

## Imaging and Minimally Invasive Biopsy for Postmortem Pulmonary Fat Embolism Diagnosis

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### Abstract

In recent years, imaging technologies and minimally invasive biopsy have been gaining importance in forensic settings. This study aimed to evaluate the role of imaging and minimally invasive biopsy in postmortem diagnosis of pulmonary fat embolism. This was a systematic literature review by using Pubmed, EBSCO-Host, and ProQuest to search for studies on postmortem diagnosis of pulmonary fat embolism with postmortem imaging and minimally invasive biopsy. Five studies were included in the systematic review. These studies employed the following diagnostic technics: postmortem computed tomography (PMCT), postmortem computed tomography angiography (PMCTA), percutaneous needle biopsy (PNB), postmortem magnetic resonance (PMMR), and traditional autopsy. Imaging and minimally invasive biopsy are potential modalities that might complement or even replace traditional autopsy in diagnosing PFE. Further studies are needed to confirm the sensitivity and specificity of each technique.

**Keywords:** Imaging, minimally invasive biopsy, postmortem computed tomography, postmortem magnetic resonance, pulmonary fat embolism

## Pencitraan dan Biopsi Minimal Invasif Pada Diagnosis Postmortem Emboli Lemak Paru

### Abstrak

Beberapa tahun terakhir, teknologi pencitraan dan biopsi minimal invasif semakin berkembang dalam ranah forensik. Penelitian ini bertujuan mengevaluasi peran pencitraan dan biopsi minimal invasif pada diagnosis *postmortem* dari emboli lemak paru. Pencarian literatur dengan Pubmed, EBSCO-Host, dan ProQuest dilakukan untuk mencari penelitian mengenai diagnosis emboli lemak paru pada *postmortem* dengan pencitraan *postmortem* dan biopsi minimal invasif. Lima penelitian diikutsertakan dalam telaah sistematis, dengan metode diagnosis yang dilaporkan dalam penelitian adalah *postmortem computed tomography* (PMCT), *postmortem computed tomography angiography* (PMCTA), *percutaneous needle biopsy* (PNB), *postmortem magnetic resonance* (PMMR), dan autopsi tradisional. Pencitraan dan biopsi minimal invasif berpotensi melengkapi atau bahkan menggantikan autopsi tradisional dalam mendiagnosis emboli lemak paru. Penelitian lebih lanjut diperlukan untuk mengonfirmasi sensitivitas dan spesifisitas tiap-tiap teknik.

**Kata kunci:** Biopsi minimal invasif, emboli lemak paru, pencitraan, *postmortem computed tomography*, *postmortem magnetic resonance*

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## Introduction

Fat embolism syndrome is a disease affecting mainly capillaries, particularly on the venous side. Hence, the lung is the most common organ affected in fat embolism syndrome. The manifestations of fat embolism are varied, and thus, the exact pathophysiology of fat embolism is still a controversy. Fat embolism syndrome usually presenting with a delay of 12–72 hours, the classical triad consists of respiratory distress, cerebral signs, and petechiae. These can go unnoticed clinically or may present as an acute fatal event within hours of the inciting injury. There is no specific treatment for FES, but we can do supportive management and prevention or prompt management of complications. Examples include early fixation of long bone fractures within 24 hours, prophylactic corticosteroids, albumin for volume resuscitation, and other measures that can be adapted to the existing symptoms. The incidence of fat embolism and fat embolism syndrome is not known with certainty, as milder forms of fat embolism may not be clinically detectable. With the help of postmortem examination, the incidence increases to 20%. Embolization following major trauma is reported to be a quite common event, while a clinical fat embolization syndrome seems to be a much rarer event.<sup>1</sup> Fat embolism can be caused by

fracture of long bones, injury to adipose tissue which forces fat into damaged blood vessels, injecting oil into circulation, burns, septicemia, natural disease without any trauma, as in sickle cell anemia, diabetes, blood transfusion, or in chronic alcoholic.<sup>2</sup> Distinguishing antemortem violence with other causes of fat embolism is crucial in forensic settings. Histopathological analysis is currently used for definitive diagnosis of PFE.<sup>3</sup>

In recent years, imaging technologies such as postmortem computed tomography (PMCT), postmortem computed tomography angiography (CTA), multislice computed tomography (MSCT), and postmortem magnetic resonance (PMMR) imaging had been implemented in medicolegal settings. Minimally invasive biopsy has also been gaining importance in this field.<sup>4</sup>

Are imaging and minimally invasive biopsy superior to traditional autopsy in postmortem diagnosis of pulmonary fat embolism cases? This question will be addressed in this systematic review.

## Methods

This systematic review was designed and conducted in accordance with the guideline based on the Preferred Items for Systematic

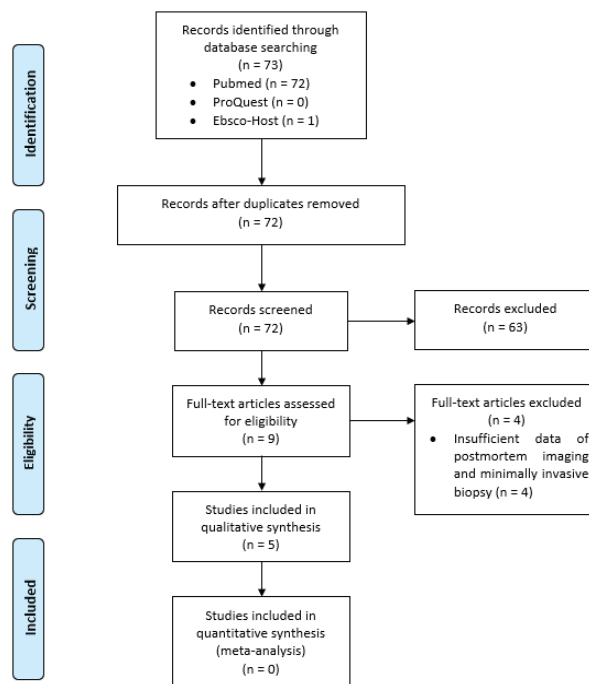


Figure Flow Diagram of Study Selection

**Table 1 Medical Subject Heading Used for Literature Search**

Library	Medical Subject Heading
Pubmed	((("fat embolism"[MeSH Terms]) OR fat embolism) OR "fat embolism syndrome"[MeSH Terms]) OR fat embolism syndrome)) AND (((("post mortem examination"[MeSH Terms]) OR post mortem examination) OR post mortem) OR postmortem))) AND (("computed tomography scanner, x ray"[MeSH Terms]) OR computed tomography scanner, x ray) OR ct scan) OR x ray) OR imaging) OR "radiology"[MeSH Terms]) OR radiology) OR "magnetic resonance imaging"[MeSH Terms]) OR magnetic resonance imaging) OR mri) OR "ultrasonography"[MeSH Terms]) OR usg)) OR (("minimally invasive surgery"[MeSH Terms]) OR "minimally invasive surgical procedure"[MeSH Terms]) OR minimally invasive surgical procedure) OR minimally invasive technique) OR "needle biopsy"[MeSH Terms]) OR needle biopsy) OR "laparoscopy"[MeSH Terms]) OR laparoscopy)))
EBSCO-Host	(TI fat embolism OR AB fat embolism OR TI fat embolism syndrome OR AB fat embolism syndrome) AND (TI post mortem examination OR AB post mortem examination OR TI post mortem OR AB post mortem) AND (TI computed tomography scanner, x ray OR AB computed tomography scanner, x ray OR TI ct scan OR AB ct scan OR TI imaging OR AB imaging OR TI radiology OR AB radiology OR TI magnetic resonance imaging OR AB magnetic resonance imaging OR TI mri OR AB mri OR TI ultrasonography OR AB ultrasonography OR TI usg OR AB usg OR TI minimally invasive surgery OR AB minimally invasive surgery OR TI minimally invasive surgical procedure OR AB minimally invasive surgical procedure OR TI minimally invasive technique OR AB minimally invasive technique OR TI needle biopsy OR AB needle biopsy OR TI laparoscopy AND AB laparoscopy)
ProQuest	(ab(fat embolism) OR ti(fat embolism) OR ab(fat embolism syndrome) OR ti(fat embolism syndrome)) AND (ab(post mortem examination) OR ti(post mortem examination) OR ab(post mortem) OR ti(post mortem)) AND (ab(computed tomography scanner, x ray) OR ti(computed tomography scanner, x ray) OR ab(ct scan) OR ti(ct scan) OR ab(imaging) OR ti(imaging) OR ab(radiology) OR ti(radiology) OR ab(magnetic resonance imaging) OR ti(magnetic resonance imaging) OR ab(mri) OR ti(mri) OR ab (ultrasonography) OR ti(ultrasonography) OR ab(usg) OR ti(usg) OR ab(minimally invasive surgery) OR ti(minimally invasive surgery) OR ab(minimally invasive surgical procedure) OR ti(minimally invasive surgical procedure) OR ab(minimally invasive technique) OR ti(minimally invasive technique) OR ab(needle biopsy) OR ti(needle biopsy) OR ab(laparoscopy) OR ti(laparoscopy))

Reviews and Meta-Analysis (PRISMA) statement. We include cross-sectional, cohort, case control, case report, and case series studies. Conversely, review, conference abstract, book section, commentaries or editorial work were excluded. Laboratories and non-human studies, also articles with unavailable full-text, languages other than English, and irrelevant topics were omitted. We included every study with pulmonary fat embolism examined with postmortem imaging and minimally invasive biopsy.

We performed a literature search using several search engines, including Pubmed, EBSCO-Host, and ProQuest by the year of 2021. Studies were identified by six independent authors using medical subject heading listed in Table 1.

All the search outputs were exported to the EndNote X9 software. After duplicates removal,

retrieved articles were screened based on their titles and abstracts. Potentially eligible articles were thoroughly assessed in full text using the eligibility criteria described above. Any emerging discrepancies were resolved among the review team.

Included studies were analyzed and the following data was extracted: first author, country of origin, study design, population (age and sex), postmortem examination, and outcomes.

**Results**

The study selection is presented in Figure 1. We conducted a search in PubMed, EBSCO-Host, and ProQuest by the year of 2021. A total of 73 records were identified, from which 72 remained after duplicate removal. Titles and abstracts were screened, leaving 9 potential studies. Full-

Table 2 Study Characteristics

Author, Year	Country	Type of Study	N	Age	Sex	Outcomes Assessed
Filigrana et al, <sup>3</sup> 2010	Switzerland	Case report	1	78	Female	Postmortem imaging using MSCT technique and microscopic examination of the lung tissue sampled using percutaneous needle biopsy as additional tools alternative to traditional autopsy.
Filigrana et al, <sup>17</sup> 2012	Switzerland	Cross-sectional diagnostic accuracy study	26	20–92 (mean 55.1 ± 15.9 years)	Male and female	PNB and DEK in PFE detection, PFE grading, diagnosis of PFE as a vital sign and as a cause of death
Flach et al, <sup>7</sup> 2012	Switzerland	Case report	1	89	Female	Findings of lethal systemic FE on unenhanced PMCT, PMCTA, and image-guided lung biopsy, with correlation to conventional autopsy and histopathology
Chatzaraki et al, <sup>9</sup> 2019	Switzerland	Case series	830	Case group: 60.54 ± 18.74 Control group: 53.79 ± 17.8	Case group: 119 females, 247 males Control group: 151 females, 313 males	Sensitivity and specificity of PMCT for diagnosis of PFE in relation to the Falzi histological grade based on the presence of macroscopically visible fat layers in the large pulmonary vessels
Makino et al, <sup>10</sup> 2020	Japan	Retrospective diagnostic correlation study	27	4–90 (mean 59, median 73)	9 females, 18 males	Correlation between histopathological, PMCT, and PMMR findings of fat embolism Comparison between PMCT and PMMR according to histopathological findings.

DEK: double-edged knife, MSCT: multiple slice computed tomography, PFE: pulmonary fat embolism, PMCT: postmortem computed tomography, PMCTA: postmortem computed tomography angiography, PMMR: postmortem magnetic resonance, PNB: percutaneous needle biopsy

Table 3 Results of Studies

Author, Year	Outcomes	Conclusion
Filigrana et al, <sup>3</sup> 2010	<p><b>PMCT findings:</b> Bilateral, near complete opacification of the pulmonary parenchyma and of the large airways, Absence of pleural effusion, Multiple bilateral rib fractures resulted from resuscitation manoeuvres, Heart enlargement, The left femoral prosthesis, No evidence of vascular damage in the operative field. <b>Histological (percutaneous needle biopsy) findings:</b> all over mid-level vessels and the capillaries massive fat embolization disseminated throughout the mid-level vessels and the capillaries. A grading score of III, according to Falzi et al classification</p>	<p>Postmortem imaging enhanced by postmortem tissue sampling by PNB may offer a new alternative to traditional autopsy.</p>
Filigrana et al, <sup>17</sup> 2012	<p>All PFE cases are examined by Percutaneous Needle Biopsy and Double Edge Knife Technique as Gold Standard. From 26 cases, one case of PFE was detected in PNB but not found in DEK. There was 1 diagnostic discrepancy in which PFE was detected by PNB but not by DEK. There was no disagreement between PNB and DEK when it came to determining the relevance of PFE to the cause of death. The PFE grade, or severity significantly differed between PNM and DEK in 6 out of 26 cases.</p>	<p>The PNB sampling approach for PFE, offers potential advantages beyond virtual autopsy. It might be used to analyze PFE in cases when autopsy is refused and virtual autopsy is unavailable, or simply as an alternative to DEK or frozen sections in conventional autopsy.</p>
Flach et al, <sup>7</sup> 2012	<p>Unenhanced PMCT: distinct fat level on top of sedimented layers of corpuscular blood particles and serum in the arterial system and pulmonary trunk. Subsequent PMCTA and image-guided biopsy confirmed fatal FE. Prior to autopsy, MCT PMCTA and image-guided biopsy revealed that the cause of death was right cardiac failure caused by systemic lethal FE. All imaging findings were consistent with traditional autopsy and histological specimens.</p>	<p>Prior to autopsy, the diagnosis of fatal systemic FE could be made in this patient. The emerging use of minimally invasive virtual autopsy as a viable replacement for traditional autopsy in certain situations and when the cause of death is clearly determined by imaging and image-guided biopsy is supported by this case description.</p>
Chatzaraki et al, <sup>9</sup> 2019	<p>Fat layers on PMCT was found in 2 cases from control group and 16 cases from case group. Fat layers (+) on PMCT in Falzi grade <math>\leq 2</math> were 8 cases and in Falzi grade <math>\geq 2.5</math> were 10 cases. Fat layers (-) PMCT in Falzi grade <math>\leq 2</math> were 762 cases and in Falzi grade <math>\geq 2.5</math> were 50 cases. In positive PFE with Falzi grade <math>\geq 1</math>: sensitivity 4.37, specificity 99.57, PPV 88.89 and NPV 56.9. In severe PFE with Falzi grade <math>\geq 2.5</math>: sensitivity 16.67, specificity 98.96, PPV 55.56 and NPV 93.84.</p>	<p>Fat layer findings is uncommon on PMCT, however it is associated with PFE diagnosis, particularly in cases of severe histopathological grade. In a typical position within the pulmonary trunk, this is to be expected.</p>

Table continued on next page

**Table 3 (continued)**

Author, Year	Outcomes	Conclusion
Makino et al, <sup>10</sup> 2020	<p>Detection of "fat fluid level"</p> <p>In 1 case, PMCT showed clearly fat densities floating in the blood in the right ventricle or pulmonary trunk; PMMR showed corresponding findings including an upper bright and lower dark layer separated by a sharp horizontal border.</p> <p>In 1 case, PMCT showed unclear "fat-fluid level"; PMMR showed more clearly.</p> <p>In 1 case in the case group and 24 cases in the control group, PMCT and PMMR showed no findings suggestive of massive pulmonary fat embolization in the right heart.</p> <p>Fat in distal pulmonary arteries</p> <p>In 1 case, PMCT showed fat densities in the pulmonary arteries in both sides of the first lobar branches of the left and right pulmonary arteries; PMMR showed clearer findings.</p> <p>In 1 case, PMCT showed unclear fat densities in the pulmonary arteries; PMMR showed scattered bright intensities in the lobar and segmental arteries on both sides.</p> <p>In 1 case in the case group and 24 cases in the control group, no evidence of fat emboli in the distal pulmonary arteries.</p> <p>Lung findings</p> <p>Case group:</p> <p>In 2 cases, PMCT showed patchy opacities (ground-glass opacities and/or consolidations) and/or centrilobular nodules in the lungs bilaterally</p> <p>In 1 case, PMCT showed consolidation of most of the lungs</p> <p>Control group:</p> <p>In 18 cases, PMCT showed patchy or centrilobular opacities of the lungs bilaterally</p> <p>In 6 cases, PMCT showed no bilateral patchy or centrilobular opacities</p>	<p>Massive fat embolism can be suggested by a "fat-fluid level" in the right heart or intraluminal fat in the pulmonary arterial branches seen with imaging. PMMR suggests fat embolism more clearly compared to PMCT.</p>

DEK: double-edged knife, FE: fat embolism, PFE: pulmonary fat embolism, PMCT: postmortem computed tomography, PMMR: postmortem magnetic resonance, PNB: percutaneous needle biopsy.

**Table 4 Fat Embolism Syndrome Diagnostic Criteria**

Major criteria	Minor criteria
1. Petechial rash	1. Tachycardia >120 beats/min
2. Respiratory insufficiency	2. Fever
3. Cerebral involvement	3. Retinal changes: fat or petechiae
	4. Jaundice
	5. Renal signs: anuria or oliguria
	6. Thrombocytopenia
	7. Anemia
	8. High erythrocyte sedimentation rate
	9. Fat macroglobulinemia

text paper of each 9 studies was evaluated for eligibility criteria and 4 was excluded due to insufficient data of postmortem imaging and minimally invasive biopsy. The remaining five studies were included in the systematic review. There are five studies included in this systematic review. Table 2 shows details on the selected studies for the systematic review. Most studies included were conducted in Switzerland. There are two case reports, one cross sectional study, one case series, and one retrospective diagnostic correlation study. Four studies evaluating PMCT are Filograna et al<sup>3</sup>; Flach et al<sup>7</sup>; Chatzaraki et al.<sup>9</sup> We also found four studies evaluating biopsy technique, which were conducted by Filograna et al<sup>3</sup>; Flach et al<sup>7</sup>; Makino et al<sup>10</sup> respectively. In addition, there is one study evaluating PMMR, which was conducted by Makino et al.<sup>10</sup>

We summarize the included studies by the outcome and conclusion as shown in Table 3.

## Discussion

Fat embolism (FE) is the finding of fat globules in the pulmonary or peripheral circulation, otherwise FE syndrome is its manifestations followed by a remarkable insult resulting in triad of respiratory distress, neurologic symptoms and petechial rash.<sup>5</sup>

Diagnostic criteria for fat embolism syndrome according to Gurd et al. are at least one major or four minor criteria as described in Table 4.<sup>6</sup>

Fat embolism often occurs due to major fractures (in particular long bones pelvis or spine) and severe soft tissue damage concomitant to trauma. Furthermore, in general,

orthopaedic interference of the intramedullary region consequently lead to fat embolism complication. This procedure contributes to higher intramedullary pressure which enforces the entry of fat and bone marrow into the venous circulation. Among patients with fat embolism, 1-5% represent fat embolism syndrome, despite the manifestation being commonly asymptomatic. Subsequently, this could be fatal in up to 20% cases. The distinct pattern of FES sign and symptoms as a sequel of some organs dysfunction (mainly lungs, brain, and skin) denoted by gradual onset predominantly 12-36 h after the accompanying injury.<sup>3</sup>

As respiratory symptoms is the major clinical presentation of FES, it is reported that within 50% of patients with FES whereupon turn dyspnoeic, which then require mechanical ventilation due to hypoxemia. The lungs is the initial organ interfered by fat embolism and its risk of fatalities in FE commonly influenced by the volume of the fat that gets through the lungs and capillary bed. These mortality cases of FE involving lungs have been described by two pathophysiology consisting of mechanical and chemical mechanisms. Firstly, in an early mechanical phase, fat droplets derived from the sites of injury, then gain entry to the circulation which further impairs the process of gas exchange by occluding lung capillaries. The latter is associated with chemical pneumonitis, vasculitis and related perivascular haemorrhage and edema, which furthermore results in mechanical obstruction. Both mechanical and chemical effects of FE in the pulmonary system generate acute respiratory distress whereas causing hypoxia that lead to death.<sup>3</sup>

The importance of fat embolism presence during autopsy in determination of related cause of death have remained uncertain. Histopathological analysis is the most commonly applied system by a lot of authors regarding the severity of embolism assessment by quantitative or semi-quantitative methods. However, it is still controversial between the correlation of the quantitative amount of FE and the severity of its clinical presentation. Several authors support the theory of an immediate correlation, in contrast, the others hypothesize that there is a crucial role of unusual reaction to fat in the capillary bed. Nevertheless, whichever the case, diagnosis of death due to FE is a diagnosis of exclusion. The other fatal contributing factors and required correlation of the degree of fat embolism with pre-existing diseases, remarkably cardio-respiratory pathologies should be excluded.<sup>3</sup>

**Table 5 Falzi Grading of Pulmonary Fat Embolism**

Grading Scale	Shape of Emboli	Localization
0 (no PFE)	(Punctiform)	Sporadic, not in every microscopic field
I (light)	Drop-shaped	Sporadic, in every microscopic field
II (moderate)	Sausage-shaped or rounded	Multiple, disseminated in every microscopic field
III (massive)	Antler-shaped	Numerous everywhere, in every microscopic field

Pulmonary fat embolism (PFE) in postmortem computed tomography (PMCT) was found as bilateral, near complete opacification of the pulmonary parenchyma in the study conducted by Filograna et al.<sup>3</sup> The forensic importance of fat embolism discovered at autopsy in relation to cause of death determination is still an unresolved issue. Many researchers have used quantitative or semi-quantitative approaches to grade the severity of embolism, the most common of which is histological analysis. Nonetheless, the relationship between the amount of FE in the blood and the severity of its clinical symptoms remains a source of debate.<sup>3</sup>

Some researchers believe there is a direct link, while others believe that an individual's aberrant sensitivity to fat in the capillary bed plays a key role. In any instance, FE death can only be diagnosed when other lethal reasons have been ruled out and a mandatory correlation of the degree of fat embolism with pre-existing disorders, particularly cardio-respiratory abnormalities.<sup>3</sup>

In the study performed by Flach et al.,<sup>7</sup> unenhanced pmCT revealed a distinct fat level on top of sedimented layers of corpuscular blood particles and serum in the arterial system and pulmonary trunk. Subsequent pmCTA showed reproducible results, and image-guided biopsy confirmed fatal FE.

In clinical radiology some reports describe the visualization of fat in the pulmonary arteries on computed tomography or transesophageal echocardiography. A patchy ground-glass opacities or consolidations resembling acute respiratory distress syndrome and subpleural centrilobular nodules in the lungs are more frequent findings in fat embolism syndrome.<sup>8</sup>

PMCT done by Chatzaraki et al. showed fat layers based on Falzi grading, 2 in the control group and 16 in the case group. The sensitivity in positive PFE with Falzi grade  $\geq 1$  was 4.37, specificity 99.57, PPV 88.89 and NPV 56.9. This shows that the fat layer in PMCT can be used in diagnosing PFE but it is rarely found. Fat layer is

specific in determining the severity of PFE, but with more sensitivity. If found, it shows 55.56% of severe PFE, and negative fat layer 93.84% showed PFE with Falzi grade  $< 2$ . Fat layered findings on PMCT can also reveal CPR-induced PFE that has no connection to antemortem trauma. In high Falzi grade, determining the severity has similar specificity and slightly higher sensitivity. Fifty five percent of the result shows true positive and 93% of the result shows true negative in high Falzi grade.<sup>9</sup>

As stated earlier, PMCT conducted by Makino et al.<sup>10</sup> revealed fat densities that were clearly evident floating in the blood in the right ventricle or pulmonary trunk, displaying a "fat-fluid level" in one of the cases, while one of the other cases also showed fat around the ventricle wall without apparent "fat-fluid level". PMCT also showed fat densities in the pulmonary arteries in two of the cases, although one of them was unclear. Based on these findings, there are two possible signs of fat embolism: the "fat-fluid level" in the right ventricle or pulmonary trunk and fat in the pulmonary arterial branches. In their control subjects, these findings were absent. Their study showed that these findings did not always correspond with the histopathological diagnosis of massive fat embolism, and a negative scan did not rule out massive fat embolism. CT can detect fat based on its density, however it can also miss fats. When combined with other materials that increase the density of the fat, it will result in inaccurate imaging.<sup>11</sup>

Although all of the studies show promising use of PMCT to determine the cause of death in PFE cases, it is still unclear whether PMCT examination is necessary in cases without showing signs of FE syndrome or whether PMCT can be used as a routine forensic practice in the future. A larger sample study is still needed to obtain more specific signs in PMCT imaging.

Percutaneous needle biopsy (PNB) was done in studies done by Filograna et al. in 2010 and 2012, and by Falch et al.<sup>7</sup> In 2010, a massive fat embolization was found throughout the mid-



level vessels and capillaries and had a Falzi grade III after stained with Sudan.

In the study demonstrated by Filograna et al.,<sup>17</sup> PFE detection and grading using samples taken with PNB and double-edged knife (DEK) autopsy technique were compared. This study shows no disagreement in detection and diagnosis of PFE, except in diagnosis of 1 case out of 26. Similarly, there was no disagreement in the determination of the relationship of PFE to the cause of death between PNB and DEK. Although a significant difference of grading was found in 6 cases out of 26, this difference did not affect the ultimate determination of cause of death. According to Filograna et al., this difference might be affected by different operators performing the DEK cuts.

Falch et al. use image-guided PNB and found PFE with grade IV according to Mason and Grade III according to Falzi. This finding were in accordance with histological findings using double-edge knife autopsy.

PNB has several advantages, such as its acceptability, simplicity, and decreased risk of disease transmission compared to complete autopsies. Furthermore, PNB is not as dependent on operator expertise and has a high success rate, especially guided with imaging techniques.<sup>12</sup> Compared to autopsy, sampling using PNB requires less time, in which around 10 minutes was needed. Autopsy in the other time takes at least 30 minutes. Minimally invasive technique is also beneficial in settings in which autopsy was rejected due to religion and cultural belief.

Some considerations should be made on blind biopsies of the target organ. A study performed by Cox et al.<sup>12</sup> showed a lower success rate when biopsy was done blindly without guidance of imaging modalities. Without a macroscopic view of the organs, some data important for determining other causes of death might also be missed even with the guidance of imaging.<sup>13</sup> Moreover, a full minimally invasive autopsy with full body imaging and sampling of all major organs may need more time than autopsy.

In general, MR imaging produces higher quality of images compared to CT scan. However, the use of MR imaging in forensic medicine is still limited. This might be due to the relatively long time and higher cost needed to perform MR imaging. Moreover, there are several factors that may influence the quality of the images produced and render the interpretation; the presence of gas, temperature, and vascular stasis.<sup>14</sup> Nevertheless, Makino et al. have found that PMMR displayed fat-fluid level and fat in distal pulmonary arteries more clearly than

PMCT. The reason for this is that MR imaging is able to detect the fat resonant frequency more specifically. Additionally, fat-specific techniques can be used to further confirm the presence of fat, such as spectral attenuated inversion recovery (SPAIR) and fast field echo sequences (FFE), as seen in this study. Thus, PMMR might be beneficial in detecting fat-fluid level in cases where PMCT findings of PFE are uncertain.

There are several cases in which PMMR was found to be useful, such as cardiovascular pathologies, internal hemorrhage or fluid accumulation, brain and pulmonary edema, pleural effusion, and neonatal or pediatric death.<sup>16</sup> To date, studies have investigated the use of PMMR in fat embolism, mainly cerebral fat embolism, and some reported that PMMR has a high sensitivity for such cases.<sup>15,16</sup> Further studies are still needed to validate the use of PMMR in diagnosing PFE.

Imaging and minimally invasive biopsy are potential modalities that might complement or even replace traditional autopsy in diagnosing PFE. Although in some cases imaging findings do not always correlate with the histopathological diagnosis, they show promising results. Further studies with larger sample sizes are needed to confirm the sensitivity and specificity of each technique, and thus, to support the use of minimally invasive techniques in forensic medicine.

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