Legal Medicine 20 (2016) 68–74

Contents lists available at ScienceDirect

Legal Medicine

journal homepage: www.elsevier.com/locate/legalmed

# Pulmonary thromboembolism on unenhanced postmortem computed tomography: Feasibility and findings

Garyfalia Ampanozi [a,*], Ulrike Held [b], Thomas D. Ruder [a,c], Steffen G. Ross [a], Wolf Schweitzer [a], Juergen Fornaro [a], Sabine Franckenberg [a], Michael J. Thali [a], Patricia M. Flach [a]

[a] Department of Forensic Medicine and Imaging, Institute of Forensic Medicine, University of Zurich, Winterthurerstrasse 190/52, 8057 Zurich, Switzerland
[b] Horten Centre, University of Zurich, Pestalozzistrasse 24, 8091 Zurich, Switzerland
[c] Institute of Diagnostic, Interventional and Pediatric Radiology, University Hospital Bern, Freiburgstrasse, 3010 Bern, Switzerland

ARTICLE INFO

*Article history:*
Received 19 February 2016
Received in revised form 16 April 2016
Accepted 18 April 2016
Available online 19 April 2016

*Keywords:*
Pulmonary thromboembolism
Postmortem CT
Autopsy
Virtopsy
Deep venous thrombosis

ABSTRACT

*Purpose:* The purpose of this study was to evaluate the feasibility of diagnosing fatal pulmonary thromboembolism (PTE) with unenhanced postmortem computed tomography (PMCT).
*Materials and methods:* Twelve cases with autopsy confirmed PTE and matched controls (n = 19) were retrospectively examined for PTE signs on PMCT. The following variables were evaluated: edema of the lower extremities (areal and Hounsfield Unit measurements) and observer dependent patterns of the morphology of the sedimentation in the pulmonary arteries and trunk.
*Results:* The median absolute difference between the areal measurements of the right and left lower leg and thigh and the attenuation of the popliteal adipose tissue did not differ significantly between the groups. In contrast, the categorical assessment of soft tissue edema in the lower extremities was significantly different. A statistically significant difference could also be found in the shape of the vascular content within the pulmonary trunk and arteries.
*Conclusion:* PTE may be assessed on unenhanced PMCT using diagnostic clues such as a distinct pattern of the pulmonary artery content and the presence of perivascular edema in the lower extremities.


## 1. Introduction

Pulmonary thromboembolism (PTE) rates, although declining primarily from a decreasing case fatality rate in stable patients [1,2], still comprise a significant cause of both morbidity and mortality, and PTE incidence increases with age [3,4]. The postmortem gold standard in the diagnosis of this pathologic entity is autopsy, as many cases can be missed by clinical examination [4] if they are not suspected. Certainly in clinical practice, computed tomography pulmonary angiogram (CTPA) is considered the gold standard. PTE fatalities occur sudden, unexplained and unexpected leading to an exceptional death which are subsequently investigated by forensic institutes.

Deep venous thrombosis, usually located in the lower extremities, is typically found after identification of PTE. The triplet of factors leading to thrombosis, namely vascular endothelial damage, stasis or deceleration of blood flow, and hypercoagulability of blood, are well known as Virchow's triad [5]. Clinical manifestations of lower extremity thrombosis include soft tissue edema below the level of thrombosis and swelling of the affected extremity [6]. However, edema of the legs does not have to be necessarily related to PTE, but rather to other etiologies e.g. cardiac failure. Sporadic case reports can be found in the literature also describing pelvic vein thrombosis as a source of the embolus [7]. Many risk factors for PTE have been suggested, with the most significant ones being surgeries, older age, increased body mass index (BMI), multiple traumas [8,9], malignancy, thrombophilia and a theory of de novo PTE [10].

Postmortem imaging has become a routine examination in many forensic institutes across the world [11], with postmortem computed tomography (PMCT) being the most widespread modality. Its limitations regarding natural causes of death, and in particular PTE, have been mentioned in the literature [12,13]. PMCT angiography (PMCTA) offers a possibility of diagnosing contrast medium filling defects of the pulmonary arteries [14–16], but in contrast to the clinical setting, these findings are not always due to PTE; the differentiation between true PTE and postmortem clotting is challenging. Postmortem clot formation, sedimentation of blood particles and the separation from blood plasma with typical leveling of the components are frequent postmortem findings due

* Corresponding author.
*E-mail address:* garyfalia.ampanozi@irm.uzh.ch (G. Ampanozi).

http://dx.doi.org/10.1016/j.legalmed.2016.04.005

to a lack of circulation and concomitant clotting, have been described in the literature [17,18]. For a precise diagnosis in a minimally invasive manner, a postmortem biopsy has to be performed – preferably based on PMCT and PMCTA findings [15]. Furthermore, there are few references with only small numbers of cases claiming that postmortem magnetic resonance (PMMR) imaging can provide reliable evidence regarding PTE [19]. Even if larger studies on PMMR prove that the technique is reliable for diagnosing PTE, access to such technology for most forensic institutes is impossible or restricted. Therefore, reliable diagnostic criteria using unenhanced PMCT are desirable.

Recent literature reports the use of PMCT in PTE diagnoses based on indirect signs such as increased venous diameter as a sign of venous congestion [20].

The purpose of this study was to identify possible characteristic patterns in cases of PTE pertaining to signs of thrombosis of the lower extremities and the morphology of the pulmonary trunk and main pulmonary artery branches in unenhanced PMCT.

## 2. Materials and methods

The Forensic Institute‘s database was retrospectively searched for a 4 year period. All fatal pulmonary thromboembolism cases were identified by using specific keywords (pulmonary embolism and pulmonary thromboembolism) and by reviewing the written autopsy reports. All cases referred to our institute in the above mentioned time period had undergone a whole-body PMCT examination, which was part of the post mortem examination commissioned to us by the responsible local justice authorities. Cases with advanced decomposition [21], amputation of at least one lower extremity, fractures of the lower extremities, non-parallel positioned legs on the CT couch, that exceeded the field of view, or with medical emergency infusions at the lower extremities (e.g., intraosseous infusions) were excluded.

### 2.1. PTE case group

Twelve cases with autopsy confirmed PTE as the cause of death (matching the inclusion and exclusion criteria) and available PMCT data were identified (3 females and 9 males, mean age 65.2 years, age range 44–93 years, mean BMI (kg/m$^2$) 27.9).

### 2.2. Control group

For each individual of the case group, the PMCT database was searched with the filtering functions for age and sex matched controls. Then – as close as possible – BMI-matched individuals with causes of death other than PTE were selected as controls for the PTE case group. At least one control was included in the group for each case. The control group consisted of 19 individuals (8 females and 11 males, mean age 58.7 years, age range 35–91 years, mean BMI (kg/m$^2$) 29.2).

### 2.3. PMCT scan protocol and image analysis

PMCT was performed on a 128-slice dual-source CT scanner (Flash Definition, Siemens, Forchheim, Germany). The scan parameters used followed those recommended by recent literature [22]: tube voltage 120 kVp; variable mAs values (reference 400 mAs) using automatic dose modulation software (CARE dose 4D, Siemens, Forchheim, Germany); 128 $\times$ 0.6 mm slice collimation; rotation 0.5 s; and pitch 0.6. Images were reconstructed with a soft tissue kernel and bone kernels. Whole body and thoracic/abdominal reconstructions were used for the evaluation of the lower extremities and the pulmonary artery.

For image analysis, the cases and controls were intermingled into one single group to blind image review concerning the group assignment. The images were evaluated by a forensic pathologist and a radiologist, both with distinct expertise in postmortem imaging.

A picture archiving and communication system (PACS workstation, IDS7, Sectra, Linköping, Sweden) was used for image assessment and analysis. As the viewer did not allow assessment of the circumference, we decided instead to assess the area of the axial slices of the lower extremities at pre-defined levels. Image review of the pulmonary trunk and arteries included a soft tissue window with 2 different settings: a broad window (center: 50, width: 350; preset: mediastinal window) and narrow window (center: 60, width 110; preset: liver window). The latter allowed for a better differentiation of the vascular content.

The cross sectional area of the lower leg was assessed in mm$^2$ at the level below the head of the fibula. The area was defined with the specific PACS tool by manually placing markers at the perimeter of the lower leg (Fig. 1a). In the same manner, the cross sectional area of the thigh was assessed at the level of the insertion of the musculus adductor longus at the linea aspera, located at the middle third of the medial lip of linea aspera (Fig. 1b). Differences between the two legs were then calculated. In one case, the thighs reached the margin of the extended field of view impeding measurements.

Focal soft tissue edema was assessed subjectively on the lower leg by assessing visual differences in the perivascular fatty tissue fluid concentration, namely fat stranding between the two legs (Fig. 2). Additionally, popliteal fat stranding was measured in Hounsfield Units (HU) of the adipose tissue of the popliteal fossa. The measurement was performed at the level directly above the patella by placing a circular region of interest (ROI) in a vessel-free fatty area (Fig. 1c). Differences between the two legs were then calculated. There was one case with unilateral knee arthroplasty and significant metal artifacts disabling assessment of fatty tissue HU.

Both the main pulmonary arteries and trunk were assessed by attribution to one of the categories idealized in a schematic diagram covering all encountered appearances of morphology detected in this study (Fig. 3a and b). Each individual of the study group was initially assigned to one of these categories, and finally, two clusters were formed throughout the data. The first one is shown in Fig. 3a with pulmonary arteries presenting either no sedimentation at all, a clear sedimentation line, or a homogenous clot of any shape. Fig. 3b depicts heterogeneities with an irregular shaped content within the pulmonary trunk or the main pulmonary arteries. In the cases containing irregular shapes, the main features were hyper- or hypodensities with irregular borders (Fig. 4). The morphology of the pulmonary trunk and the branching main artery content were assessed first by one reader and afterwards by both readers in consensus.

### 2.4. Autopsy

The diagnosis of PTE was assessed by autopsy. An autopsy was performed by two forensic pathologists, at least one of them board certified, assisted by an autopsy technician, and included standardized the opening of all 3 body cavities.

### 2.5. Statistical analysis

Categorical variables were described as percentages of the total, and continuous variables were described using median and interquartile ranges. The median absolute difference between the measurements on the right and left side for the cross sectional area (in mm$^2$) of the lower leg and the upper leg (thigh) were calculated