

## Examining the Relationship between Quality of Life and Baseline Hemoglobin Level in Lung Cancer with Chemotherapy Treatment Using EORTC QLQ-LC13

Adelin Kole<sup>1</sup>, Suryanti Dwi Pratiwi\*<sup>1</sup>, Ngakan Putu Parsama Putra<sup>1</sup>, Ungky Agus Setyawan<sup>1</sup>, Deden Permana<sup>2</sup>

<sup>1</sup>Department of Pulmonology and Respiratory Medicine, Faculty of Medicine, Universitas Brawijaya, dr. Saiful Anwar Hospital, Malang, East Java, Indonesia

<sup>2</sup>Department of Pulmonology and Respiratory Medicine, Faculty of Medicine, Universitas Brawijaya, Karsa Husada General Hospital, Batu, East Java, Indonesia

### ABSTRACT

**Background:** The effect of lung cancer and its various treatments on the overall well-being can be substantial. This study seeks to examine the correlation between quality of life and baseline hemoglobin (Hb) levels in lung cancer patients who are receiving chemotherapy.

**Method:** This study involved 30 patients with non-small cell lung cancer (NSCLC) who underwent platinum-based chemotherapy. Baseline Hb level were collected from medical records. The patients' quality of life was assessed using interviews utilizing the EORTC QLQ-LC13 questionnaire.

**Result:** Baseline Hb levels and pain relief after medication score was positively correlated ( $r=0.559$ ,  $p=0.001$ ). Baseline Hb levels and difficulty swallowing score was negatively correlated ( $r=-0.386$ ,  $p=0.035$ ). Determined cut-off point for the total score was 303.5. However, the correlation between Hb levels and overall quality of life was insignificant ( $r=-0.096$ ,  $p=0.615$ ).

**Conclusion:** According to the quality of life indicators in the questionnaire, there is a notable association between lower baseline Hb levels and reduced effectiveness of pain relief medication, as well as an increase in difficulty swallowing. However, the underlying cause for this correlation is unclear. On the other hand, the correlation between baseline Hb levels and the overall scores of quality of life in the questionnaire was not found to be significant.

**KEYWORDS:** baseline haemoglobin, anemia, quality of life, EORTC QLQ LC 13

### ARTICLE DETAILS

**Published On:**  
01 May 2024

**Available on:**  
<https://ijmscr.org/>

### I. INTRODUCTION

Lung cancer is a multifaceted illness influenced by various internal and external factors. The overall well-being and social ability of individuals with lung cancer can be significantly impacted by the disease itself and its treatment. Anemia, among other concurrent conditions, is substantially impacting the quality of life experienced by individuals with lung cancer.<sup>1,2,3,4</sup>

Anemia is a prevalent occurrence among cancer patients, particularly those undergoing chemotherapy, due to its myelosuppressive effects. The causes of anemia are often multifactorial and can be attributed to chronic inflammatory conditions, malignant invasion of the bone marrow,

treatment side effects, or nutritional deficiencies. The onset rapidly, the extent of anemia, and other concurrent conditions resulted in the symptoms severity. The impact of anemia can vary across different organs, influenced by factors such as its severity, duration, and the medications used in cancer treatment. Patients with anemia may exhibit symptoms like shortness of breath, palpitations, and fatigue, ultimately leading to a decline in their quality of life.<sup>5,6,7</sup>

The management of cancer involves a multidisciplinary approach, with various medical specialties involved in diagnosis and the use of multimodal treatment strategies. Comprehensive patient care encompasses a wide range of factors, including addressing organ dysfunctions caused

# Examining the Relationship between Quality of Life and Baseline Hemoglobin Level in Lung Cancer with Chemotherapy Treatment Using EORTC QLQ-LC13

directly or indirectly by cancer. Most lung cancer patients are diagnosed in advanced stages, limiting curative treatment options. As a result, systemic palliative treatment has minimal impact on overall survival.<sup>8</sup> Therefore, the primary objective of treatment becomes maintaining or improving the quality of life for patients. Recent studies have placed increasing emphasis on examining the quality of life in cancer patients. This research evaluated the association between quality of life and Hb levels in lung cancer patients undergoing platinum-based chemotherapy.

## II. METHOD

A cross-sectional study was conducted from January 2023 to February 2023 at Saiful Anwar General Hospital. The study involved patients with lung cancer who were receiving platinum-based chemotherapy. The study received approval from the Ethics Committee of Saiful Anwar General Hospital under the reference number 400/285/K.3/102.7/2022. Hemoglobin levels were analyzed using venous blood samples. The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Lung Cancer 13 (EORTC QLQ-LC13) was used to evaluate the quality of life.

To be eligible for inclusion in the study, a definite assessment of a non-small-cell lung cancer should be done on the patient, and the patient have undergone one round of platinum-based chemotherapy. Hb data prior to chemotherapy were collected from the patients' medical records. Patients with severe illness, specific blood-related disorders, nephropathy, or those with secondary lung cancer were excluded from the study.

Categorical data were presented as frequency (%). Numerical data were presented as mean  $\pm$  SD. The Kolmogorov-Smirnov (KS) test was used to assess the distribution of the data. The significance between baseline Hb categories and quality of life was evaluated using the T-test., the optimal cut-off point for the total scores of the EORTC QLQ-LC13 questionnaire was determined using a combination of cluster analysis, followed by ROC analysis.

## III. RESULTS

30 individuals were enrolled in this study, with a mean age of  $58.97 \pm 10.46$  years. Among the participants, 63.3% were male. Approximately 40% of the participants had comorbidities, with hypertension being the most common (26.7%), followed by diabetes (10.0%). The chemotherapy used were cisplatin-paclitaxel (3.3%), cisplatin-etoposide (3.3%), cisplatin-pemetrexed (30.0%), and carboplatin-paclitaxel (63.3%). Table 1 provides further details on the clinical characteristics of the subjects.

**Table I. Clinical Characteristics of The Study Subjects**

Variable	Freq (%) or Mean $\pm$ SD
• Male gender	19 (63.3)
• Age (years)	$58.97 \pm 10.46$
• Smoking history	19 (63.3)
• Smoking history duration (years)	$28.83 \pm 11.56$
• Baseline Hb	$11.90 \pm 2.03$
• Transfusion history	15 (45.5)
<b>Baseline Hb Category</b>	
• Normal	8 (26.7)
• Anemia Grade 1	17 (56.7)
• Anemia Grade 2	5 (16.7)
<b>Comorbidity</b>	
• Hypertension	8 (26.7)
• Diabetes Mellitus	3 (10.0)
• Heart Disease	1 (3.3)
• Hepatitis B	1 (3.3)
• Lung Tuberculosis	1 (3.3)
<b>Karnofsky Score</b>	
• 50 – 60	5 (16.7)
• 70 – 80	25 (83.3)
<b>Combination of Chemotherapy Regimen</b>	<b>Freq (%)</b>
• Carboplatin-paclitaxel	19 (63.3)
• Cisplatin-pemetrexed	9 (30.0)
• Cisplatin-etoposide	1 (3.3)
• Cisplatin-paclitaxel	1 (3.3)
<b>Chemotherapy Series</b>	<b>Freq (%)</b>
• Series 1	4 (13.3)
• Series 2	7 (23.3)
• Series 3	5 (16.7)
• Series 4	4 (13.3)
• Series 5	4 (13.3)
• Series 6	6 (20.0)

The average baseline Hb level was 11.90 g/dL. In terms of the EORTC QLQ LC-13 questionnaires, the mean scores were as follows: LCCO (31.97), LCHA (2.2), LCD (30.67), LCSM (3.3), LCDS (2.2), LCPN (15.4), LCHR (46.43), LCPC (28.63), LCPA (18.70), LCPO (18.70), and the pain-relief-after-medication score (82.39). Between demographic variables and the total scores of the EORTC QLQ LC-13 questionnaire, no correlation or difference were found.

**Table II. Baseline Hb and Quality of Life of Study Subjects**

Baseline Hb (Anemia Grade)	EORTC QLQ LC-13 Score (Mean $\pm$ SD)	P
Normal	$236.75 \pm 150.56$	0.836
Grade 1	$268.18 \pm 87.22$	
Grade 2	$277.60 \pm 244.50$	

## Examining the Relationship between Quality of Life and Baseline Hemoglobin Level in Lung Cancer with Chemotherapy Treatment Using EORTC QLQ-LC13

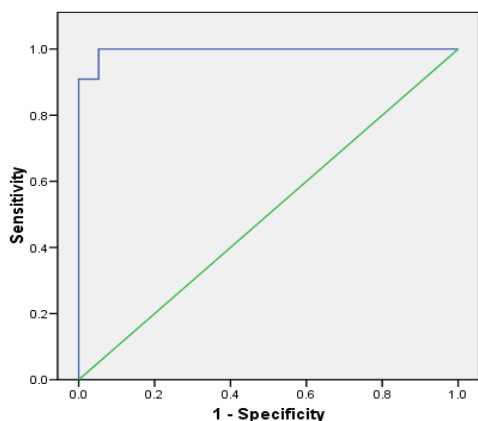
The relationship between the EORTC QLQ LC-13 questionnaire score and the baseline Hb anemia grade was examined. It was observed that as the anemia grade became more severe, there was a gradual increase in the EORTC QLQ LC-13 questionnaire score. The results of the ANOVA test indicated that there was no significant difference between the baseline Hb groups regarding the questionnaire scores ( $p = 0.836$ ).

**Table III. Correlation between Baseline Hb and EORTC QLQ LC-13**

Variable Correlated with Hb Values	R	p
• LCCO	-0.290	0.120
• LCHA	-0.086	0.652
• LCDY	-0.003	0.987
• LCSM	-0.276	0.139
• LCDS	-0.386	<b>0.035*</b>
• LCPN	-0.005	0.978
• LCHR	0.202	0.284
• LCPC	0.007	0.969
• LCPA	-0.109	0.566
• LCPO	0.117	0.539
• Pain relief after medication	0.559	<b>0.001*</b>
• Total EORTC QLQ LC-13 Scores	-0.096	0.615

Note: R: Correlation coefficient; p: significance ( $p < 0.05$ ); LCCO: coughing; LCHA: haemoptysis; LCDY: dyspnea; LCSM: sore mouth; LCDS: dysphagia; LCPN: peripheral neuropathy; LCHR: alopecia; LCPC: pain in chest; LCPA: pain in arm or shoulder; LCPO: pain in other parts; \*) With a  $p < 0.05$ , there is a significant difference.

To assess the relationship between different questionnaire questions and baseline Hb, Pearson correlation tests were performed. The results indicated that there was no significant correlation between the total score of the questionnaire and baseline Hb ( $p = 0.615$ ). However, Hb and LCDS was negatively correlated ( $r = -0.386$ ,  $p = 0.035$ ). Additionally, Hb and the pain-relief-after-medication was positively correlated ( $r = 0.559$ ,  $p = 0.001$ ).



**Figure 1. ROC Curve of The Total EORTC QLQ LC-13 Scores**

ROC analysis was done to decide the cut off point for the total EORTC QLQ LC-13 scores. After cluster analysis, the following ROC analysis showed a significantly strong area under the curve (AUC 0.995;  $p < 0.05$ ). The most optimal cut off point was 303.5 (sensitivity 0.909; specificity 0.947). A tabular analysis was done by quality of life (classified using the cut-off point) and degree of anemia. There was no significant quality of life differences in classifications between subjects within normal baseline Hb, grade 1 anemia, or grade 2 anemia ( $p < 0.05$ ).

**Table IV. Baseline Hb and Quality of Life of Study Subjects**

Baseline Hb (Anemia Grade)	EORTC QLQ LC-13 Score (Mean $\pm$ SD)		p
	>303.5	<303.5	
Normal	2	6	1.000
Grade 1	7	10	0.661
Grade 2	2	3	1.000

## IV. DISCUSSION

This study found no significant correlation between the total score of the EORTC QLQ LC13 questionnaire and Hb levels. However, specific points within the questionnaire were found to be related to Hb. Hb and dysphagia was negatively correlated, indicating that higher Hb levels are associated with decrease of dysphagia-like symptoms. Previous study showed that anemia can be linked to iron deficiency, which can significantly affect iron-dependent oxidative enzymes. An activity decrease of these enzymes can lead to degraded pharyngeal structures, resulting in dysphagia.<sup>10</sup>

The pain-relief-after-medication and Hb was positively correlated. This suggests that higher levels of Hb are associated with increased effectiveness of pain-relief drugs. However, there is currently a lack of previous studies specifically examining the relationship between drug efficacy and anemia in cancer. For instance, a study conducted by Joshi et al. found no significant phenytoin bioavailability differences between individuals with anemia and those without.<sup>11</sup> Further research is needed to investigate the connection between anemia and the efficacy mechanisms of different drugs, particularly pain relief medications.

Compared to other forms of cancer, individuals with lung cancer face unique and significant challenges. Symptoms related to both the treatment and the disease itself, including pain, difficulty breathing, fatigue, and loss of appetite, are common and have a detrimental impact on patients' functional abilities, ultimately reducing their quality of life. Furthermore, patients diagnosed with lung cancer often experience heightened levels of anxiety and depression and have an increased risk of suicide compared to individuals with other types of cancer. This can be

## Examining the Relationship between Quality of Life and Baseline Hemoglobin Level in Lung Cancer with Chemotherapy Treatment Using EORTC QLQ-LC13

attributed in part to the poor side effects of therapy and prognosis.<sup>12</sup>

Quality of life refers to an individual's subjective satisfaction with their overall well-being and lifestyle. It encompasses various aspects, including physical health, relationships with family and friends, emotional well-being, and functional abilities. In the context of cancer patients, the assessment of quality of life is commonly done using standardized questionnaires that provide quantitative measurements. These assessments are typically completed by the patients themselves or sometimes by their proxies. The evaluation of quality of life can play a significant role in informing clinical decision-making by providing insights into the effectiveness of treatments. This is particularly relevant in advanced-stage cancer cases, where patient-reported outcome assessments like quality of life can be utilized to assess treatment efficacy or be included as part of composite endpoints to demonstrate the clinical benefits of interventions.<sup>3</sup>

The quality of life of patients was evaluated using the EORTC QLQ LC 13 questionnaire in this study. This questionnaire includes a combination of multiple questionnaire items to assess various symptoms such as dyspnea, as well as individual items to measure cough, alopecia, dysphagia, hemoptysis, sore mouth, pain, and peripheral neuropathy. Each scale and individual item is scored on a scale from 0 to 100. Higher scores on the scales and individual items indicate a greater presence of symptoms or problems experienced by the patients.<sup>13</sup>

Anemia is a common complication in cancer. Cancer-related anemia specifically refers to a condition that occurs in the absence of hemolysis, bleeding, bone marrow infiltration by cancer cells, or kidney and liver failure. It primarily arises due to chronic inflammation in relation to the cancer itself and the production of cytokines. The key mechanisms through which inflammation can lead to anemia include the faster metabolism of erythrocytes, suppressed erythrocyte production by the bone marrow, the inflammatory impact on erythropoietin production, and the restriction of iron availability caused by elevated levels of hepcidin.<sup>14</sup>

Higher rates of cancer recurrence and reduced survival following radiation therapy were linked to anemia. This may be due to a more aggressive or extensive tumor burden rather than the direct effects of anemia. However, there is some evidence suggesting that tumor cell hypoxia, which can be worsened by anemia, can negatively impact the effectiveness of radiation treatment. Nonetheless, there is currently no strong evidence indicating a direct association between anemia and tumor radiosensitivity. Radiation therapy can cause a long-lasting damage to the bone marrow, affecting the production of red blood cells, particularly when the radiation field encompasses a significant portion of the bone marrow. Chemoradiotherapy

agents can also have unintended effects that disrupt the production of red blood cells. Additionally, immunotherapy can lead to autoimmune hemolytic anemia.<sup>15</sup>

Anemia in lung cancer patients can have detrimental effects on both their overall well-being and treatment options. For instance, cancer therapy typically require patients to have an Hb level above 10 g/dL.<sup>16,17</sup> The most common form of anemia associated with cancer is normochromic normocytic anemia. Cancer-related anemia is typically characterized by low reticulocyte counts and low reticulocyte index values, indicating a hypoproliferative type of anemia. The prevalence of cancer-related anemia varies across different types of cancer, with lung cancer having the highest reported percentage. In lung cancer, approximately 37.6% of patients experience anemia, and this incidence increases to around 80% after undergoing chemotherapy treatment.<sup>14</sup>

Decreased Hb levels can have a significant impact on bodily functions and overall quality of life due to disruptions in oxygen transport. When oxygen transport from the lungs to the rest of the body is impaired, it can result in metabolic dysfunction, affecting the production of adenosine triphosphate (ATP), which is essential for energy production. This can manifest in symptoms like fatigue, ultimately reducing the individual's quality of life. Additionally, impaired energy production can have negative consequences on various bodily functions, including immunity, which can ultimately impact life expectancy and overall well-being.<sup>19</sup>

In chemotherapy patients, there is often a noticeable decline in Hb levels in line with the progression of chemotherapy. This can be attributed to both the advancement of the cancer and the effects of chemotherapy itself. Cancer progression can contribute to the worsening of anemia through factors such as malignancy-related bleeding and inadequate nutrition.<sup>6</sup> In the case of lung cancer, an additional factor such as hemoptysis can lead to anemia, which is observed in up to 35% of cases.<sup>20</sup> Furthermore, the myelosuppressive effects of the therapy can reduce Hb levels, potentially impacting the overall wellbeing.<sup>21</sup>

Previous research has different findings compared to our study. In a study conducted by Barca-Hernando et al. utilizing the EORTC QLQ-C30 questionnaire, the study found that anemia negatively impacts the overall well-being and was associated with a higher number of symptoms.<sup>9</sup> The difference in findings could be related to the variation in the assessment tools. While the previous study utilized the EORTC QLQ-C30, which is a comprehensive questionnaire covering broader aspects of overall wellbeing, our study employed the EORTC QLQ LC13, a more specific questionnaire.<sup>13</sup> Although more user-friendly for the participants, the use of this questionnaire may restrict our study to comprehensively assess the entirety of the study subjects' quality of life.



## Examining the Relationship between Quality of Life and Baseline Hemoglobin Level in Lung Cancer with Chemotherapy Treatment Using EORTC QLQ-LC13

A previous study yielded contrasting results when compared to our study. In the study by Palasamudram et al., they also found that anemia was associated with diminished well-being, which was assessed using the EORTC-QLQ-30 questionnaire.<sup>22</sup> Buckstein et al. reported similar findings. Both of these studies had a higher prevalence of severe anemia compared to our study. Previous study determined that an optimal Hb cut-off for distinguishing subjects' quality of life was 10 g/dL.<sup>23</sup> In our study, grade II anemia was defined as an Hb level below 10 g/dL, which accounted for only 16.7% of the subjects. Additionally, our study had a smaller sample size compared to the aforementioned studies, ranging from 204 to 689 participants.

There is evidence to suggest that higher Hb levels in cancer patients are associated with improved quality of life and better prognosis, particularly in cases of lung cancer. Over the past two decades, the association between cancer-related anemia and the prognosis of lung cancer has been studied. A study by Liu et al., which analyzed 23 studies, revealed that patients with preoperative anemia were found to have a 1.6 times higher risk of death compared to those without anemia.<sup>24</sup> Another study by Zhang et al. reported that patients with normal hemoglobin levels before treatment had a higher chance of longer survival compared to patients with low pre-treatment hemoglobin levels.<sup>25</sup> Similar findings were also observed in a study by Chen et al., which studied stage IV NSCLC patients. In this study, 32% of the patients were diagnosed with anemia, with 19% classified as mild anemia. Older age, smoking history, and bone metastasis were correlated with a higher prevalence of baseline anemia. The overall survival of patients without anemia was significantly higher compared to those with anemia. Furthermore, the severity of anemia was inversely associated with overall survival, with mild anemia being linked to the longest survival duration compared to more severe anemia.<sup>26</sup>

No significant association was observed between demographic variables and the overall EORTC QLQ LC-13 score in this study. Among the 30 subjects, 12 had various comorbidities. Comorbidity has been shown to impact both the overall well-being and life expectancy of lung cancer in previous research. It has also been linked to treatment effectiveness in lung cancer. Furthermore, risk factors of lung cancer such as age, smoking, and comorbidity is known to be related.<sup>27</sup> However, in this study, neither of those were significantly related to the overall EORTC QLQ LC-13 score. This suggests that the patients' overall well-being was not directly impacted by these factors.

### V. CONCLUSIONS

The majority of lung cancer patients in this study experienced anemia prior to chemotherapy. Then, chemotherapy further exacerbated the severity of anemia. Previous research has demonstrated a connection between

anemia and the overall well-being in cancer patients. Although no correlation of Hb levels and the overall well-being was found in this study, we observed that baseline Hb levels were associated with specific quality of life issues, such as dysphagia and the effectiveness of pain medication. This suggests that the utilization of shorter and more specific questionnaires may not comprehensively assess the overall well-being, and consequently the relationship between anemia and overall quality of life. As a result, the use of more comprehensive, general quality of life questionnaires to assess the overall well-being in lung cancer patients is recommended.

### ACKNOWLEDGMENT

The authors are grateful to Faculty of Medicine, Universitas Brawijaya and dr. Saiful Anwar Hospital for the assistance.

### REFERENCES

- I. de Groot PM, Wu CC, Carter BW, Munden RF. The epidemiology of lung cancer. *Translational Lung Cancer Research*. 2018 Jun;7(3):220–33.
- II. Barta JA, Powell CA, Wisnivesky JP. Global Epidemiology of Lung Cancer. *Annals of Global Health*. 2019;85(1):8.
- III. Prapa P, Papathanasiou IV, Bakalis V, Malli F, Papagiannis D, Fradelos EC. Quality of Life and Psychological Distress of Lung Cancer Patients Undergoing Chemotherapy. *World J Oncol*. 2021 May 14;12(2–3):61–6.
- IV. Pizzoli SFM, Renzi C, Arnaboldi P, Russell-Edu W, Pravettoni G. From life-threatening to chronic disease: Is this the case of cancers? A systematic review. *Monacis L*, editor. *Cogent Psychology*. 2019 Jan 1;6(1):1577593.
- V. Gluszk C, de Vries-Brilland M, Seegers V, Baroin C, Kieffer H, Delva R, et al. Impact of Iron-Deficiency Management on Quality of Life in Patients with Cancer: A Prospective Cohort Study (CAMARA Study). *The Oncologist*. 2022 Apr 5;27(4):328–33.
- VI. Abdel-Razek H, Hashem H. Recent update in the pathogenesis and treatment of chemotherapy and cancer induced anemia. *Critical Reviews in Oncology/Hematology*. 2020 Jan 1;145:102837.
- VII. Nooreldeen R, Bach H. Current and Future Development in Lung Cancer Diagnosis. *Int J Mol Sci*. 2021 Aug 12;22(16):8661.
- VIII. Balboni TA, Hui KKP, Kamal AH. Supportive Care in Lung Cancer: Improving Value in the Era of Modern Therapies. *American Society of Clinical Oncology Educational Book*. 2018 May 23;(38):716–25.

## Examining the Relationship between Quality of Life and Baseline Hemoglobin Level in Lung Cancer with Chemotherapy Treatment Using EORTC QLQ-LC13

- IX. Barca-Hernando M, Muñoz-Martin AJ, Rios-Herranz E, Garcia-Escobar I, Beato C, Font C, et al. Case-control analysis of the impact of anemia on quality of life in patients with cancer: A Qca study analysis. *Cancers*. 2021 Jun 1;13(11):2517.
- X. Goel A, Bakshi SS, Soni N, Chhavi N. Iron deficiency anemia and Plummer–Vinson syndrome: current insights. *J Blood Med*. 2017 Oct 19;8:175–84.
- XI. Joshi MV, Pohujani SM, Mehta BC, Acharya VN, Kshirsasgar NA. Effect of iron deficiency anaemia and its treatment on single dose phenytoin bioavailability. *Eur J Clin Pharmacol* [Internet]. 1993 Nov [cited 2023 May 19];45(4). Available from: <http://link.springer.com/10.1007/BF00265961>
- XII. Cochrane A, Woods S, Dunne S, Gallagher P. Unmet supportive care needs associated with quality of life for people with lung cancer: A systematic review of the evidence 2007–2020. *European Journal of Cancer Care*. 2022 Jan 1;31(1):e13525.
- XIII. Coon CD, Schlichting M, Zhang X. Interpreting Within-Patient Changes on the EORTC QLQ-C30 and EORTC QLQ-LC13. *Patient*. 2022 Nov 1;15(6):691–702.
- XIV. Madeddu C, Gramignano G, Astara G, Demontis R, Sanna E, Atzeni V, et al. Pathogenesis and Treatment Options of Cancer Related Anemia: Perspective for a Targeted Mechanism-Based Approach. *Frontiers in Physiology* [Internet]. 2018 [cited 2023 Mar 8];9. Available from: <https://www.frontiersin.org/articles/10.3389/fphys.2018.01294>
- XV. Anand S, Burkenroad A, Glaspy J. Workup of anemia in cancer. *Clinical Advances in Hematology & Oncology*. 2020 Oct;18(10):640–6.
- XVI. Macciò A, Gramignano G, Madeddu C. A Multitargeted Treatment Approach for Anemia and Cachexia in Metastatic Castration-Resistant Prostate Cancer. *Journal of Pain and Symptom Management*. 2015 Aug;50(2):e1–4.
- XVII. Ganti AK, Klein AB, Cotarla I, Seal B, Chou E. Update of Incidence, Prevalence, Survival, and Baseline Treatment in Patients With Non–Small Cell Lung Cancer in the US. *JAMA Oncol*. 2021 Dec;7(12):1–9.
- XVIII. Menga M, Sjattar E, Irwan A. ANALYSIS OF FACTORS AFFECTING FATIGUE IN CANCER PATIENTS WITH CHEMOTHERAPY : LITERATURE REVIEW. *Jurnal Ilmiah Perawat Manado*. 2020;
- XIX. Busti F, Marchi G, Ugolini S, Castagna A, Girelli D. Anemia and Iron Deficiency in Cancer Patients: Role of Iron Replacement Therapy. *Pharmaceuticals (Basel)*. 2018 Sep 30;11(4):94.
- XX. Beckles MA, Spiro SG, Colice GL, Rudd RM. Baseline evaluation of the patient with lung cancer: symptoms, signs, laboratory tests, and paraneoplastic syndromes. *Chest*. 2003 Jan;123(1 Suppl):97S-104S.
- XXI. Yuliandra Y, Nasif H, Ermayanti S, Sulistyowati L, Juwita DA. Hematologic Toxicities of Chemotherapy in Lung Cancer Patients: A Retrospective Study in Dr. M. Djamil Hospital Padang, Indonesia. *Indonesian Journal of Clinical Pharmacy*. 2019 Jun 28;8(2):129–40.
- XXII. Palasamudram K, Kaiser J. Study on the impact of anemia on the Quality of Life (QoL) of cancer patients. *Eur J Oncol*. 2014 Feb 26;43–51.
- XXIII. Buckstein R, Wells RA, Zhu NY, Geddes M, Sabloff M, Leber B, et al. Quality of Life Scores Improve with Increasing Hemoglobin but Optimal Thresholds Vary According to Transfusion Dependence and Clinical Risk Scores: A Canadian Cross Sectional Study of 689 Patients with 2969 Measurements. *Blood*. 2016 Dec 2;128(22):3192.
- XXIV. Liu Y, Bai YP, Zhou ZF, Jiang CR, Xu Z, Fan XX. Preoperative anemia as a prognostic factor in patients with lung cancer: a systematic review and meta-analysis of epidemiological studies. *J Cancer*. 2019;10(9):2047–56.
- XXV. Zhang YH, Lu Y, Lu H, Zhang MW, Zhou YM, Li XL, et al. Pre-treatment hemoglobin levels are an independent prognostic factor in patients with non-small cell lung cancer. *Mol Clin Oncol*. 2018 Jul;9(1):44–9.
- XXVI. Chen C, Song Z, Wang W, Zhou J. Baseline anemia and anemia grade are independent prognostic factors for stage IV non-small cell lung cancer. *Molecular and Clinical Oncology*. 2021 Mar 1;14(3):1–7.
- XXVII. Megasari A, Bagiada M. Ketahanan hidup 1 tahun karsinoma paru di divisi Pulmonologi RSUP Sanglah Denpasar. *Medicina* [Internet]. 2020 Jan 9 [cited 2023 May 11];51(1). Available from: <https://www.medicinaudayana.ejournals.ca/index.php/medicina/article/view/323>