Predictors of long-term survival in nonagenarians: the NonaSantfeliu study

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Abstract

Background: few studies have prospectively evaluated long-term predictors of mortality in nonagenarians. 
Objective: to determine predictors of death in a nonagenarian cohort after 5 years of follow-up.
Design: a prospective community-based study.
Setting: a community-based study.
Subjects: one hundred and eighty-six nonagenarians both living in the community and institutionalised.
Methods: functional status was determined by the Lawton–Brody and Barthel Indexes (BI) and cognition by the Spanish version of the mental state examination (MEC). The Charlson Index was used to measure comorbidity. Nutritional status was evaluated by the short version of the Mini-Nutritional Assessment questionnaire.
Results: mortality after 5 years was 75.53%. Patients who did not survive were significantly older, with lower cognitive and functional performance, with diminished visual acuity, higher comorbidity, higher risk of malnutrition, higher number of drugs taken and a higher percentage of patients with the diagnosis of dyslipidaemia, heart failure or previous stroke. Cox regression analysis, identified the Charlson Index (hazard ratio 1.23, 95% CI 1.09–1.37) and MEC (hazard ratio 0.98, 95% CI 0.97–0.99) as independent predictors of mortality after 5 years.
Conclusions: better cognitive status and lesser comorbidity at baseline are the best predictors to identify which nonagenarians survived after a 5-year follow-up period.

Keywords: nonagenarian, comorbidity, elderly; cognitive status, mortality, elderly

Introduction

The prevalence of nonagenarians or older in the population has increased in the recent decades. This increase in longevity is likely to be associated with an increase in multimorbidity rates [1–3]. Prior studies of nonagenarians in our geographical area have shown a predominance of women, usually widows, many of whom have maintained functional...
independence [1, 2]. However, male nonagenarians with low comorbidity probably experience more successful ageing than females or than nonagenarians with high comorbidity [1, 3].

Few studies have prospectively evaluated predictors of mortality in nonagenarians, but even less information is available on the long-term mortality in this segment of the population [4–7]. The results of the Danish 1905 cohort survey reported that in the oldest old, several known predictors of mortality (for example, sociodemographic factors) have lost their importance and have been replaced by high disability level, poor physical and cognitive performance and self-related health (women only) [4]. In the first year of our follow-up study of the NonaSantfeliu cohort, we found a mortality rate of 19.3% [6]. Age, heart failure and nutritional risk remained associated with mortality in multivariate analyses. After 2 years of follow-up, 64 failures and nutritional risk remained associated with mortality. The results of the Danish 1905 cohort survey reported that in the oldest old, several known predictors of mortality (for example, sociodemographic factors) have lost their importance and have been replaced by high disability level, poor physical and cognitive performance and self-related health (women only) [4]. In the first year of our follow-up study of the NonaSantfeliu cohort, we found a mortality rate of 19.3% [6]. Age, heart failure and nutritional risk remained associated with mortality in multivariate analyses. After 2 years of follow-up, 64 failures and nutritional risk remained associated with mortality.

In the present study we evaluated long-term follow-up (at 5 years) in a cohort of non-selected nonagenarians, including institutionalised subjects, in order to determine predictors of death in this oldest-old group. We hypothesised that predictors of mortality may change over the 5 years of follow-up.

Methods

The data were taken from the NonaSantfeliu study, a population-based study of nonagenarians in the town of Sant Feliu de Llobregat (Barcelona, Catalonia, Spain). The survey has been described in detail elsewhere [1–3, 6, 7]. In brief, all 305 nonagenarian residents both in the community and institutionalised were contacted, and 61% (= 186 participants) replied. Geriatric assessment and sociodemographic data (gender, marital status, place of residence and educational level) were recorded. There were no differences in age and gender of individuals included in the study that when compared with those who were not.

Global geriatric assessment

The methodology was similar to that reported in previous studies of mortality in the NonaSantfeliu cohort [6, 7]. Functional status was measured using the Barthel Index (BI) [8] for basic ADL (BADL) and the LI [9] for instrumental ADL (IADL). The total score of the BI ranges from 0 to 100 points. Nonagenarians with scores of 59 or lower on the BI were defined as individuals with significant functional impairment. The LI scale ranges from 0 to 8 points (a score of 8 meaning that no help is needed). Cognitive function was measured by the Spanish version of the mini-mental state examination (MEC) [10] with a maximum score of 35 and scores below 24 indicating cognitive impairment. Nutritional risk was evaluated by the short version of the Mini-Nutritional Assessment (MNA-SF) questionnaire [11]. MNA-SF scores range from 0 to 14 points, with scores below 11 denoting patients at risk of, or suffering from, protein-energy malnutrition.

Sensorial status

Short sightedness was measured with Snellen charts. A score below 20/40 at 40 cm, with the best eye and wearing glasses was considered abnormal. Hearing ability was measured by the Whisper test, with the examiner sitting 60 cm behind the subject so that his or her lips could not be read [12].

Co-morbidity and cardiovascular risk factors

The Charlson comorbidity Index was calculated by medical chart reviews and the information provided by the participants’ caregivers [13]. This score ranges from 0 to a theoretical maximum of 33. Our investigation placed special emphasis on the presence of hypertension, diabetes, dyslipidaemia, ischaemic cardiopathy, heart failure, chronic obstructive pulmonary disease (COPD), dementia, presence of previous stroke and chronic drug prescription.

Successful ageing group

Twenty-three of 186 (12%) non-institutionalised inhabitants who scored 91 or more on the BI and 24 or more on the MEC were considered non-disabled nonagenarians and assigned to the ‘successful ageing group’.

Overall 5-year mortality

Vital status for the total cohort was evaluated. Mortality was coded as dead (1) or alive (2). Individuals were followed up for 60 months or until they died, whichever occurred first. Vital status was confirmed by the participants’ caregivers and in case of doubt by consulting the National Population Register records. We compared the patients who had survived with those deceased.

Statistical analyses

SPSS 15.0 statistical software (SPSS Inc, Chicago, IL, USA) was used to perform the analyses. Normally, distributed continuous variables are reported as means ± standard deviation (SD). Categorical variables are reported as proportions. Student’s t-test was used to compare normally distributed continuous variables and the chi-square statistic or Fisher’s exact test was used to compare categorical or dichotomous variables.

The 5-year survival rate was evaluated. Cox proportional-hazard regression analysis was used to model the time to death data to identify possible predictors of mortality. The first step was the selection of the variables
using bivariate analysis. The final model 1 was constructed using backward stepwise Cox regression models (the $P$ for entry was 0.5 and for removal was 0.10). The results were considered significant when $P<0.05$. Variables examined were age, gender, diminished visual acuity, dyslipidaemia, stroke, heart failure and number of chronic drug prescriptions and BI, LI, MEC, Charlson Index and short-MNA as continuous variables. The term 'successful ageing' was not included in the model since it was composed by several variables, which were already included separately. Two alternative models were conducted to explore the importance of functionality (BADL) on mortality in more depth. In model 2, we treated the BI value as a dichotomous variable (BI greater or less than 60). Finally, in a third model, due to the possible relationship between LI and BI, we excluded the LI values from the model.

**Results**

The sample comprised 143 (76.5%) women and 43 men. The mean ± SD of age at baseline was 93.1 ± 3.2 years. Most subjects lived in community-based housing (72.3%) and the remaining 27.1% were institutionalised. With regard to marital status, 149 (80.2%) were widowed, 17 (9.1%) married and 20 (10.7%) unmarried. Two (1.1%) had a university degree, 13 (6.9%) had reached high school, 67.2% had completed primary school and 24.3% had received no basic education.

**Geriatric assessment**

The mean values of geriatric assessment scales at the beginning of the follow-up study period were: LI 2.1 ± 2.2 for IADL and BI 60.8 ± 30 for BADL. Six patients (3%) had a BI of 100 and 26 (14%) had a BI > 90. Moreover, 71 (38%) had a BI < 61 and 31 (17%) had a BI < 21. As regards cognition, the mean MEC score was 21 ± 11 and was <24 in 102 subjects (56%). Forty-seven subjects (25.2%) had a previous diagnosis of dementia. At baseline, in the subgroup of community-dwelling subjects, the successful ageing group comprised 23 nonagenarians (17.7%; 11: 5.9%, women and 12: 6.4%, men).

The evaluation of nutritional risk showed a mean MNA-SF score of 11.1 ± 2.4. Fifty-three (28.4%) subjects had MNA-SF values <11. Sensory evaluation found auditory impairment in 76 (40.8%) and visual impairment in 71 (38.1%).

**Evaluation of co-morbidity and cardiovascular risk factors**

The mean Charlson Index score was 1.4 ± 1.7. Hypertension was found in 109 (58.6%), diabetes in 25 (13.4%) and dyslipidaemia in 35 (18.8%). Previous clinical history of ischaemic cardiopathy (21, 11.2%), heart failure (48, 25.8%), COPD (28, 15%) and stroke (36, 19.3%) were recorded. Patients were taking an average of 4.3 ± 2.5 drugs, with 114 patients (61.2%) receiving three or more.

**Evaluation after 5 years follow-up**

One-hundred and thirty-six patients died during the 60 months of the follow-up period (75.5%), giving an annual average mortality rate in the overall cohort of 15.1%, distributed as follows: 19.3% for the first year, 36.3% for the second, 55.9% for the third, 62.3% for the fourth and 75.5% for the fifth. The median survival was 25 months (95% CI: 20.9–29 months). At the end of the follow-up period, the mean age of the 50 survivors was 97.1 ± 3 (range 95–104). Mean BI was 52.5 ± 27 and was 60 or higher in 24 (48%), and mean MEC was 15 ± 9, being 24 or higher in 13 (26%). Twelve of the 23 subjects (52%) with ‘successful ageing’ at baseline were alive at the end of the follow-up period, their mean age was 96.7 ± 2 (range 95–99).

**Predictors of mortality**

The bivariate analysis of baseline variables associated with 5-year survival is shown in Table 1. Patients who did not survive were significantly older and had lower cognitive (MEC) and functional performance (BADL and IADL), diminished visual acuity, higher comorbidity (Charlson Index), high risk of malnutrition (MNA-SF), took more drugs and were more likely to have dyslipidaemia, heart failure or previous stroke.

Cox regression analysis (model 1) identified two significant clinical variables (Charlson Index and MEC) as independent predictors of mortality in these patients after 5 years (Table 2). Therefore, better cognitive status and lower comorbidity at baseline predicted survival in nonagenarians at 5-year follow-up. Neither model 2 nor model 3 changed the predictors of 5-year mortality: the Charlson Index and MEC values presented hazard ratios almost identical to those of model 1.

**Discussion**

The results of the present study show a very low 5-year survival rate, estimated in 24.5% in these very old subjects. The average mortality rate in the overall cohort was 15.1% per year, lower than the rate in nonagenarians aged 90–94 (20.7%) and the >94 age group (37.4%) reported in Catalonia for 2007 [14]. This difference could be explained in part due to high percentage of nonagenarians who refused to participate in the study (39%), and although there were no differences in age and gender, we could not evaluate parameters of function, cognition or comorbidity, which could indicate a population likely to have a poorer overall health status. In a previous study evaluating Danish nonagenarians, mortality was found to be 25.7% after 15 months [4]. With studies of longer periods, the proportion of deaths reaches 60%, as reported in a study in a Finnish nonagenarian cohort after 4 years of follow-up [15]. In the Nona Santfeliu study, the mortality rate was very similar at 4
The main aim of this study was to identify predictors of long-term mortality in nonagenarians. We found that better cognitive status and lower comorbidity at baseline predict which nonagenarians are likely to survive at 5-year follow-up.

Though the reports in the literature are not entirely consistent, it does seem that cognitive impairment is associated with increased mortality [16]. Evaluating data from the Danish 1905 cohort survey, Andersen et al. [17] found that cognitive impairment also predicts mortality among nonagenarians, even controlling for most known predictors of mortality. We found MEC values, as an objective measure of cognitive status, to be long-term predictors of mortality, as in our earlier evaluation after 2 years of follow-up. With regard to the instrument used to detect cognitive impairment, it is important to note that age in itself has not been shown to be a major limitation when using the MEC [18]. Although it has been reported that different domains predict mortality in older subjects, we did not conduct a subanalysis of MEC items.

Comorbidity is a term used to describe the variety of illnesses or burdens that may affect a patient's clinical outcome and issues such as health-care cost, utilisation and survival. It is a common characteristic in the elderly population. The Charlson Index is the score that is most widely used for its assessment. In our study, the mean Charlson Index score is 1.4 ± 1.7, which is not especially high and in fact is similar to the score previously reported in a multicentre study of hospitalised nonagenarians in our area [19]. In a previous study on nonagenarians after 15 months of follow-up, self-reported comorbidity failed to predict mortality [4]. In the NonaSantfeliu cohort, the Charlson Index was associated with 1-year mortality in the bivariate analysis, but lost statistical significance in the multivariate analysis [5]; however, the association remained significant when the cohort was evaluated after 2 years [7].

As well as high comorbidity and a high percentage of cognitive impairment at baseline, the bivariate analysis found that patients who did not survive were significantly older, had lower functional performance (BADL and IADL), diminished visual acuity and high risk of malnutrition (MNA-SF), took a higher number of drugs and presented a higher percentage of diagnoses of dyslipidaemia, heart failure or previous stroke. The majority of these associations seem logical.

Age remained significant at the 1-year evaluation [6], despite the narrow age range of the outpatients included, but at 2 years it was no longer a predictive factor [7]. Age could not be assessed in the Danish 1905 cohort study because all the patients included were born in the same year [4]. A decline in functional status has been reported as a significant risk factor for mortality in nonagenarians [4], and in fact in the 2-year study, we reported an association between LI and mortality [7]. We designed two alternative statistical models to explore the possible predictive value of physical function (BADL) in more depth, but neither showed changes in the predictors of mortality. It is known that there is an association between visual impairment and disability in the elderly population and that visual impairment has a predictive effect on mortality regardless of comorbidity [20]. A body mass index below 28 has also been associated with an increase in mortality in nonagenarians [4]. The MNA-SF has proved its usefulness in predicting short-term mortality in the NonaSantfeliu study [6]. The high numbers of drugs taken for the comorbidity may explain its association with poor prognosis. The association between dyslipidaemia and mortality in the elderly is controversial [21, 22]. High total cholesterol seems to remains a strong risk factor for coronary mortality in elderly men [21] but very low cholesterol levels do not

Table 1. Comparison of variables associated with 5-year survival

<table>
<thead>
<tr>
<th></th>
<th>Not survivors (n = 136)</th>
<th>Survivors (n = 50)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>93.3 ± 3.2</td>
<td>92.1 ± 2.8</td>
<td>0.02</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td>0.84</td>
</tr>
<tr>
<td>Female</td>
<td>106 (77.9%)</td>
<td>38 (76%)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>30 (22.1%)</td>
<td>12 (24%)</td>
<td></td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td>0.37</td>
</tr>
<tr>
<td>Widowed</td>
<td>111 (81.6%)</td>
<td>38 (76%)</td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>10 (7.4%)</td>
<td>7 (14%)</td>
<td></td>
</tr>
<tr>
<td>Unmarried</td>
<td>15 (11%)</td>
<td>5 (10%)</td>
<td></td>
</tr>
<tr>
<td>Studies</td>
<td></td>
<td></td>
<td>0.64</td>
</tr>
<tr>
<td>No studies</td>
<td>35 (25.7%)</td>
<td>11 (22%)</td>
<td></td>
</tr>
<tr>
<td>Primary studies</td>
<td>92 (67.6%)</td>
<td>33 (66%)</td>
<td></td>
</tr>
<tr>
<td>High school</td>
<td>8 (5.9%)</td>
<td>5 (10%)</td>
<td></td>
</tr>
<tr>
<td>University degree</td>
<td>1 (0.7%)</td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>BI</td>
<td>55.7 ± 3.0</td>
<td>74.8 ± 24.6</td>
<td>0.0001</td>
</tr>
<tr>
<td>BI &lt; 60</td>
<td>63 (46.3%)</td>
<td>18 (16%)</td>
<td>0.0001</td>
</tr>
<tr>
<td>MEC</td>
<td>18.6 ± 11.8</td>
<td>27 ± 8.9</td>
<td>0.0001</td>
</tr>
<tr>
<td>MEC &lt; 24</td>
<td>63 (46.3%)</td>
<td>39 (78%)</td>
<td>0.0001</td>
</tr>
<tr>
<td>LI</td>
<td>1.7 ± 1.9</td>
<td>3.3 ± 2.4</td>
<td>0.0000</td>
</tr>
<tr>
<td>Diminished hearing</td>
<td>60 (44.1%)</td>
<td>16 (32%)</td>
<td>0.13</td>
</tr>
<tr>
<td>Diminished visual acuity</td>
<td>60 (44.1%)</td>
<td>11 (22%)</td>
<td>0.006</td>
</tr>
<tr>
<td>Charlson Index</td>
<td>1.7 ± 1.8</td>
<td>0.7 ± 1.1</td>
<td>0.0001</td>
</tr>
<tr>
<td>MNA-SF</td>
<td>10.7 ± 2.5</td>
<td>12.0 ± 1.8</td>
<td>0.002</td>
</tr>
<tr>
<td>Hypertension</td>
<td>76 (55.9%)</td>
<td>33 (66%)</td>
<td>0.21</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>19 (14%)</td>
<td>6 (12%)</td>
<td>0.72</td>
</tr>
<tr>
<td>Dyslipidaemia</td>
<td>20 (14.7%)</td>
<td>15 (30%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>16 (11.8%)</td>
<td>5 (10%)</td>
<td>0.73</td>
</tr>
<tr>
<td>COPD</td>
<td>18 (13.2%)</td>
<td>10 (20%)</td>
<td>0.25</td>
</tr>
<tr>
<td>Heart failure</td>
<td>41 (30%)</td>
<td>7 (14%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Medical history of stroke</td>
<td>32 (23.5%)</td>
<td>4 (8.2%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Previous diagnosis of dementia</td>
<td>43 (31.6%)</td>
<td>4 (8%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Number of drugs taken</td>
<td>4.5 ± 2.5</td>
<td>3.6 ± 2.2</td>
<td>0.03</td>
</tr>
<tr>
<td>Institutionalised</td>
<td>36 (26.5%)</td>
<td>13 (26%)</td>
<td>0.94</td>
</tr>
<tr>
<td>Not successful ageing</td>
<td>125 (91.9%)</td>
<td>38 (76%)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Table 2. Multiple regression analysis model of baseline variables for nonagenarians death after 5 years of follow-up

<table>
<thead>
<tr>
<th>Variable</th>
<th>P-value</th>
<th>Hazard ratio</th>
<th>95 % confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Charlson Index</td>
<td>0.0001</td>
<td>1.23</td>
<td>1.09–1.37</td>
</tr>
<tr>
<td>MEC</td>
<td>0.02</td>
<td>0.98</td>
<td>0.97–0.99</td>
</tr>
</tbody>
</table>

years (62.3%) and reached 75.5% after 5 years of follow-up.
prolong survival in the elderly. The association between low total cholesterol and high mortality observed in some studies in crude analysis may be confounded by common cardiovascular risk factors, rather than reflect underlying inflammation or undernutrition [22]. In recent years, heart failure has gradually become one of the most prevalent cardiovascular disorders, with a particularly high mortality in the elderly [23]. Heart failure also showed to be a good predictor of global mortality in our first 1-year study [6], but at the 2-year time point it was no longer significant [7]. However, it must be noted that we measured comorbidity using the Charlson Index, which includes heart failure among its variables. Stroke is a major cause of disability and death among the elderly; nevertheless, we only recorded stroke as an epidemiological register in the medical history of stroke survivors.

Previously, in the baseline evaluation of the NonaSantfeliu study, we reported that male nonagenarians with low comorbidity probably experience more successful ageing than females or those with high comorbidity [3]. Nearly half of our nonagenarians remained non-disabled after 2 years of follow-up [24]. Male nonagenarians with more successful ageing are more likely to maintain this status than females. We did not include this combined index of good functional and cognitive status and non-institutionalisation in the multivariate analysis. However, we stress that a significant percentage of subjects in the successful ageing group survived.

The main limitations of this study are the sample size, especially as the males are concerned, and the absence of biological data. Furthermore, causes of death were not recorded. With respect to dyslipidaemia, we only recorded its diagnosis, not the values of total cholesterol and subtypes.

In conclusion, the 5-year mortality ratio observed in our cohort of nonagenarians is very high. Our study highlights the importance of comorbidity and poor cognition as predictors of long-term mortality among the oldest-old subgroup of elderly subjects. These predictors differ from the ones observed when only short-term, 1-year mortality is considered (age, heart failure and nutritional status), but are consistent with the ones related to mid-term, 2-year mortality.

Key points

- Few studies have prospectively evaluated predictors of mortality in nonagenarians, but even less information is available on the long-term mortality in these older-old subjects.
- A very low 5-year survival rate, estimated in 24.5% in these very old subjects was found. The average mortality rate in the overall cohort was 15.1% per year.
- Our study highlights the importance of comorbidity and poor cognition at baseline as predictors of long-term mortality among the oldest-old subgroup of elderly subjects.

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Conflicts of interest

None declared.

References

O. Grimaud


Incidence of ischaemic stroke according to income level among older people: the 3C study

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Abstract

Background: stroke has been shown to follow a social gradient with incidence rising as socioeconomic status decreases.

Objective: to examine the relationship between socioeconomic status and ischaemic stroke risk amongst older people.

Setting: the Cities of Bordeaux, Dijon and Montpellier in France.

Subjects and methods: nine thousand and two hundred and ninety-four non-institutionalised persons aged 65 years or more followed for 6 years.

Results: the distribution of cardiovascular risks factors was consistent with the classical finding of more favourable risk profiles among the advantaged socioeconomic groups. One hundred and thirty-six individuals developed a first ever ischaemic stroke (incidence rate: 3.2 per 1,000 py (person-years), 95% CI 2.7–3.8). The age- and sex-adjusted incidence of ischaemic stroke increased with increasing level of income (from 2.4 to 4.1 per 1,000 py, P = 0.04). In the multivariable analysis adjusting for cardiovascular risk factors, the higher income group displayed a 80% increased risk of ischaemic stroke.

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