Update on the Management of Iatrogenic Gas Embolism

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42.1 Introduction

Gas embolism remains a poorly known medical problem albeit it is often of iatrogenic origin and is associated with an unacceptably high rate of morbidity and mortality. In this chapter, we will summarize the physiopathology, diagnosis, and management of iatrogenic gas embolism.

42.2 Definition and Epidemiology

Gas embolism results from a vascular breach leading to the entry of gas into the circulation. Gas embolism is defined by the onset of clinical manifestations resulting from circulating gas. Gas embolism occurs in three main circumstances: pregnancy, trauma, and following medical or surgical procedures, i.e., iatrogenic gas embolism. In this chapter, we will focus on iatrogenic gas embolism. According to where gas enters into the circulation, the terms venous or arterial gas embolism are used. Gas embolism is a potentially catastrophic complication of numerous medical or surgical procedures [1]. The prevalence of iatrogenic gas embolism is estimated to be at least 2.6/100,000 hospitalizations [2]. Gas embolism is likely underdiagnosed, undertreated, and thus underreported. Its mortality rate in the short-term is approximately

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Table 42.1 Mortality and neurological sequelae of gas embolism

First author [ref]	Number of patients	Hyperbaric oxygen therapy	Death (%)	Neurological sequelae (%)
Murphy [3]	16	One session at 6 ATA (US Navy 6A)	12.5	37.5
Bitterman [31]	5	One session at 6 ATA (US Navy 6A)	20	20
Massey [32]	14	One session at 6 ATA (US Navy 6A)	21.4	71.4
Kol [33]	6	One session at 6 ATA (modified US Navy 6A) One patient was treated for 90 min at 2.8 ATA	33	17
Muskat [34]	4	One session at 6 ATA (US Navy 6A)	25	0
Ziser [4]	17	One session at 6 ATA (US Navy 6A) One patient was treated for 90 min at 2.8 ATA	18	35
Blanc [5]	86	One session at 6 ATA (US Navy 6A)	8	33
Bessereau [2]	125	One session at 4 ATA for 15 min with a decompression plateau pressure at 2.8 ATA for 90 min	21	33
Beevor [35]	36	One session at 6 ATA (US Navy 6A)	9	36

ATA atmospheres absolute

8–12% [2–5]. Severe sequelae affect 9–35% of survivors (Table 42.1) [2–5]. The diagnosis is challenging in particular during general anesthesia. Indeed, visualization of gas in the circulation on its own may not mean that there will be clinical consequences and is not sufficient to confirm the diagnosis of gas embolism.

42.3 Physiopathology

There are two main mechanisms by which gas embolism may cause organ damage: mechanical obstruction and inflammation. First, the gas embolus interrupts flow when reaching a vessel with a smaller diameter causing ischemia in corresponding tissues. A venous gas embolus originates before the pulmonary filter and progresses to the right cardiac cavities. When the volume of the bubble is sufficiently large, acute cardiac obstruction may occur [6]. Moderate size bubbles lodged in the pulmonary arteries increase pulmonary vascular resistance and cause pulmonary hypertension [7], abnormal ventilation/perfusion ratios, and subsequently hypoxemia [8]. Small-sized bubbles may remain *asymptomatic* and clear through the pulmonary alveoli without causing any circulatory disorder. The brisk increase in right ventricular pressure may promote the migration of bubbles originating in the venous system into the arterial system, causing a paradoxical embolism. A paradoxical embolism occurs through the existence of a right-left shunt, including patent foramen ovale, a condition present in 20–30% of the adult population [9]. Mechanical ventilation, particularly with positive end-expiratory pressure (PEEP), promotes bubble progression through right-to-left shunting. Gas entering the systemic circulation may affect multiple organs, sometimes simultaneously. In experimental models of arterial gas embolism, there was evidence of gas in the cerebral, mesenteric, femoral, and coronary arteries [10].

A bubble of gas entering the systemic circulation will travel until the caliber of the vessel is too small, forcing the bubble to slow down and then to stop, leading to end-organ ischemia. During this process, a bubble will break up into smaller entities leading to multiple sites of ischemia. Owing to natural dissolution of gas into blood, the diameter of the intravascular bubbles decreases enabling the bubble to progress downstream to a vessel with a smaller diameter. As a result, ischemia-reperfusion injuries may occur. In addition, bubbles interact with the endothelium, triggering activation of platelets, leukocytes, complement system, coagulation cascade, fibrinolysis, and kinin systems [11–13]. The gas embolus may then become covered with fibrin and inflammatory cells or even lead to the formation of a blood clot. This will prevent the natural dissolution of the gas into the blood and prolong tissue ischemia.

A number of factors contribute to the severity of gas embolism. First, the type of gas will determine the speed of the natural dissolution of the bubbles into the blood with nitrogen being less soluble in the blood than oxygen or carbon dioxide. Intravascular gas volume of >50 ml may cause cardiac arrest, and administration of 90 ml/s of air may be lethal in man. In case of venous air embolism, the gradient of pressure between the vessel breach and the right atrium is a major determinant of the volume and flow of air entering the circulation. Typically, the sitting position during neurosurgery or during manipulation of a central venous line is an important risk factor for serious cerebral air embolism [14]. Thus, maintaining the gradient of pressure at zero (supine position) or even negative (Trendelenburg position) usually prevents eruption of gas into the venous circulation. In addition to patient position, hypovolemia and early phase of inspiration in spontaneously breathing patients may also contribute to a positive gradient of pressure between the vessel's hole and the right atrium.

42.4 Diagnosis

Sometimes entry of gas (usually air) into the vessels is directly seen, particularly following extracorporeal circulation or intravascular radiographic procedures. In this context, the diagnosis is immediate and does not require any further investigations. Likewise, clinical manifestations in circumstances such as a disconnected central venous line are sufficient to confirm the diagnosis of air embolism.

42.4.1 Conditions with Risk of Iatrogenic Gas Embolism

42.4.1.1 Venous Gas Embolism

A number of surgical procedures are particularly at risk of gas embolism. They include procedures requiring gas insufflation in a virtual cavity such as the pleura or the peritoneum [15] or in the gastroduodenal tract [16]. High-frequency jet ventilation during surgery is also a common cause of venous air embolism. Surgical procedures in areas of no collapsible veins (i.e., epiploic and emissary veins and dural venous systems) may also promote gas entry into the circulation. For example,

neurosurgery of the posterior fossa in a patient in the sitting position is associated with gas embolism in 39% of cases [17]. Hysteroscopy or self-inflicted abortions, through damage to the veins of the myometrium is often associated with gas embolism.

Placement, manipulation, or removal of central venous lines, Swan-Ganz catheters, and dialysis catheters is the primary cause of iatrogenic air embolism [18] with a prevalence of 1/750 to 1/3000 [2, 19]. Gas embolism may also occur following invasive chest procedures, such as thoracoscopy and transthoracic punctures, and during mechanical ventilation with dynamic hyperinflation-induced alveolar breach.

42.4.1.2 Arterial Gas Embolism

Cardiopulmonary bypass (CPB) exposes to arterial gas embolism, and transcranial Doppler monitoring shows the presence of cerebral microbubbles in almost all patients [20]. Gas embolism-related death or major brain injuries may occur in 1/2500 to 1/8000 cases [21]. There are many other procedures, particularly invasive radiography, that may be complicated by gas embolism [2, 22] (Table 42.2).

42.4.2 Clinical Manifestations

Symptoms of gas embolism are of sudden onset during procedures at risk. Sometimes symptoms may be delayed after the procedure, for example, following mobilization of the patient, or during recovery from general anesthesia. Symptoms are usually nonspecific signs of ischemia and/or inflammation.

A precordial "millwheel murmur" can occasionally be heard at the time of gas embolism, indicating gas in the cardiac chambers. More common are cardiac signs of obstruction of the pulmonary arteries, including pulmonary artery hypertension, reduced right ventricular preload, which may lead to lower left ventricular preload and reduced cardiac output, or signs of myocardial ischemia including chest pain, faintness, hypotension, cardiovascular collapse, bradycardia, tachyarrhythmia, or asystole. Neurological signs are related to cerebral ischemia, cerebral edema, and intracranial hypertension, and include headaches, coma, focal neurological signs (anosognosia, hemiparesis, or hemiplegia, ataxia), pyramidal signs, visual anomalies (cortical blindness, hemianopsia), and seizures.

During general anesthesia for at-risk surgery, gas embolism can be diagnosed by a sudden decrease in end-tidal CO_2 indicating a fall in cardiac output. Delayed awakening following surgery may be related to gas embolism of the pons or both hemispheres.

42.4.3 Laboratory Investigations

The diagnosis of gas embolism is often straightforward in the context of sudden onset of neurological and/or cardiorespiratory symptoms during a medical or

Table 42.2 Procedures at risk for iatrogenic gas embolism

Procedures	Mechanisms
Cardiac and vascular surgery	Arterial air embolism
Valve repair	
Coronary artery bypass grafting	
Inter-cavity communication closure	
Aortic aneurysm repair	
Interventional radiology	Arterial air embolism
Coronary angiogram	
Arteriography	
Transarterial chemo-embolization	Arterial air embolism
Neurosurgery	Venous air embolism
Posterior fossa	
Spinal surgery	
Endovascular intervention (e.g., thrombectomy)	Arterial air embolism
Extracorporeal circulation	Arterial air embolism
Arterio-venous ECMO	
Veno-venous ECMO	Venous air embolism
Hemodialysis	
Central vascular access	Venous air embolism
Placement, manipulation, removal of central line	
Cardiac catheterization	
Pacemaker placement	
Peripheral venous access	Venous air embolism
Thoracic procedures	Venous air embolism
Pleural puncture/drainage	
Transparietal puncture/biopsy	
Bronchoscopy	
Laser treatment of the airways	
Thoracoscopy/pleuroscopy	Venous CO_2 embolism
Mechanical ventilation	Venous air embolism
High positive end-expiratory pressure	
Jet ventilation	
High frequency oscillatory ventilation	
Endoscopic procedures requiring gas insufflation	Venous CO_2 embolism
Laparoscopy	
Coelioscopy	
Endoscopic retrograde cholangio-pancreatography	

ECMO extracorporeal membrane oxygenation

surgical procedure at risk. There is no biomarker of gas embolism and electrophysiological studies, whether cerebral or cardiac, are useless and only provide evidence of nonspecific brain injuries or cardiac ischemia. During surgery, monitoring of end-tidal CO_2, or monitoring by transesophageal echocardiography or transcranial Doppler allows early detection of gas embolism. In cases such as delayed awakening from general anesthesia, brain computed tomography (CT) scan may show gas in cerebral vessels (Fig. 42.1). Likewise, presence of gas in intrathoracic vessels or the cardiac cavity can also be demonstrated on chest X-ray, echocardiography, or CT scan.

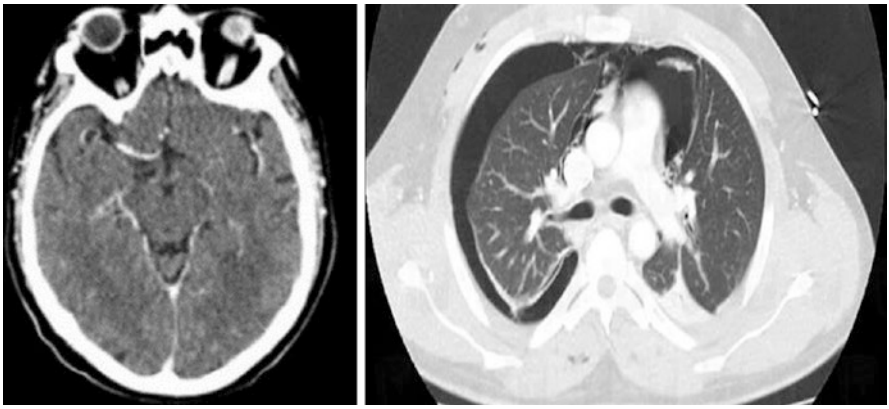

Fig. 42.1 Computed tomography (CT) scan of the brain (left panel) and the thorax (right panel), in a 38-year-old woman who presented suddenly with headaches, bilateral blindness, and chest pain 4 h after coelioscopy for ovarian resection. CT scan showed multiple air-density areas in both cerebral hemispheres (left panel) and a right pneumothorax and air in the intrathoracic vessels (right panel)

42.5 Treatment

42.5.1 Immediate Interventions

Any suspicion of gas embolism should prompt specific management. First, the invasive procedure should be terminated without delay and the patient be placed in the supine or Trendelenburg position. Whenever possible, gas should be removed from the right atrium and or the superior vena cava through the central venous line, and sometimes chest compression may help split a large embolus obstructing the heart [23, 24]. To further reduce the gradient pressure between a vessel's breach and the right atrium, rapid volume expansion or shockproof trousers may be used [1]. Patients should be breathing at a fraction of inspired oxygen of 100%, and mechanical ventilation may help accelerate the clearance of gas from the cerebral circulation [25].

42.5.2 Hyperbaric Oxygen Therapy

Hyperbaric oxygen therapy is the gold standard treatment of gas embolism, and patients should be referred to the hyperbaric center without delay [1, 26, 27]. The administration of hyperbaric oxygen therapy is based on solid rationale. First, according to gas physics, increasing atmospheric pressure will mechanically reduce the volume of bubbles in the body. The Boyle and Marriote law states that for a given mass of confined gas, and as long as the temperature is constant, the product of pressure and volume is constant. As shown in Fig. 42.2, increase of absolute pressure to

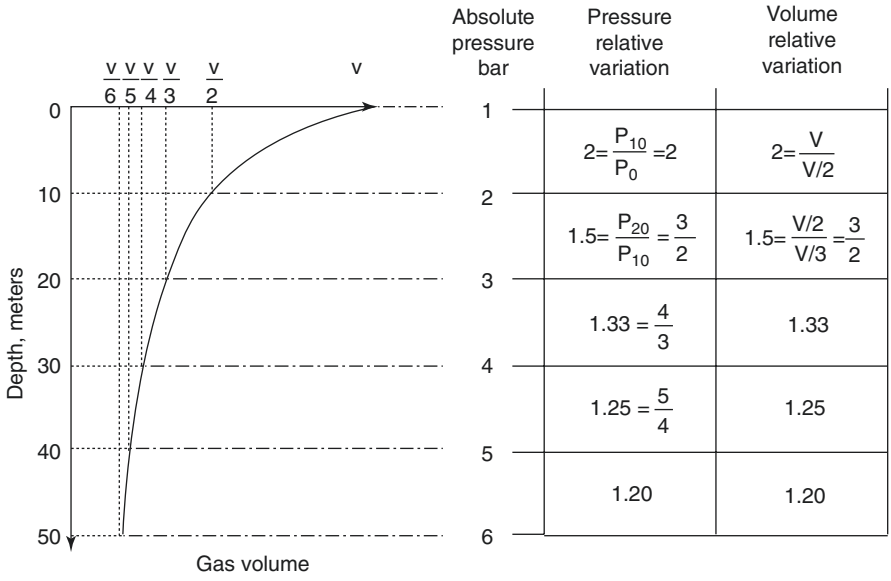

Fig. 42.2 Relationship between atmospheric pressure (P) and volume (V) of gas

Table 42.3 Relationship between atmospheric pressure, alveolar oxygen pressure (P_AO_2), and arterial oxygen content (CaO_2)

Atmospheric pressure		P_AO_2 FiO_2: 21%	P_AO_2 FiO_2: 100%	CaO_2 FiO_2: 21%	CaO_2 FiO_2: 100%
ATA	mmHg	mmHg	mmHg	Vol (%)	Vol (%)
1	760	102	673	0.32	2.09
2	1520	262	1053	0.81	3.26
3	2280	422	1433	1.31	6.80
4	3040	582	1813	1.80	9.34
6	4560	902	2193	2.80	14.53

FiO_2 inspired fraction of oxygen, *ATA* atmospheres absolute

2 and 3 bars reduced the volume of gas by two- and threefold, respectively. The magnitude of the reduction in the size of bubbles is much less above 3 bar, suggesting that in medical practice there is limited added value of high pressurization (i.e., above 2.8 bar). Second, according to the Dalton law, increase in absolute pressure increases blood oxygen content with denitrogenation accelerating the dissolution of nitrogen into the blood and subsequently diminishing the size of circulating air bubbles [21, 24]. Table 42.3 illustrates the relationship between increase in atmospheric pressure and alveolar oxygen pressure and arterial oxygen content. Finally, hyperbaric oxygen therapy contributes to reducing brain vascular permeability, edema, and intracranial pressure improving the cerebral perfusion pressure [28, 29].

In patients, the evidence supporting hyperbaric oxygen therapy comes from cohort studies (Table 42.1). The most recent and largest cohort study found that 1

year after one session of hyperbaric oxygen therapy, 78/119 patients had survived severe iatrogenic gas embolism free of sequelae [2]. Long-term major neurological sequelae, i.e., a Glasgow outcome scale of three or lower, were seen in only 12/119 patients. Risk factors for mortality at 1 year included an initial cardiac arrest and a Babinski sign. Likewise, a Babinski sign upon ICU admission was a strong and independent predictor of major neurological sequels at 1 year. There is no randomized trial comparing hyperbaric oxygen therapy versus normobaric oxygen therapy. Such a trial would be ethically challenging owing to the iatrogenic nature of gas embolism, the strong rationale and the consistency in the results of cohort studies. One large cohort study found that when hyperbaric oxygen therapy was delivered within 6 h from gas embolism, the recovery rate was dramatically better than if this treatment was delayed (38/56 versus 12/30) [5]. Furthermore, with appropriate preventative measures for oxygen neurotoxicity and barotrauma, hyperbaric oxygen therapy has consistently been reported to be safe with infrequent undesirable effects [30]. Nevertheless, a number of issues have not been addressed so far, including which absolute pressure, which duration, and how many hyperbaric sessions are optimal.

42.6 Conclusion

Gas embolism is an underestimated and potentially cataclysmic complication of invasive procedures. Physicians should suspect gas embolism whenever there is sudden onset of cardiac, neurological, or respiratory symptoms during an at-risk procedure. Whenever suspected, gas embolism should prompt termination of the procedure and rapid management of patients, including positioning and breathing high oxygen concentrations, while being referred to the hyperbaric center. Iatrogenic gas embolism remains associated with an unacceptably high morbidity and mortality.

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