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RESEARCH PROGRESS ON THE APPLICATION OF PHASE ANGLE IN POSTOPERATIVE COMPLICATIONS OF LUNG CANCER

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Abstract: Phase angle (PhA) is the result of bioresistivity analysis (BIA) and is a physiological marker. In the past few years, the field of medical research has attracted more and more attention. In the field of oncology, PhA is particularly useful because it is related to the nutritional status and cell integrity of patients, and provides an important estimate of the risk of postoperative complications in surgical lung cancer population. Existing research shows that there may be a link between PhA and postoperative complications in lung cancer patients, but so far, research has been limited in terms of small sample size or lack of standard methods for evaluating PhA. This review outlines the physiological basis of PhA, the methods of measuring PhA, and the possibility of PhA affecting the risk of postoperative complications in patients with postoperative lung cancer. This review expands the study to integrate the latest articles published before to discuss the potential value and opportunities of using PhA in risk assessment in the future. This review ultimately aims to solve the current relationship between PhA and postoperative complications, evaluate the use of influencing factors or clinical interventions, and inform the basic practice of the evidence of lung cancer population in the postoperative nursing environment.
Keywords: Phase angle; Lung cancer; Postoperative complications; Bioelectrical impedance analysis; Risk prediction; Nutritional assessment

1 INTRODUCTION

Lung cancer is one of the main causes of cancer-related death, and surgical resection is still the main treatment for patients with early disease. However, postoperative complications, such as lung infection, anastomosis leakage and respiratory failure, have a significant impact on the prognosis and quality of life of postoperative patients. In recent years, traditional risk assessment tools, such as the American Association of Anesthesiologists (ASA) classification and the physiological and surgical severity score (POSSUM) classification system for mortality and morbidity, have been introduced and used to predict the risk of postoperative complications. However, their value to people with lung cancer surgery has been questioned. In addition, neither ASA nor POSSUM classification can accurately capture the physiological and nutritional status of patients, which is usually related to the development of postoperative complications.

BIA is a non-invasive, easy-to-use and inexpensive valuable method, which is now widely used for clinical nutrition assessment and prognostic measurement. As a functional parameter for BIA evaluation, PhA occurs in cell membranes, indicating the integrity and cellular function of the membrane. It has been proven to be related to nutritional status and nutritional status related to systemic inflammation and metabolic disorders. Many studies have shown that low preoperative PhA is associated with a higher rate of postoperative complications and a lower rate of positive results, regardless of surgical intervention for various malignant diseases or known malignant diseases. In a study, it was reported that there was a correlation between preoperative PhA (4.7 ± 0.7°) and higher Clavien-Dindo ≥ II complications, and identified PhA as an independent predictive factor [1]. This shows that PhA may be used as a valuable preoperative variable to assess the risk of postoperative complications in patients with lung cancer surgery.

So far, no systematic review has been carried out to evaluate the role of PhA in postoperative complications or results of lung cancer surgery. The summary of the findings provided in Table 1 provides a systematic review to summarize the latest findings and use of PhA, mainly to improve the perioperative management strategy of lung cancer patients. By offering clinicians a more effective risk assessment tool and supporting individualized perioperative care strategies, PhA has the potential to improve patient outcomes and enhance evidence-based clinical practice.

Table 1 Associations of PhA with Postoperative Complications in Lung Cancer and Its Potential Applications

Categories of Postoperative Complications	Association with PhA	Potential Mechanistic Explanations	Potential Applications
Malnutrition / Cachexia	Low PhA is significantly associated with low albumin and low BMI.	Reflects decreased cell membrane integrity, systemic inflammation, and skeletal muscle loss.	Used for preoperative nutritional risk stratification and dynamic monitoring of nutritional intervention efficacy.
Pulmonary Complications (pneumonia, ARDS, persistent air leak, atelectasis)	Decreased PhA → increased risk; low PhA is an independent adverse prognostic factor; patients with low PhA have higher incidence of pneumonia and respiratory failure.	Malnutrition and impaired immunity lead to poor sputum clearance, reduced respiratory muscle endurance, and compromised mucosal barriers.	Preoperative risk assessment; identification of patients who require "prehabilitation" and enhanced nutritional support; dynamic monitoring for early warning of complications.
Pleural Complications (pleural effusion, empyema)	Decreased PhA → increased risk of pleural complications.	Low PhA is often accompanied by hypoalbuminemia and skeletal muscle loss, resulting in delayed pleural repair and poor lung re-expansion.	Combined with prognostic nutritional index (PNI), albumin (Alb), and other markers to guide individualized nutritional support and respiratory training.
Cardiovascular Complications	Evidence specific to lung cancer is limited; cardiac surgery studies show that low PhA is associated with increased risk of postoperative atrial fibrillation (POAF) and mortality.	Low PhA represents frailty, inflammatory status, and fluid imbalance, increasing susceptibility to arrhythmias.	Can serve as a secondary risk marker, used in conjunction with age, electrocardiogram findings, and other factors for risk stratification.
Hemorrhage / Thromboemboli sm	Data in lung cancer are lacking; cardiac surgery studies show that low PhA is associated with increased transfusion risk.	Vulnerability along the "nutrition–sarcopenia–inflam mation" axis impairs hemostatic ability and destabilizes hemodynamics.	Can be combined with hemoglobin (Hb), albumin (Alb), and D-dimer for high-risk screening; indicates the need for early correction of anemia and nutritional optimization.

2 PHYSIOLOGICAL BASIS, MEASUREMENT METHODS, AND INFLUENCING FACTORS OF PHA

PhA represents the phase shift between voltage and current as electrical impulses pass through biological tissues, typically expressed in degrees. Its value is directly associated with cell membrane integrity and cellular function [2, 3]. PhA is measured using BIA, particularly at higher frequencies (e.g., 50 kHz), where it mainly reflects overall cellular mass. A higher PhA typically reflects preserved cell membrane integrity, increased cellular mass, and superior nutritional condition, whereas a lower PhA may indicate cellular injury or poor nutritional status [2].

BIA in clinical practice is carried out through a four-pole or eight-pole electrode system using single-frequency or multi-frequency current (usually 50 kHz). The patient is evaluated and measured in a supine position, and the limbs are separated from the body position to maintain the stability of appropriate electrode placement and reading [4]. Compared with traditional body composition analysis, PhA does not rely on predictive equations, reducing biases arising from body shape, race or disease status. This makes PhA particularly important when evaluating nutritional and prognostic results during critically ill patients, tumors and postoperative acute diseases [5]. In addition, the use of multi-frequency BIA and the progress of phase-sensitive impedance imaging are improving the accuracy and clinical applicability of PhA, allowing PhA to be more widely used in nutrition monitoring, fluid management and disease outcome prediction [6].

Finding the appropriate cut-off value of PhA is a key research area for its clinical application. Generally speaking, research shows that the cut-off range is about 4.5° to 5.5°. For example, in a study of 1,814 cancer patients, the researchers reported a cut-off value of 4.8° for men and 4.4° for women; therefore, support requires a gender-specific reference value [7]. Age is another important variable that leads to PhA, because the reference value varies between young and elderly patients 1. Therefore, the establishment of a comprehensive reference range specific to age, gender and race will help provide clinical utility for full adaptation to PhA. Further large-scale multi-center research is needed to verify the cut-off values of different populations, especially among multi-ethnic populations, in order to provide accurate clinical practice advice.

PhA measurement is affected by many factors that affect the accuracy of measurement. First of all, the liquid state plays an important role. Both dehydration and fluid retention can lead to inaccurate PhA values, especially if the patient's fluid balance is abnormal [8-10]. Secondly, age and gender also play an important role in determining PhA. PhA usually decreases with age, and there is a significant difference between men and women [11-13]. The overall body composition plays an important role in determining PhA. Due to the better electrical conductivity of muscle, a larger muscle mass usually corresponds to a higher PhA value [14, 15]. In diseases such as cancer, liver disease and chronic kidney disease, the PhA value often decreases by due to poor cell membrane function and changes in fluid state and balance [16-18]. In addition to physiological and clinical variables, there are also technical and procedural variables that help measure the variability. If there is a difference in the measurement of single-frequency and multi-frequency BIA, this difference can promote the variability of the measurement, even the operation details of electrode placement, and the positioning of the patient or participant will lead to deviation and reduce the accuracy of the measurement [19, 20].

In addition, dietary intake and physical activity levels may also change the PhA value, and change slightly, which is especially evident in the PhA value assessment after exercise or after meals [21-23]. In view of the findings of the influencing factors mentioned above, clinical practice must consider other variables to maintain the accuracy and reliability of PhA measurement.

3 PHA AND POSTOPERATIVE NUTRITIONAL STATUS IN LUNG CANCER PATIENTS

As a key parameter of BIA, PhA reflects cell membrane integrity, body cell mass, and fluid distribution. In lung cancer patients, a low PhA is typically associated with impaired cell membrane function, cellular depletion, and the progression of cancer-related malnutrition or cachexia a mechanism supported by multiple studies. A systematic review of 11 studies conducted over the past two decades [24, 25] reported that low PhA was significantly associated with poorer nutritional status, functional impairments (e.g., reduced handgrip strength and lower Karnofsky performance scores), and shorter survival. However, the review also emphasized inconsistencies in PhA cutoff points due to variations in measurement devices and study populations, suggesting that a universal standard cannot be applied. Suzuki et al. 1 retrospectively analyzed 240 patients with non-small cell lung cancer who underwent primary surgical resection. The mean preoperative PhA measured by BIA was 4.7 ± 0.7°, notably lower than the reference value of approximately 6.5° observed in healthy Asian populations. The study further showed that PhA was significantly lower in women compared with men (4.5 ± 0.7° vs. 4.9 ± 0.7°, $p < 0.001$) and declined with advancing age ($\rho = -0.51$, $p < 0.001$). Moreover, PhA was positively correlated with body mass index ($\rho = 0.29$), skeletal muscle mass ($\rho = 0.47$), hemoglobin ($\rho = 0.33$), albumin ($\rho = 0.33$), total lymphocyte count ($\rho = 0.17$), and the prognostic nutritional index ($\rho = 0.32$), all with statistical significance ($p < 0.01$). Perioperative studies show that low preoperative phase angle (PhA) can independently predict postoperative complications after cancer surgery. The author has framed the potential of PhA as a nutritional marker with the evaluation tools in preoperative risk assessment [26-28].

The diet pattern is also positively correlated with the PhA value. Among 82 male samples with stage IV non-small cell lung cancer, Detopoulou et al. reported a positive correlation between PhA and dietary patterns characterized by high consumption of potatoes, meat and poultry ($r = 0.254$, $p = 0.02$) [29]. After adjusting for age, lean weight and Mediterranean diet, the diet pattern is still an independent positive predictor of PhA ($\beta = 0.165$, $p = 0.05$). In addition, lean weight is positively correlated with PhA ($\beta = 0.018$, $p = 0.02$), and age is negatively correlated ($\beta = -0.022$, $p = 0.02$). The model jointly explains the variability of about 24% in PhA. A high-protein diet may help maintain muscle quality, which may allow the physical condition of cancer patients and ensure beneficial results.

So far, most studies have been observational and single-center studies, so the overall strength of the evidence is weak. For this reason, it is necessary to conduct large-scale, multi-center and prospective clinical research to further use the clinical efficacy of PhA to evaluate nutritional status and guide the perioperative intervention of lung cancer patients.

4 PHA AND POSTOPERATIVE PULMONARY COMPLICATIONS IN LUNG CANCER

The overall complication rate following lung cancer surgery ranges from 9.0% to 53.4%, with respiratory complications such as pneumonia, atelectasis, persistent air leak (PAL), and respiratory failure being the most common. Postoperative pulmonary complications (PPCs) in lung cancer primarily include pneumonia, acute respiratory distress syndrome (ARDS), PAL, atelectasis, and bronchospasm [30].

Evidence from prospective studies suggests that PhA can independently predict the occurrence of PPCs after lung cancer surgery. Suzuki et al. reported that, as assessed by the Clavien–Dindo grading system, 22.0% of patients ($n = 53$) developed postoperative complications of grade II or higher, with prolonged air leak (12.0%) and pneumonia (0.4%) representing the most frequent complications [1]. In terms of risk prediction, univariate analysis showed that for every 1° increase in PhA, the risk of postoperative complications decreased significantly (OR = 0.50, 95% CI: 0.32–0.78, $p = 0.002$). Multivariate regression further confirmed PhA as the only independent predictor of Clavien–Dindo grade ≥ II complications (OR = 0.51, 95% CI: 0.29–0.90, $p = 0.018$), whereas sex, age, BMI, and PNI were not significant predictors [1].

Low preoperative PhA in lung cancer patients has also been associated with poorer physical performance and shorter survival, while simultaneously indicating an increased risk of postoperative complications, supporting its role as a perioperative risk stratification tool [24]. Similar associations have been repeatedly observed in perioperative studies of colorectal cancer, where low PhA predicted higher complication rates and prolonged hospitalization [27]. Although not lung cancer–specific, these findings suggest external reproducibility of PhA as an integrated biomarker of perioperative nutritional and functional status. Retrospective analyses involving mixed cohorts of lung and colorectal surgery patients further showed that standardized PhA was associated with medical complications within 30 days after surgery [31]. Mechanistically, low PhA reflects malnutrition, sarcopenia, and impaired immune function, which may predispose patients to PPCs through reduced coughing and expectoration ability, decreased respiratory muscle endurance, impaired mucosal immunity, and delayed wound healing factors contributing to pneumonia, atelectasis, and PAL [32-34]. Moreover, reduced PhA, representing compromised cell membrane integrity and increased extracellular water, may synergize with skeletal muscle loss, hypoalbuminemia, and systemic inflammation (elevated CRP and IL-6) to impair alveolar epithelial repair and airway clearance capacity after surgery [32].

From the above studies, patients with low PhA may represent key candidates for targeted “prehabilitation plus nutritional optimization” interventions, including high-protein and high-energy dietary supplementation, omega-3 fatty

acids, and vitamin support, combined with resistance training and respiratory muscle rehabilitation. Such comprehensive strategies may help reduce the risk of pulmonary complications such as pneumonia, atelectasis, and persistent air leak [24, 35]. Furthermore, PhA should be integrated with established nutritional and functional assessment tools such as the Patient-Generated Subjective Global Assessment (PG-SGA), the Global Leadership Initiative on Malnutrition (GLIM) criteria, body composition measures (e.g., CT-derived skeletal muscle cross-sectional area), and inflammatory markers for a more precise and multidimensional perioperative evaluation. In perioperative management, PhA may also serve as a dynamic monitoring parameter, with repeated measurements during hospitalization and early postoperative recovery to assess the efficacy of nutritional support and fluid management. When used alongside early clinical signs of pulmonary complications (e.g., oxygenation status, imaging findings, and temperature changes), PhA may enhance the sensitivity of complication surveillance. Considering that there is no consensus on the cut-off value between the population and the tool, it is more suitable for risk assessment to use institution-specific thresholds (for example, median or quartile distribution) or gender and age-standardized PhA (S-PhA). In addition, for a more reasonable and continuous explanation, it may be more intuitive to explain to patients that "higher PhA means lower risk" [24].

In a word, the preoperative and early postoperative evaluation of PhA not only provides independent prognostic information on pulmonary complications after surgery for lung cancer treatment, but also a useful indicator for evaluating the impact of nutritional and immune methods. The uniqueness of PhA gives it potentially important clinical efficacy and may promote its use in perioperative clinical management.

5 PHA AND POSTOPERATIVE PLEURAL COMPLICATIONS IN LUNG CANCER

Pleural effusion and empyema are common complications following lung cancer surgery, with an incidence of approximately 0.9%, and are associated with male sex, advanced pathological stage, and open thoracotomy [36]. Similar to pulmonary complications, PAL is also one of the most frequent pleural complications after lung cancer surgery. PAL occurs at a relatively high rate and is significantly linked to prolonged hospital stays and extended chest tube drainage. Studies have shown that PAL is strongly associated with factors such as fragile lung parenchyma, low body weight, and surgical procedures such as upper lobectomy [37,38].

The core pathophysiological basis of pleural complications lies in impaired pleural integrity and disturbed intrathoracic negative pressure. A low PhA reflects decreased cell membrane integrity and extracellular water imbalance, which when combined with preoperative skeletal muscle loss, hypoalbuminemia, and systemic inflammation may weaken pleural healing capacity and delay postoperative lung re-expansion, thereby increasing the risk of pleural effusion [32]. Since malnutrition-related indicators such as hypoalbuminemia and low prognostic nutritional index (PN) have been shown to be significantly associated with pleural complications [39, 40], and PhA has already been established as an independent predictor of postoperative complications in lung cancer, PhA may be considered in combination with PNI, albumin, pulmonary function, and imaging features (e.g., upper lobectomy status) for precise risk stratification. For patients with low PhA or reduced PNI and albumin levels, individualized preoperative nutritional interventions and prehabilitation strategies such as enteral nutrition, exercise, and respiratory training are recommended to reduce the incidence of postoperative complications [41]. In addition, postoperative monitoring of PhA dynamics, particularly in patients with increased air leakage or drainage volume, may serve as an early warning indicator for complications such as empyema. This may achieve timely treatment interventions, including negative pressure drainage and bronchoscopic closure strategies.

Although PhA has aroused interest as a predictor of postoperative complications, there is no standardized measurement and a standardized cut-off threshold. In addition, most studies conducted so far have not directly evaluated PhA and specific pleural endpoints, such as PAL, pleural effusion or empyema. Future work should emphasize multicenter prospective cohort studies to evaluate the predictive utility of PhA on pleural complications, including its potential utility in nutritional intervention and pre-rehabilitation. Overall, PhA holds considerable promise in the identification, risk stratification, and management of postoperative complications in lung cancer, but further standardization and validation are required.

6 PHA AND POSTOPERATIVE CARDIOVASCULAR COMPLICATIONS IN LUNG CANCER

Among cardiovascular complications following surgical treatment of lung cancer, postoperative atrial fibrillation (POAF) is the most common and clinically significant, with an incidence of approximately 10–40% after pulmonary resection. POAF is associated with hypotension, heart failure, stroke, and increased mortality, with advanced age and right-sided resections being recognized risk factors [42, 43].

At present, there is no direct evidence linking PhA to postoperative cardiovascular complications in lung cancer patients. However, evidence from cardiac surgery indicates that low preoperative PhA is associated with frailty, in-hospital mortality, all-cause mortality, and increased risk of POAF and related complications [44-47], supporting the feasibility of using PhA as a perioperative cardiovascular risk biomarker. Additionally, several studies in lung cancer and other malignancies have suggested that PhA values in the range of 4.4°–5.5° are associated with stratification of adverse outcomes [27, 48, 49]. Taken together, existing data in thoracic oncology provide direct evidence of the association between PhA and overall complications, while robust background evidence supports its relevance to cardiovascular vulnerability. Although the evidence of PhA specificity of cardiovascular complications of lung cancer is in the

accumulation stage, the mechanism logic is similar: the path from low PhA indicating weakness, systemic inflammation and fluid disorders to the vulnerability of cardiovascular events seems to be generally effective in the perioperative environment and provides for the study of lung cancer-specific cardiovascular results. External validity.

In view of this background, any future research exploring Lung Cancer PhA can be included in the preoperative cardiovascular risk assessment of lung cancer as a "second layer" indicator, supporting traditional "first layer" indicators, such as age, hypertension or smoking history and right resection. Absolute PhA and standardized Z scores (relative to age and gender matching population) should be reported in order to customize the risk according to individual patients. For example, if an individual's PhA is lower than the institutional cut-off value or significantly lower than the age-matching control group, intervention can be initiated earlier (for example, even within the normal range), including targeted nutrition, rehabilitation training (respiratory muscle, resistance exercise), stricter perioperative fluid management, intermittent rather than continuous Electrocardiogram monitoring.

7 PHA AND POSTOPERATIVE HEMORRHAGE AND THROMBOEMBOLISM IN LUNG CANCER

Postoperative bleeding in lung cancer is defined as blood loss caused by a variety of reasons, including surgical trauma, vascular damage and possible postoperative use of anticoagulants. The impact of bleeding severity is important for overall recovery and/or even survival in some cases [50]. Venous thromboembolism (VTE) involving pulmonary embolism (PE) and deep vein thrombosis (DVT) is a potentially fatal complication with a relatively high prevalence in patients undergoing surgical intervention. The development of VTE is related to embolism and thrombosis, through immobility, tumor characteristics, surgical insults, and coagulation factors of inflammation and non-inflammatory mechanisms [51]. Due to inflammation caused by tumors, hemodynamic changes in tumors and long-term bed rest after surgery, lung cancer patients are particularly prone to thrombosis.

At present, there is no specific evidence linking PhA with postoperative bleeding or thromboembolism in lung cancer. However, the data comes from other major surgical fields and is equivalent. For example, in heart surgery, PhA preoperative <15% of the population is an independent predictor of the need for postoperative red blood cell transfusion (OR = 2.326) [50]. Therefore, preoperative low PhA (such as malnutrition, cell state) may be related to an increase in postoperative blood loss [50]. Furthermore, low PhA has been linked to adverse perioperative outcomes, including higher transfusion requirements, indicating its potential role in perioperative risk stratification [47].

These data are the potential theoretical basis for evaluating PhA when considering postoperative bleeding and thromboembolism in lung cancer. Integrating preoperative PhA with key laboratory indicators, such as hemoglobin, albumin, and D-dimer, may help identify patients at high risk for bleeding or thromboembolic complications [52]. In the context of anemia, prolonged antiplatelet or anticoagulant therapy, and extensive resection, a low PhA may indicate vulnerability along the “nutrition–sarcopenia–inflammation” axis, prompting preoperative correction of anemia and nutritional optimization. However, PhA alone should not be used to adjust hemostatic or transfusion thresholds [47, 50]. Although PhA is not currently included in VTE guideline pathways, when combined with high-risk surgery, a history of VTE, or postoperative D-dimer elevation, low PhA may help guide enhanced attention to early mobilization, mechanical and pharmacologic prophylaxis adherence, and, where guidelines allow, extended prophylaxis duration or intensified monitoring with D-dimer and ultrasonography. Importantly, clinical decisions should remain guided primarily by patient condition, surgical risk, and established guideline recommendations.

8 CONCLUSION AND FUTURE PERSPECTIVES

As a key parameter derived from BIA, PhA has received increasing attention in clinical medicine in recent years. Current evidence indicates that PhA reflects both the general health and nutritional condition of patients with lung cancer, while also offering distinct utility in evaluating the risk of postoperative complications. In particular, low PhA levels are significantly associated with moderate to severe postoperative complications, which indicates that PhA may be an important independent predictor in postoperative risk stratification. Although a lot of research has been carried out in this field, there are still obstacles to the clinical use of PhA. Although there is still a clinically acceptable, non-invasive and cost-effective option to measure PhA through BIA, the procedure for measuring PhA must still be standardized to ensure accurate and repeatable measurements. Secondly, the combination of PhA with other biomarkers is crucial to promote the clinical implementation of PhA into a multimodal assessment method. In addition to risk assessment, there is also the additional potential of using PhA, especially in the postoperative management of lung cancer. A continuous dynamic assessment of PhA will further support health care practitioners to measure recovery, promote treatment adjustments through timely evaluation, and ultimately promote patient-centered care, which may reduce complications and improve outcomes. As part of postoperative management, the continued implementation of PhA assessment will require multi-site and large-scale research to prove sufficient evidence for making clinical decisions on postoperative risks. In addition, it is possible to develop portable devices to evaluate PhA and help promote clinical acceptance by improving accuracy, which may use smart devices.

In summary, PhA is a promising biomarker that will be a predictor of postoperative risk, recovery monitoring and prognosis indicators, even lung cancer. Although these findings pave the way for the clinical application of PhA through clinical application research, it is necessary to verify and standardize PhA as a biomarker to further solve the inconsistent findings I-related research. PhA and other biomarkers will require interdisciplinary scientific work interdisciplinary cooperation to quantify PhA into actual clinical use, so that lung cancer patients can get better

treatment and quality of life.

COMPETING INTERESTS

The authors have no relevant financial or non-financial interests to disclose.

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