Exploratory Analysis of Survival and Mortality Rates among Older Lung Cancer Patients Utilizing Different Treatment Modalities

Abdulmajeed Alotaibi, PharmD, MS, PhD[1]; Askal Ali, PhD[2]; Clyde Brown, DrPH, MSPH[3]; Fatimah Sherbeny, PharmD, MS, PhD[4]
[1]Florida A&M University, School of Pharmacy; [2]Florida A&M University, School of Pharmacy;
[3]Florida A&M University, School of Public Health; [4]Florida A&M University, School of Pharmacy

Abstract
Objective: *To explore the impact of different lung cancer treatment modalities on survival time and mortality rates in older patients.*
Methods: *The Surveillance Epidemiology and End Results (SEER) database was used to identify lung cancer patients aged ≥50 years old in the United States. Descriptive statistics and trend charts from 2000 to 2016 were generated. Regression analysis was performed among lung cancer patients to explore the association between survival time and treatment utilization (chemotherapy, radiation, and surgery). A regression model was also applied to explore the association between treatment modalities and odds of dying.*
Results: *A total of 826,217 patients were diagnosed with lung cancer between 2000-2016. The number of lung cancer cases increased by 7%, and the average annual frequency was 48,529 cases per year. Survival, mortality, and treatment utilization varied over the years based on demographic, clinical characteristics, and social status. Five-year survival rate was less than 10% among the study population, and 84% of included lung cancer patients died. Chemotherapy was more commonly used (62%), followed by radiation (35%) and surgical interventions (22%). Chemotherapy and surgery showed a survival advantage. The odds of dying were two times higher among patients treated with surgery than those who were not (OR: 2.62, 95%Cl: 2.58- 2.67).*
Conclusion: *This study highlighted the importance of considering treatment modalities and individual patient characteristics, which may impact survival times and mortality rates among older lung cancer patients.*

Keywords: survival rate, lung cancer, treatment, mortality

Introduction

Lung cancer remains the most frequent cancer and is among the top global causes of morbidity and mortality.[1,2] In the United States, lung cancer is the second most common malignancy in men after prostate cancer and in women after breast cancer, with an incidence rate of 71.3 and 52.3 per 100,000, respectively.[3] Lung cancer is categorized into two main histopathological types: non-small-cell lung cancer (NSCLC) and small cell lung cancer (SCLC). NSCLC is the most common type and accounts for 85% of all lung cancer cases with its three subtypes, which are adenocarcinoma (ADC), squamous cell carcinoma (SCC), and large cell carcinoma (LCC).[4]

Lung cancer mortality rates in the United States closely mirror the incidence rates due to high fatality, with 51.6 and 34.4 deaths per 100,000 men and women.[3] Fortunately, the decline in smoking rates and treatment advances have resulted in a significant decline in lung cancer mortality over the past decades and is projected to further decline by 79% between 2015 and 2065.[5,6] However, the 5-year survival rate of patients diagnosed with lung cancer has only marginally improved and remains significantly low at around 20% as most patients are diagnosed in late stages.[3,7] Nearly half of the lung cancer patients in the United States are diagnosed with distant tumors, which have a particularly low 5-year survival rate of 6%, while the 5-year survival rates of localized and regional tumors are relatively higher (60% and 33%, respectively).[3,7]

Corresponding author: Fatimah Sherbeny, PharmD, MS, PhD
Assistant Professor, Florida A&M University
School of Pharmacy, East Wing Pharmacy Building
Suite # L154N; Phone: (850)-412-5712
E-mail: fatimah.sherbeny@famu.edu

Moreover, most patients are diagnosed with lung cancer at an older age. In the United States, the probability of developing lung cancer increases from 0.1% in <50-year-old males to 0.6% in 50-59-year-old, 1.4% in 60-69-year-old, and 6.0% in ≥70-year-old (the corresponding probabilities in females are 0.1%, 0.6%, 1.4%, and 4.7%).[8] Consequently, 47% of all lung cancer in the United States is diagnosed in ≥70-year-old patients.[9] Lung cancer diagnosis at an older age also complicates treatment delivery. Nearly 28% of 70–79-year-old and 47% of ≥80-year-old lung cancer patients in the United States could not be treated by surgery or radiation.[9] In comparison, only 19% of patients <70 years of age received neither surgery nor radiation therapy.[9]

While surgery is considered the most effective and curative treatment for early-stage tumors or advanced respectable lesions, it often leads to perioperative morbidity and mortality in patients with coexistent medical conditions, heart and respiratory diseases, or elderly patients.[10-13] Postoperative radiation therapy can improve local control and potentially improve the survival rate for lung cancer, but it can also cause severe toxicity. However, chemotherapy as a postoperative therapy can benefit those with resected tumors. On the other hand, radiation therapy combined with chemotherapy can give

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curative results in a small number of patients but provide palliation in most patients with NSCLC, although the results have been inconsistent reported in the literature.[14] For instance, concomitant treatment with chemotherapy and radiation (concurrent chemoradiation) did not improve overall survival in patients older than 70 years with Stage III NSCLC compared to when radiation therapy was administered following chemotherapy (sequential chemoradiation) or radiation alone.[15] On the contrary, other studies have shown a survival advantage with chemoradiation over radiotherapy alone[16,17], although sequential chemoradiation was associated with lower mortality risks relative to concurrent chemoradiation in older patients with stages IIIA and IIIB NSCLC.[16] It has been hypothesized that these inconsistency arise from varying frailty of patients recruited in different studies and that functional age and not necessarily a higher age may determine treatment tolerance and survival in elderly patients.[15]

Consequently, it is imperative to investigate factors associated with survival and mortality rates among elderly lung cancer patients utilizing different treatment modalities using data from cancer registries with large population datasets. Therefore, this study aims to explore the impact of lung cancer treatment on survival time and mortality rates using the Surveillance Epidemiology and End Results database (SEER) to help healthcare providers achieve optimal therapeutic strategies for lung cancer patients. The specific aims include: (1) Describe lung cancer patients' characteristics. (2) Describe lung cancer patients' treatment modalities and utilization from 2000 to 2016. (3) Explore how different treatment modalities, that is, chemotherapy, radiation, or surgery, affect the survival time of older patients (4) Describe the characteristics of lung cancer patients who died during the study period. (5) Determine the association between mortality with different treatment modalities.

Methods

Data Source

The SEER database of the National cancer institute (NCI), which is the only comprehensive population cancer registry in the United States covering 28% of the population, was used in this study. The details of the SEER database have been described previously.[18] Briefly, longitudinal trends of cancer diagnosis, treatment, and survival have been available from the SEER database since 1973. It includes data from 16 long-standing, high-quality, population-based registries (California [San Francisco, Los Angeles, San Jose, and Oakland], California excluding SF/SJM/LA, Connecticut, Georgia [Atlanta only], Hawaii, Iowa, Michigan [Detroit only], New Mexico, Seattle, Utah, Kentucky, Louisiana, New Jersey, and Greater Georgia.[19] A limited-use data agreement was signed to comply with the National Cancer Institute's requirements. No patient informed consent was directly obtained.

Population

Lung cancer patients were identified by using the International Classification of Diseases for Oncology (ICD-O-3/WHO 2008). Six main histologic type categories were extracted: SCLC, SCC, LCC, ADC, other specified carcinoma, and unspecified types. The morphology codes were: SCLC (8002, 8041-5); SCC (8051-2, 8070-6, 8078, 8083-4, 8090, 8094, 8120, 8123); ADC (8015, 8050, 8140-1, 8143-5, 8147, 8190, 8201, 8211, 8250-5, 8260, 8290, 8310, 8320, 8323, 8333, 8401, 8440, 8470-1, 8480-1, 8490, 8503, 8507, 8550, 8570-2, 8574, 8576); LCC (8012-4, 8021, 8034, 8082); other specified carcinoma (8003-4, 8022, 8030-3, 8035, 8200, 8240-1, 8243-6, 8249, 8430, 8525, 8560, 8562, 8575); and unspecified malignant neoplasms (carcinoma not otherwise specified [NOS] 8010-1, 8020, 8230; NSCLC 8046; malignant neoplasm NOS 8000-1).

The inclusion criteria were patients diagnosed primarily with lung cancer aged ≥50 years. Children and patients less than 50 years old, which was relatively few, were excluded from the study. Whites, Blacks, American Indian/Alaska Native, and Asian or Pacific Islanders were selected as the main ethnic group for our study. Patients whose race was unspecified or unknown were excluded. Tumor-node-metastasis (TNM) staging system was used to identify the extent of the disease. Those who had an unspecified or unknown stage at diagnosis were excluded from the study. Patients who were insured or covered by non-Medicaid (insured or insured/no specifics) or Medicaid insurance (any Medicaid) were selected. However, those with unknown insurance status were excluded from the study. The database included information from all 16 long-standing, high-quality, population-based registries.

Study Variables and Outcomes

Patients' demographic characteristics included age (50-59, 60-69, 70-79, and >80), ethnicity/race (Whites, Blacks, American Indian/Alaska Native, and Asian/Pacific Islander), and gender (male and female). Socioeconomic status included marital status (single/never married, married including common-law, separated, divorced, widowed, and unmarried/domestic partner unknown), and insurance status from 2007 (uninsured, any Medicaid, insured, and insured/no specifics). The lung cancer stage was identified as localized, regional, or distant using the TNM staging system. Histology type (adenocarcinoma, squamous cell carcinoma, small cell carcinoma, neuroendocrine carcinoma, neoplasm/malignant, carcinoma, large cell carcinoma, bronchioloalveolar adenocarcinoma, non-small cell carcinoma, squamous cell carcinoma keratinizing, and another site/histology) was based on the 2000 International Classification of Diseases for Oncology version 3 or ICD-O-3. In addition, treatment utilization or lack thereof was identified using several variables such as chemotherapy use, radiation, and surgery (yes, or no/ unknown). Vital status (alive or deceased) was also extracted, and the survival periods were classified into 0-6 months, 1-year, 2-years, 3-years, 4-years, and 5-years. Survival time was defined as the time from diagnosis to the date of death. Finally, data relating to the cause of death, including lung and bronchus malignancy, chronic obstructive pulmonary disease, heart diseases, miscellaneous malignant cancers, or other causes of death, were extracted for descriptive analysis. Our primary study outcomes were the length of survival and mortality rate.

Data Analysis

A descriptive analysis was performed to describe lung cancer patients' characteristics using Microsoft® Excel 2016. Trend analysis was performed to explore the incidence of lung cancer cases and the utilization of chemotherapy, radiation, and surgery from 2000 to 2016. The study population dataset was dichotomized based on vital status for the regression analysis. Linear regression was performed among the surviving participants to assess the association between the length of survival and treatment utilization. Independent variables assessed in the regression model include patient demographics and lung cancer characteristics such as age, gender, race, stage, histology type, and the utilization of surgery, chemotherapy, or radiotherapy treatment modalities. For histology type, we set "other histology type" as the reference group to assess if defined and undefined histological data in the SEER database affects survival outcomes. Logistic regression was performed to measure the odds of dying among lung cancer patients utilizing different treatment modalities. An analysis was performed to assess the association of demographic, clinical characteristics, and treatment utilization on mortality among patients who died during the study period. The mortality rate was calculated based on demographic characteristics (age, gender, and race) using the following formula: total number of deceased patients in the subpopulation/total number of patients living or dead in the subpopulation*100. Finally, descriptive analysis was applied to identify the secondary cause of death besides lung cancer. A p-value of < 0.05 was considered statistically significant. All statistical analysis was performed by Stata software version 16.1 (Stata Corp, College Station, TX, USA).

Results

Descriptive Analysis

We identified 826,217 patients aged ≥50 years with a lung cancer diagnosis between 2000-2016 in the SEER database. Of these 440,819 (53.35%) patients were males and 385,398 (46.65%) were females (Table 1). Lung cancer was more prevalent among patients aged 60-69 (29.44%) and 70-79-year-old (34.20%) and less prevalent among patients aged 50-59 (15.25%) and >79-year-old (21.12%). White patients comprised the majority of the patients accounting for (83.47%) of the population, followed by Black patients (10.54%), Asian or Pacific Islander (5.33%), and American Indian/Alaska Native (0.48%) (Table 1). Half of the population diagnosed with lung cancer were married (50%), followed by widows (22%), then single and divorced patients with 11% for each group (Table 1). Separated and unmarried domestic partners had the lowest prevalence, with only 1% prevalence (Table 1). Overall, 65.37% of patients had specified insurance, Medicaid covered 13.27%, 19.02% had unspecified insurance, and 2.34% were uninsured (Table 1).

Overall, the prevalence of lung cancer increased by approximately 7% from 2000 to 2016, with an annual average frequency of 48,529 cases per year (Figure 1). However, the trends of lung cancer prevalence among males were stable from 2000 to 2016, with the average annual percent change (APC) of -0.10±1.70% (Figure 2). In contrast, year-by-year prevalence among females increased throughout the study period with an average annual percent change of 1.14±1.63% (Figure 2). More importantly, the annual prevalence gap between genders decreased consistently throughout the study period from 22.26% in 2000 to 5.32% in 2016 (Figure 2).

Lung Cancer Clinical Characteristics

More than half of the cases were diagnosed with distant lung cancer (52%), while the percentages of localized, regional, and un-staged tumors were 18%, 22%, and 8%, respectively (Table 1). NSCLC comprises most lung cancer cases (54.75% for adenocarcinoma, squamous cell carcinoma, large cell carcinoma, squamous cell carcinoma keratinizing, bronchioalveolar adenocarcinoma and unspecified non-small cell carcinoma combined) compared to SCLC (11.45%). NSCLC was further categorized into subtypes: From 2000 to 2016, the cases included in our analysis had a higher proportion of adenocarcinoma (30.54%), followed by squamous cell carcinoma (17.95%), large cell carcinomas (1.94%), and bronchioloalveolar adenocarcinoma (1.91%) (Table 1).

Treatment Utilization

The most utilized treatment for lung cancer between 2000 to 2016 was chemotherapy (62%), followed by radiation (35%) and surgery (22%) (Figure 3). The annual average frequency of chemotherapy, radiation, and surgery was 512,038, 17,064, and 10,554 during the study period. The percentage of chemotherapy patients showed year-by-year fluctuation (APC=0.07±2.08%) and peaked in 2009 with 30,814 patients (Figure 3). Substantial changes in the percentage of patients treated with chemotherapy were observed in 2004 (-4.37%), 2006 (3.91%), and 2010 (-3.25%) from the preceding year (Figure 3). In contrast, the percentage of patients receiving radiation dropped each year between 2000 and 2005 and has consistently increased between 2005 and 2016, and as a result, the APC (0.49±2.62%) only marginally changed during the entire study period (Figure 3). The percentage of patients receiving surgery declined in 2003 sharply by 18.15% from the preceding year, while the trend has been fluctuating considerably since 2003, with relatively large changes noted in 2006 (4.41%), 2010 (-4.16%), and 2016 (3.26%) from the preceding year (APC through the study period for surgery=-0.39±5.13%) (Figure 3).

The number of patients receiving a combination of chemotherapy with radiation accounted for 23% of the population (Figure 4). On the other hand, most patients who received chemotherapy did not receive or refused radiation therapy (77%), while those who received radiation but did not use chemotherapy accounted for 56% (Figure 4). Out of 798,313 patients for whom data on surgery was available (for

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27,904 patients, it was unknown if surgery was performed or not and were, therefore, excluded from the analysis), only 16% had a surgical intervention with radiation therapy, while most of the participants (84%) had surgery and did not receive radiation therapy (Figure 5). Around 42% had radiation therapy refused/did not perform the surgery (Figure 5). Patients who neither received surgery nor chemotherapy accounted for 43% of the study population (Figure 6). Postoperative or preoperative chemotherapy was administered in 75% of the cases (Figure 6).

Furthermore, early-stage (localized and regional) lung cancer was mainly treated with surgical intervention (57% and 38%, respectively). However, the surgical rate significantly dropped to 5% in the distant stage. In contrast, chemoradiation was more frequent in patients with distant tumors (37%) (Figure 7).

Mortality-related outcomes

Out of the 826,217 patients included in this study, 692,467 died, representing 83% of the total population. Among the study population, the primary cause of death was lung cancer (79.01%). The most common secondary causes of death were cardiovascular diseases (4.08%), followed by other cancer (3.18%), chronic obstructive pulmonary diseases (2.93%), and other causes of death combined accounted for 10% of all deaths (Table 2). While the mortality rate increased with age from 79.07% in 50-59-year-old patients to 90.76% in those aged >79-year-old, males had a higher mortality rate than females (86.51% vs. 80.85%, respectively) (Table 2). We also observed a higher mortality rate among Blacks and Whites (84.14% and 84.92%), while Asian/Pacific Islanders had the lowest mortality rate (77.43%) (Table 2). Among the 91,183 surviving patients, the 6-month, 1-year, 2-years, 3-years, 4-years and 5-years survival rates were 26.54%, 14.92%, 21.62%, 15.46%, 11.84% and 9.61% respectively (Table 2).

Association Between Survival Rate and Treatment Modalities Among Lung Cancer Patients

For the linear regression, data from 132,307 patients who were alive were extracted from the total study population. The survival period was the primary predictor in our regression analysis. The independent variables in the linear regression model included demographic, clinical, and treatment modalities. All parameters had a significant association (*p*-value<0.05) with the length of survival (Table 3). Based on gender, females had prolonged survival compared to males, while older age groups had worst survival outcomes compared to the 50–59-year-old reference group (Table 3). All ethnicity/race groups (Black, American Indian/Alaska Native, and Asian/Pacific Islander) had substantially lower survival periods than Whites (Table 3).

Further, the prognosis of patients with regional and distant stage lung cancer was significantly worse than that of patients with localized lung cancer, while patients with un-staged lung cancer had higher odds of prolonged survival (Table 3). Also, there was a significant association between all defined histology types of lung cancer and the survival period compared to other histology (Table 3). Further, our linear regression model showed that patients who did not receive chemotherapy or surgery had worst survival outcomes compared to patients treated with chemotherapy or surgery, respectively, while those who received radiation had an exacerbated survival outcome compared to patients not receiving radiation therapy (Table 3).

Association Between Mortality Rate and Treatment Modalities Among Lung Cancer Patients

For the logistic regression, vital status was the dependent variable. The association between the odds of dying among lung cancer patients utilizing different treatment modalities was analyzed after controlling for demographic variables, lung cancer characteristics, and treatment modalities. Demographic variables were significantly associated with mortality (Table 4). Mortality odds increased with age. Older patients aged >79 years had over two times the odds of dying compared to younger patients aged 50-59 years (OR: 2.09, CI: 2.04-2.14) (Table 4). On the other hand, females were less likely to die than males (OR: 0.69, CI: 0.68-0.70). Based on ethnicity/race, all groups, including Black, American Indian/ Alaska Native, and Asian/Pacific Islanders, were less likely to die than Whites [OR (95%CI): 0.97(0.94-0.99), 0.87(0.79-0.96), and 0.56(0.54 – 0.57), respectively] (Table 4).

In terms of lung cancer characteristics, patients with more advanced lung cancer stages, such as regional and distant tumors, had two to five times higher odds of dying [OR (95%CI): 2.23(2.19-2.27) and 5.84(5.72-5.95), respectively) compared to patients with localized tumors (Table 4). Also, histological types of lung cancer were significantly associated with mortality (Table 4). Patients diagnosed with large cell carcinoma were five times more likely to die due to lung cancer (OR: 5.04, 95%CI: 4.71-5.38), followed by neuroendocrine carcinoma (OR: 3.55, 95%CI: 3.44-3.67) compared to “other” histological type. Based on treatment modalities, chemotherapy, radiation, and surgery were significantly associated with mortality (Table 4). Patients who received radiation had lower odds of dying than patients who did not (OR: 0.82, 95%CI: 0.81-0.84). Also, patients who received surgery were less likely to die due to lung cancer. In fact, the odds of dying were two times higher among the patients who did not perform surgery (OR: 2.63, 95%CI: 2.58-2.67). However, chemotherapy was not associated with lower odds of dying among lung cancer patients.

Discussion

The present epidemiological study highlights the differences in survival time and mortality of older lung cancer patients based on their demographic and clinical profiles. We observed a prolonged survival time and lower mortality rates among females compared to males, while older patients had worst survival and mortality outcomes compared to 50-59-years-old patients. The trends in survival time of patients with lung cancer observed in our study are consistent with pre-2000 trends in the United States. Fry *et al.* analyzed lung cancer diagnoses in the National Cancer Database between 1985 and 1995 and reported better 5-year survival among patients who were females, of younger age at diagnosis, or Hispanic and non-Hispanic white.[20]

In general, lung cancer is more prevalent in males than females. This has been primarily attributed to a higher smoking prevalence among males.[21] It is important to note that the prevalence of smoking among females peaked in the 1960s while daily cigarette consumption among women peaked in the 1980s in the United States—an entire decade after males—but the gender gap in smoking prevalence and daily cigarette consumption has been decreasing in the past two decades.[22] In line with these historical trends, we observed a narrowing gender gap in lung cancer incidence from 2000 to 2016. However, despite this narrowing gender gap, our analysis indicated longer survival time and lower mortality risk among female lung cancer patients, consistent with an earlier meta-analysis of studies from the United States that showed an improved survival rate among females across all stages with low heterogeneity.[23]

Further, ethnic and racial differences in lung cancer mortality have been widely reported. For instance, lower smoking-related lung cancer mortality has been reported among Asian populations compared to Western countries.[24] This phenomenon has been termed the "smoking paradox" and has largely been attributed to epidemiological factors such as the age of initiation and amount of cigarette consumption.[24] Even within the United States, Hispanics and Asians have lower lung cancer mortality, while African Americans and Caucasians have similar mortality risks.[23] However, in our study, although Black, Asian, or Pacific Islanders and American Indian/Alaska Native had a shorter survival time than White participants, we noted a lower mortality risk among these minority ethnic groups. In addition, although Black males are more likely to be diagnosed with advanced cancers than whites[25], it is noteworthy that our study cohort predominantly comprises White patients (83.48%).

Gender and ethnic/racial factors are strongly associated with the histological types of lung cancer and the clinical prognosis of patients. An earlier analysis of the SEER database showed that adenocarcinomas are the predominant histological type[25,26], as also observed in our study cohort (33.54%), with increasing incidence across gender and ethnic/racial groups between 1973 and 2010 while squamous, large and small cell carcinoma rates continue to decrease for all racial and gender groups.[25] In our analysis, patients with defined histological features, that is, NSCLC (including adenocarcinomas), SCLC, neuroendocrine carcinoma, neoplasm, or carcinoma, had prolonged survival time, albeit with higher mortality risk compared to patients with other sites/histological presentation. This is in line with pre-2000 trends in the United States, where patients with squamous cell, adenocarcinoma, large cell carcinoma, or sarcoma had similar or better 5-year survival compared to other/unknown histological presentation.[20] However, in the earlier study, patients with SCLC had the worst survival outcomes compared to other/unknown histological presentation.[20]

Further, we observed that patients with unstaged cancer had prolonged survival time while those with regional and distant cancers had a poorer survival time than those with localized cancer. However, patients in all cancer stages had higher mortality risks than patients with localized lung cancer. Although cancer-directed treatment generally favored better 5-year survival rates, the treatment advantage was minimal with higher cancer staging.[20] Moreover, 5-year survival rates varied substantially depending on histological presentation. For instance, the 5-year survival rates among patients with Stage II adenocarcinoma treated with surgery, radiation therapy, or a combination of the two were 32%, 5%, and 30%, respectively.[20] Similarly, the 5-year survival rates among patients with Stage II SCLC treated with chemotherapy or chemoradiotherapy were 4% and 13%, respectively.[20]

Notably, nearly 98% of our study population were insured and were, therefore, more likely to receive cancer-directed surgery and radiation therapy, as demonstrated in previous studies.[27] A recent meta-analysis of studies from the United States showed that surgery was associated with the most significant survival benefit among lung cancer patients with a two-thirds reduction in mortality risk, and while radiation and chemotherapy were also associated with improved prognosis, the effect size was smaller with high heterogeneity.[23] Consistent with these earlier observations, we noted that patients undergoing surgical resection had prolonged survival and lower mortality risk. However, patients who were not treated with chemotherapy/refused chemotherapy had a shorter survival time than those who were. We hypothesize that this may be because most chemotherapy patients were diagnosed with extensive stage lung cancer. Surprisingly, patients not treated with chemotherapy also had lower mortality risks. Since the mortality rate was measured among the original data, which mainly consisted of deceased patients, chemotherapy's mortality rate contradicts the linear regression readings. In contrast, recipients of radiation therapy had a shorter survival time but lower mortality risks.

An earlier analysis of the SEER database by Lu et al. reported relatively stable surgical rates at around 25%, a downward trend for radiotherapy, and increased use of chemotherapy for lung cancer patients in the United States between 1973 and 2015.[26] In contrast, our analysis from 2000 to 2016 showed that surgery and chemotherapy utilization was stable, while radiation therapy utilization increased during the study period. This contrasting trend may be attributed to the fact that we specifically recruited older patients while Lu et al. reported data

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from all age groups. As demonstrated by Dalwadi et al., some treatment modalities can be replaced in older age groups.[28] For example, radiation therapy has replaced surgery as the most used modality for early-stage NSCLC in older patients. The treatment of the elderly diagnosed with lung cancer is challenging, and it will remain an obstacle for the health care sector in the United States. However, using different treatment modalities might improve the survival rates. For instance, Lee et al. examined the survival rate in patients treated with different therapeutic strategies for NSCLC and demonstrated that radiofrequency ablation could be used as an alternative treatment to surgery with a better survival rate at 12, 24, and 60 months in patients with inoperable stage I to II NSCLC.[29] Similarly, in elderly patients with stage III NSCLC, combined modality therapy with chemoradiation improved overall survival compared with radiation alone.[30] In addition, sequential therapy appears to have a survival advantage over concurrent therapy. However, the linear regression analysis did not examine the combination therapeutic approach for lung cancer. It also did not indicate whether the patients were treated with neoadjuvant or adjuvant chemotherapy.

The present study of long-term survivors indicates that cardiovascular diseases, chronic obstructive pulmonary disease, and other malignancies were common secondary causes of death other than lung cancer. Although the reasons for this are not fully elucidated, it is likely that some of these diseases share common risk factors and that lung cancer or cancer treatment increases the risks of other diseases. For instance, Kanitkar et al. indicated that the secondary cause of death after heart disease was the existence of other malignancies and that elderly male patients older than 65 years who underwent surgical resection for lung cancer faced a higher risk of dying of other causes.[31]

Implications

While the 5-year survival rate of lung cancer in the overall population is relatively low at 20%,[3,7] we observed an even lower survival rate of 10% in our study population of older patients. Although advancing age decreases the odds of survival, the lower survival rate in our study population may also be attributed to late diagnosis and the decision to forgo curative therapy and opt for palliative care, thereby affecting the survival and mortality trends with chemotherapy, radiation therapy and surgery as observed in this study. These trends highlight the critical implication of lung cancer screening in the older, at-risk population to leverage the advances in treatment and improve overall survivability. Given that the national cancer screening in the United States only marginally increased from 3% in 2010 to 5% in 2018 among eligible individuals[7], in March 2021, the US Preventive Services Task Force recommended expanding the eligibility criteria for screening to include all 50-80-year-old adults with a 20 pack-year history from the previous age bracket of 55-80 years and 30-pack-year smoking history.[32]

Limitations

There are some limitations to our study. First, there is an inherent risk of selection bias by the non-random allocation of interventions, the risk of coding errors, and missing data in any large database study. However, the data collection process of SEER databases is well-validated, and we used a relatively large sample size. Second, our findings are only relevant to older patients. The impact of treatment modalities on survival and mortality outcomes in younger age groups warrants separate investigation. Third, the findings of this retrospective observational study are hypothesis-generating and warrant confirmation in future prospective trials. Fourth, although Cox regression models may provide better analysis of time-to-event outcomes, given the retrospective nature of this study[33,34], the lack of clearly defined follow-up data[33,34], and that 52% of the study population had distance cancer and therefore lower survival rate than other stages, we have used logistic regression in this study. Fifth, we could not include relevant pre-patient covariates such as smoking history, clinical covariates such as genetic mutations and targeted therapy, or whether the patients received adjuvant or neoadjuvant therapy due to database limitations. However, recent studies associate adjuvant and neoadjuvant therapies with only modest benefits, and this exclusion is unlikely to affect the validity of our findings dramatically.[35] Lastly, although the worst prognosis can be expected among patients in advanced stages, we did not assess the effects of treatment modalities on different stages of lung cancer, given our study's descriptive and exploratory focus. Additionally, the concurrent or sequential use of different treatment modalities may have important prognostic implications, and these limitations need to be addressed in future outcome-focused research.

Conclusion

This study provided an exploratory overview of lung cancer in older patients in the United States over 17 years. Lung cancer incidence, mortality, and treatment utilization varied based on age, gender, race, clinical characteristics, and social status. We noted a narrowing gender gap in lung cancer prevalence while patients aged 70-79-year-old were disproportionately affected. Chemotherapy was more commonly used among lung cancer patients during the study period, followed by radiation, then surgical interventions. Based on the regression analysis, chemotherapy and surgery showed a survival advantage. In addition, patients who had surgery and radiotherapy had a lower mortality risk than those who did not. However, regardless of medical innovations and improvements in treatment modalities, the 5-year survival rate of lung cancer was less than 10% among the study population. Overall, 84% of the patients diagnosed with lung cancer during the study period had died, and cardiovascular disease was the most common cause of death besides lung cancer. The findings of this study highlight the importance of considering individual patient characteristics and managing existing health conditions among lung cancer patients that may impact their disease progression and survival rates. These findings can inform decision-making and help health care professionals to optimize patient safety and improve treatment protocol.

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Conflict of Interest: None

The opinions expressed in this paper are those of the author(s).

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Table 1: Patients' characteristics

Variables	Patients with Lung Cancer Diagnosis (%) *n*=826,217
Gender	
Male	53.35%
Female	46.65%
Age	
50-59	15.25%
60-69	29.44%
70-79	34.20%
>79	21.12%
Race/Ethnicity	
White	83.47%
Black	10.57%
Asian or Pacific Islanders	5.33%
American Indian/Alaska Native	0.48%
Marital Status	
Single	11%
Married	50%
Separated	1%
Divorced	11%
Widowed	22%
Unmarried	1%
Unknown	5%
Insurance status	
Uninsured	2.34%
Any Medicaid	13.27%
Insured	65.37%
Insured/No specifics	19.02%
Lung cancer stage	
Localized	18%
Regional	22%
Distance	52%
Unknown	8%
Lung cancer histological type	
Adenocarcinoma (NSCLC)	30.54%
Squamous cell carcinoma (NSCLS)	17.95%
Large cell carcinoma (NSCLC)	1.94%
Squamous cell carcinoma keratinizing (NSCLC)	1.18%
Bronchioalveolar adenocarcinoma (NSCLC)	1.91%
Unspecified non-small cell carcinoma (NSCLC)	1.23%
Small cell carcinoma (SCLC)	11.45%
Neuroendocrine carcinoma	10.60%
Neoplasm/Malignant	7.63%
Carcinoma/NOS	6.74%
Other sites/histology	8.83%

Table 2: Mortality and survival rate of patients with lung cancer based on demographic characteristics

Variables	Mortality (%) *n*=692,467
Gender	
Male	86.51%
Female	80.85%
Age	
50-59	79.07%
60-69	80.38%
70-79	84.75%
>79	90.76%
Race/Ethnicity	
White	84.14%
Black	84.92%
Asian or Pacific Islanders	77.43%
American Indian/Alaska Native	84.19%
Primary causes of death	
Lung cancer	79.01%
Other malignancies	3.18%
Heart disease	4.08%
Chronic obstructive pulmonary disease	2.93%
Other causes of death	10.8%
Survival rate (*n*=91,183)	
6-months	26.54%
1-year	14.92%
2-years	21.62%
3-years	15.46%
4-years	11.84%
5-years	9.61%

Table 3: Linear regression analysis of length of survival by demographic and clinical characteristics of lung cancer patients

Survival Months	Coefficient [95% Confidence Interval]	P>t
Gender		
Female vs Male	2.86 [95%CI (2.39 – 3.34)]	<0.001
Lung Cancer Stage		
Regional vs. Local	-1.73 [95%CI (-2.33 – -1.12)]	<0.001
Distance vs. Local	-10.19 [95%CI (-10.96 – -9.43)]	<0.001
Un-staged vs. Local	6.98 [95%CI (5.3 – 8.67)]	<0.001
Age		
60-69 vs. 50-59	-9.12 [95%CI (-9.77 – -8.47)]	<0.001
70-79 vs. 50-59	-17.7 [95%CI (-18.38 – -17.03)]	<0.001
>79 vs. 50-59	-24.33 [95%CI (-25.21 – -23.45)]	<0.001
Race		
Black vs. White	-4.06 [95%CI (-4.84 – -3.27)]	<0.001
American Indian/Alaska Native vs. White	-5.48 [95%CI (-8.89 – -2.07)]	0.002
Asian or Pacific Islander vs. White	-3.49 [95%CI (-4.39 – -2.6)]	<0.001
Histology		
Adenocarcinoma vs. Other histology	2.89 [95%CI (2.23 – 3.55)]	<0.001
Squamous cell carcinoma vs. Other histology	4.36 [95%CI (3.58 – 5.14)]	<0.001
Small cell carcinoma vs. Other histology	7.2 [95%CI (5.99 – 8.4)]	<0,001
Neoplasm/Malignant vs. Other histology	22.79 [95%CI (21.53 – 24.05)]	<0.001
Carcinoma vs. Other histology	4.75 [95%CI (2.97 – 6.53)]	<0.001
Large cell carcinoma vs. Other histology	14.08 [95%CI (12.34 – 15.82)]	<0.001
Bronchioloalveolar adenocarcinoma vs. Other histology	43.4 [95%CI (40.78 – 46.02)]	<0.001
NSCLC vs. Other histology	43.22 [95%CI (41.87 – 44.56)]	<0.001
Neuroendocrine carcinoma vs. Other histology	11.2 [95%CI (9.06 – 13.33)]	<0.001
Squamous cell carcinoma keratinizing vs. Other histology	2.56 [95%CI (0.33 – 4.79)]	0.025
Treatment		
Did not receive chemotherapy vs received chemotherapy	-2.43 [95%CI (-3.06 – -1.81)]	<0.001
Received radiation vs. did not receive radiation	-0.74 [95%CI (-1.39 – -0.1)]	0.023
Did not perform surgery vs performed surgery	-29.5 [95%CI (-30.2 – -28.81)]	<0.001

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Table 4: Mortality odds ratio of patients with lung cancer

Variables	Odds Ratio [95% Confidence Interval]	P>z
Gender		
Female vs. Male	0.69 [95%CI (0.68 – 0.70)]	<0.001
Race		
Black vs. White	0.97 [95%CI (0.94 – 0.99)]	0.002
American Indian/ Alaska Native vs. White	0.87 [95%CI (0.79 – 0.96)]	0.004
Asian or Pacific Islander vs. Whites	0.56 [95%CI (0.54 – 0.57)]	<0.001
Age		
60-69 vs. 50-59	1.16 [95%CI (1.14 – 1.19)]	<0.001
70-79 vs. 50-59	1.59 [95%CI (1.56 – 1.62)]	<0.001
>79 vs. 50-59	2.09 [95%CI (2.04 – 2.14)]	<0.001
Lung Cancer Stage		
Regional vs. Local	2.23 [95%CI (2.19 – 2.27)]	<0.001
Distance vs. Local	5.84 [95%CI (5.72 – 5.95)]	<0.001
Un-staged vs. Local	3.9 [95%CI (3.74 – 4.07)]	<0.001
Histology Type		
Adenocarcinoma vs. Other histology	1.27 [95%CI (1.24 – 1.29)]	<0.001
Squamous cell carcinoma vs. Other histology	1.86 [95%CI (1.82 – 1.91)]	<0.001
Small cell carcinoma vs. Other histology	2.59 [95%CI (2.51 – 2.68)]	<0.001
Neuroendocrine carcinoma vs. Other histology	3.55 [95%CI (3.44 – 3.67)]	<0.001
Neoplasm/Malignant vs. Other histology	2.32 [95%CI (2.22 – 2.43)]	<0.001
Carcinoma vs. Other histology	3.25 [95%CI (3.11 – 3.39)]	<0.001
Large cell carcinoma vs. Other histology	5.04 [95%CI (4.71 – 5.38)]	<0.001
Bronchioloalveolar adenocarcinoma vs. Other histology	1.7 [95%CI (1.64 – 1.78)]	<0.001
NSCLC vs. Other histology	1.47 [95%CI (1.39 – 1.56)]	<0.001
Squamous cell carcinoma keratinizing vs. Other histology	2.25 [95%CI (2.11 – 2.39)]	<0.001
Treatments		
Did not received chemotherapy vs. received chemotherapy	0.71 [95%CI (0.7 – 0.72)]	<0.001
Not performed surgery vs. Preformed surgery	2.63 [95%CI (2.58 – 2.67)]	<0.001
Received radiation vs. did not radiation	0.82 [95%CI (0.81 – 0.84)]	<0.001

Figure 1: The prevalence of lung cancer cases among older adults, 2000-2016

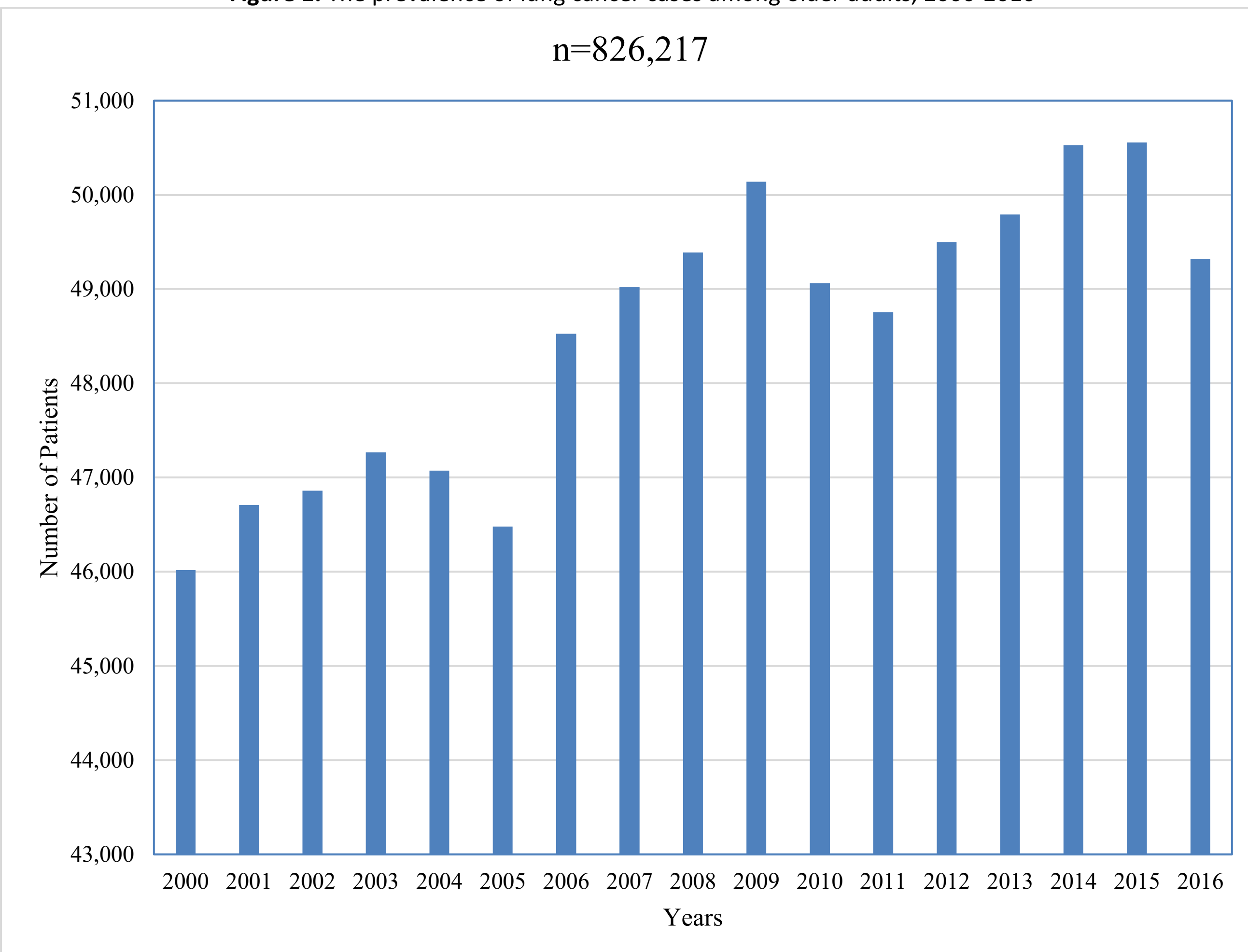

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Figure 2: Lung cancer trends among older adults by gender from 2000-2016
The year-to-year difference in the prevalence of lung cancer between males and females is shown as percentages

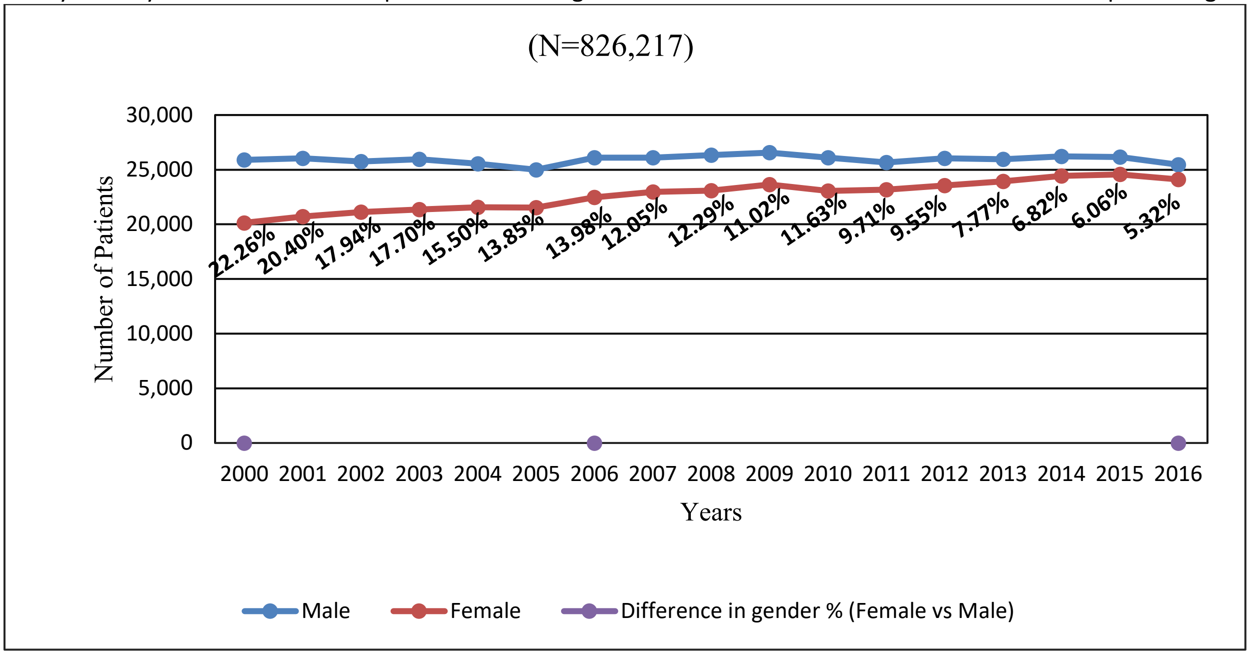

Figure 3: Treatment utilization for lung cancer among older adults, 2000 to 2016. The change in the rate of patients receiving surgery, radiation, or chemotherapy from the preceding year is shown in percentage

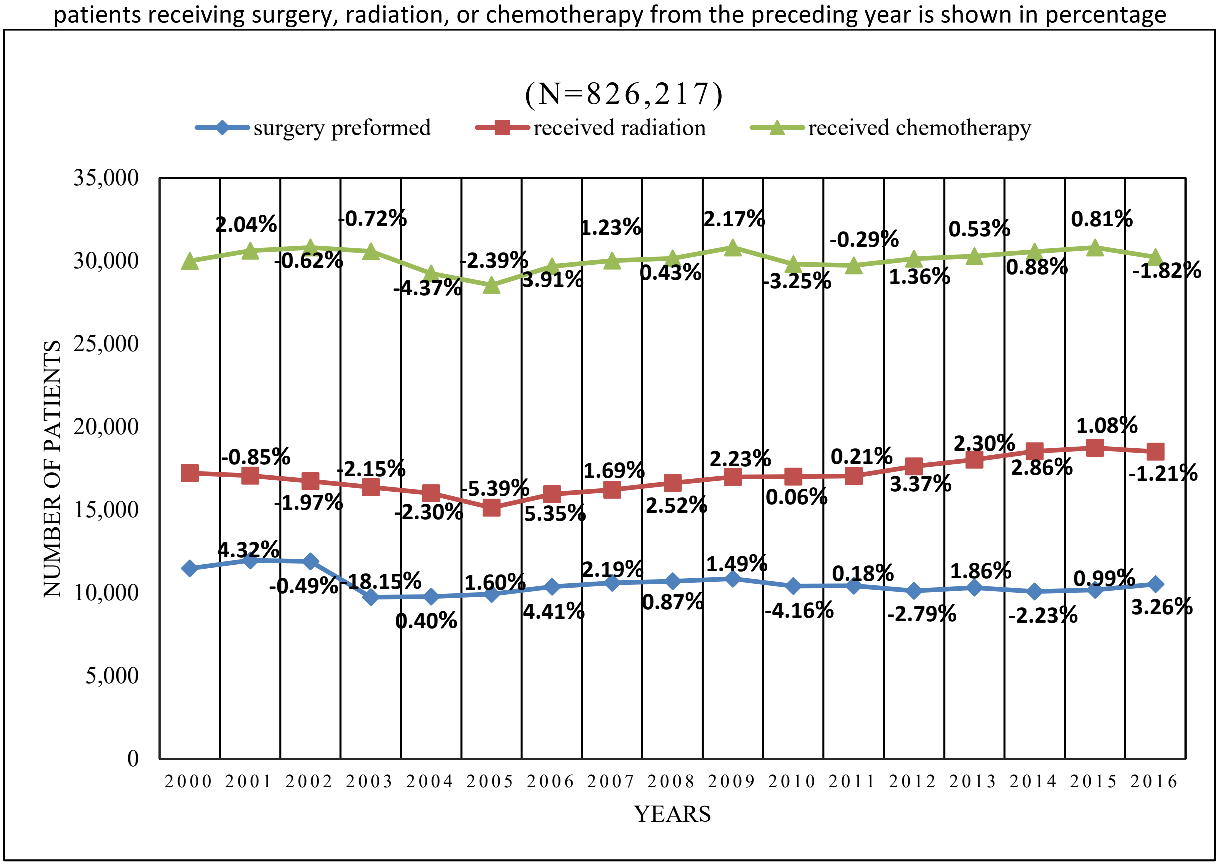

Figure 4: Chemotherapy and radiotherapy utilization among older adults, 2000-2016

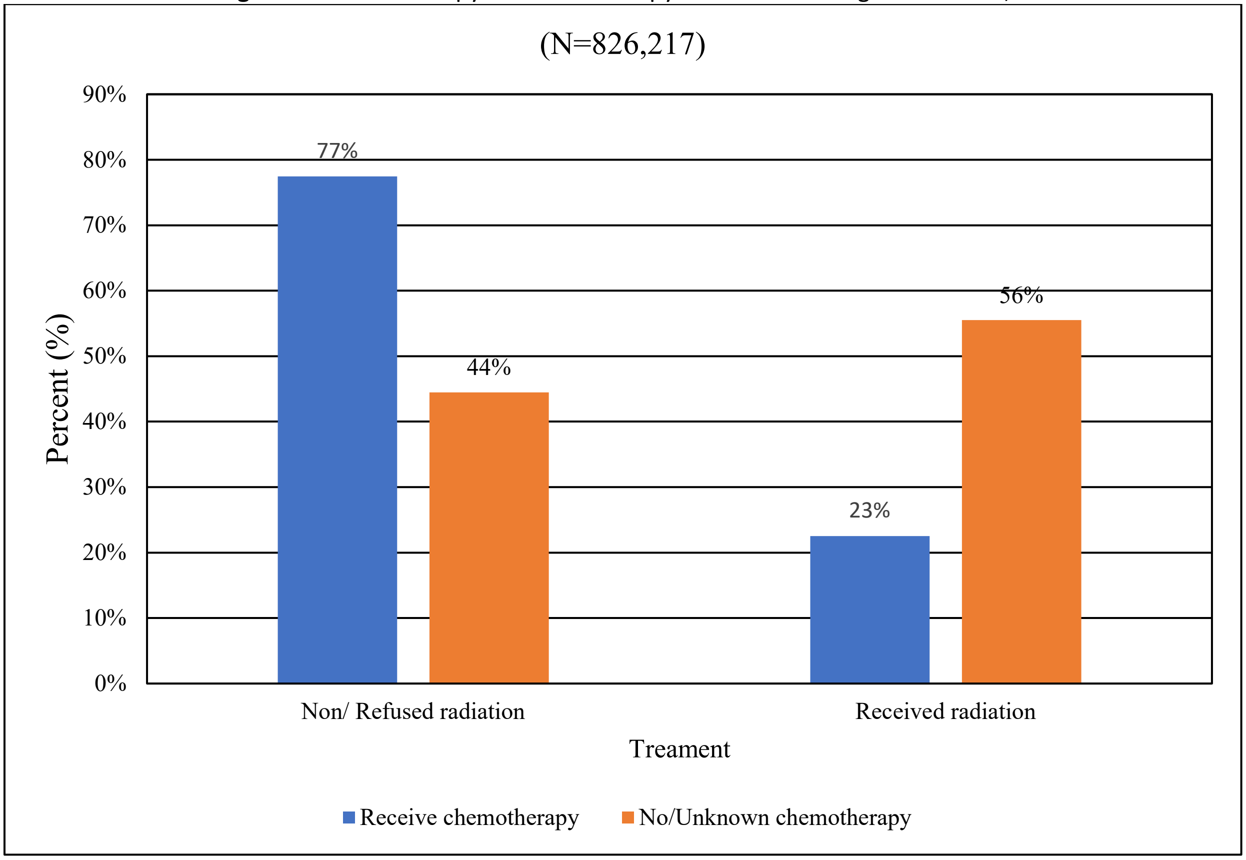

Figure 5: Surgery and radiotherapy utilization among older adults, 2000-2016

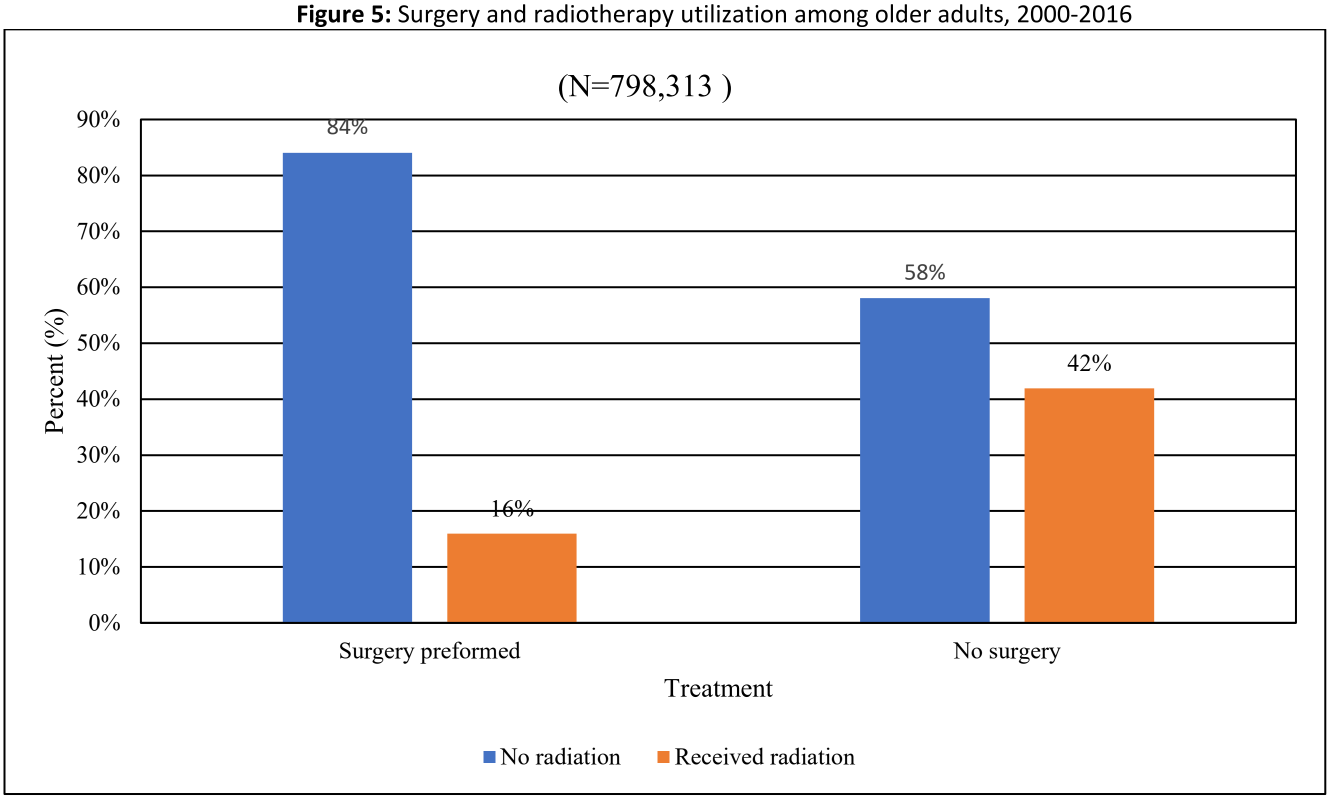

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Figure 6: Surgery and Chemotherapy utilization among older adults, 2000-2016

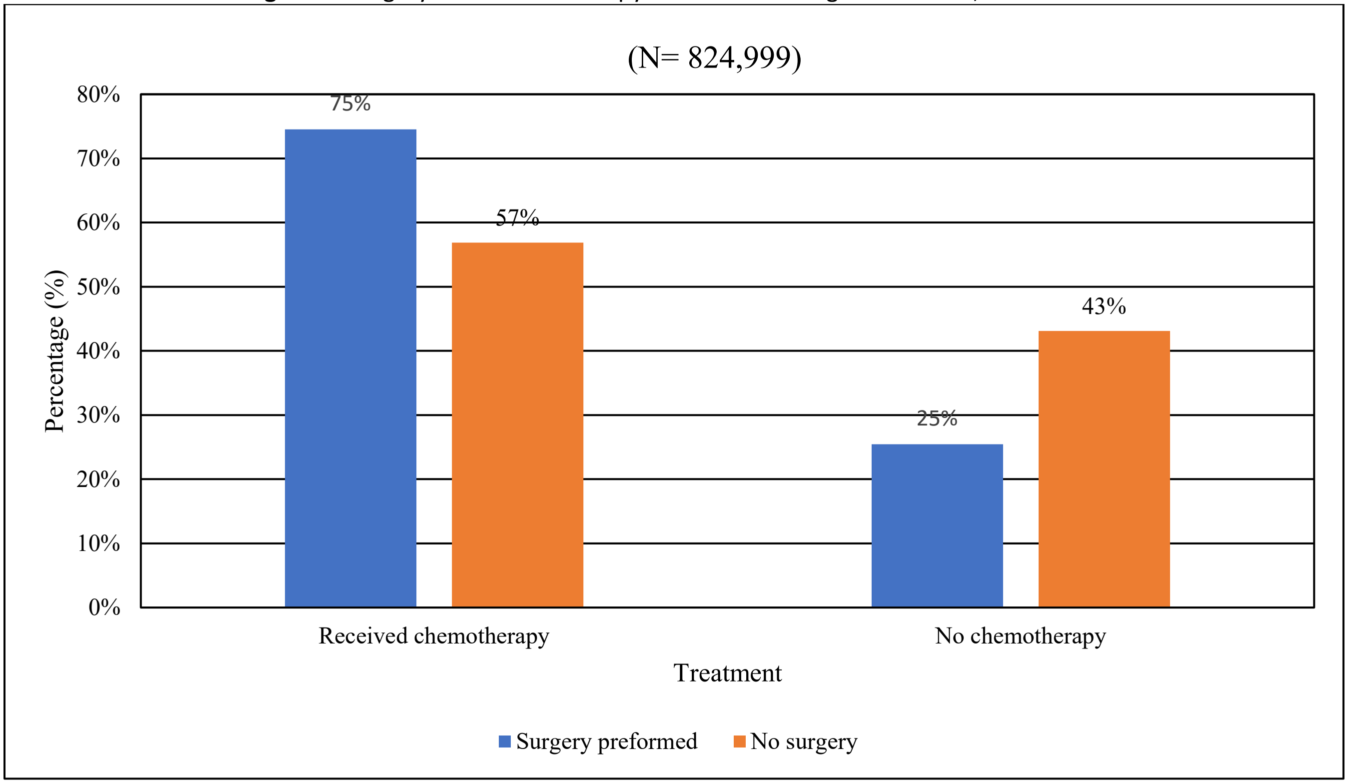
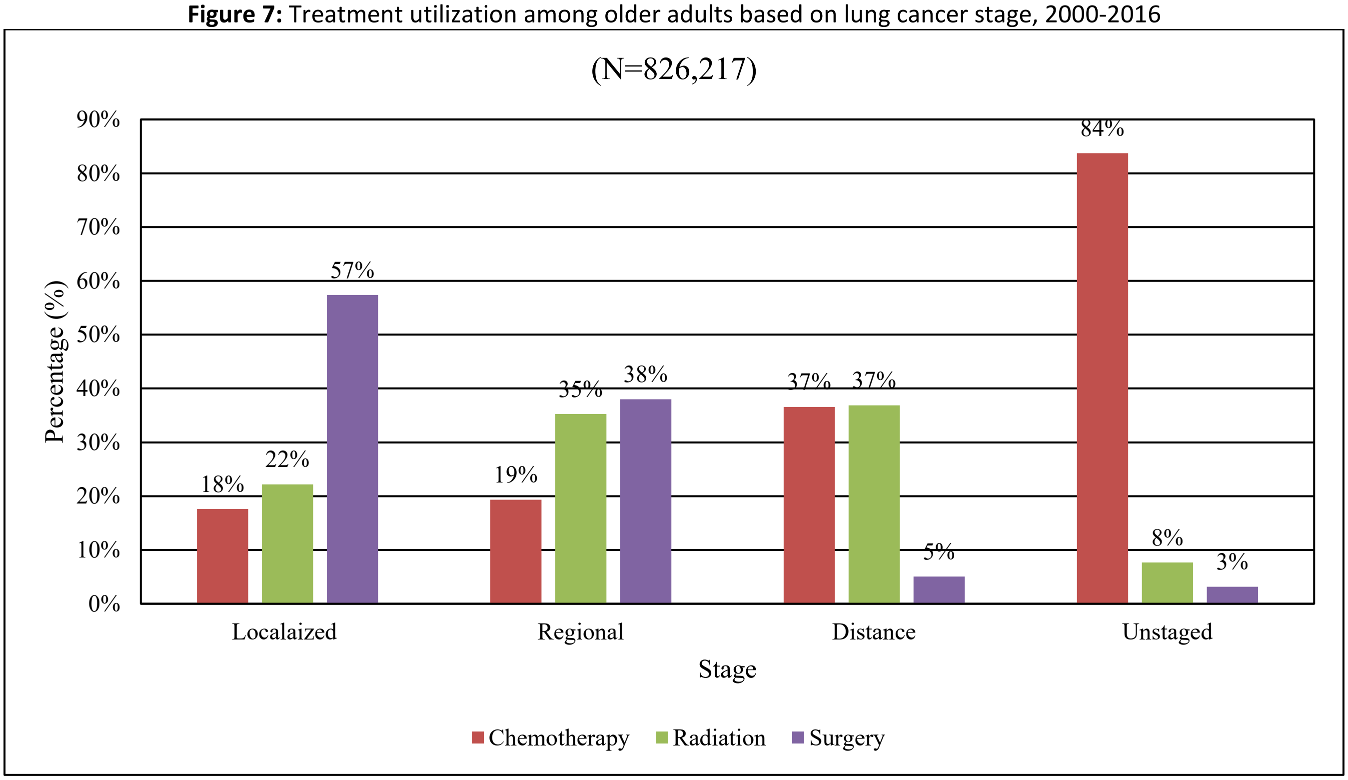


Figure 7: Treatment utilization among older adults based on lung cancer stage, 2000-2016



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