International Journal of Gerontology 14 (2020) 260–264
https://doi.org/10.6890/IJGE.202011_14(4).0002

International Journal of Gerontology

journal homepage: http://www.sgecm.org.tw/ijge/

Original Article

Hemoglobin, Albumin and Cholesterol as Potential Malnutrition Risk Biomarkers Associated with Coronary Artery Disease in Older People: A Cross-Sectional Analysis

Yujiao Sun [a], Jinyang Li [a], Ling Chen [a], Liye Shi [a], Shijie Zhao [a], Wen Tian [a], Haiyan Zhang [b], Guoxian Qi [a *]

[a] *Department of Geriatric Cardiology, The First Affiliated Hospital of China Medical University, Shenyang 110001, China,* [b] *Department of Geriatrics, The First Affiliated Hospital of China Medical University, Shenyang 110001, China*

ARTICLE INFO

Accepted 30 January 2020

Keywords:
hemoglobin,
albumin,
cholesterol,
coronary artery disease,
older people

SUMMARY

Aims: To observe the associations of hemoglobin, albumin and cholesterol as potential malnutrition risk biomarkers with coronary artery disease in the elderly.
Methods: Individuals who were aged 80 or older took annual medical examination were included, they were divided into two groups based on the median levels of hemoglobin, albumin or cholesterol respectively. The incidences of coronary artery disease between two groups were compared. The levels of hemoglobin, albumin or cholesterol were compared in coronary artery disease and non-coronary artery disease group respectively. The relationships between hemoglobin, albumin and cholesterol and coronary artery disease were assessed by univariate and multivariate logistic regression analysises.
Results: 1007 individuals with ≥ 80 years old were enrolled. The incidences of coronary artery disease were significantly higher in the lower level of hemoglobin and cholesterol groups than the higher level of hemoglobin and cholesterol groups respectively (both $p < 0.05$). The levels of hemoglobin and cholesterol were siginificantly lower in coronary artery disease than non-coronary artery disease group (both $p < 0.05$). After adjusting for potential confounding factors, hemoglobin was only protective factor for coronary artery disease in people with ≥ 80 years old ($p < 0.05$).
Conclusions: The general elderly population with lower levels of hemoglobin and cholesterol had the higher incidence of coronary artery disease, but only hemoglobin was a significant protective factor for coronary artery disease.

1. Introduction

In today's world, with the increasing intensification of old aging, the health problems of older people are becoming the focus of attention of global society. Malnutrition is a common problem in elderly population. But malnutrition yet remained underdiagnosed, especially in elderly population.[1,2] Now, many nutrition screening and assessment tools have been used in clinical practice, such as Mini Nutritional Assessment, Nutritional Risk Screening 2002, and Malnutrition Universal Screening Tool and so on.[3] The different nutrition assessments lead to the different judging standards for malnutrition, and the process of nutrition assessment is complicated, so nutrition assessments are still difficult to carried out in general elderly population. More convenient and faster routine blood markers are widely used to predict the presence of malnutrition in clinical practice. Recently, a meta-analysis summarized malnutrition-related blood biomarkers and further assessed them against nutrition screening tools, the results showed hemoglobin (Hb), albumin (ALB), total cholesterol (TC) were the most common and valuable biomarkers for potential malnutrition risk, even under chronic inflammatory state.[4]

Malnutrition have negative effects on organs and systems of human and strongly associate with health and illness outcomes.[5] Malnutrition lead to a poor quality of prognosis and increased mortality in patients with cardiovascular disease, including heart failure,[6] stable coronary artery disease (CAD),[7] acute coronary syndrome,[8] peripheral arterial disease,[9] but most of researches focused on the relationship between protein malnutrition and prognosis in cardiovascular disease. CAD is one of the commonest illness in older people, which would risk the health and life of older people. Therefore, preventing CAD of older people have received more and more attention worldwide.

But few studies have investigated the relationship between potential malnutrition risk and the incidence of CAD, especially in older people. In order to evaluate whether potential malnutrition risk is associated with CAD in older people, we survey the relationships between Hb, ALB and TC as potential malnutrition risk biomarkers and the incidence of CAD in older people (≥ 80 years). The results of study will confirm the impact of potential malnutrition risk biomarkers on CAD in general elderly population.

2. Methods

A total of 14414 consecutive individuals took annual physical examination were investigated at the first affiliated hospital of China Medical University from June 2014 to July 2017. Individuals who

* Corresponding author. Department of Geriatric Cardiology, The First Affiliated Hospital of China Medical University, No. 155, Nanjing North Street, Heping Ward, Shenyang 110001, China
E-mail address: qiguoxiantg@163.com (G.x. Qi)

were aged 80 or older were enrolled. Individuals were excluded if they had known malignancy; immune system disease; acute comorbidity such as acute stroke, sepsis and infection; known chronic inflammatory disease; hepatic cirrhosis; stage V chronic kidney disease; trauma/burns/post-surgery within a year, or incomplete data. Finally 1007 individuals were enrolled in the study. The study was approved by the ethics committee of the First Affiliated Hospital of China Medical University.

The demographic characteristics, disease histories and drug-taking histories of all individuals were investigated by experienced and trained clinicians. Height and body weight were measured, body mass index (BMI) was calculated by dividing weight in kiograms by height in meters squared. Smoking, hypertension, diabetes mellitus, stroke and CAD were defined as described previously.[10]

Blood biochemical markers such as low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), triglyceride (TG), TC, fasting plasma glucose (FPG), ALB and Hb were measured by standard methods and fasting time should be longer than 12 hours. Then all results of blood biochemical markers were recorded. Individuals were divided into two groups based on the median levels of Hb, ALB or TC respectively.

The baseline characteristics, the incidences of CAD were compared. The levels of Hb, ALB and TC were compared in CAD and non-CAD group respectively. Continuous datas were expressed as mean ± standard deviation and compared by Student t test, categorical datas were expressed as percentage and compared by chi-square test. The relationships between Hb, ALB or TC and CAD were assessed by univariate and multivariate logistic regression analyses. Furthermore, three models were used to further evaluate the associations between Hb, ALB or TC and CAD. All datas were analysed by SPSS 21.0. P(2-tailed) < 0.05 was considered statistical difference.

3. Results

3.1. Baseline characteristics

A total of 1007 individuals with ≥ 80 years old were enrolled in this study. The average age was 84.95 ± 2.99 years, 79.1 percent of individuals were men. The median Hb level was 139 g/l, 513 individuals had Hb ≤ 139 g/l, and 494 individuals had Hb > 139 g/l. The median ALB level was 41.6 g/l, 519 individuals had ALB ≤ 41.6 g/l, and 488 individuals had ALB > 41.6 g/l. The median TC level was 4.76 mmol/l, 510 individuals had TC ≤ 4.76 mmol/l, and 497 individuals had TC > 4.76 mmol/l.

The general characteristics, histories of disease, laboratory findings and histories of medication were summarized in Table 1. Age and the level of HDL were significantly higher in Hb ≤ 139 g/l than Hb > 139 g/l group (both p < 0.001); the levels of ALB, Hb, BMI and the prevalences of male, smoker, stroke were significantly lower in Hb ≤ 139 g/l than Hb > 139 g/l group (all p < 0.05). Age was significantly higher in ALB ≤ 41.6 g/l than ALB > 41.6 g/l group (85.23 ± 3.04 years vs. 84.66 ± 2.92 years, p = 0.002); the levels of TG, FPG, ALB, Hb and the prevalences of DM, HBP, statins, ACEI/ARB, antihyperglycemic/insulin were significantly lower in ALB ≤ 41.6 g/l than ALB > 41.6 g/l group (all p < 0.05). The levels of TC, TG, HDL and LDL were significantly lower in TC ≤ 4.76 mmol/l than TC > 4.76 mmol/l group (all p < 0.001); the prevalences of male, HBP, antiplatelet drugs, statins, ACEI/ARB, antihyperglycemic/insulin were significantly higher in TC ≤ 4.76 mmol/l than TC > 4.76 mmol/l group (all p < 0.05).

3.2. The levels of Hb, ALB, TC and CAD

The incidence of CAD was depicted in Figure 1. The incidence of CAD was significantly higher in Hb ≤ 139 g/l than Hb > 139 g/l group (33.1% vs. 27.3%, p = 0.045). There was not statistical significance in CAD rate between the ALB ≤ 41.6 g/l and ALB > 41.6 g/l group (28.1% vs. 32.6%, p = 0.124). The significantly higher incidence of CAD was in TC ≤ 4.76 mmol/l than TC > 4.76 mmol/l group (36.7% vs. 23.7%, p < 0.001).

In order to further analyse the relationships between Hb, ALB or TC and CAD, all individuals were divided into CAD (n = 305) and non-CAD (n = 702) groups. The results found the levels of Hb and TC were siginificantly lower in CAD than non-CAD group (Hb: 136.92 ± 15.54 g/l vs. 140.08 ± 15.28 g/l, p = 0.003; TC: 4.53 ± 1.04 mmol/l vs. 4.90 ± 0.94 mmol/l, p < 0.001). The level of ALB was no significant difference between CAD and non-CAD group (41.58 ± 2.75 g/l vs.

Table 1
Baseline characteristics.

Variables	Total N = 1007	Hb ≤ 139 g/l N = 513	Hb > 139 g/l N = 494	ALB ≤ 41.6g/l N = 519	ALB > 41.6 g/l N = 488	TC ≤ 4.76 mmol/l N = 510	TC > 4.76 mmol/l N = 497
Age (y)	84.95 ± 2.99	85.35 ± 3.05	84.54 ± 2.88*	85.23 ± 3.04	84.66 ± 2.92*	84.86 ± 3.10	85.04 ± 2.88
Male (%)	797 (79.1)	335 (65.3)	462 (93.5)*	410 (79)	387 (79.3)	446 (87.5)	351 (70.6)*
BMI, kg/m^2	24.04 ± 3.52	23.77 ± 3.92	24.28 ± 3.03*	24.05 ± 3.89	23.99 ± 3.09	24.14 ± 3.40	23.90 ± 3.64
Smoker (%)	66 (6.6)	23 (4.5)	43 (8.7)*	41 (7.9)	25 (5.1)	38 (7.5)	28 (5.6)
Hypertension (%)	587 (58.3)	300 (58.5)	287 (58.1)	281 (54.1)	306 (62.7)*	313 (61.4)	274 (55.1)*
DM (%)	240 (23.8)	132 (25.7)	108 (21.9)	101 (19.5)	139 (28.5)*	132 (25.9)	108 (21.7)
Stroke (%)	26 (2.6)	8 (1.6)	18 (3.6)*	15 (2.9)	11 (2.3)	16 (3.1)	10 (2.0)
LDL-C (mmol/l)	2.98 ± 0.85	2.97 ± 0.88	2.99 ± 0.83	2.96 ± 0.88	2.99 ± 0.83	2.36 ± 0.52	3.61 ± 0.65*
HDL-C (mmol/l)	1.32 ± 0.35	1.38 ± 0.37	1.26 ± 0.32*	1.31 ± 0.36	1.43 ± 0.35	1.23 ± 0.31	1.42 ± 0.37*
TG (mmol/l)	1.37 ± 0.76	1.30 ± 0.74	1.45 ± 0.77	1.27 ± 0.71	1.48 ± 0.79*	1.23 ± 0.66	1.52 ± 0.82*
TC (mmol/l)	4.78 ± 0.99	4.80 ± 1.03	4.78 ± 0.95	4.74 ± 1.02	4.84 ± 0.96	4.02 ± 0.54	5.58 ± 0.67*
FPG (mmol/l)	5.87 ± 1.46	5.78 ± 1.27	5.96 ± 1.64	5.69 ± 1.32	6.06 ± 1.57*	5.84 ± 1.28	5.89 ± 1.62
ALB (g/l)	41.50 ± 2.72	40.86 ± 2.82	42.18 ± 2.44*	39.46 ± 1.88	43.69 ± 1.52*	41.37 ± 2.70	41.64 ± 2.75
Hb (g/l)	139.13 ± 15.42	127.63 ± 11.18	151.06 ± 8.67*	136.02 ± 15.87	142.43 ± 14.21*	138.88 ± 14.90	139.38 ± 15.95
History of medication (%)							
Antiplatelet drug	66 (6.6)	31 (6.0)	35 (7.1)	29 (5.6)	37 (7.6)	45 (8.8)	21 (4.2)*
Statins	73 (7.2)	39 (7.6)	34 (6.9)	29 (5.6)	44 (9.0)*	52 (10.2)	21 (4.2)*
Beta blocker	57 (5.7)	28 (5.5)	29 (5.9)	25 (4.8)	32 (6.6)	35 (6.9)	22 (4.4)
ACEI/ARB	208 (20.7)	100 (19.5)	108 (21.9)	90 (17.3)	118 (24.2)*	125 (24.5)	83 (16.7)*
Antihyperglycemic/insulin	144 (14.3)	76 (14.8)	68 (13.8)	56 (10.8)	88 (18)*	87 (17.1)	57 (11.5)*

* The two groups (Hb ≤ 139 g/l vs. Hb > 139 g/l, ALB ≤ 41.6 g/l vs. ALB > 41.6 g/l or TC ≤ 4.76 mmol/l vs. TC > 4.76mmol/l) were significantly different (p < 0.05).
BMI, body mass index; DM, diabetes mellitus; LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol; TG, triglyceride; TC, total cholesterol; FPG, fasting plasma glucose; Hb, hemoglobin; ALB, albumin; ACEI/ARB, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker.

41.47 ± 2.71 g/l, p = 0.569) (as shown in Figure 2).

3.3. Logistic regression analysis

In our research, three models were used to evaluate the associations between Hb, ALB and TC as biomarkers of malnutrition risk and CAD in aged individuals (details seen in Table 2). Model 1 was univariate analysis. Model 2 adjusted for age and sex. Model 3 further adjusted for age, sex, BMI, smoker, hypertension, diabetes, stroke, LDL-C, HDL-C, TG, TC, FPG, Hb, ALB, antiplatelet drugs, statins, beta blocker, ACEI/ARB, antihyperglycemic/insulin. In model 1 and model 2, Hb and TC were the significant protective factors for CAD in individuals with ≥ 80 years old (all p < 0.05). After adjusting for potential confounding factors in Model 3, Hb was only protective

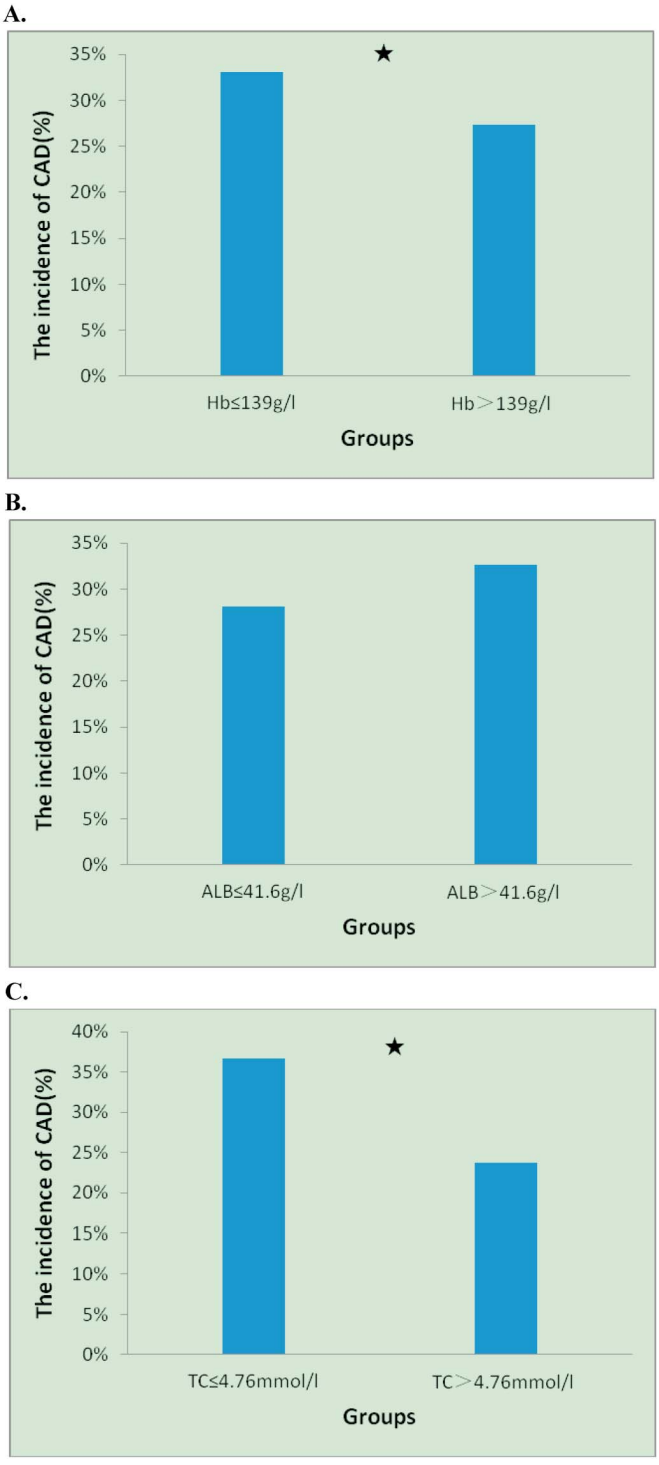

Figure 1. The incidence of CAD in different groups. A. The incidence of CAD in Hb ≤ 139 g/l and Hb > 139 g/L group. ★ Indicates Hb ≤ 139 g/l vs. Hb > 139 g/L (33.1% vs. 27.3%, p = 0.045). B. The incidence of CAD in ALB ≤ 41.6 g/l and ALB > 41.6 g/L groups. ALB ≤ 41.6 g/l vs. ALB > 41.6 g/L (28.1% vs. 32.6%, p = 0.124). C. The incidence of CAD in TC ≤ 4.76 mmol/l and TC > 4.76 mmol/l groups. ★ Indicates TC ≤ 4.76 mmol/l and TC > 4.76 mmol/l (36.7% vs. 23.7%, p < 0.001).

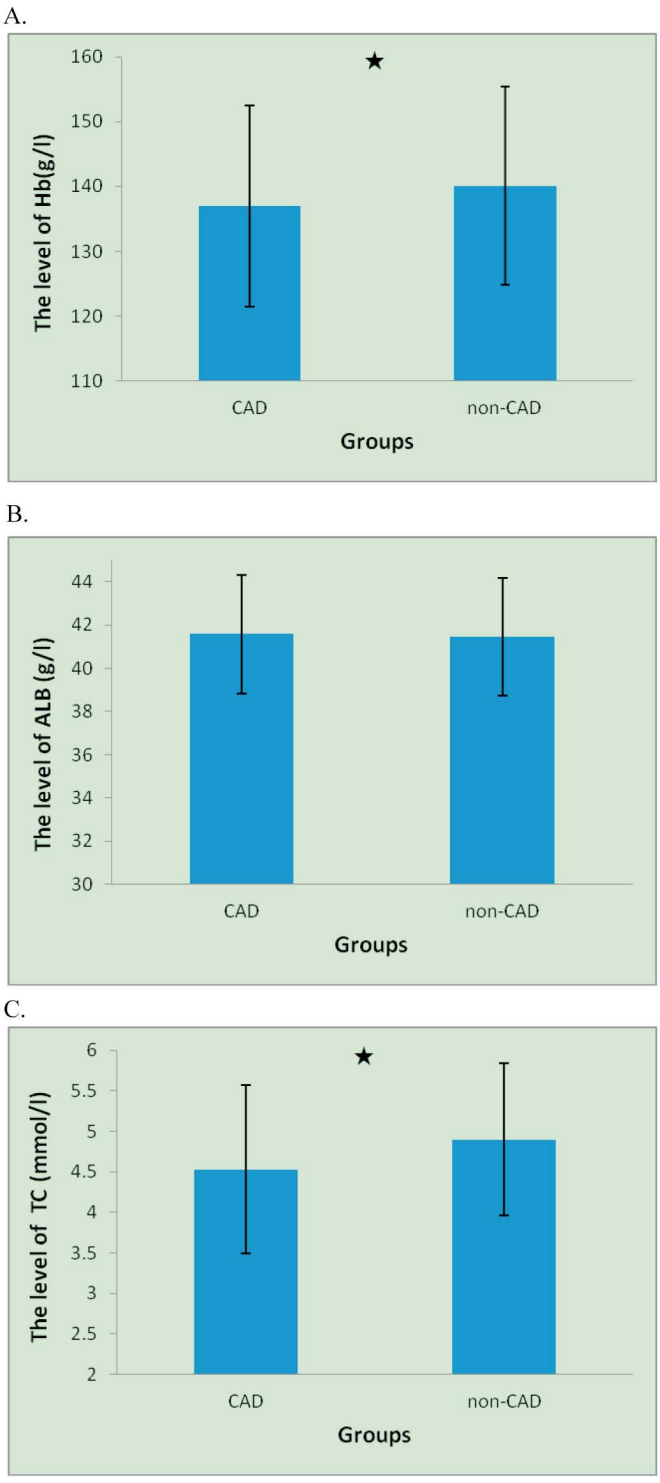

Figure 2. The levels of Hb, ALB and TC in CAD and non-CAD groups. A. The level of Hb in CAD and non-CAD group. ★ Indicates CAD vs. and non-CAD (136.92 ± 15.54 g/l vs. 140.08 ± 15.28 g/l, p = 0.003). B. The level of ALB in CAD and non-CAD group. CAD vs. and non-CAD (41.58 ± 2.75 g/l vs. 41.47 ± 2.71 g/l, p = 0.569). C. The level of TC in CAD and non-CAD group. CAD vs. and non-CAD (4.53 ± 1.04 mmol/l vs. 4.90 ± 0.94 mmol/l, p < 0.001).

Table 2
The associations of Hb, ALB and TC with CAD in older people.

	Model1			Model 2			Model 3		
	HR	95% CI	p	HR	95% CI	p	HR	95% CI	p
Hb	0.987	(0.978–0.995)	0.003	0.990	(0.980–0.999)	0.028	0.988	(0.976–0.999)	0.048
ALB	1.015	(0.965–1.066)	0.569	1.021	(0.972–1.073)	0.409	1.022	(0.960–1.089)	0.496
TC	0.672	(0.581–0.779)	< 0.001	0.628	(0.539–0.732)	< 0.001	1.073	(0.552–2.084)	0.835

Model 1: univariate analysis.
Model 2: Data adjusted for age, sex.
Model 3: Data adjusted for age, sex, BMI, body mass index; smoker, hypertension, DM, diabetes mellitus; stroke, LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol; TG, triglyceride; TC, total cholesterol; FPG, fasting plasma glucose; Hb, hemoglobin; ALB, albumin; antiplatelet drugs, statins, beta blocker, ACEI/ARB, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; antihyperglycemic/insulin.

factor for CAD in individuals with ≥ 80 years old ($p < 0.05$).

4. Discussion

The present study was a cross-sectional survey in older individuals (≥ 80 years), the purpose of study was to assess the relationships between potential malnutrition risk biomarkers and CAD. The results found the incidences of CAD were siginificantly higher in lower levels of Hb and TC than the higher levels of Hb and TC, respectively. The levels of Hb and TC were siginificantly lower in individuals with CAD than non-CAD. The level of ALB was not significantly associated with the incidence of CAD. Further, multivariate analysis showed Hb as a biomarker of malnutrition risk was the only independent predictor of the occurrence of CAD, but ALB and TC were not. In short, the novel finding was that Hb as the malnutrition risk biomarker was the independent protective factor for CAD in older individuals with ≥ 80 years old.

Anemia is considered as the marker of malnutrition in the elderly.[11] Anemia in adult is Hb < 130 g/L in men and 120 g/L in women.[12] Hb < 120 g/L in men and 115 g/L in women is considered as anemia in older people (> 70 years).[13] A research found that anemia increased the presence of malnutrition and the risk of malnutrition, malnutrition lead to decrease albumin synthesis in the liver and serum proteins such as hemoglobin, and malnutrition with insuffificient erythropoiesis may cause anemia.[14] Anemia is associated with cardiovascular complications and mortality.[15,16] Some studies have found that increasing Hb level was able to improve patients' cardiac function, left ventricular hypertrophy and quality of life.[17] But most of those studies were carried out from the relationship between anemia and the prognosis of cardiovascular disease, that very little research work has been done on the relationship the level of Hb and CAD, particularly in the elderly. In the study, the participants were the general elderly population (age ≥ 80 years and average Hb: 139.13 ± 15.42 g/L), the vast majority of them did not meet the definition of having anemia, so our study evaluated the relationship between the level of Hb and CAD in general elderly population. The low level of Hb predict malnutrition risk, and Hb is relatively stable and insensitive to acute and chronic disease stress.[4] The results showed that individuals with lower level of Hb had significantly higher incidence of CAD, and further analysis found that only Hb was the independent protective factor for CAD in older individuals. The lower level of Hb as biomarker of malnutrition risk is a new target for prevention of CAD in general elderly population. The underlying mechanism may be the low level of Hb is a risk factor for myocardial ischemia, and associate with other CAD risk factor such as inflammation,[18] but the exact mechanisms are unclear.

Numerous studies have found that the closely association of low ALB level and adverse cardiovascular outcomes in patients with stable coronary heart disease,[7] acute myocardial infarction,[19] percutaneous coronary intervention[20] and heart failure.[21] Low ALB level may have potential to reduce inhibition of platelet aggregation and attenuate fibrinolysis, and increase blood viscosity, disrupt endothelial functions, and decrease antioxidant capacity.[22] ALB as a negative-phase protein decreases in response to inflammation in acute disease and chronic disease with inflammatory process.[23] All the above-mentioned factors may increase the risk of atherothrombosis, leading to adverse cardiovascular outcome. Our study excluded some diseases which might induce hypoproteinemia, including acute or chronic inflammation, hepatic and renal dysfunction and so on. The average value of ALB was 41.50 ± 2.72 g/l in our study. Coincidently, a study showed the ALB value was above 38 g/l in healthy elder people until the age over 90 years.[24] ALB could be a good biomarker of nutritional situation in general elderly population,[25] so we think that the level of ALB should be a ture reflection of nutritional status in our study. To data, the research of the association ALB with the incidence of CAD in the general older population is less, especially in those greater than age 80 who had a higher incidence of CAD. Our study found the level of ALB was not significantly associated with the incidence of CAD in the general elderly population. Our result was consistent with prior study in which the olderly population (aged 65–74 years) was enrolled,[26] but our study population was more older. In the Framingham Offspring study, the level of ALB could predict the risk of myocardial infarction.[27] The study population and the level of ALB were different in different researches. Our results represented the relatively healthy older individuals with aged 80 or older, in which the ALB as a biomarker of malnutrition risk did not predict the incidence of CAD.

It is well known that the higher level of TC is closely associated with cardiovascular disease and mortality in middle-aged people.[28] But a research showed that the higher TC level no significant association with CAD in individuals with an average age of 79 years.[29] A meta analysis suggested that a lower TC concentration of 1 mmol/L was associated with a lower risk CAD mortality in older individuals.[30] And older individuals with TC ≥ 6.2 mmol/l were significantly associated with higher CAD mortality.[31] Most of the previous studies assessed the relationship TC and long-term prognosis. Our results found the low level of TC was closely associated with the higher incidence of CAD, the negative correlation between TC and the incidence of CAD in older population was consistent with the negative relationship between TC and mortality in previous research.[30] In our study, the average value of TC was 4.78 ± 0.99 mmol/l in the relatively healthy elderly population, TC cutoff of 4.76 mmol/l as a dividing line, the TC level was still in the normal range which may partly explain why our results is different from previous study.[28] With increasing age, the level of TC is trending downward.[32] In the elderly population, TC could be considered as marker of frailty and malnutrition.[4,33] Studies have already found age may attenuate the relative impact of TC on cardiovascular disease, the low level of TC

has been associated with an increased risk of mortality in elderly people.[33] The relationship may be partly explained by frailty and malnutrition. In the study, TC was not an independence protective factor for CAD after adjusting for these recognized risk factors.

Our study has some limitations, the results are limited to older Chinese adults and may not be generalizable to other ethnic and age groups cohorts. In the real word, older men tend to be more health-conscious than older women in the northern regions of China, so men in a greater proportion than women in the physical older population of the study, which may influence the result. The study was a cross-sectional observational research, we did not assess longitudinal relationships between biomarkers of malnutrition risk and CAD, and not further evaluate treatment benefits from improving potential malnutrition risk on the prevention and treatment of CAD in the elderly. Further large-scale longitudinal and interventional studies are needed to verified our finding. Despite the limitations, the associations of malnutrition risk biomarkers with CAD in the general elderly population have an important clinical significance to help us to understand the role of malnutrition risk in CAD.

In the study, we assessed the associations of Hb, ALB and TC as biomarkers of malnutrition risk with the incidence of CAD in the general elderly population (≥ 80 years). The unadjusted results showed the lower levels of Hb and TC had the higher incidence of CAD, only Hb was a significant protective factor for CAD after adjusting for these recognized risk factors in older individuals, but ALB and TC were not. The finding suggested that malnutrition risk may participate in the development of CAD in elderly, which could provide novel therapeutic strategies to treat and prevent CAD in older adults. But targeted therapy, such as nutritional intervention and administration should be futher researched in older individuals.

Conflicts of interest statement

All authors ensure that there is no conflict of interest in the study.

References

1. Corkins MR, Guenter P, DiMaria-Ghalili RA, et al. Malnutrition diagnoses in hospitalized patients: United States, 2010. *JPEN J Parenter Enteral Nutr.* 2014;38(2):186–195.
2. Agarwal E, Miller M, Yaxley A, et al. Malnutrition in the elderly: a narrative review. *Maturitas*. 2013;76(4):296–302.
3. Skipper A, Ferguson M, Thompson K, et al. Nutrition screening tools: an analysis of the evidence. *JPEN J Parenter Enteral Nutr.* 2012;36(3):292–298.
4. Zhang Z, Pereira SL, Luo M, et al. Evaluation of blood biomarkers associated with risk of malnutrition in older adults: a systematic review and meta-analysis. *Nutrients*. 2017;9(8):E829.
5. Corish CA, Kennedy NP. Protein-energy undernutrition in hospital inpatients. *Br J Nutr.* 2000;83(6):575–591.
6. Rahman A, Jafry S, Jeejeebhoy K, et al. Malnutrition and cachexia in heart failure. *JPEN J Parenter Enteral Nutr.* 2016;40(4):475–486.
7. Chien SC, Chen CY, Leu HB, et al. Association of low serum albumin concentration and adverse cardiovascular events in stable coronary heart disease. *Int J Cardiol.* 2017;241:1–5.
8. Kurtul A, Murat SN, Yarlioglues M, et al. Usefulness of serum albumin concentration to predict high coronary SYNTAX Score and in-hospital mortality in patients with acute coronary syndrome. *Angiology.* 2016; 67(1):34–40.
9. Ishii H, Aoyama T, Takahashi H, et al. Serum albumin and C-reactive protein levels predict clinical outcome in hemodialysis patients undergoing endovascular therapy for peripheral artery disease. *Atherosclerosis.* 2013;227(1):130–134.
10. Sun Y, Zhang H, Tian W, et al. Association between serum uric acid levels and coronary artery disease in different age and gender: a cross-sectional study. *Aging Clin Exp Res.* 2019;31(12):1783–1790.
11. Mitrache C, Passweg JR, Libura J, et al. Anemia: an indicator for malnutrition in the elderly. *Ann Hematol*. 2001;80(5):295–298.
12. Broadway-Duren JB, Klaassen H. Anemias. *Crit Care Nurs Clin North Am.* 2013;25(4):411–426.
13. Locatelli F, Aljama P, Bárány P, et al. Revised European best practice guidelines for the management of anaemia in patients with chronic renal failure. *Nephrol Dial Transplant.* 2004;19(Suppl 2):ii1–ii47.
14. Sahin S, Tasar PT, Simsek H, et al. Prevalence of anemia and malnutrition and their association in elderly nursing home residents. *Aging Clin Exp Res.* 2016;28(5):857–862.
15. Lee WC, Fang HY, Chen HC, et al. Anemia: a significant cardiovascular mortality risk after ST-segment elevation myocardial infarction complicated by the comorbidities of hypertension and kidney disease. *PLoS One.* 2017;12(7):e0180165.
16. Martinsson A, Andersson C, Andell P, et al. Anemia in the general population: prevalence, clinical correlates and prognostic impact. *Eur J Epidemiol.* 2014;29(7):489–498.
17. Hirakata H, Tsubakihara Y, Gejyo F, et al. Maintaining high hemoglobin levels improved the left ventricular mass index and quality of life scores in pre-dialysis Japanese chronic kidney disease patients. *Clin Exp Nephrol.* 2010;14(1):28–35.
18. Sarnak MJ, Tighiouart H, Manjunath G, et al. Anemia as a risk factor for cardiovascular disease in the Atherosclerosis Risk in Communities (ARIC) Study. *J Am Coll Cardiol*. 2002;40(1):27–33.
19. Plakht Y, Gilutz H, Shiyovich A. Decreased admission serum albumin level is an independent predictor of long-term mortality in hospital survivors of acute myocardial infarction. Soroka Acute Myocardial Infarction II (SAMI-II) project. *Int J Cardiol*. 2016;219:20–24.
20. Wada H, Dohi T, Miyauchi K, et al. Impact of serum albumin levels on long-term outcomes in patients undergoing percutaneous coronary intervention. *Heart Vessels.* 2017;32(9):1085–1092.
21. Polat N, Aydin M, Yildiz A, et al. The prognostic significance of serum albumin in patients with acute decompensated systolic heart failure. *Acta Cardiol.* 2014;69(6):648–654.
22. Joles JA, Willekes-Koolschijn N, Koomans HA. Hypoalbuminemia causes high blood viscosity by increasing red cell lysophos phatidylcholine. *Kidney Int.* 1997;52(3):761–770.
23. Horwich TB, Kalantar-Zadeh K, MacLellan RW, et al. Albumin levels predict survival in patients with systolic heart failure. *Am Heart J.* 2008; 155(5):883–889.
24. Campion EW, Delabry LO, Glynn RJ. The effect of age on serum albumin in healthy males: report from the Normative Aging Study. *J Gerontol.* 1988; 43(1):M18–M20.
25. Cabrerizo S, Cuadras D, Gomez-Busto F, et al. Serum albumin and health in older people: review and meta analysis. *Maturitas.* 2015;81(1):17–27.
26. Arques S. Human serum albumin in cardiovascular diseases. *Eur J Intern Med.* 2018;52:8–12.
27. Djoussé L, Rothman KJ, Cupples LA, et al. Serum albumin and risk of myocardial infarction and all-cause mortality in the Framingham Offspring Study. *Circulation.* 2002;106(23):2919–2924.
28. Tanabe N, Iso H, Okada K, et al. Serum total and non-high-density lipoprotein cholesterol and the risk prediction of cardiovascular events-the JALS-ECC-. *Circ J.* 2010;74(7):1346–1356.
29. Krumholz HM, Seeman TE, Merrill SS, et al. Lack of association between cholesterol and coronary heart disease mortality and morbidity and all-cause mortality in persons older than 70 years. *JAMA.* 1994;272(17): 1335–1340.
30. Prospective Studies Collaboration, Lewington S, Whitlock G, et al. Prospective Studies Collaboration. Blood cholesterol and vascular mortality by age, sex, and blood pressure: a meta analysis of individual data from 61 prospective studies with 55,000 vascular deaths. *Lancet*. 2007; 370(9602):1829–1839.
31. 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(10):753–760.
32. Schatz IJ, Masaki K, Yano K, et al. Cholesterol and all-cause mortality in elderly people from the Honolulu Heart Program: a cohort study. *Lancet.* 2001;358(9279):351–355.
33. Spada RS, Toscano G, Cosentino FI, et al. Low total cholesterol predicts mortality in the nondemented oldest old. *Arch Gerontol Geriatr.* 2007; 44(Suppl 1):381–384.