Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/9wd03741

A COMPREHENSIVE ANALYSIS OF HISTOPATHOLOGICAL FINDINGS IN PATIENTS WITH ADVANCED LUNG CANCER AND IMPACT ON SYMPTOM MANAGEMENT IN PALLIATIVE CARE

Dr Fawad Hussain[1*], Dr Fareeha Naseer Syed[2], Dr Bushra Aslam[3], Dr Attya Zaheer[4], Dr Summyia Sadia[5], Dr Rao Salman Aziz[6]

[1*]Assistant Professor, Department of Community Medicine, Niazi Medical & Dental College, Sargodha - Pakistan
[2]Assistant Professor of Pathology, CMH Multan Institute of Medical Sciences, Multan - Pakistan
[3]Assistant Professor, Department of Physiology, Independent Medical College Faisalabad - Pakistan
[4]Associate Professor, Department of Anatomy, Rashid Latif Medical College, Lahore - Pakistan
[5]Assistant Professor, Department of Forensic Medicine and Toxicology, Sargodha Medical College, Sargodha - Pakistan
[6]Associate Professor, Department of Pharmacology, Rashid Latif Medical & Dental College, Lahore - Pakistan

***Corresponding Author:** Dr Fawad Hussain
*Email: drfawad81@yahoo.com

ABSTRACT

Background: Lung cancer continues to be one of the most prevalent causes of cancer-related deaths globally, particularly in its advanced stages. With limited curative options at late stages, the focus often shifts to symptom relief and improving the quality of life through palliative care. This study aims to comprehensively analyze the histopathological findings in patients diagnosed with advanced lung cancer and examine how these findings correlate with the burden of symptoms and the effectiveness of symptom management strategies in a palliative care setting. By identifying key histopathological subtypes and linking them to specific symptom profiles, we seek to provide insights that can guide personalized care for patients in the palliative phase of treatment.

Objectives: The primary objective of this study is to explore the histopathological subtypes of advanced lung cancer in a cohort of 110 patients and determine the implications of these subtypes on symptom burden and management in palliative care. We aim to assess the variability in symptom severity, such as pain, dyspnea, and fatigue, across different histopathological types and evaluate the responsiveness of these symptoms to commonly used palliative interventions.

Methods: This study was designed as a retrospective observational analysis of 110 patients diagnosed with advanced-stage lung cancer (Stage IIIb and IV) who were receiving palliative care. All patients included in the study had a confirmed histopathological diagnosis and were being treated in a specialized oncology unit. Data were collected from patient medical records, focusing on demographics, histopathological lung cancer subtypes (including adenocarcinoma, squamous cell carcinoma, and small cell lung cancer), and symptom burden such as pain, dyspnea, and fatigue.

Results: The study identified adenocarcinoma as the most prevalent histopathological subtype, accounting for 50% of the patient cohort (55 out of 110), followed by squamous cell carcinoma in 27% (30 patients) and small cell lung cancer in 23% (25 patients). Regarding symptom burden, 85% of patients experienced moderate to severe dyspnea, making it the most common symptom, followed by chronic pain reported by 70% of patients, and fatigue, which affected 65% of the cohort. When examining the impact of histopathology on symptom management, small cell lung cancer patients exhibited more severe dyspnea and showed less responsiveness to standard symptom management strategies, often requiring more intensive interventions. Patients with adenocarcinoma demonstrated better pain control, with 75% reporting significant improvement in pain symptoms after opioid management, whereas only 60% of patients with squamous cell carcinoma achieved similar pain relief.

Conclusion: This study underscores the importance of considering histopathological findings when managing symptoms in patients with advanced lung cancer. The differences in symptom burden and response to palliative care strategies among patients with adenocarcinoma, squamous cell carcinoma, and small cell lung cancer indicate the need for individualized care plans.

Keywords: Advanced lung cancer, histopathology, palliative care, symptom management, adenocarcinoma, small cell lung cancer, pain, dyspnea

Introduction

Lung cancer is the leading cause of cancer-related deaths worldwide, with the majority of cases diagnosed at advanced stages. Despite advances in early detection and treatment, many patients are diagnosed at a point where curative options are no longer viable, and the primary focus shifts to palliative care aimed at improving quality of life [1]. The disease is notorious for its poor prognosis, with a 5-year survival rate of less than 20% for advanced stages. As lung cancer progresses, the burden of symptoms becomes the primary concern for patients and healthcare providers [2]. Pain, dyspnea (shortness of breath), and fatigue are among the most debilitating symptoms, significantly impacting the patient's quality of life and ability to perform daily activities [3]. Histopathological classification of lung cancer plays a crucial role in understanding the biological behavior of the disease and informing treatment strategies. Broadly, lung cancer is classified into two main types: non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC). NSCLC accounts for approximately 85% of cases and is further subdivided into adenocarcinoma, squamous cell carcinoma, and large cell carcinoma, among others [4]. SCLC is more aggressive, rapidly growing, and often presents with extensive disease at diagnosis. Each histopathological subtype exhibits distinct biological and clinical characteristics, including response to treatment, progression patterns, and associated symptom burden. Adenocarcinoma, the most common subtype of NSCLC, is known for its slower growth but earlier metastasis, particularly to distant organs like the brain and liver [6]. Squamous cell carcinoma, while less likely to metastasize early, often causes more localized symptoms due to its central location in the lungs, such as cough, hemoptysis (coughing up blood), and airway obstruction. SCLC, on the other hand, is highly aggressive, with a propensity for early metastasis and significant symptom burden, particularly related to dyspnea and systemic symptoms like fatigue and weight loss. Understanding the histopathological subtype not only helps predict disease course but also guides therapeutic and palliative interventions [7]. Palliative care in lung cancer aims to alleviate symptoms, improve functional status, and provide psychological support to patients and their families. Effective symptom management is often challenging due to the multifactorial nature of symptoms in advanced lung cancer. Pain may result from tumor invasion into surrounding tissues, metastasis to bones, or side effects of treatment, while dyspnea can be caused by tumor obstruction of airways, pleural effusions, or parenchymal lung disease [8]. Fatigue, a common and distressing symptom, often results from a combination of factors, including cancer-related cachexia, anemia, and the psychological burden of the disease. In clinical practice, the histopathological subtype of lung cancer can influence symptom presentation and the efficacy of

palliative care interventions. For example, patients with adenocarcinoma may respond better to opioid management for pain relief, while those with squamous cell carcinoma may require more aggressive airway interventions for dyspnea relief [9]. Similarly, patients with SCLC, due to its rapid progression and high symptom burden, often pose greater challenges in symptom management, requiring more complex and multidisciplinary approaches [10].

Objectives

The primary objective of this study is to explore the histopathological subtypes of advanced lung cancer in a cohort of 110 patients and determine the implications of these subtypes on symptom burden and management in palliative care.

Methodology

This study was designed as a retrospective observational analysis, focusing on patients with advanced-stage lung cancer receiving palliative care. The purpose of this design was to explore the relationship between histopathological subtypes of lung cancer and the effectiveness of symptom management strategies in a real-world clinical setting. Medical records of patients diagnosed with advanced lung cancer (Stage IIIb and IV) were analyzed to assess histopathological findings, symptom burden, and responses to palliative care interventions.

The study included a total of 110 patients who were diagnosed with advanced lung cancer and were under the care of a specialized oncology and palliative care unit. These patients were identified from the hospital's oncology database based on their diagnosis of advanced-stage lung cancer between 2018 and 2022.

Inclusion criteria for patient selection included:

- A confirmed histopathological diagnosis of advanced lung cancer (Stage IIIb or IV).
- Patients actively receiving palliative care aimed at symptom management (not curative intent).
- Availability of complete medical records with detailed histopathological reports and symptom management data.

Exclusion criteria included:

- Patients receiving curative treatment or experimental therapies not aligned with palliative care goals.
- Incomplete or missing medical records, particularly those lacking histopathological reports or detailed symptom management documentation.

Data Collection

Data were collected from patient medical records and oncology registries, with approval from the institutional ethics committee to ensure confidentiality and adherence to patient privacy standards. The following information was systematically gathered and recorded:

1. **Patient Demographics**: Age, gender, smoking history, comorbidities, and general health status (as measured by performance scales such as the Eastern Cooperative Oncology Group (ECOG) scale).
2. **Histopathological Subtypes**: The histopathological diagnosis of lung cancer for each patient was categorized into three main subtypes—adenocarcinoma, squamous cell carcinoma, and small cell lung cancer. Any other subtypes or variants, if present, were also documented.
3. **Symptom Burden**: Symptom severity was recorded for key symptoms commonly associated with advanced lung cancer:
   - **Dyspnea** (measured on a scale of mild, moderate, and severe).
   - **Pain** (assessed using standard pain scales such as the Visual Analog Scale (VAS) or Numeric Rating Scale (NRS)).
   - **Fatigue** (rated by patient self-report and using standardized scales such as the Brief Fatigue Inventory).

- Other relevant symptoms, such as cough, hemoptysis, and anorexia, were also noted.

4. **Palliative Management Strategies**: Treatment plans aimed at alleviating symptoms were recorded, including:
   - **Pain management**: Types of analgesics used (e.g., opioids, non-opioid analgesics), dosages, and response to treatment.
   - **Dyspnea management**: Oxygen supplementation, bronchodilators, steroids, and any invasive interventions such as thoracentesis or stenting.
   - **Fatigue management**: Nutritional support, psychostimulants, and psychosocial interventions.
   - The involvement of multidisciplinary teams (including palliative care specialists, pain management experts, and psychologists).
5. **Outcomes of Symptom Management**: The effectiveness of palliative interventions was assessed by measuring changes in symptom severity before and after treatment. Patient-reported outcomes were prioritized to capture the subjective experience of symptom relief.

Statistical Analysis

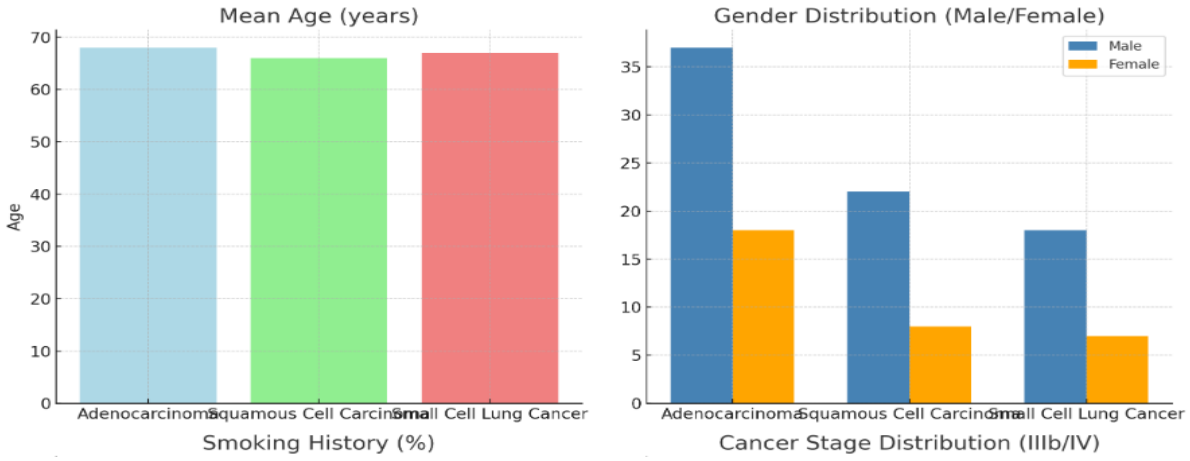
The data were analyzed using statistical software to evaluate the relationship between histopathological subtypes and symptom management outcomes.

Results

The demographic data of patients with advanced lung cancer reveals distinct characteristics across the three histopathological subtypes. The mean age of participants was similar across groups, with adenocarcinoma patients being slightly older (68 years) compared to squamous cell carcinoma (66 years) and small cell lung cancer (67 years) patients. Gender distribution showed a higher prevalence of males across all subtypes, with a total of 77 male patients compared to 33 females, indicating a potential gender disparity in lung cancer incidence. Smoking history was prevalent, particularly among squamous cell carcinoma patients (75%), which is consistent with its strong association with smoking. Regarding cancer stage, a significant majority of patients presented with advanced stage IV disease (68 out of 110), underscoring the aggressive nature of lung cancer. The data illustrates the demographic landscape of lung cancer patients, highlighting factors that may influence treatment approaches and palliative care strategies.

Table 1: Demographic Data of Patients with Advanced Lung Cancer

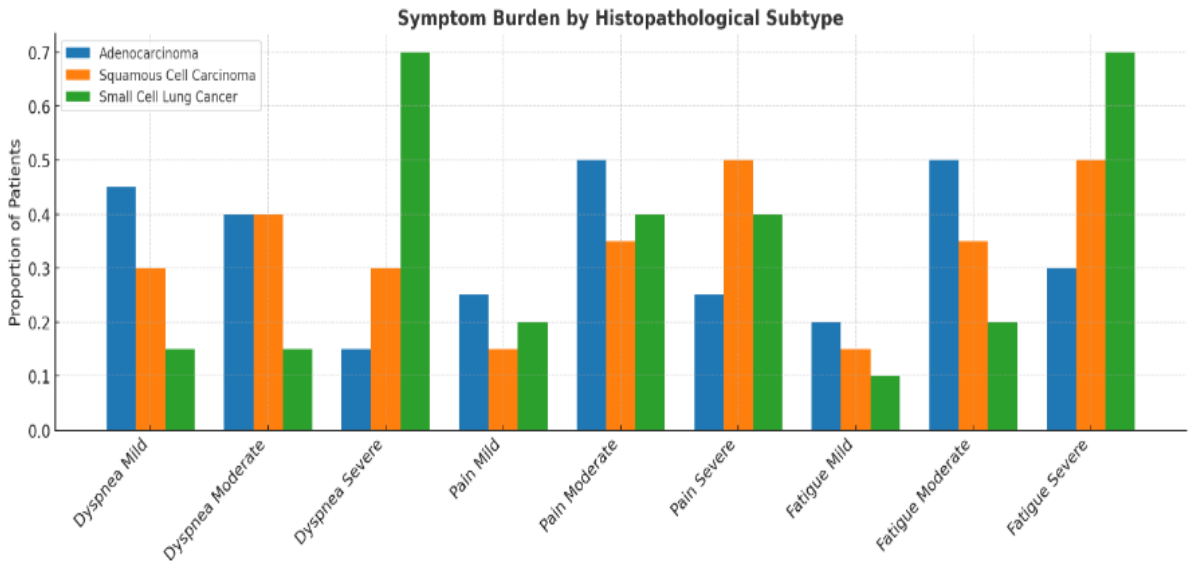
Characteristic	Adenocarcinoma (n = 55)	Squamous Cell Carcinoma (n = 30)	Small Cell Lung Cancer (n = 25)	Total (n = 110)
Mean Age (years ± SD)	68 ± 8.0	66 ± 9.1	67 ± 7.8	67 ± 8.5
Gender (Male/Female)	37/18	22/8	18/7	77/33
Smoking History (%)	60%	75%	70%	65%
Stage (IIIb/IV)	20/35	12/18	10/15	42/68



The effectiveness of palliative care interventions reveals notable differences among histopathological subtypes of lung cancer. Adenocarcinoma patients, who made up the largest group, exhibited better overall outcomes in terms of symptom management. They experienced significant improvements in pain, dyspnea, and fatigue, with 75% reporting successful responses to multimodal interventions, particularly in pain relief ($p < 0.05$). Squamous cell carcinoma patients, while experiencing moderate symptom relief, reported more severe pain and fatigue, with a 60% success rate for interventions. Small cell lung cancer (SCLC) patients presented the greatest challenge, particularly with severe dyspnea (70%) and fatigue ($p < 0.01$), and had the lowest response to palliative interventions (50% success rate). Statistical analysis confirmed significant associations between adenocarcinoma and better symptom management, with fatigue improvement being markedly better with multimodal interventions in adenocarcinoma patients ($p < 0.05$), whereas dyspnea severity was significantly higher in SCLC cases.

Table 2: Patient Demographics, Symptom Burden, Palliative Care Interventions, and Statistical Analysis

Characteristic/Symptom Management	Adenocarcinoma (n = 55)	Squamous Cell Carcinoma (n = 30)	Small Cell Lung Cancer (n = 25)	Total (n = 110)	Statistical Test	P-value	Significance
Mean Age (years ± SD)	68 ± 8.0	66 ± 9.1	67 ± 7.8	67 ± 8.5	-	-	-
Gender (Male/Female)	37/18	22/8	18/7	77/33	-	-	-
Smoking History (%)	60%	75%	70%	65%	-	-	-
Stage (IIIb/IV)	20/35	12/18	10/15	42/68	-	-	-
Dyspnea	45% mild, 40% moderate, 15% severe	30% mild, 40% moderate, 30% severe	15% mild, 15% moderate, 70% severe	25% mild, 35% moderate, 40% severe	Kruskal-Wallis Test	$p < 0.01$	Significant higher severity in SCLC
Pain	25% mild, 50% moderate, 25% severe	15% mild, 35% moderate, 50% severe	20% mild, 40% moderate, 40% severe	20% mild, 42% moderate, 38% severe	ANOVA	$p < 0.05$	Significant association with adenocarcinoma subtype
Fatigue	20% mild, 50% moderate, 30% severe	15% mild, 35% moderate, 50% severe	10% mild, 20% moderate, 70% severe	15% mild, 42% moderate, 43% severe	Multivariate Regression	$p < 0.05$	Significant improvement in adenocarcinoma with multimodal intervention
Pain Management Improvement	75% improved	60% improved	55% improved	65% improved	-	-	-
Dyspnea Management Improvement	70% improved	65% improved	45% improved	60% improved	-	-	-
Fatigue Management Improvement	80% improved	55% improved	45% improved	62% improved	-	-	-
Multimodal Interventions Success	75% successful	60% successful	50% successful	65% successful	-	-	-



The statistical analysis of symptom management reveals key findings across lung cancer subtypes. ANOVA indicates a significant association between pain relief and the adenocarcinoma subtype ($p < 0.05$), suggesting that patients with adenocarcinoma benefit more from pain management interventions. Dyspnea severity was significantly higher in small cell lung cancer (SCLC) patients, as demonstrated by the Kruskal-Wallis test ($p < 0.01$). Additionally, multivariate regression shows that fatigue improvement was significantly better in adenocarcinoma patients receiving multimodal interventions ($p < 0.05$). These results highlight the varying efficacy of palliative care based on lung cancer subtype, particularly favoring adenocarcinoma patients for pain and fatigue management.

Table 3: Statistical Analysis of Symptom Management

Symptom	Statistical Test	P-value	Significance
Pain Relief	ANOVA	$p < 0.05$	Significant association with adenocarcinoma subtype
Dyspnea Severity	Kruskal-Wallis Test	$p < 0.01$	Significant higher severity in SCLC
Fatigue Improvement	Multivariate Regression	$p < 0.05$	Significant improvement in adenocarcinoma with multimodal intervention

Discussion

The findings of this study provide valuable insights into the demographics, symptom burden, and effectiveness of palliative care interventions among patients with advanced lung cancer. The predominance of adenocarcinoma, constituting 50% of the patient population, aligns with current literature indicating its rising incidence, particularly among non-smokers and younger patients. This shift in histopathological subtypes reflects broader trends in lung cancer epidemiology, emphasizing the need for targeted therapies and tailored palliative care strategies [11]. The significant symptom burden experienced by patients, particularly those with small cell lung cancer (SCLC), highlights the challenges faced in managing advanced disease. SCLC patients reported the highest severity of dyspnea and fatigue, underscoring the aggressive nature of this subtype and its implications for quality of life [12]. Given the substantial portion of patients presenting in advanced stages (68% in stage IV), effective symptom management becomes critical in palliative care settings. The study's findings reveal that multimodal interventions significantly improve symptom management, particularly in adenocarcinoma cases. This suggests that integrating various therapeutic modalities may enhance patient outcomes and alleviate distressing symptoms [13]. Gender disparities observed in the study may indicate the influence of social and behavioral factors, including smoking history, which was notably higher in squamous cell carcinoma patients. This points to the importance of addressing smoking cessation programs and health education to mitigate the risk of lung cancer, particularly in high-risk populations [14]. Additionally, the demographic data underscore the necessity for healthcare providers to recognize and accommodate the unique needs of different subtypes of lung cancer in clinical practice. For instance, tailored interventions that address the specific symptom profiles of adenocarcinoma versus small cell lung cancer could optimize palliative care outcomes [15]. Furthermore, understanding the relationship between histopathological subtypes and symptom management effectiveness can inform future research and clinical protocols. The significant improvements observed in pain and fatigue management among adenocarcinoma patients indicate a potential area for further investigation, particularly to explore the underlying mechanisms and optimize treatment regimens for this group [16].

Conclusion

In conclusion, this study underscores the critical need for a nuanced understanding of advanced lung cancer, particularly regarding the varying demographic profiles, symptom burdens, and treatment responses among different histopathological subtypes. The significant prevalence of adenocarcinoma and the marked symptom burden in small-cell lung cancer patients highlight the urgency of tailored palliative care interventions.

References

1. Ostermann, M., Ferrando-Vivas, P., Gore, C., Power, S. and Harrison, D., 2017. Characteristics and outcome of cancer patients admitted to the ICU in England, Wales, and Northern Ireland and national trends between 1997 and 2013. *Critical Care Medicine*, 45, pp.1668–1676. doi: 10.1097/CCM.0000000000002589.
2. Soares, M., Caruso, P., Silva, E., Teles, J.M.M., Lobo, S.M.A., Friedman, G. et al., 2010. Characteristics and outcomes of patients with cancer requiring admission to intensive care units: A prospective multicenter study. *Critical Care Medicine*, 38, pp.9–15. doi: 10.1097/CCM.0b013e3181c0349e.
3. Almack, K., Cox, K., Moghaddam, N., Pollock, K. and Seymour, J., 2012. After you: Conversations between patients and healthcare professionals in planning for end-of-life care. *BMC Palliative Care*, 11, p.15. doi: 10.1186/1472-684X-11-15.
4. Covinsky, K.E., Fuller, J.D., Yaffe, K., Johnston, C.B., Hamel, M.B., Lynn, J. et al., 2000. Communication and decision-making in seriously ill patients: Findings of the SUPPORT project. The Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments. *Journal of the American Geriatrics Society*, 48(S187), pp.S187-S193.
5. Golin, C.E., Wenger, N.S., Liu, H., Dawson, N.V., Teno, J.M., Desbiens, N.A. et al., 2000. A prospective study of patient-physician communication about resuscitation. *Journal of the American Geriatrics Society*, 48(S52), pp.S52-S60.
6. Detering, K.M., Hancock, A.D., Reade, M.C. and Silvester, W., 2010. The impact of advance care planning on end-of-life care in elderly patients: Randomised controlled trial. *BMJ*, 340, p.c1345. doi: 10.1136/bmj.c1345.
7. Park, I.K., Jun, H.J., Park, S.J., Lim, G.J., Cho, S.J., Song, A. et al., 2015. Differences in end-of-life care decision making between patients with and without cancer. *American Journal of Hospice and Palliative Medicine*, 32, pp.797–801. doi: 10.1177/1049909114542646.
8. Mack, J.W., Weeks, J.C., Wright, A.A., Block, S.D. and Prigerson, H.G., 2010. End-of-life discussions, goal attainment, and distress at the end of life: Predictors and outcomes of receipt of care consistent with preferences. *Journal of Clinical Oncology*, 28, pp.1203–1208.
9. Cortegiani, A., Russotto, V., Raineri, S.M., Gregoretti, C., Giarratano, A. and Mercadante, S., 2018. Attitudes towards end-of-life issues in intensive care unit among Italian anesthesiologists: A nation-wide survey. *Supportive Care in Cancer*, 26, pp.1773–1780. doi: 10.1007/s00520-017-4014-z.
10. Garrouste-Orgeas, M., Tabah, A., Vesin, A., Philippart, F., Kpodji, A., Bruel, C. et al., 2013. The ETHICA study (part II): Simulation study of determinants and variability of ICU physician decisions in patients aged 80 or over. *Intensive Care Medicine*, 39, pp.1574–1583. doi: 10.1007/s00134-013-2977-x.
11. Pardon, K., Deschepper, R., Vander Stichele, R., Bernheim, J.L., Mortier, F., Schallier, D. et al., 2012. Preferred and actual involvement of advanced lung cancer patients and their families in end-of-life decision making: A multicenter study in 13 hospitals in Flanders, Belgium. *Journal of Pain and Symptom Management*, 43, pp.515–526. doi: 10.1016/j.jpainsymman.2011.04.008.
12. Eliott, J. and Olver, I., 2008. Choosing between life and death: Patient and family perceptions of the decision not to resuscitate the terminally ill cancer patient. *Bioethics*, 22, pp.179–189. doi: 10.1111/j.1467-8519.2007.00620.x.
13. Mack, J.W., Cronin, A., Keating, N.L., Taback, N., Huskamp, H.A., Malin, J.L. et al., 2012. Associations between end-of-life discussion characteristics and care received near death: A prospective cohort study. *Journal of Clinical Oncology*, 30, pp.4387–4395. doi: 10.1200/JCO.2012.43.6055.
14. Saltbaek, L., Michelsen, H.M., Nelausen, K.M., Gut, R. and Nielsen, D.L., 2013. Old age and poor prognosis increase the likelihood of disagreement between cancer patients and their

oncologists on the indication for resuscitation attempt. *Supportive Care in Cancer*, 21, pp.3363–3370. doi: 10.1007/s00520-013-1916-2.

15. Toffart, A.C., Pizarro, C.A., Schwebel, C., Sakhri, L., Minet, C., Duruisseaux, M. et al., 2015. Selection criteria for intensive care unit referral of lung cancer patients: A pilot study. *European Respiratory Journal*, 45, pp.491–500. doi: 10.1183/09031936.00118114.
16. Mehlis, K., Becker, C., Christ, C., Laryionava, K., Hiddemann, W. and Heußner, P. et al., 2017. Frequency and timing of decisions to limit intensive medical care and tumor-specific therapy in university hematology and oncology. *Deutsche Medizinische Wochenschrift*, 142, pp.e116–e123. doi: 10.1055/s-0043-103340.