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Hemoglobin discriminates stages of chronic kidney disease in elderly patients

YING CHEN[1], MINGZHAO QIN[1], JIE ZHENG[2], HONG YAN[3], MEI LI[4], YAO CUI[1], RUIHUA ZHANG[1], WEI ZHAO[1] and YING GUO[1]

Divisions of [1]Geriatrics, [2]Nephrology, [3]Laboratory and [4]Nuclear Medicine, Beijing Tongren Hospital, Capital Medical University, Beijing 100730, P.R. China

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Abstract. The prevalence of chronic kidney disease (CKD) increases with age, and anemia is known to affect the outcome of subjects with CKD. However, little is known with regard to the associations between metabolic complications and stages of CKD among elderly patients. Thus, the aim of the present study was to investigate the prevalence of CKD in elderly Chinese patients, as well as the associations between stages of CKD and clinically important complications of anemia. In total, 2,258 individuals with CKD, divided into younger (n=989) and elderly (n=1,269) groups, were enrolled in the study between June 2009 and December 2011. The glomerular filtration rate (GFR) was assessed using a 99mTc-DTPA renal dynamic imaging method (modified Gate's method). The levels of serum creatinine (SCr) and hemoglobin (Hb), and the hematocrit (HCT) were measured simultaneously per manufacturer's instructions. In the elderly group, the levels of SCr and proportional ratios were higher, while the GFR, Hb level, HCT and proportional ratios were lower when compared with the values in the younger group. Statistically significant differences were observed in the Hb concentrations when comparing individuals classified with different stages of CKD in the younger and elderly groups. In the younger group, there was no significant difference in the Hb concentrations between the stage 3a and 3b CKD patients. However, in the elderly group, the Hb concentrations were significantly higher in patients classified with stage 3a CKD when compared with those with stage 3b, whose GFR cutoff point was <60 ml/min/1.73 m^2. In conclusion, the results indicated that Hb levels may be used to discriminate stages of CKD in elderly patients; thus, Hb may be used as a biomarker to assess the severity of CKD.

Correspondence to: Professor Mingzhao Qin, Division of Geriatrics, Beijing Tongren Hospital, Capital Medical University, 1 Dong Jiao Min Xiang Street, Beijing 100730, P.R China
E-mail: dr.mingzhao.qin@gmail.com

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Introduction

The prevalence of chronic kidney disease (CKD) is high in the general population and increases significantly with age (1). As reported in the National Health and Nutrition Examination Survey, the prevalence of a reduced estimated glomerular filtration rate (GFR; <60 ml/min/1.73 m^2) was 37.8% among participants aged >70 years (1). However, the clinical implications of a low GFR in elderly individuals remains controversial, particularly among the Chinese population. Certain studies have proposed that a gradual decline in the GFR is an expected consequence of aging, and that rigid cutoffs of the GFR result in the arbitrary 'labeling' of individuals with disease, particularly when the GFR is considered to indicate mild CKD (45-59 ml/min/1.73 m^2) (2,3). However, this estimate of the GFR is cumbersome and susceptible to record errors in elderly individuals (4). An additional approach for evaluating the significance of a low GFR in the elderly population is to assess the association between a lower GFR and metabolic disorders, typically observed in patients with CKD (5). Furthermore, anemia is common in CKD (6); however, it remains unknown whether hemaglobin (Hb) levels may be used to discriminate the stages of CKD in elderly patients, and whether Hb can be used as a biomarker to assess the severity of CKD. The association of CKD and anemia in elderly Chinese patients is not well studied and thus further investigation is necessary. Studies on the above mentioned gaps would yield valuable information for elderly Chinese patients with chronic kidney disease, particularly those with different hematocrit levels and anemia. Therefore, the aim of the present study was to investigate the prevalence of CKD in elderly Chinese individuals, and subsequently the associations with stages of CKD and complications of anemia.

Materials and methods

Study population. The present study was approved by the Ethics Committee of Capital Medical University (Beijing, China), and written informed consent was obtained from all of the patients. In total, 2,258 subjects (male, 1,138; female, 1,120; age, 30-99 years; mean age, 62.3±12.0 years), admitted to Beijing Tongren Hospital affiliated to Capital Medical University,

Table I. Clinical and demographic characteristics of the study population (n=2,258) at the baseline.

Patient characteristics	Young group	Elderly group	P-value
Subjects, n	989	1,269	
Age, years	51.17±6.34	70.95±7.32	<0.001
Gender			
Male, n (%)	508 (51.4)	630 (49.6)	0.421
Creatinine, mg/dl	0.96±0.83	1.20±0.94	<0.001
Hb, g/l	136.63±18.35	124.80±18.26	<0.001
HCT	0.40±0.05	0.37±0.05	<0.001
GFR, ml/min/1.73 m^2	91.19±23.81	64.84±23.60	<0.001
≥60, %	90.6	59.3	
45-59, %	5.1	20.3	
30-44.99, %	2.2	12	
<30, %	2	8.4	

Hb, hemoglobin; HCT, hematocrit; GFR, glomerular filtration rate.

were recruited for the study based on their 99 mTc-DTPA renal clearance value. Patients were categorized into six groups according to their age: 30-39, 40-49, 50-59, 60-69, 70-79 and ≥80 years-old. Young and elderly groups were assigned using a cutoff value of 60 years, according to the latest standards of the World Health Organization (WHO). CKD was diagnosed according to the National Kidney Foundation-Kidney Disease Outcomes Quality Initiative (K/DOQI) clinical practice guidelines; subjects were classified into five CKD stages according to the K/DOQI guidelines (7). Information was collected as part of the routine care. All subjects were ambulatory without active comorbidities, and were under regular control and in a stable condition. For subjects with multiple samples, only the sample with the lowest serum creatinine (SCr) value was used for analysis. Subjects with edema, pleural effusion or ascites, heart failure, skeletal muscle atrophy, malnutrition, amputation, ketoacidosis or acute kidney function deterioration were excluded from the study. In addition, subjects who were receiving any form of renal replacement therapy or had been administered recombinant human erythropoietin were excluded.

Blood sampling. Biochemical profiles included those for Hb, the hematocrit (HCT) and SCr (i-STAT 04J60-20; Abbott Diagnostics Inc., Abbott Park, IL, USA). The levels of Hb and SCr, and the HCT value, were determined in a single laboratory at Beijing Tongren Hospital using a Stanbio 900900SP (Stanbio Laboratory, Boerne, TX, USA). Blood samples were obtained simultaneously with the reference GFR (rGFR) measurement.

Measurement of the rGFR. GFRs were calculated based on the 99mTc-DTPA-clearance rate, with the rGFR. The 99mTc-DTPA-clearance rate was assayed using a radionuclide imaging method, known as the modified Gates' method (8), which was performed using a GE SPECT Millennium VG Hawkeye Nuclear Medical System (GE Healthcare Life Sciences, Little Chalfont, UK). Following Gates' method, the subjects were asked to drink 300-500 ml water after breakfast, which was 20 min prior to the investigation. Between 2-3 min following the arrival of the radiotracer in the kidneys, the fractional renal uptake of the intravenously administered 99mTc-DTPA is proportional to the GFR. The GFR was computed from the scintigraphic determination of the 99mTc-DTPA uptake within the kidneys, and modified according to the Chinese population (9). Results obtained from the rGFR method were corrected for the body surface area (BSA; m^2) as follows: rGFR (ml/min/1.73 m^2) = GFR/standard BSA. The BSA was calculated according to the method outlined by Du Bois and Du Bois (10).

Statistical analysis. All statistical analyses were conducted using SPSS version 16.0 (SPSS, Inc., Chicago, IL, USA). Descriptive statistics for continuous variables were presented as the mean ± standard deviation, while categorical variables (number and percentage) were used to characterize the study population. Levels of Hb and SCr, the HCT and the rGFR were assessed for the young and elderly individuals separately, across the various CKD stages. Analysis of variance was used to assess the effect of aging on the CKD stages, and the effect of CKD severity on the Hb level and number anemia cases. In addition, comparisons were performed for the prevalence rates of significant anemia cases among subjects with an rGFR of <30, 30-44, 45-59 and >60 ml/min/1.73 m^2. The associations among anemia, rGFR and age were also analyzed based on the WHO definitions of Hb (females, <120 g/l; males, <130 g/l) (11). $P<0.05$ was considered to indicate a statistically significant difference.

Results

Subjects and their characteristics. Baseline characteristics of all the participants are shown in Table I. The mean rGFR

Table II. Distribution of subjects according to their rGFR stage and age group.

Age, years	Cases, n	GFR[a], ml/min/1.73 m^2	CKD stage, n (%)			
			CKD 1-2	CKD 3a	CKD 3b	CKD 4-5
30-39	59	100.61±26.21	54 (91.5)	4 (6.8)	0 (0)	1 (1.7)
40-49	275	96.75±24.36	254 (92.4)	13 (4.7)	2 (0.7)	6 (2.2)
50-59	655	88.00±22.70	588 (89.8)	34 (5.2)	20 (3.0)	13 (2.0)
60-69	550	74.67±22.06	416 (75.6)	80 (14.6)	37 (6.7)	17 (3.1)
70-79	558	60.49±21.69	297 (53.2)	131 (23.5)	75 (13.4)	55 (9.9)
≥80	161	46.37±19.16	40 (24.8)	47 (29.2)	40 (24.8)	34 (21.2)

[a]Results are presented as the mean ± standard deviation. rGFR, reference glomerular filtration rate; CKD, chronic kidney disease.

Table III. Hb concentration and anemia are associated with the reduced rGFR in the two age groups.

Group	Parameters	CKD 1-2	CKD 3a	CKD 3b	CKD 4-5	P-value
Young	Hb, g/l	139.01±15.72	120.53±22.81	114.18±23.33	95.7±24.37	<0.001
	Anemia, n (%)	138 (15.4)	28 (54.9)	13 (59.1)	16 (80)	<0.001
Elderly	Hb, g/l	131.00±13.02	124.32±17.50	113.66±18.31	97.93±19.88	<0.001
	Anemia, n (%)	206 (27.4)	131 (50.8)	103 (67.8)	92 (86.8)	<0.001

rGFR, reference glomerular filtration rate; CKD, chronic kidney disease; Hb, hemoglobin.

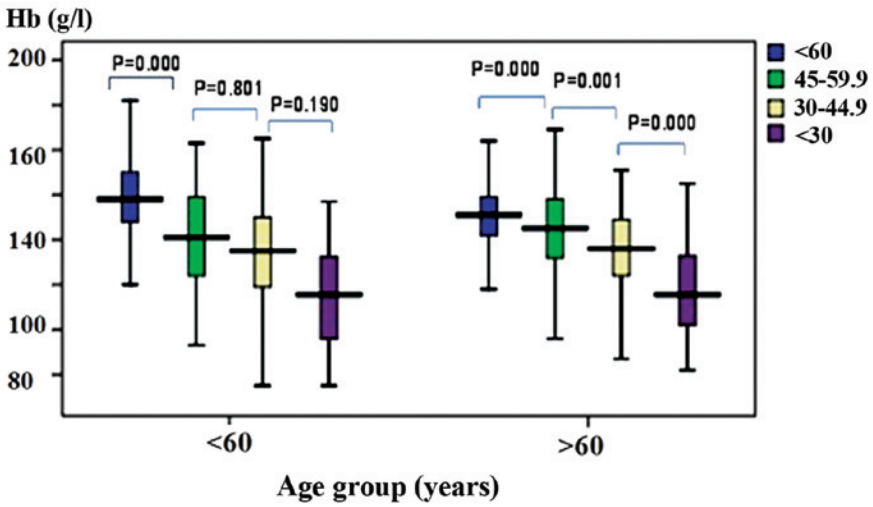

Figure 1. Hemoglobin concentrations by age group and chronic kidney disease stage.

was 91.19±23.81 ml/min/1.73 m^2 in the young group and 64.84±23.60 ml/min/1.73 m^2 in the elderly group. The prevalence of a rGFR of <60 ml/min/1.73 m^2 was higher in the elderly group compared with the young group (Table I). As shown in Table II, the number of patients with stage 3 CKD increased with aging, with the number of stage 3 CKD cases >50% in the ≥80 years age group. With regard to the percentage of cases of CKD stage 3a or higher, there was a small difference between the young and elderly groups. However, statistically significant differences were observed in the percentage of CKD among the different decade of age groups.

rGFR and anemia. In the young and elderly groups, the Hb concentration was shown to decrease and anemia was shown to deteriorate with increasing CKD stage (Table III). A rGFR of 45 ml/min/1.73 m^2 was an important cutoff, particularly in the elderly group. In the young group, there were no statistically significant differences in the Hb concentration or number of anemia cases between the patients with CKD of stage 3a and 3b. However, in the elderly group, the Hb levels were significantly higher and the number of anemia cases was alleviated in patients with stage 3a CKD, as compared with patients with CKD of stage 3b (Fig. 1).

Discussion

In 2002, the K/DOQI proposed a CKD definition and staging system, which is now regarded as the millstone of CKD development. The study focused attention towards CKD in the public and for non-nephrology physicians, moved the research on the epidemiology of CKD forward, and had a significant impact on the policy of public health (12). However, there was limited evidence-based therapy available at that time. With the development of clinical practice and increasing evidence-based treatment, much controversy has been aroused (13,14). One major focus is the K/DOQI definition and staging, based on the epidemiology survey. The prevalence of CKD is between 6 and 16% in the elderly population (15). The increasing population of CKD patients are predominantly classified as stage 3, particularly within the elderly population. The results of the present study revealed that the prevalence of CKD increases with age. In the elderly group, 40.7% of the subjects had a GFR of <60 ml/min/1.73 m^2, among which 20.3% were classified as CKD stage 3a, indicating that >50% of patients with stage 3 CKD are at stage 3a. In subjects aged between 70 and 79 years, almost 50% had a GFR of <60 ml/min/1.73 m^2, while for those aged >80 years, ~75% had a GFR of <60 ml/min/1.73 m^2. These observations are consistent with previously published results (16), indicating that this is a common finding in the elderly population.

Anemia is very common in CKD and an independent predictor for cardiovascular complications of CKD. Not only does anemia affect the life quality of patients, the condition worsens their kidney function. Patients at any stage of CKD may be accompanied with different degrees of anemia. The common causes are inadequate erythropoietin levels due to kidney disease, the metabolic products of renal dysfunction, and the toxins produced by uremia, which are renal-derived (17). However, anemia caused by nutritional insufficiency is more common in stages 1 and 2 CKD (18). A positive correlation between the degree of anemia and the degree of kidney insufficiency has been previously reported (19,20). The results of the present study indicated that the level of Hb decreased with decreasing renal function. Using a GFR of 60 ml/min/1.73 m^2 as the cutoff point, in the young group, a statistically significant difference was observed in the level of Hb, with higher values observed in those with a higher GFR. There was no statistically significant difference in the level of Hb between patients with stage 3 and 4 CKD. However, in the elderly group, statistically significant differences were observed in the Hb level between patients with stages 1-5 of CKD. Furthermore, a statistically significant difference was observed between patients with stage 3a and 3b CKD, demonstrating the importance of staging in this age group.

Compared with the Hb level, the prevalence of anemia appears to be more important clinically. The present study demonstrated that in the young group, there was a significantly higher prevalence of anemia cases in those with stage 3b compared with stage 3a CKD, when the GFR was >60 ml/min/1.73 m^2. However, no statistically significant difference was observed when the GFR cutoff was set at 45 ml/min/1.73 m^2. In the elderly group, the prevalence of anemia differed between patients with stage 3a and 3b CKD, regardless of the GFR cutoffs. This observation indicated that in an elderly population, a GFR cutoff of 45 ml/min/1.73 m^2 may be more successful for use in clinical practice.

However, there are limitations to the present study. Although the current study used a large patient population, including more patients is likely to improve the accuracy of the results. In addition, as the focus of the study was Hb and anemia, the associations among metabolic acidosis, electrolytes, parathyroid function, proteinuria and other factors were not evaluated and require further investigation.

In conclusion, the results of the present study demonstrated that Hb levels can be used to discriminate stages of CKD in elderly Chinese patients. Therefore, Hb may be used as a biomarker to assess the severity of CKD.

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