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ORIGINAL ARTICLE

Determinants of further survival in centenarians

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Background: We studied the impact of selected clinical and demographic variables on further survival in subjects over 100-year-old.

Methods: In 1992, we assessed activities of daily living, cognitive function, and nutritional status in 38 centenarians (7 men and 12 women living in the Tokyo metropolitan area as well as 3 men and 16 women living in Aichi prefecture; mean age, 100.9Å}1.6 years). Cox proportional hazard regression analysis was used to identify variables influencing likelihood of further survival in centenarians.

Results: While 21 subjects had died by 1996, 17 were still living. Of the 38 subjects, 9 had illnesses at initial evaluation such as hypertension or other cardiovascular disease. Centenarians with a high cognitive level tended to show an independent activity of daily livings or a good nutritional condition. Cognitive levels were higher in men than in women. Cox proportional hazard regression analysis indicated that a high level of activity of daily livings, cognitive function, or nutritional status tended to be advantageous for further survival in centenarians. After adjustment for clinical variables, only a high serum albumin concentration was a significant factor favoring survival in centenarians (hazard ratio, 0.44 for a 1-SD increment in serum albumin concentration; 95% confidence interval, 0.23–0.85).

Conclusion: We conclude that undernourishment jeopardizes survival even in late life.

Key words: centenarian, albumin, nutrition, hazard ratio, survival.

Introduction

At least 10 000 people over 100-year-old (centenarians) presently live in Japan. Including such individuals, persons over 65-year-old will comprise one-fourth of the Japanese population in 2025. In such a society, advancing age of the population will make independence of daily living an increasingly important priority, since dependence represents an overall social burden. Centenarians are considered a group that has achieved successful aging; analysis of their clinical status could provide cue for healthy late life. We therefore investigated the relationship between clinical status and further survival in centenarians.

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Materials and methods

Subjects

A total of 38 centenarians were assessed with respect to present illnesses, activities of daily living (ADL), cognitive function, and nutritional status. Their mean age in 1992 was 100.9±1.6 years. Of the subjects, 7 men and 12 women lived in the Tokyo metropolitan area while 3 men and 16 women lived in Aichi prefecture. Informed consent was obtained before the study from either the centenarians or their representatives.

Evaluation of clinical status in centenarians

We determined whether significant diseases such as hypertension, other cardiovascular disease, cerebral atherosclerosis, chronic lung disease, and diabetes were present in the centenarians. ADL were assessed with respect to toilet care, eating, dressing, grooming, walking, and bath-

ing using a physical self-maintenance scale.[1] Subjects were scored on a 6-point scale from 0 (completely dependent) to 6 (completely independent). Cognitive function was classified semiquantitatively into five categories based on the clinical dementia ratings[2] (CDR) of stage 0 (normal), 0.5 (subnormal), 1 (mildly demented), 2 (moderately demented), or 3 (severely demented). For evaluation of nutritional status, serum albumin concentrations were measured with an autoanalyzer (model 7170; Hitachi Instruments, Ibaraki, Japan).

We recorded survival of study subjects yearly based on residence registration until 1996. In the present study, survival duration was semiquantitated as follows: 0.5 years if a centenarian was no longer registered in 1993; 1 years if registered until 1993 but not in 1994; 2 years if registered until 1994 but not in 1995; 3 years if registered until 1995 but not in 1996; or 4 years if still registered in 1996.

Cox proportional hazard regression model

Clinical parameters can be associated with each other. Therefore we firstly investigated mutual relationships between clinical variables. Then we calculated both crude and adjusted hazard ratios for each variable by using the Cox proportional hazard regression analysis[3] and identified variables influencing likelihood of further survival in centenarians. We considered gender (male = 0, female = 1), clinically important illness (presence = 1, absence = 0), ADL score (points), cognitive function (CDR stage), serum albumin concentration (g/dL), and age in 1992 (years) as covariables.

Figure 1 (a) survival curve depicts centenarians during 4 years of follow-up concerning survival (1992–1996). Of 28 centenarians, 21 died during the study and 17 were still living in 1996. Closed circles indicate decreased subjects.

Statistics—sample heading 3

Statistical analyses were performed using Statistica software (StatSoft, Tulsa, OK). Differences in mean were investigated by Mann–Whitney *U*-test while differences in prevalence were compared by chi-squared test (Yates' modification where needed). Correlations were evaluated by Spearman's rank correlation coefficient. Hazard ratios were investigated by Wald's test. Results were presented as the mean ±SD. *P*-values < 0.05 were considered to indicate statistical significance.

Results

Clinical status in centenarians

The following diseases were present in nine centenarians: chronic lung disease (three individuals), hypertension (three individuals), cerebral atherosclerosis (one individual), cardiovascular disease (one individual), and impaired glucose tolerance (one individual).

ADL scores ranged from 0 to 6 points (mean, 3.3 ± 2.1) while CDR stages ranged from 0 to 3 (mean, 1.6 ± 1.2). Mean value of serum albumin concentrations was 3.6 ± 0.4 g/dL (range, 2.8–4.3).

Tables 1–4 show mutual relationships between clinical variables. Centenarians with a high cognitive level tended to show an independent activity of daily livings or a good nutritional condition. Cognitive levels were higher in men than in women. Presence of illness was not related to other clinical variables.

Clinical parameters and mortality risk

Figure depicts a survival curve for the 4 years from 1992 to 1996. Twenty-one centenarians died during the study period while 17 were still living in 1996. Tables 5 and 6 show crude and adjusted hazard ratios for each variable, respectively. A high level of activity of daily livings, cognitive function, or nutritional status tended to be advantageous for further survival in centenarians. However, when adjusted for clinical variables, only a serum albumin concentration was found to have a significant influence on survival. Presence of illness, age in 1992, or gender was not related to mortality risk in centenarians.

Discussion

Only limited studies have considered prognostic factors for survival in the oldest elderly individuals. The Framingham Heart Study found short-term fluctuation of heart rate, i.e. heart rate variability, to be related to mortality risk in an elderly cohort.[4] In the Kahoku Longitudinal Aging Study, low ADL scores indicated high risk for subsequent death in an elderly Japanese population.[5] In previous studies comparing elderly survivors and non-survivors,[6,7] serum albumin concentration in non-survi-

vors was significantly lower than in survivors. In the present study, only a serum albumin concentration was identified as a significant factor positively associated with prognosis for survival in centenarians. Impact of ADL and cognitive function on survival was lessened by adjustment for other clinical parameters including serum albumin concentration. ADL status, cognition, and nutrition correlate closely with each other.[8,9] Apparent impact of ADL and cognitive function on mortality risk might depend on nutritional status.

Recently we found that C-reactive protein, an indicator of inflammation, was higher in centenarians with lower serum albumin than in those with higher concentrations.[9] This finding indicates that decreased albumin observed in the centenarians might result not only from reduced protein synthesis or intake,[10,11] but also possibly from an age-associated exaggeration of the inflammatory response. Ross *et al*. have recently suggested that atherosclerosis can be regarded as an inflammatory disease.[12,13] Atherosclerosis causes cerebrovascular and cardiovascular diseases, which generally are disadvantageous for survival and quality of life.

Table 1 Correlations between clinical variables

	ADL	CDR	ALB
Age (years)	–0.05	0.04	–0.31
ADL (points)	–0.05	–0.42**	0.08
CDR (stage)	0.04	–0.42**	–0.36*
ALB (g/dL)	– 0.31	0.08–0.36*	

*:$P < 0.05$, **:$P < 0.01$
ADL, activities of daily living; CDR, clinical dementia rating; ALB, serum albumin concentration.

One would expect that age and gender might influence further survival in centenarians. However, in the present study, the two variables were unrelated to survival in centenarians. In people who have reached the age of 100 years, clinical factors such as age or gender might have a minimal influence on survival.

The present study has some limitations. The number of the subjects seems small in size. Additionally the centenarians studied may not be representative of their age group because we examined only centenarians from whom informed consent was obtained. For survival data, we depended on residence registration, and therefore we could plot survival only crudely. Future study of survival will require more direct observation in a large population.

We conclude that undernourishment threatens survival even in centenarians, while good nutrition is important for a fuller late life.

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