Five-Year Survival of Older People with Anemia: Variation with Hemoglobin Concentration

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OBJECTIVES: To investigate the significance of low hemoglobin concentration and longevity in older people.

DESIGN: Randomized prospective study.

SETTING: Nursing home and geriatric hospital ward in a metropolitan welfare center.

PARTICIPANTS: Apparently stable older residents from 1990 to 1996.

MEASUREMENTS: Survival rates were estimated by statistical analysis. Sixty-three older subjects with low hemoglobin (Hb<11g/dl) and age/sex-matched normal controls (Hb≥11g/dl) were observed for 60 months. Scores of activities of daily living (ADLs) did not significantly differ between the two groups. Cerebrovascular disease was the main complication in both, and malignant neoplasms were not apparent initially.

RESULTS: After 60 months, the 5-year survival rate (FSR) of normal controls was significantly higher than that of cases with anemia ($P = .0078$). FSR was 67% in normal controls and 48% in anemic individuals age 70 to 79. The figures for individuals age 80 to 89 were 62% and 41%, respectively, and for individuals age 90 to 99 were 25% and 13%, respectively, the survival rate significantly decreasing with age in both groups ($P < .001$). FSR with severe anemia (Hb≤ 8.9g/dl) was 0% in males, and 27% in females. Values for moderate anemia (9.0g/dl to 10.9g/dl) were 25% and 51%, respectively, for normal hemoglobin (11.0g/dl to 12.9g/dl) were 44% and 61%, respectively, and for high hemoglobin (13.0g/dl≤Hb) were 50% and 70%, respectively. Advanced carcinomas were often detected at autopsy in anemic individuals. No death by cancer occurred in normal controls.

CONCLUSION: Low hemoglobin concentration predicts early death in nursing home residents. Anemia-associated conditions that might be life-threatening risks in older people require further investigation. **J Am Geriatr Soc 49: 1226–1228, 2001.**

Key words: survival rate; anemia; nursing home

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Although many investigations of hemoglobin concentration have been performed, the situation regarding optimal levels in older people is still controversial.[1] Anemia is primarily caused by impaired hematopoiesis with aging, and secondarily caused by various conditions associated with chronic diseases.[2,3] A low hemoglobin concentration causes chronic circulation load, and prognosis of chronic diseases is usually poorer than with a normal hemoglobin concentration.[4] However, hemoglobin concentration decline in older people may not be of major prognostic significance.[3] The World Health Organization (WHO) has recommended cutoff points of 13.0g/dl for males and 12.0g/dl for females.[5] In Japan, cross-sectional data and statistical analysis indicate that older people with hemoglobin concentrations of 11.0g/dl or less are considered to be anemic.[6] However, the clinical meaning of these thresholds is obscure because longitudinal studies with change of hemoglobin level have been limited. The present investigation of long-time survival of older people with low hemoglobin concentration was therefore performed with subjects in a nursing home and a metropolitan welfare center.

METHODS

The subjects were 63 individuals, in a nursing home with 400 residents, having a hemoglobin concentration <11g/dl and 63 age/sex-matched controls with values above this threshold. All were residing in the nursing home from the initial blood examination through the termination of the study, after 60 months. Blood tests were performed with an E-4000 automatic complete blood cell counter (Sysmex, Kobe, Japan). Assessment of activities of daily living (ADL) was carried out using the previously described 15-grade summed index,[7] modified from the Barthel Index method;[8] there were four grades for ambulation, four for mobility, three for feeding, three for dressing, three for bathing self, and four for controlling bowel and bladder movement. In 60 months, blood cell counts were rechecked. Blood films and screening for malignancy were conducted, and subjects with hematological malignancies, malignant tumors, or bone fractures were not included. If subjects died before the endpoint, reference was made to the last blood test before death. The maximum period between examination and death was 10 days. Causes of death were ascertained by autopsy. Statistical parameters

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were evaluated: average numbers by the Student's *t*-test, survival rates by the log rank test, and decrease of 5-year survival rate (FSR) according to age and to hemoglobin concentration by the chi-square test.

RESULTS

The average ages of the 15 male and 48 female controls were 81 (70 to 89) and 83 (72 to 98), respectively, and those for the 15 male and 48 female anemic individuals were 81 (70 to 89) and 83 (72 to 98), respectively. There were no significant differences. Hemoglobin concentration of the subjects at start varied between 6.7g/dl and 15.3g/dl; hematocrits were between 23.4% and 51.6%. All subjects were in apparently stable condition and were admitted to the clinic because of chronic disease, most commonly cerebrovascular disease (47 of normal controls (75%) and 39 of those with anemia (62%)), and not anemia itself. Senile dementia (9 and 7), organized pulmonary tuberculosis (3 and 4), and reflux esophagitis (4 and 3) were apparent in both groups, and three cases of stable rheumatoid arthritis were included in the anemia group. There were no significant differences between the two groups. When ADL was assessed by a 15-grade summed index, 24 controls and 34 anemic individuals had poor ADL scores (0–5), 10 and eight had impaired ADL scores (6–10), and 29 and 21 had good ADL scores (11–15); the differences were not significant between the two groups.

FSRs were 67% in normal controls and 48% of the anemic cases in their eighth decade (70–79), 62% and 41% in their ninth decade (80–89), and 25% and 13% in their tenth decade (90–99); FSRs significantly decreased with age increase in both groups ($P < .001$ in both). FSRs of those with hemoglobin concentrations <8.9g/dl were 0% in males and 27% in females. FSRs for those with hemoglobin levels of 9.0g/dl to 10.9g/dl were 25% and 51% ($P < .001$), respectively, with 11.0g/dl to 12.9g/dl were 44% and 61% ($P < .001$), respectively, and with ≥13.0g/dl were 50% and 70% ($P < .001$), respectively. Survival rates significantly improved with hemoglobin concentration increase ($P < .001$ in both). Survival curves indicated that average survival rate of anemic subjects was lower than that for individuals with normal hemoglobin levels at all points over 60 months, especially in females (Figure 1).

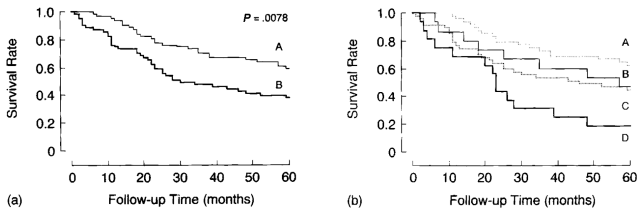

Figure 1. Cumulative Kaplan-Meier survival rates over 5 years.

(a) A = survival curve for subjects with a normal hemoglobin concentration
B = survival curve for subjects with anemia
(b) A = survival curve for females with a normal hemoglobin concentration
B = survival curve for males with a normal hemoglobin concentration.
C = survival curve for females with anemia
D = survival curve for males with anemia
The survival of females was better than that of males ($P < .001$). Survival rate in A is better than C ($P = .041$), whereas survival rate in B is better than D, without significance ($P = .068$). *P*-values were estimated using the log rank test.

Data for change in hemoglobin level of older people with initially normal hemoglobin concentrations are summarized in Table 1, with 41% of surviving patients demonstrating increase.

Causes of death determined by clinical investigation in 26 normal controls and 38 anemic cases were cardiovascular disease in 10 (38%) and 12 (32%), anemia, pneumonia in seven and five, neoplasia in two and six, accidents in two and three, renal failure in zero and three, tuberculosis in zero and two, and cerebral disease in zero and two. There were no primary hematological malignancies or associated conditions in either group. Three additional neoplasms were found by postmortem investigation in normal controls, but none in the anemic subjects.

The cellularity of bone marrow from fifth lumbar vertebral bone at autopsy was investigated in 12 cases of initially normal subjects and 29 cases with anemia, and hypercellularity was not found. Eighteen anemic cases (62%) showed hypocellularity, whereas nine normal controls (75%) showed

Table 1. Change in Hemoglobin Level of Older People, over 60 Months

Hb* (g/dl)		Total n (%)	Died n (%)	Alive n (%)			
>+1.1	normal	9 (14)	3 (12)	6 (15)			
	anemia	11 (18)	5 (16)	6 (22)	$P = .58$		
0–+1.0	normal	15 (24)	5 (18)	10 (26)			
	anemia	16 (30)	9 (31)	7 (28)	$P = .2$		
−0.1–−1.0	normal	13 (24)	2 (7)	11 (31)			
	anemia	10 (20)	6 (22)	4 (17)	$P = .026$		
<−1.1	normal	25 (38)	15 (63)	10 (28)			$P = .046$
	anemia	17 (32)	9 (31)	8 (33)	$P = .65$		
Total†	normal	62 (100)	25 (100)	37 (100)			
	anemia	54 (100)	29 (100)	25 (100)	$P = .15$		

*Change of hemoglobin in peripheral blood.
†Total number of subjects for whom data were available just before death.

normocellularity, the difference being statistically significant ($P = .031$). Regarding abnormal iron deposits in bone marrow, they were found in one (8%) normal subject and four (14%) of those with anemia ($P = .063$).

DISCUSSION

To our knowledge, this is the first study of the relationship between longitudinal survival and hemoglobin concentration in older people living under defined conditions. In terms of survival, a hemoglobin level >11.0 g/dl was here found to be favorable. Furthermore, the higher the hemoglobin concentration was, between 6.7g/dl and 15.3g/dl, the better the survival rate. The WHO criterion for adults appears more suitable for the older population than the 11.0g/dl threshold. Improvement of hemoglobin concentration might be expected to be significantly beneficial for longevity because decline of hemoglobin concentration bears a significant relationship with early death.

All the subjects in this study required some support or assistance from others for toileting, eating, transfer to/from wheelchair, or changing clothes. There was no significant difference between the ADL scores of the two groups, but basic complications associated with anemia might have importance. It has been suggested that comprehensive management in stroke rehabilitation, by removing additional risks other than arteriosclerotic conditions,[9] is necessary for good prognosis.[10] A recent case-control study in nursing homes elucidated that not only neurological deficits, but also other factors such as social support might affect the prognosis.[11] Our results suggest that anemia is a significant risk-increasing factor that requires further investigation.

Anemia may be caused by chronic diseases, as reported elsewhere.[2,3,12] Chronic infectious, inflammatory, and neoplastic disorders induce decline of erythropoieisis through modulation of action or responses to various cytokines.[13–15] Our results from postmortem subjects indicated that hypocellularity and iron deposits are more frequently observed in subjects suffering from anemia. Considering that hypocellularity reflects ineffective erythropoiesis in bone marrow, primary impairment could be concealed by overt disease.[5,16] Under these circumstances, bone marrow aspiration is indispensable for differential diagnosis of anemia.

That recovery from anemia might be important for improvement of survival in older people is supported by the previous retrospective finding that decline in hemoglobin concentration needs continuous clinical monitoring.[17,18] Survival rate of subjects with improvement from the initial hemoglobin level was here significantly higher than that observed with decline of >1.1g/dl (Table 1). It is known that anemia is associated with circulation overload,[4] with general deleterious effect for the prognosis of all illness.[19,20]

In conclusion, the present study confirmed a significance for preservation of hemoglobin concentration even in very old people. The effects of very high hemoglobin concentrations are still unclear, although increased risk of disease, such as vascular events, due to high hematocrit has been suggested.[21] From our results with older people, a hemoglobin level <13.0g/dl should be carefully monitored and adequately treated to improve quality of life.

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