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CLINICAL RESEARCH STUDY

Impact of Anemia on Mortality, Cognition, and Function in Community-Dwelling Elderly

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ABSTRACT

PURPOSE: To explore the impact of varying hemoglobin levels on mortality, function, and cognition in a representative population of older persons.

METHODS: Participants in this prospective cohort study included 1 744 men and women, aged 71 years or older, from a random household sample living in Durham and surrounding counties in North Carolina. Hemoglobin levels were obtained from participants at baseline in 1992. Functional status was measured at the 4-year follow-up interview using Katz and instrumental activities of daily living. Cognition was measured using the Short Portable Mental Status Questionnaire (SPMSQ). Death was determined by search of the National Death Index, and all deaths through 2000 are included.

RESULTS: Using World Health Organization (WHO) criteria, the prevalence of anemia was 24%. There was a strong racial difference with an odds ratio, adjusted for age, education, estimated glomerular filtration rate and comorbidity of 3.0 (95% CI, 2.3-3.9) in African Americans compared with Caucasians. The risk ratio for 8-year mortality was 1.7 (95% CI, 1.5-2.0) for anemic subjects ($P = .0001$) and did not differ by sex or race. Anemia was strongly associated with poorer physical function ($P = .0001$) and cognitive function ($P = .0001$), and predicted decreases in both over a 4-year period.

CONCLUSIONS: In an elderly community-based population, anemia is more prevalent in African Americans and is independently associated with increased mortality over 8 years for both races and sexs. Anemia also is a risk factor for functional and cognitive decrease.

KEYWORDS: Aging; Elderly; African American; Anemia

Although numerous studies have examined the effect of anemia on the chronically ill, the magnitude of risk associated with anemia in the elderly remains largely unknown. As the American population ages, this often underdiagnosed and undertreated condition will increasingly impact the health of our nation. According to the 1996 National Health Interview Survey, a national household survey of the civilian noninstitutionalized population, the prevalence of anemia in those aged over 65 years is 2.3%.[1] This conservative measure of anemia would translate to over 800 000 community-dwelling elderly Americans currently suffering from anemia, with numbers climbing to over 1.8 million by the year 2050.[2] The true prevalence in the geriatric community is likely much higher, given that anemia frequently is not diagnosed or reported to the patient.[3] Recent data from the noninstitutionalized U.S. population assessed in the third National Health and Nutrition Examination Survey (1988-1994) revealed an anemia prevalence of 11.0% in men and 10.2% in women aged 65 years and older.[4] In the geriatric literature there is a wide range of anemia prevalence, from 2.9% to 61% in elderly men and 3.3% to 41% in elderly women.[5]

The diversity in the reported prevalence of anemia

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may be due to differences in the characteristics of the elderly populations studied and, in part, to study methodology.[5,6] The majority of studies use the World Health Organization (WHO) definition of anemia (hemoglobin values 12.0 g/dL for women and 13.0 g/dL for men). Although this definition has been widely used in the geriatric literature, it is based on hemoglobin values from studies that did not include subjects aged >64 years.[7-10] Recent studies have questioned the use of this traditional method for determining anemia by examining the relationship between hemoglobin levels and the risk of clinically relevant outcomes in the geriatric population.[11-12]

To improve the diagnosis and treatment of anemia, it is essential that appropriate clinical criteria such as mortality, function, and cognition be used to appropriately define anemia in the geriatric population. These criteria must be studied in populations that are sufficiently diverse and representative of the general elderly population. Our study was conducted in a racially diverse, community-dwelling elderly population followed over 8 years with the purpose of answering the following four questions. At what hemoglobin concentration is optimal survival seen in men and women? Are there racial differences in the relationship of anemia with mortality? Is anemia associated with an increase in mortality beyond 5 years? Is anemia associated with a decrease in cognition as well as function?

CLINICAL SIGNIFICANCE

- Anemia is 3-fold more common in elderly African Americans than Caucasians.
- For both races and genders, anemia is equally and independently associated with mortality over an 8-year period.
- Anemia is associated with lower physical and cognitive function and predicts further functional decline (both cognitive and physical) over a 4-year period.

METHODS

Subjects

Subjects were participants in the Duke Established Populations for Epidemiologic Studies of the Elderly, a component of the four-site National Institute on Aging study.[13-15] This study was approved by the Duke institutional review board, and informed consent was obtained from each participant and proxy. The study enrolled 4162 participants aged 65 years or older who were selected in a random household sample of a five-county area including and adjacent to Durham, NC in 1986.

African Americans were oversampled (54% of sample) to allow for comparison by race. Participants were contacted annually. In 1992, at the sixth annual contact, 2569 interviews were conducted, functional status and cognition were measured, and blood samples permitting determination of hemoglobin levels were obtained on 1744 participants. Blood was not obtained from those who refused, from those who were unable to give consent because of cognitive impairment, when there were technical difficulties in the blood draw, or from those who had moved from the in-person interview area. Those unable or refusing to give blood tended to be older and more impaired than those who gave blood.[16] Forty-three of the participants had incomplete interview data and were not included in the final analysis. In 1996, a follow-up in-person interview was conducted, and functional status and cognition were again determined. Mortality status was obtained on all 1701 remaining participants 8 years after initial blood draw.

Measures

Information on demographic characteristics was obtained at entry into the study. At the sixth annual interview, when the blood draw occurred, height and weight were measured, and body mass index (BMI; kg/m^2) was calculated. Blood was obtained from participants by venipuncture. Hemoglobin was measured using a Coulter counter. Kidney function was determined using the estimated glomerular filtration rate (GFR) in mL/min/1.73 m^2 units based on the Modification of Diet in Renal Disease (MDRD) study.[17] At this and the follow-up interview 4 years later, we obtained information on smoking status, alcohol use, hospitalization, institutionalization, and health status. Information was gathered on 5 physical health conditions including heart attack, hypertension, diabetes, stroke and cancer. A simple weighted summary score, the health index, was developed to provide a snapshot of medical status based on the presence of these selected chronic physical health conditions.[18] Two measures of functional status were obtained at each interview and included Katz (basic personal maintenance tasks, such as toileting and bathing), range 0-5, and instrumental activities of daily living (ability to function in society, such as shopping and handling money) range 0-5. Cognition was measured using the Short Portable Mental Status Questionnaire (SPMSQ), a test measuring orientation, personal history, remote memory and calculations, range 0-10.[19] Anemia was defined by the WHO criteria: hemoglobin concentration 12.0 g/dL for women and 13.0 g/dL for men. Death was determined by search of the National Death Index, and all deaths as of December 31, 2000 are included in the current analyses.

Statistical Analysis

Differences in baseline characteristics between anemics and nonanemics were determined using chi-squared tests and *t* tests, for categorical and continuous independent variables, respectively. Unadjusted and adjusted logistic regression analyses were conducted to examine the association between anemia and race. All multivariate analyses were adjusted for age, education, BMI, estimated GFR, as a continuous variable, hospitalization, institutionalization, and

Table 1 Baseline Characteristics of the Study Population be Anemia Status

Characteristic	No Anemia (n = 1318) Number (%) or Mean ± SD	Anemia (n = 426) Number (%) or Mean ± SD	*P* Value
Female	854 (65)	280 (66)	.73
African American	624 (47)	312 (73)	<.0001
Age			
65-74	493 (37)	100 (23)	
75-79	405 (31)	131 (31)	
>80	420 (32)	195 (46)	<.0001
Education	569 (43)	249 (58)	
<9			
9-12	508 (39)	116 (27)	
>12	241 (18)	61 (14)	<.0001
Hospitalized in past year	256 (19)	127 (30)	<.0001
Currently institutionalized	66 (5)	27 (6)	.29
Body mass index	25.93 ± 4.52	25.47 ± 4.51	.07
Health index			
Mild	244 (19)	76 (18)	
Moderate	527 (40)	152 (36)	
Severe	534 (41)	191 (46)	.21
Glomerular filtration rate* (GFR) (mL/min/1.73 m^2)	56.1 (13.0)	51.5 (17.3)	<.0001

Anemia was defined using World Health Organization criteria as a hemoglobin level <13 g/dL for men and <12 g/dL for women.
*Calculated using abbreviated MDRD Study equation based on age, sex, race and serum creatinine.

health condition. Kaplan-Meier curves were used to examine the 8-year survival by anemic status, separately, by sex and race. Cox-proportional hazards model were used to examine the adjusted risk-ratios for survival separately by anemic status and by race, and for the whole sample. Cox proportional hazards models were are also used to examine risk for survival by the hemoglobin levels for men and women. This analysis was done to obtain the possible optimum hemoglobin level for survival**.** In addition, we examined baseline activities of daily living (ADL), instrumental activities of daily living (IADL), and SPMSQ by anemic status, sex, and race using a nonparametric Wilcoxon test. Changes in Katz ADL, IADL, and cognition from baseline to 4 years later were examined by anemic status, sex and race using *t* tests. We also examined the change in function and cognition, separately, by anemic status, sex and race, using analysis of co-variance and adjusting for all the above covariates. Using full sample and change in Katz ADL, IADL, and cognition as the dependent variable, in 3 separate models, we examined the interaction of anemic status by sex and anemic status by race after adjusting for covariates.

RESULTS

Baseline characteristics of the study participants are shown in Table 1. Participants consisted of 1744 community-dwelling men and women aged 71 to 102 years. The mean (± SD) age of the total sample was 78 (± 5.42) years, and 65% were female. Using WHO criteria, the prevalence of anemia was 24%. It was age related; 17% (65-74), 25% (75-79), 32% (>80), P <.0001, but not sex related. Two hundred eighty women (33%) and 146 men (31%) met criteria for anemia, P = .73. Those with anemia were older, more likely to be African American, to have been hospitalized in the past year, to have lower estimated GFR, and to have lower education levels.

The average hemoglobin level among Caucasians was 13.60 g/dL, compared with 12.76 g/dL among African Americans. Both races had similar decreases in hemoglobin (Hg) concentrations with advancing age. Caucasians aged 65 to 80 years had an average Hg of 13.75 g/dL, whereas those over age 80 had an average of 13.16 g/dL (P = .001). African Americans had an average hemoglobin concentration of 12.91 and 12.41 in those aged 65 to 80 and over 80, respectively (P = .001). Using WHO criteria, the prevalence of anemia among African Americans was 33.6%, compared with only 13.8% in Caucasians, P = .0001. The unadjusted odds ratio (OR) for anemia in African Americans was 3.2 (95% CI, 2.5-4.1). The odds ratio remained statistically significant after adjustment for age, education, BMI, estimated GFR, hospitalization, institutionalization, and health condition (OR 3.0; 95% CI, 2.3-3.9).

Table 2 Risk Ratios for Mortality

Variable	Unadjusted RR (95% CI)	Adjusted* RR (95% CI)
Anemic vs nonanemic	1.7 (1.5-2.0)	1.4 (1.2-1.6)
Anemic women	1.9 (1.6-2.3)	1.4 (1.2-1.8)
Anemic men	1.5 (1.2-1.9)	1.3 (1.0-1.7)
Anemic Caucasians	1.8 (1.4-2.4)	1.3 (1.0-1.6)
Anemic African Americans	1.7 (1.4-2.1)	1.4 (1.2-1.8)

*Adjusted for age, education, BMI, GFR, hospitalization, institutionalization and health condition.

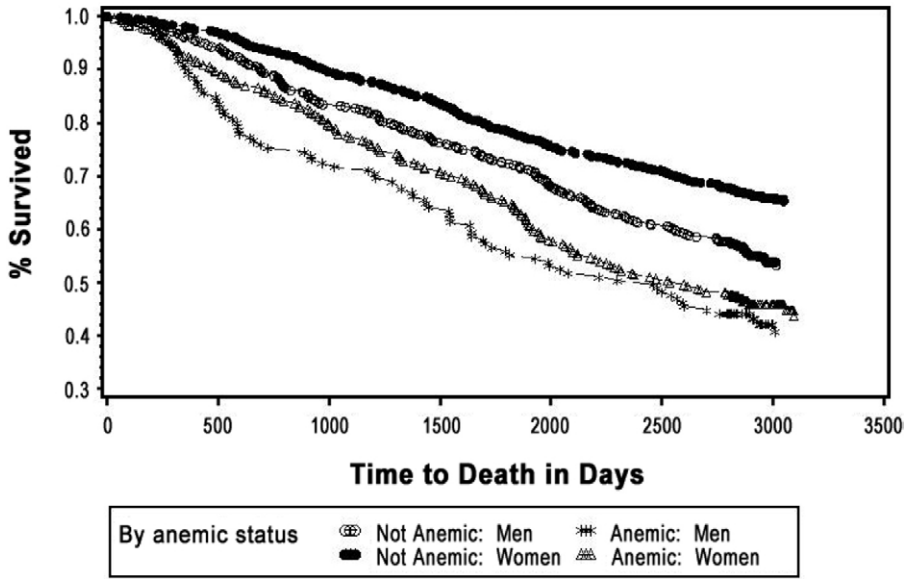

Figure 1 Survival by sex. Survival over 8 years by sex and anemia status. Sex difference ($P = .3173$), anemia vs nonanemia: men ($P = .0027$), women ($P = .0001$).

There was a statistically significant increase in mortality among the entire sample of anemic participants compared with nonanemic participants, relative risk (RR) 1.4; 95% CI, 1.1-1.6, which persisted after breakdown by sex (Table 2). Figure 1 shows survival curves among men and women with and without anemia over a period of 8 years. There was no sex difference in survival among anemic participants ($P = .3173$), however both men and women with anemia were more likely to die than their nonanemic counterparts (women $P = .0001$, men $P = .0027$). Despite the marked difference in anemia prevalence by race, survival analysis indicated that the average survival over 8 years did not differ significantly by race among anemic ($P = .5549$) or nonanemic ($P = .4893$) participants (Figure 2). Table 2 shows the adjusted risk ratios for death at 8 years among African Americans with anemia (RR 1.7; 95% CI, 1.4-2.1) compared with Caucasians with anemia (RR 1.8; 95% CI, 1.4-2.4). The adjusted relative risk of death did not differ significantly among African Americans with anemia compared with Caucasians with anemia (RR 0.85; 95% CI, 0.6-1.2).

Figure 3 reveals the percent survival by hemoglobin concentration in women and men. Those with intermediate hemoglobin concentrations had the highest survival,

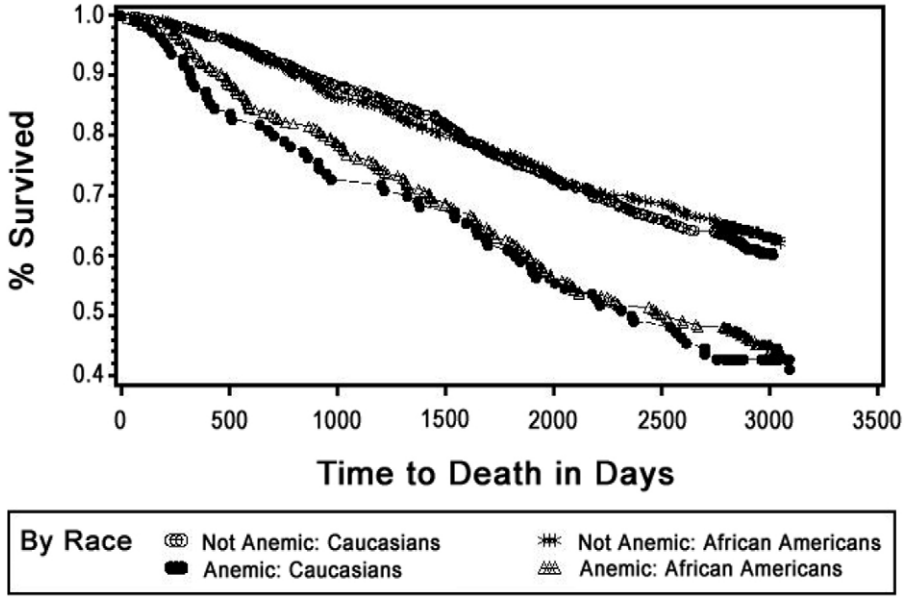

Figure 2 Survival by race. Survival by race and anemia status over 8 years. No difference by race whether anemic ($P = .5549$) or nonanemic ($P = .4813$).

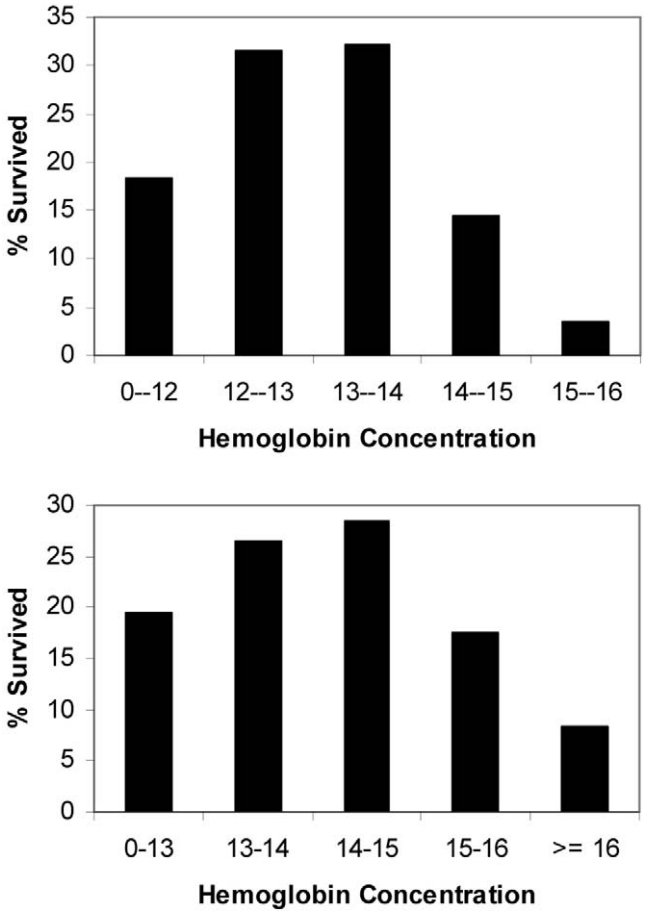

Figure 3 Survival by hemoglobin concentration. Top panel is women, bottom panel men. Survival is over 8 years. *P* values for overall differences: women ($P < .0001$), men ($P = .0950$).

whereas the lowest survival rates were found in the extreme concentrations. The survival differences between hemoglobin concentrations were statistically significant in women (*P* .0001) but not in men ($P = .0950$). The highest percent survival at 8 years occurred in women with hemoglobin concentrations between 13.0 and 14.0 g/dL and in men with hemoglobin concentrations between 14.0 and 15.0 g/dL.

Table 3 shows the unadjusted and adjusted risk ratios for all-cause mortality by specific hemoglobin concentrations in both men and women. Those women with hemoglobin concentrations 12.0 g/dL had higher risks of mortality at 8 years in the unadjusted analysis when compared with women whose hemoglobin levels were between 12.0 and 13.0 g/dL. After controlling for baseline characteristics, those women with hemoglobin concentrations between 10.0 and 11.0 g/dL maintained a higher risk of mortality (RR 2.1; 95% CI, 1.5-3.1), however, those women with hemoglobin concentrations between 11.0 and 12.0 g/dL did not have a statistically significant increase in mortality. In the unadjusted analyses, men with hemoglobin levels between 10.0 and 11.0 g/dL suffered a statistically significant increase in mortality at 8 years compared with men whose levels were between 13.0 and 14.0 g/dL, but not in the adjusted model

Table 3 Adjusted and Unadjusted Mortality by Hemoglobin Levels in Men and Women

Hemoglobin (g/dL)	Unadjusted RR (95% CI)	Adjusted* RR (95% CI)
Women		
0-10	3.9 (2.6-6.0)	1.9 (1.2-3.0)
10-11	2.3 (1.7-3.3)	2.2 (1.5-3.1)
11-12	1.6 (1.2-2.1)	1.2 (1.0-1.8)
12-13	1.0 (reference)	1.0 (reference)
13-14	0.9 (0.7-1.2)	1.0 (0.7-1.3)
14-15	1.1 (0.8-1.6)	1.2 (0.9-1.7)
15-16	1.7 (1.1-2.6)	1.6 (1.0-2.5)
>16	3.9 (1.7-8.9)	4.1 (1.8-9.4)
Men		
0-10	1.9 (0.8-4.8)	1.3 (0.5-3.3)
10-11	2.2 (1.1-4.1)	1.7 (0.9-3.3)
11-12	1.3 (0.7-2.3)	1.3 (0.7-2.4)
12-13	1.3 (0.9-1.8)	1.2 (0.9-1.7)
13-14	1.0 (reference)	1.0 (reference)
14-15	0.9 (0.6-1.3)	1.1 (0.7-1.4)
15-16	0.9 (0.6-1.3)	1.0 (0.7-1.4)
>16	0.8 (0.5-1.4)	0.9 (0.5-1.5)

*Adjusted for age, education, BMI, GFR, hospitalization, institutionalization and health condition.

Table 4 Baseline Katz ADL, IADL and SPMSQ by Anemia Group, Race and Sex

Variable	No Anemia	Anemia	*P* Value*
Full sample			
Katz ADL (0-5)	0.27 (0.86)	0.47 (1.14)	.0001
IADL (0-7)	0.80 (1.44)	1.17 (1.68)	.0001
SPMSQ (0-10)	1.58 (1.75)	2.03 (1.78)	.0001
By sex			
Katz ADL			
Male	0.17 (0.67)	0.39 (1.14)	.0313
Female	0.32 (0.95)	0.51 (1.14)	.0007
IADL			
Male	0.64 (1.39)	0.82 (1.54)	.1880
Female	0.89 (1.46)	1.35 (1.73)	.0001
SPMSQ			
Male	1.48 (1.75)	1.80 (1.79)	.0224
Female	1.63 (1.75)	2.15 (1.77)	.0001
By race			
Katz ADL			
African Americans	0.34 (0.98)	0.49 (1.18)	.0807
Caucasians	0.20 (0.73)	0.43 (1.01)	.0002
IADL			
African Americans	1.03 (1.57)	1.19 (1.70)	.2138
Caucasians	0.61 (1.29)	1.10 (1.64)	.0002
SPMSQ			
African Americans	2.18 (2.02)	2.28 (1.78)	.1014
Caucasians	1.03 (1.23)	1.34 (1.58)	.0425

Ranges: Katz ADL, 0-5; IADL, 0-7; SPMSQ, 0–10.
*P value based on nonparametric Wilcoxon test.

Table 5 Decrease of Katz ADL, IADL, SPMSQ by Anemia Group, Race, and Sex

Variable	No Anemia	Anemia	*P* Value*
Full sample			
Katz ADL (0-5)	0.57 (1.29)	0.79 (1.45)	.0241
IADL (0-7)	0.69 (1.51)	0.75 (1.58)	.6100
SPMSQ (0-10)	1.04 (1.98)	1.40 (2.16)	.0106
By sex			
Katz ADL			
Male	0.46 (1.14)	0.37 (1.13)	.5245
Female	0.63 (1.35)	0.99 (1.54)	.0041
IADL			
Male	0.55 (1.41)	0.55 (1.29)	.9864
Female	0.76 (1.56)	0.84 (1.70)	.5631
SPMSQ			
Male	0.97 (1.90)	0.91 (1.76)	.7929
Female	1.07 (2.02)	1.66 (2.29)	.0033
By race			
Katz ADL			
African Americans	0.61 (1.31)	0.81 (1.46)	.0840
Caucasians	0.54 (1.27)	0.75 (1.42)	.1956
IADL			
African Americans	0.69 (1.55)	0.80 (1.68)	.6596
Caucasians	0.69 (1.48)	0.61 (1.27)	.4325
SPMSQ			
African Americans	1.28 (1.96)	1.49 (2.20)	.1707
Caucasians	0.83 (1.97)	1.17 (2.04)	.2498

Ranges: Katz ADL, 0-5; IADL, 0-7; SPMSQ, 0–10.
**P* value based on *t* test.

(RR 2.2; 95% CI, 1.1-4.1 and RR 2.0; 95% CI, 0.9-3.3, respectively).

At baseline, there was more impairment in functional status (both Katz ADL and IADL) and cognition among those with anemia (Table 4) than in those with no anemia. The difference between the anemic and nonanemic groups is statistically significant for baseline Katz and IADL, as well as cognition. Both anemic women and men had higher levels of impairment compared to those with no anemia, but women had more impairment than men (Table 4). In both men and women the difference in the impairment levels between the anemic and non-anemic groups is statistically significant for Katz ADL and cognition, while IADL is significant only in women. Although both Caucasians and African Americans with anemia had larger impairments than nonanemics on ADL, IADL, and cognition, these differences are significant only in Caucasians (Table 4).

Anemic subjects had significant decrease in ADL and cognition compared with those who were not anemic (Table 5). Anemic women, but not men, had a larger significant decrease in ADL and cognition than those who were not anemic. In both African Americans and Caucasians, there are no statistical differences between the anemics and non-anemics on Katz ADL, IADL, and cognition, even though the anemics have a larger decrease. In analyses with the full sample, using analyses of covariance, there is a significant interaction of sex by anemic status, with decrease in Katz ADL and SPMSQ as the outcome in separate models. Women showed higher levels of decrease on both outcomes than men (adjusted mean decrease in women on Katz ADL = 0.85 and adjusted mean decrease in men on Katz ADL = 0.29; $P = .0012$; adjusted mean decrease in women on SPMSQ = 1.48 and adjusted mean decrease in men on SPMSQ = 0.29; *P* value for the difference = .0248). Race by anemic status interaction was not significant for both the outcomes. Interactions were not significant in the model with IADL as the outcome.

DISCUSSION

This study of 1744 community-dwelling persons aged 71 years or older provides important information about the impact of anemia in an ethnically diverse population. The prevalence of anemia found in our patient population was higher than that seen in other community-dwelling elderly populations of predominantly Norwegian ancestry and higher than the prevalence recently reported from the NHANES III data.[3,4,20,21] African Americans accounted for 54% of our patient population and had a significantly increased prevalence of anemia compared with Caucasians. Even after adjusting for significant social confounders and health status, African Americans were over three times more likely to suffer from anemia than their Caucasian counterparts. There has been some debate as to whether anemia criteria should be adjusted based on race, as several prior studies have shown lower hemoglobin levels in African Americans versus Caucasians across varying age groups.[22-26] However, there is a paucity of data evaluating the clinical consequences of racial differences in anemia prevalence. This is the first study, to our knowledge, to evaluate whether or not this racial difference in prevalence correlates with increased mortality in the community-dwelling elderly. African Americans who met the WHO criteria for anemia did not have a significantly higher mortality rate over 8 years, when compared to Caucasians with anemia after controlling for significant differences in health condition and chronic disease burden. Thus, race does not independently increase the risk of mortality in elderly with anemia. This is important because justification for race-specific criteria for anemia would depend on evidence of adverse clinical outcomes at different hemoglobin levels.

Two prior studies have shown that decreases in hemoglobin concentration are associated with increased mortality over 5 years in community-dwelling elderly persons.[27,28] Our study followed both men and women over 8 years and found an overall increase in mortality of 40% in anemic patients. Neither the prevalence nor the overall risk of death differed significantly among men and women. Our study attempted to identify the hemoglobin concentration at which optimal survival is obtained in the community-dwelling elderly population. Optimal survival was obtained at a hemoglobin concentration of 13.0-14.0 g/dL in women and 14.0-15.0 g/dL in men in an unadjusted analysis.

Recent studies have examined whether clinically relevant outcomes such as mobility and function are better in people with hemoglobin levels above the WHO threshold for anemia.[11,12] A study by Chaves et al[11] showed that women with a hemoglobin concentration between 13.0 g/dL and 14.0 g/dL had significantly lower mobility difficulty prevalence when compared with those with hemoglobin levels of 12 g/dL. Penninx et al found that both men and women with hemoglobin concentrations above the WHO threshold for anemia had decreased muscle strength and a significant decrease in physical performance over 4 years compared to persons with higher hemoglobin levels.[12,29] The impact of anemia on cognition has likewise been of considerable interest. Prior studies have suggested an association between Alzheimer's Disease and anemia and vascular dementia and anemia in retrospective case-control analyses.[30-32] Other studies, in patients with chronic renal disease and cancer, also have suggested such an association and have indicated modest improvement in cognition following treatment with erythropoietin, suggesting a direct relationship.[33-35] There have been no studies evaluating this relationship in community-dwelling elderly. In our studies, there is a clear association of anemia and both physical function and cognitive status. Moreover, the presence of anemia predicts subsequent decrease in physical function and cognitive status. This impact is seen to a greater extent in females than males but with no difference between Caucasians and African Americans. This is consistent with the generally greater prevalence of disability in older women than in men.[36] The greater decrease in cognition for women is a bit surprising given the generally greater prevalence of memory impairment in men in the community.[37] This may indicate a particular sensitivity of women to the effects of anemia than other causes of memory impairment. As was the case for mortality, despite the greater prevalence of anemia in African Americans, they appear to be no more functionally disadvantaged by it than Caucasians. The data available to us did not allow us to address the relationship of anemia to frailty, often considered a precursor to functional decrease. However, a recent study has shown that anemia is associated with frailty in elderly women, lending further support to the potential role of anemia in the evolution to functional decrease.[38]

This study has several potential weaknesses that should be acknowledged. Although our analyses were adjusted for common chronic health conditions and baseline patient characteristics known to influence our measured outcomes, there is a possibility that subclinical disease or other diseases not measured (such as lung disease) may have themselves contributed to decreases in survival, function and cognition. Clinical disease was determined by patient self-report, which is a source for potential bias; however, previous research has found self-report to be reasonably accurate.[39] We did not have information allowing assessment of cause of anemia nor whether there had been any treatment for anemia. Finally, subjects who refused blood draw tended to be older and more impaired, thus causing a potential for nonresponse bias. If present, this bias would have underestimated the risk associated with lower hemoglobin levels.

By measuring clinically relevant outcomes in a large, racially diverse, community-dwelling, randomly selected population, our study is readily generalizable to our nation's growing elderly population. We conclude that the proportion of older persons who meet the WHO criteria for anemia is substantial and that they are at an increased risk for mortality and functional and cognitive decrease. African Americans, despite a higher prevalence of anemia, are at no greater risk than Caucasians for these adverse outcomes.

References

1. Adams PF, Hendershot GE, Marano MA, for the National Center for Health Statistics. Current estimates from the National Health Survey, 1996. *Vital Health Stat 10*. 1999;1–203.
2. U.S. Census Bureau. National Population Projections. I. Summary Files. Total population by age, sex, race, and Hispanic origin. (NP-T3) Projections of the total resident population by 5-year age groups, and sex with special age categories: middle series, 1999 to 2100. Revised August 2, 2002. Available at: http://www.census.gov/population/www/projections/natsum-T3.html. Accessed May 4, 2004.
3. Ania B, Suman V, Fairbanks V, et al. Incidence of anemia in older people: an epidemiologic study in a well-defined population. *J Am Geriatr Soc*. 1997;45:825-831.
4. Guralnik JM, Eisenstaedt RS, Ferucci L, et al. Prevalence of anemia in persons 65 years and older in the United States: evidence for a high rate of unexplained anemia. *Blood*. 2004;104:2263-2268.
5. Beghe C, Wilson A, Ershler W. Prevalence and outcomes of anemia in geriatrics: a systematic review of the literature. *Am J Med*. 2004;116:3S-10S.
6. Balducci L. Epidoemiology of anemia in the elderly: information on diagnostic evaluation. *J Am Geriatr Soc*. 2003;51(Suppl):2-9.
7. Natvig K. Studies on hemoglobin values in Norway. V. Hemoglobin concentration and hematocrit in men aged 15-21 years. *Acta Med Scand*. 1966;180:613-620.
8. De Leeuw NK, Lowenstein L, Hsieh YS. Iron deficiency and hydremia in normal pregnancy. *Medicine (Baltimore)*. 1966;45:291-315.
9. Sturgeon P. Studies of iron requirements in infants. III. Influence of supplemental iron during normal pregnancy on mother and infant. A. The mother. *Br J Haematol*. 1959;5:31-44.
10. Kilpatrick GS, Hardisty RM. The prevalence of anemia in the community: a survey of a random sample of the population. *BMJ*. 1961;1:778-782.
11. Chaves PH, Ashar B, Guralnik JM, et al. 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 by reevaluated? *J Am Geriatr Soc*. 2002;50:1257-1264.
12. Penninx, B, Guralnik, J, Onder G, et al. Anemia and decline in physical performance among older persons. *Am J Med*. 2003;115:104-110.
13. Cornoni-Huntley J, Ostfeld AM, Taylor JO, et al. Established populations for epidemiologic studies of the elderly: study design and methodology. *Aging Clin Exp Res*. 1993;5:27-37.
14. Cornoni-Huntley J, Brock DB, Ostfeld AM, et al., eds. *Established Populations for Epidemiologic Studies of the Elderly: Resource Data Book* (NIH publication 86-2443). Washington, DC: U.S. Government Printing Office; 1986.
15. Cornoni-Huntley J, Blazer DG, Lafferty ME, et al, eds. *Established Populations for Epidemiologic Studies of the Elderly: Resource Data Book, Vol. 2* (NIH publication 90-495). Washington, DC: U.S Government Printing Office; 1990.
16. Pieper CF, Rao KMK, Currie MS, et al. Age, functional status and racial differences in plasma D-dimer levels in community-dwelling elders. *J Gerontol Med Sci*. 2000;55A:M649-M657.

17. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. *Ann Intern Med.* 1999;130:461-470.
18. Fillenbaum GG, Leiss JK, Cohen HJ. Developing a summary measure of medical status. *Aging Clin Exp Res*. 1998;10:395-400.
19. Gallo JJ, Reichel W, Anderson L. *Handbook of Geriatric Assessment*. Rockville, MD: Aspen Publishers; 1988.
20. 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.
21. Nilsson-Ehle H, Jagenburg R, Landahl S, Svenborg A, Westin J. Decline of blood haemoglobin in the aged: a longitudinal study of an urban Swedish populations from age 70 to 81. *Br J Haematol*. 1989; 71:437-442.
22. Owen GM, Lubin AH, Garry PJ. Hemoglobin levels according to age, race and transferrin saturation in preschool children of comparable socioeconomic status. *J Pediatr*. 1973;82:850-851.
23. Perry GS, Byers T, Yip R, Mergen S. Iron nutrition does not account for the hemoglobin differences between blacks and whites. *J Nutr*. 1992;122:1417-1424.
24. Pan W-H, Habicht J-P. The non-iron-deficiency-related difference in hemoglobin concentration distribution between blacks and whites and between men and women. *Am J Epidemiol*. 1991;134:1410-1416.
25. Johnson-Spear MA, Yip R. Hemoglobin difference between black and white women with comparable iron status: justification for race-specific anemia criteria. *Am J Clin Nutr*. 1994;60:117-121.
26. Jackson RT. Separate hemoglobin standards for blacks and whites: a critical review of the case for separate and unequal hemoglobin standards. *Med Hypotheses*. 1990;32:181-189.
27. Izaks GJ, Westendorp RG, Knock DL. The definition of anemia in older persons. *JAMA*. 1999;281:1714-1717.
28. Chaves PH, Volpato S, Fried L. Challenging the World Health Organization criteria for anemia in the older woman. *J Am Geriatr Soc*. 2001;49:S3.
29. Penninx BWJH, Pahor M, Cesari M, et al. Anemia is associated with disability and decreased physical performance and muscle strength in the elderly. *J Am Geriatr Soc*. 2004;52:719-724.
30. Beard CM, Kokmen E, O'Brien PC, et al. Risk of Alzheimer's disease among elderly patients with anemia: population-based investigations in Olmstead County, Minnesota. *Ann Epidemiol*. 1997; 7:219-224.
31. Argyriadou S, Vlachonikolis I, Melisopoulou H, et al. In what extent anemia coexists with cognitive impairment in elderly; a cross-sectional study in Greece. *BMC Fam Pract*. 2001;2:5.
32. Milward EA, Grayson DA, Creasey H, et al. Evidence for association of anemia with vascular dementia. *Neuroreport*. 1999;10:2377-2381.
33. Pickett JL, Theberge DC, Brown WS, et al. Normalizing hematocrit in dialysis patients improves brain function. *Am J Kidney Dis*. 1999;33: 1122-1130.
34. Littlewood TJ. Bajetta E, Nortier JWR, Vercammen E, Rappoport B. Effects of epoetin alfa on hematologic parameters and quality of life in cancer patients receiving nonplatinum chemotherapy: results of a randomized, double-blind placebo-controlled trial.*J Clin Oncol*. 2001;19: 2865-2874.
35. O'Shaughnessy J, Vukelja S, Savin M, et al. Impact of epoetin alpha on cognitive function, asthenia, and quality of life in women with breast cancer receiving adjuvant or neoadjuvant chemotherapy: analysis of 6-month follow-up data. Abstract presented at the 25th Annual San Antonio Breast Cancer Symposium; December 11-14, 2002; San Antonio, TX.
36. Indicator 18 (Depressive Symptoms) and Indicator 19 (Disability), Health Status. *Older Americans 2004: Key Indicators of Well-Being Report*, pp. 27-28.
37. Indicator 17 (Memory Impairment), Health Status. *Older Americans 2004: Key Indicators of Well-Being Report*, p. 26.
38. Chaves PHM, Semba RD, Leng SX, et al. Impact of anemia and cardiovascular disease on frailty status of community-dwelling older women: the Women's Health and Aging Studies I and II. *J Gerontol Biol Sci Med Sci*. 2005;60:729-735.
39. Lagaay AM, Van der Meij JC, Hijmans W. Validation of medical history taking as a part of a population-based survey in subjects aged 85 and over. *BMJ*. 1992;304:1091-1092.