Original Article

Frequency of Incidental Pulmonary Findings Detected on PET/CT Images of Elderly Patients Diagnosed with Extrapulmonary Malignant Neoplasm

Ekstrapulmoner Malign Neoplazm Tanılı Yaşlı Hastaların PET/BT Görüntülerinde İnsidental Pulmoner Bulguların Sıklığı

Sibel Göksel[1], Dilek Karadoğan[2]

[1]Department of Nuclear Medicine, Recep Tayyip Erdoğan University, Rize, Turkey
[2]Department of Chest Diseases, Recep Tayyip Erdoğan University, Rize, Turkey

ABSTRACT

Introduction: Reporting thorax imaging findings on 18F-fluorodeoxyglucose (18F-FDG) positron emission tomography/computed tomography (PET/CT) is important for patient management. Even if some pulmonary findings are benign, they can have serious life-threatening consequences. This study aimed to investigate the frequency of benign or malignant pulmonary findings, which were simultaneously detected in PET/CT scans, of elderly patients with extrapulmonary malignant neoplasms.

Methods: Patients aged ≥65 years, applying to nuclear medicine department of a tertiary level health unit between November 2017 and April 2018 were retrospectively evaluated. Demographic and clinical information and PET/CT scans were obtained from their previous hospital records. Data obtained were analyzed using the SPSS version 22.

Results: A total of 112 patients (mean age, 72.8 ± 7.0; females, 58.9%) were included in the study. In total, 38.4% of the patients had a smoking history, and 39.2% were exposed to second-hand smoke. The most common indications for PET/CT imaging were post-treatment evaluation (42.9%) and staging (35.7%). Predominantly diagnosed malignancies were cancers of the gastrointestinal system (26.8%), breast (26.8%), and urogenital system (17%). While most patients had benign or malign pulmonary findings in thoracic images, no abnormal pulmonary findings were observed in only 24 patients (21.4%). The most common findings were emphysema (39.3%), metastatic nodules (27.7%), bronchial wall calcifications (14.3%), and air trapping/cysts (9.8%).

Discussion and Conclusion: This study revealed that 78.6% of elderly patients with extrapulmonary malignant neoplasms undergoing PET/CT scans had at least one pathologic lung finding. Although most of these findings are benign, reporting of them is important in the management and clinical outcomes of patients with malignancy.

Keywords: Elderly patient, PET/CT, malignant neoplasm, incidental pulmoner findings

ÖZET

Giriş ve Amaç: 18F-fluorodeoksiglukoz (18F-FDG) pozitron emisyon tomografi-bilgisayarlı tomografide (PET/BT) malignite kuşkulu lezyonlara ilaveten, benign karakterdeki bulguların raporlanması da hasta yönetiminde önemlidir. Bazı pulmoner bulgular benign olsa bile hayati tehlike oluşturan ciddi sonuçlara yol açabilir. Bu çalışmanın amacı, ekstrapulmoner malign neoplazm tanısı ile PET/BT çekilmiş olan yaşlı hastalarda benign ya da malign pulmoner bulguların sıklığını araştırmaktır.

Yöntem ve Gereçler: Üçüncü basamak sağlık kuruluşu nükleer tıp bölümüne Kasım 2017-Nisan 2018 tarihleri arasında başvuran 65 yaş ve üzeri hastalar retrospektif değerlendirildi. Demografik verileri, klinik bilgileri ve PET/BT görüntüleri hastane kayıtlarından elde edildi. Bulgular SPSS 22 kullanılarak analiz edildi.

Bulgular: Toplam 112 hasta (yaş ortalaması 72.8±7.0; %58.9' u kadın olan) çalışmaya dahil edildi. Hastaların %38.4' ü aktif, %39.2' si pasif sigara içicisiydi. En sık PET/BT çekimi endikasyonu, tedavi sonrası yanıt değerlendirme (%42.9) ve evreleme (%35.7) idi. Tanıların çoğunluğunu gastrointestinal

First Received: 05.02.2020, Accepted: 26.04.2021

sistem (%26.8), meme (%26.8) ve ürogenital sistem (%17) maligniteleri oluşturmaktaydı. Hastaların çoğunda toraks kesitlerinde benign yada malign pulmoner bulgulara rastlanırken, sadece 24 hastada (%21.4) hiçbir anormal pulmoner bulgu izlenmedi. En sık saptanan bulgular; amfizem (%39.3), metastatik nodül (%27.7), bronş duvarı kalsifikasyonu (%14.3) ve hava hapsi/kisti (%9.8) idi.
Tartışma ve Sonuç: Bu çalışma, ekstrapulmoner malign neoplazm tanısı ile PET/BT çekilen yaşlı hastaların %78.6' sında en az bir anormal pulmoner bulgunun olduğunu gösterdi. Bu bulguların çoğu iyi huylu olmakla birlikte, bunların raporlanması malignitesi olan hastaların yönetimi ve klinik gidişatında önemlidir.

Anahtar Kelimeler: Yaşlı hasta, PET/BT, malign neoplazm, insidental akciğer bulguları

Introduction

18F-fluorodeoxyglucose (18F-FDG) positron emission tomography/computed tomography (PET/CT) is a valuable imaging modality commonly for early detection, accurate staging, and evaluating treatment response of many cancers. Its main advantage in relation to other radiological imaging methods is the availability of functional imaging [1]. Oncologic PET/CT scans can be used to view cross-sectional tomographic and functional images from the vertex to the proximal thigh. Besides its ability to detect malignancies, PET/CT also reveals non-malignant findings.

The incidence of malignant diseases is increasing due to several factors such as advanced age, increased smoking rate, genetic factors, poor nutrition, air pollution, and occupational exposure. Imaging techniques exert an important role in the management of patients with malignant diseases. Among them, PET/CT has gained relevance not only for diagnosis but also for staging and treatment outcome evaluation. The rate of incidental findings has increased along with the use of low dose CT, and the importance of non-malignant incidental findings for patient management is well established among clinicians [2]. Therefore, during clinical evaluation it is crucial to carefully examine non-diagnostic CT images in the oncologic PET/CT scans [3]. It is recommended that such additional findings should be taken into account, as they are important for disease management and prognosis [4].

In the elderly patients, it is crucial to distinguish between age-related and pathological findings to avoid misdiagnoses [5]. Therefore, special knowledge on diagnostic imaging of elderly patients is required [6].

The aging causes reduced lung elasticity due to the loss of supportive tissue. Homogeneous airway dilatation may occur in the absence of inflammation, fibrosis, alveolar wall destruction or distortion [7,8]. Emphysematous and fibrotic changes in the basal segments of lung parenchyma are commonly seen, as well as morphological changes such as progressive calcifications of the airways and thorax [7-9].

A previous study reported that the CT images of elderly (> 65 years) showed a significant number of asymptomatic emphysema than those of young adults (<55 years). The same study found that 60% of elderly adults exhibited interstitial changes of the subpleural reticular pattern [10]. Another study reported that asymptomatic air cysts were frequently observed in elderly patients [11]. A study showed that asymptomatic older patients had greater prevalence of air trapping and extensive degree of air trapping also correlated with aging [12].

The aim of the present study was to evaluate pulmonary findings of elderly patients undergoing PET/CT scans due to extrapulmonary malignant neoplasms. The results will also provide an overview on the

non-malignant uses of PET/CT in elderly population.

Materials and Method

Setting and participants

The PET/CT scan of cancer patients sent to the department of nuclear medicine at a tertiary care unit in Turkey was retrospectively analyzed. The institutional ethical committee approved this study.

Demographic (i.e., age, gender, smoking status, comorbidities) and clinical (i.e., diagnosis, PET/CT indications) information were obtained from the hospital's database and the PET records/CT informed consent forms. Patients aged <65 years and diagnosed with lung cancer were excluded from the study.

The study was approved by the Recep Tayyip Erdoğan University of Local Ethics Committee (protocol number: 2018/109), and Helsinki declaration principles were followed.

18F-FDG PET/CT scan

All patients fasted for at least 6 hours before PET/CT scans. For all patients, information about the PET/CT scanning indication, clinical history, chemotherapy and radiotherapy history, height and weight, and fasting blood glucose levels were recorded before 18F-FDG injection. All patients had a fasting and blood glucose level was <200 mg/dL before imaging. The approximately 220–370 MBq 18F-FDG was intravenously administered to each patient. Following a resting period of approximately 50–60 min in the waiting room, the patients were taken for the PET/CT scan (by Siemens Biograph mCT, 20 excel). Images were acquired from the vertex to the upper thigh. CT images were taken with a 5 mm slice thickness and an average of 120-kVp/100-mAs dose range without intravenous contrast. PET images were acquired within 2–4 min per bed. Both the PET and CT images were obtained during normal tidal breathing.PET images were reconstructed using CT for attenuation correction. PET, CT, and fused PET/CT images displayed as coronal, sagittal, and transaxial planes were viewed on a syngo-via workstation (Siemens Healthineers). A nuclear medicine physician interpreted all images. All incidental lung findings detected on the PET/CT images were reported.

Statistical analysis

All statistical analyses were performed using the SPSS version 22. Descriptive statistical methods were used for demographic, clinical, and radiological features. Categorical variables were analyzed using the Pearson's Chi-square test, whereas continuous variables were analyzed using the student's t-test. A level of $p<0.05$ was considered statistically significant.

Results

A total of 112 patients were evaluated. The mean age was 72.8±7 and 58.9 % were females. The proportion of current and past smokers was 38.4%, and 24% reported second-hand smoke exposure. A total of 76.8% of the patients had at least one comorbid disease, including hypertension (65.2%), diabetes mellitus (14.3%), and coronary artery disease (11.6%). The patients' demographic data is presented in Table 1.

The patients were referred from the medical oncology (51.8%), general surgery (13.4%), hematology (12.5%), radiation oncology (9.8%) departments respectively for PET/CT scan.

Most patients undergoing PET/CT scan had gastrointestinal malignancies (26.8%), breast cancer (26.8%), and urogenital malignancies (17%). The proportion of patients with chemotherapy and radiotherapy histories was 63.4%and 25.8%, respectively. PET/CT scan indications included staging (35.7%), post-

Table 1. Demographic characteristics of all patients

Variable	n (%)
Age (mean, ±SD)	72.8 ± 7
Gender	
Female	66 (58.9)
Male	46 (41.2)
Smoking status	
Current/former smoker	43 (38.4)
Presence of second hand smoke exposure	27 (24.1)
Presence of comorbid disease	86 (76.8)
Presence of obstructive lung disease	21 (18.8)
Presence of inhaler medication use	22 (19.6)
Presence of tuberculosis or pneumonia history	11 (9.8)

Table 2. Pulmonary findings of the study population

Pulmonary findings	n (%)
Emphysema	44 (39.3)
Metastasis	31 (27.7)
Bronchial wall calcification	16 (14.3)
Air trapping/Cyst	11 (9.8)
Calcific nodule	10 (8.9)
Sequela fibrotic changes in apex	10 (8.9)
Bilateral pleural effusion	4 (3.6)
Reticular/Reticulonodular infiltration	6 (5.4)
Pleural thickening	5 (4.5)
Solitary pulmonary nodule	3 (2.7)
Calcific pleural thickening	2 (1.8)
Subsegment atelectasis	3 (2.7)
Bronchiectasis	1 (0.9)
Collapse and consolidation	1 (0.9)
Ground glass opacity	1 (0.9)

treatment evaluation (42.9%), and re-staging (21.4%) respectively.

Pathologic lung imaging findings were observed in 78.6% of the patients. The most common findings were emphysema (39.3%), metastatic nodular lesion (27.7%), and bronchial wall calcification (14.3%). Emphysema and metastatic lung nodules are shown in Figure 1, 2 and collapse-consolidation image determined by PET/CT for evaluation of treatment response after chemotherapy is given in Figure 3.

Table 3. Comparison of the variables according to patients' smoking status

	Current/former smoker (n:43)	Non-smoker (n:69)	p
Gender male	38 (88.4%)	8 (11.6%)	<0.001
Presence of obstructive pulmonary disease*	9 (20.9%)	12 (17.4%)	>0.05
Incidental pulmonary findings	41 (95.3%)	47 (68.1%)	<0.001
History of tuberculosis and pneumonia	5 (11.6%)	6 (8.7%)	>0.05

*Asthma+ COPD patients

Information about pulmonary findings is presented in Table 2.

A total of 43 patients (38.4%) had current/former smoking history and most were male (88.4%). The most of the smokers (95.3%) had pathologic lung findings (p <0.005). Table 3 shows the patient characteristics according to their smoking status.

Among the 112 patients, 21 of them were diagnosed with obstructive pulmonary disease, 11 patients had chronic obstructive pulmonary disease (COPD) (52.4%), and 10 patients had asthma (47.6%). The rate of current/former smokers was 20.9% of the total but it was 72.8% among patients with COPD.

Lung metastases were most commonly caused by breast (29%) and colon cancers (22%). Other cancers associated with lung metastasis were bladder cancer (6%), renal cell carcinoma (6%), endometrium carcinoma (6%), cancers of undifferentiated origin (6%), gastric cancer (3%), larynx cancer (3%), pancreatic cancer (3%), liver cancer (3%), sarcoma (3%), and multiple myeloma (3%) respectively.

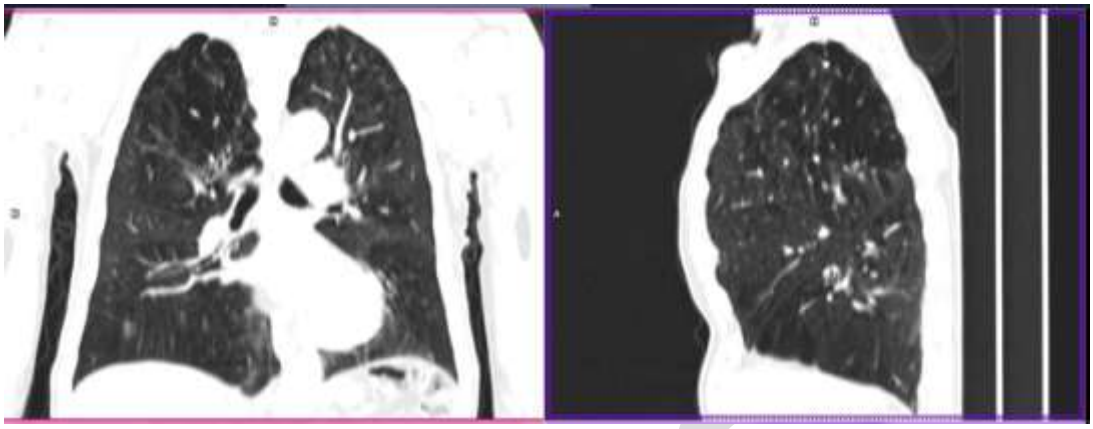

Figure 1. Emphysematous lung image in coronal and sagittal sections on CT

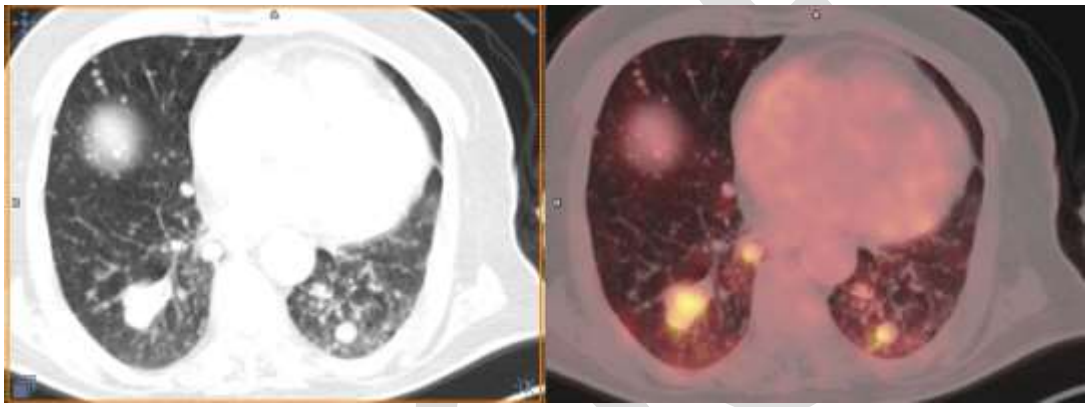

Figure 2. Transaxial CT (a) and fusion image (b) on PET/CT scan showed multiple lung metastases in a 64-year-old male patient diagnosed with a rectal cancer

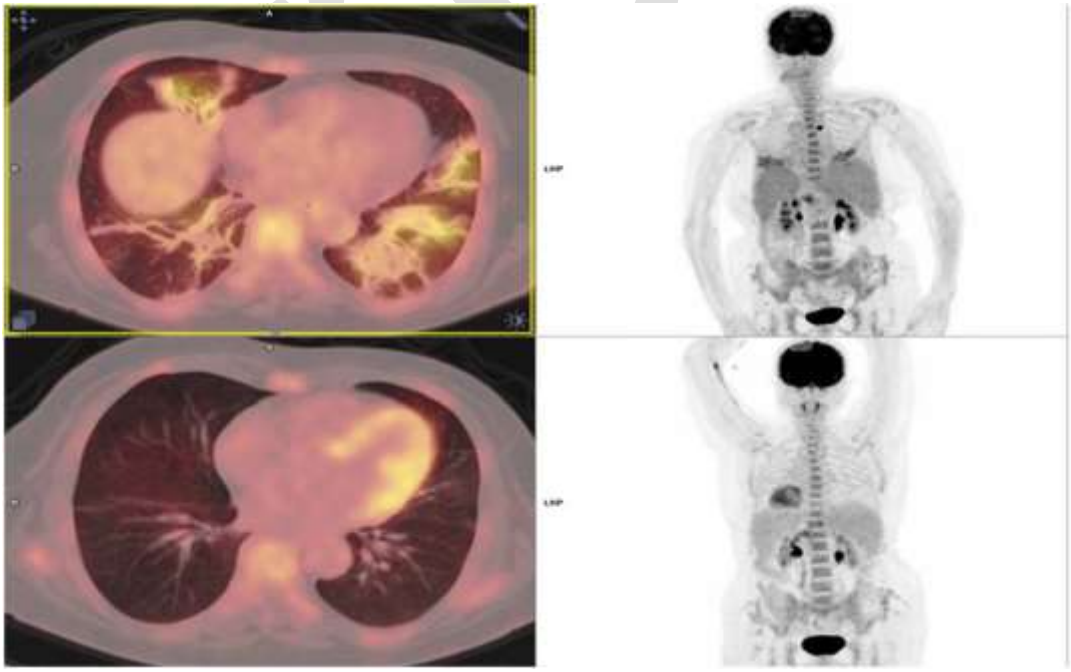

Figure 3. Transaxial fusion PET/CT (a, b) and maximum intensity projection (c, d) images showed post-chemotherapy collapse and consolidation (a, c) in a 77-year-old male patient diagnosed with a hematologic malignancy

Discussion

In the present study, thoracic CT images of 112 elderly patients undergoing PET/CT scans were retrospectively examined. Among all patients, only 24 of them (21.4%) had no pathologic lung findings on thoracic CT images. The most common pathologic findings were emphysema (39.3%), metastatic lung nodules (27.7%), bronchial wall calcifications (14.3%), and air trapping/air cysts (9.8%). Other findings included calcific nodules, sequelae fibrotic changes in the apex, subpleural reticular/ reticulonodular infiltration, and solitary pulmonary nodules. Calcific pleural thickening, subsegmental atelectasis, bronchiectasis, collapse/ consolidation, and ground glass opacity were less commonly found. All these findings significantly more frequent in the patients with a smoking history ($p < 0.001$).

It is known that with aging, distal airspaces expand due to the loss of supportive tissue, resulting in changes designated as "senile lung, senile hyperinflation, or senile emphysema". Homogeneous airway dilatations can be observed in elderly patients in the absence of inflammation, fibrosis or other structural pathologies [7]. A study comparing the radiological findings in the lung parenchyma of elderly (>75 years) and younger individuals (<55 years), found a higher rate of centrilobular emphysematous changes in the elderly group. The same study found a 60% rate of interstitial changes with subpleural reticular pattern among elderly individuals [10]. Another study showed that 25% of asymptomatic elderly patients presented small cystic lesions [11]. In the present study, the most common incidental lung finding was emphysema, which is consistent with that observed in the existing literature (39.3%). However, the rate of interstitial changes associated with the subpleural reticular pattern was only 4.5%, which may have been due to the CT image technique used. In the present study, CT images were acquired at an average of 120-kVp and 100-mAs dose, in 4-mm section thickness and in inspiratory or expiratory phases instead of 120-kVp and 400-mAs dose, 1-mm section thickness, thin-section CT. This may have caused the inconsistency between the results of the present study and those of the existing literature [11,12]. In the present study, the rate of air cysts was 9.8%, whereas previous studies report a rate of 25% [11]. This discrepancy may have also been caused by the used image section thickness.

Lung is one of the most common sites for primary and metastatic malignancies and a challenging site to diagnose primary versus a metastatic origin of the tumor on cytology. The developments in CT technology have led to an increasing detection of pulmonary nodules in thorax CT. A previous study reported that 20% of the patients with extrapulmonary malignant neoplasm presented metastatic lung nodules on thorax CT images [13]. In the latter study, thorax images were evaluated using thin-section CT (section thickness, 1 mm). The detection of incidental pulmonary nodules has increased with the use of thin-section thorax CT [14]. In our study, metastatic lung nodules were detected in 27.7% of the cases, although images were not acquired using thin-section CT (section thickness, 4 mm). This ratio is relatively high compared with that reported in the literature. In our department, PET/CT images have a 5-mm thickness and thus have low sensitivity for nodules <4 mm. Therefore, there is a possibility for small nodules to go undetected. However, histopathological sampling of the detected lung nodules was not performed. The presence of multiple nodules on PET/CT images and FDG uptake levels of nodules are findings that support the occurrence of metastases. Since most available nodules present these features, they

have been clinically accepted as metastases. The clinical history of a known extrapulmonary primary and the radiologic findings of multiple nodules in the lung are useful in arriving at the right diagnosis but is not always reliable. The approach to the diagnosis of metastatic tumors in the lung on cytology should be largely guided by the previous clinical history and comparison with previous tissue/cellular material if available [15]. Some nodules classified as malignant may, in fact, be benign, which helps to explain our findings of a higher rate of lung metastases compared with those reported by previous studies.

When the high occurrence of lung metastasis is analyzed from a different perspective, it becomes questionable whether cancer diagnosis is delayed in elderly patients. In the previous literature, 20% of lung metastases were detected without discriminating between old and young patients [13]. Pulmonary metastases are hematogenous distant metastases. In the present study, a higher rate of metastatic lung nodules than that reported in the previous literature was found, which may be related to the fact that elderly patients are diagnosed with advanced stage cancers. Comorbidities in elderly patients may overshadow cancer-related symptoms, thereby delaying cancer diagnosis. Therefore, a careful evaluation of geriatric patients should be performed, excluding malignancies in the differential diagnosis.

According to the previous literature, lung metastases were most commonly caused by breast cancer, followed by colon cancer [16]. Accordingly, in the present study the most common causes of lung metastasis were breast (29%) and colon cancers (22%).

Among the patients analyzed in the present study, only 21.4% had normal thorax CT images. Most patients had one or more pathologic findings. Beside the metastatic malignant lesions, reporting other incidental lung findings such as emphysema, collapse/ consolidation, bronchiectasis, pleural effusion, and interstitial pattern can contribute to improve the patients' quality of life through administration of adequate treatment and interventions. Such findings are therefore important for the subsequent management of cancer patients.

Conclusion

The prevalence of the geriatric patient population is increasing nationally and worldwide, leading to a higher cancer incidence. The present study investigated thorax images obtained from PET/CT scans of the geriatric patient population with extrapulmonary malignant neoplasms. Most patients (78.6%) had one or more pathologic lung findings. Consistent with the previous literature, our most frequent finding was emphysema. We found lung metastasis as the second most common finding, which contradicts previous studies. Although the interstitial changes are reported with a high rate in the existing literature, our study found a low rate, which was considered to be caused by the imaging procedures' differences.

CT scans of the lung parenchyma show common findings in elderly patients, which are thought to be related with collagen changes. The differential diagnosis between aging-related imaging findings and those secondary to disease is difficult and can not be achieved using imaging studies alone. These lesions should be compared with previous examinations and follow-up [7,10,17-19]. Therefore, the reporting of incidental findings in the geriatric population diagnosed with extrapulmonary malignancy may contribute to improve patient management.

References

1. Pfannenberg C, Gueckel B, Wang L, et al. Practice-based evidence for the clinical benefit of PET/CT-results of the first oncologic PET/CT registry in Germany. Eur J Nucl Med Mol Imaging. 2019; 46: 54–64.
2. Tsai EB, Chiles C, Carter BW, et al. Incidental Findings on Lung Cancer Screening: Significance and Management. Semin Ultrasound CT MR. 2018; 39: 273-281.
3. Hochhegger B, Meirelles GS, Irion K, et al. The chest and aging: radiological findings. J Bras Pneumol. 2012; 38: 656–65.
4. Britt CJ, Maas AM, Kennedy TA, Hartig GK. Incidental Findings on FDG PET/CT in Head and Neck Cancer. Otolaryngol. Head Neck Surg. 2018; 158: 484–488.
5. Gossner J, Nau R. Geriatric chest imaging: when and how to image the elderly lung, age-related changes, and common pathologies. Radiol Res Pract. 2013; 2013: 584793.
6. Occhipinti M, Larici AR, Bonomo L, Raffaele Antonelli Incalzi. Aging Airways: between Normal and Disease A Multiidimensional Diagnostic Approach by Combining Clinical, Functional and Imaging Data. Agind and Disease. 2017; 8: 471-485
7. Brandsma CA, de Vries M, Costa R, Woldhuis RR, Königshoff M, Timens W. Lung ageing and COPD: is there a role for ageing in abnormal tissue repair? Eur Respir Rev. 2017; 26(146).
8. Araki T, Nishino M, Gao W, et al. Pulmonary cysts identified on chest CT: are they part of aging change or of clinical significance? Thorax. 2015; 70: 1156–62.
9. Chopra A, Ford A, De Noronha R, Matthews S. Incidental findings on positron emission tomography/CT scans performed in the investigation of lung cancer. Br J Radiol. 2012; 85: 229-37.
10. Copley SJ, Wells AU, Hawtin KE, et al. Lung morphology in the elderly: comparative CT study of subjects over 75 years old versus those under 55 years old. Radiology. 2009; 251: 566–73.
11. Winter DH, Manzini M, Salge JM, et al. Aging of the lungs in asymptomatic lifelong nonsmokers: findings on HRCT. Lung. 2015; 193: 283–90.
12. Leelakanok N, Piyavisetpat N. CT features of normal lung change in asymptomatic elderly patients. Asian Biomedicine. 2015; 613-623.
13. Hanamiya M, Aoki T, Yamashita Y, Kawanami S, Korogi Y. Frequency and significance of pulmonary nodules on thin-section CT in patients with extrapulmonary malignant neoplasms. Eur J Radiol. 2012; 81: 152–7.
14. Rubin GD. Lung Nodule and Cancer Detection in Computed Tomography Screening. J Thorac Imaging. 2015; 30: 130–138.
15. Manucha V, Hansen JT, Gonzalez MF. Role of cytology and immunochemistry in diagnosis of metastatic malignancies in the lung: A critical appraisal. Diagn Cytopathol. 2018; 46: 936-944.
16. Chalmers N, Best JJ. The significance of pulmonary nodules detected by CT but not by chest radiography in tumour staging. Clin Radiol. 1991; 44: 410–2.
17. Hansell DM. Thin-section CT of the lungs: the Hinterland of normal. Radiology 2010; 256: 695–711.
18. Copley SJ. Morphology of the Aging Lung on Computed Tomography. J Thorac Imaging. 2016; 31: 140-50.
19. Choromańska A, Macura KJ. Role of computed tomography in quatitative assessment of emphysema. Pol J Radiol. 2012; 77: 28-36.

Corresponding author e-mail: sibelkandemirgoksel@gmail.com

Orcid ID:
Sibel Göksel 0000-0003-2584-1386
Dilek Karadoğan 0000-0001-5321-3964

Doi:

