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# Cardiac Findings of Pulmonary Thromboembolism by Autopsy: A Review of 48 Cases

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**Background:** To identify the overall effects of pulmonary thromboembolism (PTE) on the heart, we evaluated the heart findings and clinical characteristics of deceased patients diagnosed with PTE.

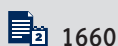
**Material/Methods:** PTEs were classified into 2 categories: fatal and contributory. Cases with a history of cardiopulmonary disease or a finding of significant disease at autopsy, including valvular heart disease and coronary artery obstruction >50%, were excluded from the cardiac evaluation. We defined an LV wall  $\geq 1.2$  cm thick and an RV wall  $\geq 0.8$  cm thick as abnormal.

**Results:** Forty-eight cases were included to the study (21 males and 27 females). The mean age was  $41.42 \pm 16.5$  years. Of the 48 cases, 5 were excluded due to cardiopulmonary diseases for determining heart findings. The thicknesses of the LV and RV walls were not measured in some patients. In the 43 cases, cardiac hypertrophy was detected in 28 patients (65.1%). The mean heart weight was  $387 \pm 83.5$  g. The mean thickness of the left ventricle (LV) wall was  $1.40 \pm 0.41$  cm in 40 cases, and the mean thickness of the RV wall was  $0.41 \pm 0.135$  cm in 41 cases. The LV walls of 35 (87.5%) cases and the RV walls of 2 cases met criteria for abnormal wall thickness. There were histopathological findings of heart in 24/43 cases (56%); these findings were necrosis, fibrosis, and hypertrophy.

**Conclusions:** The RV is affected by massive pulmonary embolism; however, the LV may also play a role in the pathogenesis of PTE.

**MeSH Keywords:** **Autopsy • Hypertrophy, Left Ventricular • Pulmonary Embolism**

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## Background

Pulmonary thromboembolism, consisting of deep vein thrombosis (DVT) and associated complications, is associated with serious and fatal outcomes. For almost one-quarter of such patients, the initial clinical presentation is sudden death. Autopsy is the criterion standard method of establishing death due to PTE [1–3].

There have been a number of studies on the pathophysiology of PTE [4–7]. PTE causes right ventricle (RV) dysfunction, which is associated with a dramatically higher incidence of mortality [8,9]. Few reports have addressed the heart findings of patients with PTE by autopsy [10,11].

To identify the overall effects of PTE on the heart, we evaluated the heart findings and clinical characteristics of deceased patients that had been diagnosed with PTE.

## Material and Methods

Forensic files stored at the Council of Forensic Medicine, Ministry of Justice in Istanbul, Turkey, from January 2010 to December 2014 were screened for deaths with autopsy-confirmed PTE. The following data were collected: demographic information, medical history, clinical diagnosis, signs and symptoms before death, BMI, point of origin of PTE, thicknesses of the LV and RV walls, and heart weight. Symptoms and clinical courses of the deceased were determined using reports by the bereaved family recorded in the patient's files.

PTE were classified into 2 categories: fatal (no other cause of death found at autopsy, the emboli occluding at least 2 lobar arteries) and contributory (factors other than PTE also implicated, the emboli occluding at least 1 lobar artery or multiple segmental artery).

Cases with a history of cardiopulmonary disease or a finding of significant disease at autopsy, including valvular heart disease and >50% coronary artery obstruction, were excluded from the cardiac evaluation. Right and left ventricular hypertrophy was quantitatively assessed by autopsy using recommendations of the American Society of Echocardiography [12]. We defined LV wall thickness  $\geq 1.2$  cm and RV wall thickness  $\geq 0.8$  cm as abnormal.

### Data analysis

All data were managed and analyzed using the Statistical Package for the Social Sciences version 13.0 software. Quantitative data are presented as means  $\pm$  standard deviations, and categorical data are presented as counts and percentages.

## Results

Of the 48 cases with PTE, 21 (43.8%) were males and 27 (56.3%) were females. The mean age was  $41.42 \pm 16.5$  years, with a range of 16–80 years. There were 26 cases (54.16%) over the age of 40 years, and 22 (45.83%) under the age of 40 years. Obesity, defined as a body mass index (BMI)  $\geq 25$ , was detected in 30 patients (62.5%) and the mean value was  $27.16 \pm 4.67$ .

The majority of patients exhibited large, coiled thromboemboli in the pulmonary trunk and its major branches. In 7 patients, dissection of lobar and segmental pulmonary arteries demonstrated large numbers of smaller thromboemboli.

PTE was the main cause of death in 83.3% (40/48) of the cases, and was a contributing factor in 16.7% (8/48). Of the 48 autopsy-confirmed PTE cases, 19 (39.6%) had shortness of breath, 13 (27.08%) had syncope, and 6 (12.5%) were in shock (Table 1).

In all, 76% (32/48) had 2 or more risk factors, 52% (13/48) had 3 or more risk factors, 18 (37.50%) suffered multiple traumas, and 21 (44%) underwent surgery (Table 2). Deaths occurred after the second week of certain risk factors for PTE in the 24/32 (75%).

Of the 48 cases, 5 were excluded due to cardiopulmonary diseases for determining heart findings. In addition, the thickness of the LV and RV walls were not measured in some patients. Data about diameter of ventricles are not routinely recorded in autopsy studies. In the 43 cases (mean age  $40.16 \pm 14.8$  years), cardiac hypertrophy, defined as a heart weighing  $\geq 300$  g for females and  $\geq 400$  g for males, was detected in 28 patients (65.1%). The mean heart weight was  $387 \pm 83.5$  g. The mean thickness of the left ventricle (LV) wall was  $1.40 \pm 0.41$  cm in 40 cases, and the mean thickness of the RV wall was  $0.41 \pm 0.13$  cm in 41 cases.

We defined an LV wall  $\geq 1.2$  cm thick and an RV wall  $\geq 0.8$  cm thick as pathogenic. The LV walls of 35 (87.5%) cases and the RV walls of 2 cases met these criteria (Table 3).

Twenty-four cases (56%) had remarkable histopathological findings (necrosis, hypertrophy, or fibrosis) while the other 19 (44%) cases had mild congestion or normal tissue findings. Necrosis was identified as myocardial necrosis without evident thrombus at the coronaries or atheroma plaques. Fibrosis was present either at perivascular or interstitial areas. Cardiac hypertrophy (enlargement of myocardial cells) was described in 9 cases (21%). Of these, 2 had hypertrophy of the LV; however, the side of hypertrophy was not indicated for the other cases. Acute myocardial infarction (AMI) with concomitant pulmonary embolism was diagnosed in 1 case.

**Table 1.** Clinical features prior to death.

Findings	No. of PTE (%)
Dyspnea	19 (39.6)
Syncope	13 (27.08)
Chest pain	2 (4.16)
Tachycardia	1 (2.08)
Hemoptysis	1 (2.08)
Hyperemia, swelling on the leg	5 (10.41)
Hypovolemic shock	6 (12.5)
Presentation with exitus	21 (43.8)

PTE – pulmonary thromboembolism.

**Table 2.** Potential risk factors.

Risk factor	Number of cases (%)
Trauma	18 (37.50)
Surgery	21 (44)
Immobilization	13 (27.1)
Age >40 years	26 (54.16)
Pregnancy	9 (19)
Others*	17 (35.4)

\* Behçet’s disease, chronic obstructive lung disease, obesity, chronic liver disease, hypertension, diabetes, heart disease, depression.

**Table 3.** Abnormal heart findings of PTE cases.

	Heart weight (≥400 g in males, ≥300 g in females)		Thickness of LV (12 mm ≥)	
	<40 years	≥40 years	<40 years	≥40 years
Male (n)	3	6	7	9
Female (n)	10	9	11	8
Total(n)	13	15	18	17
	65.1% (28/43)		87.5% (35/40)	

g – gram; LV – left ventricle; mm – milimeters; PTE – pulmonary thromboembolism.

## Discussion

A sudden increase in pulmonary artery pressure reflects an abrupt increase in RV afterload, with consequent elevation of RV wall tension, followed by RV dilation and dysfunction. In addition, elevated wall tension also increases RV myocardial oxygen demand, resulting in ischemia, which may promote further RV dysfunction and cardiogenic shock. Perpetuation of this cycle can lead to RV infarction, circulatory collapse, and death [13–15]. There are a few autopsy and experimental studies on pathogenesis of RV in PTE [10,11,16,17]. RV tissue obtained at autopsy from humans with PTE also showed the presence of inflammation in 2 studies [10,11].

In the present study, the aim of autopsy was to determine the cause of death, so a detailed examination of the heart was not performed histopathologically. However, the thicknesses of the LV and RV walls and heart weight were measured in most cases, and we found pathogenic thickness of LV wall in the majority of cases. Orde et al. [11] reported inflammatory changes within the RV myocardium but not the LV myocardium; in addition, PTE cases had thicker RV walls than controls.

Iwadata et al. [10] reported a mild increase in the number of macrophages in the LV wall in some cases. In a report of 2 cases by Iwadata et al. [17], the LV wall of 1 case was 17 mm thick in patients with massive PTE.

In the present study, most cases had LV walls of pathogenic thickness; thus, the LV might also play a role in the pathogenesis of PTE. This finding can be explained as follows. In PTE, when the RV dilates, the interventricular septum shifts toward the LV, which may lead to underfilling of this chamber. In addition, RV contractile dysfunction and acute tricuspid regurgitation may decrease RV output and further reduce LV preload. With underfilling of the LV, systemic cardiac output and pressure decrease, potentially compromising coronary perfusion [13,14]. However, the RV is less susceptible to ischemic injury than the LV because of its relatively thin wall and lower systolic pressure. Therefore, decreases in coronary pressure due to diminished cardiac output may also induce ischemia in the LV [13,14]. When ischemia leads to damage to cardiomyocytes or when there is an increased load on the heart leading to inadequate contraction, the heart undergoes hypertrophy, with a compensatory response. Cardiomyocytes become thicker

and longer, and the thickness of the ventricular wall increases [18–20]. Hypertrophy of the left ventricle was supported in at least 2 of 9 cases histopathologically; the small number was due to failure to perform detailed histopathological examination of the heart, and this is a limitation of the present study.

Abnormal LV geometry has been identified in patients who are older (>70 years) and more obese (>30 kg/m<sup>2</sup>) [21–23]. In the present study, the mean age and BMI were 40.16 years (SD 14.863 years) and 27.16 (SD 4.678), respectively. Only 10 cases (10/35, 22%) were more obese. This suggests that the LV was affected by PTE.

Deaths occurred after the second week of certain risk factors for PTE in the 24/32 (75%). Clinically, patients might delay going to the hospital for complaints due to PTE in our community. Thus, physicians should provide appropriate information to patients who have certain risk factors (e.g., trauma, surgery, and pregnancy) to predict acute PTE at a preventable stage. This can be effective for preventing sudden death due to acute PTE.

PTE may cause ventricular myocardial inflammation and necrosis, distinct from that seen in typical myocardial infarction due to atherosclerotic diseases. Typical pathological findings of myocardial infarction are transmural or subendocardial coagulation necrosis [10,11,17]. In the present study, coronary arteries of cases with myocardial necrosis were free of significant atherosclerotic disease. This finding proves that necrosis is related to PTE.

There was only 1 case that had been diagnosed as having AMI with concomitant pulmonary embolism, a 64-year-old woman who presented to the Emergency Department with acute dyspnea and chest pain. AMI (MI) and pulmonary embolism

concomitantly were diagnosed by autopsy. There was occlusive disease in the left coronary artery. Therefore, we determined that PTE was a contributing factor of the main cause of death in this case. Acute myocardial infarction and pulmonary embolism lead to life-threatening conditions such as sudden cardiac death and congestive heart failure [24]. These diseases have common risk factors, such as obesity and metabolic syndrome [25]. Some studies have shown an association between pulmonary embolism and arterial cardiovascular events [25–27]. We hypothesized that patients with venous thrombosis may be at increased risk for myocardial infarction because a large right ventricle and hypertrophy of the left ventricle were identified in this case by autopsy, potentially compromising coronary perfusion.

Shortness of breath is more common in cases with pulmonary thromboembolism (PTE) [28]. Our study illustrates the importance of considering fatal pulmonary thromboembolism, especially in the differential diagnosis of patients presenting with syncope.

## Conclusions

PTE is a fatal disorder. Physicians should provide appropriate information to patients who have certain risk factors (e.g., trauma, surgery, and pregnancy) to predict acute PTE at a preventable stage. The RV is known to be affected by massive PTE. However, the LV may also play a role in the pathogenesis of PTE. This should be investigated in further studies.

## Conflict of interest

There are no conflicts of interest for any author.

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