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The Incidental Diagnosis of Lung Cancer Through Chest Tomography During the COVID-19 Pandemic

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ABSTRACT Objective: This study aims to determine the frequency of incidental lung cancers detected during chest computed tomography (CT) scans performed for guiding the diagnosis or treatment of coronavirus disease-2019 (COVID-19). **Material and Methods:** In this single-center retrospective study, the chest CT scans taken during the beginning of COVID-19 pneumonia (mostly pre-vaccination era) between April 2020 and December 2020 were examined. Patients who were younger than 18 years and those with a prior history of cancer were excluded. Moreover, the clinicopathological factors and radiologic findings of those patients with pulmonary nodule size on CT ≥3 mm or masses were recorded. **Results:** We assessed the CT scans of 2994 patients. A pulmonary nodule ≥3 mm or a mass was detected in 473 patients, while nine of them were diagnosed with lung cancer. The median age of lung cancer patients was 65 years (48-71 years). The most common subtype of lung cancer was adenocarcinoma (44.4%), followed by squamous cell carcinoma (33.3%) and small cell lung cancer (22.2%). Furthermore, all patients were diagnosed at the non-metastatic stage. **Conclusion:** Our study showed that early-stage lung cancers were detected incidentally on CT scans in suspected COVID-19 pneumonia patients. While the COVID-19 pandemic resulted in significant mortality worldwide, early diagnosis and treatment of these cases can save several lives.

Keywords: Cancer screening; COVID-19; incidence; incidental finding; lung cancer

Coronavirus disease-2019 (COVID-19) is caused by severe acute respiratory syndrome-coronavirus-2, which primarily affects the respiratory tract. After emerging in China in late 2019, it was declared a pandemic by the World Health Organization (WHO) on March 11, 2020.[1] As of March 13, 2023, 760,360,956 cases have been reported globally, and 17,042,722 cases in Türkiye were reported until November 27, 2022.[2,3] Reverse transcription-polymerase chain reaction (RT-PCR) is considered the standard diagnostic test for COVID-19 infection.[4] Furthermore, chest computed tomography (CT) is used to assess the severity of lung involvement in the COVID-19 patients with a positive RT-PCR result. However, chest CT can also help in diagnosing and guidance on the treatment for COVID-19 patients with a negative RT-PCR report.[5] Thus, CT scans are increasingly used by emergency departments and outpatient clinics for diagnostic purposes. Moreover, the number of incidental findings has increased due to the enhanced utilization of CT scans during the COVID-19 pandemic.[6]

Lung cancer is one of the most frequently diagnosed cancers and a leading cause of cancer-related deaths worldwide. The majority of lung cancer patients have locally advanced or metastatic

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diseases at the initial diagnosis. Moreover, less than 20% of the patients are diagnosed early, and one patient in 5 can survive. However, survival improves when cancer is detected early, and localized disease in lung cancer has a 5-year survival of nearly 60%.[7]

Numerous studies have reported disruptions in cancer screenings and treatments during the pandemic process.[8-10] However, we have not come across any study that has investigated whether the multitude of chest CT scans conducted during the pandemic could create an opportunity for early diagnosis, similar to a screening program, for early-stage lung cancer cases. This study aimed to investigate the prevalence of incidental detection of lung cancer on chest CT in suspected COVID-19 patients.

MATERIAL AND METHODS

This retrospective study included those suspected COVID-19 patients who were admitted to our hospital's COVID-19 outpatient clinics between April 01, 2020, and December 31, 2020, and only those who underwent chest CT scans. Moreover, patients who were <18 years of age and patients with a prior history of cancer were excluded. A total of 2,994 patients were screened by chest CT scans, while data from 473 patients with pulmonary nodules on CT ≥3 mm or masses were collected. Only histopathologically confirmed cases of lung cancer were included. However, the recommended criteria for standardization could not be established due to variability in clinical evaluations conducted by different physicians during the pandemic. Biopsies were then performed on patients in whom the physician's assessment indicated a suspicion of malignancy and those who agreed to the procedure. The study was approved by the University of Health Sciences Dışkapı Yıldırım Beyazıt Training and Research Hospital Clinical Research Ethics Committee, dated December 28, 2020, with the number 101/03, and was conducted according to the principles of the Helsinki Declaration.

All CT scans were performed with the devices reserved for COVID-19-suspected patients in our hospital (16-slice Toshiba Alexion CT scanner, Toshiba Medical Systems, Nasu, Japan). All CT scans were obtained in the supine position during end-inspiration without any intravenous contrast material and covered the whole lung tissue. The technical parameters used were: 00-250 mAs tube current, 90-120 kV tube voltage, 3 mm slice thickness, a step factor of 0.8, 75 s of turnaround time, a field of view of 250-300 mm, and a matrix size of 512×512.

Statistical analyses were performed using SPSS 22.0 software (IBM, Armonk, NY, USA). The patients' clinical and demographic characteristics were analyzed by descriptive analysis. Chi-square and Fisher's exact tests were used for categorical parameters. A p-value <0.05 was considered significant.

RESULTS

A total of 2,994 patients, aged ≥18 years were screened. Furthermore, 473 patients with ≥3 mm lung nodules or masses on CT were included in the final analysis. Of them, 263 (55.6%) patients were men. The median age of 473 patients with a ≥3 mm lung nodule or a mass was 57 (19-95) years, while the median age of the nine lung cancer patients was 65 (48-71) years. Moreover, the number of patients aged ≤55 years was 223 (47.1%).

The CT images of 266 (56.2%) patients were not consistent with COVID-19 infection findings. However, the COVID-19 RT-PCR results were positive in 213 (45%) patients. In additionally, 237 (50.1%) and 23 (4.9%) patients displayed negative and unidentified PCR results, respectively. After excluding 23 patients with unidentified PCR results, the CT scans of 103 (72%) patients with positive PCR results were compatible with COVID-19 findings, while CT scans were consistent with COVID-19 findings in 40 (28%) patients with negative PCR results. A total of 192 (40.4%) patients did not have any smoking history, while 161 (34%) patients reported smoking history. Moreover, the smoking history of 121 (25.6%) patients remained unidentified. The patients' demographic data and clinicopathological characteristics are shown in Table 1.

Biopsy-confirmed incidental lung cancer was detected in 9 (0.3%) of 2,994 patients. When evaluated among 473 patients with ≥3 mm nodules, this rate was 1.9%. Of all lung cancer patients, 7 (77.8%) patients were male. Of all patients diagnosed with

TABLE 1: Demographic data and clinicopathological characteristics of the patients.

	n (%)
Age	
Median	57 (19-95)
≤55	223 (47.1)
>55	266 (52.9)
Gender	
Male	263 (55.6)
Female	210 (44.4)
Smoking history	
Yes	161 (34)
No	191 (40.4)
Unknown	121 (25.6)
CT COVID-19 compatible	
Yes	146 (30.9)
No	266 (56.2)
Indeterminate	61 (12.9)
COVID-19 PCR	
Positive	213 (45)
Negative	237 (50.1)
Unknown	23 (4.9)

CT: Computed tomography; PCR: Polymerase chain reaction.

lung cancer, 4 (44.4%), 3 (33.3%), and 2 (22.2%) patients were compatible with adenocarcinoma, with squamous cell carcinoma, and with small cell lung cancer (SCLC), respectively. Among the 9 lung cancer patients, 3 (33.3%) patients were evaluated as Stage 3, 4 (44.4%) patients as Stage 2, and 2 (22.2%) patients as Stage 1 as per American Joint Committee on Cancer 8th ed. Additionally, 6 (66.7%) lung cancer patients were in the smoker Group, 1 (11.1%) was in the non-smoker group, and 2 (22.2%) were in the group with unidentified smoking history. After excluding patients with unidentified smoking history, a statistically significant difference was observed between the groups with and without smoking history in terms of lung cancer (p=0.032). Among 9 incidental lung cancer patients, 7 (77.8%) patients were >55 years of age; however, the difference between the age groups was not statistically significant (p=0.13). Characteristics of lung cancer patients are presented in Table 2.

DISCUSSION

We investigated incidentally diagnosed lung cancer cases by reviewing thorax CT scans that were taken at the COVID-19 outpatient clinic at our hospital. Thus, we aimed to answer the following question: "Did thorax CT scans taken during the COVID-19 pandemic contribute to early diagnoses of lung cancer?"

The COVID-19 pandemic has disrupted healthcare services in several countries worldwide.[10] According to the IQVIA Institute for Human Data Science, patients reporting to oncology outpatient clinics decreased by 50%.[9] Moreover, a 39% reduction was also observed in CT lung cancer screenings.[9] Additionally, Dinmohamed et al. reported a 36% decrease in non-cutaneous cancer diagnoses during the pandemic.[8]

RT-PCR mRNA test is the globally accepted method for COVID-19 diagnosis. Although not routinely recommended for diagnosing COVID-19, a majority of thoracic CT scans were performed for rapid and accurate interpretation.[11] However, espe-

TABLE 2: Characteristics of patients diagnosed with lung cancer.

Case	Gender	Age	TNM	Final stage	Diagnosis
1	M	66	T2aN0M0	Stage 1B	Squamous cell carcinoma
2	M	65	T1cN2M0	Stage 3A	Squamous cell carcinoma
3	M	62	T4N2M0	Stage 3B	Adenocarcinoma
4	M	66	T2aN2M0	Stage 3A	Adenocarcinoma
5	M	68	T2bN1M0	Stage 2B	Small cell carcinoma
6	M	71	T2aN1M0	Stage 2B	Adenocarcinoma
7	F	48	T2aN1M0	Stage 2B	Adenocarcinoma
8	F	59	T2bN0M0	Stage 2A	Small cell carcinoma
9	M	55	T1bN0M0	Stage 1A	Squamous cell carcinoma

TNM: Tumor node metastasis classification.

cially in the early pandemic stage, a large number of CT scans were performed due to a lack of standard algorithms while diagnosing COVID-19 and laboratory inadequacies. However, an increased frequency of thorax CT scans resulted in an enhanced number of incidental findings found in those images.

Most lung cancer patients are diagnosed at advanced stages, and the 5-year survival rate is approximately 20%.[7] Thus, lung cancer screening has been recommended for high-risk individuals owing to high mortality rates and risk factors associated with cancer.[12]

Although there were studies on incidental findings in thorax CTs in terms of aiding the diagnosis of suspected COVID-19 infection, not much research was available on incidental lung cancer findings in such patients.

In our study, we screened 2,994 patients who had been admitted to our hospital because of suspected COVID-19 infection and had undergone CT scans. Of these, 473 patients who had a lung nodule of ≥3 mm in diameter or a mass were categorized as the target group. The median age of the target group was 57 (range 19-95), and 52.9% (n=266) were >55 years of age. Among 9 incidental lung cancer patients, 7 (77.8%) patients were >55 years of age; however, the difference between age groups was not statistically significant (p=0.13).

Dündar et al., in a retrospective study, investigated 1,540 suspected COVID-19 pneumonia patients who underwent thorax CT scans with a mean age of 41.96 (±17.08) and 2 (0.13%) patients who had a primary lung malignancy.[13] In a prospective screening study by Ronit et al., lung cancer was detected in 3 (0.33%) out of 901 HIV patients whose median age was 50.4 (43.5-59).[14] In another retrospective study by Manser et al., the prevalence of incidental lung cancer in patients dying from natural causes (n=24,708) was 0.34%, while the median age of incidental lung cancer patients was 72 years.[15]

In our study, lung cancer was detected in 9 (0.3%) patients. Although the median age of our study population was 57 years (19-95), the median age of incidental lung cancer patients was 65 years (48-71).

According to 2018 data, the incidence of lung cancer in the United States is 50.8/100,000. While most people diagnosed with lung cancer are ≥65 years of age, few diagnosed patients are <50 years.[7] The United States Preventive Services Task Force recommends annual lung cancer screening for adults aged 50-80 years, the American Association of Thoracic Surgery recommends screening for high-risk individuals >55 years, and the United Kingdom Lung Screening trial recommends screening for high-risk individuals aged 50-75 years.[12,16,17] Hence, we suggest that the variability in lung cancer incidence in all these studies is related to the patient's age and other risk factors.

WHO has classified lung cancers into two groups: SCLC and non-SCLC (NSCLC). NSCLC accounts for 80% of all lung cancer cases; adenocarcinoma is the most common form of NSCLC.[18] According to 2017 Turkish cancer statistics, approximately 80% of lung cancers were NSCLC. Moreover, the main subtypes of NSCLC were adenocarcinoma (47.7%) and squamous cell carcinoma (36.8%).[19] In the study of Ronit et al., all three lung cancer patients reported adenocarcinoma.[14] Manser et al. revealed that approximately 40% and 44% of all invasive cancers were adenocarcinoma and squamous cell carcinomas, respectively.[15] However, we observed that adenocarcinoma, squamous cell carcinoma, and SCLC were detected in 44.4%, 33.3%, and 22.2% of all lung cancer cases, respectively.

According to the WHO and the National Cancer Institute, most lung cancer patients usually report at the advanced or metastatic stages.[7,18] In low-dose computed tomographic (LDCT) screening studies with defined risk groups like The National Lung Screening Trial and The Dutch-Belgian lung-cancer screening trial (Nederlands-Leuvens Longkanker Screenings Onderzoek), lung cancer was detected earlier in the screened groups. Furthermore, reduced lung cancer-related deaths were observed in patients who underwent screening as compared with the non-screened group during the follow-ups.[12,16,20] In a meta-analysis by Hoffman et al., LDCT increased the probability of detecting early-stage lung cancer. In our study, 66.6% of the patients had early-stage lung cancer. However, while lung cancer-related mortality decreases with early screening, overall mortality remains the same.[21]

Since lung cancer is more common in men, we reported that 7 (77.8%) lung cancer patients were male. In the studies by Quadrelli et al. and Ronit et al., the incidence rates of patients with a smoking history were 84.4% and 92.9%, respectively.[14,22] In our study, 6 (66.7%) lung cancer patients had a smoking history, while 1 (11.7%) patient had never smoked. Although there was no statistically significant difference between the groups, lung cancer was more prevalent in smokers (p=0.088). Hence, our results support the prevailing theory that the use of tobacco products is a potential risk factor for developing cancer and that lung cancer is more commonly found in smokers.

Additionally, Yekedüz et al. suggested that the COVID-19 pandemic has interrupted many cancer screening programs; however, an increase in incidental cancer diagnoses was observed with chest CT scans taken during the pandemic period.[23] The incidence of lung cancer in Türkiye is 56.7/100,000 people.[19] However, we found a lung cancer rate of 300/100,000 persons. Thus, we suggest that enhanced CT scans during the pandemic led to increased incidental lung cancer diagnoses.

In 2022, Goncalves et al. stated that cancer diagnosis delay might be caused because of the pandemic; however, the large number of CT scans performed during this period helped in the early detection of incidental pulmonary nodules and lung cancers.[24] Moreover, other studies reported that the chances of survival were higher because incidental cancer cases were detected at an earlier stage.[25,26] While supporting the finding that incidentally detected cancers were detected at earlier stages, none of our 9 lung cancer cases were in the metastatic stage, and most of them were diagnosed at early stages (Stages 1 or 2).

Nonetheless, this study had a few limitations. Firstly, the retrospective design, conducted within a single-center framework, inherently introduced potential biases, thereby constraining the generalizability of the findings. Secondly, the lack of standardized biopsy criteria posed a challenge in determining the extent to which biopsies were performed on relevant patients. Lastly, the inclusion of those patients who did not undergo biopsy despite its indications could have exerted an impact on the study's outcomes. Hence, it is important to interpret the study's results correctly with due consideration of these limitations. Acknowledging these constraints underscores the need for more robust research studies that should encompass larger and more diverse patient cohorts to enhance the reliability of our conclusions.

CONCLUSION

Despite the difficulties posed by the COVID-19 pandemic in cancer screening, follow-up, and treatment, we found that early-stage lung cancers were detected incidentally on the CT scans that were conducted for suspected COVID-19 pneumonia patients. Although the pandemic caused significant mortality worldwide, the incidental detection of lung cancer cases at an earlier stage might contribute to longer survival. Therefore, we suggest that the pandemic may have created an opportunity for early diagnoses of lung cancer, especially in low-income and underdeveloped countries where lung cancer screenings are not readily available.

Source of Finance

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Yakup Düzköprü, Abdülkadir Koçanoğlu, Özlem Doğan;* ***Design:*** *Yakup Düzköprü, Gökşen İnanç İmamoğlu, Ebru Çılbır;* ***Control/Supervision:*** *Hayriye Şahinli, Doğan Yazılıtaş, Mustafa Altınbaş;* ***Data Collection and/or Processing:*** *Yakup Düzköprü, Abdülkadir Koçanoğlu, Özlem Doğan, Yeliz Aktürk, Yunus Gürbüz;* ***Analysis and/or Interpretation:*** *Yeliz Aktürk, Tülay Eren, Yunus Gürbüz;* ***Literature Review:*** *Yakup Düzköprü, Gökşen İnanç İmamoğlu, Ebru Çılbır;* ***Writing the Article:*** *Yakup Düzköprü, Abdülkadir Koçanoğlu, Özlem Doğan, Tülay Eren, Doğan Yazılıtaş;* ***Critical Review:*** *Hayriye Şahinli, Doğan Yazılıtaş, Mustafa Altınbaş.*

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