Chapter

Introductory Chapter: Defining the True Global Impact of Embolic Phenomena

Samantha Wolfe, Stanislaw P. Stawicki, Mamta Swaroop, Jennifer C.B. Irick and Michael S. Firstenberg

1. Introduction

In the realm of medical practice, the word "embolism" has many implications to many people [1, 2], with most providers instinctively placing this word within a negative context [3–5]. Derived from the Greek word, ἐμβολισμός, this term most literally means "interposition" [6]. Yet regardless of how benign the etymology may be, the clinical context is quite the opposite—synonymous with much dreaded morbidity and mortality [1, 2, 7–10]. Whether the embolus consists of a blood clot [8], a fat globule [11], a bubble of gas [12], amniotic fluid [9, 10], or even an iatrogenic or traumatic foreign body [13, 14], the unfavorable connotations persist even if the patient has few or no associated symptoms and requires no intervention.

The primary goal of this book is to provide the reader with an overview of the most common types of embolic phenomena encountered in clinical practice, including some of the key related diagnostic and therapeutic areas. The current collection of chapters includes important contributions in the areas of pulmonary embolism (PE), fat embolism (FE), embolic complications of nonmalignant cardiac tumors, acute arterial embolism (AAE) of the lower extremity, thrombophilia in pregnancy, bullet and shrapnel embolization (BSE), and coronary artery embolization (CAE), as well as a comprehensive chapter on venous interventions utilized in the management of thromboembolic disorders.

Perhaps the best way to paint the picture of the tremendous impact of "embolism" globally is to present the human costs and the resources required to treat various types, manifestations, and complications of embolic diseases. Although challenging to gather, such information was compiled by our team for the purposes of this introductory chapter and summarized in **Table 1** [12, 14–37]. Although far from comprehensive, we hope to provide the reader with valuable insight into the gravity of the collective problem.

2. Embolism types: a synopsis

No discussion of "embolism" can be complete without the discussion of risk factors, diagnostics including laboratory and imaging tests, and therapeutic considerations. Here, one must emphasize the importance of looking at the "totality of evidence," considering things like clinical suspicion, presence/absence of specific risk factors, positive/negative predictive values, diagnostic test sensitivity/specificity, and the pre−/posttest probabilities.

Embolism type (alphabetical) [Reference]	Number affected	Mortality	Morbidity	Healthcare costs	Other considerations
Air emboli [12, 15–18]	0.2–1% (with central line) 0.003–0.007% (cardiac bypass) Overall, 2.65 per 100,000 cases	14% 21.7%	Neurologic complications–encephalopathy to focal cerebral lesions (19–50%)	Legal: median payment $325,000/claim	ICU admission
Amniotic fluid [19, 20]	1/22,000 pregnancies Overall, 2–8/100,000 cases	10% of all maternal deaths 13–44% case maternal mortality 7–38% fetal mortality	Seizures (2.22%) Maternal neurologic damage (4.44%) Fetal neurologic damage (25–50%) Shock (15%) Coagulopathy (8.8%) Cardiac arrest (22.2%) Fetal NICU admission 8.8–20%	Prolonged hospitalization Average maternal LOS–2.92 days Average infant LOS–3.78 days	ICU admission Massive blood transfusion Long-term neurologic effects
Fat emboli [21–24]	Symptomatic: 1–20% patients with long bone fractures (true incidence is likely much higher)	5–15%	ARDS, pneumonia CVA Seizures, epilepsy (2.86%) DIC, thrombocytopenia (37%) Cardiac failure		ICU admission
Iatrogenic foreign body [14, 25–27]	Retained guidewire Approximately 1 in 3000 cases	<2% mortality	Cerebral ischemia Infarction Cardiac dysrhythmia, tamponade 5–32% symptomatic	Medicare: endovascular retrieval of foreign body—9.03 RVU which equates to $342.15 reimbursement Potential legal costs if foreign body not immediately recognized	Requirement for endovascular or operative removal
Peripheral emboli [28–30]	About 14 per 100,000 cases	17–18% death	Amputation (28.9%) Reperfusion injury (6%)		Requirement for fasciotomy, limb amputation, loss of function
Pulmonary embolism (PE) [31–37]	97.8 per 100,000 population/year (hospitalization rate)	0.1–4.2% in hospitalized patients ~25% at 7 days Up to 16% at 1 year	Bleeding related to thrombolytics and/or anticoagulants (4–7.5%) Right ventricular systolic dysfunction (20–60%)	Between $5,500 and $11,665 (depending on severity) with mean cost of $8800 $99,286/PE death (Cox)	Need for long-term anticoagulation Venous stasis Pulmonary hypertension Recurrent PE

ARDS = Acute respiratory distress syndrome; CVA = Cerebrovascular accident; DIC = Disseminated intravascular coagulation; ICU = Intensive care unit; LOS = Length of stay; NICU = Neonatal ICU; PE = Pulmonary embolism; RVU = Relative value unit.

Table 1.
Selected metrics demonstrating the global impact of embolic diseases, including considerations of both patient- and health system level considerations.

2.1 Pulmonary embolism

Initial clinical tests obtained when a patient exhibits symptoms of a PE are commonly electrocardiogram (EKG), arterial blood gas (ABG) analysis, and chest X-ray (CXR). However, none of these studies are sufficiently sensitive or specific for this diagnosis. Clinical scoring systems such as the Wells or PERC score have been established but in isolation are not able to diagnose PE [38]; rather, they provide clinically relevant risk stratification. Based on such risk stratification, it is recommended that a test of exclusion (e.g., one with a high negative predictive value) such as D-dimer be performed in the setting of low or intermediate clinical probability of a PE [39]. In the cases where a PE is highly suspected or likely, it is preferred to proceed directly to imaging such as a computed tomography pulmonary arteriography (CTPA). The ease of obtaining it, combined with the high predictive value (92–96%), has placed CTPA as the dominant imaging modality for suspected PE [40]. In patients unable to receive iodinated contrast, a ventilation-perfusion (V-Q) scan or a contrast-enhanced magnetic resonance angiography (MRA) may represent a valid alternative. MRA has a sensitivity of 78% and specificity of 99%. This imaging study, however, relies on patient participation and compliance, and therefore a nontrivial proportion of studies will be inadequate to obtain sufficient level of diagnostic accuracy [40]. Once diagnosed, the treatment of PE involves systemic anticoagulation, with more invasive measures such as thrombolysis or embolectomy performed in patients with significant hemodynamic instability, respiratory decompensation, or acute right ventricular dysfunction [37].

2.2 Fat emboli

Fat embolism syndrome (FES) differs in that there is no reliably accurate diagnostic or imaging test. Rather, the diagnosis is primarily clinical [11]. Multiple scoring systems exist which utilize the findings of petechiae, respiratory symptoms, fever, tachycardia, and radiographic changes with these either being identified as “major” or “minor” in magnitude or assigned a value on a pre-determined scale [11, 21, 41]. The lack of an imaging confirmatory test, however, makes it difficult to evaluate the true diagnostic accuracy or sensitivity of these indices. Ultrasound and echocardiography have been used to detect circulating fat globules; however, several studies suggest that a much higher percentage of patients with long bone fractures have circulating fat globules than previously thought, and only a fraction of these patients develop symptoms or FES [21, 42]. Computed tomography (CT) and magnetic resonance imaging (MRI) have been used, often with few abnormal findings reported. Treatment is mainly supportive and consists of intravenous fluids, respiratory support, and other forms of symptomatic management as appropriate. Medications such as steroids, heparin, alcohol, and dextran have not been proven beneficial [21].

2.3 Amniotic fluid embolism

Amniotic fluid embolism (AFE) is another condition that requires a high degree of clinical suspicion, as the diagnosis is based on a heterogeneous constellation of symptoms [9, 10]. AFE should be suspected in any case of sudden maternal cardiovascular collapse with accompanying coagulopathy, hypotension, seizures, or distress, with no other clearly identifiable cause [43–45]. There are currently no truly reliable laboratory tests that are diagnostic of AFE [46]. Detection of formed amniotic fluid components (epidermal squamous cells, meconium, or lanugo hairs) in the maternal pulmonary blood flow is sufficient for histologic diagnosis of AFE [20]. Unfortunately, in many cases AFE goes unrecognized until these findings are

Embolism type (alphabetical)	Risk factors
Air emboli [12, 16, 17, 48]	• Venous catheterization, removal, manipulation, unintended disconnection • CABG on CP bypass • Craniotomy, especially in sitting position • Fistulization between air filled viscus and vessel (aortoesophageal, atriobronchial) • Traumatic or iatrogenic pulmonary alveoli-venous fistula • PFO, VSD (for paradoxical air emboli) • Hemodialysis, cell saver transfusion
Amniotic fluid [19, 20]	• Multi-fetal pregnancy, placenta previa, placental abruption, eclampsia • Uterine rupture • Cell saver blood transfusion • Induction, C-section, fetal distress, cervical laceration/trauma, instrument delivery • Maternal age > 35 years
Fat emboli [24, 49, 50]	• Long bone fracture (pelvis, femur) • Joint arthroplasty • Percutaneous vertebroplasty • Liposuction, fat grafting • CABG • CPR • Organ transplant (lung, renal) • Bone marrow transplant or harvest • Chronic corticosteroid use • Severe burn
Iatrogenic foreign body [14]	• Guidewire–placement of central line, improper technique, or failure to control guidewire during procedure (more likely in emergency situations, inexperienced staff, inadequate supervision) • Catheter–fracture of catheter secondary to repetitive mechanical stress, damage during removal, and improper connection during placement • Coils–improperly sized or placed coils; tortuous vessels; usage of angioplasty balloon for deployment
Peripheral emboli [28–30]	• PFO in setting of venous thrombosis • Atrial fibrillation • History of central or peripheral atherosclerosis
Pulmonary embolism (PE) [51]	• Trauma • Prolonged hospitalization/immobility • Malignancy • Central venous catheterization, venous thrombosis, thrombophilia

CABG = Coronary artery bypass grafting; CP = Cardiopulmonary; CPR = Cardiopulmonary resuscitation; PFO = Patent foramen ovale; VSD = Ventricular septal defect.

Table 2.
Listing of the most common risk factors by embolism type.

seen on autopsy [9, 10]. Treatment is supportive, involving respiratory support, Cesarean section (if not already delivered), correction of coagulopathy, blood/blood product transfusion, vasopressors/inotropes, and fluids [9, 10, 43–45].

2.4 Air embolism

The most sensitive test for diagnosing an air embolism is the transesophageal echo (TEE), detecting as little as 0.02 ml/kg of air administered by bolus injection [12, 37]. In fact, it has been deemed almost "too sensitive," in that it will detect air in circulation that is not associated with any symptoms. A precordial Doppler is also highly sensitive, detecting as little as 0.25 ml of air (0.05 ml/kg) [37]. It is highly operator dependent, however, as one must rely on the detection of a change in sound with air interrupting the blood flow within the cardiac chambers. Much less sensitive is the pulmonary artery catheter, with a detection threshold of 0.25 mL/kg of air [47]. Additionally, it is of limited use therapeutically as its small caliber internal lumen is often insufficient to withdraw air from the chamber as a therapeutic maneuver (or at least quickly enough to be truly effective). In the operating room, the most practical diagnostic tool is a sudden fall in end-tidal CO_2, albeit this is highly nonspecific. Other times, air emboli will go undiagnosed by any formal means and may well end up being "presumed" based on clinical symptomatology presenting in a scenario where an air embolus is possible (**Table 2**).

2.5 Foreign body embolism

The method of detecting a foreign body embolus (FBE) is dependent on the resting intravascular location of the embolus, which may vary according to the etiology, object type, and route of introduction [13, 14, 52, 53]. For cardiac emboli, transesophageal echocardiography (TEE) is commonly used and is beneficial in that it can also assess for any structural damage associated with such FBEs [54]. This imaging modality may be limited, however, especially in instances when the emboli are small, minimally echogenic, located in difficult-to-access locations, or obscured by acoustic shadowing. In these cases, computed tomography (CT) imaging may represent a helpful adjunct to determine location and operative or endovascular plan for removal. CT angiography is also useful for more peripherally located FBEs [52, 53]. The decision on whether to remove the foreign body is also highly dependent on symptomatology and potential complications of the emboli, especially when considered in the context of any downstream anatomic structures as well as immediately surrounding tissues. In the current age, an endovascular approach is the most common, with open approaches often reserved for failure of endovascular retrieval. Rarely, an embolus may be left in place if it is unlikely to further migrate and the patient is asymptomatic, though this does leave the patient at potential risk for future complications that can occur remotely, even years later [13, 14, 55, 56].

3. Conclusion

Perhaps the most valuable take-away message of this book is that diagnostic relativity—rather than absolutism—continues to prevail in the realm of "embolic diseases." Such is the state of modern medical decision-making in this important area of active clinical investigation and management. **Table 2** summarizes the most common risk factors, organized by "embolism" type. Compiled from variety of sources, this information represents an good foundation for clinical discussions based on diagnostic probabilities.

In summary, this book represents a collection of contributions by a multidisciplinary team of clinicians and medical researchers. The editors' goal was to solicit the highest quality contributions from some of the top experts in their respective fields. We hope we were able to achieve this goal satisfactorily. Ultimately, the book's readers will be the best arbiters of its success, whether it is determined by the number of downloaded chapters or the cumulative number of citations attributable to this collection of chapters. To be able to contribute to the generation and dissemination of new knowledge in this important area of clinical investigation is a true privilege.

Author details

Samantha Wolfe[1], Stanislaw P. Stawicki[1,2]*, Mamta Swaroop[3], Jennifer C.B. Irick[4] and Michael S. Firstenberg[5]

1 Department of Surgery, St. Luke's University Health Network, Bethlehem, Pennsylvania, USA

2 Department of Research and Innovation, St. Luke's University Health Network, Bethlehem, Pennsylvania, USA

3 Department of Surgery, Northwestern University School of Medicine, Chicago, Illinois, USA

4 Department of Emergency Medicine, Richard A. Anderson Campus, St. Luke's University Health Network, Easton, Pennsylvania, USA

5 Department of Cardiothoracic Surgery, The Medical Center of Aurora, Aurora, Colorado, USA

*Address all correspondence to: stawicki.ace@gmail.com

References

[1] Nielsen HK et al. 178 fatal cases of pulmonary embolism in a medical department. Acta Medica Scandinavica. 1981;**209**(1-6):351-355

[2] Stawicki SP et al. Septic embolism in the intensive care unit. International Journal of Critical Illness and Injury Science. 2013;**3**(1):58

[3] Piqué-Angordans J, Posteguillo S. Peer positive and negative assessment in medical English written genres. Advances in medical discourse analysis: Oral and written. Contexts. 2006;**45**:383

[4] McCurdy T. Air-embolism complicating artificial pneumothorax: A case with autopsy. American Review of Tuberculosis. 1934;**30**(1):88-91

[5] Gross AF, Smith FA, Stern TA. Dread complications of catatonia: A case discussion and review of the literature. Primary Care Companion to the Journal of Clinical Psychiatry. 2008;**10**(2):153

[6] Wikipedia. Embolism. 2019. Available from: https://en.wikipedia.org/wiki/Embolism [Accessed: August 19, 2019]

[7] Ericsson JA, Gottlieb JD, Sweet RB. Closed-chest cardiac massage in the treatment of venous air embolism. New England Journal of Medicine. 1964;**270**(25):1353-1354

[8] Stawicki SP et al. Deep venous thrombosis and pulmonary embolism in trauma patients: An overstatement of the problem? The American Surgeon. 2005;**71**(5):387-391

[9] Thongrong C et al. Amniotic fluid embolism. International Journal of Critical Illness and Injury Science. 2013;**3**(1):51

[10] Balinger KJ et al. Amniotic fluid embolism: Despite progress, challenges remain. Current Opinion in Obstetrics and Gynecology. 2015;**27**(6):398-405

[11] Kwiatt ME, Seamon MJ. Fat embolism syndrome. International Journal of Critical Illness and Injury Science. 2013;**3**(1):64

[12] Gordy S, Rowell S. Vascular air embolism. International Journal of Critical Illness and Injury Science. 2013;**3**(1):73

[13] Moffatt-Bruce SD et al. Intravascular retained surgical items: A multicenter study of risk factors. Journal of Surgical Research. 2012;**178**(1):519-523

[14] Wojda TR et al. Foreign intravascular object embolization and migration: Bullets, catheters, wires, stents, filters, and more. In: Embolic Diseases: Unusual Therapies and Challenges. London, England: IntechOpen; 2017. 109p

[15] Bessereau J, Genotelle N, Chabbaut C, et al. Long-term outcome of iatrogenic gas embolism. Intensive Care Medicine. 2010;**36**(7):1180-1187

[16] Brull SJ, Prielipp RC. Vascular air embolism: A silent hazard to patient safety. Journal of Critical Care. 2017;**42**:255-263

[17] Pinho J, Amorim JM, Araujo JM, et al. Cerebral gas embolism associated with central venous catheter: Systematic review. Journal of the Neurological Sciences. 2016;**362**:160-164

[18] Hammon JW, Hines MH. Cardiac surgery in the adult. In: Cohn LH, editor. Extracorporeal Circulation. 4th ed. New York: McGraw-Hill; 2012

[19] Spiliopoulos M, Puri I, Jain NJ, et al. Amniotic fluid embolism-risk factors, maternal and neonatal outcomes. The

Journal of Maternal-Fetal & Neonatal Medicine. 2009;**22**(5):439-444

[20] Rath WH, Hofer S, Sinicina I. Amniotic fluid embolism: An interdisciplinary challenge: Epidemiology, diagnosis and treatment. Deutsches Ärzteblatt International. 2014;**111**(8):126

[21] Talbot M, Schemitsch EH. Fat embolism syndrome: History, definition, epidemiology. Injury. 2006;**37**(Suppl 4):S3-S7

[22] Habashi NM, Andrews PL, Scalea TM. Therapeutic aspects of fat embolism syndrome. Injury. 2006;**37**(Suppl 4):S68-S73

[23] Kavi T, Teklemariam E, Gaughan J, et al. Incidence of seizures in fat embolism syndrome over a 10-year period: Analysis of the national inpatient sample database. The Neurologist. 2019;**24**(3):84-86

[24] Kosova E, Bergmark B, Piazza G. Fat embolism syndrome. Circulation. 2015;**131**(3):317-320

[25] Vannucci A, Jeffcoat A, Ifune C, et al. Special article: Retained guidewires after intraoperative placement of central venous catheters. Anesthesia and Analgesia. 2013;**117**:102-108

[26] Schechter MA, O'Brien PJ, Cox MW. Retrieval of iatrogenic intravascular foreign bodies. Journal of Vascular Surgery. 2013;**57**:276-281

[27] Roddy SP. Endovascular foreign body retrieval. Journal of Vascular Surgery. 2013;**57**(2):599

[28] Costantini V, Lenti M. Treatment of acute occlusion of peripheral arteries. Thrombosis Research. 2002;**106**(6):V285-V294

[29] Aune S, Trippestad A. Operative mortality and long-term survival of patients operated on for acute lower limb ischaemia. European Journal of Vascular and Endovascular Surgery. 1998;**15**:143-146

[30] Fagundes C, Fuchs FD, Fagundes A, et al. Prognostic factors for amputation or death in patients submitted to vascular surgery for acute limb ischemia. Vascular Health and Risk Management. 2005;**1**(4):345

[31] Heit JA, Silverstein MD, Mohr DN, et al. Risk factors for deep vein thrombosis and pulmonary embolism: A population-based case-control study. Archives of Internal Medicine. 2010;**160**(6):809-815

[32] Cox CE, Carson SS, Biddle AK. Cost-effectiveness of ultrasound in preventing femoral venous catheter-associated pulmonary embolism. American Journal of Respiratory and Critical Care Medicine. 2003;**168**(12):1481-1487

[33] Kempny A et al. Incidence, mortality, and bleeding rates associated with pulmonary embolism in England between 1997 and 2015. International Journal of Cardiology. 2019;**277**:229-234

[34] Brennan P et al. Real World Outcomes for "Intermediate-High" Mortality Risk Patients Presenting with Submassive Pulmonary Embolism in a Tertiary Cardiothoracic Centre. London, United Kingdom: BMJ Publishing Group Ltd and British Cardiovascular Society; 2019

[35] Fanikos J et al. Hospital costs of acute pulmonary embolism. The American Journal of Medicine. 2013;**126**(2):127-132

[36] Dismuke SE, Wagner EH. Pulmonary embolism as a cause of death: The changing mortality in hospitalized patients. JAMA. 1986;**255**(15):2039-2042

[37] Jaff M, McMurty MS, Archer SL, et al. Management of massive and submassive pulmonary embolism, iliofemoral deep vein thrombosis, and chronic thromboembolic pulmonary hypertension: A scientific statement from the American Heart Association. Circulation. 2011;**123**(16):1788-1830

[38] Stawicki SP et al. Transthoracic echocardiography for suspected pulmonary embolism in the intensive care unit: Unjustly underused or rightfully ignored? Journal of Clinical Ultrasound. 2008;**36**(5):291-302

[39] Stein PD, Woodard PK, Weg JG, et al. Diagnostic pathways in acute pulmonary embolism: Recommendations of the PIOPEDII investigators. Radiology. 2007;**242**(1):15-21

[40] Sherk WM, Stojanovska J. Role of clinical decision tools in the diagnosis of pulmonary embolism. American Journal of Roentgenology. 2017;**208**(3):W60-W70

[41] Shaikh N. Emergency management of fat embolism syndrome. Journal of Emergencies, Trauma, and Shock. 2009;**2**(1):29

[42] Eriksson EA, Pellegrini DC, Vanderkolk WE, et al. Incidence of pulmonary fat embolism at autopsy: An undiagnosed epidemic. Journal of Trauma and Acute Care Surgery. 2011;**71**(2):312-315

[43] Clark SL. Amniotic fluid embolism. Obstetrics & Gynecology. 2014;**123**(2):337-348

[44] Killam A. Amniotic fluid embolism. Clinical Obstetrics and Gynecology. 1985;**28**(1):32-36

[45] Pacheco LD et al. Amniotic fluid embolism: Diagnosis and management. American Journal of Obstetrics and Gynecology. 2016;**215**(2):B16-B24

[46] Stawicki SP, Papadimos TJ. Challenges in managing amniotic fluid embolism: An up-to-date perspective on diagnostic testing with focus on novel biomarkers and avenues for future research. Current Pharmaceutical Biotechnology. 2013;**14**(**14**):1168-1178

[47] Mirski MA, Lele AV, Fitzsimmons L, et al. Diagnosis and treatment of vascular air embolism. Anesthesiology: The Journal of the American Society of Anesthesiologists. 2007;**106**(1):164-177

[48] Brook OR, Hirshenbaum A, Talor E, et al. Arterial air emboli on computed tomography (CT) autopsy. Injury. 2012;**43**(9):1556-1561

[49] Morales-Vidal SG. Neurologic complications of fat embolism syndrome. Current Neurology and Neuroscience Reports. 2019;**19**(3):14

[50] Molière S, Kremer S, Bierry G. Case 254: Posttraumatic migrating fat embolus causing fat emboli syndrome. Radiology. 2018;**287**(3):1073-1080

[51] Bělohlávek J, Dytrych V, Linhart A. Pulmonary embolism, part I: Epidemiology, risk factors, and risk stratification, pathophysiology, clinical presentation, diagnosis and nonthrombotic pulmonary embolism. Experimental and Clinical Cardiology. 2013;**18**(2):129

[52] Huebner S, Ali S. Bilateral shotgun pellet pulmonary emboli. Journal of Radiology Case Reports. 2012;**6**(4):1

[53] Bach AG et al. Imaging of nonthrombotic pulmonary embolism: Biological materials, nonbiological materials, and foreign bodies. European Journal of Radiology. 2013;**82**(3):e120-e141

[54] Herbert JT, Kertai MD. Transesophageal echocardiography use in diagnosis and management of

embolized intravascular foreign bodies. In: Seminars in Cardiothoracic and Vascular Anesthesia. Los Angeles, CA: SAGE Publications Sage CA; 2018

[55] Elison RMA et al. Surgical management of late bullet embolization from the abdomen to the right ventricle: Case report. International Journal of Surgery Case Reports. 2017;**39**:317-320

[56] Adegboyega PA, Sustento-Reodica N, Adesokan A. Arterial bullet embolism resulting in delayed vascular insufficiency: A rationale for mandatory extraction. Journal of Trauma and Acute Care Surgery. 1996;**41**(3):539-541