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Research Article

The Incidence and Clinical Characteristics of Pulmonary Embolism (PE) in Oncologic Patients: Cohort Study

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Abstract

Background: The clinical characteristics of pulmonary embolism (PE) in Oncological outpatients for different types of cancer are unknown.

Purpose of the Study: To estimate the incidence and type of pulmonary embolism among oncologic patients with an assessment of related clinical characteristics.

Patient and Methods: Prospective cohort study was carried out on (540) patients with different cancers at one day care unit of the oncology department at king Fahd hospital, Kingdom of Saudi Arabia. CT chest with contrast and CT pulmonary angiography was done when indicated.

Results: Our study was carried out on (540) patients who have different cancers, of which 24 (4.44%) developed PE. PE group was 9 (37.5%) males while 15 (62.5%) females with M ± SD of age (54.95 ± 17.3). PE was represented (50%) of patients with seminoma, germ cell tumor while larynx Cancer was represented (33.4%) and less common in colon, prostate, and breast Cancers (6.68%, 4.7%, 2.54%) respectively. 7 PE patients (1.3%) were incidentally discovered during the staging of cancer while 17 patients (3.14%) have symptomatic PE. In the symptomatic group: (10) patients developed PE during chemotherapy, (4) patients developed PE during hormonal therapy, (2) patients developed PE during the staging of cancer and (1) patients developed PE during follow-up after chemotherapy. 20/24 (84%) of PE developed in the first 6 months from diagnosis of cancer while 4/24 (16%) of PE developed during follow up of the patients within the first year from diagnosis patients had cancer prostrate, one patient has cancer larynx and one patient has cancer breast. The most degree of PE was low-risk PE (75%) while massive and sub-massive were in (3) patients (12.5%) each. Most of the patients were given low molecular weight heparin (LMWH) (22/24) patients while thrombolytic therapy (TPA) was given for only one patient and IVC filter was inserted in 2 patients.

Conclusion: Among oncological patients in outpatients' settings with Different Types of Cancers, PE incidence was 4.4% with Most common of these were seminoma, germ cell tumor, prostate, lung, and larynx cancers but the least common in Breast Cancer. Noted that patients with (lung, pancreas, uterus, and bladder) cancer have a higher risk of Incidental PE. Low-risk PE type was the most common, while sub-massive and Massive were rare.

Keywords: *PE; Different Cancer Type; Characters; Oncology; Outpatient*

Abbreviations

PE: Pulmonary Embolism; CTA: Computed Tomography Pulmonary Angiography; IVC: Inferior Vena Cava; KSA: Kingdom of Saudi; VTE: Venous Thromboembolism; ESC: European Society of Cardiology; ICD: International Classification of Disease; TPA: Tissue Plasminogen Activator

Background

The incidence of venous thromboembolism (VTE) is three-fold in cancer patients compared to patients without cancer and many factors contributed to the increased incidence of thrombophilic state in cancer patients as oncological treatment such as radiotherapy, chemotherapy and hormone therapy increases the risk of thrombosis and embolism, among other things due to the release of procoagulants and cytokines from cancer cells as well as the toxic effect acting on the vascular endothelium, the reduction in the concentration of natural anticoagulants [1], resistance to activated protein C [2], factor V Leiden mutation [3], increased levels of anti-phospholipid antibodies [4], hyperhomocysteinemia, surgery, disease progression and aging of the patients. Now, the majority of cancer patients are treated and followed up in an outpatient setting, and recognition of PE as an important complication in those patients even they are ambulatory [5]. Despite many of literature on PE, the clinical features of PE in oncology outpatients, as a whole, and in different cancer types, is unknown. There are several studies that report the incidence of PE in cancer patients in general [6] or in individual cancer types [7]. However, most of them focus on hospitalized patients, and many of them report the incidence of VTE in general and not PE specifically. A few studies that do report the clinical characteristics of PE in outpatients do not specifically focus on oncology patients [8].

Advances in multi-detector computed tomography (CT) have allowed better assessment of the pulmonary arterial tree and have led to improved detection of pulmonary embolism making CT pulmonary angiography the imaging modality of choice for the diagnosis of PE [9]. Although the technique used for a routine chest CT is different from that used for CT pulmonary angiography, clinically unsuspected PE is frequently detected on routine chest CT during staging and follow-up of the patients [10].

Aim of the Study

The aim of this study is to estimate the incidence and type of pulmonary embolism and assessment of some clinical characteristics in oncologic patients.

Methods

Our prospective study was conducted on (540) cancer patients treated in the daycare unit of oncology of king Fahd hospital, KSA from January 2016 through June 2020. For patients with more than one malignancy being actively treated, the patient was classified under the more advanced stage of malignancy. The type of primary cancer was recorded according to the International Classification of Diseases, ten Revision, Clinical Modification (ICD-9-10) 2012 - 2016. We divide our patients into 2 groups incidental and symptomatic group.

All patients were evaluated by a pulmonology consultant for any chest symptoms at any time for the possibility of pulmonary embolism for all patients who underwent. The demographic data including age, sex, and smoking history were obtained. Moreover, the type, staging, and type of treatment of primary cancer according to (ICD-9-10) 2012 - 2016. CT chest with contrast: scan of the chest was performed -3 using a 64-row multi-detectors CT scanner (Aquilion 64; Toshiba, The USA). Patients were scanned in the supine position from the cranial to caudal direction from the clavicles to the adrenal glands at end- inspiration. One hundred milliliters of iopromide (300 mg I/mL; Ultravist 300, Bayer HealthCare Pharmaceuticals) was injected intravenously with an automated injector (Stellent, Medrad) at a rate of 2 - 3 mL/s, with a scan delay of 30 seconds. Done for all patients; in the initial staging of cancers, after completion of the treatment and during the follow up of the patients each (3-6-9-12) months according to the protocol of each cancer. CT pulmonary angiography (CTA): if

the patient has clinically suspected PE. Done for (27) patients. The cardiac enzyme (serum troponin I) and echo-cardiology: were done for the patients who had sub massive PE (acute PE in hemodynamic stable patient). Done for only (3) patients. The degree of PE; according to (The American Heart Association2011): Massive PE, Sub massive PE, low risk. The time of PE: during the first 6 months or during follow up) after 6 months). Treatment of PE: according to ESC guidelines, 2019 [11]: Unfractionated heparin was given for two patients and fractionated one given for (22) patients. Thrombolytic which was given was tissue plasminogen activator (TPA) (alteplase) dose 100 mg given for one patient. IVC filter: Done for two patients one has cancer colon and- another one has cancer larynx. Insertion of IVC filter due to patients developed a complication from anticoagulation. Follow up of the patients for one year.

Exclusion criteria: Incomplete data collection, the patient developed PE in the hospital, age of the patient less than 18 years. The participant's rights, privacy, health, and well-being were safeguarded through informed consent forms that they asked to read and sign if they agreed to participate in the study.

Statistical analysis: Data were analyzed using IBM SPSS for Windows version 18.0.was performed with respect to the main study aim. The risk of PE for patients in each cancer group was compared with that of all other patients using Fisher's exact test.

Using the Bonferroni correction to adjust for multiplicity $p < 0.0031$ was considered to indicate a significant difference in the incidence of PE. descriptive data are tabulated Descriptive statistics such as means and standard deviation mean (± SD) were used to describe the age of the patients, degree and time of PE, and type and stage of cancer. We also did a correlation with the outcome using the t-test and Fisher's exact test as appropriate with a significant value at $p \leq 0.05$.

Results

Our study conducted on (540) cancer outpatients. Patients with PE were divided into two subgroups, depending on whether the PE was clinically suspected or unsuspected. For patients clinically suspected CT pulmonary angiography (CTA) study was done. PE was incidentally detected on routine staging or follow-up CT. Regarding the incidence of PE (symptomatic versus incidental): Total no and % of PE was 24 (4.445%) and symptomatic was 17 (3.14%) while an incidental PE was 7 (1.3%). An incidental PE was 100% in cancer lung, pancreas, and uterus. While symptomatic PE was common in cancer breast, prostate, colon, seminoma, and germ cell tumor 7/8 (87.5%), 2/2 (100%), 4/2 (50%), 4/5 (80%), respectively.

Demography and characters of PE in different types of cancers of PE were in stage VI of cancer (75%) 18/24. Regarding treatment of cancers (100% of cancer lung uterus, seminoma and germ cell tumor) took chemotherapy and (100% of prostate cancer and 25% of breast cancer) took hormonal therapy while (100% of larynx, pancreas cancers, 60% of cancer colon and 12.5% of breast cancer) not take any medication due to late-stage of cancers and patients were unfit for treatment.

About 20/24 (84%) of PE developed in the first 6 months from diagnosis while 4/24 (16%) of PE developed during follow-up of the patients within the first years from diagnosis (2 patients have prostate cancer, one patient has larynx cancer, and one patient has breast cancer). The most degree of PE type was low-risk PE (75%) while massive and sub-massive were in 3 patients (12.5%) for each one. Most of the patients were given LMWH (22/24) patients while thrombolytic therapy (TPA) was given for only one patient and an IVC filter was inserted in 2 patients.

Some clinical characteristics of (symptomatic versus: incidental) PE: No significant differences between incidental and symptomatic PE regarding age, sex, and smoking history. PE in cancer of lung and pancreas was 100% incidental and, on another side, PE in cancer prostate, larynx, seminoma, and germ cell tumor was 100% symptomatic. While the incidence of symptomatic PE in cancer breast, colon, and bladder were (7/8) 87.5%, (4/5) 80% (1/2) 50% respectively. Low-risk PE is represented in 100% of incidental PE and (70.7%) of

symptomatic PE. 100% of incidental PE diagnosed during the staging of cancers in the first 6 months while (82.5%) of symptomatic PE developed during (chemo/ hormonal) therapy. All patients with incidental PE took LMWH while thrombolytic therapy (TPA) was given for only one patient and an IVC filter was inserted in 2 patients with symptomatic PE.

Discussion

This is the first large study on the incidence of suspected and unsuspected PE in oncologic outpatients in Almadina Almonwara, KSA. The incidence of PE among different cancer types has also not been previously reported in this patient population. Over a period of four years, we found an incidence of PE was 4.4% in a total of (540) patients with different types of cancer this, in agreement with Reynolds., *et al*. 2008; found an incidence of PE in cancer patients ranging from 0.13% to 8.65% in general [12].

In the current study, the higher risk of PE was in pancreatic, bladder, larynx, genitourinary especially prostate cancer, uterine cancers, and lung adenocarcinoma with relatively less common in breast cancer which is in agreement with the prior studies which have reported a higher incidence of PE in the pancreas, and lung malignancies, as well as in renal and uterine cancers [13]. The possible reasons for the higher risk of PE include immobility, staging of cancer, and aging of the patients [14]. Chew., *et al*. 2006 reported a lower incidence of PE in the breast [6]. Recently, the risk of PE in lung cancer patients increased 20-fold compared to the general population and especially in histologic types of adenocarcinoma [7].

In this study: Most PE 20/24 (84%) developed in the first 6 months from diagnosis and in advanced stages of cancer while only 16% (4/24) of PE developed within (1 - 2) years during follow up of the patients 50% of those patients have prostate Cancer; this agreement with Biedka., *et al*. 2012 [15]. Several mechanisms may contribute to the development of PE in the first 6 months from diagnosis such as effect of active cancer, and treatment (chemo/ radio/ hormonal) therapy which leads to down-regulation of anticoagulants and upregulation of procoagulant proteins [1], endothelial damage, or stimulation of endothelial cells to produce procoagulant materials [16], inflammation due to necrosis or release of acute-phase Reactants and other causes like surgery and immobilization [17].

The most common degree of PE in cancer patients was the type with low risk (18/24) 75% regardless of the type of cancer while central PE represented only (6/24) 25% of PE results from disagreement with Karippot., *et al*. 2019 who showed that cancer patients have a high rate of central pulmonary embolism this may be due to different in the total number of patients and number of patient in different cancers [18].

Our study revealed the incidence of incidental PE was 1.3%, this result disagrees with multiple previous studies that concluded that the incidence of incidental PE was 4.3%. This difference may be due to the heterogeneity of the patient population studied and tumor characteristics: such as disease stage [19].

The incidental PE was common in (pancreatic, lung and uterine) cancers and 100% of PE discovered in MDCT chest during staging of cancers, so that patients need close follow up and search for any PE in MDCT chest during staging. while the incidental PE was less common in (colon, prostate, and breast) cancers [20].

Conclusion

Pancreas, Larynx, Uterus and Prostate cancers had a higher incidence of PE, while the Incidence of PE was low in Breast cancer. The most common type of PE was the low-risk type in cancer patients. Within the first 6 months of Discovering Cancer, it was the most common period associated with PE. So, Careful watch should be carried out on cancer patients especially during the first 6 months not to miss a PE is recommended.

Declarations

This study was approved by ethics approval and consent to participate in king Fahd hospital-medina, KSA. Number (66) at March 2019.

Consent for Publication

The written consent form of the patient was taken and was available when needed.

Availability of Data and Materials

All data of the patient is available on a computerized patient file in the recording department of king Fahd hospital-Almadina Almonoura-KSA. www//KFHM-moh.gov.sa.

Competing Interests

Not present in this section.

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Authors Contributions

Habib M is responsible for data collection interpretation of data and writing the manuscript.

Dr/Fouad M was responsible for the collection of data, sharing in discussion.

All authors have read and approved the manuscript.

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