Anemia among Chinese patients with chronic kidney disease and its association with quality of life - results from the Chinese cohort study of chronic kidney disease (C-STRIDE)

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Abstract

Background: Anemia is one of the common complications in patients with chronic kidney disease (CKD). However, there is no systematic investigation on the prevalence of anemia in CKD patients and its relationship with the quality of life in China.

Methods: The data for this study comes from baseline data from the Chinese Chronic Kidney Disease Cohort Study (C-STRIDE), which recruited predialysis CKD patients in China. The kidney disease quality of life summary (KDQOL-TM) was used to assess health-related quality of life (HRQoL). Use linear regression model to estimate the relationship between hemoglobin level and quality of life.

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Background

Chronic kidney disease (CKD) is highly prevalent in China, which has been recent estimates indicating that up to 10.8% of people aged 18 years or older have the disease [1]. Anemia commonly occurs in people with chronic kidney disease (CKD) [2–4]. In the United States, the prevalence of anemia in CKD patients was 15.4%, which is increased with stage of CKD, from 8.4% at stage 1 to 53.4% at stage 5 [5]. In the research work conducted in Shanghai, China, the total prevalence of anemia was 51.5% in CKD patients with 22.4% in stage 1, 30.0% in stage 2, 51.1% in stage 3, 79.2% in stage 4, and 90.2% in stage 5, respectively, which also reported that 44.9% patients has being treated for anemia [6]. With the progress of CKD stages, the treatment rate of anemia increased, 19.4% in stage 1, 11.4% in stage 2, 26.9% in stage 3, 46.3% in stage 4, and 73.0% in stage 5, respectively. However, in total chinese population the current prevalence of anemia is still unknown.

According to recent clinical guidelines, health-related quality of life (HRQoL) is an important key indicator for CKD anemia management [7, 8]. HRQoL provides a comprehensive appraisal of disease burden, incorporating assessment of symptoms, functional capacity, and well-being related to an effective treatment. A recent systematic review [9] showed that treatment of anemia comparing with untreated anemia among patients with CKD was associated improvement of HRQoL. However, the aimed of higher hemoglobin level may not be necessary, which has a connection with a certain outcome of HRQoL improvement. In addition, Wyatt et al [10] reported some individual patients may benefit in their subjective overall well-being from slightly higher hemoglobin levels in the range of 115–130 g/L, but the parameters were difficult to quantify.

This study is a multi-center prospective cohort study and the first national CKD cohort study in China. We aim to provide the prevalence of different hemoglobin levels and the treatment of anemia in Chinese CKD patients, and to explore the relationship between different hemoglobin levels and quality of life.

Methods

Study design

The Chinese Cohort Study of Chronic Kidney Disease (C-STRIDE) is an ongoing multicenter prospective cohort and the first national CKD cohort in China, which contains 39 clinical centers located on 28 cities in 22 provinces in China. Screening visit was conducted by nephrologists at each clinical center. The design and methods of the Chinese Cohort Study of Chronic Kidney Disease (C-STRIDE) study were published in detail already [11]. This study is a cross-sectional analysis based on the baseline data of C-STRIDE.

The C-STRIDE study was conducted in accordance with the Declaration of Helsinki. The study has been approved by the ethics committee of Peking University First Hospital (Approval Number: 2011[363]). All participants provided informed consent.

Measurements

Ascertainment of Level of Kidney Function- Kidney function was quantified using eGFR derived from the four-variable Modification of Diet in Renal Disease (MDRD) study equation [12].

Hemoglobin- Serum hemoglobin (HGB) was measured using a coulter LH 750 Hematology Analyzer (Beckman Coulter, Brea, CA,USA). The patients were divided into four groups according to the hemoglobin level at enrollment: hemoglobin level <100 g/L, hemoglobin level 100 g/L, hemoglobin level 130–150 g/L, and hemoglobin level ≥150 g/L.
hemoglobin level 116–129 g/L, hemoglobin level ≥ 130 g/L.

HRQoL was assessed using KDQOL-TM at the same time [13]. The Mandarin Chinese version of kidney disease quality of life (KDQol)-36 instrument, a globally accepted tool for evaluating HRQoL in patients with CKD [8]. The disease-related section consisted of 24 items which made up three scales: Symptoms and Problems (12 items), Burden of Kidney Disease (4 items), and Effects of Kidney Disease (8 items). The generic core was the 12-item Short-Form Health Survey (SF-12). The results of the SF-12 instrument were summarized into the Physical Component Summary (PCS) score and the Mental Component Summary (MCS) score. The raw scores were transformed linearly into a range of 0–100 with higher scores representing greater HRQoL [10].

Other laboratory measurements and patient characteristics were in contained as well, including demographics (age, gender, education, income), lifestyle (smoking), medical history (diabetes, anemia treatment: ESAs, iron [include oral and IV], or ESA combined with iron. Hypertension treatment physical examination findings (height, weight, body mass index, systolic blood pressure and diastolic blood pressure), urinary albumin-creatinine ratio (UACR) and left ventricular hypertrophy (LVH).

A two-dimensional guided M-mode echocardiographic study was performed at each nephrology center. Measurements included the diastolic thickness of the interventricular septum (IVST), left ventricular posterior wall (PWT), and the internal diameter of the left ventricle at the end of diastole (LVDd). Left ventricular mass (LVM) was calculated by using the formula: LVM = 0.8 (1.04 [LVDd+IVST+PWT] 3 – [LVDd] 3) + 0.6 [14]; left ventricle mass index (LVMI) was measured by dividing left ventricle muscle mass to body surface area (BSA). BSA = 0.0061 × height (cm) + 0.0128 × weight(kg) – 0.1529. LVMI > 125 g/m² in males and > 120 g/m² in females were considered as LVH.

Statistical analysis
Continuous data are presented as means with standard deviations (SDs) except for UACR, which is presented as median (inter-quartile range, IQR) because of skewed distribution of data. Categorical variables are presented as proportions. Hemoglobin was divided into four groups with the levels of < 100 g/L, 100–115 g/L, 116–129 g/L, and ≥ 130 g/L, respectively. Relevant characteristics were described and compared according to different hemoglobin levels. One-way ANOVA or Kruskal-Wallis test was used for comparison of continuous variables and the chi-square test for binary variables between hemoglobin levels. The prevalence of anemia based on different Hb levels and the use of anemia treatments of anemia are reported among total population and different eGFR levels.

Hemoglobin was analyzed as a categorical variable with 4 categories in the regression models and the hemoglobin of ≥130 g/L was used as a reference when comparing the difference in KDQOL scores among different hemoglobin groups. Generalized linear models were used to test the effects of the independent variables on the KDQOL scores. Each adjusted mean difference from the reference group was computed based on the estimated marginal means of the KDQOL scores. Starting with an unadjusted model, we sequentially introduced blocks of variables to evaluate their effects on the association between hemoglobin and HRQoL. Model 1 was unadjusted, model 2 was adjusted for social-demographics (age, sex, education, income), model 3 was additionally adjusted for cardiovascular risk factors (smoking, BMI, hypertension, and diabetes), and model 4 was further adjusted for comorbid conditions (LVH). The marginal means were estimated as the mean value averaged of all cells generated by the rest of the categorical variables, with the value of each covariate set to its overall mean estimate. Statistical analyses were performed with SAS (version 9.4; SAS institute, Cary, NC). P value of < 0.05 in two-sided test was considered as statistical significance.

Results
Altogether, 3499 Chinese urban patients with non-dialysis CKD stage 1–4 were enrolled in this study. We excluded 578 participants due to missing key demographic variables (serum creatinine or hemoglobin level), resulting in 2921 patients included in the analysis. The mean age of patients was 48.5 ± 13.6 years, and 1710 (58.5%) were male, of which 2016 (69.0%) patients had an eGFR less than 60 mL/min per 1.73 m². The mean hemoglobin level of the patients was 127.8 ± 21.9 g/L. When stratified by four stages of hemoglobin levels, there were significant differences in age, gender, diabetes, education level, income, UACR levels, blood pressure, BMI, albumin, ACR, eGFR; The adjusted prevalence of anemia were reported among total population and different eGFR levels.
treatment with combined usage was 14.7%. An increased trend for anemia treatment was observed with reduced levels of eGFR. For example, the patients of CKD stage 3a, 3b and 4 with hemoglobin< 100 g/L, 15.8, 32.8 and 38.2% were receiving anemia treatment, respectively. Similar patterns can be found in the group of the treatment with ESA and iron. To be noted, only 5.3% of ESA-treated patients in CKD Stage 3a were observed to be with hemoglobin< 100 g/L and 5.2% patients with hemoglobin 100-115 g/L treated with ESA in CKD stage 3a, compared to the prevalence of patients treated with iron was 15.8 and 13.8%, respectively (Table 3).

Among 2921 patients, 2333 (79.9%) received baseline echocardiography, of which 227 (7.8%) were eligible for LVM assessment. As hemoglobin levels decrease, the prevalence of left ventricular hypertrophy increases. The ratio of more than 100 g/L was 18.3% (95% CI: 9.9–11.4%), and it showed a significant downward trend with the increase of hemoglobin level.

As shown in Table 1, the HRQoL scores in all dimensions impaired progressively and significantly (p < 0.001) across hemoglobin level. The lowest scores were found in hemoglobin< 100 g/L. Scores across all the five dimensions of the KDQOL included Symptoms and Problems (S), Effects of the Kidney Disease (E), Burden of the Kidney Disease (B), SF-12 Physical Functioning (PCS), SF-12 Mental Functioning (MCS) were 81.2 ± 23.5, 62.7 ± 26.6, 72.9 ± 19.7, 86.8 ± 13.0, 74.1 ± 27.1, respectively. Scores of KDQOL were negatively associated with the decreased levels of hemoglobin. The strength of association increased through the decreased levels of hemoglobin.

HRQoL Scores by Hb level and CKD stage are presented in Table 2, with the patients divided into three groups according to their renal function; CDK 3a, with GFR range 45–59 ml/min/1.73 m², CDK 3b, with GFR range 30–44 ml/min/1.73 m² and CDK 4, with GFR range 15–29 ml/min/1.73 m². HRQoL scores of CDK deteriorated with the decrease of hemoglobin level. But the change was not significant at hemoglobin level 100–115 g/L and 116–129 g/L specifically PCS and MCS (Fig. 1).

In unadjusted analyses (model 1), HRQoL scores in patients with CKD decreased sharply as hemoglobin declined to 100 g/L. After adjusting for sociodemographics (model 2) and additionally for cardiovascular risk factors (model 3), the degree of decrease became somewhat blunted. In the final model (model 4), further adjusted for comorbid conditions, these adjusted means also decreased progressively as hemoglobin level declined (Table 3).

**Discussion**

Understanding the epidemiology of hemoglobin level in persons with CKD is important when considering the development and implementation of effective prevention and treatment strategies. This study is the first extensive cohort in China. Our findings demonstrate that among persons with CKD, the prevalence of lower hemoglobin increases linearly as eGFR declines and that this association is consistent across age, sex, race, and other clinically important patient groups.

Several studies have documented a high prevalence of anemia in patients with chronic kidney disease. However, most of these studies were regional. We used a standard design for a population survey and a strict quality control procedure to ensure the representativeness of our study. In this cohort of patients with CKD, the prevalence of hemoglobin<100 g/L was 10.3%, and also detected that the prevalence increased with decreasing level of eGFR (from 2.7 to 23.4% when eGFR decreased from CKD stage 2 to CKD stage 4). Similar patterns were observed in other study. In the US, McClellan et al. reported that prevalence of 47.7 and 8.9% for hemoglobin<120 g/L and hemoglobin<100 g/L, respectively [15]. The prevalence was comparable to that reported of urban Chinese patients (52.8% for hemoglobin<130 g/L and 10.3% for hemoglobin<100 g/L).

In our study, 34.0% of patients with hemoglobin<100 g/L were under treatment with either ESA or iron, 24.0% of patients using ESA and 24.7% of patients using iron (including both intravenous and oral iron). But the majority of patients were not treated. With the decrease of eGFR, the treatment rate increased gradually. According to the current clinical guideline, the recommended hemoglobin target is 100-110 g/L [16]. There were 11.2% of patients with hemoglobin of 116-129 g/L and 1.7% with hemoglobin<130 g/L using anti-anemia treatment. It is unknown whether the treatment is due to aims of maintaining an appropriate hemoglobin level or misuse of treatment. We observed largely similar proportion for the treatment of ESA or iron through all the hemoglobin levels, as well as after being stratified by eGFR levels. However, we found that prevalence of iron use was higher than ESA use. The treatment pattern may be due to the primary or initial intervention in these patients.

In the past years, clinical trials have shown that higher hemoglobin treatment targets and/or use of high ESA doses may increase cardiovascular risk for CKD patients [17–20]. These findings may help to reduce the prescribed ESA dose [21] and target hemoglobin levels [16, 22]. However, complex pathogenesis processes other than anemia itself may contribute to the adverse outcomes for patients with CKD [23]. For example, Hung and colleagues found that anemia together with fluid retention instead of only anemia was associated with adverse outcomes of CKD [2]. Nonetheless, higher hemoglobin targets for some patients (that is, individualization of treatment) continues to be discussed and practiced.
Table 1: Baseline Characteristics of participants according to hemoglobin levels

| Characteristic | Total (N = 2921) | < 100 (n = 300) | 100–115 (n = 525) | 116–129 (n = 716) | ≥130 (n = 1380) | Missing value | p-value |
|---------------|------------------|-----------------|------------------|------------------|-----------------|--------------|---------|
| Age (years)   | 48.5 ± 13.6      | 52.8 ± 13.0     | 51.2 ± 13.1      | 50.8 ± 13.6      | 45.5 ± 13.4     | 0            | < 0.001 |
| Men (%)       | 1710 (58.5)      | 129 (7.5)       | 199 (11.6)       | 312 (18.2)       | 1070 (62.7)     | 0            | < 0.001 |
| eGFR          | 52.3 ± 33.4      | 29.9 ± 22.5     | 38.2 ± 27.8      | 49.9 ± 31.4      | 63.7 ± 33.6     | 0            | < 0.001 |
| Prevalence (%) |                 |                |                  |                  |                 |              |         |
| ≥60 (CKD1–2)  | 10.3 (9.2,11.4)  | 18.0 (16.6,19.4)| 24.5 (23.0,26.1) | 47.2 (45.4,49.1) |                 |              |         |
| 45–59 (CKD3a) | 2.7 (1.5,3.6)    | 8.0 (6.2,9.7)   | 12.1 (9.4,15.3)  | 24.5 (20.7,28.2) | 59.4 (54.8,63.6)|              |         |
| 30–44 (CKD3b) | 8.4 (6.3,10.5)   | 19.5 (16.6,22.5)| 27.8 (24.3,31.4) | 44.3 (40.6,48.3) |                 |              |         |
| 15–29 (CKD4)  | 23.4 (20.5,26.2) | 30.7 (27.7,34.0)| 25.5 (22.6,28.7) | 20.4 (17.4,23.2) |                 |              |         |
| Hemoglobin (g/L) | 127.8 ± 21.9 | 89.3 ± 8.0     | 108.4 ± 4.5      | 122.7 ± 4.0      | 146.3 ± 12.7    | 0            | 0.001   |
| Diabetes (%)  | 393 (13.5)       | 100 (25.4)      | 97 (24.7)        | 101 (25.6)       | 95 (24.2)       | 48           | 0.056   |
| ≥High school education (%) | 1625 (55.6) | 125 (7.7)     | 240 (14.8)       | 381 (23.4)       | 879 (54.1)      | 28          | < 0.001 |
| Income, yuan (%) |                |                |                  |                  |                 | 123         | < 0.001 |
| < 30,000       | 997 (34.1)       | 136 (13.6)      | 176 (17.7)       | 249 (25.0)       | 436 (43.7)      |              |         |
| 30,000–50,000  | 726 (24.9)       | 75 (25.0)       | 157 (29.9)       | 171 (23.9)       | 323 (23.4)      |              |         |
| 50,000–100,000 | 1075 (41.0)      | 89 (29.7)       | 192 (36.6)       | 296 (41.3)       | 621 (45.0)      |              |         |
| Current smoker (%) |          |                |                  |                  |                 | 0.72        |         |
| Use anemia drug (%) |          |                |                  |                  |                 | 0            | < 0.001 |
| EPO           | 206 (7.1)        | 72 (24.0)       | 75 (14.3)        | 44 (6.1)         | 15 (1.1)        |              |         |
| Iron          | 234 (8.0)        | 74 (24.7)       | 87 (16.6)        | 57 (8.0)         | 16 (1.2)        |              |         |
| EPO + Iron    | 117 (4.0)        | 44 (14.7)       | 44 (8.4)         | 21 (2.9)         | 8 (0.6)         |              |         |
| SBP (mm Hg)   | 130.0 ± 18.8     | 135.8 ± 19.7    | 131.9 ± 17.4     | 128.3 ± 17.3     | 126.9 ± 16.2    | 178          | < 0.001 |
| DBP (mm Hg)   | 81.1 ± 11.7      | 80.3 ± 10.5     | 80.0 ± 10.5      | 79.7 ± 10.2      | 81.4 ± 10.6     | 178          | 0.001   |
| BMI (kg/m²)   | 24.6 ± 3.8       | 24.2 ± 4.1      | 23.4 ± 3.6       | 24.4 ± 3.6       | 25.2 ± 3.9      | 80           | < 0.001 |
| LHV(%)        | 227 (7.8)        | 55 (18.3)       | 55 (10.5)        | 54 (7.5)         | 63 (4.6)        | 427          | < 0.001 |
| ACR (mg/g creatinine) | 418.3 (113,898.5) | 718.5 (219,91676.6) | 554.3 (181.0, 1226.6) | 410.0 (98.0,952.5) | 349.8 (105,1814.2) | 407 | < 0.001 |
| Use antihypertensive drugs (%) | 463 (15.9) | 147 (49.0) | 107 (20.4) | 104 (14.5) | 105 (7.6) | 0 | < 0.001 |
| ACEI/ARB      | 324 (11.1)       | 93 (31.0)       | 69 (13.1)        | 81 (11.3)        | 81 (5.9)        |              |         |
| CCB           | 361 (12.4)       | 120 (40.0)      | 80 (15.2)        | 84 (11.7)        | 77 (5.6)        |              |         |
| ALB (g/L)     | 38.9 ± 7.3       | 34.9 ± 7.5      | 38.0 ± 7.1       | 38.6 ± 7.0       | 40.2 ± 7.1      | 130          | < 0.001 |
| Hs-CRP (mg/L) | 3.7 ± 1.2        | 5.3 ± 12.0      | 5.3 ± 6.8        | 5.7 ± 9.9        | 5.7 ± 5.8       | 288          | 0.038   |
| TC (mmol/L)   | 5.5 ± 7.0        | 4.6 ± 2.0       | 4.4 ± 15.9       | 3.3 ± 7.8        | 3.3 ± 12.2      | 196          | 0.075   |
| Symptoms and Problems (S) | 81.2 ± 23.5 | 72.8 ± 27.5 | 77.5 ± 25.3 | 81.9 ± 22.5 | 84.0 ± 21.8 | 395 | < 0.001 |
| Effects of the Kidney Disease (E) | 62.7 ± 26.6 | 55.5 ± 26.7 | 58.7 ± 27.4 | 63.4 ± 27.1 | 65.4 ± 25.5 | 395 | < 0.001 |
| Burden of the Kidney Disease (B) | 72.9 ± 19.7 | 66.9 ± 22.4 | 70.1 ± 20.1 | 72.6 ± 19.7 | 75.4 ± 18.2 | 395 | < 0.001 |
| SF-12 Physical Functioning (PCS) | 86.8 ± 13.0 | 81.0 ± 16.5 | 84.5 ± 12.5 | 86.7 ± 13.1 | 89.0 ± 11.2 | 395 | < 0.001 |
| SF-12 Mental Functioning (MCS) | 74.1 ± 27.1 | 60.6 ± 30.8 | 69.7 ± 27.0 | 73.7 ± 26.9 | 79.0 ± 24.9 | 395 | < 0.001 |

Continuous variables are presented as mean ± SD, or median with interquartile ranges. Categorical data are presented as numbers (n) of patients. Abbreviations: eGFR estimated glomerular filtration rate, SBP Systolic blood pressure, DBP Diastolic blood pressure, BMI Body mass index, LVH Left ventricular hypertrophy, ACR albumin:creatinine ratio, ALB Albumin, Hs-CRP high-sensitivity C-reactive protein, TC Serum cholesterol.
Table 2  KDQOL Scores by Hb level and CKD stage

|                      | CKD3a  |        |        |        | CKD3b  |        |        |        | CKD4   |        |        |
|----------------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|                      | < 100  | 100–115| 116–129| ≥130   | < 100  | 100–115| 116–129| ≥130   | < 100  | 100–115| 116–129| ≥130   |
| Symptoms and Problems (S) | 75.0 ± 4.6  | 77.2 ± 4.0 | 80.7 ± 2.6 | 84.7 ± 1.4 | 73.2 ± 4.3  | 78.3 ± 2.5 | 81.8 ± 1.7 | 81.1 ± 1.6 | 71.7 ± 12 | 76.6 ± 18 | 80.8 ± 1.7 | 78.8 ± 2.0 |
| Effects of the Kidney Disease (E) | 60.0 ± 5.3  | 64.3 ± 3.3 | 63.3 ± 2.8 | 65.2 ± 1.6 | 56.6 ± 3.7  | 57.9 ± 2.6 | 63.3 ± 2.0 | 63.4 ± 1.7 | 54.5 ± 19 | 574 ± 20 | 602 ± 21 | 620 ± 23 |
| Burden of the Kidney Disease (B) | 76.7 ± 3.3  | 766 ± 29 | 75.1 ± 20 | 77.3 ± 1.1 | 69.4 ± 3.2  | 71.9 ± 2.0 | 72.0 ± 1.5 | 74.1 ± 1.2 | 65.6 ± 16 | 681 ± 15 | 704 ± 15 | 739 ± 1.6 |
| SF-12 Physical Functioning (PCS) | 84.8 ± 5.9  | 852 ± 2.1 | 85.1 ± 1.1 | 88.9 ± 0.7 | 82.8 ± 2.3  | 84.4 ± 1.3 | 86.2 ± 1.0 | 88.0 ± 0.8 | 79.7 ± 12 | 833 ± 09 | 844 ± 10 | 859 ± 1.2 |
| SF-12 Mental Functioning (MCS) | 64.3 ± 6.3  | 755 ± 41 | 73.2 ± 26 | 79.9 ± 1.6 | 61.6 ± 4.4  | 66.8 ± 2.6 | 70.8 ± 2.1 | 74.6 ± 1.8 | 59.3 ± 22 | 676 ± 20 | 680 ± 18 | 743 ± 2.1 |
### Table 3 Adjusted Mean Differences of KDQOL Scores Among Different Levels of Hemoglobin

| Model | < 100 (n = 300) | 100–115 (n = 525) | 116–129 (n = 716) | ≥130 (n = 1380) |
|-------|-----------------|------------------|------------------|-----------------|
|       | Symptoms and Problems (S) |                       |                   |                 |
| Model 1 | -0.104(-0.105,-0.102) | 0.048(-0.049,-0.046) | -0.032(-0.033,-0.031) | ref |
| Model 2 | -0.083(-0.085,-0.082) | 0.031(-0.032,-0.030) | -0.018(-0.019,-0.017) | ref |
| Model 3 | -0.074(-0.078,-0.071) | -0.009(-0.013,-0.006) | -0.012(-0.016,-0.008) | ref |
| Model 4 | -0.047(-0.049,-0.045) | -0.014(-0.015,-0.012) | -0.013(-0.014,-0.012) | ref |
|       | Effects of the Kidney Disease (E) |                       |                   |                 |
| Model 1 | -0.094(-0.096,-0.092) | -0.052(-0.054,-0.051) | -0.027(-0.028,-0.026) | ref |
| Model 2 | -0.088(-0.089,-0.086) | -0.049(-0.050,-0.047) | -0.026(-0.027,-0.025) | ref |
| Model 3 | -0.095(-0.098,-0.091) | -0.016(-0.020,-0.012) | -0.026(-0.030,-0.022) | ref |
| Model 4 | -0.047(-0.049,-0.044) | -0.020(-0.021,-0.018) | -0.016(-0.018,-0.015) | ref |
|       | Burden of the Kidney Disease (B) |                       |                   |                 |
| Model 1 | -0.348(-0.351,-0.345) | -0.162(-0.164,-0.160) | -0.058(-0.060,-0.056) | ref |
| Model 2 | -0.304(-0.307,-0.300) | -0.105(-0.132,-0.128) | -0.048(-0.050,-0.046) | ref |
| Model 3 | -0.287(-0.294,-0.281) | -0.117(-0.123,-0.110) | -0.075(-0.081,-0.070) | ref |
| Model 4 | -0.207(-0.212,-0.203) | -0.061(-0.064,-0.058) | -0.032(-0.035,-0.030) | ref |
|       | SF-12 Physical Functioning (PCS) |                       |                   |                 |
| Model 1 | -0.266(-0.269,-0.264) | -0.196(-0.198,-0.194) | -0.115(-0.116,-0.114) | ref |
| Model 2 | -0.179(-0.181,-0.176) | -0.131(-0.133,-0.130) | -0.057(-0.059,-0.056) | ref |
| Model 3 | -0.205(-0.201,-0.199) | -0.108(-0.114,-0.103) | -0.082(-0.088,-0.077) | ref |
| Model 4 | -0.112(-0.115,-0.109) | -0.047(-0.049,-0.045) | -0.064(-0.066,-0.062) | ref |
|       | SF-12 Mental Functioning (MCS) |                       |                   |                 |
| Model 1 | -0.378(-0.381,-0.376) | -0.201(-0.203,-0.199) | -0.143(-0.145,-0.142) | ref |
| Model 2 | -0.317(-0.320,-0.315) | -0.165(-0.166,-0.163) | -0.113(-0.115,-0.111) | ref |
| Model 3 | -0.334(-0.341,-0.328) | -0.172(-0.178,-0.166) | -0.048(-0.053,-0.042) | ref |
| Model 4 | -0.295(-0.299,-0.292) | -0.098(-0.101,-0.096) | -0.101(-0.103,-0.099) | ref |

Note: Values are given as adjusted mean difference (95% confidence interval) of the KDQOL scores

Model 1 was unadjusted
Model 2 was adjusted for age, sex, education, and income
Model 3 was adjusted for model 2 + smoking, BMI, diabetes, and hypertension
Model 4 was adjusted for model 3 + LVH, eGFR

Abbreviations: BMI Body mass index, eGFR estimated glomerular filtration rate, LVH left ventricular hypertrophy, eGFR estimated glomerular filtration rate

Fig. 1 Mean Physical Composite summary (PCS) and Mental Composite Summary (MCS) scores related to declining levels of hemoglobin in CKD
Left ventricular hypertrophy (LVH) is considered an important risk factor for adverse cardiovascular (CV) outcomes in patients with chronic kidney disease (CKD). Hemoglobin (Hb) levels have been found to predict the degree of LVH in long-term dialysis patients. Cardiovascular disease (CVD) is the leading cause of morbidity and mortality in patients with chronic kidney disease (CKD). This increased risk begins during the earlier stages of CKD before the onset of kidney failure. Our results show that among CKD patients, the prevalence of LVH among all patients was 7.8%. The next analysis demonstrated variety in LVH with changes in hemoglobin level among patients with CKD, which is consistent with cross-sectional studies of patients with equivalent levels of renal dysfunction. Our results show that hemoglobin less than 100 g / L increases the incidence of left ventricular hypertrophy in CKD patients, and indicating an increased cardiovascular risk in this group.

Although monitoring biomarkers is central to the successful treatment of patients with CKD, it is necessary but insufficient to understand fully patients’ overall burden of illness. HRQoL is an important outcome measure in patients with chronic kidney disease. It also has been shown repeatedly to predict mortality in various patient populations. We conducted this systematic review first to establish which domains of HRQOL are most affected by hemoglobin in CKD and then to pool data to measure the magnitude of relationships between traditional biomarkers, including those supported by Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines and tracked by Medicare, and patient-reported HRQOL.

Our study has several key findings. First, we assessed the association between HRQoL and different hemoglobin level in CKD. Present results indicate that HRQoL dimensions were significantly impaired across CKD stages. As expected, the lowest HRQoL scores were seen in the patients with the most declined hemoglobin level. Specifically, the HRQOL decrement in CKD is most pronounced in physical function and vitality. In contrast, the impact of hemoglobin decreased in CKD is pronounced in mental health. This shows that the mental burden of CKD patients is heavy when hemoglobin is decreased, and the quality of life can be significantly improved by increasing hemoglobin.

Second, we found that although the quality of life increased with hemoglobin levels, the KDQOL scores between 100 and 115 and 116–119 showed a downward trend. Compared to hemoglobin levels in the 100–115 group, the quality of life score in the CKD3–4 group of hemoglobin 115–129 did not improve significantly, especially in PCS and MCS. The findings are likely to be related to small differences between groups in HRQoL scores, but they also suggest that keeping hemoglobin levels above 100 g/L may be physical and mental function in CKD patients.

Last, in the multivariable model with adjustment for traditional cardiovascular risk factors and kidney function, lower hemoglobin levels were consistently associated with lower KDQOL scores. Although this finding suggests that improvement of hemoglobin levels can be associated with a better quality of life, a recently published meta-analysis of 17 randomized trials involving 10,049 patients (7616 pre-dialysis CKD patients, 2387 hemodialysis recipients, and 46 peritoneal dialysis recipients) did not support a significant improvement in quality of life with ESA therapy targeting higher hemoglobin levels [24]. However, it is noteworthy that the individual study findings included in the meta-analysis were highly heterogeneous and few of them were categorized as high quality. Hence, more high-quality clinical trials are warranted to determine the efficacy of anemia treatment on the patient-relevant outcomes such as HRQoL.

Although our study bears a large sample size, simultaneous assessment between hemoglobin and KDQOL and investigation of major types of treatment for anemia, there are some limitations still. First, our study was based on the baseline survey of the cohort study, thus the cross-sectional analysis cannot elucidate causal relationships. Second, KDQOL was assessed only once and cannot reflect the dynamic status of patients. Third, the study participants were recruited from outpatient clinics in large clinical centers around China and the majority of etiology was glomerulonephritis. Thus, the generalizability to other populations will be limited. Also, mild CKD (Stages 1, 2) made up 1/3 of the study cohort, so that anemia prevalence may be higher if these are excluded then the patients with CKD Stage 5 included. The lower QoL scores showed up, the more treatments would be likely given.

Conclusions

In summary, our study reported the prevalence of different levels of hemoglobin and treatment against anemia in a cohort of Chinese patients with CKD. Increased prevalence of anemia and treatment was associated with decreased eGFR. KDQOL scores in all five domains were reduced through the decreasing level of hemoglobin and the trend was independent of traditional cardiovascular risk factors and kidney function. More observational studies are needed to confirm this finding, and randomized clinical trials are needed to explore the target of hemoglobin in the treatment of CKD-related anemia to improve patient-centered results.

Abbreviations

CKD: Chronic kidney disease; HRQoL: Health-related quality of life; KDQOL-TM: Kidney Disease Quality of Life Short Form; C-STRIDE: Chinese Cohort Study of Chronic Kidney Disease; MDRD: Modification of Diet in Renal
Disease; HGB: Hemoglobin; Serum hemoglobin; PCS: SF-12 Physical Functioning; MCS: SF-12 Mental Functioning; UACR: urinary albumin-creatinine ratio; LVH: left ventricular hypertrophy; IVST: interventricular septum; PWT: left ventricular posterior wall

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Authors’ contributions

JW analyzed and interpreted the patient data regarding the chronic kidney disease disease. JY has made some contributions to the conception, LY and FY have made some contributions interpretation of data, KW has made some contributions to analysis of data, MH and LZ have made some contributions to design of work. YZ performed the design and revision of the thesis, and was a major contributor in writing the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analysed during the current reach are available from the corresponding author on reasonable request.

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The study was approved by the ethics committee of Peking University First Hospital (Approval Number:2011[363]). All participants provided their written informed consent. The permission to access and use the C-STRIDE data was provided by the steering committee of the project.

Consent for publication

Not applicable.

Competing interests

All authors declare no competing Interests.

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