

A survey of physicians' opinions about the treatment of subsegmental pulmonary embolism

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Introduction: The aim of this study was to survey the attitudes of internists, cardiologists, and pulmonologists regarding treatment or no treatment of isolated subsegmental pulmonary embolism (ISSPE) with anticoagulant drugs.

Methods: Qualified physicians were asked to select their management options from a questionnaire that included a patient scenario with subsegmental pulmonary embolism (SSPE) and negative past medical history of thromboembolism.

Results: A total of 113 physicians responded to the survey. Of these, 8.8% preferred not to treat patients without further evaluation; 15% decided not to treat, but follow-up the patient with a serial lower-limb colour Doppler ultrasonography; 1.7% preferred anticoagulant treatment only during hospitalization and follow-up without medication; 5% preferred anticoagulant treatment for less than 3 months; and 34.5% chose a 3–6-month treatment with anticoagulation. Furthermore, 24% of physicians opted for anticoagulant treatment for more than 6 months, and 9.7% left the decision up to the patient. Opting not to treat was an option selected by more board-certified faculty members specialized in cardiology, internal medicine, and pulmonology compared with residents ($p = 0.038$). Willingness to provide anticoagulant therapy in the internal medicine, cardiology and pulmonology groups was 56.6%, 37.3% and 6%, respectively ($p = 0.007$).

Conclusion: The majority of physicians surveyed prefer anticoagulant therapy in patients with SSPE.

Key Words: pulmonary embolism; anticoagulants; computed tomography angiography

INTRODUCTION

Pulmonary embolism (PE) is one of the most common dilemmas in medicine that could lead to hospitalization [1]. Complications of the disease, including chronic pulmonary hypertension, the adverse effect of anticoagulant therapy, and increased likelihood of death, are associated with a decrease in life quality and an increase in socioeconomic costs [2]. The high sensitivity of the computed tomography pulmonary angiography (CTPA) has led to the detection of filling defects as small as 2 to 3 mm in size, which is called subsegmental pulmonary embolism (SSPE) [3]. Carrier et al. [4] investigated the rate of detection of SSPE based on the technique of CT angiography. In single-detector computed tomography (SDCT), 4.7% of patients had SSPE versus 9.4% in multidetector computed tomography (MDCT). However, in untreated cases with normal CTPA, the venous thromboembolism (VTE) recurrence rate had not changed much (0.9% in SDCT vs. 1.1% in MDCT). Moreover, VTE recurrence within 3 months of follow-up with 4 and 64 detectors CTPA was 1.4% and 0.8%, respectively, meaning many patients with negative SDCT could have SSPE that did not receive treatment. Therefore, despite the high percentage of SSPE detected by MDCT, the treatment of these patients would not prevent the occurrence of more episodes of thromboembolic events [4].

In the Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) study, 17% of patients with low-probability ventilation/perfusion (V/Q) scan had SSPE on pulmonary angiography [5]. Many studies show that patients with SSPE who had a nondiagnostic V/Q scan and a negative colour Doppler ultrasonography of lower extremities for deep vein thrombosis (DVT) did not need to receive anticoagulant treatment [6–8]. A systematic review and meta-analysis by Bariteau et al. [9] found that bleeding occurred in 8.1% of SSPE patients who were subsequently treated with anticoagulants. Moreover, VTE recurrence within 3 months after the treatment with anticoagulant was 5.3% compared with 3.9% in untreated patients. The mortality rate in treated patients was 2.1% versus 3% for untreated patients [9], which demonstrated a decrease in no significant difference between the two groups. A study by Donato et al. [10] reported that 1.05% of patients with isolated SSPE (ISSPE) treated with anticoagulant had recurrent ISSPE 15 days after being initiated on anticoagulant agents. Within 3 months of follow-up, 8.5% experienced hemorrhage. None of the patients in their study died as a result of VTE.

Bleeding is an important and dangerous complication of anticoagulant drugs, so there is a need for agreement on whether to treat or not to treat these patients. Therefore, the aim of this study was to survey current practice patterns and opinions of physicians about the management of ISSPE.

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METHODS

In this cross-sectional study, we included physicians who were internal medicine/cardiology residents, board-certified cardiologists/internists, and pulmonologists working as faculty members from three academic tertiary referral hospitals for cardiac and pulmonary disorders in Tehran from May 2016 to November 2016. These centers receive referrals from all over the country. Therefore, most cardiologists and pulmonologists are present at these three centers. One hundred and fifteen physicians were invited to participate in the study; two physicians were reluctant to cooperate due to lack of time. Therefore, 113 participants who met the inclusion criteria were asked to answer a questionnaire. One hundred four responded face to face, and nine participated by email.

The exclusion criteria were physicians who did not have the expertise described above. The sample size was determined based on the census of three available medical training centers. The 115 eligible physicians in the three centers were recruited.

This study was conducted according to the Declaration of Helsinki. Participants signed the informed consent form. The information provided by the respondents was kept confidential. Ethical approval from the Tehran University of medical science was obtained.

The questionnaire collected data pertaining to age, education, the amount of medical experience, and the average number of PE they encountered in patients in 1 month. The survey questionnaire included a scenario of a patient with SSPE and negative past medical history. Physicians were asked to select their opinions about patient management based on multiple-choice questions. Options ranged from treatment, no treatment but follow-up with serial colour Doppler ultrasonography, leaving the decision-making up to the patient, treatment with an anticoagulant agent for 3–6 months, or treatment for more than 6 months. Physicians who chose not to treat were additionally asked about their opinion on starting anticoagulant in the following circumstances: previous DVT or pulmonary thromboembolism, history of cancer who underwent surgery and chemotherapy 3 months earlier, number of ISSPE, the presence of any medical or surgical problems that cause immobility for a long time and the probability of having a 3-month recurrence rate. They could select more than one of the options.

The frequency and percentage were calculated for qualitative variables such as the type of medical specialties and physicians' management options. The Chi-square test was used to evaluate the qualitative- qualitative variables. Questionnaires were evaluated using the test-retest method, based on Cronbach's alpha (about 0.8 was calculated), which was used for the main population. Data were entered into SPSS software version 21. $p < 0.05$ was considered statistically significant.

RESULTS

A total of 113 physicians responded to the questionnaire. The characteristics of physicians are shown in Table 1. Seventeen percent ($n = 20$) had clinical experience of 10 years and more. Physicians' choices according to their selected management options are shown in Table 2. The mean age

TABLE 1

Demographics characteristics of physicians

| Parameter | n (%) |
|------------------------------------|------------|
| Specialty | |
| Internists | 57 (50.4) |
| Pulmonologists | 14 (12.4) |
| Cardiologist | 42 (37.2) |
| Status | |
| Residents | 81 (72) |
| Board certified specialist | 32 (28) |
| Age (average, max–min) | 33 (26–55) |
| Work experience (average, max–min) | 5.7 (1–28) |
| Experience ≥ 10 years | 20 (17) |

of physicians in the group who chose not to give treatment to their patients was 34.5 years old. In the group who decided to give treatment, the mean age was 32.4 ($p = 0.076$). As shown in Table 3, 34.5% ($n = 39$) of physicians who chose no treatment (or let the patients make the decision themselves) were asked about the factors that influenced their decision to start the treatment.

There was a significant statistical difference in treatment with anticoagulant between residents and board-certified specialists ($p = 0.038$), with residents more likely to treat (79% vs. 59.3%) (see Table 4). In addition, willingness to provide anticoagulant therapy differed significantly across specialties, with internists being most likely and pulmonologists least likely ($p = 0.007$) (see Table 5).

Physicians were asked about the relationship between the mean numbers of patients seen during 1 month with their unwillingness to give treatment to these patients. There was no significant difference between the number of patients seen and the unwillingness to treatment ($p = 0.33$). The results are shown in Table 6.

Physicians were asked to describe how the probabilities of SSPE recurrence would affect their decision to provide anticoagulant treatment. With an increased probability of recurrence, the likelihood of physicians prescribing anticoagulation therapy also increased (Table 7).

DISCUSSION

The introduction of CTPA has led to an increase in PE diagnosis. However, the mortality rates of PE have remained unchanged, suggesting an increase in the diagnosis of lower severity disease [3]. The current CHEST

TABLE 2

Physician choices regarding treatment in patients with SSPE and negative past medical history

| Management options | n (%) |
|---|-----------|
| No anticoagulant treatment without further observation | 10 (8.8) |
| No anticoagulant treatment + Performing V/Q scan | 1 (0.9) |
| No anticoagulant treatment +Following the patient with serial color Doppler ultrasonography | 17 (15) |
| Anticoagulant treatment only during hospitalization and then follow-up without medication | 2 (1.7) |
| Anticoagulant treatment for less than 3 months | 6 (5) |
| Anticoagulant treatment for 3–6 months | 39 (34.5) |
| Long-term treatment with anticoagulant for more than 6 months | 27 (24) |
| Leave the decision to the patient | 11 (9.7) |

TABLE 3

Factors that would influence physician's decision to begin anticoagulation treatment in patients with SSPE

| Clinical considerations | Physician's options (%) |
|--|-------------------------|
| Past medical history of DVT or PTE | 87 |
| Past medical history of cancer surgery and chemotherapy during the last 3 months | 58 |
| Both above listed risk factors | 44 |
| Immobilization | 76 |
| More than one SSPE | 46 |

Note: DVT, deep vein thrombosis; PTE, pulmonary thromboembolism; SSPE, subsegmental pulmonary embolism.

TABLE 4
Willingness to treat based on physician board certification

| Board certification | Willingness to treat | | | Patient's decision | Total |
|---------------------|----------------------|------|------|--------------------|-------|
| | Yes | No | | | |
| No | <i>n</i> | 64 | 15 | 2 | 81 |
| | % | 79 | 18.5 | 2.46 | 71.6 |
| Yes | <i>n</i> | 19 | 9 | 4 | 32 |
| | % | 59.3 | 28.1 | 12.5 | 28.3 |
| Total | <i>n</i> | 83 | 24 | 6 | 113 |
| | % | 73.4 | 21.2 | 5.3 | 100 |

TABLE 5
Willingness to treat as per speciality

| Specialty | Willingness to treat | | | Patient's decision |
|---------------|----------------------|-------|-------|--------------------|
| | Yes | No | | |
| Internist | <i>n</i> | 47 | 8 | 2 |
| | % | 56.6 | 33.3 | 33.3 |
| Cardiologist | <i>n</i> | 31 | 8 | 3 |
| | % | 37.3 | 33.3 | 50.0 |
| Pulmonologist | <i>n</i> | 5 | 8 | 1 |
| | % | 6.0 | 33.3 | 16.7 |
| Total | <i>n</i> | 83 | 24 | 6 |
| | % | 100.0 | 100.0 | 100.0 |

Guidelines for antithrombotic therapy in VTE diseases suggested, in patients with SSPE without proximal DVT and who have low-risk for recurrent VTE, follow-up without anticoagulant therapy [11]. While the guidelines became available online during the first months of 2016, our study was conducted from May 2016 to November 2016. Therefore, many of the physicians involved were possibly not familiar with the new guidelines at the time of this study. Unfortunately, we did not survey the respondents about their awareness regarding these updated recommendations.

Raslan et al. [12] reported that 34% of patients with ISSPE who received anticoagulation therapy had at least a 2 g/dL drop in hemoglobin level and (or) needed a blood transfusion within 3 months of follow-up. *There were no VTE-related deaths.* Lim et al. [13] investigated the attitudes of oncologists, pulmonologists, and palliative care physicians about the subsegmental PE treatment with anticoagulants in cancer patients. The least interest in the treatment of asymptomatic single SSPE patients with sigmoid cancer who received chemotherapy was among palliative medicine specialists (46.2%), followed by pulmonologists (56%); most interested in giving treatment were oncologists (83.6%). In our study, 56.6% of internists and 6% of pulmonologists prefer to treat their patients. Moreover, respondents preferred to initiate anticoagulant agents in the presence of metastatic cancer, symptoms like dyspnea, multiple SSPE, and previous DVT.

A survey conducted among the Thrombosis Interest Group of Canada (TIGC) investigated Canadian thrombosis physicians' opinion about treating a patient with symptomatic unprovoked single SSPE who have not contraindication to anticoagulation. Results showed that 7.1% of physicians chose not to treat with anticoagulation without further diagnostic imaging, compared to 8.8% in our study; 40.5% chose not to treat, but they followed up patients with serial colour Doppler ultrasonography versus 15% in our study; 28.6% chose not to treat but performed V/Q scan versus 0.9% in our study; 12% of TIGC physicians selected 3–6 months of anticoagulation therapy versus 34.5% in our study [14]; 76.3% of TIGC physicians chose not to treat versus 24.7% of physicians in our study who chose not to treat; and 9.7% of our respondents left the decision on the patients.

TABLE 6
The relationship between physician's unwillingness to treat the ISSPE patients and the mean number of patients with ISSPE who visited over 1 month

| Mean number of patients with ISSPE typically seen during 1 month | Percent of physicians reporting | Tend to "NO treatment" |
|--|---------------------------------|------------------------|
| 0–5 | 48.7% | 21.8% |
| 5–10 | 31.9% | 33.3% |
| >10 | 19.5% | 18.2% |

Note: ISSPE, isolated subsegmental pulmonary embolism.

TABLE 7
Reluctance to treat according to the probability of the recurrence of ISSPE within 3 months

| Probability of recurrence within 3 months after ISSPE | No treatment (%) |
|---|------------------|
| Any probability | 29.2 |
| 1% | 46.1 |
| 5% | 21.2 |
| 10% | 3.5 |

Note: ISSPE, isolated subsegmental pulmonary embolism.

In a study conducted by Pesavento et al. [15], 219 physician attendees of medical conferences and members of thrombosis research programs were questioned about treating an asymptomatic and symptomatic ISSPE. Most respondents were in Internal Medicine or Cardiology department, Thrombosis Centre or Vascular Medicine Service; 90.9% of them chose anticoagulant treatment regardless of other risk factors in symptomatic patients, while 5% chose no treatment. Asymptomatic patients were treated by 58.7% of physicians anyway, but 34.5% would prefer to treat the patients with underlying risk factors. The most common risk factors for treatment, like in our study, were the presence of active cancer and a history of VTE. Moreover, a reduction in cardiopulmonary reserve was another common risk factor in the Pesavento et al. study [15].

In a study conducted by Den Exter et al. [16], physicians were asked about treating asymptomatic SSPE in patients with and without cancer; 10.9% of physicians would prefer not to treat cancer patients while 89% of physicians started anticoagulant treatment. In our study, 58% of physicians started treatment in patients with a past medical history of cancer surgery and chemotherapy during the last 3 months. On the other hand, 28% of physicians in the Den Exter et al. study [16] would prefer not to treat patients without cancer, 23% started anticoagulants for 3 months, 43.5% anticoagulated patients for 6 months, and 5.6% for patients treatment undetermined period. In our study, 34.5% of physicians preferred anticoagulant treatment for 3–6 months, and 24% chose long-term anticoagulant treatment for more than 6 months.

Most physicians tend to initiate anticoagulant agents in symptomatic patients or in patients with underlying risk factors. But the most challenging part is to treat single SSPE patients without underlying risk factors. A 3-month prognosis in ISSPE patients is good, and the risk of side effects of anticoagulant drugs is higher than the risk of VTE recurrence in patients with an increased risk of hemorrhage complications [10].

One of the limitations of the current study is it was conducted very shortly after the release of new clinical practice guidelines on this topic, and practitioners may not have had time to implement the recommendations. A future study should evaluate current practice beliefs and determine whether practice change results from those guidelines. Another limitation of this type of study is recall bias. For example, in one part of the survey, participants were asked to recall how many patients with PE they see in a month.

Finally, future studies with larger sample sizes would also be recommended.

CONCLUSION

Our findings showed that most physicians tend to treat SSPE patients with anticoagulation drugs. On the other hand, more experienced physicians were more likely not to treat the patients with SSPE. Our study showed that management options can vary by specialty and years of experience, so the reasons for the difference should also be explored in future studies. Based on physician perspectives, anticoagulation treatment should be individualized based on underlying risk factors for bleeding or recurrence and patients' preferences.

DISCLOSURES

Contributors

All authors contributed to the conception or design of the work, the acquisition, analysis, or interpretation of the data. In addition, all authors were involved in drafting and commenting on the paper and have approved the final version.

Conflict of interest

The authors declare they have no conflict of interest.

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Ethical approval

This study was conducted according to the Declaration of Helsinki. Participants signed the informed consent form. The information provided by the respondents was kept confidential. Ethical approval from the Tehran University of medical science was obtained.

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