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High Systemic Immune-Inflammation Index is Associated with Low Mid-Upper Arm Circumference and High Malnutrition Universal Screening Tool Score in Non-Small Cell Lung Cancer Patients

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ABSTRACT

Background: Non-small cell lung cancer (NSCLC) accounts for 82% of all lung cancer-related fatalities worldwide in 2020. Inflammation is a characteristic feature of all malignancies, including lung cancer, and it can worsen nutritional status and result in malnutrition. In order to evaluate inflammation, nutritional status, and malnutrition risk, the systemic immune-inflammation index (SII), mid-upper arm circumference (MUAC), and malnutrition universal screening tool (MUST), are chosen, respectively. ***Methods:*** From August to October 2023, an analytical observational study employing a cross-sectional design was conducted at Prof. Dr. I Goesti Ngoerah Gde Ngoerah Hospital Denpasar on patients diagnosed with NSCLC. SII was used for the association with MUAC and MUST score by using bivariate analysis and logistic regression. ***Results:*** The total number of participants comprised 63 individuals. The bivariate analysis yielded inconclusive findings regarding the relationship between SII and MUAC; however, the multivariate analysis identified a significant relationship (p=0.033, odds ratio 4.197, 95% CI 1.119–15.735). SII was significantly associated with the MUST score, according to the findings of bivariate analysis (p=0.011; odds ratio of 4.675; 95% CI: 1.345–16,255). SII was an independent risk factor for a higher MUST score in NSCLC patients, according to a multivariate analysis (p=0.015, odds ratio: 4.675). ***Conclusion:*** An association has been observed between high SII and low MUAC, as well as between SII and MUST score ≥ 1, among patients diagnosed with NSCLC at Prof. Dr. I.G.N.G. Ngoerah Hospital.

Keywords: inflammation index; nutrition; non-small cell lung cancer

INTRODUCTION

Lung cancer is a disease that is responsible for a significant number of fatalities among both men and women on a global scale. The global prevalence of lung cancer in 2020 was 11.4%, making it the second most common form of cancer, following breast cancer. The mortality rate attributed to lung cancer was 18.0%. Lung cancer accounts for 15.9% of all cancer cases in Indonesia, making it the second most common cause of cancer-related fatalities, following breast cancer. In 82% of lung cancer cases, the occurrence of non-small cell lung cancer (NSCLC) was observed, whereas small cell lung cancer (SCLC) was detected in 14% of lung cancer cases.[1]

Inflammation contributes to malnutrition by inducing anorexia through reduced food consumption and heightened tissue breakdown, resulting in diminished muscle and fat mass.[2] The prevalence of malnutrition in individuals with lung cancer was found to be 26.0%, placing it as the third highest incidence among cancer types, following gastrointestinal and head and neck cancer.[3] The prognostic parameters associated with overall survival, quality of life, and therapeutic responsiveness include both malnutrition risk and nutritional status.[4,5] Moreover, the Malnutrition Universal Screening Tool (MUST) is a commonly employed instrument for evaluating the risk of malnutrition in the United Kingdom.[6]

The Systemic Inflammation Index (SII) is a recently developed index that is utilized for the evaluation of inflammation and immune response. It accomplishes this by quantifying the neutrophil-lymphocyte ratio (NLR) and thrombocyte count.

NLR is commonly employed as a prognostic biomarker in NSCLC, and thrombocytes play a significant role in cancer spreading. Therefore, the integration of NLR and thrombocyte in SII has the capacity to forecast tumor progression and overall prognosis in individuals diagnosed with cancer.[7,8]

Body mass index (BMI) measures are commonly employed to assess malnutrition in patients when measuring their nutritional status. Nevertheless, some circumstances, such as impaired mobility, may restrict the direct assessment of weight and height. Consequently, in 37.6% of instances, it becomes imperative to approximate the BMI. Under these circumstances, it is necessary to do an additional assessment that is both convenient and practical, such as measuring the mid-upper arm circumference (MUAC).[9]

Given the elevated occurrence of malnutrition in cancer patients and the impact of inflammation on malnutrition, researchers aim to investigate the correlation between inflammation and nutritional status, as well as the risk of malnutrition in patients with NSCLC. Hence, the present study aims to evaluate the correlation between SII and MUAC and MUST scores in individuals diagnosed with NSCLC.

METHODS

The study employed an analytical observational approach, utilizing a cross-sectional design, to examine NSCLC patients residing at Prof. Dr. I Goesti Ngoerah Gde Ngoerah Hospital in Denpasar, Bali. The investigation spanned a duration of three months, from August to October 2023. Criteria for inclusion: 1) Individuals who are at least 18 years of age; 2) Attended the pulmonary clinic at Prof. Dr. I Goesti Ngoerah Gde Ngoerah Hospital; 3) Diagnosed with NSCLC. Criteria for exclusion: 1) Edema or dermatological conditions resulting in swelling of both upper arms; 2) Presently undergoing statin and nonsteroidal anti-inflammatory drug (NSAID) treatment; 3) Diagnosed with primary malignancy other than NSCLC; 4) Diagnosed with other chronic ailments such as diabetes mellitus, kidney failure, or liver disease; 5) Immunocompromised state due to HIV infection; 6) Impairment of mobility causing difficulty in measuring body weight and height; 7) Lack of willingness to engage in the study.

The estimation of SII levels is derived from the computation of full blood count data that are collected within a one-week timeframe before or following the subject examination and divided into low (< 1,270) and high (≥ 1,270). The MUAC and MUST scores were obtained simultaneously while the subjects came to the outpatient clinic. The MUAC is categorized as falling between the normal range (< 24 cm) and low range (≥ 24 cm), while the MUST score is classified as low risk (score 0) and medium-high risk (score ≥ 1) of malnutrition. The data analysis in this study utilizes the International Business Machines Statistical Package for Social Sciences (SPSS), version 27.0 (IBM SPSS Corp., Armonk, NY, USA) to examine the features, ascertain proportions, and explore the association between SII and MUAC and MUST scores in patients diagnosed with NSCLC using bivariate analysis and logistic regression. Inferences are made according to a 95% confidence interval with a p-value < 0.05. Research protocol and consent forms were approved by the Research Ethics Committee Faculty of Medicine Universitas Udayana. Informed consent was obtained from all participants.

RESULT

A total of 63 samples, meeting the specified inclusion and exclusion criteria, were collected over a period of 3 months. Most subjects in this study are adults 18-65 years old (73%), males (57.1%), currently unemployed (73%), have completed education below the high school level (54%), have previously undergone therapy for NSCLC (71.4%), and have been hospitalized for NSCLC in the past (66.7%). The prevalence of SII in patients is predominantly low, with a median of 1,076.83. The median MUAC readings are 24.5, and most of them are within the normal range, accounting for 61.9%. Most individuals had a median score of 2 for the MUST score, indicating a medium-high risk of malnutrition (66.7%). Table 1, Table 2, Table 3, and Table 4 present the outcomes according to characteristics, SII, MUAC, and MUST scores, respectively.

TABLE 1: Subject characteristics.

Variables	n=63
Age (years), mean ± deviation standard	59,4 ± 10,8
Adult (18 – 65 years), n (%)	46 (73%)
Elderly (> 65 years), n (%)	17 (27%)
Gender	
Male, n (%)	36 (57.1%)
Female, n (%)	27 (42.9%)
Working status	
Not working, n (%)	46 (73%)
Currently working, n (%)	17 (27%)
Last education	
Below high school, n (%)	34 (54%)
High school or above, n (%)	29 (46%)

Variables	n=63
History of therapy	
Yes, n (%)	45 (71.4%)
No, n (%)	18 (28.6%)
History of hospitalization	
Yes, n (%)	42 (66.7%)
No, n (%)	21 (33.3%)

TABLE 2: SII calculations.

Variables	n=63
Absolute neutrophil (x 10^3 cells/µl), median (min – max)	5.49 (0.56 – 18.01)
Absolute lymphocyte (x 10^3 cells/µl), median (min – max)	1.56 (0.52 – 3.99)
Absolute thrombocyte (x 10^3 cells/µl), median (min – max)	315 (81 – 786)
SII, median (min – max)	1,076.83 (46.73 – 16,148.73)
High SII, n (%)	26 (41.3%)
Low SII, n (%)	37 (58.7%)

TABLE 3: MUAC measurements.

Variables	n=63
MUAC (cm), median (min – max)	24.5 (15.5 – 30.0)
Low MUAC, n (%)	24 (38.1%)
Normal MUAC, n (%)	39 (61.9%)

TABLE 4: MUST score results.

Variables	n=63
Body mass index, mean ± deviation standard	20.8 ± 3.3
Normal nutritional intake, n (%)	63 (100%)
Weight loss (%), mean ± deviation standard	8,6 ± 8.7
MUST score, median (min – max)	2 (0 – 4)
Low malnutrition risk, n (%)	21 (33.3%)
Medium-high malnutrition risk, n (%)	42 (66.7%)

The analysis of this study revealed a correlation between SII and MUAC. Specifically, 13 participants (50.0%) with a high SII value (≥ 1,270) had a low MUAC (< 24 cm), while 13 subjects (50.0%) with a high SII value had a normal MUAC (≥ 24 cm). Nevertheless, it is worth noting that out of the total sample size of 1,270 participants, 11 individuals (29.7%) exhibited normal SII values but had low MUAC. Additionally, 26 people (70.3%) with normal SII values also had normal MUAC. The obtained odds ratio value was 2.364, with a 95% confidence interval ranging from 0.833 to 6.708. The results of this data analysis indicate that there is no statistically significant association between the SII value and MUAC, as evidenced by a p-value of 0.103. The results of logistic regression analysis indicate that there is a significant association between SII and MUAC in subjects with NSCLC. The adjusted odds ratio for this association is 4.197, with a 95% confidence interval ranging from 1.119 to 15.735. Furthermore, after accounting for confounding variables such as age, gender, employment status, educational status, therapy history, and hospitalization history, the association remains statistically significant with a p-value of 0.033.

Regarding the correlation between SII and MUST score, the results revealed that 84.6% of the participants exhibited high SII values, indicating a medium-high risk of malnutrition. Additionally, 15.4% of the subjects with high SII values had a MUST score of 0, indicating a low risk of malnutrition. Among the subjects, 20 individuals (54.1%) had normal SII values with a MUST score of 1 or above, while 17 individuals (45.9%) had normal SII values with a MUST score of 0. The obtained odds ratio value was 4.675, with a 95% confidence interval ranging from 1.345 to 16.255. The results of this data analysis indicate a statistically significant association between the SII value and the MUST score, as evidenced by a p-value of 0.011. In addition, logistic regression analysis reveals that SII has a substantial impact on the MUST score in patients with NSCLC, as indicated by an adjusted odds ratio of 4.675 (95% CI ranging from 1.345 to 16.255). This association is statistically significant, with a p-value of 0.015.

DISCUSSION

The study reported a median MUAC of 24.5 cm, with a lower limit of 15.5 cm and an upper limit of 30.0 cm.

A study conducted on patients with different types of advanced malignancies, including lung cancer, found that the mean measurement of MUAC was 26.5 ± 3.8 cm, with a median of 26.5 cm. The smallest value recorded was 14, while the maximum value was 39 cm.[10] These findings indicate that lung cancer patients in this investigation, as well as in other studies, exhibit a normal interpretation of MUAC.

In this investigation, it was shown that 41.3% of the participants exhibited SII values exceeding 1,270. Prior studies revealed that 57.2% exhibited a SII exceeding 1,270. A high SII is related to a poorer OS and progression-free survival (PFS) in patients with locally progressed or metastatic chronic kidney disease.[11]

The risk of malnutrition was assessed using the MUST score. The results showed that 66.7% of participants had a moderate-severe degree of malnutrition, while 33.3% had a mild degree. The median MUST score was 2, with a minimum value of 0 and a maximum value of 4. In a separate study with 643 participants, it was shown that 29.4% of the subjects had a mild level of malnutrition risk, 53.0% had a moderate level, and 17.6% had a severe one. The study elucidated that there exists a strong correlation between an elevation in the MUST score and a deterioration in OS among individuals diagnosed with advanced lung cancer.[12]

The study found a strong correlation between SII and MUAC in patients with NSCLC. Previous research has not investigated the potential correlation between systemic inflammatory markers, specifically SII, and a specific anthropometric measurement, MUAC.

Prior studies have conducted a comparative analysis of MUAC and inflammatory markers, including C-reactive protein (CRP), NLR, and CRP/Albumin Ratio, in relation to the survival outcomes of outpatient patients with advanced cancer at both 12-week and 24-week intervals. The findings elucidated that MUAC has comparable efficacy, along with the benefits of ease of implementation and non-invasiveness. In summary, the inclusion of MUAC as a predictive tool should be seen as a viable alternative.[10]

A separate study conducted on hemodialysis patients found that both MUAC and hs-CRP, which are markers of inflammation, were significant predictors of mortality from any cause. Nevertheless, the research conducted in the study could not provide an explanation for the association between MUAC and hs-CRP. Furthermore, it was noted that an alternative measurement, specifically mid-upper arm muscle circumference, had a stronger predictive capability for mortality compared to MUAC.[13]

A separate study has shown that a low MUAC resulted in a prolonged hospital stay of at least 7 days and had an impact on the duration of hospital readmission. The precise explanation of the association between anthropometry and the impact of duration of hospitalization and duration of discharge remains uncertain. The potential confounding variable of nutrition and medical treatments during therapy was not documented.[14]

The findings of this study indicate a significant correlation between rising SII and higher MUST scores, as evidenced by an odds ratio of 4.675 (95% CI, 1.345 - 16.255) and a p-value of 0.011. No prior research has been identified that establishes a direct correlation between SII and MUST scores. However, an alternative study demonstrated a noteworthy correlation between the MUST score and several systemic inflammatory responses, including the modified Glasgow Prognostic Score (mGPS), which includes components such as CRP and albumin. Therefore, the findings of the multivariate analysis revealed that there exists an independent association between the MUST score, NLR, and OS.[15]

The study found no correlation between the history of NSCLC treatment and the MUST score. The prognosis nutritional index (PNI) differs from the retrospective study that evaluated malnutrition by measuring albumin and lymphocyte counts. The research conducted revealed that there was no statistically significant correlation between the pre-chemotherapy PNI value in patients with advanced NSCLC and the outcomes of progressing disease (PD), partial response (PR), and stable disease (SD) following four cycles of chemotherapy. Nevertheless, there was a notable disparity in the PNI value between the PD with PR and SD with PR groups following 4 cycles of platinum-doublet treatment. The PR group exhibited greater PNI values in comparison to the SD and PD groups. In addition, it was observed that increased PNI levels were associated with decreased PFS and OS.[16]

Aside from predicting disease response, PFS, and OS, there are further cohort studies that demonstrate that an elevated MUST score leads to an extension of inpatient days and is strongly linked to mortality.[17]

This study in Bali is the first to investigate the correlation between SII and MUAC and MUST scores in patients with NSCLC. This preliminary investigation aims to enhance understanding of the nutritional status and malnutrition risk among patients with NSCLC. The determination of nutritional status and the assessment of malnutrition risk can be effectively achieved through the measurement of MUAC and the calculation of the MUST score. These methods can be utilized in routine examinations. Furthermore, additional investigation can be undertaken to compute prognosis by considering nutritional status and the likelihood of malnutrition.

A potential limitation of this study is the presence of instrument bias in the measurement tools employed during the review of the medical record, as well as variations in data collection methods. Nevertheless, the instruments employed in the inspection undergo frequent calibration.

CONCLUSION

There are association between high systemic immune-inflammation index and less upper arm circumference and also association between high systemic immune-inflammation index and malnutrition universal screening tool score ≥ 1 in non-small cell lung cancer patients at Prof. Dr. I.G.N.G. Ngoerah Hospital.

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DECLARATIONS

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