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Review article in:

Incidence of fat embolism syndromes after femoral fractures

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Abstract

Fat embolism refers to the presence of fat droplets within the peripheral and lung microcirculation with or without clinical sequelae. However, not all fat emboli progress to fat embolism syndrome (FES). FES is a clinically relevant syndrome that occurs in the presence of intravasation of fat in the pulmonary tree, and is characterized by clear signs and symptoms. Fat emboli can be demonstrated in a number of ways. Gurd showed that 67% of trauma patients without evidence of FES had circulating fat globules. Allardyce and found that 95% of patients had circulating fat globules in blood draining from the fracture site. Urinary fat droplets are also a frequent finding after trauma. Rates of FES in orthopedic trauma patients vary from <1 percent to >30 percent, with the wide range likely reflecting study population heterogeneity and a lack of standardization for diagnostic criteria. Cerebral fat embolism (CFE) is a rare and potentially fatal condition that may occur following a long bone fracture or pelvis trauma, showing an incidence ranging from 0.9 to 11% with a mean mortality rate around 10%.

Keywords: fat , embolism, incidence

Introduction

Fat embolism refers to the presence of fat droplets within the peripheral and lung microcirculation with or without clinical sequelae. However, not all fat emboli progress to fat embolism syndrome (FES). FES is a clinically relevant syndrome that occurs in the presence of intravasation of fat in the pulmonary tree, and is characterized by clear signs and symptoms. FES is a serious manifestation of fat embolism that involves petechial rash, deteriorating mental status, and progressive respiratory insufficiency, usually occurring within 24 hours of injury. At autopsy, presence of fat can be identified in the lung vessels in more than 90% of patients with skeletal trauma,16 and in pulmonary arterial blood samples in up to 70% of patients with pelvic or long bone fractures. However, the clinical picture of the more clinically relevant FES does not develop in all patients who demonstrate the presence of intravascular or pulmonary fat (1).

Although various criteria have been used to characterize and define FES, the criteria suggested by Gurd and Wilson with some modification by Lindeque and colleagues are those that have been most widely adopted. The criteria of Gurd and Wilson require the presence of at least two of the following major clinical features: respiratory insufficiency, petechial rash or cerebral involvement, or one major and four of the five minor clinical features, defined as pyrexia, tachycardia, retinal changes, jaundice, renal changes (anuria or oliguria), fat in the urine or sputum, unexplained drop in hematocrit or platelet values, and fat macroglobulinemia. The Gurd and Wilson definition has been criticized for excluding an objective assessment of hypoxemia documented by arterial blood gas, which precedes other clinical symptoms and signs (2).

Lindeque and colleagues included the results of arterial blood gases in the formulation of their criteria. they demonstrated a much higher incidence of FES by using arterial blood gases as part of the criteria (13% vs 29%) (3).

Schonfeld proposed a fat embolism index. However, this has limited value in patents with concomitant cerebral, thoracic, or abdominal injuries.20 The clinical signs and symptoms of FES are nonspecific. Thus the differential diagnosis for each of these signs can be broad, and typically the diagnosis of FES is a diagnosis of exclusion (4).

Table 1. the commonest criteria in the diagnosis of FES

Three criteria used to define fat embolism syndrome

Criterion	Features
Gurd and Wilson (FES = 1 major + 4 minor + fat microglobulinemia)	Major criteria Respiratory insufficiency Cerebral involvement Petechial rash Minor criteria Pyrexia Tachycardia Retinal changes Jaundice Renal changes (anuria or oliguria) Thrombocytopenia (a drop of >50% of the admission thrombocyte value High erythrocyte sedimentation rate Fat macroglobulinemia
Fat embolism index (FES = 5 or more points)	Diffuse petechiae (5 points) Alveolar infiltrates (4 points) Hypoxemia (<70 mm Hg) (3 points) Confusion (1 point) Fever 38°C Heart rate >120/min Respiratory rate >30/min
Lindeque criteria (FES = femur fracture ± tibia fracture + 1 feature)	A sustained PaO_2 <60 mm Hg A sustained $PaCO_2$ >55 mm Hg) or pH <7.3 A sustained respiratory rate >35/min even after adequate sedation Increased work of breathing judged by dyspnea, use of accessory muscles, tachycardia, and anxiety

In this short review, we will discuss the incidence of Fat embolism syndrome among femoral fracture patients.

Literature review

The phenomenon of fat embolism is extremely common among trauma patients, especially those with long bone or pelvic fractures. However, in the context of trauma, fat embolism is also common following extensive injury to subcutaneous fat, such as occurs in severe beatings. Fat emboli can be demonstrated in a number of ways. Gurd showed that 67% of trauma patients without evidence of FES had circulating fat globules. Allardyce studied 43 cases of femoral shaft fractures and found that 95% of patients had circulating fat globules in blood draining from the fracture site. Urinary fat droplets are also a frequent finding after trauma (5). *Mudd* (6) found pulmonary fat in 68% of patients dying from blunt trauma, most of whom had associated fractures.

With recent studies reporting the mortality rates of FES between 1% and 10%, this inconsistency in the diagnostics appears to call for a more standardized approach to the risk analysis and a rapid diagnosis. This appears to be relevant, since patients suffering from FES show rates of full recovery of approximately 90% when receiving proper supportive care (7).

A prospective randomized controlled trial conducted in 1989 on 178 patients on femoral fractures reported that early stabilization of femoral fractures had significantly decreased fat embolization, as well as other pulmonary complications such as adult respiratory-distress syndrome and pneumonia. Similarly, a prospective study held on 18 patients with long bone fracture stated that

immediate fixation had significantly reduced pulmonary complications (including fat embolism) than delayed fixation (8).

Furthermore, a study carried out on 274 patients with isolated femoral shaft fractures in 1998 revealed that 11 patients (4%) developed fat embolism syndrome.

Sixty of the 247 patients were early operated (within 24 hours of insult) and none of them developed fat embolism, whereas, among the 109 patients whose operation was delayed to more than 24 hours, fat embolism occurred in 10%. The difference between the 2 groups was statistically significant (9).

Rates of FES in orthopedic trauma patients vary from <1 percent to >30 percent, with the wide range likely reflecting study population heterogeneity and a lack of standardization for diagnostic criteria. As an example, in a matched case-controlled study of the Japan Trauma Data Bank from 2004 to 2017, the incidence of FES in trauma patients was 0.1 percent. However, patients who did not survive >48 hours were excluded such that cases could have been missed (10).

FES is most commonly associated with long bone (especially the femur) and pelvic fractures and less commonly with fractures of other marrow-containing bones (eg, ribs). The rate of FES is also higher in those with multiple rather than single fractures (1.29 versus 0.17 percent in one series) and in patients with open fractures than closed fractures. A delay in the time to reduction of the fracture is also associated with FES. In another retrospective study, hypomagnesemia, hyperphosphatemia, hypoalbuminemia, and blunt traumatic mechanism of injury were identified as risk factors for FES in patients with orthopedic injuries .FES is more common in men than in women and its incidence is highest in those

between 10 and 40 years, likely reflecting the incidence of trauma in this age group (11).

A study in Brazil showed that the incidence rate of femoral fracture per 10,000 inhabitants standardized by gender and age (≥ 60 years) was higher in females compared to males in the state of Paraná (25.14 / 10 thousand, females and 13.12 / 10 thousand, males, respectively) and in the whole country (22.58 / 10 thousand and 13.52 / 10 thousand respectively). The fracture rate in the female population of Paraná (25.14 / 10 thousand) was higher than the national female rate (22.58 / 10 thousand). Considering both sexes, the total standardized rate of fractures in Paraná (19.80 / 10 thousand) exceeded the national rate (18.55 / 10 thousand) (12).

A clinical evident FES occurs in only ~2.5% (range 0.5-4%) of individuals with demonstrable fat embolism, seen relatively frequently in patients with long bone fractures and during orthopedic prosthetic procedures. FES has an incidence of 1-3% following long bone fractures and 33% in patients with bilateral long bone fractures (13).

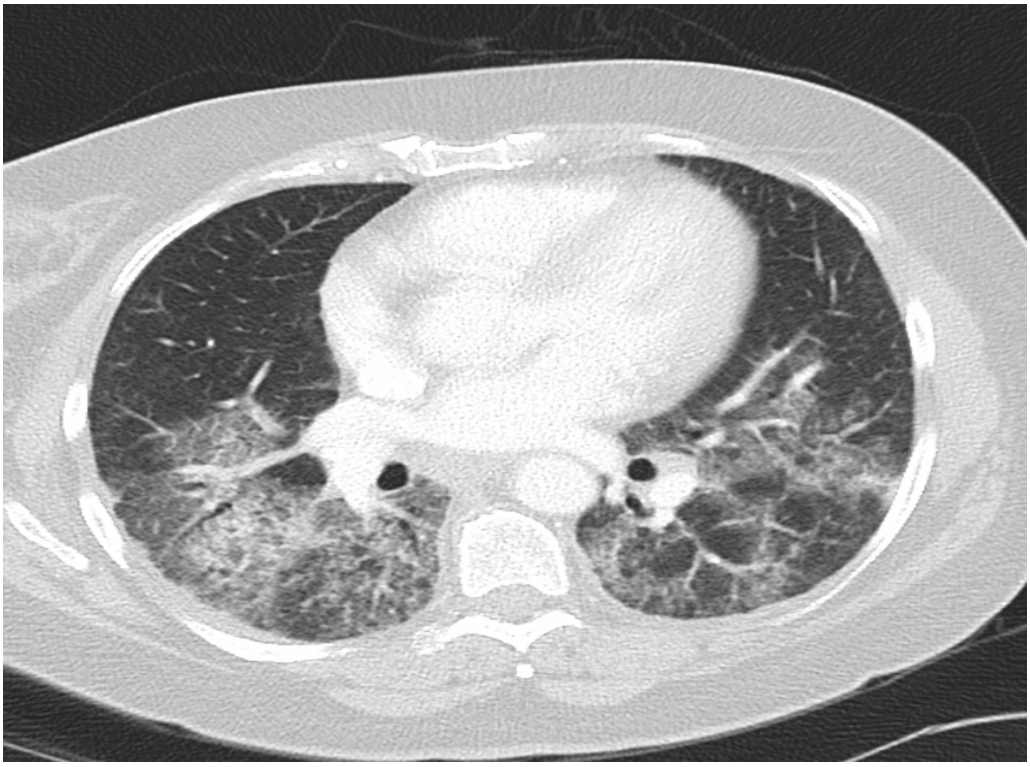

Figure 1. lung CT scan in FES

Results

The results of *Pinney et al.* study support the view that nailing of the isolated femoral shaft fracture within 10h of injury minimizes the risk of fat embolism syndrome. Ten hours was chosen as a cut-off point because it is the goal at our institution to fix all femoral shaft fractures in the young adult within this time period. Unfortunately the logistics of transportation, and access to the operating room means that this goal is not always achieved. For the cohort of young adult patients fixed between 10 and 30h after injury there is a trend towards an increased rate of fat embolism syndrome as the time from injury increases up to 25 h after

injury. However, this trend does not reach statistical significance. Those patients

who have not developed clinical signs of fat embolism syndrome within 30h of their injury appear unlikely to manifest the syndrome (14).

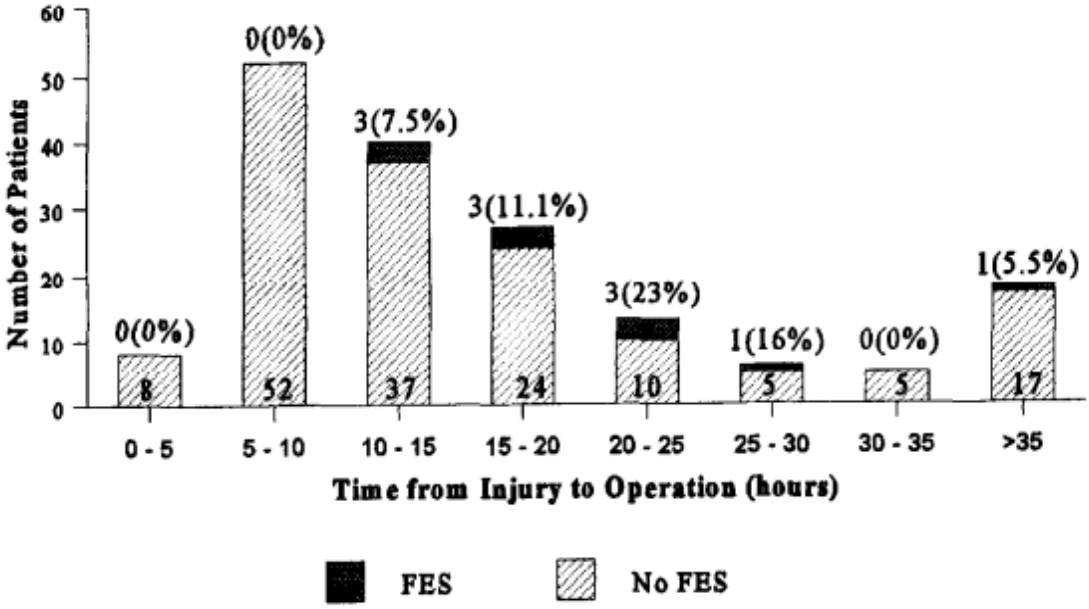

Figure 2. the rate of incidence as *Pinney et al.* study showed (14).

Cerebral fat embolism (CFE) is a rare and potentially fatal condition that may occur following a long bone fracture or pelvis trauma, showing an incidence ranging from 0.9 to 11% with a mean mortality rate around 10%. After a 'bone burst', according to the accepted pathophysiology, 'fat droplets' are shot into the systemic circulation, giving rise to emboli. But no univocal explanation exists to describe how the syndrome develops from hereon (15).

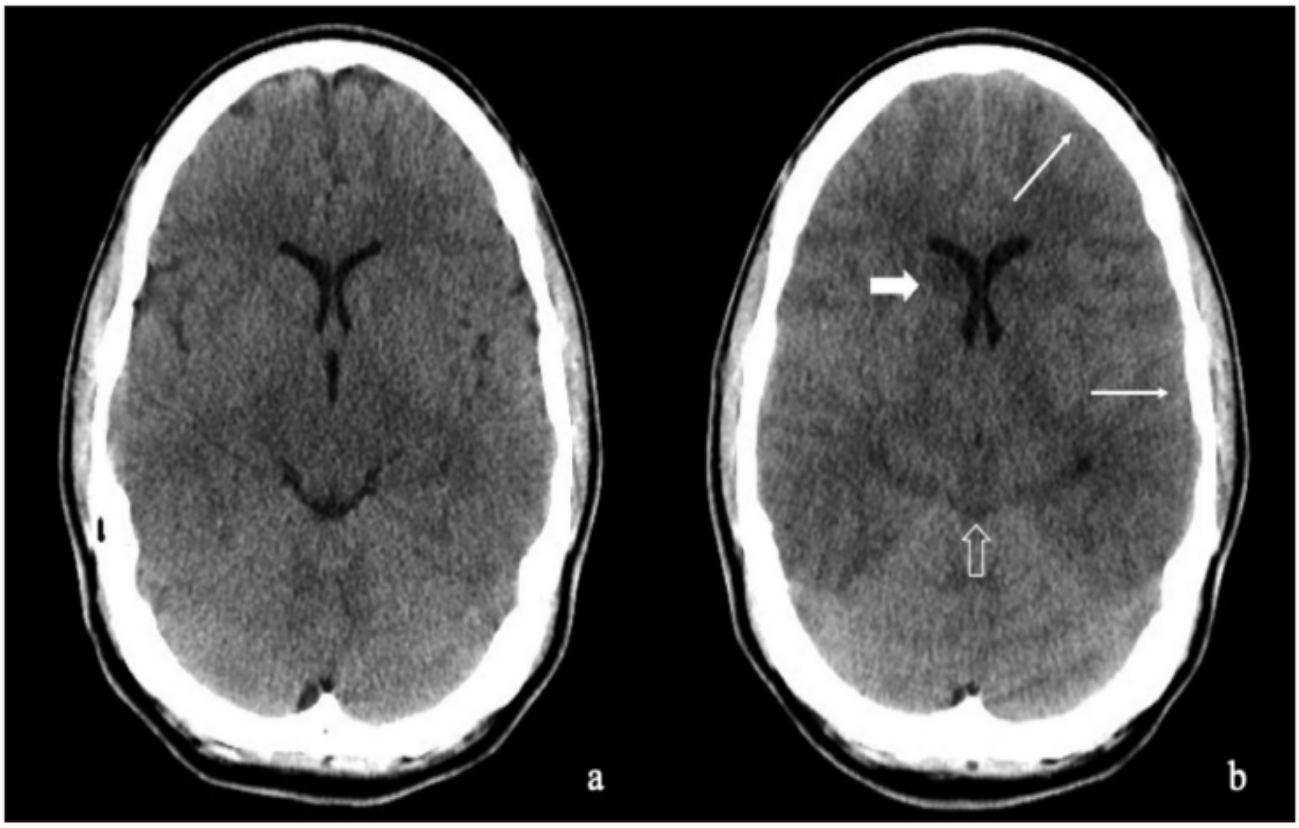

Figure 3. Brain CT of patient with CFE, a) at the time of trauma, b) after 24 hrs.

Kosova et al., revealed the incidence of FE/FES to be higher in bilateral femoral fractures and following intramedullary nail fixation, i.e. in the long bones of the lower limbs. Multivariate analysis revealed men to be affected by FES syndrome more frequently than women. They also revealed evidence for the percentage of patients positive for FES to drop significantly after 30 years of age, although a trend for a slight rise in the number of patients was observed in those aged 51–60 years (associated with the use of MR imaging) and over 70 years. The

strong reduction in the frequency of FES after 30 years of age may signify that the energy of the impacts causing bone fractures decreases as the age of the subject increases. This supports previous reports suggesting that FES is more frequently associated with complicated trauma (16).

Vetrugno et al., concluded that FE/FES is more frequent in men aged less than 30 years following multiple fractures of the legs. It appears that the laterality of the fracture is not related to the development of the syndrome. However, FES may be more frequent after a burst fracture in which the fat marrow is pushed to the upper region of the body through the lungs. Although most cases of FES occur 48–72 h after a fracture, further work is required to establish whether acute brain presentation (i.e., within 24 h) is related to the presence of PFO.

Conclusion

Based on what we reviewed, the incidence of FES is about 5% in all bone injuries especially the femoral fractures. The timing of the operation of fixation plays central role in the development of the FES.

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