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Analysis of the Correlation between Malnutrition and Prognosis in Patients with Coronary Artery Disease and Cancer

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Abstract: *To investigate the association between malnutrition and all-cause and cause-specific mortality in Coronary Artery Disease (CAD) patients with cancer. This study used a retrospective cohort design to analyze data of patients with CAD and cancer admitted to five teaching hospitals in southern China between 2007 and 2020. Nutritional Status was assessed by CONUT (Controlled Nutritional Status) scoring system. The primary outcomes were all-cause mortality and cause- specific mortality to explore the association between malnutrition and these clinical outcomes. A total of 1063 CAD patients with cancer (mean age 68.0±9.7 years, female 26.6%) were included in this study. 698 (65.7%) patients were malnourished. During a mean follow-up of 3.3 years (range, 1.7 to 5.4 years), 250 patients (35.8%) in the malnourished group and 69 patients (18.9%) in the nonmalnourished group died. Cardiovascular Disease (CVD) was the leading cause of death in the nonmalnourished group, whereas cancer surpassed CVD as the leading cause of death in the malnourished group. After adjustment for potential confounders, undernutrition was associated with a significantly increased risk of all-cause mortality (adjusted hazard ratio [aHR]: 1.89, 95% confidence interval [CI]: 1.40-2.56), as well as an increased risk of death from cancer (aHR: 3.11, 95% CI: 1.67-5.80) and an increase in the trend of cardiovascular mortality (aHR: 1.78, 95%CI: 0.98-3.23). This study found that about two-thirds of CAD patients with cancer were malnourished and that malnutrition was associated with significantly increased all- cause and cancer mortality. Therefore, malnutrition is an important independent risk factor for patients with CHD and cancer, which significantly increases the risk of all-cause death and cancer death. These findings highlight the importance of valuing and improving the nutritional status of such patients in clinical management.*

Keywords: *malnutrition; CONUT score; Coronary artery disease; cancer*

1. Introduction

1.1 Research Background

Coronary Artery Disease (CAD) refers to a heart condition caused by reduced blood flow in the coronary arteries due to the formation of atherosclerotic plaques, coronary artery spasm, or inflammation, leading to an imbalance in the oxygen supply and demand of the myocardium, resulting in myocardial ischemia and hypoxia. In severe cases, this can lead to myocardial cell necrosis. CAD is an important component of cardiovascular diseases, including stable angina, unstable angina, non- ST elevation myocardial infarction (NSTEMI), and ST elevation myocardial infarction (STEMI). The main risk factors for CAD include age, gender, hypertension, diabetes, hyperlipidemia, smoking, and others. With the aging population and changing lifestyles, the incidence of CAD has been rising annually, making it one of the leading health threats worldwide [1-2]. The prevalence of CAD is increasing globally. In China, the incidence of CAD has been rising annually due to the aging population and changes in lifestyle. Current treatment for CAD primarily includes pharmacological therapy, interventional therapy, and surgical treatment. Pharmacological treatments include antiplatelet agents, anticoagulants, lipid-lowering drugs, and vasodilators. Interventional treatments mainly involve percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG). Surgical treatments include CABG and heart transplantation. With advancements in medical technology, the treatment outcomes for CAD continue to improve, but prevention remains the most effective strategy [3-4].

Cancer is a type of malignant tumor originating from epithelial tissues, characterized by uncontrolled proliferation, infiltration, and metastasis. The development of cancer is a complex,

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multifactorial process, including gene mutations, activation of oncogenes, and inactivation of tumor suppressor genes [5]. The harm of cancer primarily manifests in local infiltration, distant metastasis, and destruction of the body's normal physiological functions. The incidence of cancer is influenced by various factors such as age, genetics, environment, and lifestyle. In recent years, with advancements in medical technology, cancer diagnosis and treatment levels have continuously improved, but cancer remains one of the major public health problems globally. The incidence of cancer is also rising worldwide. In China, both the incidence and mortality rates of cancer are high. Current cancer treatments include surgery, radiotherapy, chemotherapy, targeted therapy, and immunotherapy. Surgical treatment is suitable for early-stage cancer patients, while radiotherapy and chemotherapy are mainly used for patients with advanced-stage cancer. Targeted therapy and immunotherapy are newer treatment methods developed in recent years. With the progress in medical technology, the early diagnosis and treatment of cancer continue to improve, but cancer prevention and early screening remain crucial [6-7].

Coronary Artery Disease (CAD) and cancer are two major health threats globally, with multifaceted impacts on the global burden, including economic costs, loss of healthy life years, and decreased quality of life. CAD is one of the leading causes of death worldwide, responsible for approximately 17.5 million deaths annually, with its treatment and management imposing a significant burden on the global economy, including direct healthcare costs and indirect costs. Cancer is the second leading cause of death globally, with approximately 10 million deaths each year, and its treatment and management also place a substantial burden on the global economy. With population aging and known carcinogenic factors, the incidence of cancer continues to rise. Globally, the burden of CAD and cancer is unevenly distributed, with death rates declining in developed countries due to better healthcare systems and preventive measures, while the burden is increasing in low- and middle-income countries [8-9]. In response to the global burden of these two diseases, governments and international organizations are implementing various measures, including raising public awareness of both diseases and their risk factors, promoting healthy lifestyles, improving the accessibility and quality of healthcare systems, and investing in research and prevention programs. Additionally, global health organizations are promoting early detection, diagnosis, and treatment of both cancer and cardiovascular diseases to reduce the impact of these diseases on individuals and society. Due to overlapping risk factors such as smoking, side effects of cancer treatment, and the negative impact of cancer on cardiovascular health, CAD and cancer are becoming increasingly common in aging populations. Despite progress in prevention and treatment, the comorbidity rate of CAD and cancer remains high, with these patients often poorly managed and having a worse clinical prognosis. Therefore, it is necessary to explore other effective treatment and intervention targets to improve the prognosis of this population [10-12].

Malnutrition refers to a condition in which the body lacks essential nutrients due to insufficient intake, digestive or absorption disorders, metabolic abnormalities, or excessive consumption, affecting physiological functions and health. Malnutrition is common in CAD and cancer patients, and it may lead to muscle wasting, decreased immunity, delayed wound healing, increased risk of complications, and reduced survival rates [13-14]. Malnutrition is a modifiable clinical variable, and it has been reported as common in CAD patients and widespread in cancer patients. However, the impact of malnutrition on all-cause mortality and disease-specific mortality in CAD and cancer patients has not been fully addressed. Recently, the Controlled Nutritional Status (CONUT) score, a simple and effective nutritional tool, has been used to predict prognosis in different clinical scenarios during hospitalization. The CONUT (Controlled Nutritional Status) score system is a tool for assessing the nutritional status of patients [15-17]. It evaluates the nutritional status using several simple clinical parameters, thereby predicting clinical outcomes and surgical risks. The CONUT score system includes three indicators: serum albumin levels, total cholesterol levels, and lymphocyte count. These indicators reflect the patient's nutritional status, immune function, and inflammatory state. Each indicator has a corresponding score based on laboratory test values or clinical data. The scores for each of the three indicators are then summed to obtain a total score, which is used to assess the patient's nutritional status. The higher the total score, the worse the nutritional status of the patient, which may lead to worse clinical outcomes and higher surgical risks [18-19].

The CONUT score system is simple to implement, requiring no complex tests or calculations, allowing for quick assessment of a patient's nutritional status in clinical practice. It helps doctors make treatment plans, adjust therapy, reduce surgical risks, and improve patient outcomes. Therefore, the CONUT score system has been widely applied in clinical practice, particularly in surgery, intensive care, and oncology. Our study aims to report the prevalence of malnutrition, overall mortality, and cause-specific mortality in CAD and cancer patients [20].

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1.2 Literature Review

For the global burden of Coronary Artery Disease (CAD) and cancer, Haidong Wang's study points out that the impact of CAD and cancer on the global burden includes economic costs, loss of healthy life years, and reduced quality of life. CAD is one of the leading causes of death worldwide, responsible for approximately 17.5 million deaths annually, while cancer is the second leading cause of death, with approximately 10 million deaths each year. With the aging population and the influence of known carcinogenic factors, the incidence of these two diseases continues to rise. Globally, the burden of CAD and cancer is unevenly distributed. In developed countries, death rates have declined due to better healthcare systems and preventive measures, but the burden in low- and middle-income countries is increasing.

Regarding the impact of nutritional status on CAD and cancer, the studies by Ignacio de Ulíbarri and Hideki Wada highlight that the CONUT score system has significant application value in assessing the nutritional status of CAD and cancer patients. The CONUT (Controlled Nutritional Status) score system is a tool to evaluate a patient’s nutritional status by using several simple clinical parameters, thus predicting clinical outcomes and surgical risks. The CONUT score system includes three indicators: serum albumin levels, total cholesterol levels, and lymphocyte count.

These indicators reflect the patient's nutritional status, immune function, and inflammatory state. Studies have found that the CONUT score is closely related to the prognosis of CAD and cancer patients. A higher CONUT score (indicating poorer nutritional status) is associated with worse clinical outcomes and increased surgical risks. Therefore, the CONUT score system has been widely used in clinical practice, especially in fields such as surgery, intensive care, and oncology.

Regarding the impact of nutritional intervention on CAD and cancer patients, Yeh ET and Sadeer G Al-Kindi, among others, believe that nutritional intervention plays a crucial role in improving the prognosis of CAD and cancer patients. In CAD patients, good nutritional status helps reduce the risk of cardiovascular events and improve clinical outcomes. In cancer patients, nutritional interventions can improve nutritional status, enhance quality of life, and even extend survival. Research by Arends J and Hébuterne X points out that nutritional interventions include nutritional screening, nutritional assessment, and nutritional therapy. Nutritional screening and assessment help detect and diagnose malnutrition early, enabling timely interventions. Nutritional therapy includes dietary adjustments, nutritional supplementation, and nutritional support, aiming to improve the patient's nutritional status and immune function, thus enhancing treatment outcomes and survival rates.

In summary, Coronary Artery Disease (CAD) and cancer are two major global health threats, with impacts on the global burden including economic costs, loss of healthy life years, and decreased quality of life. The CONUT score system has significant application value in assessing the nutritional status of CAD and cancer patients and is closely related to their prognosis. Nutritional intervention has an important impact on the prognosis of CAD and cancer patients, including measures like nutritional screening, assessment, and therapy, which aim to improve nutritional status and immune function, thereby improving treatment outcomes and survival rates.

2. Study Subjects and Methods

2.1 Research object

The data for this study were sourced from the Heart and Kidney Improvement Registry Cohort Study conducted at several hospitals in Southern China from January 2007 to December 2020. This registry study included consecutive patients who underwent Coronary Angiography (CAG) and/or Percutaneous Coronary Intervention (PCI). The diagnosis of Coronary Artery Disease (CAD) was based on the International Classification of Diseases, 10th Edition (ICD- 10) codes, and the diagnosis of cancer was also based on ICD- 10 codes. Clinical data were collected from 1,063 patients during their first hospitalization. These data included, but were not limited to, patients' demographic characteristics (such as age, gender), comorbidities (including other medical diseases and complications), laboratory test results (such as blood biochemical markers, inflammatory markers, etc.), and medication treatment at discharge. The collection of these data aimed to comprehensively assess the patients' clinical conditions and treatment background.

The inclusion criteria were as follows:

1) Patients diagnosed with Coronary Artery Disease (CAD);

2) Patients diagnosed with cancer.

The exclusion criteria included:

1) Patients with incomplete or missing follow-up information;

2) Patients lacking data required to calculate the Controlled Nutritional Status (CONUT) score. After screening, a total of 1,063 CAD patients with concurrent cancer were included in the final statistical analysis.

2.2 Data Preprocessing

The primary outcome measures of this study include overall mortality and cause- specific mortality. To assess the nutritional status of the patients, the CONUT (Controlled Nutritional Status) score system was used. The CONUT score is a composite index that considers several biochemical parameters: serum albumin level (g/dL), total cholesterol level (mg/dL), and total lymphocyte count (mm^3). According to the CONUT score system, the severity of malnutrition can be classified into four levels: no malnutrition (0- 1 points),mild malnutrition (2-4 points), moderate malnutrition (5-8 points), and severe malnutrition (9- 12 points).

In this study, patients were divided into two groups based on the CONUT score: those with a CONUT score of 0 or 1 were classified as the non-malnutrition group, while those with a CONUT score of 2 or higher were classified as the malnutrition group. This classification method helps researchers distinguish the impact of different nutritional statuses on patient mortality, providing a better understanding of the clinical significance of malnutrition in CAD patients with concurrent cancer.

2.3 Data Analysis

2.3.1 Statistical Method

The baseline characteristics of the subjects were described by continuous variables and categorical variables. For continuous variables, if the data follow normal distribution, the mean ± standard deviation (SD) is used to represent; If the data is not normally distributed, the median and interquartile (IQR) are used to describe it. For categorical variables, they are represented by counts and percentages. When comparing continuous variables, the appropriate statistical test method is selected according to the distribution characteristics of the data. If the data were normally distributed, Student's t test was used to compare the two groups. If the data is not normally distributed, anon-parametric test, such as the Kruskal-Wallis H test, is used to compare the differences between multiple groups. For categorical variables, Chi-squared test was used to compare the difference in frequency distribution between two or more groups.

2.3.2 Survival Analysis

Survival analysis is used to analyze time-to-event data, where the event of interest is typically something such as death, disease recurrence, equipment failure, etc. Survival analysis primarily focuses on two key outcomes: the time until the event occurs and whether or not the event occurs. Common survival analysis methods include:

1) Kaplan-Meier Curve (Survival Curve): This is a non-parametric method used to estimate the survival function, i.e., the probability of an event not occurring over time. The Kaplan-Meier curve calculates the survival rate at each time point and connects these points to form a curve, providing an intuitive way to observe survival differences between different groups.

2) Cox Proportional Hazards Model: This is a semi-parametric method used to analyze the relationship between survival time and one or more covariates. The Cox model does not require assumptions about the distribution of survival times and can handle censored data. The formula for the model is as follows:

$$h(t, x) = h_0(t)\exp(\beta_1 x_1 + \beta_2 x_2 + \cdots + \beta_p x_p) \quad (1)$$

In this model, h(t,X) is the hazard function at time *t* for covariates X,h_0 (t) is the baseline hazard function, β is the coefficient of the covariates, representing the effect of the covariates on the

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risk.

3) Parametric Survival Models: These models assume that survival times follow a specific distribution, such as the Weibull distribution or log-normal distribution. Parametric models can provide more accurate survival time estimates but require the assumption of a specific distribution.

4) Competing Risks Models: When individuals in the study face multiple possible events, competing risks models (such as the multi-event version of the Cox proportional hazards model) are used for analysis. This model considers the competition between different events and estimates the probability of each event occurring.

The choice of survival analysis method depends on the characteristics of the data and the research objectives. Kaplan-Meier curves and Cox models are the most commonly used methods due to their minimal assumptions and wide applicability.

2.3.3 Gray Test

Gray's test, also known as Gray's test for proportional hazards, is a statistical test used in survival analysis with the Cox proportional hazards model to assess whether the effect of covariates remains constant over time, i.e., whether the proportional hazards assumption holds. In the Cox model, the proportional hazards assumption implies that the hazard ratio of covariates remains constant over the observation period. If this assumption is violated, traditional Cox model analysis may yield misleading results.

Gray's test is based on the residuals process and evaluates the validity of the proportional hazards assumption by comparing the observed residuals with the expected residuals. If the difference between the two is significant, the proportional hazards assumption can be rejected, suggesting that the effect of covariates changes overtime.

The common approach to Gray's test is to perform individual tests for each covariate in the Cox model or a global test for all covariates. The global test typically uses a statistic based on the integral of the relationship between residuals and time, to assess whether the entire model satisfies the proportional hazards assumption. The statistic for Gray's test can be calculated using the following formula:

$$U^2 = \int ((\hat{\lambda}_0 (t)\hat{R}(t))^2 dN(t) \tag{2}$$

λ_0 (t) is the estimate of the baseline hazard function.

R(t) is the estimate of the covariate effects in the hazard function, i.e., the hazardratio.

dN(t) is the number of deaths at time t.

The statistic U2 follows a chi-square distribution, and its corresponding p-value can be calculated to determine whether to reject the proportional hazards assumption. If the p-value is less than the given significance level (e.g., 0.05), the proportional hazards assumption is considered violated. In practice, Gray'stest is typicall performed using statistical software. For example, the coxph function in the R package survival can be used to fit the Cox model, and the ggcoxdiag function in the ggcoxdiag package can be used to generate diagnostic plots for Gray's test.

Survival analysis uses the Kaplan-Meier method to estimate the overall survival time of patients with different nutritional statuses, and the Log-rank test is applied to compare differences between survival curves. To more intuitively describe the impact of competing risks on prognosis, the study also generates cumulative incidence function curves for cancer mortality and cardiovascular (CV) mortality based on nutritional status, and Gray's test is used for comparison.

To assess the correlation between malnutrition and all-cause mortality, the study uses the Cox proportional hazards regression model. Additionally, considering the potential competing risks of cancer death and CV death, competing risks regression analysis (such as the Fine-Gray model) is used to determine the hazard ratios for these endpoints. In all regression analyses, adjustments are made for demographic factors (such as age, sex), acute myocardial infarction (AMI), diabetes (DM), chronic kidney disease (CKD), low-density lipoprotein cholesterol (LDL-C), chronic heart failure (CHF), prior PCI treatment, anemia, and atrial fibrillation (AF).

All data processing and statistical analyses are conducted using R 4.0.3 software. For statistical significance, a two-sided p-value < 0.05 is used as the threshold to determine whether the results are

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statistically significant.

3. Research Result

3.1 Baseline Feature

A total of 1,063 patients with coronary artery disease (CAD) and cancer were included in the study, with a median age of 68.0 years (standard deviation: 9.7 years). Female patients accounted for 26.6% of the cohort. Among all patients, 698 (65.7%) were diagnosed with malnutrition. Other clinical characteristics included: 232 patients (21.8%) with a history of acute myocardial infarction (AMI), 642 patients (60.4%) with hypertension, 411 patients (38.7%) with diabetes, 305 patients (28.7%) with chronic kidney disease (CKD), 483 patients (45.4%) with anemia, and 683 patients (64.3%) who underwent percutaneous coronary intervention (PCI). Compared to the control group, patients in the malnutrition group were older, had a higher proportion of females, and had significantly higher incidences of CKD (31.7% vs. 23.0%), chronic heart failure (CHF) (19.9% vs. 13.7%), and anemia (55.2% vs. 26.9%). In addition, the estimated glomerular filtration rate (eGFR) and baseline low-density lipoprotein cholesterol (LDL-C) levels were lower in the malnutrition group. Detailed baseline characteristics of the patients are shown in Table 1 - Table 5.

Table 1: Baseline Characteristics Stratified by Nutritional Status

trait	Total	Non-malnutrition	malnutrition	P value
	N = 1063	n = 365	n = 698	

Table 2: Demographic Data

Age	68.0±9.7	66.4±9.9	68.9±9.5	< 0.001
Gender,n (%)	283 (26.6)	129 (35.3)	154 (22.1)	< 0.001
Acute Myocardial Infarction,n(%)	232(21.8)	72(19.7)	160(22.9)	0.263

Table 3: Discharge diagnostic information

Hypertension,n(%)	642(60.4)	216(59.2)	426(61.0)	0.603
DM,n(%)	411(38.7)	136(37.3)	275(39.4)	0.540
Chronic Kidney	305(28.7)	84(23.0)	221(31.7)	0.004
Disease,n(%)				
Heart Failure,n(%)	189(17.8)	50(13.7)	139(19.9)	0.015
Atrial Fibrillation , n (%)	76(7.2)	28 (7.7)	48(6.9)	0.725
Stroke , n (%)	92(8.7)	26 (7.1)	66(9.5)	0.242
COPD, n (%)	58(5.5)	16(4.4)	42(6.0)	0.331
Anaemia , n (%)	483(45.4)	98(26.9)	385(55.2)	< 0.001
CABG, n (%)	2(0.2)	1(0.3)	1(0.1)	> 0.99
Pre-PCI,n (%)	122(11.5)	32(8.8)	90(12.9)	0.057
PCI, n (%)	683(64.3)	231(63.3)	452(64.8)	0.684

Table 4: Laboratory test index

Hemameba,10^9/ L	7.88±3.10	7.83±3.02	7.90±3.14	0.700
eGFR, ml/min/1.73 m²	75.69 [56.69-89.55]	78.97 [62.56-92.76]	74.22 [54.82-88.06]	< 0.001
LDL-C, mmol/L	2.69 [2.08-3.37]	3.30 [2.81-3.93]	2.32 [1.86-2.90]	< 0.001
HDL-C ,mmol/L	1.01 [0.85-1.21]	1.08 [0.91-1.28]	0.96 [0.82-1.16]	< 0.001
Glycosylated	6.56±1.37	6.63±1.36	6.53±1.38	0.321
Hemoglobin ,mmol/L				
Albumin, g / L	36.89±5.00	40.09±3.52	35.22±4.84	< 0.001

Table 5: Medication Information

Beta blockers, n (%)	730 (75.0)	250 (73.5)	480 (75.8)	0.476
Statins, n (%)	903 (92.8)	313 (92.1)	590 (93.2)	0.596
Aspirin, n (%)	811 (83.4)	287 (84.4)	524 (82.8)	0.575
Spironolactone, n (%)	148 (15.2)	44 (12.9)	104 (16.4)	0.177
CCB, n (%)	261 (26.8)	85 (25.0)	176 (27.8)	0.387
ACEI, n (%)	334 (34.3)	117 (34.4)	217 (34.3)	> 0.99
ARB, n (%)	294 (30.2)	116 (34.1)	178 (28.1)	0.062

AMI: Acute Myocardial Infarction; DM: Diabetes Mellitus; CKD: Chronic Kidney Disease; CHF:

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Congestive Heart Failure; COPD: Chronic Obstructive Pulmonary Disease; CABG: Coronary Artery Bypass Grafting; Pre-PCI: Pre- Percutaneous Coronary Intervention; WBC: White Blood Cells; eGFR: Estimated Glomerular Filtration Rate; LDL-C: Low-Density Lipoprotein Cholesterol; HDL-C: High-Density Lipoprotein Cholesterol; HbA1c: Glycated Hemoglobin; CCB: Calcium Channel Blockers; ACEI: Angiotensin-Converting Enzyme Inhibitors; ARB: Angiotensin Receptor Blockers.

3.2 Study Outcome and Subgroup Analysis

During a median follow-up of 3.32 years (range: 1.7 to 5.4 years), 319 participants died. The proportion of deaths due to cancer was lower than the proportion of deaths due to cardiovascular disease (CVD) (3.8% vs. 5.2%, respectively). However, in malnourished patients, cancer became the leading cause of death, surpassing CVD (12.3% vs. 11.0%, respectively). Similar results were observed in male, female, and patients under 70 years of age. When the age reached or exceeded 70 years, CVD became the primary cause of death, regardless of nutritional status.

The Kaplan-Meier survival curve indicated that the all-cause mortality rate was higher in malnourished patients compared to those with good nutritional status (Log- rank test, $p < 0.001$). The cumulative incidence function (CIF) curve showed a significant association between malnutrition and higher cancer mortality and cardiovascular mortality rates (all Log-rank tests, $p < 0.001$). After adjusting for confounding factors such as age, gender, AMI, DM, CKD, LDL-C, CHF, previous PCI treatment, anemia, and atrial fibrillation, multivariable analysis revealed that malnutrition was significantly associated with increased all-cause mortality (adjusted hazard ratio [aHR]: 1.89, 95% confidence interval [CI]: [1.40-2.56]) and also significantly associated with increased cancer mortality (aHR: 3.11, 95% CI: [1.67-5.80]). Additionally, malnutrition showed a trend toward increased cardiovascular mortality (aHR: 1.78, 95% CI: [0.98-3.23]) (see Table 6).

Table 6: Risk of all-cause, cancer, and cardiovascular (CV) death

variable	All-cause Death[a]		Cancer Death[b]		Cardiovascular Death[b]	
	aHR (95% CI)	P value	aHR (95% CI)	P value	aHR (95% CI)	P value
Non-malnutrition	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
malnutrition	1.89 (1.40-2.56)	< 0.001	3.11 (1.67-5.80)	< 0.001	1.78 (0.98- 3.23)	0.057
age	1.02 (1.00- 1.03)	0.015	1.00 (0.98- 1.02)	0.720	1.02 (1.00- 1.05)	0.071
sex	0.60 (0.46- 0.80)	< 0.001	0.45 (0.25- 0.79)	0.005	0.47 (0.27- 0.83)	0.009
AMI	1.16 (0.88- 1.53)	0.302	1.23 (0.75-2.02)	0.420	0.77 (0.45- 1.31)	0.330
DM	1.16 (0.92- 1.46)	0.197	1.26 (0.84- 1.91)	0.270	1.45 (0.95-2.19)	0.083
Chronic Kidney Disease	1.45 (1.13- 1.85)	0.003	1.08 (0.67- 1.74)	0.750	1.95 (1.25- 3.04)	0.003
LDL-C	1.34 (1.19- 1.50)	< 0.001	1.24 (1.03- 1.51)	0.025	1.44 (1.12- 1.84)	0.004
CHF	1.46 (1.11- 1.93)	0.007	0.75 (0.40- 1.39)	0.360	1.97 (1.22- 3.18)	0.006
PCI	0.79 (0.62- 0.99)	0.045	0.78 (0.51- 1.19)	0.240	1.15 (0.72- 1.83)	0.550
Anemia	1.41 (1.12- 1.79)	0.004	1.48 (0.95-2.31)	0.080	1.61 (1.04-2.51)	0.034
Atrial Fibrillation	1.11 (0.74- 1.66)	0.613	0.97 (0.42- 2.25)	0.950	1.40 (0.73-2.70)	0.310

[a.] A Cox regression analysis was used to evaluate the relationship between malnutrition and all-cause mortality.
[b.] A competing risk regression analysis was used to evaluate the relationship between malnutrition and mortality from malignant tumors and cardiovascular disease.

Adjusted for age, gender, acute myocardial infarction, diabetes, chronic kidney disease, low-density lipoprotein cholesterol, congestive heart failure, and percutaneous coronary intervention.

4. Discussion

To the best of our knowledge, this is the first study to explore the prevalence of malnutrition and its prognostic impact in patients with coronary artery disease (CAD) and cancer. Our study found that approximately two-thirds of CAD and cancer patients were malnourished. After adjusting for confounding factors, malnutrition was associated with a 1.9-fold increased risk of all-cause mortality and a 3.1-fold increased risk of cancer-specific mortality, with a trend toward an increased risk of cardiovascular mortality as well.

Malnutrition is a common issue among CAD and cancer patients. In our study, two-thirds of the patients were classified as malnourished based on the CONUT score. Other studies have reported similar high rates of malnutrition, such as Roubín et al.'s cohort study in Canada, which found that 49.8%

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of patients with acute coronary syndrome (ACS) were malnourished. Wada et al.'s study showed that 43.3% of CAD patients undergoing PCI treatment were malnourished. In cancer patients, the prevalence of malnutrition varies depending on cancer type, stage, or treatment methods, typically ranging from 50% to 65%. Malnutrition in cancer patients may be related to factors such as inflammation, catabolism caused by tumors, gastrointestinal obstruction, and the side effects of cancer treatments.

Malnutrition not only increases the risk of all-cause mortality in CAD and cancer patients but is also associated with an increased risk of death from specific causes. In our study, malnutrition was associated with a 3.11-fold increased risk of cancer-specific mortality. Other studies have also found similar associations, such as in patients with colorectal and gastric cancers, where high malnutrition risk was significantly associated with an increased risk of cancer-specific death. Malnutrition is also linked to an increased risk of cardiovascular death, although in our study, this association became non-significant after adjusting for confounding variables. This may be due to cancer death acting as a competing risk, which weakened the association between malnutrition and cardiovascular death. Notably, in non- malnourished patients, the proportion of deaths due to cardiovascular disease was higher than that due to cancer. However, in malnourished patients, cancer became the leading cause of death, surpassing cardiovascular disease. This phenomenon was observed in male, female, and patients younger than 70 years old. However, in patients aged 70 years or older, cardiovascular disease was the leading cause of death regardless of nutritional status. This suggests that age is a significant risk factor for cardiovascular disease-related mortality.

Our findings have important implications for secondary prevention strategies for cardiovascular diseases and cancer. The results highlight the importance of incorporating malnutrition screening into daily clinical practice. The CONUT score, as a simple and effective tool, can help physicians identify high-risk patients for malnutrition, thereby enabling the development of targeted secondary prevention strategies, including nutritional supplementation, to improve patient outcomes. The implementation of optimal evidence-based monitoring guidelines should aim to reduce morbidity and mortality in cancer patients with comorbid cardiovascular diseases.

5. Deficiency and Prospect

The limitations of this study are as follows:

1) Retrospective Study Design: Since this study employed a retrospective design, it cannot establish causal relationships, and only correlations can be observed. Future prospective studies are needed to further validate the causal relationship between malnutrition and prognosis in CAD patients with cancer.

2) Selection Bias in the Study Population: The study population was selected based on patients who underwent coronary angiography (CAG) and/or percutaneous coronary intervention (PCI), which may have excluded patients with advanced cancer who did not undergo CAG unless they presented with acute and life-threatening conditions, such as acute coronary syndrome. Therefore, the study population may not fully represent all CAD patients with cancer.

3) Missing Cancer Characteristics: Detailed information regarding cancer grading, histology, and staging was not available in this study. These factors are crucial for understanding how different types and stages of cancer impact patients' nutritional status and prognosis. Certain types of cancer, especially those requiring radiotherapy or chemotherapy, or those in active phases, may more rapidly affect patients' appetite and nutritional status, or result in poorer prognosis.

4) Limitations of the Nutritional Assessment Tool: The CONUT score, used in this study to assess malnutrition, was the only tool applied and was calculated only once at the time of patient admission. While the CONUT score is an effective tool for nutritional assessment, it may not fully account for the dynamic changes in nutritional status throughout the patient's course of illness. Additionally, the CONUT score may not capture all factors associated with malnutrition.

Despite these limitations, the results of this study reveal the high prevalence of malnutrition in CAD patients with cancer and emphasize the importance of nutritional assessment in this population. Future studies should adopt prospective designs and incorporate more comprehensive nutritional assessment tools to better understand the impact of malnutrition in CAD patients with cancer.

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6. Conclusion

According to the assessment results using the CONUT score, approximately one- third of patients with coronary artery disease (CAD) and cancer are malnourished.

This finding indicates that malnutrition is a prevalent and significant health issue among patients with CAD and cancer. Malnutrition is significantly associated with an increased risk of all-cause mortality, as well as with a higher risk of cancer-related death and a trend towards increased cardiovascular mortality. These findings highlight the potential impact of malnutrition on prognosis in CAD patients with cancer.

However, the clinical effectiveness of malnutrition interventions in this high-risk population still requires further investigation. Future research should explore whether specific interventions targeting malnutrition, such as nutritional support therapy, can improve clinical outcomes in CAD patients with cancer, including survival rates, cardiovascular event incidence, and quality of life. Additionally, studies are needed to determine the optimal timing, duration, and personalized approach for these interventions.

In conclusion, the CONUT score, as a simple and effective nutritional assessment tool, helps identify malnourished CAD and cancer patients. The efficacy and cost-effectiveness of nutritional intervention strategies for these patients is an important direction for future research. Such studies could provide stronger evidence for clinical practice to improve the treatment and prognosis of CAD patients with cancer.

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