Turk Neurosurg 33(1):87-93, 2023

Original Investigation

Received: 13.10.2021
Accepted: 11.02.2022

DOI: 10.5137/1019-5149.JTN.36806-21.2

Published Online: 10.08.2022

Silent Pulmonary Thromboembolism in Patients Undergoing Craniotomy for Brain Tumor

Haydar GOK[1], Ozan BASKURT[2], Buse SARIGUL[1], Defne GURBUZ[3], Suat Erol CELIK[1]

[1]Prof. Dr. Cemil Tascioglu City Hospital, Department of Neurosurgery, Istanbul, Turkey
[2]Hakkari State Hospital, Department of Neurosurgery, Hakkari, Turkey
[3]Prof. Dr. Cemil Tascioglu City Hospital, Department of Radiology, Istanbul, Turkey

Corresponding author: Haydar GOK ✉ haydarctf@hotmail.com

ABSTRACT

AIM: To detect the silent pulmonary thromboembolism (SPTE) frequency in patients who underwent craniotomy for a brain tumor, and to examine the correlation based on the data obtained from patients.

MATERIAL and METHODS: Overall, 100 patients with brain tumors were included in the study. The mean age was 54.29 years (±12.5 years), with the youngest patient being 19 years old and the oldest 73 years. All patients underwent craniotomy, and a pulmonary ventilation-perfusion scintigraphy was performed 48 h after surgery to detect SPTE. The frequency of SPTE and the conditions related to it were investigated.

RESULTS: The incidence of SPTE was 26% in patients with a brain tumor who underwent craniotomy. Statistically, no correlation was observed between SPTE and data obtained from patients (tumor histopathology, tumor localization, perilesional edema, midline shift, bleeding time, surgical positioning, smoking history, age, duration of surgery, etc.).

CONCLUSION: Our study revealed a high rate of SPTE in patients with a brain tumor who underwent craniotomy. Although most articles suggest using anticoagulant therapy in these patients, the literature lacks definite evidence for the same.

KEYWORDS: Silent pulmonary thromboemboli, Pulmonary embolism, Brain tumor, Craniotomy, Pulmonary scintigraphy

INTRODUCTION

Despite signs and symptoms, such as chest pain, shortness of breath, and hemoptysis, not being specific or sensitive for pulmonary embolism (PE), 90% of cases are diagnosed based on clinical suspicion (10,12). Notably, PE should be suspected if the patient has adequate predisposing factors (10).

Silent pulmonary thromboembolism (SPTE) has been labeled as incidental, unsuspected, asymptomatic, or a combination thereof (6). It is detected unexpectedly, and there are no clinical findings. SPTE can cause rapid neurological and clinical changes and should be considered in postoperative patients with a brain tumor. Nonetheless, no clear treatment algorithm is available upon detection, and no clinical findings are noted. In addition, because the treatment involves using anticoagulants, there is an impending risk of bleeding in the postoperative patient.

In this study, we used pulmonary ventilation-perfusion scintigraphy (V/Q scan) to detect SPTE in patients who underwent craniotomy for cranial tumors. The incidence of SPTE and its correlation with patients' data were analyzed.

MATERIAL and METHODS

This study included 100 patients who underwent surgery for a brain tumor at Prof. Dr. Cemil Taçcıoğlu City Hospital and underwent a pulmonary V/Q scan in the first 48 hours.

Haydar GOK : 0000-0002-5211-7388
Ozan BASKURT : 0000-0003-1021-6529
Buse SARIGUL : 0000-0003-3732-3850
Defne GURBUZ : 0000-0003-0280-1197
Suat Erol CELIK : 0000-0003-3825-9854

Patients with preoperative lung lesions (atelectasis, lung cancer, chronic obstructive pulmonary disease, etc.) were not included. Moreover, patients who were intubated for more than 1 day in the preoperative or postoperative periods were not included.

The neurological and clinical findings of patients, comorbidities, medications, tumor localization, presence and degree of perilesional edema, operative procedure, surgery duration, amount of preoperative bleeding, postoperative neurological and clinical findings, and tumor pathology were recorded. A pulmonary V/Q scan was performed in the first 48 hours postoperatively to detect SPTE. Perfusion defects were recorded by the nuclear medicine department.

The incidence of SPTE during the postoperative period in patients with a brain tumor and the correlation between patient data and SPTE were investigated.

Statistical analysis was performed using the SPSS 17.0 statistical package software. Continuous variables were summarized as medians or means and SDs. The effect of various categorical variables on the occurrence of SPTE was tested using the chi-square test. A two-sided p value of <0.05 was considered statistically significant. Furthermore, a multivariate analysis was conducted using a forward stepwise logistic regression analysis to evaluate the risk factors associated with SPTE.

RESULTS

A total of 100 patients who underwent a craniotomy at our institute between 2017 and 2019 were included. Of these, 52 patients were women and 48 men. The ages of patients were between 19 and 73 years, with an average of 54.29 years.

Patients were grouped based on the result of the pulmonary scintigraphy performed in the postoperative period to evaluate SPTE. Groups were named as group A (no perfusion defect on the scintigraphy) (Table I) and group B (segmental perfusion defect on scintigraphy) (Table II).

Table I: Patients Who Had No Perfusion Defect on the Scintigraphy After Cranial Operation (Group A)

Pathology	n
Glioblastoma	21
Meningioma WHO Grade 1	19
Astrocytoma WHO Grade 3	10
Carcinoma Metastasis	8
Oligodendroglioma WHO Grade 2	6
Meningioma WHO Grade 2	6
Astrocytoma WHO Grade 2	3
Colloid Cyst	1

Table II: Patients Who Had Segmental Perfusion Defect on Scintigraphy After Cranial Operation (Group B)

Pathology	n
Meningioma WHO Grade 1	9
Glioblastoma	7
Astrocytoma WHO Grade 3	4
Oligodendroglioma WHO Grade 2	2
Meningioma WHO Grade 2	2
Astrocytoma WHO Grade 2	2

Preoperative Evaluation

Group A had 74 patients, with ages between 19 and 73 years (average 52.5 years). Of these, 40 were women and 34 men. Among these, 34 patients were either a pre-smoker or current smoker, with an average of 16 packets per year. 14 patients had a history of hypertension, 10 had diabetes mellitus (DM), and six had both. Four patients had breast cancer, two patients had lymphoma, and four had gastrointestinal cancer. Preoperative examination revealed only 12 patients with hemiparesis.

Tumor was located on the left side in 38 patients, on right side in 30, and midline in 6. Tumors were located in the frontal lobe (n=20), frontoparietal lobe (n=4), temporal lobe (n=14), temporoparietal lobe (n=6), parietal lobe (n=18), occipital lobe (n=4), cerebellum (n=4), and lateral ventricle (n=4). Perilesional edema was graded as 0 (no edema) or 1 (prominent edema in T2 and FLAIR sequences). Overall, 61 patients had perilesional edema and 33 of them had a midline shift.

Group B comprised 26 patients, with ages between 19 and 73 years (average 59.4 years). Of these, 12 were women, and 14 were men. 10 patients were either a pre-smoker or current smoker with an average of 18 packets per year. Furthermore, 10 patients had primary hypertension, and four patients had both hypertension and diabetes. Preoperative neurological evaluation revealed six patients with hemiparesis. Tumor was located in the right hemisphere in 12 patients, left hemisphere in 10, and in the midline in 4. Tumor locations were the frontal lobe (n=8), thalamus (n=2), temporal lobe (n=2), parietal lobe (n=4), frontoparietal (n=4), temporoparietal (n=4), and frontotemporoparietal (n=2). 19 patients had perilesional edema, and 11 of them had midline shift.

Some cranial images of each group are illustrated in Figure 1.

Surgery

In group A, 67 patients were operated in the supine position, and 7 were operated in the prone position. The average duration of surgery was 180 min (120–255 min). For head positioning, the Mayfield head holder was used in 59 patients, and the horse-shoe shaped headrest was used in 15. Subtotal resection was performed in 28 patients, and 46 patients underwent total tumor excision. The average blood loss was 338 cc (338 ml). Overall, 64 patients were extubated in the operating room, and 10 were extubated in the intensive care unit after 6 hours postoperatively on an average.

In group B, all patients were treated in the supine position. The average duration of surgery was 204 min (90–300 minutes). For head positioning, the Mayfield head holder was used in all patients. Subtotal resection was performed in eight patients, and total excision was achieved in 18 patients. The average blood loss was 367 mL for all patients. Overall, 22 patients were extubated immediately in the operating room, and four were extubated in the intensive care unit after 8 hours postoperatively on an average.

Compression stockings were worn on all patients during surgery and postoperative intensive care and removed when they begin to mobilize. All patients stayed in the intensive care unit for 1 day and were mobilized an average of 2-4 hours after transfer to the neurosurgery service. Since all patients included in the study were mobilized within the first 30 hours postoperatively, no prophylaxis was applied. Compression stockings were worn on all patients during surgery and postoperative intensive care and removed when they begin to mobilize. Pulmonary scintigraphy was performed in 48 h after surgery to avoid the possible effects of pulmonary embolism in the late postoperative period. As previously described, no perfusion defects were noted in group A (Figure 2). In group B, 16 patients had bilateral, and 10 had unilateral segmentary perfusion defects (Figures 3-5). These defects were either

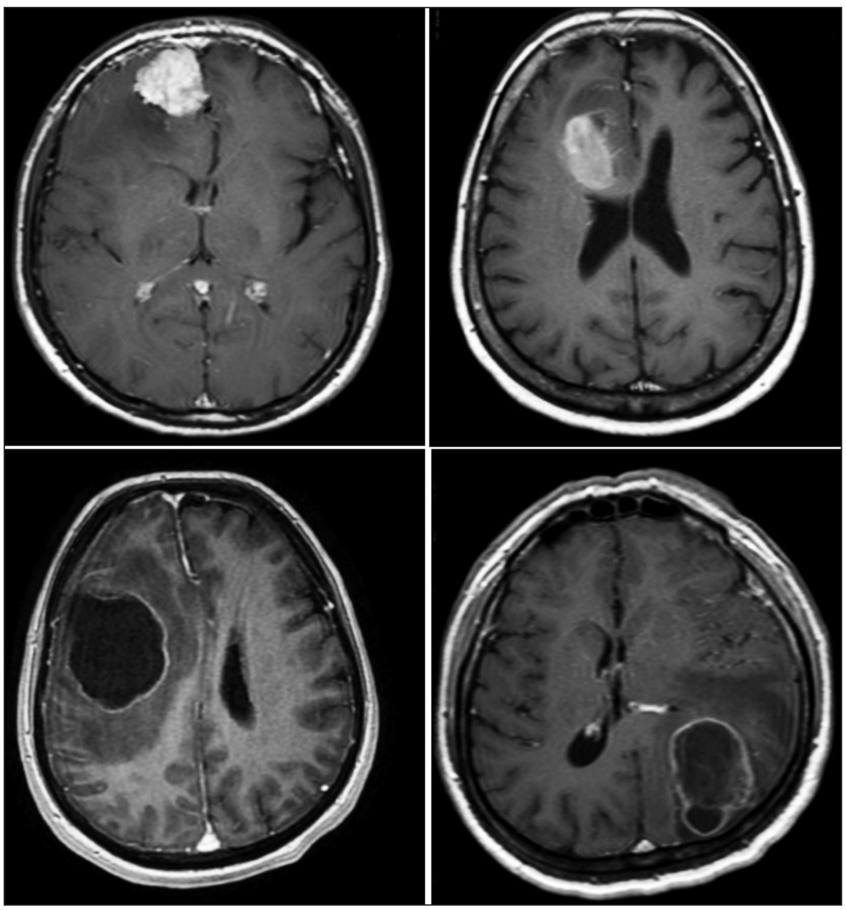

Figure 1: Contrast enhanced T1W axial brain MRI of patients. Images of two patients with contrast enhancement are presented above. Images of two cystic tumors with prominent perilesional edema and midline shift are presented below.

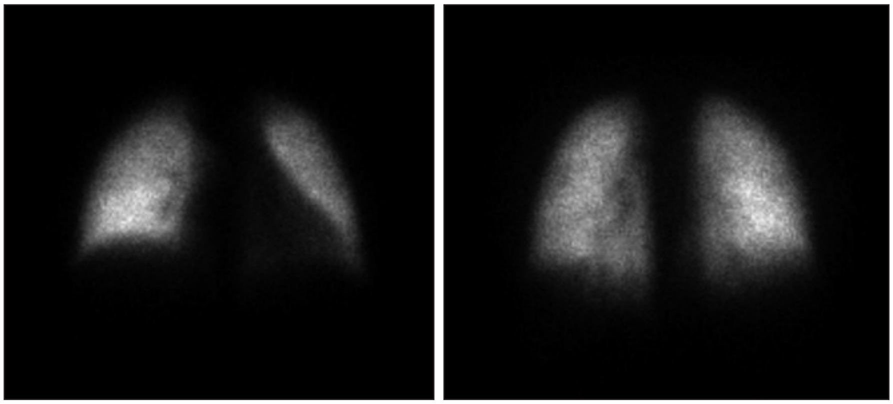

Figure 2: A patient with a normal scintigraphy imaging.

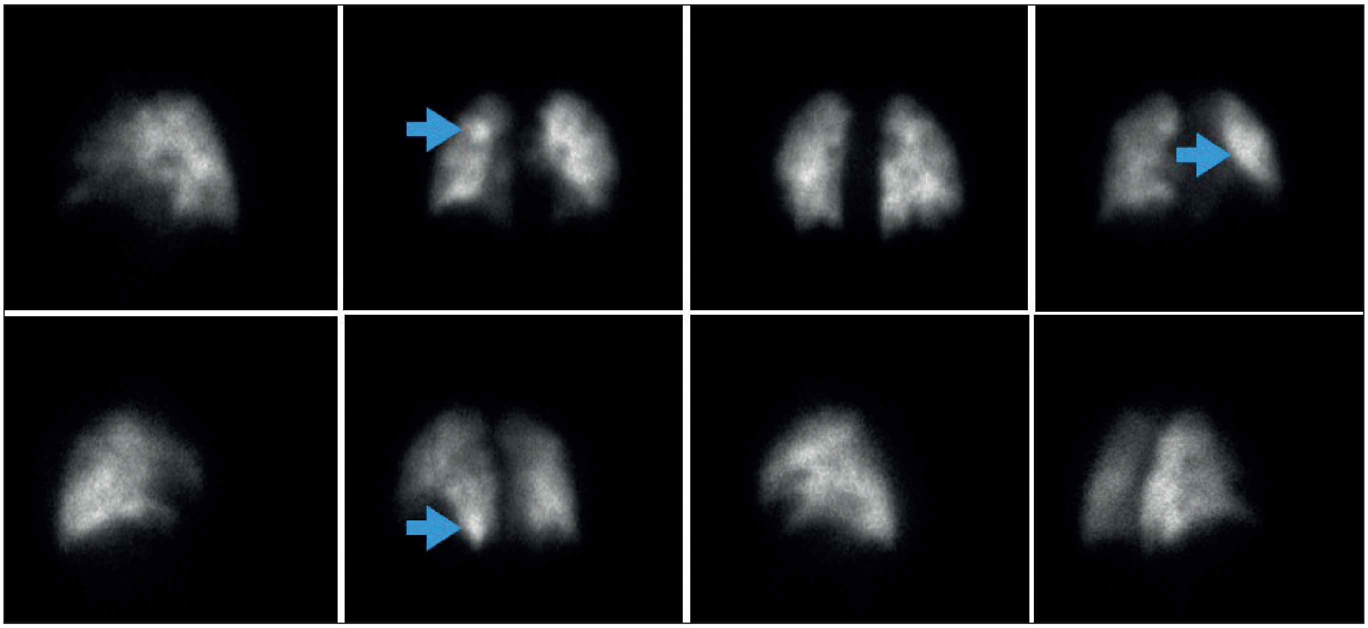

Figure 3: A patient with an abnormal signaling observed on pulmonary scintigraphy. The patient has perfusion defects in both basal and apical segments bilaterally.

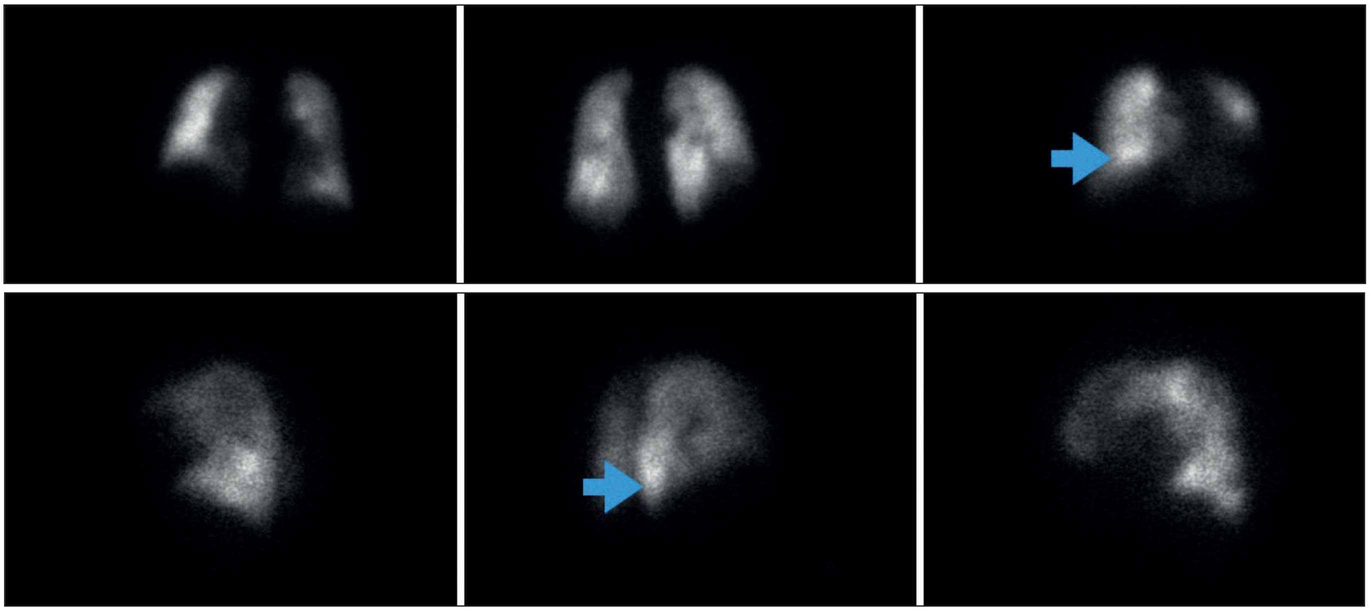

Figure 4: A patient with perfusion defect in the left basal segments.

in the upper lobe or basal lung segments. A pulmonologist assessed all patients with perfusion defects, and only one patient was continued on low-molecular-weight heparin (enoxaparin sodium). Lower extremity Doppler ultrasound was performed in all patients. D-dimer levels were evaluated, and were in the normal range (0–500 µg/L) for all patients except one patient whose D-dimer was calculated to be 702 µg/L and consequently received treatment. The rest of the patients were continued on subcutaneous injection until postoperative mobilization except if they had been previously on oral anticoagulant therapy. These patients received the injections until it was decided that the use of oral anticoagulants was safe with no risk of intracranial bleeding.

SPTE was detected in 26% of our patients. No correlation was observed with either tumor histopathology or localization ($p>0.05$). Perilesional edema and midline shift were not relevant in PE ($p>0.05$). In addition, the amount of bleeding, surgical positioning, and smoking history did not alter the results ($p>0.05$). Even though statistically, no correlation was noted with the patient's age and duration of surgery, this study observed that PE occurred more frequently in older patients and those with a longer surgery duration.

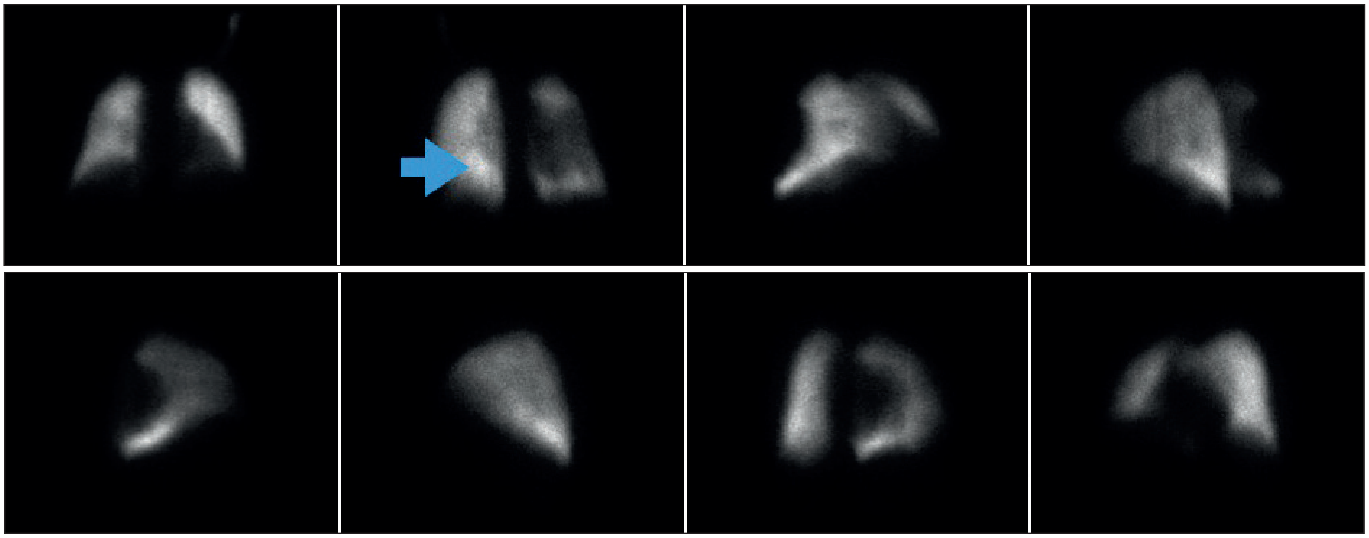

Figure 5: A patient with right basal segmentary perfusion defect on pulmonary scintigraphy.

DISCUSSION

PE is the obstruction of pulmonary arteries by a thrombus, causing pulmonary circulation and respiratory failures (6,19). SPTE is an earlier stage of PE and has an atypical presentation (19).

The mean prevalence of SPTE is 2.6% (ranging from 1.2% in outpatients to 4% in inpatients). It is more common in patients with cancer than those without cancer (4). V/Q scan may be an ideal method for detecting SPTE in patients with younger age, normal chest X-ray, low clinical risk, pregnancy, suspected contrast mediated allergy, and renal failure because it involves neither radiation exposure nor contrast agent (3,9,12).

For neurosurgical patients, the risk of PE is estimated to be 5% and mortality 9%–50% (20). Notably, prolonged bed rest, cancer, and preoperative hypercoagulability may increase the risk for PE (10). Moreover, a history of thromboembolism, cardiac disease, cancer, obesity, and prolonged immobility have been proven to be the predisposing factors (10). In our analysis, it was observed that prolonged surgery increased the risk of SPTE. Moreover, the horseshoe-shaped headrest was used in 40% of patients with segmentary pulmonary defects. This finding could be explained based on the more unstable positioning of the patient with the horseshoe headrest apparatus.

In a study by Sawaya et al., it was noted that the duration of symptoms correlated with the risk of venous thromboembolism (VTE) (15). It is suggested that a longer period of tumor growth may be associated with increased release of thrombogenic material (15). In the same study, edema was not observed to increase the risk of VTE (15).

Immobility is related to stasis of blood flow, as included in the Virchow triad of stasis, endothelial injury, and hypercoagulability (11). Notably, the risk in neurosurgical patients may increase with the premorbid state, type of surgical procedure, specific conditions (risk of VTE in meningioma is 72%), hypercoagulable state, steroid use, and tumor-induced hemostatic alterations (20).

The risk is estimated to be 15% for glial tumors and 7.1% for meningiomas (19). Longer duration of surgical procedure, osmotherapeutic drugs, intraoperative bleeding, chemotherapy, and steroids were associated with an increased risk (15,19). A study determined that the risk was more for patients undergoing a cranial procedure compared with spinal interventions (19).

All these data were obtained by evaluating patients who had signs of PE in the clinic and who were determined to have PE radiologically or with blood tests.

Notably, no information is available in the literature regarding the incidence of STPE in brain surgery patients, its clinical reflections, and treatment modalities if detected because there are no other studies similar to ours. In our department, we make patients wear compression stockings preoperatively and provide low-molecular-weight heparin subcutaneously on the first postoperative day as prophylactic measures. However, no consensus and strict guidelines are available that suggest these measures.

Nevertheless, with the development of imaging techniques and frequent thoracic imaging, especially in patients with cancer and trauma, the detection rates of SPTE have increased. However, based on the high detection rates, some researchers have questioned whether the detected SPTE was indeed clinically silent. Abdel-Razeq et al. noted that some patients had signs and symptoms of PE on their retrospective investigations (1). O'Connell et al. observed that 44% of their 52 study patients had PE symptoms or signs but missed them (14).

Nonetheless, no precise information is available regarding the treatment modality when SPTE is detected (5). Until date, several physicians have applied anticoagulant therapy in patients with PE, whether symptomatic or non-symptomatic (1,7,18).

Notably, small emboli often indicate accompanying DVT. Therefore, considering these emboli as a precursor to recurrent small embolism that can cause chronic pulmonary thromboembolic hypertension and affect cardiorespiratory reserve, patients are typically treated with therapeutic or prophylactic anticoagulants as if they had symptomatic PE (2,8,16).

Several researchers have argued that treatment is not necessary if the clot burden is small, risk factors for thromboembolism are transient, and DVT has been ruled out because the present situation could become worse owing to the risks of anticoagulant therapy (8,17). This situation is precarious concerning the bleeding risk in our postoperative patients.

Fred reported that it was easier to visualize pulmonary arteries and subsegmental branches with a multidetector computed tomographic scanner, but raised questions regarding the management of asymptomatic patients with PE who were incidentally detected. He reported that thromboembolism was observed in all parts of the pulmonary arterial tree, especially in patients with cancer who had pulmonary pathology, and stated that it could be overlooked on the first CT imaging. They stated that definitive studies are needed to analyze the natural history and optimal management (6).

According to our data, the probability of postoperative SPTE was high in patients with a brain tumor. This finding raises the question of whether postoperative lung imaging should be performed for each patient. Notably, no statistically significant data could be obtained for the development of SPTE. However, it was observed to be more common in elderly patients and those undergoing prolonged surgery. Although most articles suggest using anticoagulant therapy in these patients, no definite information is available in the literature. Nevertheless, the new protocols for preventing SPTE include intraoperative leg elevation, intermittent pneumatic compression, and the use of low-molecular-weight heparin (13).

CONCLUSION

This study investigated the prevalence of SPTE in patients who underwent craniotomy. The correlation between SPTE and several preoperative and perioperative parameters were evaluated. Nonetheless, no correlation was observed between the parameters and SPTE. Hence, further studies with a higher patient number are warranted to ascertain a correlation. Postoperative respiratory imaging as a routine procedure should be investigated to facilitate postoperative prophylactic management of thromboembolism. Our study sample was not large, but a study with more patients may explain if SPTE affects patient outcomes and morbidity. Moreover, V/Q scan could be an ideal method for detecting SPTE in patients with younger age, normal chest X-ray, low clinical risk, pregnancy, suspected contrast mediated allergy, and renal failure because it involves neither radiation exposure nor contrast agent (3,9,12).

AUTHORSHIP CONTRIBUTION

Study conception and design: SEC, HG
Data collection: OB, BS, DG
Analysis and interpretation of results: HG, OB
Draft manuscript preparation: SEC
Critical revision of the article: SEC, HG
Other (study supervision, fundings, materials, etc...): DG, OB, BS
All authors (HG, OB, BS, DG, SEC) reviewed the results and approved the final version of the manuscript.

REFERENCES

1. Abdel-Razeq HN, Mansour AH, Ismael YM: Incidental pulmonary embolism in cancer patients: clinical characteristics and outcome-a comprehensive cancer centre experience. Vasc Health Risk Manag 7:153-158, 2011
2. Browne AM, Cronin CG, English C, NiMhuircheartaigh J, Murphy JM, Bruzzi JF: Unsuspected pulmonary emboli in oncology patients undergoing routine computed tomography imaging. J Thorac Oncol 5(6):798-803, 2010
3. Celebioglu E, Ozgen Kıratlı MP, Coplu L: Ventilation/perfusion scintigraphy in pulmonary embolism. Turkiye Klinikleri J Cardiol-Special Topics 8(6):37-41, 2015
4. Dentali F, Ageno W, Becattini C, Galli L, Gianni M, Riva N, Imberti D, Squizzato A, Venco A, Agnelli G: Prevalence and clinical history of incidental, asymptomatic pulmonary embolism: A meta-analysis. Thromb Res 125(6):518-522, 2010
5. Desai SR: Unsuspected pulmonary embolism on CT scanning: Yet another headache for clinicians? Thorax 62(6):470-472, 2007
6. Fred HL: Unsuspected pulmonary thromboemboli: A continuing clinical challenge. Tex Heart Inst J 40(1):9-12, 2013
7. Gladish GW, Choe DH, Marom EM, Sabloff BS, Broemeling LD, Munden RF: Incidental pulmonary emboli in oncology patients: Prevalence, CT evaluation, and natural history. Radiology 240(1):246-255, 2006
8. Goodman LR: Small pulmonary emboli: What do we know? Radiology 234(3):654-658, 2005
9. Gottschalk A, Sostman HD, Coleman RE, Juni JE, Thrall J, McKusick KA, Froelich JW, Alavi A: Ventilation-perfusion scintigraphy in the PIOPED study. Part II. Evaluation of the scintigraphic criteria and interpretations. J Nucl Med 34(7):1119-1126, 1993
10. Hall D: Perioperative pulmonary embolism: Detection, treatment and outcomes. Am J Ther 20:64-72, 2013
11. Kimmel KT, Jahromi BS: Clinical factors associated with venous thromboembolism risk in patients undergoing craniotomy. J Neurosurg 122(5):1004-1011, 2015

12. Konstantinides SV, Torbicki A, Agnelli G, Danchin N, Fitzmaurice D, Galiè N, Gibbs JSR, Huisman MV, Humbert M, Kucher N, Lang I, Lankeit M, Lekakis J, Maack C, Mayer E, Meneveau N, Perrier A, Pruszczyk P, Rasmussen LH, Schindler TH, Svitil P, Noordegraaf AV, Zamorano JL, Zompatori M, Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC): 2014 ESC Guidelines on the diagnosis and management of acute pulmonary embolism. Eur Heart J 35(43):3033-3069, 3069a-3069k, 2014
13. Nunno A, Li Y, Pieters TA, Towner JE, Schmidt T, Shi M, Walter K, Li YM: Risk factors and associated complications of symptomatic venous thromboembolism in patients with craniotomy for meningioma. World Neurosurg 122:e1505-e1510, 2019
14. O'Connell CL, Boswell WD, Duddalwar V, Caton A, Mark LS, Vigen C, Liebman HA: Unsuspected pulmonary emboli in cancer patients: Clinical correlates and relevance. J Clin Oncol 24(30):4928-4932, 2006
15. Sawaya R, Zuccarello M, Elkalliny M, Nishiyama H: Postoperative venous thromboembolism and brain tumors: Part I. Clinical profile. J Neurooncol 14(2):119-125, 1992
16. Schoepf UJ, Kessler MA, Rieger CT, Herzog P, Klotz E, Wiesgigl S, Becker CR, Exarhos DN, Reiser MF: Multislice CT imaging of pulmonary embolism. Eur Radiol 11(11):2278-2286, 2001
17. Schultz DJ, Brasel KJ, Washington L, Goodman LR, Quickel RR, Lipchik RJ, Clever TBS; Weigelt J: Incidence of asymptomatic pulmonary embolism in moderately to severely injured trauma patients. J Trauma 56(4):72-33, 2004
18. Sun JM, Kim TS, Lee J, Park YH, Ahn JS, Kim H, Kwon OJ, Lee KS, Park K, Ahn MJ: Unsuspected pulmonary emboli in lung cancer patients: The impact on survival and the significance of anticoagulation therapy. Lung Cancer 69(3):330-336, 2010
19. Tian R, Gao J, Chen A, Bao X, Guan J, Feng M, Li Y, Ma W, Ren Z, Wang R, Wei J: Silent pulmonary thromboembolism in neurosurgery patients: Report of 2 cases and literature review. Medicine (Baltimore) 95(33):e4589, 2016
20. Wang X, Zhou YC, Zhu WD, Sun Y, Fu P, Lei DQ, Zhao HY: The risk of postoperative hemorrhage and efficacy of heparin for preventing deep vein thrombosis and pulmonary embolism in adult patients undergoing neurosurgery: A systematic review and meta-analysis. J Investig Med 65(8):1136-1146, 2017