A population-based study on dementia and stroke in 97 year olds

MATS ANDERSSON1, XINXIN GUO2, ANNE BÖRJESSON-HANSON2, MARTIN LIEBETRAU3, SVANTE ÖSTLING2, INGMAR SKOOG2

1Neuropsykiatri, Neuropsychiatric Epidemiology, Wallinsgatan 6, SU/Mölndal SE-431 41, Sweden
2Department of Psychiatry, Sahlgrenska University Hospital, Göteborg SE-413 45, Sweden
3Neurology, HSK Dr. Horst Schmidt Klinik, Wiesbaden, Germany

Address correspondence to: M. Andersson. Tel: (+46) 31 343 86 40; Fax: (+46) 31 776 04 03. Email: mats.andersson@neuro.gu.se

Abstract

Background: the number of nonagenarians increases dramatically worldwide.
Objectives: to examine the prevalence of stroke/transient ischaemic attack (TIA) and dementia, their inter-relationship and their relation to 2-year mortality and institutionalisation in 97 year olds.
Methods: a population-based sample of 97 year olds (n = 591) was examined. Information on stroke/TIA was obtained from self-reports, key informants and hospital discharge registers. Dementia was diagnosed according to DSM-III-R criteria.
Results: the response rate was 65%. The prevalence of dementia was 32.7% in men and 59.3% in women (P < 0.001). The prevalence of stroke/TIA was 21.5% (17.8% in men, 22.3% in women). Stroke/TIA was related to dementia in women (odds ratio = 1.9, 95% CI: 1.2–3.0), but not in men. Dementia, but not stroke/TIA, was related to 2-year mortality and institutionalisation in logistic regression models.
Conclusion: dementia was very common in this age group, and related to mortality and institutionalisation. Stroke/TIA in 97 year olds showed less association with dementia, mortality and institutionalisation than reported in studies of younger elderly populations. The finding that stroke was not associated with dementia in men needs to be taken cautiously due to the small number of men. The findings also emphasise that more studies are needed to scrutinise the aetiology of dementia in nonagenarians.

Keywords: stroke, dementia, epidemiology, mortality, ageing, elderly

Introduction

The number of nonagenarians in the world will increase from 3.3 million in 2010 to 21 million in 2050 [1]. Stroke and dementia are major causes of disability and death [2–4]. It seems that stroke is related to a higher death rate and more disability in the very elderly [5]. Stroke increases the risk of dementia approximately nine times in younger elderly [6], but the risk for dementia after stroke may decrease with age [3, 7, 8]. Demented patients with stroke history are generally given a diagnosis of vascular dementia (VaD) or mixed dementia (co-existing Alzheimer’s disease and cerebrovascular disease). VaD is the second most common cause of dementia after Alzheimer’s disease, and may be caused by several different cerebrovascular diseases, e.g. stroke, silent infarcts, ischaemic white matter lesions, cerebral amyloid angiopathy and cerebral vasculitis [9]. Alzheimer encephalopathy, the neuropathological hallmark of Alzheimer’s disease, was recently reported to be less related to dementia in nonagenarians than in younger age groups [10]. It is not clear whether this is true also for stroke.

The primary aim of this study was to estimate the prevalence of stroke/transient ischaemic attack (TIA) and dementia, and their inter-relationship in 97 year olds using information from self-reports, key informants and a hospital discharge register. The second aim was to study consequences of stroke/TIA and dementia in 97 year olds...
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olds in relation to a 2-year mortality rate, and institutionalisation.

Methods

The study is part of the Gothenburg 95+ study, which is a population survey conducted on individuals above age 95 years. All 97 year olds living in Gothenburg, Sweden, and born between 1 July 1901 and 31 December 1909 were included. Names and addresses were obtained from the Swedish Population Register. The examinations were conducted between 1998 and 2007.

The Ethics Review Board approved the study. All participants gave their written informed consent. In those with dementia where informed consent could not be obtained, consent was obtained from a close relative.

All participants were examined by trained psychiatric research nurses, supervised by neuropsychiatrists. The nurses were able to discuss with neuropsychiatrists in cases of doubt regarding assessments, but the participants were not seen by neuropsychiatrists. The examination included physical examinations, neuropsychiatric examinations and a history of previous and current disorders, drug use, assessments of activities of daily living and social factors. The semi-structured examinations included ratings of psychiatric symptoms and signs in accordance with the Comprehensive Psychopathological Rating Scale (CPRS) and assessment of cognitive function.

After the personal examination, participants were asked for permission to interview a key informant. Key informant interviews included questions about changes in behaviour, intellectual function, and in cases of dementia, questions about age at onset and course. It also included questions about stroke and other somatic disorders.

Both interviews were structured but allowed clarifying questions. The interviews included questions about sudden onset of focal symptoms or acute aphasia, symptom duration, age at stroke/TIA and admission to hospital due to stroke/TIA.

Information from the interviews, including side notes, was evaluated by two of the authors (I.S., M.A.). Stroke/TIA was only diagnosed in cases with a definite history of acute focal symptoms (i.e. paresis or aphasia).

Information about the diagnosis of stroke or TIA was also obtained from the Swedish Hospital discharge register. Since 1978, everybody admitted to a Swedish hospital are registered in a computerised hospital-discharge system, using diagnoses according to the International Statistical Classification of Diseases and Related Health Problems. In Gothenburg, individuals with stroke are admitted to Sahlgrenska University Hospital, and are therefore mainly diagnosed by neurologists and internists.

Dementia was diagnosed according to the DSM-III-R criteria [11] based on data from neuropsychiatric examinations and key informant interviews, as described previously [12]. The final diagnosis of dementia was made by neuropsychiatrists, who reviewed information from interviews and examinations. The diagnosis was made if the participant had dementia according to both sources of information or if there was clear evidence of dementia from one source and subthreshold symptoms in the other.

Institutionalisation was defined as living permanently in homes for the elderly, special dementia units or in nursing homes, based on information obtained at the home visits.

Dates of death were obtained from the Swedish Population Register, a national register comprising all Swedish citizens. This register is complete regarding mortality data. Mortality was calculated from time of examination.

Statistical methods

Differences in proportions were tested with Fisher’s exact test and differences in means with t-test [13]. Odds ratios (ORs) and 95% confidence intervals (95% CI) were calculated when appropriate. The associations between stroke, dementia, mortality and institutionalisation were tested with logistic regression models.

Results

There were 973 (156 men and 817 women) 97 year olds living in Gothenburg, Sweden, and born between 1 July 1901 and 31 December 1909. Of those, eight individuals were excluded due to not speaking Swedish, four had emigrated outside Sweden, two could not be traced and 48 died before they could be contacted, leaving 911 eligible. Among these, 591 (107 men and 484 women) agreed to participate (response rate 64.9%). Participants and non-participants were similar regarding 2-year mortality rate (52.8 versus 50.9%; P = 0.627) and diagnosis of stroke in the hospital discharge register (18.6 versus 14.7%; P = 0.134). Participants more often had a diagnosis of dementia according to the hospital discharge register than non-participants (16 versus 11%; P = 0.01), and men had a higher response rate than women (72.8 versus 63.3%; P = 0.03). Key informant interviews were performed in 450 (76%) individuals (11 participants and 11 key informants declined, 17 participants did not have a key informant, 8 key informants could not be traced and 96 key informant provided incomplete information).

Prevalence of dementia was 54.5% (n = 322; 32.7% in men, 59.3% in women; P < 0.001), and of stroke/TIA 21.5% (n = 127; 22.3% in women, 17.8% in men), including 105 cases with stroke, and 22 cases with only TIA. Seventeen cases had a history of both stroke and TIA (Table 1). Among those with stroke/TIA according to hospital discharge register (n = 110), 104 had a primary diagnoses of stroke/TIA on at least one occasion. Among those with dementia, 83 (25.8%) also had a stroke/TIA. The mean age of stroke onset was 90.5 years (no gender difference), and 81.9% (n = 104) had their first stroke/TIA after age 85, and 55.9% (n = 71) after age 90. The mean age of
dementia onset was 91.0 years (93.1 years for men and 90.8 years for women) [P = 0.011]. Among those with dementia, 92.2% (n = 297) had onset after age 85, and 75.3% (n = 204) after age 90.

The prevalence of dementia was higher in those with a history of stroke/TIA than in those without (65.4 versus 51.5%, OR: 1.8, 95% CI: 1.2–2.7). However, a history of stroke/TIA was associated with dementia only in women (70.4 versus 56.1%, OR: 1.9, 95% CI: 1.2–2.9), but not in men (36.8 versus 31.8%, OR: 1.2, 95% CI: 0.4–3.5) (Table 2). In one-third (28.9%, n = 24), the stroke/TIA occurred after dementia onset, in one-third (33.7%, n = 28) within the same year and in one-third (27.7%, n = 23) before dementia onset. In 9.6% (n = 8) dementia onset age was not possible to determine.

The 2-year mortality rate was 52.8% (56.1% in men and 52.1% in women, P = 0.453). The 2-mortality rate was higher in those with dementia than in those without (67.7 versus 34.9%, OR: 3.9, 95% CI: 2.8–5.5), and higher in those with a history of stroke/TIA than in those without (62.2 versus 50.2%, OR: 1.6, 95% CI: 1.1–2.4). Stroke/TIA was associated with increased mortality in women (OR: 1.6, 95% CI: 1.0–2.5), but not in men. In a logistic regression analysis, including gender, dementia and stroke/TIA, the 2-year mortality rate was associated with dementia (OR: 4.3, 95% CI: 3.0–6.1) and male gender (OR: 1.8, 95% CI: 1.2–2.9), but not with stroke/TIA (OR: 1.4, 95% CI: 0.9–2.2).

Among 97-year-olds, 31.7% of the men and 63.4% of the women were institutionalised. Dementia was associated with institutionalisation both among men (79.4 versus 16.9%; OR: 19.0, 95% CI: 6.7–53.5) and women (84.5 versus 32.8%; OR: 11.1, 95% CI: 7.2–17.2). Those with stroke/TIA were more often institutionalised than those without (68.8 versus 55.9%; OR: 1.7, 95% CI: 1.1–2.6).

Among the non-demented, 32.6% of those with stroke/TIA and 27.8% of those without stroke/TIA were institutionalised (OR: 1.2, 95% CI: 0.6–2.5). Among the demented, 87.8% of those with stroke/TIA and 82.6% of those without stroke/TIA were institutionalised (OR: 1.5, 95% CI: 0.7–3.2). In a logistic regression analysis including gender, dementia and stroke/TIA, institutionalisation was associated with dementia (OR: 11.9, 95% CI: 7.9–17.8) and female gender (OR: 1.9, 95% CI: 1.2–3.3), but not with stroke/TIA (OR: 1.4, 95% CI: 0.8–2.3).

**Discussion**

We examined the relation between stroke/TIA and dementia in a large representative sample of 97-year-olds from Gothenburg, Sweden, using several sources of information. More than one-fifth of 97-year-olds had a history of stroke/TIA, and almost two-thirds of the women and one-third of men had dementia. However, stroke/TIA was associated with dementia to a lesser extent than in younger age groups [7, 14]. In contrast to reports from younger age groups, stroke/TIA was not associated with institutionalisation [15] and mortality rate [3], after controlling for dementia. These findings may look contrasting to reports that case fatality rate in stroke is higher among very old stroke/TIA patients than in younger cases [5, 16]. However, our study is looking at a history of stroke. Our group thus comprises chronic survivors of a previous stroke event. Nevertheless, our findings suggest that stroke may have less consequence in extreme old age, while the consequences of dementia remain substantial.

Although the prevalence of dementia in those with stroke/TIA was high, the OR for dementia after stroke/TIA was only 1.8. This finding is in line with other reports that the odds of dementia in relation to stroke/TIA decreases with age [7]. OR for dementia in those with stroke/TIA was 6.7 at ages 70–80 [7], 4.8 after age 80 [7] and 4.3 in 85 year olds [3]. However, the prevalence of dementia among those without stroke/TIA was much higher at age 97 (51%) than in younger ages. Prevalence of

| Table 2. The prevalence of dementia in relation to stroke/TIA in 97 year olds |
|-----------------|-----------------|-----------------|
| Stroke/TIA      | Men (n = 107)   | Women (n = 484) |
| ND/NA %         | ND/NA %         | ND/NA %         |
| No              | Yes             | No              | Yes             |
| ND/NA           | ND/NA           | OR (95% CI)     |
| All             | 239/464         | 51.5            | 83/127          | 65.4            | 1.8 (1.2–2.7)* |
| Men             | 28/88           | 31.8            | 7/19            | 36.8            | 1.2 (0.4–3.5)  |
| Women           | 211/376         | 56.1            | 76/108          | 70.4            | 1.9 (1.2–2.9)* |

ND/NA = number demented/number of all.

*P < 0.01.

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dementia for other reasons than stroke/TIA is thus high in this age, and stroke/TIA does not add as much to the risk as in younger ages. Also Alzheimer encephalopathy (deposition of extracellular senile plaques and intracellular neurofibrillary tangles in the hippocampus and the frontal and temporal cortex) is common in nonagenarians, and not associated with dementia to the same extent as in younger age groups [10]. The two most common causes of dementia may thus not have the same impact on dementia in nonagenarians, the age group with the highest prevalence of dementia. It is therefore important to further scrutinise the aetiology of dementia in this age group.

Among those with dementia, 25.8% had a history of stroke/TIA. The proportion with VaD is thus lower than reported at age 85 (57.0%) [12] and 95 years (30.5%) [8], in line with several studies reporting that the proportion of VaD decreases with age [17]. One reason may be that the frequency of silent stroke increases with age [18]. The lack of brain imaging in our study may thus underestimate frequency of VaD in this age group. We also need to emphasise that the contribution of stroke/TIA for dementia is not always easy to elucidate. Stroke/TIA may be the main cause of dementia, it may be the event that finally overcomes the brain’s compensatory capacity in individuals whose brains are already compromised by Alzheimer pathology, albeit not yet clinically manifest and often minor manifestations of both disorders which individually would not be enough to produce dementia may produce it together.

Our prevalence of stroke/TIA (22%) was only slightly higher than the 19% reported in 85 year olds using the same methods [3], and the 16% in centenarians using self-report or key informants [19]. In a study on individuals aged 70 and above (mean age 81 years), the prevalence of stroke/TIA was 7.4% [7].

Dementia was the major cause of mortality and institutionalisation, as previously reported in other studies [4, 12, 20]. Stroke/TIA did not increase the risk of mortality or institutionalisation in 97 year olds after adjusting for dementia and gender. This is in contrast to findings in younger ages [3, 21]. It may be that stroke/TIA has less severe consequences in this extreme age or that the competing risk of dementia diminishes the effect of stroke/TIA on mortality. The mortality rate and institutionalisation for other reasons than stroke/TIA is already high in this age, and stroke/TIA does thus not add as much to the risk as in younger ages.

There were some gender differences. First, the prevalence of dementia was higher in women (59.3%) than in men (32.7%) at age 97, as also found at age 95 [8]. Second, in contrast to other studies [3, 7], stroke/TIA was only related to dementia in women at age 97. These gender differences may have several explanations. One reason might be that fewer men survive to the age 97 years (ratio women/men increased from 2.6 at age 85 to 4.5 at age 97). Surviving men may thus constitute a group with high resistance to dementia. It has to be acknowledged that despite that this is a relatively large population study, it is under-powered when exploring gender differences. It is thus a possibility of a type 2 error in relation to the association between stroke and dementia in men.

Strengths of this study are the population-based design, the large sample, the comprehensive examinations, the use of several information sources, and that all diagnoses were made by geriatric neuropsychiatrists. Some possible limitations should also be considered. First, the validity of the information sources could be questioned. However, information from self-reports and key informants was evaluated by neuropsychiatrists. Furthermore, criteria for dementia and stroke were strict, allowing only cases with a clear history of focal symptoms for a stroke diagnosis and requiring information from both neuropsychiatric examinations and key informant interviews for a dementia diagnosis. Second, it is possible that we underestimated the prevalence of stroke/TIA, as only 450 out of 591 individuals had key informant interviews. Third, information from the hospital discharge register may be questioned since diagnoses were made by many different physicians working under different circumstances. However, most cases were diagnosed by neurologists or interns at the university hospital in Gothenburg. Fourth, the response rate was 65%, a fairly satisfactory response rate in this age group. Although comparisons between responders and non-responders showed that the sample investigated was similar to non-responders regarding stroke/TIA hospitalisation and mortality rate, participants more often had dementia according to the hospital discharge register (16 versus 11%) and men had a higher response rate than women (72.8 versus 63.3%). These differences are probably too small to have major influences on our findings. It is also noteworthy that the hospital discharge register only captured a small minority of those with dementia. However, we cannot exclude that there may be other differences that may have influenced the results. Fifth, although this is the largest population study performed in this age group, some of the subgroups were small, e.g. the number of men. Finally, the cross-sectional design of our study makes it difficult to discuss the cause–effect relationship between dementia and stroke/TIA. Our cross-sectional design may also overestimate cases of mild stroke, as those with severe stroke may die before they come to examination.

Key points

• The increased risk for dementia in relation to stroke/TIA decreases with age.
• Stroke may have less consequence in extreme old age.
• Consequences of dementia remain substantial also in extreme ages.
• Stroke/TIA did not increase the risk of mortality or institutionalisation in extreme old age.
• Two-thirds of women and one-third of men had dementia at the age of 97.
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Conflicts of interest
None declared.

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