

## Postprint: Study on the Predictive Value of Lipid Profile Features in Digestive System Tumors for Phase Angle

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### Abstract

**Background:** Blood lipids play a crucial role in maintaining normal physiological functions. Cancer patients frequently exhibit lipid abnormalities, which can affect prognosis. Phase angle (PA) is an objective indicator reflecting the integrity of cell membrane structure and functional status, positively correlates with nutritional status, and is commonly used for survival and efficacy prediction. Currently, the characteristics of lipid profiles in cancer patients and their impact on PA remain unclear.

**Objective:** To analyze the characteristics of blood lipids in patients with digestive system tumors and examine their influence on PA.

**Methods:** A retrospective study included 142 patients admitted to the First People's Hospital of Anqing between July 2020 and December 2023. General patient information, Performance Status (PS) scores, and Patient-Generated Subjective Global Assessment (PG-SGA) scores were collected. Serum lipid parameters and PA were measured. Patients were divided into normal PA and low PA groups based on PA values, and differences in general characteristics and lipid levels between the two groups were compared. Binary logistic regression analysis was used to identify factors influencing PA. Receiver Operating Characteristic (ROC) curves were plotted, and the area under the curve (AUC) was calculated to evaluate the predictive value of lipid indicators for PA.

**Results:** Among the 142 patients, 104 were male (73.24%) and 38 were female (26.76%), with a mean age of (65±10.8) years. The low PA group included 64 cases (45.07%), while the normal PA group comprised 78 cases (54.93%). Statistically significant differences were observed between the two groups in gender, age, PS scores, and PG-SGA scores ( $P < 0.05$ ). Levels of TC, TG, and LDL in the low PA group were significantly lower than those

in the normal PA group ( $P < 0.05$ ). No statistically significant difference in HDL was observed between the two groups ( $P > 0.05$ ). Binary logistic regression analysis revealed that female gender (OR=0.223, 95%CI=0.078~0.635) and age (OR=0.282, 95%CI=0.110~0.727) were risk factors for PA, whereas TC (OR=5.522, 95%CI=2.632~11.584) was a protective factor for PA. The AUC of TC for predicting PA was 0.803 (95%CI=0.733~0.874), with sensitivity of 75.6%, specificity of 71.9%, and optimal cutoff value of 4.25 mmol/L. The AUC of LDL for predicting PA was 0.790 (95%CI=0.717~0.863), with sensitivity of 76.9%, specificity of 67.2%, and optimal cutoff value of 2.46 mmol/L. The AUC of TG for predicting PA was 0.609 (95%CI=0.517~0.702), with sensitivity of 55.1%, specificity of 64.1%, and optimal cutoff value of 1.05 mmol/L.

Conclusion: Blood lipid profiles in digestive system tumors are influenced by multiple factors. Maintaining lipid control within an appropriate range is beneficial for preserving normal PA and may potentially improve prognosis.

## Full Text

### Research on Lipid Characteristics and Predictive Value for Phase Angle in Digestive System Tumors

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## Abstract

**Background:** Lipids play a crucial role in maintaining normal physiological functions, and cancer patients often exhibit dyslipidemia that can affect prognosis. Phase angle (PA) is an objective indicator reflecting the structural integrity and functional status of human cell membranes, which is positively correlated with nutritional status and commonly used to predict survival and therapeutic efficacy. Currently, the lipid profile characteristics of cancer patients and their impact on PA remain unclear.

**Objective:** To analyze the lipid profile characteristics of patients with digestive system tumors and investigate their influence on PA.

**Methods:** A retrospective study was conducted on 142 patients admitted to the Affiliated Anqing First People's Hospital between July 2020 and December 2023. General patient data, performance status (PS) scores, and Patient-Generated Subjective Global Assessment (PG-SGA) scores were collected. Lipid profile indicators and PA were measured, and patients were divided into normal PA and low PA groups based on PA levels. Differences in general characteristics and lipid levels between the two groups were compared. Binary logistic regression was used to analyze influencing factors of PA. Receiver operating characteristic (ROC) curves were plotted, and the area under the ROC curve (AUC) was calculated to evaluate the predictive value of lipid indicators for PA.

**Results:** Among the 142 patients, 104 (73.24%) were male and 38 (26.76%) were female, with a mean age of  $(65 \pm 10.8)$  years. The low PA group comprised 64 patients (45.07%), while the normal PA group included 78 patients (54.93%). Significant differences were observed between the two groups in terms of sex, age, PS score, and PG-SGA score ( $P < 0.05$ ). The low PA group had lower levels of TC, TG, and LDL compared to the normal PA group ( $P < 0.05$ ), while no significant difference was found in HDL levels ( $P > 0.05$ ). Binary logistic regression analysis revealed that female sex (OR=0.223, 95%CI=0.078-0.635) and age (OR=0.282, 95%CI=0.110-0.727) were risk factors for PA, whereas TC (OR=5.522, 95%CI=2.632-11.584) was a protective factor. The AUC for TC in predicting PA was 0.803 (95%CI=0.733-0.874), with a sensitivity of 75.6%, specificity of 71.9%, and an optimal cutoff value of 4.25 mmol/L. The AUC for LDL was 0.790 (95%CI=0.717-0.863), with a sensitivity of 76.9%, specificity of 67.2%, and an optimal cutoff value of 2.46 mmol/L. The AUC for TG was 0.609 (95%CI=0.517-0.702), with a sensitivity of 55.1%, specificity of 64.1%, and an optimal cutoff value of 1.05 mmol/L.

**Conclusion:** Lipid metabolism in digestive system tumor patients is influenced by multiple factors. Maintaining lipid levels within an appropriate range may help preserve normal PA and potentially improve prognosis.

**Keywords:** Digestive system tumors; Blood lipid; Phase angle; Nutritional status; Logistic regression analysis

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## Introduction

Lipids are essential nutrients for the human body, and blood lipids play a positive role in maintaining normal physiological functions. Cancer patients often experience lipid metabolism disorders, and tumor metabolism theory suggests that secondary dyslipidemia in cancer patients results from tumor progression itself. As malnutrition worsens, this ultimately manifests as hypertriglyceridemia [1], though the clinical characteristics and mechanisms of total cholesterol (TC) changes in cancer patients remain unclear. Phase angle is an objective indicator reflecting the structural integrity and functional status of human cell membranes [2]. The human cell membrane is a lipid bilayer, and lipids serve as important

nutritional substrates for maintaining cell membrane structure and function. Previous studies have indicated that phase angle is positively correlated with nutritional status [3] and serves as a good indicator for evaluating nutritional status, gradually gaining clinical attention and application [4-5]. Human phase angle (PA) is also commonly used for survival and efficacy prediction, with patients having normal PA demonstrating better prognosis than those with low PA [6]. The normal reference range for phase angle is typically between  $4.2^\circ$  and  $5.4^\circ$  [7], with  $4.4^\circ$  used as the cutoff for nutritional status and prognosis assessment in Asian populations [8].

The 2021 Chinese Expert Consensus on Lipid Management in Cancer Patients [9] provides reference standards for the upper limit of lipid control in cancer patients based on atherosclerotic cardiovascular disease (ASCVD) management, but does not address the lower control limit. Previous studies have reported that low blood lipids are also a poor prognostic factor in cancer patients, easily leading to tumor progression [10]. Our preliminary study of 159 cancer patients showed that major lipid indicators such as TC and TG were positively correlated with phase angle, with different lipid indicators showing distinct patterns as nutritional status deteriorated. TG is associated with nutritional consumption, while TC may exhibit bipolar distribution—some patients show decreased TC due to increased consumption, while others show elevated TC due to enhanced tumor tissue anabolism [11]. Therefore, controlling blood lipids within an appropriate range may be more beneficial for improving general condition and prognosis. Building on our previous research, this study further focused on digestive system tumor patients, who have higher rates of malnutrition, to analyze lipid metabolism characteristics and their impact on phase angle, and to explore reasonable control ranges for blood lipids, aiming to provide reference for chronic disease indicator monitoring in the comprehensive nutritional management of cancer patients.

## Methods

**1.1 Study Subjects** Patients with esophageal, gastric, colorectal, liver, and pancreatic cancers admitted to the Affiliated Anqing First People's Hospital of Anhui Medical University between July 2020 and December 2023 were selected as study subjects. Inclusion criteria: (1) pathologically confirmed digestive system tumor patients; (2) age >18 years; (3) able to stand independently and undergo body composition analysis. Exclusion criteria: (1) history of hyperlipidemia before diagnosis; (2) currently taking lipid-lowering medications; (3) active severe chronic liver or kidney disease; (4) uncontrolled diabetes or thyroid dysfunction; (5) double or multiple primary cancers; (6) patients with pacemakers. A total of 169 digestive system tumor patients were initially collected, excluding 12 with pre-existing hyperlipidemia, 9 taking lipid-lowering medications, 2 with active severe chronic liver disease, 3 with uncontrolled hypothyroidism, and 1 with small intestine cancer. Ultimately, 142 patients were included. This study was approved by the Ethics Committee of the Affiliated

Anqing First People's Hospital of Anhui Medical University (approval number: AQYY-YXLL-KJXM-40), and all patients provided informed consent.

## 1.2 Data Collection and Measurements 1.2.1 General Data Collec-

**tion:** Patient sex, age, tumor type, clinical stage, and performance status (PS) scores were collected.

**1.2.2 PS Scoring:** The PS score is an important indicator for evaluating daily living ability and overall health status in cancer patients [12], typically divided into 5 grades: 0 points for normal activity capacity with no difference from pre-illness status; 1 point for ambulatory and able to perform light activities but unable to perform heavy physical labor; 2 points for ambulatory and self-caring but with lost working capacity, spending less than half of daytime in bed; 3 points for partially self-caring and spending more than half of daytime in bed; 4 points for bedridden and completely dependent; 5 points for life-threatening condition or death.

**1.2.3 Lipid Profile Measurement:** Fasting venous blood samples were collected after admission, and TC, TG, LDL, and HDL levels were measured using a Hitachi 7600 automatic biochemical analyzer.

**1.2.4 PG-SGA Scoring and Nutritional Status Classification:** Based on the Patient-Generated Subjective Global Assessment (PG-SGA) scoring system and nutritional status classification standards [13], PG-SGA evaluation was conducted within 48 hours of admission. Scores of 0-3 indicated good nutritional status, 4-8 indicated moderate malnutrition, and  $\geq 9$  indicated severe malnutrition.

**1.2.5 PA Measurement and Grouping:** PA was measured using an Inbody 770 body composition analyzer. The measurement procedure: after emptying bladder and bowels, fasting or after discontinuing food intake for 2-3 hours, patients removed shoes, socks, and gloves, cleaned their palms with 75% alcohol gauze, made contact with the analyzer's electrodes by slightly pressing thumbs against them, and stood with hands naturally hanging down and slightly separated from the body.  $PA < 4.4^\circ$  was defined as the low PA group, and  $PA \geq 4.4^\circ$  as the normal PA group [14].

**1.3 Statistical Analysis** SPSS 26.0 statistical software was used for data analysis. Normally distributed continuous variables were expressed as  $(\bar{x} \pm s)$  and compared between groups using independent samples t-test. Non-normally distributed variables were analyzed using rank sum tests. Unordered categorical variables were compared using  $\chi^2$  tests. Variables showing significant effects on phase angle in univariate analysis underwent Pearson or Spearman correlation testing. After removing highly correlated indicators, variables were included in binary logistic regression to explore independent effects on phase angle. ROC curves were plotted and AUC values were calculated to evaluate the predictive value of lipid indicators for PA.  $P < 0.05$  was considered statistically significant.

## Results

**2.1 Comparison of General Characteristics Between Low PA and Normal PA Groups** A total of 142 patients were included, comprising 104 males (73.24%) and 38 females (26.76%), with a mean age of  $(65 \pm 10.8)$  years. The low PA group included 64 patients (45.07%), while the normal PA group included 78 patients (54.93%). Significant differences were observed between the two groups in sex, age, PS score, and PG-SGA score ( $P < 0.05$ ). No significant differences were found in tumor clinical stage or tumor type ( $P > 0.05$ ).

shows the comparison of general data between low PA group and normal PA group.

**2.2 Comparison of Lipid Profiles Between Low PA and Normal PA Groups** The low PA group had significantly lower TC, TG, and LDL levels compared to the normal PA group ( $P < 0.05$ ). No significant difference was observed in HDL levels between the two groups ( $P > 0.05$ ).

shows the comparison of blood lipid levels between low PA group and normal PA group.

**2.3 Correlation Analysis Among Variables** Correlation analysis revealed a strong positive correlation between TC and LDL ( $r = 0.915$ ,  $P < 0.001$ ). TC was negatively correlated with age ( $r = -0.222$ ,  $P = 0.008$ ), PG-SGA score ( $r = -0.220$ ,  $P = 0.008$ ), and PS score ( $r = -0.201$ ,  $P = 0.017$ ). Sex was positively correlated with PS score ( $r = 0.167$ ,  $P = 0.047$ ). Age was positively correlated with PG-SGA score ( $r = 0.383$ ,  $P < 0.001$ ) and negatively correlated with LDL ( $r = -0.170$ ,  $P = 0.043$ ). PG-SGA score was positively correlated with PS score ( $r = 0.263$ ,  $P = 0.002$ ). PS score was negatively correlated with HDL ( $r = -0.187$ ,  $P = 0.026$ ). TG was positively correlated with TC ( $r = 0.365$ ,  $P < 0.001$ ) and LDL ( $r = 0.348$ ,  $P < 0.001$ ), but negatively correlated with HDL ( $r = -0.300$ ,  $P < 0.001$ ) and PG-SGA score ( $r = -0.197$ ,  $P = 0.019$ ), and negatively correlated with age ( $r = -0.183$ ,  $P = 0.029$ ). No significant correlations were found between other variable pairs.

**2.4 Binary Logistic Regression Analysis of PA Influencing Factors** After removing LDL due to its high correlation with TC, binary logistic regression analysis was performed with PA as the dependent variable ( $PA < 4.4^\circ = 0$ ,  $PA \geq 4.4^\circ = 1$ ) and TC, TG, HDL, PG-SGA, PS score, sex, and age as independent variables. The results showed that female sex (OR=0.223, 95%CI=0.078-0.635) and age (OR=0.282, 95%CI=0.110-0.727) were risk factors for PA, while TC (OR=5.522, 95%CI=2.632-11.584) was a protective factor.

shows the binary logistic regression analysis of independent influencing factors of phase angles.

**2.5 ROC Curves of TC, LDL, and TG for Predicting PA** ROC curves were plotted to evaluate the predictive value of TC, LDL, and TG for PA. The

AUC for TC was 0.803 (95%CI=0.733-0.874), with sensitivity of 75.6%, specificity of 71.9%, and optimal cutoff value of 4.25 mmol/L. The AUC for LDL was 0.790 (95%CI=0.717-0.863), with sensitivity of 76.9%, specificity of 67.2%, and optimal cutoff value of 2.46 mmol/L. The AUC for TG was 0.609 (95%CI=0.517-0.702), with sensitivity of 55.1%, specificity of 64.1%, and optimal cutoff value of 1.05 mmol/L [Figure 1: see original paper].

[Figure 1: see original paper] shows the receiver operating characteristic curves of TC, TG, and LDL in predicting PA.

## Discussion

Lipid metabolism in cancer patients is complex, particularly when accompanied by malnutrition, which may lead to characteristic lipid changes. Traditional theory suggests that tumor-associated malnutrition further exacerbates metabolic disorders, eventually manifesting as hypertriglyceridemia [15]. However, the characteristics and mechanisms of cholesterol changes remain unclear. This study focused on digestive system tumor patients, who have higher rates of malnutrition, to analyze lipid metabolism characteristics and explore appropriate lipid control ranges, providing reference for lipid management in cancer patients.

Phase angle, calculated from bioelectrical impedance analysis, effectively evaluates nutritional and health status [16] and reflects cell membrane integrity. Clinical studies have confirmed its close association with adverse disease outcomes. Due to its non-invasive nature, ease of operation, accurate measurement, and low cost, it has broad clinical application prospects [17]. Currently, there are no standardized reference values distinguishing healthy populations from patient populations. This study used  $4.4^\circ$  as the grouping standard, with  $PA < 4.4^\circ$  as the low PA group and  $PA \geq 4.4^\circ$  as the normal PA group [14]. The result showed significant differences between the two groups in sex, age (P=0.326). According to the measurement principle of PA, its value primarily depends on cell membrane structural and functional integrity rather than tumor type [20], suggesting that previously reported differences may be related to selection bias.

Correlation analysis showed a strong correlation between TC and LDL ( $r=0.915$ ,  $P < 0.001$ ) with collinearity, while other variables showed no collinearity. TC is a primary nutritional substrate for cell membrane synthesis, and LDL is the main cholesterol transport protein in the body, carrying approximately two-thirds of blood cholesterol and showing homology with TC [21]. With deteriorating nutritional status, LDL showed similar changes to TC in this study. After removing LDL due to high correlation with TC, variables without collinearity (TC, TG, HDL, PG-SGA, PS score, sex, age) were included in binary logistic regression analysis. The results indicated that male sex, younger age, and high TC were protective factors for PA, while TG, PS score, and nutritional status were not independent influencing factors. Previous studies showed some correlation between PA and PS score [22]. Although exercise can improve physical function,

few cancer patients can actively increase physical activity after diagnosis. Performance status often serves as a comprehensive evaluation of activity ability after improvement in various clinical characteristics. The significant effect of PS score on PA in univariate analysis ( $\chi^2=8.423$ ,  $P=0.004$ ) may represent a confounding variable effect. TG primarily participates in energy metabolism and is easily affected by diet and body fat reserves. Differences in dietary intake caused by different tumor types and inherent differences in body fat reserves between sexes may weaken TG's effect on PA, explaining why TG did not show independent significance in regression analysis. Previous studies demonstrated good correlation between PA and PG-SGA, with PA serving as a predictor of malnutrition [23]. However, this study's regression analysis did not show independent effects of nutritional status on PA, possibly because previous studies rarely included meaningful indicators like blood lipids for joint analysis. We hypothesize that deteriorating nutritional status in cancer patients may affect PA by regulating lipid metabolism [24-25], warranting further investigation.

The 2021 Chinese Expert Consensus on Lipid Management in Cancer Patients [9] provides reference for hyperlipidemia prevention but does not address the impact of excessively low lipids on poor prognosis, despite both high and low blood lipids being disadvantageous for cancer patients. Based on binary logistic regression results, maintaining TC and LDL within certain ranges (TC 4.25-5.55 mmol/L; LDL 2.46-3.91 mmol/L) appears valuable for maintaining normal PA. Controlling TG at 1.05-1.97 mmol/L may also help preserve normal PA. Given that tumor lipid metabolism characteristics and influencing factors differ substantially from cardiovascular diseases, stricter lipid control standards for cardiovascular disease may not be applicable to cancer patients. Further analysis revealed that the lipid levels corresponding to 100% specificity for PA in TC, TG, and LDL were only slightly above the upper limits of reference standards for major lipid indicators in low-risk populations for ASCVD primary prevention [26]. We preliminarily propose that the lower limit of appropriate lipid range for cancer patients should not be below the optimal cutoff values identified in this study, while the upper limit should not exceed the lipid levels corresponding to 100% specificity, which align with the high values of reference ranges recommended in the Chinese Lipid Management Guidelines [26] for low-risk ASCVD primary prevention populations. Since this study population has not undergone long-term follow-up, more accurate reference upper limits should be established through longer-term follow-up studies after fully weighing risks including cardiovascular events.

This study has several limitations. First, it included only digestive system tumors and cannot reflect lipid characteristics of other malignant tumors, requiring expanded sample sizes for further analysis. Second, the lack of long-term follow-up makes final prognostic conclusions difficult to obtain, which we plan to address in future retrospective studies. Third, although the included patients had PG-SGA scores ranging from 1-19 points covering most cancer patients, lipid characteristics and influencing factors in patients with more severe malnutrition beyond this range require further investigation.

In conclusion, this study preliminarily analyzed influencing factors of blood lipids in digestive system tumor patients. Tumor type, age, PS score, and nutritional status can affect blood lipids, while TC, sex, and age are independent influencing factors of phase angle. With deteriorating nutritional status, the body may regulate lipid metabolism to alter tissue cell structure and function, thereby affecting phase angle. In comprehensive nutritional management of cancer patients, besides preventing hyperlipidemia, attention should be paid to preventing excessively low blood lipids. Maintaining TC and LDL within reasonable ranges is beneficial for preserving normal PA and may potentially improve prognosis.

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