A Review: Epidemiology and Risk Factors of Lung Cancer patients in Thailand

[1*]Ananya Sirisomboon, [2]Gwinlada Tayanun, [3]Nithikorn Tanskul,
[4]Surangpimol Puedtapongpaphanij, [5]Thanique Sirisoonthornphibul,
[6]Chottanin Teerakomolwit & [7]Justin Chatpaisankun
[1]Satriwithaya School, Bangkok
[2]Demonstration School of Phranakhon Si Ayutthaya Rajabhat University, Phranakhon Si Ayutthaya
[3]Bangkok International Preparatory & Secondary School, Bangkok
[4]Assumption College Sriracha, Bangkok
[5]Chulalongkorn University Demonstration Secondary School, Bangkok
[6]Mahidol University International Demonstration School, Bangkok
[7]Nakhon Sawan School, Nakhon Sawan
*Corresponding author: ananya.19m@gmail.com

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Abstract

Lung cancer is a prominent cause of cancer-related mortality globally, with increasing incidence and mortality rates in Thailand. This review delves into the epidemiology and risk factors associated with Small Cell Lung Cancer (SCLC) and Non-Small Cell Lung Cancer (NSCLC) in Thailand. In 2021, lung cancer accounted for 17.9% of all cancer-related deaths, with a rising trend in incidence observed between 2012 and 2022. SCLC, characterized by its aggressive nature, constituted 4.5% of all lung cancer cases in Thailand between 2016 and 2021. Notably fatal, SCLC exhibited a higher mortality rate than NSCLC, with distinct survival rates in limited and extensive stages. NSCLC, comprising various subtypes, dominated the lung cancer landscape in Thailand, with adenocarcinoma being the most prevalent.

The review emphasizes smoking as a primary risk factor for lung cancer, despite a decline in smoking prevalence. Radon exposure, especially in upper-northern Thailand, emerges as a significant contributor to lung cancer incidence, with a notable proportion of deaths linked to indoor radon exposure. Additionally, air pollution, characterized by PM 2.5 and other pollutants, is implicated in lung cancer development, mirroring global trends.

This comprehensive review underscores the critical need for targeted interventions to address the rising burden of lung cancer in Thailand. Efforts should focus on smoking cessation programs, radon exposure mitigation, and air quality improvement to curb the escalating rates of lung cancer and enhance public health outcomes. Ongoing research and surveillance are crucial for refining preventive strategies and advancing our understanding of the complex interplay between environmental factors and lung cancer in the Thai population.

Keywords: Lung cancer epidemiology; Small Cell Lung Cancer (SCLC); Non-Small Cell Lung Cancer (NSCLC)

Background

Lung cancer is ranked as a leading cause of cancer-related mortality in several countries (Molina et al, 2008). There were more than 2.2 million new cases of lung cancer in 2020. In Asia, lung cancer with 59.0% of all illnesses and 21.0% of all mortality (Chhikara and Parang, 2023; Huang et al, 2022) has become a major health problem including Thailand. It was a common type of cancer found in the country. There were 122,757 new cases of lung cancer, divided into 48.6% males and 51.4% females in Thailand 2014 (National Cancer Institute (Thailand), 2018). In 2021, the mortality rate of lung cancer in Thailand was 17.9% of all cancer patients, including 63.9% males and 36.1% females (Vichapat et al, 2023). During 2012 to 2022, incidence trends of lung cancer climbed by 40.0% and 31.0%, among males and females, respectively (Virani et al, 2017).

There were two major categories of lung cancers: small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). About 15.0% of all lung cancers were SCLC (Rudin et al, 2021) and it was the more fatal type of lung cancer due to its rapid growth and spread (Wang et al, 2022). NSCLC was much more common, accounting for 80.0-90.0% of lung cancer patients (Reungwetwattana et al, 2020).

A number of lung cancer factors, smoking was one of the main risk factors. Long-term heavy smokers were tend to have SCLC. Other factors were high amounts of exposure to second-hand smoke, air pollution such as PM 2.5, radon gases, genetic susceptibility, improper diet, occupational exposures and much more (Pallis and Syrigos, 2013; Malhotra et al, 2016).

Consequently, the objective of this review is to describe the epidemiology and risk factors associated with two major categories including small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC) in Thailand.

The results of the literature review

This academic article is a systemic review or coping review of research related to the epidemiology and risk factors of lung cancer patients in Thailand. The review encompasses research articles published since 2002 that were disseminated through

the database of MEDLINE®, Springer, Google Scholar, and ScienceDirect. The search was conducted using keywords such as Lung Cancer, lung cancer worldwide, Lung Cancer in Thailand, Rick factor of Lung cancer, Lung Cancer and Air Pollution, Radon and Lung Cancer, Lung Cancer Incidence and Mortality, Small-cell lung cancer, Non-small cell lung cancer. Additionally, searches were made through books and various academic documents.

Upon reviewing research articles, it was found that there were a total of 100 research articles. Non-relevant research articles were excluded, leaving 47 articles. Among these articles, types of studies were Lung cancer, Statistics, Effects of rick factor in Lung cancer, Incidence rate survival rate, mortality rate, Treatment

LUNG CANCER IN THAILAND

Small Cell Lung Cancer

Small cell lung cancer (SCLC) is a cancer that develops quickly and aggressively in lung tissue and has the potential to spread to other organs. Looking at the cancer cells under a microscope reveals that they are tiny and oval-shaped. (PDQ Adult Treatment Editorial Board, 2002) SCLC accounting for 15.0% of all patients worldwide (Rudin et al, 2021). Approximately 250,000 patients were diagnosed with having SCLC each year globally, of which approximately 200,000 succumb to the disease (Reitsma et al, 2021). From lung cancer in United States of America were approximately 227,875 incidental lung cancer cases worldwide in 2020, with SCLC constituting approximately 14.0% of them (Paz-Ares et al, 2019; Huang et al, 2022).

In Thailand, six years of study between 2016 to 2021 found that SCLC patients accounted for approximately 4.5% of all lung cancer cases, divided into 2.7% males and 1.8% females (Benjakul et al, 2022). Mortality from SCLC would be higher than NSCLC (Siddiqui et al, 2023) by total deaths in United States of America, 69.5% of SCLC deaths occurred within the first years after diagnosis, 26.0% of SCLC deaths occurred from 1 to 3 years, and 4.5% of SCLC deaths individuals survived longer than 3 years (Wu et al, 2022). Post diagnostic survival rates in periods of 1 and 3 years in patients with lung cancer of the SCLC type were 27.9% and 11.6% respectively (Musika et al, 2021). It will

be seen that Thailand, like the United States, had an increased trend of SCLC mortality compared to treatment duration at diagnosis. The results of SCLC patient data analysis were divided into a limited stage with median overall survival 17.1 ± 3.9 months and an extensive stage with median overall survival, 6.7 ± 1.3 months (Kittiwarawut and Bunthaowong, 2014).

Non-Small Cell Lung Cancer

Non-small cell lung cancer (NSCLC) is a term that includes many different types of cancer such as adenocarcinoma, squamous cell carcinoma, and large cell carcinoma. The most prevalent type of NSCLC is adenocarcinoma, and Squamous cell carcinoma. Squamous cell carcinoma (SCC) normally originates from the tracheobronchial tree, but there are more and more cases appearing at the periphery of the lung. (Basumallik and Agarwal, 2023) Next is large cell carcinoma, most cases will show squamous glandular, or neuroendocrine differentiation. Around 80-85% of all lung cancer cases are NSCLC. From 62 cases of NSCLC studied in Thailand 67.7% were adenocarcinoma type (Supavavej et al, 2021). Adenocarcinoma is a malignant neoplasm arising from epithelial cells of the glands or glandular like structures. Adenocarcinoma can arise in multiple sites of the body. Some of the common sites that develop adenocarcinoma are the breast, lung, prostate, gastrointestinal tract like the colon, rectum, pancreas, stomach, esophagus. Adenocarcinomas also make 70 percent of cancer of unknown origin (Mullangi & Lekkala, 2024). All these subtypes start as different types of lung cells grouped together as NSCLC and due to the striking similarities between the different types, they are hard to distinguish (Siddiqui et al, 2023). From 2010 to 2017 there were 1.28 million new NSCLC cases in worldwide (Clark and Alsubait, 2023; Ganti 30et al, 2021).

Prevalence between younger patients increased while decreased for older patients, which shows that patients 65 years or above had a slimmer likelihood to be treated, earlier detection could increase the chance of NSCLC being treated (Clark and Alsubait, 2023). The median of survival for NSCLC was 11 - 12 months in adenocarcinoma group, 7.4 months for squamous cell carcinoma group (Supavavej et al, 2021). For comparison the prevalence of NSCLC in men and women respectively in Thailand is 31.0

and 10.1 patients per 100,000 (Chang et al, 2018). In a larger scale Asian country such as China the rate is much higher as 43.4% for men and 37.1% for women (Fan et al, 2015).

RISK FACTORS OF LUNG CANCER IN THAILAND

A risk factor is anything that increases the chances of someone getting a disease, such as lung cancer. Generally, risk factors for lung cancer are consistent worldwide, including Thailand, such as smoking (Malhotra et al, 2016). Lung Cancer can occur in non-smokers too, as the patient may have been exposed to other factors such as radon gas and more (Hecht, 2012).

The prevalence of lung cancer in the 20th century soared due to cigarette smoking, a primary contributor to the epidemic. Despite efforts, rates remain high, underscoring the need for significant reductions in smoking to curb this trend. Secondhand smoke exposure, particularly during childhood, also correlates with a small percentage of cases. While certain dietary factors like antioxidant-rich fruits and vegetables may offer protection, supplements like carotenoids show inconsistent effects, and some foods like cured meats may increase risk. Additionally, moderate to heavy alcohol consumption slightly raises lung cancer risk. Conversely, regular physical activity is linked to decreased risk, especially among heavy smokers. Long-term exposure to urban air pollution and occupational hazards such as silica dust and asbestos also contribute to lung cancer development. Genetic factors, particularly gene variations like TP53 and EGFR, further predispose individuals to the disease, with recent studies identifying markers associated with increased risk, potentially affecting nicotine addiction (Yaser et al, 2023). And another factor that may be considered another cause of lung cancer is family history of illness. That may determine the risk status of disease. (Yaser et al, 2023; Yin et al, 2021)

Small Cell Lung Cancer

- Tobacco Smoke

In tobacco smoking, it is the carcinogens within them that cause lung cancer. However, nicotine is a key component in tobacco smoke, as it is what causes smokers

to be addicted to smoking, but it is not a cause of lung cancer. To further clarify, the results of studies showed that nicotine causes other effects such as increased cell proliferation, stimulation of cancer cell growth, and more. Other studies also show that nicotine does not induce cancer (Hecht, 2012; Murphy et al, 2011). There are over 70 carcinogens in tobacco smoke that shows carcinogenicity in either laboratory animals or humans by the IARC Monographs (IARC, 2004). A well-known example of a carcinogen is tar. Tar is the sticky-brown substance that collects in lungs when tobacco smoke is inhaled. It contains many cancer-causing chemicals, which increases the risk of lung disease. In simple terms, tar and other carcinogens cause genetic mutations of the delicate cells' DNA inside of our lungs. These healthy cells in the lung will change and grow out uncontrollably, forming a tumor, a lesion, or a nodule. For small cell lung cancer, it begins in the neuroendocrine cells, which are the nerve cells or hormone-producing cells of the lung (Basumallik and Agarwal, 2023). In Thailand, smoking prevalence had decreased from 60.0% to 39.0% in males and 5.0% to 2.1% in females between 1991 and 2014. However, lung cancer incidence been increasing in Thailand since the 1990s, and this can explain that the high number of smokers before the 1990s have now developed lung cancer as they are now at an older age (Chang et al, 2018). There is also a pattern where, as the incidence of small cell lung cancer patients by smoking increases, the mortality rate increases (Chhikara and Parang, 2023). In the United States of America, smoking prevalence among US adults has decreased from 42.4% in 1965 to 13.7% in 2018. Lung cancer also has the highest incidence in developing countries where cigarette smoking has the most prevalence, and the leading cause of cancer mortality worldwide (Thandra et al, 2021).

- Radon

Radon exposure is considered the second cause of lung cancer and the first among non-smokers (Rodríguez-Martínez et al, 2018). Radon is a noble gas produced by the decay of the Uranium found in soil and rocks of the earth crust. The amount of radon gas worldwide varies, depending mostly on the Uranium content of the bedrocks where buildings are present (Rodríguez-Martínez et al, 2022). Radon when inhaled is mostly immediately exhaled, but inhaled progenies as solid particles are able to readily

deposit on the walls of the bronchial epithelium, where it delivers most of the radiation dose. Radon emits alpha radiation particles that is connected to cytotoxic and genotoxic effects, and may cause damage in the cell lining of the lung. Certain studies have shown a link between radon exposure and p53, ALK or EGFR alterations (which causes mutations and chromosomal rearrangements in the lungs (Riudavets et al, 2022; Ruano-Ravina et al, 2016; Ruano-Ravina et al, 2009). For small cell lung cancer, indoor radon increased the risk of lung cancer by 31.2% per 100Bq m^{-3} and 2.6% compared to other subtypes of lung cancer in 13 different European case-control studies. The indoor radon concentration of 192 participant bedrooms in the eight provinces of upper-northern Thailand is ranged from 11 to 405 Bq m^{-3}, with a mean of 105 ± 74 Bq m^{-3} (Somsunun et al, 2022) which is higher than both the global average of 39 Bq m^{-3} (World Health Organization, 2009) and the mean of 16 Bq m^{-3} in Thailand (International atomic energy agency, 2013). In upper-northern Thailand, 553 lung cancer deaths yearly was linked to indoor radon exposure between 2015 and 2019. In all of Thailand in 2012, 1660 deaths of lung cancer was linked to indoor radon exposure. This means a third of deaths linked to indoor radon exposure occurred in upper-northern Thailand (Gaskin et al, 2018). In Spain and its regions, 3.8% (838 deaths) of lung cancer mortality was linked to radon exposure of over 100 Bq m^{-3}.

- Air pollution

From current information there are no reports indicating of DNA mutations occurring in the lungs from air pollution in non-smokers. However, they found that air pollution exposure in mice and humans results in an inflammatory response involving interleukin-1beta (IL1B) that transforms lung epithelial cells into a progenitor stem cell state. If the stem cell has the EGFR or KRAS mutation, there is an increased risk of a tumor being initiated (Hill et al, 2023). The tumor may then start growing and result in lung cancer. In Urban U.S cities and around the world, air pollution is increasing. In California, a study focusing a group of 350,000 people found that people who lived in highly polluted areas are more likely to develop all types of lung cancer (Eckel et al, 2016). Similarly in Thailand, Air pollution in Thailand is a serious health threat, especially in the northern region. High levels of particulate matter (PM2.5 and PM10) are strongly

linked to severe health consequences and mortality. Air pollution is a chronic problem particularly in the northern region of Thailand. Farmers burn fields to clear land every year during the dry season, and there is also a higher risk of wildfires due to the vegetation type and climate. According to the Pollution Control Department (PCD1) of Thailand, the highest daily average of particulate matter concentrations during the haze period. from the Health Data Center (HDC3) of Ministry of Public Health in 2020 was about 588,808 cases and the incidence rate was 10,564.61 per 100,000 people. The highest number of diseases caused by air pollution were respiratory diseases equal to an incidence rate of 4124.86 per 100,000 people (Supasri et al, 2023). Also in South Korea, air pollution is linked to almost one quarter of lung cancer cases, with the highest rates of lung cancer in densely populated urban areas (Lamichhane et al, 2017).

Conclusion

In Thailand, lung cancer, encompassing both small cell (SCLC) and non-small cell (NSCLC) types, presents a significant public health challenge mirroring global trends. SCLC, despite its lower prevalence, is characterized by aggressive progression and high mortality rates, while NSCLC, particularly adenocarcinoma, dominates in incidence. Smoking remains a primary risk factor, although environmental exposures like radon and air pollution also play substantial roles, especially among non-smokers. Addressing these multifactorial influences requires comprehensive tobacco control measures, environmental regulations, and targeted interventions for high-risk populations. Efforts should focus on early detection, prevention strategies, and innovative treatments to alleviate the burden of lung cancer and improve outcomes in Thailand.

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