPA, tPA-treated patients in 2005 and 2050.
case we may have underestimated the future proportion of tPA-treated patients. In either case, however, it is unlikely that the question of thrombolytic treatment above the age of 80 years will not deserve increasing attention.

Disclosures

None.

References

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