Anemia and Decline in Physical Performance among Older Persons

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PURPOSE: Anemia is prevalent in old age and is potentially modifiable, but its effects on physical function have not been determined. We examined whether anemia in older persons increases the risk of subsequent decline in physical function, as measured by objective performance-based tests.

METHODS: Participants in this 4-year prospective cohort study included 1146 participants, aged 71 years or older, living in Iowa and Washington counties, Iowa. Anemia was defined according to World Health Organization (WHO) criteria as a hemoglobin concentration below 12 g/dL in women and below 13 g/dL in men. An assessment of standing balance, a timed 2.4-m walk, and a timed test of five chair rises were used to assess physical performance; these were combined into a 0 (poor) to 12 (excellent) summary scale.

RESULTS: After adjustment for baseline performance score, health status, and demographic characteristics, anemia was associated with greater mean decline in physical performance over 4 years; the adjusted mean decline was 2.3 (95% confidence interval [CI]: 1.7 to 2.8) in subjects with anemia and 1.4 (95% CI: 1.2 to 1.5) in those without anemia ($P = 0.003$). The association between anemia and greater physical decline was also present in participants who were free of diseases associated with anemia (cancer, infectious disease, and renal failure), and after adjustment for serum cholesterol, iron, and albumin levels. Persons with borderline anemia, a hemoglobin concentration within 1 g/dL above the WHO criteria, also showed greater mean physical decline (1.8; 95% CI: 1.5 to 2.2) than did those with higher hemoglobin concentrations ($P = 0.02$).

CONCLUSION: This study suggests that anemia in old age is an independent risk factor for decline in physical performance. **Am J Med. 2003;115:104–110.** ©2003 by Excerpta Medica Inc.

Age-related disability and loss in physical function are growing public health priorities (1). Loss in physical function threatens the independence and quality of life of older adults, and has substantial social and economic effects (2). Consequently, better understanding of common and potentially treatable conditions that affect physical function is needed.

Anemia, defined by the World Health Organization (WHO) as a hemoglobin concentration below 12 g/dL in women and below 13 g/dL in men (3), might affect physical function. Anemia could affect physical function through fatigue and weakness. Anemia also decreases myocardial function and increases peripheral arterial vasodilation and activation of the sympathetic and renin-angiotensin-aldosterone system, which affects the initiation or progression of diseases such as heart failure and renal failure (4–7).

The prevalence of anemia increases with age and averages about 13% in persons aged 70 years or older (8). A majority of the anemia in old age is assumed to be due to underlying diseases such as cancer and infectious disease or due to malnutrition or iron deficiency (9,10). However, in at least 20% of cases, it is not possible to attribute anemia to these factors (10,11). Surprisingly, the effects of late-life anemia have not received much research attention. We therefore used data from a 4-year longitudinal, observational study to examine whether anemia affects subsequent decline in physical performance among community-dwelling older persons.

METHODS

Data for this study were collected as part of the Established Populations for Epidemiologic Studies of the Elderly (EPESE), a prospective cohort study of older persons. A sample of the eligible population of all persons aged 65 years or older who lived in Iowa and Washington counties, Iowa, was selected (12). Between December 1981 and August 1982, 3673 persons were enrolled in the initial home interview. Follow-up home interviews were conducted annually for 6 years and then again at 10 years.

The sixth (last annual) follow-up assessment conducted in 1988 was considered the baseline for the anal-

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yses presented, as it was the first assessment that included physical performance measures. At that time, 2538 persons were contacted. Of these, we excluded 278 (10.9%) who were institutionalized, 111 (4.4%) who were cognitively or physically impaired and for whom a proxy had to be interviewed, 57 (2.2%) who had to be interviewed by telephone because they left the geographic area, 59 (2.3%) with missing physical performance data, and 306 (12.0%) with no available blood sample.

Of the 1727 remaining subjects with complete baseline data, 303 (17.5%) died during the next 4 years, 272 (15.7%) were lost to follow-up or unable to participate in the complete interview because of cognitive or physical impairment, and 6 (0.3%) had missing performance scores. A total of 1146 subjects with complete data remained and served as the subjects for our analyses. Compared with these subjects, those without follow-up data were older (mean, 80.1 vs. 77.7 years, $P < 0.001$), more often men (41.1% vs. 31.1%, $P < 0.001$), more physically impaired (mean performance score, 8.2 vs. 6.8, $P < 0.001$), and more often anemic (9.3% vs. 5.9%, $P = 0.009$) at baseline.

Anemia

Blood was obtained by venipuncture from participants in 1988. Specimens were sent to a commercial laboratory (Nichols Institute, San Clemente, California) where hemoglobin levels were analyzed using a Coulter counter. Anemia was defined by the WHO criteria (3): hemoglobin concentration below 12 g/dL (7.5 mmol/L) in women and below 13 g/dL (8.1 mmol/L) in men. Because these criteria were established using reference values from a much younger sample, we confirmed their appropriateness in identifying older people at risk of physical decline by also examining borderline anemia, defined as a hemoglobin level within 1 g/dL above WHO criteria (12 to 13 g/dL for women, 13 to 14 g/dL for men). Mean corpuscular volume was used to classify the anemia as macrocytic (>100 fL), normocytic (80 to 100 fL), or microcytic (<80 fL).

Physical Performance

Physical performance measures (sometimes referred to as lower extremity function measures) included tests of standing balance, walking speed, and ability to rise from a chair. For testing standing balance, subjects attempted to maintain their feet in three increasingly difficult positions (side-by-side, semi-tandem, and full tandem stand) for 10 seconds each. For testing walking speed, an 8-ft (2.4-m) walk at the subject's normal pace was timed twice, and the faster of the two walks was scored according to quartiles of the time required in three EPESE populations (13). For testing the ability to rise from a chair, subjects were asked to fold their arms across their chests and to stand up from a sitting position and sit five times as quickly as possible. The time to complete this task was categorized based on quartiles of the time required in three EPESE populations (13). Each physical performance test was categorized into a 5-level score, with 0 representing inability to do the test and 4 representing the highest level of performance (13). Scores on the three tests were added together as a summary performance measure (0 to 12), which predicts nursing home admission, mortality, hospitalization, and subsequent disability (13–15).

We used the continuous decline in physical performance (1988 score – 1992 score) as the main outcome (16). The average decline in physical performance was 1.5, which is associated with a 50% increased risk of developing disability in activities of daily living (transferring, bathing, eating, dressing, and using the toilet) (17). In addition, we also used a dichotomous indicator for substantial physical decline (decline of 3 or more points) as an outcome. During 4 years of follow-up, a 3-point difference in physical performance at baseline was associated with a greater risk of hospitalization, nursing home admission, mortality, and subsequent disability (15).

Covariates

We recorded age, sex, and education at baseline. Indicators of baseline health status included smoking status (never, ex-, or current smoker), body mass index (kg/m^2), and blood pressure (classified as normotension [systolic blood pressure <140 mm Hg and diastolic blood pressure <90 mm Hg], borderline systolic hypertension [diastolic blood pressure <90 mm Hg and systolic blood pressure 140–160 mm Hg], isolated systolic hypertension [diastolic blood pressure <90 mm Hg and systolic blood pressure ≥160 mm Hg], or diastolic hypertension [diastolic blood pressure >90 mm Hg]). Coronary heart disease was determined by any listed hospital discharge diagnosis (18) codes 410–414 in the 3 years before baseline, as ascertained from Health Care Financing Administration Medicare Provider Analysis and Review files (Baltimore, Maryland), self-report of heart attack, or a positive Rose questionnaire (19) for angina at any interview before baseline. Heart failure was considered present when participants had listed hospital discharge diagnoses in the past 3 years for this disease (code 428) or the current use of diuretic medication and either a digitalis or vasodilator drug. Diabetes, stroke, cancer, and lung disease were considered present when respondents had ever been told by a doctor that they had these diseases, or when they had listed hospital discharge diagnoses in the past 3 years for these diseases (codes 250 for diabetes, 430–434 for stroke, 140–208 for cancer, or 491–493 for lung disease). Infectious diseases were diagnosed by specific hospital discharge diagnoses in the past 3 years. Kidney disease was determined by a serum creatinine level above 1.5 mg/dL in women and above 1.7 mg/dL in men. Because low levels of serum cholesterol, iron, and albumin have

Table 1. Baseline Characteristics of the Study Sample by Anemia Status*

Characteristic	No Anemia (n = 906)	Borderline Anemia (n = 172)	Anemia (n = 68)	*P* for Trend
	Number (%) or Mean ± SD			
Age (years)	77 ± 5	78 ± 5	80 ± 6	<0.001
Female sex	623 (69)	121 (70)	46 (68)	0.94
Education (years)	11 ± 3	11 ± 3	11 ± 3	0.73
Cigarette smoking				0.03
Former	197 (22)	29 (17)	12 (18)	
Current	47 (5)	7 (4)	1 (2)	
Body mass index	25.0 ± 5.2	23.8 ± 6.0	24.5 ± 5.7	0.04
Blood pressure				0.06
Borderline systolic hypertension	327 (36)	49 (29)	25 (37)	
Isolated systolic hypertension	87 (10)	11 (6)	9 (13)	
Diastolic hypertension	67 (7)	7 (4)	3 (4)	
Coronary heart disease	183 (20)	33 (19)	10 (15)	0.31
Heart failure	71 (8)	19 (11)	6 (9)	0.38
Stroke	62 (7)	13 (8)	1 (2)	0.25
Diabetes	102 (11)	19 (11)	7 (10)	0.82
Cancer	156 (17)	27 (16)	22 (32)	0.02
Lung disease	184 (20)	34 (20)	17 (25)	0.53
Infectious disease	32 (4)	7 (4)	5 (7)	0.16
Kidney disease	42 (5)	13 (8)	8 (12)	0.05
Hospitalization past year	114 (13)	25 (15)	14 (21)	0.07
Baseline physical performance score	8.3 ± 2.7	7.7 ± 2.8	7.6 ± 2.7	0.003
Iron (μg/dL)	92 ± 27	79 ± 26	68 ± 30	<0.001
Cholesterol (mg/dL)	223 ± 43	210 ± 39	199 ± 42	<0.001
Albumin (g/dL)	4.2 ± 0.3	4.1 ± 0.3	3.9 ± 0.3	<0.001

* Borderline anemia was defined as a hemoglobin level of 13 to 14 g/dL for men or 12 to 13 g/dL for women. Anemia was defined using World Health Organization criteria as a hemoglobin level <13 g/dL for men or <12 g/dL for women.

been associated with anemia (20) and predict adverse health outcomes in old age (21–23), these biological variables were considered covariates in additional analyses.

Statistical Analysis

Because the decline score of physical performance was normally distributed, analyses of covariance were used to examine the effect of anemia status on decline in physical performance. Models included baseline physical performance score and were adjusted for age, sex, cigarette smoking, body mass index, blood pressure, and chronic diseases. Additional analyses were conducted to examine whether the effect of anemia on decline in physical performance persisted after adjustment for serum levels of cholesterol, iron, and albumin. Finally, logistic regression models were used to identify the association of anemia status with a 3-point drop in performance score. All analyses were performed using SPSS, version 10.1 (Chicago, Illinois).

RESULTS

The mean (± SD) age of the total sample at study baseline was 77 ± 5 years; about 70% were female (Table 1). The mean serum hemoglobin level was 15.0 ± 1.3 g/dL in men and 13.8 ± 1.3 g/dL in women. Twenty-two men and 46 women met criteria for anemia. Anemia was mostly normocytic (79%, n = 54), 10% (n = 7) was microcytic, and 10% (n = 7) was microcytic. A total of 172 subjects (15%; 51 men and 121 women) had borderline anemia (of which 96% [n = 165] were normocytic). Those with anemia were older, more likely to be nonsmokers, and more likely to have a history of cancer or kidney disease than were those without anemia (Table 1). Also, persons with anemia performed significantly worse on the baseline physical performance battery.

Hemoglobin Concentration and Mean Performance Decline

The 4-year decline score of physical performance ranged from 12 (largest decline) to -8 (largest improvement), with a mean decline of 1.5 ± 2.4. Overall, 66% (n = 757) had decreased physical performance, 18% (n = 204) improved their performance, and 16% (n = 184) showed no change. Women with anemia (hemoglobin <12 g/dL) showed the greatest physical decline (Figure 1), followed by women with borderline anemia (hemoglobin, 12 to 13 g/dL). Both groups showed significantly greater physical

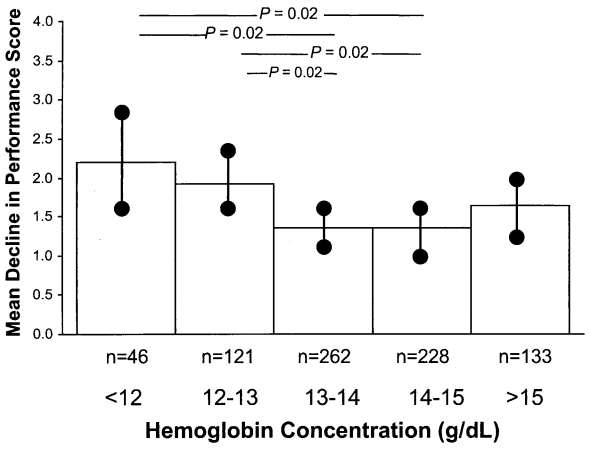

Figure 1. Adjusted mean decline in physical performance score (1988 to 1992) by hemoglobin concentration in women. Decline is adjusted for baseline performance score, age, education, smoking, blood pressure, body mass index, coronary heart disease, heart failure, stroke, diabetes, cancer, lung disease, infectious disease, and renal disease. *P* values indicate significant differences between categories. Vertical lines indicate 95% confidence intervals around the mean adjusted decline.

decline than did women with hemoglobin concentrations between 13 and 15 g/dL. A similar pattern was observed in men (Figure 2). Men with anemia (hemoglobin <13 g/dL) showed significantly greater physical decline than did men with a hemoglobin concentration ≥15 g/dL. Men with borderline anemia (hemoglobin, 13 to 14 g/dL) tended to have more physical decline than did men with a hemoglobin concentration of >16 g/dL.

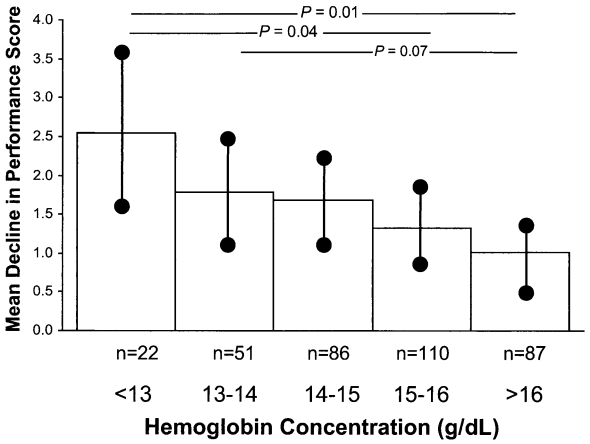

Figure 2. Adjusted mean decline in physical performance score (1988 to 1992) by hemoglobin concentration in men. Decline is adjusted for baseline performance score, age, education, smoking, blood pressure, body mass index, coronary heart disease, heart failure, stroke, diabetes, cancer, lung disease, infectious disease, and renal disease. *P* values indicate significant differences between categories. Vertical lines indicate 95% confidence intervals around the mean adjusted decline.

Anemia Status and Mean Decline in Performance

The adjusted mean decline in physical performance was significantly greater in those with borderline anemia and anemia than in those without anemia (Table 2). The mean decline in physical performance was similar among those with microcytic anemia (n = 7, decline = 2.5), normocytic anemia (n = 54, decline = 2.2), and macrocytic anemia (n = 7, decline = 2.5). Excluding subjects with diseases that were associated with anemia at baseline (infectious disease, cancer, and kidney disease), or who had been hospitalized during the year before baseline, gave similar results (Table 2). Anemia was also associated with greater decline in physical performance when subjects who were hospitalized during follow-up were excluded (Table 2). In analyses that adjusted for baseline serum levels of iron, albumin, and cholesterol, anemia ($P = 0.02$) and borderline anemia ($P = 0.02$) were associated with decline in physical performance.

Anemia Status and Substantial Decline in Performance

A total of 346 persons (30%) had a substantial decline (≥3 points) in performance during the 4 years of the study. Substantial decline in physical performance was more common in those with borderline anemia (33% [57/172]) and anemia (44% [30/68]) than in those without anemia (29% [259/906]). After adjustment for covariates, subjects with borderline anemia and anemia were more likely than the nonanemic subjects to decline substantially in performance (Table 3). Other factors associated with substantial declines in performance included worse baseline performance, increasing age, female sex, and coronary heart disease, lung disease, and infectious disease at baseline (Table 3).

DISCUSSION

In our community-based study of older persons, anemia defined according to the WHO criteria was associated with a significantly greater decline in physical performance during 4 years. Persons with borderline anemia also had significantly greater physical decline than did those with higher hemoglobin concentrations. These associations were not explained by baseline diseases or by low serum cholesterol, iron, or albumin levels. Anemia was also associated with subsequent physical decline in older persons without diseases associated with baseline anemia status (cancer, infectious disease, and renal failure).

In at least one third of cases, anemia in old age is caused by underlying chronic disease ('anemia of chronic disease') (6). In our study, anemia was associated with poor health status, especially cancer, renal failure, and infec-

Table 2. Change in Physical Performance Score during 4 Years of Follow-up by Anemia Status*

Group	Number	Mean Adjusted Decline in Performance† (95% Confidence Interval)	*P* Value‡	*P* for Trend
Total sample				
No anemia	906	1.4 (1.2–1.5)	—	0.002
Borderline anemia	172	1.8 (1.5–2.2)	0.02	
Anemia	68	2.3 (1.7–2.8)	0.003	
Sample without cancer, infectious disease, and kidney disease				
No anemia	689	1.4 (1.6–1.2)	—	0.004
Borderline anemia	128	1.8 (2.2–1.4)	0.05	
Anemia	37	2.5 (3.2–1.7)	0.004	
Sample without hospitalizations in year before baseline				
No anemia	792	1.5 (1.3–1.6)	—	0.004
Borderline anemia	147	1.9 (1.6–2.3)	0.02	
Anemia	54	2.3 (1.7–2.9)	0.009	
Sample without hospitalizations in 4 years after baseline				
No anemia	448	1.2 (1.0–1.4)	—	0.09
Borderline anemia	82	1.3 (0.9–1.8)	0.51	
Anemia	25	2.1 (1.3–2.9)	0.03	
Sample with hospitalizations in 4 years after baseline				
No anemia	458	1.6 (1.4–1.8)	—	0.03
Borderline anemia	90	2.3 (1.8–2.8)	0.02	
Anemia	43	2.2 (1.5–3.0)	0.11	

* See footnote to Table 1 for definitions of anemia and borderline anemia.
† Adjusted for baseline physical performance level, age, sex, education, body mass index, smoking, blood pressure, coronary heart disease, heart failure, stroke, diabetes, lung disease, infectious disease, kidney disease, and cancer.
‡ Compared with no anemia.

tions. However, anemia in old age is frequently multifactorial, with bleeding, malnutrition, and physiological changes as additional contributing factors (20). Physiological aging could lead to anemia through reduced bone marrow functional reserve, adaptation to a reduced lean body mass with diminished oxygen requirements, or reduced erythropoietin secretion (24,25). Although iron deficiency, either because of low iron intake or a low bioavailability of dietary iron, is a main cause of anemia in younger populations (26), it appears to be less important in old age. For older persons, there is no clear association between iron intake and anemia (27).

Overall, our results confirmed the appropriateness of the WHO criteria of anemia in old age, because persons who fulfilled the WHO anemia criteria had the greatest decline in physical performance. However, our findings also indicated that persons with borderline anemia, those with a hemoglobin level just above the WHO criteria, may also deserve attention, because they had greater physical decline than did those with higher hemoglobin levels. These findings are consistent with earlier cross-sectional findings among disabled older women (28). It is possible that some persons with borderline anemia did develop anemia after the baseline examination, which could explain the greater subsequent physical decline.

How does anemia result in greater physical decline? First, anemia may lead to feelings of weakness and fatigue that increase the risk of disability (29). Second, hypoxia resulting from anemia leads to peripheral arterial vasodilatation, myocardial dysfunction, and activation of the sympathetic and renin-angiotensin-aldosterone system to maintain blood pressure (5). These physiological changes could result in the onset or progression of diseases such as heart failure (30) and renal failure (4). Third, anemia could result in a diminished muscle oxygenation. In addition, because older persons with anemia have higher serum levels of C-reactive protein (31), acute or chronic inflammation may have caused greater physical decline. It is also possible that a decline in physical performance and anemia are associated because physicians forgo investigation and treatment of anemia in persons who are in poor physical condition. Although our

Table 3. Factors Associated with a Substantial Decline in Physical Performance (≥3 Points) during 4 Years of Follow-up*

Factor	Odds Ratio (95% Confidence Interval)	*P* Value
Baseline physical performance score (per-unit increase)	1.3 (1.2–1.4)	<0.001
Age (per 10 years)	2.3 (1.7–3.2)	<0.001
Female sex	1.4 (1.0–2.0)	0.05
Education (per year)	1.0 (0.9–1.0)	0.27
Body mass index (kg/m^2)		
<20	1.2 (0.8–1.9)	0.41
≥28	0.9 (0.6–1.3)	0.50
Smoking		
Former smoker	1.5 (1.0–2.2)	0.04
Current smoker	2.2 (1.2–4.0)	0.01
Blood pressure		
Borderline systolic hypertension	1.3 (1.0–1.7)	0.10
Isolated systolic hypertension	1.2 (0.8–2.0)	0.40
Diastolic hypertension	1.4 (0.8–2.5)	0.20
Coronary heart disease	1.7 (1.2–2.4)	0.003
Heart failure	1.3 (0.8–2.2)	0.24
Stroke	1.3 (0.8–2.2)	0.34
Diabetes	1.2 (0.8–1.9)	0.33
Lung disease	1.4 (1.0–2.0)	0.05
Infectious disease	2.1 (1.0–4.1)	0.04
Kidney disease	0.9 (0.5–1.9)	0.83
Cancer	1.2 (0.8–1.7)	0.35
Anemia status	1.5 (1.0–2.1)	0.05
Borderline anemia		
Anemia	2.1 (1.2–3.6)	0.01

* Reference groups were body mass index 20 to 28 kg/m^2, nonsmokers, subjects with normotension, and subjects without anemia. See Table 1 for definitions of anemia and borderline anemia.

analyses were adjusted for common chronic conditions, and our results were confirmed in analyses that excluded persons with diseases linked to anemia, we cannot exclude the possibility that anemia could have reflected disease severity, subclinical disease, or other diseases not measured (e.g., liver and pancreatic disease) that themselves could have resulted in physical decline.

Some limitations of the data should be acknowledged. Rates for refusing blood sampling and for patients lost to follow-up (largely due to mortality) were high. This may explain the low prevalence of anemia in our sample (5.9%) as compared with other studies (13%) (11). Loss to follow-up was higher among anemic than nonanemic older persons, which is in line with previous findings that anemia increases mortality (11). Finally, we were unable to further characterize persons with anemia through additional tests.

Nevertheless, our findings indicate that, possibly independent of its underlying cause, anemia is a risk factor for subsequent decline in physical performance in older persons. Because anemia is a potentially modifiable condition, future research should explore whether the treatment of late-life anemia results in preservation of physical function of older adults.

REFERENCES

1. Guralnik JM, Fried LP, Salive ME. Disability as a public health outcome in the aging population. *Annu Rev Public Health.* 1996;17: 25–46.
2. Fried TR, Bradley EH, Williams CS, Tinetti ME. Functional disability and health care expenditures for older persons. *Arch Intern Med.* 2001;161:2602–2607.
3. World Health Organization. *Nutritional Anaemias. Report of a WHO Scientific Group.* Geneva, Switzerland: World Health Organization; 1968. Technical Report Series No. 405.
4. Silverberg DS, Iaina A, Wexler D, Blum M. The pathological consequences of anaemia. *Clin Lab Haematol.* 2001;23:1–6.
5. Anand IS, Chandrashekhar Y, Ferrari R, et al. Pathogenesis of oedema in chronic severe anaemia: studies of body water and sodium, renal function, haemodynamic variables, and plasma hormones. *Br Heart J.* 1993;70:357–362.
6. Goldstein D, Felzen B, Youdim M, et al. Experimental iron deficiency in rats: mechanical and electrophysiological alterations in the cardiac muscle. *Clin Sci (Colch).* 1996;91:233–239.

7. Georgieva Z, Georgieva M. Compensatory and adaptive changes in microcirculation and left ventricular function of patients with chronic iron-deficiency anaemia. *Clin Hemorheol Microcirc.* 1997; 17:21–30.
8. Salive ME, Cornoni-Huntley J, Guralnik JM, et al. Anemia and hemoglobin levels in older persons: relationship with age, gender, and health status. *J Am Geriatr Soc.* 1992;40:489–496.
9. Joosten E, Pelemans W, Hiele M, et al. Prevalence and causes of anaemia in a geriatric hospitalized population. *Gerontology.* 1992; 38:111–117.
10. Ania BJ, Suman VJ, Fairbanks VF, et al. Incidence of anemia in older people: an epidemiologic study in a well defined population. *J Am Geriatr Soc.* 1997;45:825–831.
11. Izaks GJ, Westendorp RG, Knook DL. The definition of anemia in older persons. *JAMA.* 1999;281:1714–1717.
12. Cornoni-Huntley J, Ostfeld AM, Taylor JO, et al. Established populations for epidemiologic studies of the elderly: study design and methodology. *Aging (Milano).* 1993;5:27–37.
13. Guralnik JM, Winograd CH. Physical performance measures in the assessment of older persons. *Aging (Milano).* 1994;6:303–305.
14. Guralnik JM, Ferrucci L, Simonsick EM, et al. Lower-extremity function in persons over the age of 70 years as a predictor of subsequent disability. *N Engl J Med.* 1995;332:556–561.
15. Penninx BW, Ferrucci L, Leveille SG, et al. Lower extremity performance in nondisabled older persons as a predictor of subsequent hospitalization. *J Gerontol A Biol Sci Med Sci.* 2000;55:M691–M697.
16. Penninx BW, Guralnik JM, Ferrucci L, et al. Depressive symptoms and physical decline in community-dwelling older persons. *JAMA.* 1998;279:1720–1726.
17. Guralnik JM, Ferrucci L, Pieper CF, et al. Lower extremity function and subsequent disability: consistency across studies, predictive models, and value of gait speed alone compared with the short physical performance battery. *J Gerontol A Biol Sci Med Sci.* 2000; 55:M221–M231.
18. World Health Organization. *Manual of the International Statistical Classification of Diseases, Injuries, and Causes of Death.* Geneva, Switzerland: World Health Organization; 1977.
19. Rose G. The diagnosis of ischaemic heart pain and intermittent claudication in field surveys. *Bull World Health Organ.* 1962;27: 645–658.
20. Mitrache C, Passweg JR, Libura J, et al. Anemia: an indicator for malnutrition in the elderly. *Ann Hematol.* 2001;80:295–298.
21. Corti MC, Guralnik JM, Salive ME, Sorkin JD. Serum albumin level and physical disability as predictors of mortality in older persons. *JAMA.* 1994;272:1036–1042.
22. Corti MC, Guralnik JM, Salive ME, et al. Serum iron level, coronary artery disease, and all-cause mortality in older men and women. *Am J Cardiol.* 1997;79:120–127.
23. Corti MC, Guralnik JM, Salive ME, et al. Clarifying the direct relation between total cholesterol levels and death from coronary heart disease in older persons. *Ann Intern Med.* 1997;126:753–760.
24. Forbes GB, Halloran E. The adult decline in lean body mass. *Hum Biol.* 1976;48:162–173.
25. Kario K, Matsuo T, Kodama K, et al. Reduced erythropoietin secretion in senile anemia. *Am J Hematol.* 1992;41:252–257.
26. Dallman PR, Yip R, Johnson C. Prevalence and causes of anemia in the United States, 1976 to 1980. *Am J Clin Nutr.* 1984;39:437–445.
27. Joosten E, Vanderelst B, Kerkhofs P, De Boeck S. Does dietary iron intake influence the iron status in hospitalised elderly patients? *J Nutr Health Aging.* 1999;3:8–10.
28. Chaves PH, Ashar B, Guralnik JM, Fried LP. Looking at the relationship between hemoglobin concentration and prevalent mobility difficulty in older women. Should the criteria currently used to define anemia in older people be reevaluated? *J Am Geriatr Soc.* 2002;50:1257–1264.
29. Tinetti ME, Williams CS, Gill TM. Health, functional, and psychological outcomes among older persons with chronic dizziness. *J Am Geriatr Soc.* 2000;48:417–421.
30. Alexander M, Grumbach K, Remy L, et al. Congestive heart failure hospitalizations and survival in California: patterns according to race/ethnicity. *Am Heart J.* 1999;137:919–927.
31. Olivares M, Hertrampf E, Capurro MT, Wegner D. Prevalence of anemia in elderly subjects living at home: role of micronutrient deficiency and inflammation. *Eur J Clin Nutr.* 2000;54:834–839.