



# Risk Factors and Prevention of Pulmonary Embolism in Young Adults

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## Abstract

**Objective:** Pulmonary thromboembolism (PTE) importance is due to some reasons, first, it is one of the most common cardiovascular diseases, second it has high mortality and morbidity especially in some situations and third, prevention of this event is applicable and effective in most cases. The aim of this study was evaluation of predisposing factors of pulmonary emboli in young patients and defining preventive strategies in this age group.

**Materials and Methods:** In this retrospective study, recorded data including age, sex, presentation month, chief complaint, vital signs at admission, positive findings of physical examination, venous thromboembolism (VTE) risk factors, laboratory and imaging findings of patients with pulmonary embolism diagnosis who had 45 years old or less from March 2008 to March 2014 in Shahid Madani Heart hospital, Tabriz, Iran were evaluated. Statistical analysis was done via SPSS version 21.

**Results:** Eight hundred seventy patients had pulmonary emboli diagnosis during study period, 101 of them were  $\leq 45$  years old. Fifty-three patients were men and 48 of them were women. Mean age of patients was 33.6 years. Abnormal lower limb was the most frequent positive finding at physical examination. The important risk factor in women was hormonal change due to pregnancy or oral contraceptive pill use which was present in 50% of females. Smoking and immobilization due to surgery or trauma were the most common risk factor in men. Women had higher pulse rate ( $113.53 \pm 21.84$  vs  $101.33 \pm 20.27$ ,  $P = 0.005$ ) and lower hemoglobin ( $11.76 \pm 2.00$  vs  $13.52 \pm 2.21$ ,  $P = 0.000$ ) than men. The overall mortality rate was 10.8%.

**Conclusion:** Although all the risk factors of pulmonary emboli were not evaluated in our patients but the determined ones seem to be modifiable in majority of cases.

**Keywords:** Pulmonary, Thromboembolism, Young adult

## Introduction

Venous thromboembolism (VTE) which consists of pulmonary emboli and deep vein thrombosis is one of the three most common cardiovascular diseases. Mortality rate of acute pulmonary embolism could be as high as 60% (1). Apart from pulmonary emboli mortality and morbidity, it has major complications like chronic thromboembolic pulmonary hypertension (CTEPH), post-thrombotic syndrome and recurrent VTE (2). Although prevalence of pulmonary embolism is significantly lower (about 10 times) in young adults than in older patients (3), but it has shown previously that pulmonary thromboembolism (PTE) contribution to death is more prominent in young persons including 20-39 years old in comparison with other age groups (4). It is obvious that these problems on young adults are more tragic and they have also less comorbidity disorders and VTE risk factors, so preventing strategies may be more effective than older patients. Although suspicion to pulmonary emboli is the important

step in diagnosis, but establishment of it requires imaging modalities which make computed tomography (CT) the gold standard diagnostic test but some adverse complications of this technique such as radiation exposure, contrast dye consequences and the over diagnosis place the physician in challenging state (5). These problems are more obvious in young patients like in a pregnant woman so understanding various aspects of pulmonary emboli in this group is essential. Increasing trends of VTE diagnosis in adults has been found in previous years (6) and also in young women in recent years (7) but the exact cause of this curve has not been found. These studies show that VTE incidence may be changed around the world especially in young adults whereas in majority of countries this incidence has not been evaluated like in our country. Only with keeping in mind that VTE in young people is possible anyway, we could reduce the missed patients with this diagnosis. Various aspects of pulmonary embolism presentation in young adults have been evaluated in local

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studies (8) but it did not completely review in our region. Due to contribution of genetic and environmental factors in VTE incidence, the prevalence of it may be different in various territories, so finding out the nature and rate of this problem in every area could be helpful in overall prevalence of VTE and also in determining of involving factors. This understanding could be helpful in specific preventive and even treatment strategies in each region or by other means localization of proceedings.

The aim of this study was evaluation of young patients with pulmonary emboli diagnosis to find out their predisposing factors and defining preventive policies for reducing the incidence of PTE in these patients.

## Material and Methods

### Patient Selection

In this retrospective study, we selected the patients who discharged or expired with pulmonary emboli diagnosis between March 2008 to March 2014 in Shahid Madani hospital of Tabriz, Iran, which is the tertiary center of cardiovascular diseases of Northwest of Iran. The diagnosis were made by clinical evaluation, based on patients signs and symptoms combined with laboratory and imaging findings such as plasma D-dimer, chest x-ray, echocardiography and Doppler ultrasonography of lower limbs. Chest CT angiography was the mainstay of diagnosis whenever possible. Patients data including age, sex, presentation month, chief complaint, vital signs at admission, positive findings of physical examination, VTE risk factors, laboratory and imaging findings data were collected. For assessment of differences between patients younger than 30 years old from older ones, we divided them into two groups including greater or less than 30 years old. Another category of patients was about their gender, so we could define differences between men and women.

### Statistical Analyses

SPSS version 21 was used for statistical analysis. For qualitative variables, chi-square or Fisher exact test, whether which was appropriate and for quantitative ones, independent t-test were used to comparing between two groups. Significant difference was defined as  $P < 0.05$ .

## Results

Eight hundred seventy cases had PTE diagnosis in the study period and 101 patients were 45 years old or less. The proportional incidence of young patients with pulmonary emboli diagnosis has increased in our hospital in recent years (Figure 1).

From these young patients, 53 (52.5%) were men and 48 (47.5%) were women. The mean age of patients was approximately 33.6 years. Pure dyspnea was the frequent symptom (73.3%) followed by dyspnea plus chest pain which were present in 22.8% of patients. Neurological findings such as disorientation were detected in 1% of patients. Heart and lung examination were normal in almost all patients while lower limb examination was abnormal in near 15% of patients. 31.7% of patients had not identi-

fiable risk factor.

Twenty-four of women which accounts for 50% of them were pregnant or had used oral contraception pills (OCPs). Nineteen patients (18.8%) had recent surgery, trauma or immobilization and 6% of patients had active cancer. The remainder risk factors were less frequent including congestive heart failure (3%), autoimmune disease (3%), arterial disease (3%) and chronic kidney disease (2%).

Smoking as the VTE risk factor was detected in 21 patients (20.8%) and all of users were men.

The three most common risk factors for men were smoking (39.6% of men), recent surgery, trauma or immobilization and for women were pregnancy, OCP consumption and recent surgery or immobilization. Mortality rate was 10% all of patients (5.6% of men and 16.6% of women)

Women had higher pulse rate and lower hemoglobin than men, respiratory rate also tends to be higher in women, but other quantitative variables had not significant differences between two sexes.

Personal or family history of VTE was more common in males. The prevalence of PTE was higher in winter, followed by spring and then autumn and summer (Figure 2). Disease seasonal presentation was also different between two genders. While the incidence of pulmonary emboli was higher at spring in males, for females the winter was. Comparison between men and women findings are summarized in Tables 1 and 2.

In another category, comparison between patients older than 30 years old and the others showed no significant

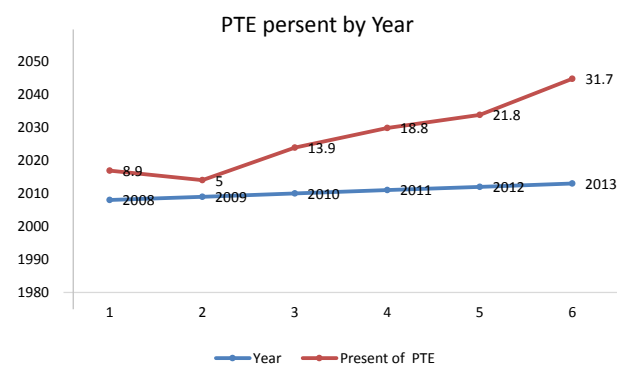


Figure 1. PTE Presented by Year (Data presented in percentage).

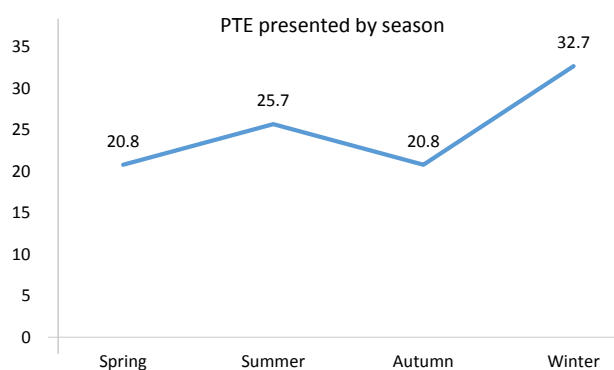


Figure 2. Prevalence of PTE by Season.

**Table 1.** Comparison of Vital Signs and Laboratory Findings Between Men and Women

Variable	Male	Female	P Value
Age	34.07± 7.28	33.06± 6.11	0.453
Systolic blood pressure	115.73± 17.22	112.70 ± 20.77	0.427
Diastolic blood pressure	73.26± 10.92	72.71± 12.45	0.815
Pulse rate	101.33± 20.27	113.53± 21.84	0.005
Respiratory rate	21.34± 4.74	23.52 ± 6.48	0.066
Blood temperature	36.93± 0.55	37.01± 0.37	0.419
Oxygen saturation	88.76± 6.45	87.42± 15.65	0.694
Lymphocyte count	4.37± 7.09	2.85± 5.09	0.348
Neutrophil count	8.11± 5.82	7.06 ± 4.54	0.462
Hemoglobin	13.52± 2.21	11.76 ± 2.00	0.000
Platelet count	267.50± 111.63	231.04± 108.88	0.113
Lactate dehydrogenase level	593.53± 362.58	793.32± 840.61	0.177
BUN	18.20± 10.16	16.18± 15.43	0.453
Cr	1.05± 0.57	1.31± 1.19	0.669
ESR1	32.00± 33.24	28.25 ± 28.87	0.654
ESR2	51.92± 48.26	49.33± 45.89	0.841
CPK	139.50± 242.93	355.90± 996.76	0.141
CK-MB	23.84± 16.17	33.61± 62.98	0.285
CTNI	0.36± 0.48	0.30± 0.60	0.528
PH	7.38 ± 0.17	7.38± 0.13	0.933
PCO2	37.62± 11.33	36.90± 17.30	0.873
HCO3	25.51± 7.34	21.65± 5.55	0.040
PO2	76.09 ± 62.21	61.50± 30.91	0.280
EF	52.04± 9.42	53.73± 5.13	0.325

Abbreviations: LDH, lactate dehydrogenase; BUN: blood urea nitrogen; Cr, Creatinine; ESR 1: erythrocyte sedimentation rate 1st hour; ESR 2: erythrocyte sedimentation rate 2nd hour; CPK: creatinine phosphokinase; CK-MB: CPK – muscle brain (type); CTNI: cardiac troponin type I; EF: Ejection Fraction.

**Table 2.** Comparison of Seasonal Presentation, Chief Complaint and VTE Risk Factors Between Men and Women

Variables	Male No. (%)	Female No. (%)	P Value
Seasonal presentation			
Spring	17 (32)	4 (8.3)	0.006
Summer	11(20.7)	15 (31.2)	0.260
Autumn	10 (18.8)	10 (20.8)	1.000
Winter	14 (26.4)	19 (39.5)	0.203
Chief complaint (dyspnea)	37 (69.8)	37 (77)	0.902
VTE risk factors			
Pregnancy/OCP consumption	-	24 (50)	0.000
Recent surgery, trauma or immobilization	14 (26.4)	10 (20.8)	0.641
Personal or family history of VTE	8 (15)	1 (2)	0.033
Cancer	3 (5.6)	3 (6.2)	1.000
CHF	2 (3.7)	1 (2)	1.000
Autoimmune disease	-	3 (6.2)	0.104
Arterial event	2 (3.7)	1 (2)	1.000
CKD	1 (1.8)	1 (2)	1.000
Smoking	21 (39.6)	-	0.000
Mortality	3 (5.6)	8 (16.6)	0.112

Abbreviations: OCP: oral contraception pill; CHF, congestive heart failure; CKD, chronic kidney disease; VTE, venous thromboembolism.

differences among them except for lower erythrocyte sedimentation rate (ESR) and the more negative Rh blood group in younger patients. This category findings are summarized in Tables 3 and 4.

## Discussion

VTE is uncommon or even rare (9) among young adults and its incidence significantly increases with aging (10). These clinical findings are also confirmed by imaging modalities (11), however due to pulmonary emboli under-diagnosis, probably actual incidence of this problem is higher than recorded ones (12).

In our study the prevalence of PTE in young adults was low but the recorded frequency has ascending tendency in recent years. It may be due to some reasons, first, awareness of physicians about this disease and so lower rate of missed cases, second, increased sensitivity of diagnostic techniques, third, it may be a real increase which is due to increase in risk factors like obesity, immobility, smoking, trauma, and also some less considered factors such as air pollution, nutritional factors and daily stresses. Previous studies have showed an association between arterial and venous thrombosis (13) or by other means between atherosclerosis and VTE risk factors (14) so the increase of coronary events in young adults (15) as well as pulmonary embolism at same place is possible.

**Table 3.** Comparison of Admission Vital Signs and Laboratory Findings Between Younger and Older of 30 Years Old

Variable	<30	>30	P Value
Age	26.56 ± 3.40	38.01 ± 3.96	0.000
SBP	114.23 ± 18.32	114.36 ± 19.47	0.974
DBP	71.64 ± 11.30	73.91 ± 11.79	0.344
PR	110.30 ± 19.63	105.00 ± 22.99	0.237
RR	22.91 ± 6.12	21.89 ± 5.32	0.398
BT	37.00 ± 0.46	36.94 ± 0.49	0.562
O2 Sat	86.88 ± 12.85	88.65 ± 11.87	0.620
Lymph	4.40 ± 7.78	3.05 ± 4.69	0.411
Neutrophil	7.77 ± 4.46	7.43 ± 5.68	0.815
Hb	12.91 ± 2.29	12.51 ± 2.27	0.413
Platelet	232.62 ± 86.89	260.71 ± 123.99	0.233
LDH	583.46 ± 291.90	733.86 ± 740.21	0.325
BUN	17.14 ± 15.53	17.31 ± 11.14	0.952
Cr	0.98 ± 0.93	1.15 ± 0.89	0.381
ESR1	20.25 ± 24.01	37.53 ± 33.69	0.037
ESR2	33.17 ± 37.35	63.58 ± 49.16	0.016
CPK	301.85 ± 1001.09	196.46 ± 412.85	0.486
CK-MB	31.89 ± 65.03	25.67 ± 19.58	0.503
CTNI	0.28 ± 0.25	0.37 ± 0.64	0.465
PH	7.38 ± 0.10	7.38 ± 0.16	0.974
PCO2	37.52 ± 19.78	37.00 ± 12.53	0.908
HCO3	22.35 ± 7.53	23.51 ± 5.99	0.554
PO2	64.76 ± 28.22	68.32 ± 52.37	0.801
EF	54.81 ± 6.22	51.50 ± 8.43	0.056

Abbreviations: LDH, lactate dehydrogenase; BUN: blood urea nitrogen; Cr, Creatinine; ESR 1: erythrocyte sedimentation rate 1st hour; ESR 2: erythrocyte sedimentation rate 2nd hour; CPK: creatinine phosphokinase; CK-MB: CPK – muscle brain (type); CTNI: cardiac troponin type I; EF: Ejection Fraction; SBP, systolic blood pressure; DBP; diastolic blood pressure.

Although our small study population, the seasonal variation in the pulmonary embolism incidence is comparable with larger studies (16,17) which indicate the higher outbreak of PTE in winter or cold weather month, however, some investigations has showed no significant seasonal differences of this disease (18).

Although the results of previous studies about VTE incidence between men and women have controversies, a systematic review has shown no differences in two sexes (19). In other word, in spite of some differences in the presentation of pulmonary embolism between two genders but the prevalence in each group in totally the same (20) same as our study.

In this study, the most common risk factors of VTE were pregnancy, OCP consumption in women and recent surgery trauma or immobilization and smoking in men.

One of the most important risk factors of venous thromboembolism in young women is various forms of contraceptives which is present in significant number of case reports even in healthy and athlete women (21-23).

All forms of combined hormonal contraception such as pill, patch or even vaginal ring could enhance the risk of

**Table 4.** Comparison of Gender, Chief Complaint, Rh Group VTE Risk Factors and Seasonal Presentation Between Younger and Older 30 Years Old

Variable	<30 y (n=39) No. (%)	>30 y (n=62) No. (%)	P
Gender (male)	20 (51)	33 (53.2)	0.849
Chief complaint (dyspnea + chest pain)	6 (15.3)	17 (27.4)	0.038
Negative Rh group	7 (20.5)	2 (4.2)	0.031
Risk factor			
Pregnancy/OCP consumption	12 (30.7)	12 (19.3)	0.232
Recent surgery, trauma or immobilization	8 (20.5)	16 (25.8)	0.635
Personal or family history of VTE	3 (7.6)	6 (9.6)	1.000
Cancer	1 (2.5)	5 (8)	0.401
Congestive heart failure	2 (5.1)	1 (1.6)	0.557
Autoimmune disease	0 (0.0)	3 (4.8)	0.282
Arterial event	0 (0.0)	3 (4.8)	0.282
Chronic kidney diseases	0 (0.0)	2 (3.2)	0.521
Smoking	7 (17.9)	14 (22.5)	0.646
Seasonal presentation			
Spring	6 (15.3)	15 (24.1)	0.325
Summer	11 (28.2)	15 (24.1)	0.816
Autumn	6 (15.3)	14 (22.5)	0.449
Winter	16 (41)	17 (27.4)	0.193
Mortality	5 (13.1%)	6 (9.6%)	0.744

Abbreviations: OCP: oral contraception pill; CHF, congestive heart failure; CKD, chronic kidney disease; VTE, venous thromboembolism.

VTE especially in the first few months of consumption. Women with a history of VTE should not take combined hormonal contraception, for these patients the progesterone - only contraception is acceptable (24).

There is similarity between pulmonary embolism nature in contraceptive use and during pregnancy (25). Near one-third of women had pregnancy as their risk factor in our study which is a high percent and with accounting the fetus life, the load of this problem is remarkable. About 0.05%-0.2% of pregnancies may be complicated by VTE. Mortality rate of antenatal pulmonary embolism was about 3.5% in one study, but majority (near 80%) of those expired women had identifiable risk factors such as history of unprovoked VTE. Therefore, women should be evaluated about VTE risk factors as soon as possible during pregnancy or even before it. High risk patients may be candidate for prophylactic therapy (26,27) .

Pregnancy related VTE was one of the most common causes of maternal death in some studies. The risk of this event in a pregnant woman is more than 20 times greater than non-pregnant ones. The important risk factors for VTE during pregnancy or post-partum period were infection, hospitalization, multiple pregnancies, hyperemesis, obesity, preeclampsia, major post-partum bleeding, cae-

sarian section, fetal death or intra uterine growth retardation (28).

The other common risk factors of VTE in this study were smoking and immobility. Smoking is a modifiable risk factor. Reducing complete bed rest days after surgery and VTE prophylactic regimens during those periods are the two important steps in PTE prophylaxis for reducing immobility effect on venous thromboembolism.

Approximately one third of patients with VTE have some form of inherited thrombophilia (29). Probably impact of this disorder on young patients with VTE is higher for example there are several reports of Pr-C deficiency presenting as venous thromboembolism in young adults (30), so evidence suggests screening of patients younger than 50 years old in special situations (31). Multiple heritable defects may be responsible for thrombotic tendency so it is not too easy to find out the exact responsible of thrombotic event. Inherited coagulopathy state was not evaluated in our patients but it might be present in some of our patients without identifiable risk factors and also in the others who have one or more risk factor.

Accounting all these factors, it seems that prevention of VTE in young adults is more applicable and helpful than older ones.

### Limitations

This study has some limitations, first due to its retrospective funds some data were not collected for example body mass index (BMI) of patients or inherited defects. There is also missing information of some patients which made the *P* value of those data less accurate.

### Conclusion

Hereditary causes may play significant role in young adults pulmonary emboli, however the increased proportional incidence of PTE in this group in recent years, suggests importance of acquired factors. Regarding this, risk stratification and preventive strategies seems to be more practical in this group of patients.

### Ethical Issues

The local ethics committee approved this study.

### Conflict of Interests

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