Literature Review

Effect of Chemotherapy on Quality of Life of Lung Cancer Patients: Scoping Review

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Abstract

Background: Lung cancer is a tumor originating from the lung parenchyma or in the bronchi. Lung cancer is the second most frequently diagnosed cancer. The treatment often used is chemotherapy as most lung cancers are diagnosed late. Chemotherapy can provide many benefits but also has side effects because it works by killing healthy replicating cells. Symptoms of cancer that appear as well as side effects of therapy have an impact on the patient's quality of life. Quality of life is a person's perception of his position in life in the context of values and culture. Quality of life can determine a person's general well-being and well-being is the main goal of treatment**.** This study aims to determine the effect of chemotherapy on the quality of life of lung cancer patients.

Method: This Scoping Review was compiled by conducting a literature search on the PubMed, ScienceDirect, SpringerLink databases, and manual searches on Google Scholar with the keywords "Lung Cancer" AND "Chemotherapy" AND "Quality of Life" from 2016 to 2021 publication period. Scoping This review is guided by the PRISMA-ScR checklist.

Results: As much as 30 journals were obtained based on inclusion and exclusion criteria from this process. We found that most of the literature states that chemotherapy has a positive effect in improving the quality of life of lung cancer patients, which are dominated by advanced NSCLC cancer types.

Conclusion: Aspects that can affect the quality of life of lung cancer patients undergoing chemotherapy are the available health facilities, the choice of chemotherapy regimen, the timing of the quality-of-life assessment, and the patient's socio-cultural background.

Keywords: lung cancer, chemotherapy, quality of life (QoL)

INTRODUCTION

Lung cancer or bronchogenic carcinoma is a tumor originating from the lung parenchyma or in the bronchi. The pathophysiology of lung cancer is very complex and not fully understood.[1] Globally, lung cancer is the leading cause

of death with a high prevalence.

Lung cancer is the second most frequently diagnosed cancer with a portion of 11.4% in 2020. However, lung cancer is still the leading cause of cancer death, with an estimated 1.8 million deaths each year.[2] Lung cancer is the most common type of cancer with highest mortality in men and second in women after breast cancer.[3] Lung cancer incidence and mortality also differ by region. In 2020, Asia has the highest incidence rate, 59.6%, and the highest mortality rate with a 61.9% percentage while Oceania has the lowest incidence rate (0.8%) and the lowest mortality rate (0.7%).[4]

In Indonesia, Basic Health Research (Riskesdas) data in 2013 and 2018 showed an increase in cancer prevalence from 1.4% to 1.8%.[5] In 2020 the number of new cancer cases reached 396,914 cases and the number of new lung cancer cases lung numbered 34,783 cases. This makes lung cancer in third place with the most cancer cases.[6] The prevalence of cancer in Aceh Province also increased from 2013 to 2018 from 1.4 to 2.[7,8]

Based on medical records of the Regional General Hospital dr. Zainoel Abidin Banda Aceh, recorded that there were 53 lung cancer patients in 2018 then increased in 2019 to 63 patients.[9] This high incidence requires serious efforts from all relevant parties in selecting and implementing therapy for patients.

There are several alternative therapies for patients, namely surge surgery, rugs including chemotherapy, targeted therapy and immunotherapy, and palliative care. All of them have a role in the treatment of lung cancer patients depending on the stage of cancer.[10]

This treatment plan should be based on the histologic and molecular characteristics of the tumor, disease stage at diagnosis, appearance status, and individual comorbidities.[10] Most lung cancers are diagnosed late because they are inoperable or metastatic. In this case, the treatment of choice is chemotherapy, either alone or in combination with radiotherapy.[11]

Chemotherapy is the application of chemicals or drugs to kill cancer cells and the effects are systemic.[12] Chemotherapy works by stopping or slowing the growth of cancer cells. Chemotherapy can make tumors smaller before surgery or radiation therapy, destroy any cancer cells that may remain after surgery or radiation therapy, help radiation therapy and immunotherapy work better, and can destroy cancer cells that come back (relapse) or spread to other parts of the body (metastasis).[13] Although chemotherapy can provide many benefits, chemotherapy has side effects as it also kills healthy replicating cells.[14] Common side effects include hair loss, nausea, and low blood cell counts.[15]

Cancer symptoms that manifested and the side effects of the therapy have an impact on the patient's quality of life. Quality of life is a person's perception of his position in life in the context of values and culture. It relates to the patient's goals, expectations, standards, and concerns.[16] Quality of life can determine a person's general well-being and well-being is the

one of the main goals of treatment. In addition, the patient's well-being is expected to prolong life expectancy. Therefore, quality of life is now widely used by clinical researchers as an outcome measure to evaluate the effectiveness of treatment so that it can provide the right therapy.[17]

Previous studies are showing the effect of chemotherapy on the quality of life of cancer patients. Studies conducted in patients with squamous NSCLC with four cycles of nab-paclitaxel or carboplatin showed a clinically significant improvement in quality of life and greater benefit compared to those who did not undergo these therapies.[18] However, a study conducted in patients with advanced NSCLC showed a negative effect on the quality of life of patients undergoing chemotherapy compared to the period before the start of therapy.[19]

Because there are still research gaps that explain the effect of chemotherapy on lung cancer quality of life, Therefore, the authors are interested in studying further regarding the effect of chemotherapy on the lives of lung cancer patients, which is then expected to provide a synthesis.

METHODS

The literature search was carried out using four databases of journal publications and articles in the literature search process related to the research topic. The databases used are Pubmed, Sciencedirect, Springerlink, and manual data searches on Google Scholar. The research was conducted in Banda Aceh from September to November 2021. The keywords used were "Lung Cancer" AND "Chemotherapy" AND "Quality of Life". Literature was obtained with a time limit of the last 5 years, namely from 2016 to 2021.

The literature that included is literature published on databases or international article publication sites. The contents of the literature that are relevant to the research objective, namely describing the topic of the effect of chemotherapy on the quality of life of lung cancer patients, literature published within a period of 5 years, from 2016 to 2021. The excluded literature is duplicates, literature in languages other than English, literature which is a literature review, and literature that does not provide full-text access.

The filter used all titles, abstracts, and full text independently. Then the following information was extracted: title, DOI/journal number, year of publication, country of the first author or international organization where the research was conducted, type of literature, and results and conclusions.

The analysis carried out is a descriptive analysis of the characteristics of the included literature. The source describes where found literature, year of publication, type of literature, and literature topics on the effect of chemotherapy on the quality of life of lung cancer patients to examine gaps in the study. The scoping review according to the PRISMA-ScR Checklist was conducted.

RESULTS

The search in the PubMed database uses a literature filtering function using English and the time range for publication is from 2016 to 2021. The selected types of articles are full text, associated data, case reports, clinical studies, journal articles, observational studies, Randomized Control Trials. The number of literatures obtained in the search was 574 pieces of literature. A total of 551 pieces of literature were excluded because they did not meet the inclusion and exclusion criteria so only 23 pieces of literature in the PubMed database search were reviewed at the stage of identifying duplicates and reviewing the overall contents of the literature.

Search on ScienceDirect using the filtering function of the literature publication time range from 2016 to 2021 and the type of literature in the form of research articles and case reports and using the advanced search title, abstract, keywords feature: The number of literature obtained is 137 pieces of literature, 116 of which do not meet the inclusion and exclusion criteria. The number of literatures reviewed at the stage of duplicate identification and review of the contents of the entire literature is a total of 21 pieces literature.

The search on SpringerLink uses a filtering function for the time range of literature publication from 2016 to 2021. The number of articles obtained is 5,151 literatures with article types, not chapters. A total of 5,150 of the entire literature is irrelevant and only 1 suitable literature meets the inclusion and exclusion criteria so that duplicates and the entire contents of the literature will be reviewed.

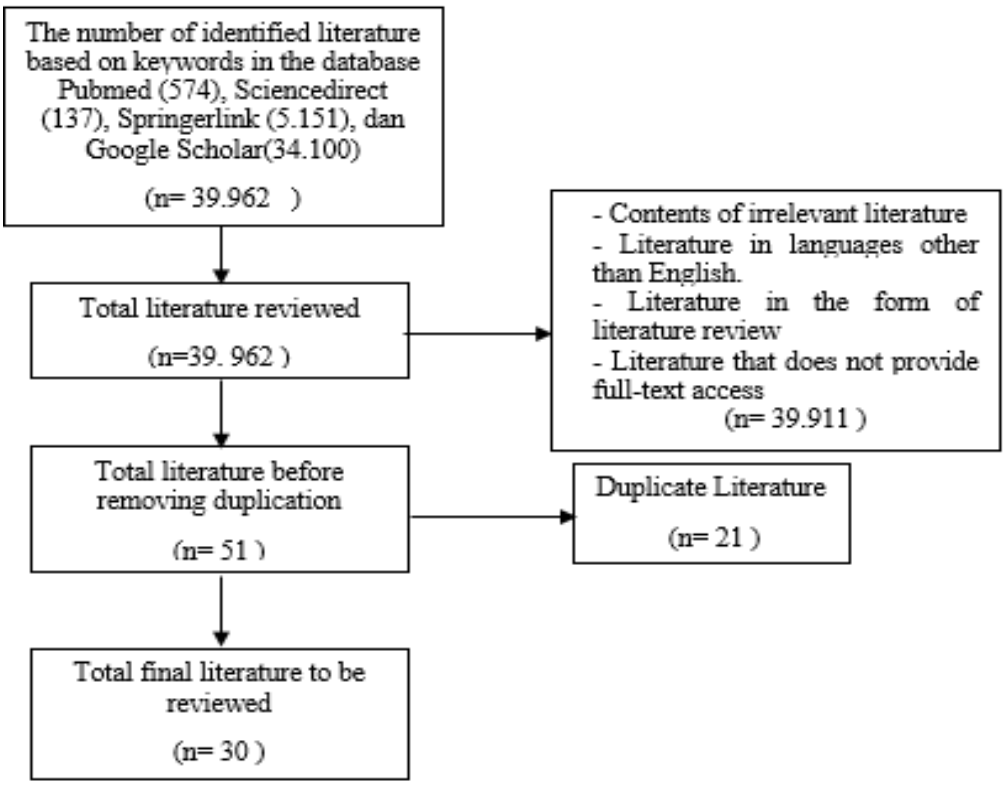

Figure 1. Flowchart of Search Results and Literature Selection

The manual search aims to obtain literature that is relevant to the research topic but unable to found in the PubMed. The number of literatures that meets the inclusion and exclusion criteria is six literature which will then be reviewed for duplicates. Furthermore, as many as 21 pieces of literature were removed as duplications of a total of 51 pieces of literature so that the remaining 30 pieces of literature will be extracted from each literature and reviewed (Figure 1).

Table 1. Characteristics of Literature

Characteristics	N	%
Journal		
Tha Lancet	3	10
European Journal of Cancer	3	10
Thoracic Cancer	3	10
Journal Lung Cancer	3	10
European Society for Medical Oncology (ESMO)	2	7
Other	16	53
First Author's Country		
China	5	17
United States	5	17
German	5	17
France	3	10
Other	12	40

Most of the literature comes from China, the United States, and Germany with a percentage of 17% in each country. Then, the journals with the highest amount of literature were The Lancet, European Journal of Cancer, Journal of Thoracic Cancer, and Lung Cancer Journal with 3 (10%) published literature (Table 1).

Figure 2 shows the cumulative amount of literature every year, starting from 2016 to 2021. During that period, there are publications of literature related to this research topic which fluctuate annually with the highest number of journal publications being in 2017 with 12 pieces of literature.

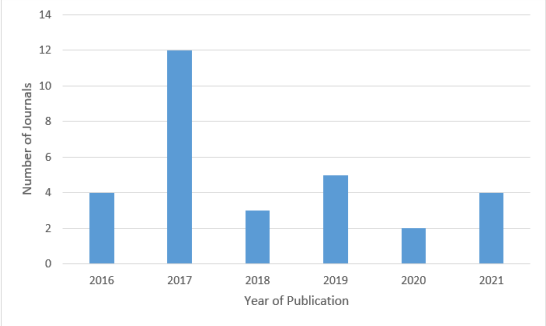

Figure 2. Number of Journals by Year of Publication

The type of literature published annually is shown in Figure 3 where the author finds literature with the type of clinical trial every year although it is fluctuating the author only gets 3 cohort studies published in 2016 and 2017 while in 2018 to 2021 there are no cohort studies.

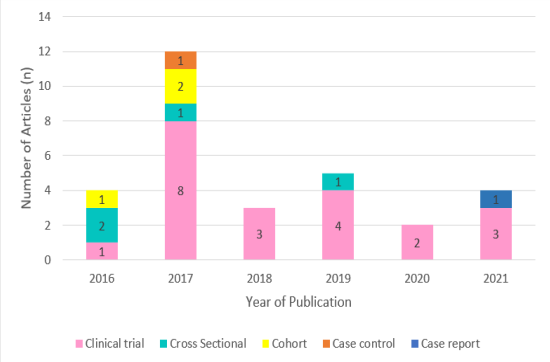

Figure 3. Types of Studies by Year of Publication

DISCUSSION

The study by Dai et al. reported that patients who achieved partial response after undergoing chemotherapy experienced stronger improvements in global quality of life and QOL emotional functional domains than patients who did not achieve a partial response. To assist

advanced NSCLC patients in optimizing their quality of life, healthcare practitioners should improve their ability to identify patients who are at high risk of experiencing poor quality of life during chemotherapy.[20]

The study was reinforced by Daroszewski et al who stated that patients who completed at least three cycles of chemotherapy had a better physical function and a good appetite compared to those who did not complete but global health status did not change in patients with advanced NSCLC.[21]

The results of another study conducted by von Verschuer et al using the The European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire-Cancer 30 (QLQ-C30) and The European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire-Lung Cancer 13 (QLQ-LC13) questionnaires stated that there was no significant difference in results in improving or maintaining the quality of life between carboplatin or cisplatin administration after 4-6 months of therapy.[22]

Another literature by Kristensen et al used the same questionnaire but with a different regimen, namely carboplatin plus vinorelbine (VC) or gemcitabine (GC) where the mean global quality of life scores showed a consistent pattern during chemotherapy. However, there were differences in mean HRQol scores between the two treatment groups at different times.[23] In contrast to the study by Juan Arraras et al, patients with advanced NSCLC showed moderate QoL scores with platinum-doublet treatment but worsened on the third assessment.[24]

The occurrence of this worsening is in line with the study by Shallwani et al who reported a decrease in the SF-36 score in advanced NSCLC patients indicating a worsening quality of life status ($P<0.05$) and the study of

Ferry et al which showed a worsening quality of life in patients who were given carboplatin or cisplatin at a low dose of 50 mg/m^2.[19,25] These results are supported by the study of

Prapa et al who found a low quality of life in lung cancer patients under chemotherapy treatment.[26]

The study was also conducted in a group of patients with advanced squamous NSCLC. The research of

Wang et al stated that there was an increase in the quality of life of lung cancer patients undergoing chemotherapy. Significant improvement in quality of life was measured by the experimental outcome index where it was seen that nab-paclitaxel improved quality of life more significantly than gemcitabine ($P<0.05$).[27]

The same result was stated by Saad et al which showed that the administration of cisplatin or carboplatin, when combined with gemcitabine in patients with advanced squamous NSCLC, had an effect in increasing the total FACTL score and TOI score significantly from baseline after administration of the regimen of three cycles and six cycles.[28] This is supported by research by Thomas et al which states that giving carboplatin can maintain or improve

quality of life.[18]

Another study using BAI chemotherapy by Zhu et al also significantly improved patients' quality of life. This study revealed that BAI chemotherapy significantly increased operative rates, prolonged PFS and OS, and improved quality of life in patients with inoperable stage III pulmonary SCC compared with intravenous neoadjuvant chemotherapy in the same group of patients.[29]

Improvements in quality of life also occurred in the non-squamous NSCLC group who were given first-line treatment to maintenance therapy.[30] However, a study by Reck et al conducted with patients with advanced squamous and non-squamous NSCLC on a regimen of docetaxel did not improve health status and did not relieve symptoms compared to nivolumab.[31,32]

In addition, there is a study comparing chemotherapy with immunotherapy, namely the comparison between nivolumab and docetaxel conducted by Reck et al who found that the docetaxel HRQoL group experienced a significant deterioration in various assessments, and the docetaxel group also experienced a significant decrease in HRQoL compared to nivolumab showing an increase in HRQoL.[33]

Research by Bordoni et al also stated that administration of docetaxel was no better in improving the patient's quality of life when compared to atezolizumab as measured using a global health status score.[34] Still in a similar study conducted by Brahmer et al also showed the same results, namely a decrease in the average score of global health status or quality of life by 0.9 points (–4.8 to 3.0) from the initial average score. before platinum-based chemotherapy. This study also showed that platinum-based chemotherapy was no better than pembrolizumab in improving or maintaining the quality of life to a better level.[35]

There are other studies comparing chemotherapy with a group of tyrosine kinase inhibitors. Chemotherapy was also shown to be no better at maintaining or improving quality of life when compared to the tyrosine kinase inhibitor group in lung cancer patients with EGFR mutations in the study of Lee et al with the administration of osimertinib and lung cancer with ALK mutations in the study of Soria et al. Ceritinib administration has been shown to improve quality of life better than chemotherapy.[36,37]

In a study conducted on the population aged over 70 years by Huerter et al, the quality-of-life assessment used the FACT-L questionnaire which is a special questionnaire to see the impact of treatment on the quality of life and performance of lung cancer patients. From this assessment, it was found that an increase in the score at week 17 in patients who had completed therapy showed an improvement in quality of life compared to the baseline, but the number of respondents who completed the questionnaire was still relatively low.[38]

A study in a similar population was also conducted by Morabito et al. The

results of the QOL response in the group with the addition of cisplatin to single-agent chemotherapy showed no signs of improvement, although the overall reduction in quality of life tended to be better when cisplatin was added (HR=0.56; 95% CI=0.31-1.01; P=0.05) so that is not sufficient to provide a positive interpretation of QOL therefore in elderly patients the addition of cisplatin does not provide any benefit.[39]

In a study conducted on NSCLC patients who had metastases by Garon et al, there were significant changes from the start of chemotherapy to week 48 which indicated an improvement or worsening.[40] The results in patients with metastatic NSCLC were strengthened in the study of Maizeres et al which showed a change after undergoing chemotherapy where for the carboplatin and paclitaxel/nab-paclitaxel group combined with placebo the average QLQ-C30 GHS/QoL score was lower than baseline. throughout the assessment until week 36.[41]

Furthermore, there was a study using docetaxel in the treatment group of NSCLC patients who had undergone previous treatment. In the study of Barlesi et al, there was a nominally significant worsening that was inversely related to pembrolizumab at a reported dose of 2 mg/kg arm and had a greater proportion of significantly improved QLQ-C30 EORTC scores across multiple domains.[42]

In the study, Nokihara et al. also described a better quality of life maintained with S-1 than with docetaxel in NSCLC patients with previous platinum-based chemotherapy treatment.[43] Similar results were also reported by the study of James Yang et al but in elderly patients who reported that administration of docetaxel did not work well in improving quality of life compared to administration of S-1.[44]

There was one literature that met the inclusion and exclusion criteria for SCLC patients conducted by Mansfield et al with the administration of atezolizumab plus Carboplatin/Etoposide group therapy. Administration of the regimen provided a significant increase in HRQoL that persisted at most visits up to week 54, whereas the initial increase in HRQoL in the placebo plus Carboplatin/Etoposide group (mostly <10 points) decreased after week 21. Health-related quality of life (HRQoL) improved in both groups after starting treatment, with a more pronounced and persistent increase in HRQoL in the atezolizumab group.[45]

The authors also found a study of adjuvant chemotherapy with vinorelbine plus cisplatin regimen compared with adjuvant gefitinib in patients with fully resected stage II-IIIA NSCLC mutant EGFR-mutants. There are similar results in studies by Zhong et al and Zeng et al. It was reported that the quality of life between the two groups fluctuated and there was a gradual improvement. However, if the logistic regression analyzed the level of OR improvement, FACT-L, TOI, and LCSS scores were significantly higher in the gefitinib treatment group and it was also stated that the timing of the decline in quality of life was delayed in the gefitinib group.[46,47]

Based on this search, research was found that examined the effect of chemotherapy on the quality of life of lung cancer patients which was dominated by advanced NSCLC cancer types, where there were variations in the quality-of-life outcomes in the study that could be influenced by several aspects, such as available health facilities, choice of chemotherapy regimen, the timing of the quality of life assessment, and the different socio-cultural backgrounds of patients.

CONCLUSION

Aspects that can affect the quality of life of lung cancer patients undergoing chemotherapy are the available health facilities, the choice of chemotherapy regimen, the timing of the quality-of-life assessment, and the patient's socio-cultural background.

Researchers who wish to conduct a similar scoping review are expected to examine other aspects that can affect chemotherapy. Health practitioners are expected to be able to choose the right regimen for lung cancer patients so that the patient's quality of life increases. Patients are expected to comply with the education provided and undergo chemotherapy to improve their quality of life.

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