Review

Management of Respiratory Failure in Cancer Patients: A Narrative Review

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ABSTRACT

Introduction: According to WHO, in 2018 18.1 million people worldwide had cancer, and 9.6 million people died. Acute organ failure is often found in cancer patients, especially respiratory failure where this is related to co-morbidities, cancer treatment, or the malignancy itself. **Purpose:** To identify management that can be done in cancer patients who experience respiratory failure. **Methods:** This literature review used a narrative review design using the PubMed, Sciencedirect, and Proquest databases. The criteria for the articles used were full-text, English-language articles, the year the research was published was between 2012-2022, the research design was a randomized control trial, quasi-experimental, qualitative study, retrospective study, and the research to be analyzed discussed the management of respiratory failure in patients with cancer. The articles obtained were extracted according to the criteria and then grouped and reviewed. **Results:** There are 6 articles that meet the requirements and contain various types of management of respiratory failure in cancer patients and are grouped into nursing interventions, ventilator installation, oxygenation support, administration of pharmacological medication. **Conclusion:** Various kinds of management in dealing with respiratory failure in cancer patients can be applied to provide benefits to patients. It is hoped that there will be further research regarding the effectiveness of the management of respiratory failure in cancer patients so that it can help patients to improve their condition and prevent death.

Introduction

According to WHO, in 2018 18.1 million people worldwide had cancer, and 9.6 million people died. By 2040, it is estimated that it will increase twice as much as the previous year. Cancer itself is the cause of 30% of PTM deaths at the age of 30-69 years (Siegel, Miller, Fuchs & Jemal, 2022). In Indonesia in 2020 there were 396,914 new cases of cancer and 234,511 deaths from cancer. Historically, this cancer is likely to trigger respiratory failure (Ministry of Health, Republic of Indonesia, 2022).

Acute respiratory failure is the most common and life-threatening cause (Ferreyro & Munshi, 2018). Diseases that cause acute respiratory failure include pneumonia, heart failure, cardiogenic pulmonary edema (Alberts et al., 2020; Im et al., 2019; Scott et al., 2021), chronic obstructive pulmonary disease (COPD) and are also found in cancer patients accompanied by complications in the respiratory system (Shebl, Mirabile, Sankari & Burns, 2022). In the study of Schnell et al. 2013 revealed that out of 424 cancer patients, 328 patients experienced respiratory failure and 142 patients ended in death in the ICU. Therefore, intensive treatment is needed in dealing with respiratory failure in cancer patients.

Apart from the various recent studies both in documenting and advancing in the care of critical cancer patients, this requires serious treatment in the Intensive Care Unit (ICU) room. In fact, 20% of patients admitted to ICU care units are diagnosed with malignancy (Kızılgöz, Akın Kabalak, Kavurgacı, İnal Cengiz & Yılmaz, 2021). The most common reason for transfer to a critical care ward is organ failure (Asim, Amin & El-Menyar, 2020). Acute organ failure may be related to co-morbidities, cancer treatment, or the malignancy itself (Vadde & Pastores, 2016). Every organ can be affected, but respiratory failure is the most common and feared indication for ICU admission (Sears, S. P. et al, 2020). Therefore, a variety of effective interventions are needed to be used during treatment at the hospital.

Management of respiratory failure, one of which can be done by administering mechanical ventilation or a ventilator with various modes that are adjusted to the patient's condition (Hikmat et al., 2022; Mokart et al., 2015; Yosep et al., 2023). In addition, several collaborative therapies that are effective enough to support patients with acute respiratory failure are also needed to improve patient condition support so that they can survive until their condition is stable. This literature aims to determine the management of respiratory failure in cancer patients in the ICU. So that the authors can review various interventions in dealing with respiratory failure in cancer patients with the narrative review method.

Method

This article used a narrative review design where the flow of writing this article starts from determining the topic, searching the literature from the database, selecting articles, processing data, and drawing conclusions.

Search Strategy

The researcher formulated the theme of the article using the PICO method (Problem, Intervention, Comparison and Outcome). The Population: cancer patient, Intervention: management of respiratory failure components, the Comparison component was not used, because the purpose of this study was only to find out the types of management techniques in cancer patients with respiratory failure, not to compare one intervention with another. The outcome component that has been determined is well-being. So a research question arises in the form of "how is the management of respiratory failure in cancer patients?".

The article search used the Preferred Items for Systematic Reviews and Meta Analyzes (PRISMA) guidelines with three databases used, namely PubMed, ScienceDirect, and ProQuest

with a range of 2012 - 2022. The main keywords of the PICO approach used were cancer OR malignant OR patient with cancer AND management OR intervention OR management of respiratory failure OR respiratory failure management OR intervention of respiratory failure AND well-being

Eligibility Criteria

The inclusion criteria that met the requirements in this article were full-text, English-language articles, 2012-2022 research, randomized control trial, quasi-experimental, qualitative study, retrospective study, HOT ICU trial design. The focus of this research is an article that discusses the management of respiratory failure in cancer patients. Articles are excluded if the article is only in the form of an abstract, not in English, is a research review, research protocol, thesis, dissertation, opinion expert article. Researchers independently carry out the process of screening articles based on titles, abstracts and full text by assessing the quality of the articles until the preparation of this article is complete.

Data Extraction and Document Results

Data extraction was carried out manually by researchers by analyzing the specified articles, then displayed in the literature review results table which contained the title, researcher, year of publication, research sample research objectives, research design, interventions and research results. After extracting the data, the results of the data analysis are then reviewed and described in more detail in the discussion by grouping similar interventions and discussing the management of respiratory failure in cancer patients.

Results

From the search results that have been carried out, we got six articles that were selected according to predetermined inclusion and exclusion criteria, which we then analyzed. Most of the journal findings from the analyzed database came from PubMed, namely 3 articles, ScienceDirect 1 article, and ProQuest 2 articles. With the research design from the article obtained Experimental study, Retrospective study, Retrospective cohort study and HOT ICU trial. The release year of the six articles ranged from 2014 to 2022 with samples ranging from 14-1614 patients. From the results of this analysis, we grouped several managements performed on patients with cancer who experienced respiratory failure as follows:

1. **Nursing interventions**

Nursing interventions carried out in cancer patients with respiratory failure are the application of an integrated perioperative nursing model that can improve lung function, quality of life and self-efficacy and can reduce negative moods in patients (Huang & Feng, 2022).

2. **Installation of ventilators**

Providing non-invasive ventilation in patients with lung cancer, the results show that the installation of non-invasive ventilation is more effective in this type of hypercapnic respiratory failure. The use of non-invasive ventilation can be given to patients with lung cancer to prevent complications (Kızılgöz, Kabalak, Kavurgacı, Cengi & Yılma, 2021). Next is the intervention of using a non-invasive ventilator with positive pressure which can be used as the first-line management of patients with respiratory failure. Management of non-invasive mechanical ventilators that fail will eventually require invasive ventilation. However, making non-invasive mechanical ventilation the first line can reduce endotracheal intubation (Rathi et al. 2017).

3. **Oxygenation Support**

Giving a higher oxygenation target can reduce mortality, organ damage, and higher use

of norepinephrine in cancer patients with respiratory failure in the ICU (Klitgard, Schjorring, & Lange, Moller, 2022). In addition, in more severe conditions, adequate oxygenation support can also be provided with the use of an ECMO device. In the article analyzed here the use of ECMO is given to selected patients with hematologic malignancies and severe acute respiratory failure whose results show a link between long-term disease-free survival in patients with hematologic malignancies and severe acute respiratory failure (Philipp Wohlfarth et al, 2014).

4. Provision of Pharmacological Medications

Giving tyrosine kinase inhibitors with the results obtained that for an average of 17 days can increase the life expectancy of lung cancer patients treated in the ICU (Lee et al., 2021).

The following are the results of the article analysis (Table 1):

Table 1. Data Extraction

No.	Author	Title	Objective	Sample	Intervention	Design	Results
1.	Huang & Feng, 2022	Effect of Refined Perioperative Nursing on The Efficacy of Noninvasive Ventilation in Elderly Patients with Lung Cancer and Respiratory Failure	This study aims to improve the quality of life and reduce the need for medical services with an integrated perioperative nursing model	104 elderly patients in Sichuan Hospital divided into 2 groups 1. Control Group (52 patients) 2. Intervention Group (52 patients)	Three nursing models were applied in this study, namely: 1. The Peer Support Nursing Model 2. The Interdisciplinary Cooperative Nursing Model 3. The Transcultural Nursing Theory (Madeleine Leininger) The intervention was carried out for 2 months and using 5 instruments, namely: 1. logical Decision Tree Regression (LDTR) models 2. Iterative Fruit Fly Optimization Algorithm (IFOA). 3. The Zung Self Rating-Anxiety Scale (SAS) 4. Zung Self-rating Depression Scale (SDS) 5. GSE (General Self-Efficacy Scale)	Experimental Study	Patients showed better results after surgery with an integrated perioperative nursing intervention model. Researchers analyzed the results using 4 comparison factors, namely: 1. Lung Function Lung function in the intervention and intervention groups was the same as before the intervention. After the intervention, the intervention group had Forced Expiratory Volume, Forced Vital Capacity, and Forced Expiratory Volume/Forced Vital Capacityhigher than the control group ($p<0.050$) 2. Negative mood after the intervention, the intervention group had lower scores on SAS and SDS than the control group ($p<0.050$) 3. Quality of Life the final results found that the quality of life of patients in the intervention group was better than the control group ($p<0.050$) 4. self-efficacy The final result was that the intervention group had a higher GSE score than the control group ($p<0.050$).
2.	Derya Kızılgöz, Pınar	The success of non-	To determine the success of NIMV in lung	A total of 42 lung cancer and respiratory	Lung cancer patients and respiratory failure are given NIMV according to	Retrospective study	- In this study, it was found that most respiratory failure was due to COPD exacerbations. Although the difference is not significant, the

No.	Author	Title	Objective	Sample	Intervention	Design	Results
	Akın Kabalak, Suna Kavurgacı, Tuba İnal Cengi, Ülkü Yılma (2021)	invasive mechanical ventilation in the lung cancer patients with respiratory failure	cancer patients and the factors that influence it.	failure patients who received NIMV between 2014-2018. With consideration of NIMV contraindications, this treatment is given to patients with GCS 15, adequate cough reflex, stable hemodynamics.	indications. One hour after initiation of treatment with NIMV, blood gas analysis, vital parameters and physical examination were performed. Every day ABG and respiratory system examinations are carried out to monitor NIMV pressure and titration duration.		success of treatment with NIMV is highest in lung cancer patients with COPD exacerbations. - Based on the type of respiratory failure, treatment with NIMV has a higher success rate in hypercapnia - The use of NIMV as an initial step can be an option for lung cancer patients in hospitals to prevent complications of IMV
3.	Rathi et al., (2017)	Non-invasive Positive Pressure Ventilation versus Invasive Mechanical Ventilation as First Line Therapy for Acute Hypoxemic Respiratory	This study aims to describe the characteristics and outcomes of critically ill cancer patients receiving non-invasive positive pressure ventilation (NIPPV) vs invasive mechanical ventilation as first-line therapy for acute hypoxemic	A sample of 1614 people aged over 18 years and hypoxemic respiratory failure (defined as PaO2:FiO2 < 200). Patients were excluded if they received NIPPV before ICU.	Variables collected included initial ventilation mode (NIPPV vs. IMV), subsequent ventilation modes, and time spent on NIPPV, and/or IMV. Time to intubation was measured for the NIPPV failure group as time from NIPPV administration to time of intubation and was stratified into four groups: less than or more than 24 hours and less than or more than 48 hours. Other data collected included cancer diagnosis, demographic data (age, race, sex, marital status), primary transfer	Retrospective cohort study	A total of 1614 consecutive patients with hypoxemic respiration Failures who received NIPPV or IMV as first-line therapy were identified and included learning. - All patients had moderate to severe hypoxemic respiratory failure with PaO2:FiO2 as ratio < 200. Patients with haematological malignancies comprised 55.7% of the total group (n = 899), whereas 44.3% had solid tumors (n = 715. - Most of the patients were referred from leukemia services (30.3%), followed by stem cell transplant services (14.4%) and lymphoma services (12.6%). The SOFA mean score for all patients was 9.6 (+) 4.5. - A total of 821 patients (51%) received IMV as first-line therapy, and 793 patients (49%) received NIPPV. Of patients who received

No.	Author	Title	Objective	Sample	Intervention	Design	Results
		Failure in Cancer Patients	respiratory failure.		services, hospital LOS prior to ICU transfer, body mass index (BMI), white blood cell count and absolute neutrophil count at admission. , ICU and Hospital mortality, Total Sequential Organ Failure Assessment (SOFA) score after 24 hours after ICU		NIPPV, 62% (n=490) improved and did not require endotracheal intubation, and 38% (n=303) failed NIPPV and subsequently required IMV.
4.	Klitgard , Thomas . Schjorri ng, Olav., Lange, Theis., Moller, Morten H. (2022)	Lower versus higher oxygenat ion targets in critically ill patients with severe hypoxae mia: secondar y Bayesian analysis to explore heteroge neous treatment effects in the Handling Oxygena tion	The aim of this study was to analyze the causes of death of patients admitted to the ICU who suffered from respiratory failure and hypoxaemia and received a FiO2 of at least 0.50 in a closed system (invasive or non-invasive mechanical ventilation or CPAP mask) or received 10 L of oxygen in the past 90 days	patients admitted to the ICU who suffer from respiratory failure and hypoxemia and receive an FiO2 of at least 0.50 in a closed system (invasive or non-invasive mechanical ventilation or CPAP mask) or is receiving 10 L of oxygen on an IV and is expected to receive supplemental oxygen	Giving a low oxygenation target which will then be seen by the following 4 variables: 1. Organ dysfunction based on SOFA (Sequential Organ Failure Assessment). 2. The PaO2:FiO2 ratio determines the severity of hypoxaemia with additional adjustments for respiratory failure 3. Highest norepinephrine dose received 4. Plasma lactate concentration	HOT ICU trials	- The mortality that occurred in this ICU room was around 63.5%. - When viewed from the administration of norepinephrine accompanied by lower oxygen levels, it shows a higher death outcome than in patients who receive a higher oxygen target. A 95% probability of interaction was found between increasing the initial dose of norepinephrine and the lower oxygenation target on death (ie the unfavorable effect of a lower oxygenation target with increasing norepinephrine dose at baseline). - There is a positive relationship between a low oxygenation target and an 85% increase in lactate that allows participant death. - There is also a positive relationship (potentially increased risk of death) between a low oxygenation target and a 65% increase in the degree of organ failure, especially the 76% percentage for the incidence of respiratory failure.

No.	Author	Title	Objective	Sample	Intervention	Design	Results
		Targets in the Intensive Care Unit (HOT-ICU) trial					
5.	(Lee et al., 2021)	Tyrosine Kinase Inhibitors Improved Survival of Critically Ill EGFR-Mutant Lung Cancer Patients Undergoing Mechanical Ventilation	analyzed the performance of tyrosine kinase inhibitors in lung cancer patients who were admitted to the ICU due to respiratory failure and who required mechanical ventilation, and all of them had epidermal growth factor receptor (EGFR) mutation status.	63 patients who were treated in the ICU using a mechanical ventilator and were diagnosed with lung cancer	The patient received EGFR-TKI as first-line therapy for lung cancer. Previously, the patients were assessed prior to demographics and initial characteristics such as age, sex, co-morbidities, ICU admission diagnosis, and disease severity on ICU admission (APACHE II score) were recorded for all patients. Data on cancer stage, histological type, etc. were reviewed. Then after that the patient underwent EGFR-TKI therapy which was carried out for 17 days of treatment. The evaluation was carried out by assessing survival in the ICU and LOS in the ICU	Retrospective study	Patients with sensitive EGFR mutations were 35 out of 63 people. Most of the patients were treated with first or second generation EGFR-TKI (gefitinib: 22 people; erlotinib: 11 people; and afatinib: 1 person). Only one patient received osimertinib treatment in the ICU. The median duration of EGFR-TKI use in the ICU was 17 days to 28 days. The ICU survival rate was 77%, and the median survival time was 67 days. In addition, 43% of patients were weaned from MV successfully, and the median days with MV use was 22 days.
6.	(Philipp Wohlfarth et al, 2014)	Extracorporeal membrane oxygenat	The results of this analysis are to report the characteristics and outcomes	14 consecutive patients with hematologic malignancies severe acute	ECMO therapy was used for an average of 8.5 (4 to 16) days, and mechanical ventilation, for 17 (12 to	Retrospective cohort study	Prior to ECMO, the PaO2/FiO2 ratio was 60 (53 to 65), (3.3 to 3.7). Three patients received venoarterial ECMO because acute circulatory failure other than ARF; all other patients received venovenous ECMO. All patients

No.	Author	Title	Objective	Sample	Intervention	Design	Results
		ion in adults patients with hematologic malignancies and severe acute respiratory failure	of patients with and hematologic malignancies severe acute respiratory failure treated with extracorporeal membrane oxygenation (ECMO)	respiratory failure who were treated with a total of 17 episodes of ECMO	35) days. In patients with VV ECMO, percutaneous cannulation was performed by inserting a 21-24-F drainage cannula into the femoral vein and 19-22-F into the right jugular vein using the ultrasound-guided Seldinger technique. In one patient, a 31-F double-lumen cannula was placed into the right jugular vein. Cannulation of VA ECMO was performed surgically using the semi Seldinger cutdown technique. Eleven patients received a continuous intravenous infusion of unfractionated heparin to maintain an activated partial thromboplastin time of approximately 55 seconds.		required vasopressors, and five patients required hemofiltration. Thrombocytopenia occurred in all patients (the lowest platelet count was 20 (11 to 21) G/L). Five major bleeding events were recorded. ECMO duration is 8.5 (4 to 16) days. ICU and hospital survival is 50%. All survivors were alive at follow-up (36 (10 to 58) months); five patients were in complete remission, one was in partial remission, and one had relapsed. ECMO therapy can be performed in selected patients with hematologic malignancies and severe acute respiratory failure and is associated with long-term disease-free survival.

Discussion

Cancer is uncontrolled cell growth, has the ability to invade and metastasize (Muray, 1997). Patients with cancer are at high risk of experiencing respiratory failure so that these patients need effective management to overcome their respiratory failure. Respiratory failure means that the supply of oxygen in the body will decrease (Bergin & Rackley, 2016). If the supply in the body is reduced, there is a risk of complications, for example organ failure in other body systems (Ervin, Rentes, Dibble, Sjoding et al., 2020). The main and most common management for respiratory failure is to install a ventilator that is tailored to the patient's needs (Kapil & Wilson, 2019). In addition to installing a ventilator, other management can be done to reduce severity and support other interventions. Therefore management of respiratory failure needs to be done in patients in the ICU, especially in patients with cancer. The management of respiratory failure analyzed in this article is divided into 4 groups, namely the therapy group with various nursing models, therapy with NIMV and NIPPV ventilator modes, oxygen support therapy, and pharmacological therapy.

The first therapy that can be applied is nursing model therapy using 3 nursing models namely The Peer Support Nursing Model, The Interdisciplinary Cooperative Nursing Model, The Transcultural Nursing Theory (Madeleine Leininger). The Peer Support Nursing Model is a model that implements interventions to help the patient physically and psychologically, helps reduce anxiety, loneliness and improves the patient's quality of life (Carvello, Zanotti, Rubbi, Bacchetti, Artioli & Bonacaro, 2019). The Interdisciplinary Cooperative Nursing Model is a model that works in collaboration with other disciplines to jointly carry out the process of disease therapy in patients (Mahdizadeh, Heydari & Karimi Moonaghi, 2015). The Transcultural Nursing Theory according to Madeleine Leininger, every patient has a different cultural and ethnic background, therefore when providing care to patients it must be adjusted to the patient's background and culture so that patients are more comfortable with what we are doing (Im & Lee, 2018). These three theoretical models are proven to improve quality of life, self-efficacy, reduce negative emotions and improve lung function. In this way, patients who are treated in the ICU with respiratory distress have good psychological strength.

The next therapy that can be done is the success of non-invasive mechanical ventilation in lung cancer patients with respiratory failure, where every patient with respiratory failure who is given NIMV is subjected to ABG examination, vital parameters and physical examination every 1 hour every day. In addition, monitoring of NIMV pressure and the duration of the titration was also carried out (Mokart et al., 2015; Ochi et al., 2022; Yosep et al., 2022). Then therapy is Non-invasive Positive Pressure Ventilation versus Invasive Mechanical Ventilation as First Line Therapy for Acute Hypoxemic Respiratory Failure in Cancer Patients. NIPPV failure is a major risk factor for death in the ICU (Wang, Wilson, Dobler, Morrow & Beuschel et al., 2019). Delay in action in the intubation process can affect the results. NIPPV failure (intubation after 48 hours or more) is associated with high mortality and on multivariate analysis is associated with increased patient mortality (Rathi et al., 2017).

Other therapy that can be done is Lower versus higher oxygenation targets in critically ill patients with severe hypoxaemia. This article discusses the use of high or low oxygen for the treatment of patients in the ICU. Lower oxygenation targets are unlikely to affect overall

mortality among critically ill adult patients with acute hypoxemic respiratory failure (MacIntyre, 2013). However, the results of this study demonstrated an increased risk of death for patients with lower oxygen targets and increased initial doses of norepinephrine (Klitgart et al., 2022).

Furthermore, there is Extracorporeal membrane oxygenation therapy in adult patients with hematologic malignancies and severe acute respiratory failure, which is therapy by administering ECMO for 8.5 days and mechanical ventilation for 17 to 35 days by inserting a 21-24-F drainage cannula into the femoral vein and 19 -22-F into the right jugular vein using the Seldinger technique (Wohlfarth et al., 2014).

Another therapy that can be done is by using Tyrosine Kinase Inhibitors treatment therapy which is described in the article Lee et al., (2021) revealed that this therapy aims to inhibit this type of cancer by suppressing protein kinases to mutate which will cause uncontrolled growth, resulting in become new cancer cells. In that study, therapy was carried out for 17 days of treatment and evaluation was carried out with indicators of reduced LOS from patients and the use of mechanical ventilators in a shorter range. The results showed that 35 of the 63 patients with EGFR mutations who were sensitive to this therapy reaction (Alberts et al., 2020; Wang et al., 2019). As for the reaction to this therapy, it was found that the 28-day ICU survival rate was 77%, and the average survival time was 67 days. In addition, 43% of patients were successfully weaned from MV, and the range of days with MV use was within 22 days. So it can be concluded that the use of this TKI therapy can extend the survival of patients in ICU with EGFR-driven lung cancer, even for patients with critical illness who require MV.

Kesimpulan

From the six articles obtained, it can be concluded that there are four categories of therapeutic approaches that can be taken to manage cancer patients who experience respiratory failure, namely the application of various nursing models, therapy with NIMV and NIPPV ventilator modes, therapy with different target oxygen levels, use of ECMO, and pharmacological therapy. It is hoped that there will be further research regarding the effectiveness of the management of respiratory failure in cancer patients so that it can help patients to improve their condition and prevent death.

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