The Role of Geriatric Nutritional Risk Index in Predicting Postoperative Pulmonary Complications in Elderly Lung Cancer Patients Undergoing Surgical Resection

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Research Article

Keywords: geriatric nutritional risk index, postoperative pulmonary complication, lung cancer, resection, predictor.

Posted Date: January 5th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1155133/v2

Abstract

Background

The relationship between immunonutritional status (eg. Prognostic nutritional index [PNI] and Controlling Nutritional Status [COUNT] score) and risk of postoperative pulmonary complications (PPCs) after surgical resection of lung cancer had reported before. However, another immunonutritional parameter-Geriatric Nutritional Risk Index (GNRI)-had never explored.

Method

To address this issue, in this study we retrospectively analyzed patients' characteristics and PPCs in a cohort of lung cancer patients who were treated by surgical resection at our center. The clinical utility of patients' characteristics for predicting PPCs was evaluated by receiver operating characteristic curve analysis and the Youden index. Univariate and multivariate analysis were applied to find the most important factors.

Result

A total of 128 patients met the inclusion criteria for this study. Significant differences in sex, GNRI, FEV1%, LY% were found between the PPC and non-PPC groups (all $P<0.05$). The difference in pathology between the 2 groups showed borderline statistical significance ($P=0.052$). We determined the best cutoff value of each parameter and calculated the corresponding sensitivity and specificity, and found that GNRI, FEV1% and LY% had similar diagnostic value. Multivariate analysis reveled GNRI, sex, LY% and FEV1% were filtered to be correlated to PPCs of elderly lung cancer patients received surgery therapy.

Conclusion

These results indicate that preoperative immunonutritional parameters of GNRI can be used to identify elderly lung cancer patients at risk of PPCs.

Introduction

Lung cancer is the leading cause of cancer-related deaths both worldwide and in China[1, 2]. Surgery is the first-choice treatment for early-stage lung cancer[3]. The mortality and postoperative pulmonary complication (PPC) rates within 30 days after lung cancer resection are about 4.4% and 20–40%, respectively[4, 5]. Many factors influence the occurrence of PPCs, including preoperative pulmonary function and immunonutritional status[6, 7].

The immunonutritional status of lung cancer patients were an important predictor of clinical outcome. Tumor cells alter the patient's metabolism and grow rapidly by usurping nutrients from the patient. It was previously reported that weight loss and low albumin (ALB) level were associated with the occurrence of PPCs after lung cancer resection[8]. Various instruments such as modified Glasgow prognostic score (mGPS), prognostic nutritional index (PNI), Controlling Nutritional Status (CONUT) score, and Geriatric Nutritional Risk Index (GNRI) have been developed to assess the preoperative immunonutritional status of cancer patients. The relationship between immunonutritional status (eg. PNI, CONUT score) and risk of PPCs after surgical resection of lung cancer had reported before[9,10]. However, another immunonutritional parameter- GNRI -had never explored.

To address the above point, in this retrospective cohort study we evaluated the clinical utility of GNRI for predicting PPCs in elderly lung cancer patients treated by surgical resection.

Methods

Patient selection

We reviewed the patient database of Shanghai Chest Hospital, Shanghai Jiao Tong University for lung cancer cases treated by resection in 2012 and 2013. The study was conducted according to the principles outlined in the Declaration of Helsinki, and the Ethics Committee of Shanghai Chest Hospital approved the protocol (no. KS1924). All patients signed the informed consent form before participating.

The inclusion criteria were as follows: (1) age between 60 and 80 years old; (2) underwent lung cancer resection at Shanghai Chest Hospital, Shanghai Jiao Tong University; (3) physical and laboratory examinations were performed within 1 week before the surgery. Exclusion criteria were as follows: (1) incomplete clinical data; (2) severe cardiac insufficiency as determined by electrocardiography and echocardiography; (3) previously underwent lung resection. Basic demographic and clinical information were collected for each patient including age, sex, smoking history, physical and laboratory examination results, major comorbidities, surgery type, pathologic diagnosis, and PPCs.

Evaluation of immunonutritional status

A standard physical examination was conducted and data including height and weight were recorded. Laboratory examinations were also performed before surgery including a routine blood test, hepatic and renal function tests, and measurement of serum lipids. The immunonutritional parameters were determined as follows.

GNRI was calculated based on serum ALB level and body weight according to the formula GNRI=1.489×serum ALB level (g/L) + 41.7×preoperative weight/ideal weight (kg) [11].

Surgery performance

Four surgeons and their respective teams performed all operations, using similar operative and perioperative procedures. All patients received similar medical care following the guidelines of enhanced recovery after surgery[12]. Preoperative medical care included health education, smoking cessation, preoperative pulmonary rehabilitation, comorbidities management, and prevention of deep venous thrombosis. Intraoperative management included general anesthesia combined with endotracheal intubation anesthesia and paravertebral nerve block under ultrasound guidance; precise controlled infusion of opioid frugal general anesthesia technology was used to reduce the dosage of muscle relaxants. Postoperative management included post-operative pulmonary rehabilitation and nutritional support. Each patient was given prophylactic antibiotics for 2–3 days after surgery.

Evaluation of PPCs

PPCs within 1 month after lung cancer resection were defined as follows: (1) pneumonia (new lung infiltration on imaging examination in addition to any of the following items: fever [body temperature ≥38°C] lasting >5 days; white blood cell count >10.5×10^9/l; and upgraded antibiotic treatment or antibiotic application for >7 days); (2) atelectasis; (3) long-term mechanical ventilation due to postoperative respiratory failure (mechanical ventilation time >48 h); (4) secondary tracheal intubation; (5) persistent air leakage or pleural effusion requiring long-term drainage (>7 days); (6) bronchopleural fistula; (7) pulmonary embolism; (8) other pulmonary complications[13, 14].

Statistical analysis

We used SPSS v20.0 software (IBM, Armonk, NY, USA) for statistical analyses. Measurement data are expressed as mean ± SD. Differences between groups were evaluated by one-way analysis of variance and with the t test. Count data were analyzed with Pearson's chi-squared test and Fisher's exact probability test. Receiver operating characteristic (ROC) curve analysis and the Youden index were used to assess the predictive value of immunonutritional parameters for PPCs. Differences were considered statistically significant for P values <0.05.

Results

Characteristics of the study population

A total of 128 patients met the inclusion criteria for this study (Fig. 1). Most patients were male (73.43%), underwent thoracotomy (93.75%), had no smoking history (45.31%), and were diagnosed with adenocarcinoma (54.69%) (Table 1). There were 29 patients with 37 PPCs in the whole cohort, the

incidence of PPCs was 22.48% (29/128). The most frequent PPCs were persistent air leakage or pleural effusion and pneumonia. Six patients had more than one PPC (Table 2).

Relationship between immunonutritional status and PPCs

We calculated the correlation between patient characteristics and PPCs. Significant differences in sex, GNRI, FEV1%, LY% were found between the PPC and non-PPC groups (all $P<0.05$). The difference in pathology between the 2 groups showed borderline statistical significance ($P=0.052$). (Table 3)

Predictors of PPCs

An ROC curve analysis was performed with GNRI, BMI, FEV1%, FVC and LY% to evaluate the predictive value of these parameters for PPCs. GNRI, FEV1%, FVC and LY% were found to be statistically significant based on the area under the ROC curve. We determined the best cutoff value of each parameter and calculated the corresponding sensitivity and specificity, and found that GNRI, FEV1% and LY% had similar diagnostic value. (Table 4 and Fig. 2). The we conducted the multivariate analysis. For the continuous variable, we used the cutoff value to define “low” or “high”. In the analysis, the variable of sex, surgery method, pathology, GNRI FEV1%, FVC% and LY% were included. Finally, GNRI, sex, LY% and FEV1% were filtered to be correlated to PPCs of elderly lung cancer patients received surgery therapy.

Discussion

PPCs are a major concern in the surgical treatment of lung cancer. Pulmonary function is one of the main predictors of PPCs, and some guidelines recommend the evaluation of preoperative immune and nutritional status[15]. The PPC rate in our study is about 22%, which is similar to previous reports[4, 5]. The main PPC is persistent air leakage or pleural effusion and pneumonia, which are affected by immune and nutritional status. Pneumonia is common in patients who are malnourished or immunocompromised. The principal causes of persistent air leakage or pleural effusion are pneumothorax or hydrothorax; persistent hydrothorax may also result from pneumonia or hypoproteinemia. Thus, in theory, immune and nutritional parameters can be predictors of PPCs.

Many researches have explored the clinical meanings of single immune and nutritional in predicting PPCs. Among all, ALB and body weight related index are most studied. ALB is synthesized by hepatocytes and maintains vascular osmotic pressure; transports hormones, fatty acids, or other compounds; and regulates blood pH. Serum ALB concentration is often used as a biochemical marker of long-term nutritional status and reflects visceral protein status[16]. A correlation between ALB insufficiency and the development of early PPCs has been reported previous[17,18]. Body weight loss is also revealed correlated to high rate of PPCs. In Busch E’s report, weight loss and ALB level are linked to PPCs following lung cancer resection[8, 19–21]. Globulin and LY% reflect the immune status of patients[22]. The cellular

immunitymainly regulates immune function through T lymphocyte subsets[23] and in tumor surveillance, immunoglobulin contributes to target cell phagocytosis[24].

Immunonutritional parameters are calculated based on multiple indices related to immune function (CRP, peripheral lymphocyte count, etc) and nutrition (BMI and ALB). Those parameters show to be useful for detecting sarcopenia, which has been linked to the survival of lung cancer patients[25]. Moreover, several studies have reported that immunonutritional parameters are prognostic indicators of survival[26–33] and could predict PPCs[28, 30, 34] in patients with lung cancer. Poor immunonutritional status may increase the risk of PPCs by impairing pulmonary function, which was improved by nutritional support during chemotherapy [33].

Among the clinical instruments included in our analysis, GNRI were found to have predictive value for PPCs, with moderate diagnostic value. GNRI are calculated based on the original index and are continuous variables. In previous study, GNRI is suggested to be not inferior to nutrition screening tool of Mini Nutritional Assessment[35]. GNRI is recognized to correlated with sarcopenia status[36]. GNRI has been widely applied in digestive tract diseases. In gastric cancer, colorectal cancer and esophageal cancer, GNRI is defined as a prognostic factor[37–39]. Previous studies reveal GNRI as a prognostic factor both in early lung cancer patients treated with surgery operation[40, 41] and advanced stage lung cancer[42–44]. Besides, GNRI can predict the treatment response of immunotherapy[45, 46]. Apart this, GNRI is suggested to be good predictor for postoperative complications after abdominal surgery or gastrointestinal malignancy[47, 48]. But, can this parameter be good predictor in elderly lung cancer surgery operation patients? There is no answer. Thus we compare the GNRI and other patients characteristic and find GNPI has moderate sensitivity for detecting PPCs; that is, patients with low values are more likely to develop PPCs after lung cancer resection and require special care. Meanwhile, it has moderate specificity; this means that patients with a high value are not likely to experience PPCs, and routine care is therefore sufficient. Thus, risk stratification is possible based on these few parameters, which would maximize the use of limited medical resources. As mention above, ALB and body weight are the most important simple index for PPCs. When calculating GNRI, both ALB and body weight are enrolled, thus it may has excellent diagnostic value than other patient characteristics.

There were some limitations to this study that should be noted. Firstly, because of the retrospective single-center design, selection bias could not be avoided. Secondly, because the sample size is relatively small, statistical bias was inevitable.

Nonetheless, our findings demonstrate that immunonutritional parameters can predict PPCs following lung cancer resection and can be used to identify high-risk patients who would benefit from preventive interventions. Among all, GNRI has the best performance.

Abbreviations

PPC: postoperative pulmonary complication

ALB: albumin

mGPS: modified Glasgow prognostic score

PNI: prognostic nutritional index

CONUT: controlling nutritional status

GNRI: geriatric nutritional risk index

ROC: receiver operating characteristic

VATS: video-assisted thoracoscope

BMI: body mass index

FEV1: forced expiratory volume

FVC: forced vital capacity

LY: lymphocyte

RBC: red blood cell

PALB: Prealbumin.

Declarations

Ethics approval and consent to participate

The study was conducted according to the principles outlined in the Declaration of Helsinki, and the Ethics Committee of Shanghai Chest Hospital approved the protocol (no. KS1924). All patients signed the informed consent form before participating.

Consent for publication

All author approved this publication.

Availability of data and materials

The datasets generated for this study will be made available from the corresponding author on reasonable request.

Competing interests

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Funding

This work was support by grants from the National Key Research and Development Program of China (no. 2018YFC1313600 to LY Jiang) and Chinese Society of Clinical Oncology (no. Y-2019AZZD-0038 to LY Jiang).

Author Contributions

Conception and design: Mao XW, Zhang W, Jiang LY; (II) Administrative support: Mao XW, Jiang LY; (III) Provision of study materials or patients: Mao XW, Zhang W, Hu F, Niu YJ, Jiang LY; (IV) Collection and assembly of data: Mao XW, Zhang W, Hu F, Wang Q, Lu AT, Liu JB; (V) Data analysis and interpretation: Mao XW, Zhang W, Hu F, Wang Q, Lu AT, Liu JB, Jiang LY; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors

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Tables

Table 1. Patient characteristics

Variable	Number (percent)
Total	128
Age, mean	65.77
Sex	
Male	94 (73.43%)
Female	34 (26.57%)
Surgery method	
Thoracotomy	120 (93.75%)
VATS	8 (6.25%)
Smoking history	
Never	58 (45.31%)
Current	52 (40.63%)
Ever	18 (14.06%)
Pathology	
Squamous	45 (35.16%)
Adenocarcinoma	70 (54.69%)
Large cell lung cancer	6 (4.69%)
Small cell lung cancer	2 (1.56%)
Other	5 (3.90%)
GNRI, mean	106.91
BMI, mean	23.92

VATS: video-assisted thoracoscope; GNRI: geriatric nutritional risk index; BMI: body mass index.

Table 2. Postoperative pulmonary complications in the study population

Item	
Total events	37
Pneumonia	10
Atelectasis	2
Mechanical ventilation >48 h	3
Re-intubation	1
Persistent air leakage or pleural effusion	19
Pneumorrhagia	1
Pulmonary embolism	1
Total patients	29
1 event	23
>1 event	6

Table 3. Correlation between postoperative pulmonary complications and immunonutritional parameters

Variable	Non-PPC	PPC	P value
Sex			
Male	67	27	0.007
Female	32	2	
Age, years	65.98±4.95	65.07±3.36	0.354
Surgery method			0.682
VATS	7	1	
Thoracotomy	92	28	
Smoking history			0.609
Never	47	11	
Current	38	14	
Ever	14	4	
Pathology			0.052
Squamous	28	17	
Adenocarcinoma	60	10	
Small cell lung cancer	2	0	
Large cell lung cancer	5	1	
Other	4	1	
GNRI	107.85±9.37	103.69±9.38	0.038
BMI	24.21±3.33	22.94±2.75	0.065
FEV1%	85.37±16.71	74.83±18.13	0.004
FVC%	86.94±15.44	81.09±14.23	0.070
LY	1.87±0.57	1.75±0.54	0.287
LY%	30.71±7.98	24.73±9.10	0.001
RBC	4.37±0.50	4.33±0.52	0.700
HB	132.80±14.22	134.52±14.79	0.571
ALB	42.06±3.75	41.03±4.39	0.213
PALB	0.22±0.06	0.21±0.06	0.407
Globin	26.68±4.20	25.69±3.32	0.246

Urea	5.54±1.41	5.83±1.90	0.366
Creatinine	62.72±10.92	65.45±15.92	0.291
Uric acid	321.60±70.54	309.93±84.38	0.456
Number of segments removed	4.13±1.69	4.24±1.55	0.754

Data represent mean ± standard deviation. Abbreviations: PPC, post pulmonary complication; VATS: video-assisted thoracoscope; GNRI, geriatric nutritional risk index; BMI: body mass index; FEV1: forced expiratory volume; FVC: forced vital capacity; LY: lymphocyte; RBC: red blood cell; HB: hemoglobin; ALB: albumin; PALB: Prealbumin.

Table 4. Receiver operating characteristic curve analysis of immunonutritional parameters

Parameter	AUC	P value	Cutoff value	Sensitivity	Specificity	Youden index
GNRI	0.639	0.023	105.736	0.646	0.655	1.301
BMI	0.599	0.104				
FEV1	0.664	0.007	77.150	0.657	0.655	1.312
FVC	0.603	0.093	89.05	0.424	0.793	1.217
LY%	0.686	0.002	27.300	0.657	0.655	1.312

Abbreviations: GNRI, geriatric nutritional risk index; BMI: body mass index; FEV1: forced expiratory volume; FVC: forced vital capacity; LY: lymphocyte; AUC: area under the curve.

Table 5: Multivariate analysis of the influence parameters of PPCs

Parameters	OR	95% CI	P value
GNRI: High Vs Low	0.377	0.145, 0.975	0.044
Sex□female vs male	0.221	0.016, 1.066	0.060
LY%: High Vs Low	0.390	0.152, 1.002	0.051
FEV1%: High Vs Low	0.296	0.116, 0.759	0.011

Abbreviations: GNRI, geriatric nutritional risk index; BMI: body mass index; FEV1: forced expiratory volume; LY: lymphocyte; OR: odd ration; CI: confidence interval.

Figures

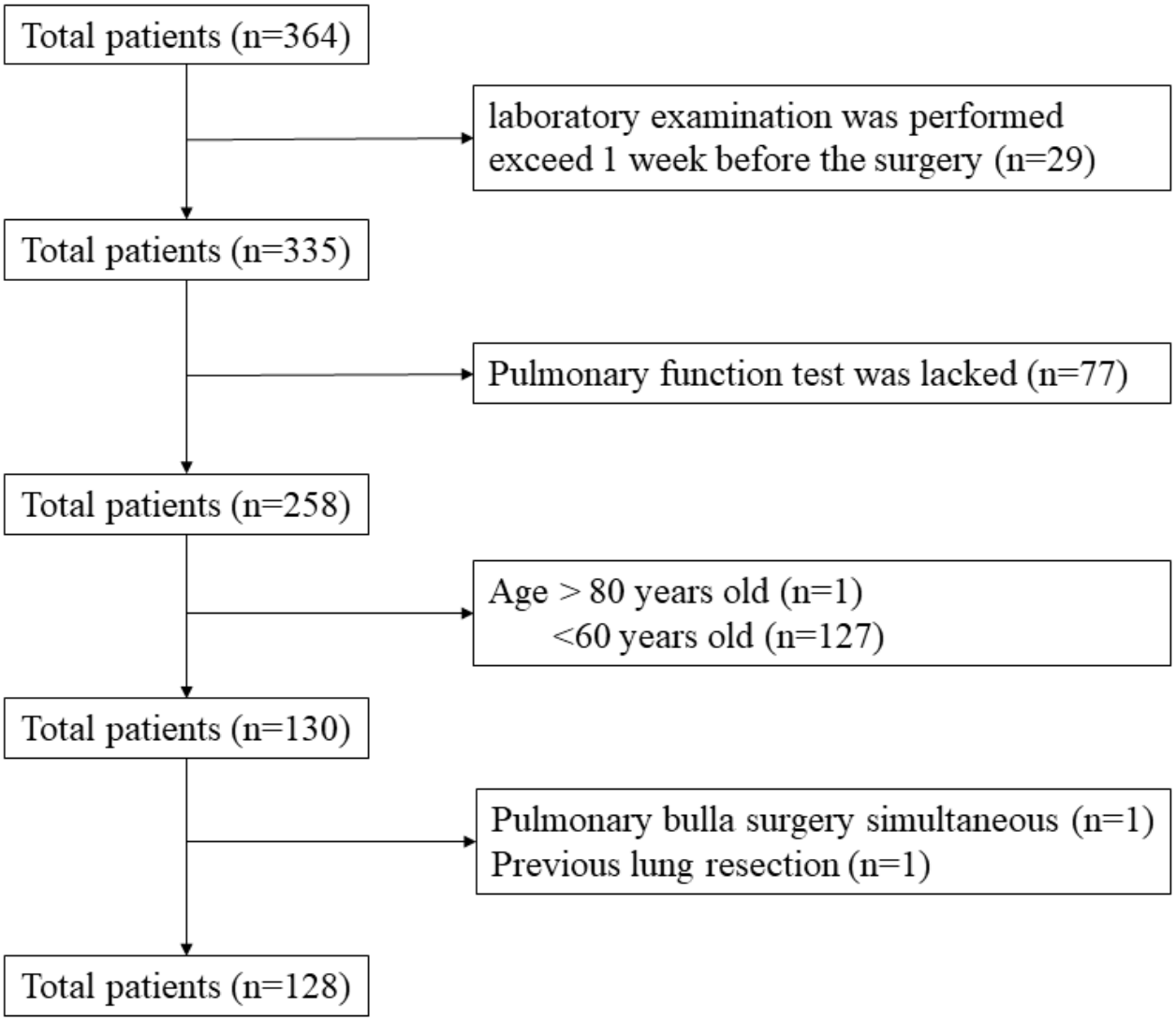

Figure 1

Patient selection flow chart

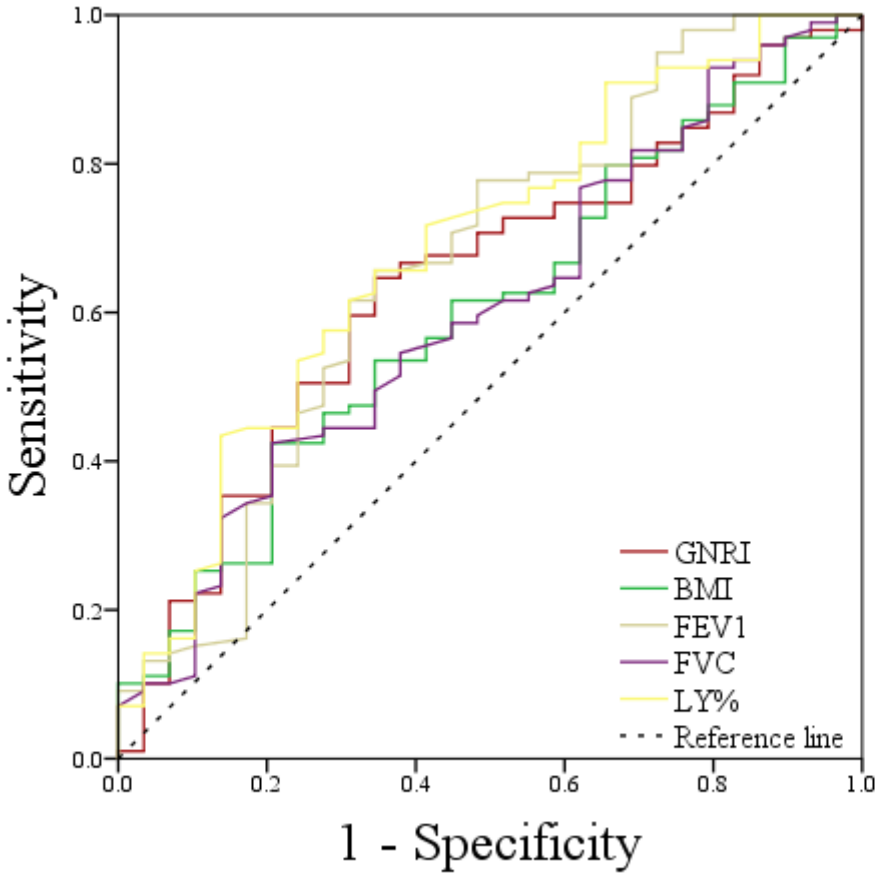

Figure 2

ROC for the patients' characteristics. Abbreviation: GNRI, geriatric nutritional risk index; BMI: body mass index; FEV1: forced expiratory volume; FVC: forced vital capacity; LY: lymphocyte; AUC: area under the curve.