Original Article

Prevalence of Coronary Artery Calcification in Non-ECG Gated Staging Chest CT Scans of Patients with Primary Lung Cancer

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Abstract

Introduction: Patients with primary lung cancer have an elevated risk of cardiovascular disease, which requires further assessment. In which, a non-ECG-gated chest CT scan performed for lung cancer staging may be used to reveal coronary artery calcification.

Objective: The objective of this study was to determine the prevalence of coronary artery calcification using a non-ECG gated staging chest CT scan in patients with primary lung cancer.

Methods: A retrospective review of fifty-one patients with primary lung cancer and at least one staging chest CT was carried out from May 1, 2020, to August 31, 2021, in Thammasat University Hospital. The prevalence of coronary artery calcification identified on the non-ECG gated staging chest CT was documented. Coronary artery calcium scores were analyzed using automated computerized software, employing the Agatston method. The association between coronary artery calcium scores and established cardiovascular disease risk factors, including age, sex, smoking behavior, systolic blood pressure, diabetes mellitus, and serum low-density lipoprotein level was examined.

Results: The observed prevalence of coronary artery calcification on non-ECG gated staging chest CT scans was 74.5%. The median coronary artery calcium score was 46.03, with an inter-quartile range (IQR) of 0-259.81. Thirteen patients did not have coronary artery calcification, twenty-five patients had coronary artery calcium scores equal to or less than 300, and thirteen patients had scores greater than 300. No significant association was identified between coronary artery calcium scores and cardiovascular disease risk factors.

Conclusions: Patients with primary lung cancer have a high prevalence of coronary artery calcification, and coronary artery calcium scores can be calculated from non-ECG gated staging CT chest scans.

Keywords: Coronary artery calcification, Coronary artery calcium score, Agatston method, Primary lung cancer.

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Introduction

Primary lung cancer is a major health concern in Thailand, representing 12.4% of all cancer cases.[1] Risk factors include cigarette smoking, exposure to air pollution, chemical substances, and a family history of lung cancer. Previous studies have shown that patients with primary lung cancer have a higher risk of developing cardiovascular disease compared to the general population.[2-3] The environmental and lifestyle risk factors that raise lung cancer risk are closely similar to those of cardiovascular disease, especially smoking.[2] In addition, the mechanisms linking atherosclerosis with cancer include chronic inflammation, oxidative stress, telomere length modifications, and clonal hematopoiesis.[8] Therefore, it is important to assess patients with primary lung cancer for cardiovascular disease in addition to their cancer.

The Thai cardiovascular risk score is a tool used to predict the risk of cardiovascular disease in the Thai population based on several risk factors, including age, gender, systolic blood pressure, cholesterol levels, history of diabetes mellitus, and smoking status. According to the Royal College of Physicians of Thailand Dyslipidemia Clinical Guideline published in 2016 (2016 RCPT),[4] statin therapy is recommended for individuals with high LDL cholesterol (equal to or greater than 190 mg/dL), familial hypercholesterolemia, or a Thai cardiovascular risk score greater than 10%. However, even primary lung cancer patients without clinical atherosclerotic cardiovascular disease should be evaluated for evidence of atherosclerosis due to their high incidence of coronary artery calcifications and increased cardiovascular mortality after surviving cancer, as shown in previous studies.[2-3]

The coronary artery calcium score is a non-invasive metric that uses a specialized non-contrast chest computed tomography (CT) scan to detect and measure the amount of calcium present in the coronary arteries, and in the reference article: either a cardiac-gated electron-beam CT scanner or a multidetector CT system was used.[5] The primary method for quantifying the coronary artery calcium score is the Agatston method. This method involves a weighted sum of the area of calcified plaques in the coronary arteries, adjusted for the size and density of the plaques. A score above 300 is strongly associated with a high risk of cardiovascular disease.[6-7] According to the 2016 RCPT, patients with a Thai

cardiovascular risk score below 10% but evidence of subclinical atherosclerosis such as a coronary calcium score above 300 Agatston units, an ankle-brachial index below 0.9, a family history of premature cardiovascular disease, or chronic inflammatory conditions may benefit from considering low- to moderate-intensity statin therapy. This approach is suggested for individuals with an LDL-C level below 190 mg/dL and no diabetes, aiming for an LDL-C target below 130 mg/dL or at least a 30% reduction from baseline levels.[4]

Routine chest CT scans are used for staging primary lung cancer. In additon to staging cancer, these chest CT scans can also be used to assess coronary artery calcification, indicating the risk of cardiovascular disease. This assessment can play a crucial role in determining the most appropriate treatment and follow-up care. ECG-gated chest CT scans with 2.5-mm slice thickness reconstruction are generally recommended for coronary artery calcium scoring.[8-9] However, some studies have suggested that non-ECG gated chest CT scans with 1-mm slice thickness may also be sensitive for detecting coronary artery calcium.[7]

The aim of this study was to determine the prevalence of coronary artery calcification in patients with primary lung cancer using a non-ECG gated staging chest CT scan.

Methods

The study was carried out with the approval of the Human Ethics Committee of Thammasat University, under the Certificate of Approval 284/2021.

Study population

The data from patients who were diagnosed with primary lung cancer for the first time and had a staging chest CT scan at Thammasat University Hospital from May 1, 2020, through August 31, 2021, were retrospectively collected and reviewed. The inclusion criteria were as follows: (a) patients who had primary lung cancer, including small cell lung cancer and non-small cell lung cancer, (b) a staging chest CT scan was performed (c) the medical records and pathological results were accessible through the hospital information system (HIS). The exclusion criteria were as follows: (a) unavailable imaging data for calculating a coronary artery calcium score using Philips IntelliSpace Portal software, (b) unavailable data for calculating a Thai

cardiovascular risk score, and (d) patients with a history of coronary artery intervention.

Out of the initial one hundred six cases with primary lung cancer, fourteen cases were excluded due to unavailable imaging data for calculating a coronary artery calcium score, thirty-seven cases were excluded due to a lack of data to calculate a Thai cardiovascular risk score, and four cases had coronary artery stents. Ultimately, fifty-one cases were eligible for our study.

This study has a relatively small sample size due to the limited number of primary lung cancer patients that meet both requirements: imaging data suitable for retrospective measurement of the Agatston score and data available for computing a Thai cardiovascular risk score. As a result, the findings may have reduced statistical power and could be subject to bias when generalized to the overall population.

Imaging technique and processing

A non-ECG gated non-contrast staging chest CT scan was performed using a Philips 256-slice scanner. Images were acquired with a slice thickness of 1.0 mm through the region of the coronary arteries during held inspiration.

Imaging interpretation

The chest CT scan images and coronary artery calcium scores were retrospectively reviewed by a radiology resident and a radiologist with 2 years of experience. All chest CT scan images were collected from the Philips IntelliSpace Portal and reviewed. The data for coronary artery calcium scores was analyzed by an automated computerized software program using the Agatston method.[8-9] The patients were categorized into three groups: coronary artery calcium scores of 0, equal to or less than 300, and greater than 300.[8-9] The number and location of affected coronary arteries was also recorded.

Clinicopathological evaluation

Patient clinical information was collected from electronic medical records, including age, sex, smoking status, systolic blood pressure, diabetes mellitus, and serum low-density lipoprotein. The Thai cardiovascular risk scores were calculated. Histopathological data was retrieved from histopathological reports and separated into two

groups: small cell lung cancer and non-small cell lung cancer.

Data analysis and statistics

Descriptive statistics were reported as mean with standard deviation or median with interquartile range (IQR) for continuous data, and count with percentage for categorical data. Multiple linear regression analyses were used to determine the association between coronary artery calcium scores and established cardiovascular disease risk factors. The statistical analyses were performed using Stata/SE 14.0 software. All statistical analyses were two-sided, with significance assigned at a P-value of less than 0.05.

Results
Patient characteristics and histopathological results

The demographic data, clinical characteristics, and histopathological results of the patients are shown in Table 1. This study recruited a total of fifty-one patients, with twenty-four patients (47.1%) being male and twenty-seven patients (52.9%) being female, with a mean age of 66.8 years. A history of smoking was recorded in twenty-two patients (43.1%), and eighteen patients (35.3%) had underlying diabetes mellitus. Systolic blood pressure and LDL cholesterol were recorded in all patients, with a mean of 137.9 mmHg and 109 mg/dL, respectively.

The analysis of patient medical records identified six patients (11.8%) with a Thai cardiovascular risk score of less than 10%, while forty-five patients (88.2%) had a Thai cardiovascular risk score equal to or greater than 10%. Additionally, a history of statin use was recorded in thirty-one patients (60.8%), of whom two patients had low Thai cardiovascular risk scores, and twenty-nine patients had high Thai cardiovascular risk scores. Among patients with Thai cardiovascular risk scores of less than 10%, no one had a coronary artery calcium score greater than 300.

Among our study patients, adenocarcinoma was the most common histopathological subtype, accounting for forty-six cases (90.2%). Squamous cell carcinoma was the second most common subtype, representing 3 cases (5.9%), followed by small cell carcinoma and round cell carcinoma, both accounting for one case each (2.0% and 2.0%).

Table 1 Demographic and data characteristics

Characteristics	Number (n = 51)
Age (years), mean ± SD	66.8 ± 9.99
Sex	
- Male, n (%)	24 (47.1)
- Female, n (%)	27 (52.9)
History of smoking, n (%)	22 (43.1)
History of DM, n (%)	18 (35.3)
SBP (mmHg), mean ± SD	137.9 ± 20.8
LDL (mg/dL), mean ± SD	109 ± 40.9
Thai cardiovascular risk score	
- < 10%, n (%)	6 (11.8)
- ≥ 10%, n (%)	45 (88.2)
Statin use, n (%)	31 (60.8)
Lung cancer subtype	
- Adenocarcinoma, n (%)	46 (90.2)
- Small cell carcinoma, n (%)	1 (2.0)
- Squamous cell carcinoma, n (%)	3 (5.9)
- Round cell, n (%)	1 (2.0)

Note: DM = diabetes mellitus; SBP = systolic blood pressure; LDL = low density lipoprotein.
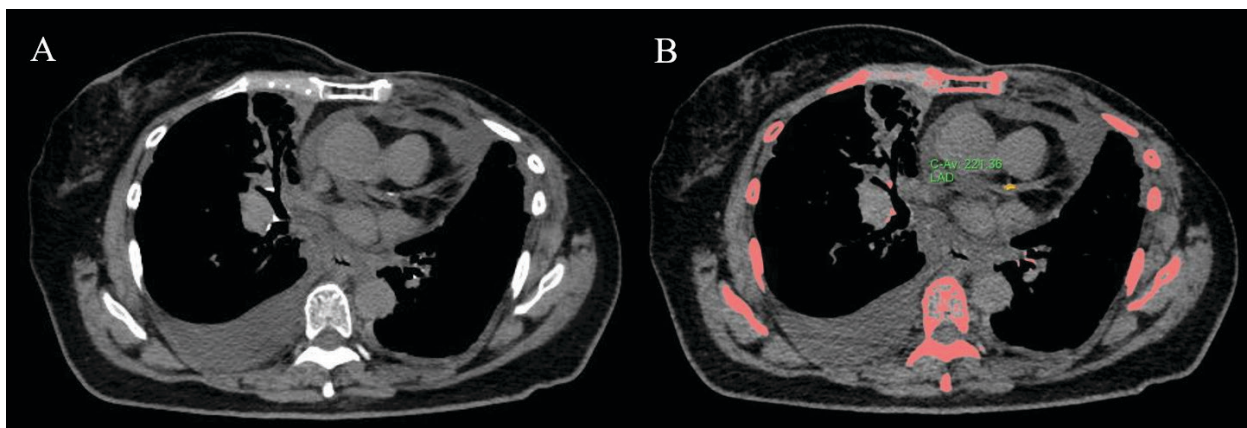
Coronary artery calcification

The coronary artery calcium score was determined in all study patients and is shown in Table 2. An example of a case is shown in Figure 1. The prevalence of the coronary artery calcification was 74.5%, with a median coronary artery calcium score of 46.0. Thirteen patients had no coronary artery calcification, twenty-five patients had coronary artery calcium scores equal to or less than 300, and thirteen patients had coronary artery calcium scores greater than 300. The analysis revealed that thirty-three patients had calcification in the left anterior descending artery (LAD), twenty-two patients had calcification in the left circumflex artery (LCX), twenty patients had calcification in the right coronary artery (RCA), nine patients had calcification in the left main coronary artery (LM), and one patient had calcification in the ramus intermedius artery (RI). Additionally, among the thirteen patients classified as high risk for cardiovascular disease based on their coronary artery calcium score (> 300), three patients (23%) were not taking statins.

The results of cardiovascular disease risk factors associated with the coronary artery calcification score in multiple linear regression analysis are listed in Table 3. The study found that there was no association between the coronary artery calcium scores and any of the cardiovascular disease risk factors that were examined in this study.

Table 2 Coronary artery calcification

Coronary artery calcification	Number
Prevalence of coronary artery calcification (%)	74.5%
Coronary artery calcium score (Agatston units), median (IQR)	46.0 (0-259.8)
- 0, n (%)	13 (25.5)
- ≤ 300, n (%)	25 (49.0)
- > 300, n (%)	13 (25.5)
Number of vessel involvement	
- LAD, n (%)	33 (64.7)
- LCX, n (%)	22 (43.1)
- RCA, n (%)	20 (39.2)
- LM, n (%)	9 (17.6)
- RI, n (%)	1 (2.0)

Note: LAD = left anterior descending artery; LCX = left circumflex artery; RCA = right coronary artery; LM = left main coronary artery; RI = ramus intermedius artery and IQR = interquartile range.

Figure 1 Non-ECG gated non contrast chest CT scan showed a calcified plaque in the proximal LAD (A). Coronary artery calcium scores were analyzed with an automated, computerized software program using the Agatston method (B).

Table 3 Multiple linear regression analysis of the association of cardiovascular disease risk factors with coronary artery calcium scores

Parameters	t	P-value	95% CI
Age	0.63	0.530	-388.3; 743.9
Sex	1.29	0.205	-7.7; 34.8
Smoking	-0.82	0.419	-812.2; 343.8
DM	0.30	0.764	-395.0; 534.3
SBP	-1.22	0.230	-15.8; 3.9
LDL	0.49	0.626	-4.2; 6.9

Note: SBP = systolic blood pressure; DM = diabetes mellitus and LDL = low density lipoprotein.

Discussion

In this study, we reported the prevalence of CT-evaluated coronary artery calcification as indicators of atherosclerotic plaques in patients with primary lung cancer. Coronary artery calcification was identified in 74.5% of all patients, with 25.5% having coronary artery calcium scores greater than 300, indicating a severe to extensive amount of coronary artery calcification. This is consistent with a previous report by S. Cuddy et al.,[3] that used non-contrast CT images to detect coronary artery calcium in early-stage non-small cell lung cancer patients and showed that 109 of 138 patients (80%) have coronary artery calcification. Similarly, E. Koutroumpakis et al.[11] reported a prevalence of severe to extensive coronary artery calcium scores ($\geq$ 300) equal to 36% when evaluating 193 patients with non-small cell lung cancer treated with concurrent chemoradiotherapy. These results support the association between primary lung cancer and coronary artery calcification, suggesting that patients with primary lung cancer may have an increased risk of cardiovascular disease. Our study also found that three patients (23%) in the group classified as high risk for cardiovascular disease, having a coronary artery calcium score > 300, were not receive statin therapy for primary prevention. It is important for physicians to consider this potential risk when treating and monitoring patients with primary lung cancer.

In the general population, several risk factors for coronary artery calcification are aligned with those for clinical cardiovascular disease, including age, male sex, hypertension, smoking, diabetes mellitus, and cholesterol levels.[12-13] In several studies, the majority of cases of coronary artery calcification were detected in older patients with lung cancer.[3, 1, 14] Our results showed similar findings, with a high incidence of coronary artery calcification (74.5%) and a mean patient age of 66.8 years. Additionally, systolic blood pressure was slightly elevated in the study population, with a mean of 137.9 mmHg. According to the report by McAvoy et al.,[15] coronary artery calcification in patients undergoing evaluation for orthotopic liver transplantation was strongly associated with systolic blood pressure and fasting glucose. However, our results from multiple linear regression analysis did not find a significant association between coronary artery calcium scores and any of the cardiovascular risk factors examined in this study. This discrepancy may be due to differences in the patient population, sample size, or other factors in study design.

There were several limitations in this study. Firstly, a retrospective design was used, which could potentially introduce selective bias. Secondly, the sample size was relatively small due to the limited number of patients with primary lung cancer and the requirement for patients to have imaging data suitable for retrospectively determining Agatston score and Thai cardiovascular risk score. Further studies involving larger populations and prospective data collection are necessary to validate our findings. Thirdly, coronary artery calcium scores calculated from staging chest CT scans were not verified with ECG-gated chest CT to assess score validity.However, non-ECG gated CT imaging results in a lower radiation dose for patients compared to an ECG-gated CT, and is a standard procedure for primary lung cancer patients.

In conclusion, we determined that patients with primary lung cancer exhibit a high prevalence of coronary artery calcification, increasing their risk of future cardiovascular events. Coronary artery calcium scores offer a valuable tool for assessing cardiovascular risk and can be calculated by using a non-ECG gated chest CT image, which is routinely performed for primary lung cancer staging.

Conflicts of interest

All authors report no conflicts of interest relevant to this article.

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