Gas embolism during endoscopic retrograde cholangiopancreatography: diagnosis and management

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Abstract   Air embolism is rarely diagnosed and is often fatal. The diagnosis is often not made in a timely manner given the rapid and severe clinical deterioration that often develops, frequently leading to cardiac arrest. Many patients are only diagnosed post-mortem. With the increasing use of endoscopic retrograde cholangiopancreatography, air embolism should be considered in the differential diagnosis in patients who experience sudden clinical deterioration during or immediately after the procedure. Clinical suspicion is key in the diagnosis and management of air embolism. Use of precordial Doppler ultrasound and transesophageal echocardiogram can aid in the diagnosis of air embolism. Once the diagnosis is made, supportive management of airway, breathing and circulation is pivotal. Advanced cardiac life support should be initiated when necessary. Fluid resuscitation and vasopressors can improve cardiac output. Hyperbaric oxygen therapy should be considered when possible in cases of suspected cerebral air embolism cases to improve neurological outcome. A multidisciplinary team approach and effective communication with experts, potentially including an anesthesiologist, cardiologist, intensivist, radiologist and surgeon, can improve the outcome in air embolism.

Keywords Endoscopic retrograde cholangiopancreatography, air embolism, precordial Doppler ultrasound, transesophageal echocardiogram, hyperbaric oxygen therapy

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Introduction

Gas embolism is defined as the undesired entry of air into the vascular structures which can be venous or arterial. Gas embolism is usually air, but it can be carbon dioxide, nitrous oxide, nitrogen or other gases. Air embolism is often a catastrophic event which can lead to significant morbidity and mortality. It is usually iatrogenic and can occur during any endoscopic procedure including esophagogastroduodenoscopy, colonoscopy, enteroscopy, sigmoidoscopy, endoscopic ultrasound, surgical procedures, intravenous catheterization, radiologic procedures, positive pressure ventilation, trauma,

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and decompression sickness [1-10]. Endoscopic retrograde cholangiopancreatography (ERCP) is a complex gastrointestinal procedure wherein a side-viewing upper endoscope is used to pass into the duodenum to facilitate instruments to access biliary and pancreatic duct. Various indications of ERCP include the treatment of biliary obstruction, acute biliary pancreatitis with cholangitis, stent placement for benign and malignant strictures, pancreatic pseudocyst drainage, and tissue sampling from pancreatic or bile ducts [11]. Complications of ERCP include pancreatitis, cholangitis, hemorrhage, and duodenal perforation [12]. Air embolism should be considered in the differential diagnosis of a patient with abrupt change in vitals or neurological status during or after ERCP. In this article, we review the etiology, pathophysiology, diagnosis, and management of air embolism in ERCP.

Pathophysiology

Gas embolism can be venous, paradoxical or arterial and the pathophysiology is described in Fig. 1 [12-16]. Physiological intrapulmonary right to left shunts, retrograde flow via superior vena cava into the cerebral veins, and passage of air via pulmonary veins into the left atrium can lead to paradoxical air embolism [17-20]. Large venous gas embolism can cause fatal cerebral artery gas embolism even in the absence of

intracardiac defects [21]. Spencer *et al* demonstrated that the size of the bubble, surface tension, and vascular pressure influence the passage of emboli across the lungs [22]. Also, the partial pressure of gas inside the bubble determines the rate of dissolution in the blood. They also showed that equivalent doses of oxygen or carbon dioxide did not cross the lungs compared with nitrogen because of differences in partial pressure and surface tension.

In endoscopy, air insufflation under pressure into an exposed vessel (gastric ulcer) can lead to air embolism [23]. Maximum flow rates during endoscopy without resistance for purified water is 100 mL/min and for air it is 2000 mL/min [23]. Lowdon *et al* described a case report of air embolism in a patient who had previously undergone Kasai procedure (hepatoportoenterostomy) for biliary atresia. The authors concluded that air embolism developed by the entry of air into the hepatic veins below the enterostomy site [17].

The various proposed mechanisms for air embolism from ERCP include endoscope-induced mechanical irritation of the bile duct wall, air entry into the bilio-venous shunts, transgression of air into adjacent veins from inflammation of the mucosa, and muscular wall, leakage of air into the portal or hepatic venous system from the bile duct secondary to pressure in the biliary system via contrast injection, removal of bile duct stents, mechanical irritation of the bile duct from bile duct stones, preexistent bilio-venous fistula, and communication via sphincterotomy to the portal vein [24,25] (Fig. 1). Portal vein cannulation can also occur from laceration of small portal vein or trauma to papilla and is more common in pancreatic adenocarcinoma patients, likely from neo-angiogenesis or aberrant vessels [26-28].

Clinical presentation

Clinical suspicion is key in the diagnosis of air embolism as most of the patients are sedated during the procedure and hence diagnosis is based on objective signs, although most cases of air embolism go undiagnosed acutely given the severity and rapidity of clinical deterioration patients often experience. Many cases are only diagnosed post-mortem. Minor cases of venous air embolism can be asymptomatic but most severe cases can be lethal. Air can be detected in retinal vessels and areas of sharply defined pallor can be noticed on the tongue [29]. Cardiovascular signs and symptoms include chest pain, dizziness, crackles, elevated jugular venous pressure, acute onset right side heart failure, tachycardia or bradycardia, hypotension, mill wheel murmur (loud churning sound likely from mixing of air and blood in the right ventricle heard throughout the cardiac cycle), cardiac arrest, arrhythmias like supraventricular tachycardia, ventricular tachycardia, ventricular fibrillation, asystole, and pulseless electrical activity [30-34]. Neurological signs and symptoms include headache, seizures, focal neurological deficits, acute change in mental status or failure to regain consciousness after the procedure, hemiparesis, conjugate eye deviation, pupillary dilation, paraplegia, quadriparesis, skin mottling, bilateral extensor plantar reflex, and coma [35-38] (Fig. 2). Pulmonary symptoms and signs include respiratory failure, tachypnea, cyanosis, rales, and wheezing [39].

Diagnosis

Diagnosis should be based on clinical suspicion as no imaging is sufficiently accurate [16] sometimes the first clue to the diagnosis of air embolism during ERCP in intubated patients is drop in end-tidal carbon dioxide (etCO$_2$) [40]. The fall in etCO$_2$ level (normal range 35-45 mmHg) can be detected by capnography. Air embolism leads to ventilation perfusion mismatch which further leads to increased physiological dead space and eventually to fall in etCO$_2$. Hypoxia is a universal finding in air embolism and any sudden drop in oxygen saturation should be evaluated immediately. Hypotension occurs due to decreased venous return. Elevated central venous pressure (CVP) is a result of air embolism causing right ventricular strain leading to right heart failure [41]. Routine complete blood count with differential, comprehensive metabolic panel, creatine kinase, brain natriuretic peptide and troponin should be ordered. Although elevated hematocrit (Hct) can be nonspecific, it can be seen in arterial gas embolism likely secondary to endothelial injury leading to leakage of intravascular fluid and elevated Hct [42]. Low platelet count with elevated creatine kinase (CK) can be seen in air embolism [43,44]. Thrombocytopenia is explained by direct air bubble and platelet binding [45]. Also, pulmonary air embolism leads to platelet aggregation because of complement activation from the release of endothelin, serotonin, and thromboxane [43]. Elevated CK-MB is commonly seen in diving-associated gas embolism likely from skeletal air embolization [44]. CK occurs in 3 different isoenzymes: MM, MB, and BB. CK-MM is more common in skeletal muscle, CK-MB in cardiac muscle, and CK-BB in brain tissue. Electrocardiogram (ECG) shows non-specific ST and T wave changes. ST-segment depression or elevation can occur which suggests myocardial ischemia [46]. Arterial blood gas shows hypoxemia and hypercarbia.

Chest x-ray findings include air in pulmonary artery, characteristic of pulmonary venous air embolism, pulmonary edema, adult respiratory distress syndrome, diminished vascularity in the upper lobes (air emboli common in upper lobes), intracardiac air, and atelectasis [47,48]. Computed tomography (CT) of the chest shows air in the pulmonary artery, heart and right ventricle [31,49,50]. CT of the abdomen can show air in the portal vein if the portal vein is cannulated (Fig. 3) [51]. CT of the brain shows intraparenchymal gas, midline shift, cerebral edema, and uncal herniation (Fig. 4) [52]. Magnetic resonance imaging (MRI) of the brain shows acute infarcts in the areas affected by air embolism [37]. Echocardiogram can identify air in cardiac chambers, patent foramen ovale (PFO), atrial septal defect, right ventricular dilation, decreased systolic function and pulmonary artery hypertension [53]. Transesophageal echocardiography (TEE) is more sensitive than transthoracic echocardiography in
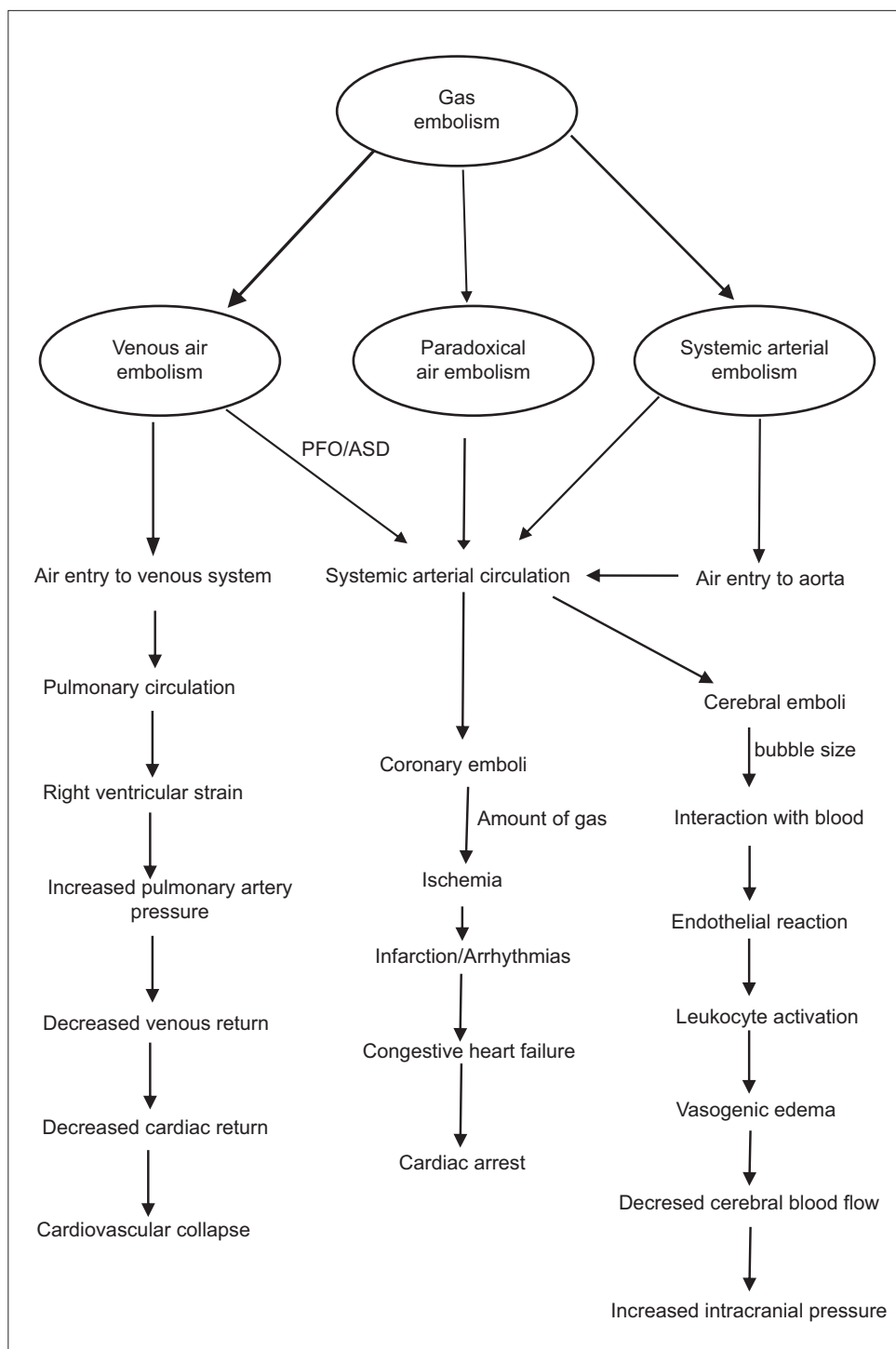
Figure 1 Pathophysiology of air embolism
PFO, patent foramen ovale; ASD, atrial septal defect

identifying PFO [54]. TEE is invasive, expensive and needs experienced personnel to do immediately [55]. Pulmonary embolism (PE) on TEE can be identified as global hypokinesis with mobile echogenic densities in the right atrium and right ventricle [40]. Precordial Doppler ultrasonography is sensitive in diagnosing air embolism and is noninvasive [56,57]. It is based on the principle that the Doppler ultrasonic signal from the transducer is reflected by moving red blood cells and cardiac structures, further electronically converted to an audible sound. The transducer is placed with a small amount of acoustic gel
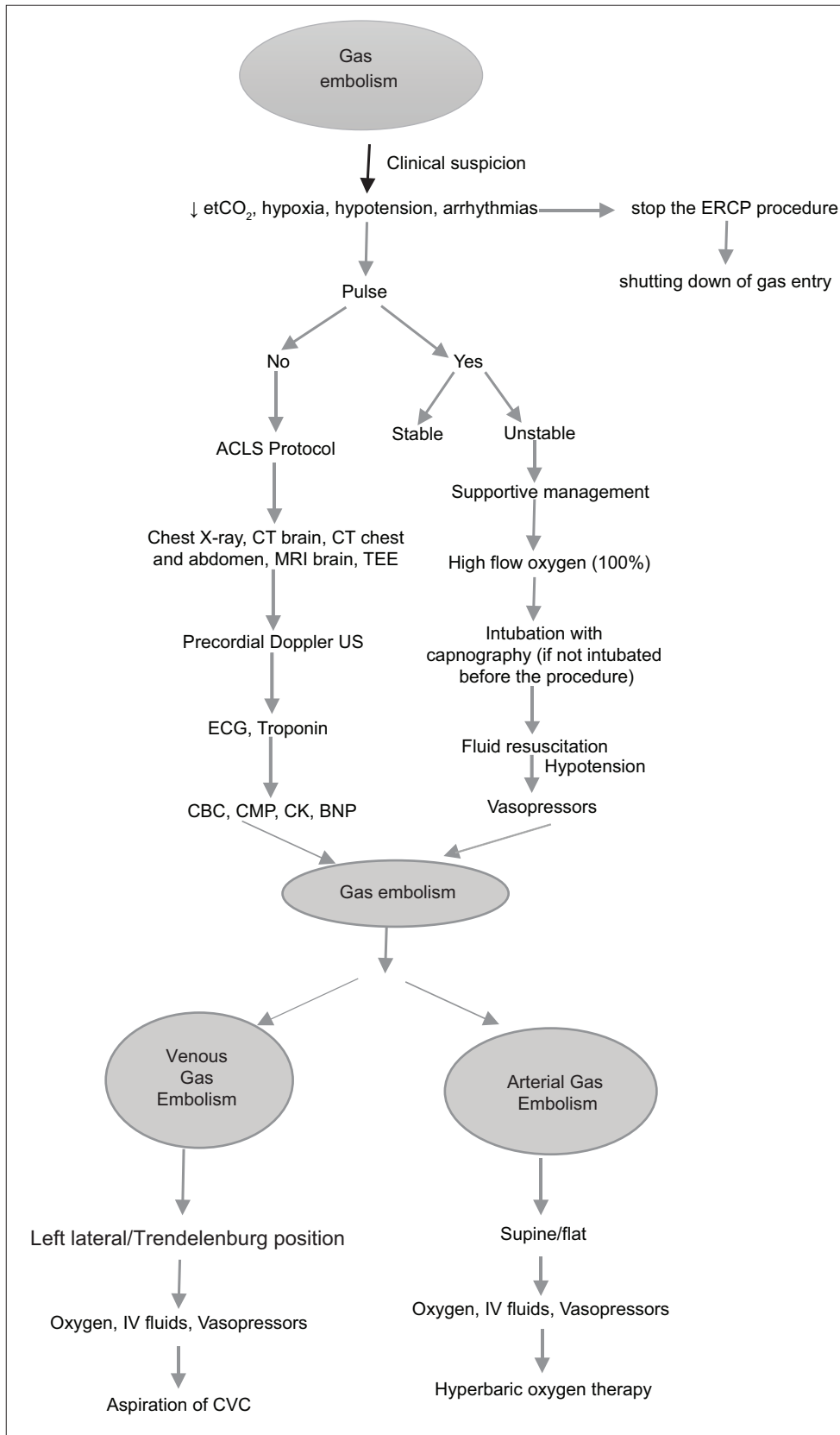
Figure 2 Proposed algorithm for diagnosis and management of gas embolism
MRI, magnetic resonance imaging; ACLS, advanced cardiac life support; ERCP, endoscopic retrograde cholangiopancreatography; TEE, transesophageal echo; CBC, complete blood count; CMP, complete metabolic panel; CK, creatine kinase; ECG, electrocardiogram; BNP, brain natriuretic peptide; IV, inferior vena; CVC, central venous catheter; etCO2, end-tidal CO2; CT, computed tomography
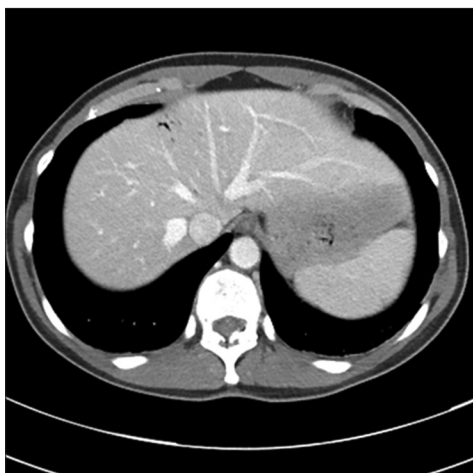
Figure 3 Computed tomography scan showing portal venous air embolism (Image courtesy Akram Shabaan, MD)
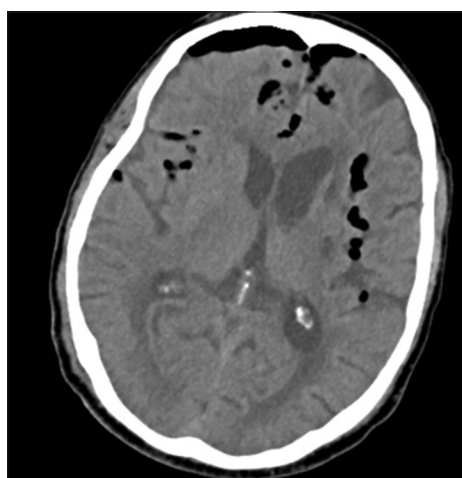
Figure 4 Computed tomography scan showing brain air embolism (Image courtesy Akram Shabaan, MD)

to the right side of the sternum between 3rd and 4th intercostal space, usually a few inches above the xiphoid process [58]. This position closely correlates with the placement of the transducer over the right atrium or right ventricle. Once the position of the transducer is confirmed it is secured with a circumferential rubber strap to avoid changes in Doppler signal with respiratory movements. A high pitched, "chirping", "scratchy", "roaring" sound is characteristic of air embolus [57]. A transient chirp is produced by small air embolus but raucous 'static' is usually produced by large air embolus. The disadvantage of precordial ultrasound Doppler is that it may be difficult to use in prone or lateral position [55]. Failure of Doppler signal can be due to slippage of the transducer especially in lengthy procedures or entrainment of air bubbles leading to decreased audible signal from the ultrasound [59]. Pulmonary artery catheter (PAC) can be used to detect air embolism. It is slightly more sensitive than etCO$_2$, but it is invasive [59]. The increase in pulmonary artery pressure correlates with the amount and rate of air entrapment [55]. However, insertion of PAC is not practical in

all cases as it needs more time and trained personnel and it is not well suited for aspiration of air from right atrium because of small atrial lumen [60,61].

Management

We were able to identify 51 cases of air embolism during or after ERCP published in literature shown in Tables 1, 2, 3 and 4). A proposed algorithm for diagnosis and management of gas embolism is included in Fig. 2. The key in management is early recognition of signs and symptoms of air embolism, although in many cases the diagnosis is only made post-mortem [62]. Termination of the procedure should be the first step in the treatment to prevent further entry of gas. Decompression of the stomach and duodenum by withdrawal of the endoscope will reduce the pressure gradient and prevent further additional entrapment of air. Hemodynamic and respiratory stabilization should be the priority. Cardiopulmonary resuscitation should be initiated immediately when needed. Endotracheal intubation with capnography should be performed in somnolent, obtunded or comatose to protect airway and provide adequate ventilation and oxygenation.

High flow 100% oxygen should be administered not only to treat hypoxia but also to help eliminate gas from bubbles by creating a diffusion gradient [63,64]. Placing the patient in left lateral (Durant) and Trendelenburg position will not only minimize the air embolism to brain but will also help force it out of the right ventricle [13,35]. As a result of these positions, the right ventricular outflow tract is placed inferior to the right ventricle cavity and air will migrate superiorly into the right ventricle making it less likely to embolize [65,66]. In arterial embolism, supine position is preferred as the buoyancy of air bubbles is not sufficient to overcome the blood flowing towards the head and head down position aggravates cerebral edema [29,67]. Evacuation of air from central venous catheter (CVC) is recommended if possible and occasionally up to 50% of entrained air can be removed with proper placement of CVC [55,68]. The optimal position of CVC for aspiration of air is at 2 cm below the junction of right atrium and superior vena cava [55,69]. Fluid resuscitation will increase CVP thereby preventing further entry of gas into the venous circulation [70]. Gas embolism can lead to hemoconcentration because of endothelial injury and leakage of intravascular fluid [42]. Animal studies in rabbits showed that minimal hemodilution (Hct approx. 30%, target hemoglobin concentration 11 g/100 mL) reduces neurologic injury after cerebral ischemia compared with marked hemodilution (Hct <30%, target hemoglobin concentration 6 g/100 mL) [71]. The authors chose rabbits for their study as they closely resemble with the physiological characteristics of humans like arterial blood pressure, cerebrovascular response to change in PaCO$_2$, arterial blood pressure and resting cerebral blood flow. This study is based on the hypothesis that cerebral blood flow and oxygen delivery is increased to ischemic tissues with minimal hemodilution but with marked hemodilution this protective effect is lost and further leads to greater cerebral infarct [72].

Table 1 Venous air embolism cases of ERCP published in literature

Age (M/F)	Indication	Risk factor	Diagnosis	Treatment	Outcome	Shunt
79 F [30]	Ascending cholangitis	Previous biliary stent	Venous air embolism	Supportive	Dead	None
24 F [103]	Replace previous stent	Previous biliary stent	Venous air embolism	HBOT	Alive	None
75 M [104]	Obstructive jaundice	Previous biliary stent	Venous air embolism	HBOT	Alive	None
69 M [105]	Common bile duct stone	Endoscopic papillary balloon dilation	Venous air embolism	HBOT	Alive	None
51 F [31]	Common bile duct stone	Biliary sphincterotomy	Venous air embolism	Supportive	Dead	PFO
56 F [32]	Common bile duct stone	Biliary sphincterotomy	Venous air embolism	Supportive	Dead	None
55 F [49]	Common bile duct stone	Previous biliary stent	Venous air embolism	Supportive	Alive	None
87 M [106]	Common bile duct stone	Biliary sphincterotomy	Venous air embolism	HBOT	Alive	None
8 M [41]	Removal of previous biliary stent	Portal cavernoma/ Splenomes-enteric portal shunt	Venous air embolism	Supportive	Alive	None
Not mentioned [107]	Common bile duct stone	Biliary sphincterotomy	Hepatic portal vein gas	Supportive	Alive	Not mentioned
31 M [108]	Pancreatic duct stricture	Biliary sphincterotomy	Hepatic portal venous gas	Supportive	Alive	None
39 F [109]	Biliary pancreatitis	Duodenal perforation/biliary sphincterotomy	Portal venous gas	Supportive	Alive	None
68 M [51]	Ascending cholangitis	Edematous papillae	Portal air	Supportive	Alive	None
74 F [110]	Ascending cholangitis	Gall bladder carcinoma	Portal air	Supportive	Alive	None
72 F [111]	Obstructive jaundice	pre-cut papillotomy	Portal air	Supportive	Alive	None
55 M [62]	Common bile duct stone	Biliary sphincterotomy	Pulmonary-air embolism	Supportive	Dead	None
76 F [40]	Common bile duct stone	Previous biliary stent	Pulmonary thrombo embolism	Thrombolytic	Alive	None
43 F [112]	Obstructive jaundice	Biliary sphincterotomy	Pulmonary embolism	Supportive	Dead	None

ERCP, endoscopic retrograde cholangiopancreatography; PFO, patent foramen ovale; HBOT, hyperbaric oxygen therapy; M, male; F, female

Table 2 Systemic air embolism cases of ERCP published in literature

Age (M/F)	Indication	Risk factor	Diagnosis	Treatment	Outcome	Shunt
66 M [36]	CBD stone	Previous biliary stent	Systemic air embolism	Supportive	Dead	PFO
51 F [113]	Recurrent pancreatitis	Recurrent pancreatitis	Spinal air	Supportive	Alive	Intra atrial
65 M [5]	Pancreatic duct stricture	Chronic pancreatitis	Cardiac air embolism	Supportive	Alive	None
82 M [46]	Removal of CBD stent	Prior biliary stent	Systemic air embolism	Supportive	Alive	None
50 F [94]	CBD stone	Bilio-venous fistula/choledochoduodenostomy	Systemic air embolism	Supportive	Dead	None
72 F [114]	Diagnostic	Cholangiocarcinoma	Systemic air embolism	Supportive	Alive	None
53 M [24]	CBD stone	Bilio-venous fistula	Systemic air embolism	Supportive	Alive	None
78 M [115]	CBD stone	Bilio-duodenal fistula	Systemic air embolism	Supportive	Dead	None
82 F [116]	Bile duct stricture	Previous biliary stent	Systemic air embolism	HBOT	Dead	None
27 M [34]	Bile leak	Hepatic trauma	Systemic air embolism	HBOT	Alive	None
63 F [117]	CBD stone	Biliary sphincterotomy	Systemic air embolism	Supportive	Dead	None
54 M [118]	Biliary obstruction	Billroth II, previous biliary stent, chronic pancreatitis	Systemic air embolism	Supportive	Dead	None

ERCP, endoscopic retrograde cholangiopancreatography; PFO, patent foramen ovale; CBD, common bile duct; HBOT, hyperbaric oxygen therapy

There is no clear consensus on whether colloids are better than crystalloids in acute cerebral ischemia [73]. However, if there are signs of raised intracranial pressure or diffuse cerebral edema, hyperosmolar therapy with hypertonic saline (3%, 7.5% or 23%) is recommended [74]. Vasopressors should be initiated if blood pressure continues to be low even after fluid resuscitation. CVC placement is strongly recommended as it has an advantage of not only monitoring CVP (goal 12 mmHg)

Table 3 Cerebral air embolism cases of ERCP published in literature

Age (M/F)	Indication	Risk factor	Diagnosis	Treatment	Outcome	Shunt
85 M [35]	Obstructed stent	Cholangiocarcinoma/Previous biliary stent	Cerebral air embolism	Supportive	Dead	None
37 M [30]	CBD obstruction	Recurrent pancreatitis	Cerebral air embolism	Supportive	Dead	None
85 M [119]	Obstructed stent	Cholangiocarcinoma/Previous biliary stent	Cerebral air embolism	Supportive	Dead	None
45 M [106]	Double duct stricture	Chronic pancreatitis	Cerebral air embolism	HBOT	Alive	PFO
36 M [37]	CBD stone	Previous biliary stent	Cerebral air embolism	Supportive	Alive	None
45 M [38]	Ascending cholangitis	Alcoholic liver cirrhosis	Cerebral air embolism	Supportive	Dead	None
66 M [113]	Bile duct stricture	Previous biliary stent	Cerebral air embolism	HBOT	Dead	PFO
58 F [52]	CBD dilatation	Unsuccessful previous biliary stent/ Cholangiocarcinoma	Cerebral air embolism	Comfort measures	Dead	None
45 M [93]	Obstructive jaundice	Percutaneous transhepatic biliary drainage	Cerebral air embolism	Supportive	Alive	PFO
79 F [39]	CBD stone	Biliary sphincterotomy	Cerebral air embolism	Supportive	Alive	None
62 F [54]	CBD stone	Biliary sphincterotomy/Intraductal balloon dilation	Cerebral air embolism	Supportive	Alive	PFO
65 M [33]	Bile duct stricture	Bilio-venous fistula	Cerebral air embolism	Supportive	Dead	None
60 F [120]	CBD stone	Biliary sphincterotomy/choledochal varices	Cerebral air embolism	Supportive	Alive	None
87M [118]	Bile duct stricture	Previous biliary stent	Cerebral air embolism	Supportive	Alive	PFO
56 M [25]	Ascending cholangitis	Previous biliary stent/Biliary adenocarcinoma	Cerebral air embolism	Comfort measures	Dead	None
50 F [121]	CBD stone	Biliary sphincterotomy	Cerebral air embolism	HBOT	Dead	PFO
59 F [50]	Recurrent cholangitis	Choledochojejunostomy/Previous biliary stent	Cerebral air embolism	Supportive	Dead	PFO
82 M [122]	CBD stone	Pancreatitis	Cerebral air embolism	Supportive	Dead	None

ERCP, endoscopic retrograde cholangiopancreatography; HBOT, hyperbaric oxygen therapy; PFO, patent foramen ovale; CBD, common bile duct

Table 4 Gas embolism from cholangioscopy published in literature

Age (M/F)	Indication	Risk factor	Diagnosis	Treatment	Outcome	Shunt
68 F [97]	Hepatolith	Hepaticojejunostomy	Systemic air embolism	Supportive	Dead	None
Not mentioned [98]	Choledocholithiasis	Papillotomy/previous ERCP	Venous air embolism	Supportive	Dead	None
Not mentioned [98]	Cholangitis	papillotomy	Systemic air embolism	Supportive	Dead	None

ERCP, endoscopic retrograde cholangiopancreatography

but also to evacuate air. Seizures can occur with cerebral gas embolism and first line of treatment is benzodiazepines and phenytoin. However, if seizures are refractory, then barbiturates should be added. Barbiturates are shown to decrease oxygen consumption, intracranial pressure and the release of free radicals [75,76].

Anticoagulation is not routinely recommended as there is risk of hemorrhagic transformation in the infarcted tissue. However, if PE is diagnosed, then anticoagulation is recommended. Risk factors for PE can be genetic or acquired. Genetic risk factors include factor V Leiden mutation and prothrombin gene mutation (G20210-A) [77]. Acquired risk factors can be provoked from recent surgery, trauma, immobilization, initiation of hormone therapy, and active cancer [78]. Unprovoked risk factors include obesity and heavy cigarette smoking [78]. Treatment choices for PE depends on whether the patient is hemodynamically stable or unstable. For stable PE, treatment choices include unfractionated heparin and low molecular weight heparin. Heparin can induce

antibodies to platelets which can predispose to arterial and venous thrombosis [79]. When unfractionated heparin cannot be used, low molecular weight heparin is safe to use [80]. For unstable PE, treatment options include thrombolytic therapy, transvenous catheter embolectomy, inferior vena cava (IVC) filter and pulmonary embolectomy with or without cardiopulmonary bypass [81]. Thrombolytic therapy with tissue plasminogen activator (tPA), such as alteplase, streptokinase and urokinase, can be used in unstable PE when rate of clot resolution is critical. Absolute contraindications for tPA use include intracranial neoplasm, recent intracranial or spinal surgery or trauma (less than 2 months), history of a hemorrhagic stroke, active bleeding or bleeding diathesis, or nonhemorrhagic stroke within the previous 3 months. IVC filter placement is recommended when there is absolute contraindication to therapeutic anticoagulation or complication to anticoagulation. Surgical embolectomy is recommended in unstable PE when there is contraindication to tPA or failed thrombolysis.

Corticosteroids are not recommended in cerebral gas embolism as they can potentiate ischemic injury to neurons [82]. In an effort to understand the cause of death in cerebral air embolism, studies on animals showed that autonomous nervous system could mediate cardiac arrhythmias. As a result, an animal study was done to evaluate the effect of lidocaine on cerebral air embolism. The role of lidocaine in humans is not clear, although prophylactic treatment with lidocaine in animal models showed benefit in cerebral air embolism by reduction in somatosensory evoked potential and intracranial pressure [83,84]. Hence, future studies on humans can potentially investigate the role of lidocaine in cerebral ischemia from air embolism. Therapeutic hypothermia in cerebral air embolism after cardiac arrest can be neuroprotective, more studies need to be done to make it standard of care in cerebral air embolism [85]. However, therapeutic hypothermia is not recommended in active infection or coagulation disorder [38,86].

Hyperbaric oxygen therapy (HBOT) is recommended in severe cases of air embolism with hemodynamic compromise and neurologic deficits [70]. Hyperbaric oxygen is based on the principle of Boyle's law that surface area and volume of gas bubble is inversely proportional to pressure at constant temperature. HBOT provides 100% oxygen at a pressure above that of the atmosphere at sea level and the partial pressure of arterial oxygen is greater than 2000 mmHg [70]. With increasing ambient pressure from HBOT, the gas bubble shrinks and leads to hyperoxia. Hyperoxia creates diffusion gradient which promotes oxygen into the bubble and nitrogen out of the bubble [67]. Hyperoxia also increases the extent of diffusion of oxygen into the tissues by dissolving large amounts of oxygen into the plasma [87]. HBOT has been shown to decrease cerebral edema by decreasing the adherence of leukocytes to damaged endothelium and by reducing the permeability of blood vessels [88,89]. The ideal time to initiation of HBOT is not clear, however patients who received HBOT within 5 h from the onset of symptoms are likely to have good recovery [90]. HBOT is generally safe when standard protocol of atmospheric pressure not more than 3 and maximum treatment exposure time of 120 min is used [91]. Most common side effect of HBOT is reversible myopia from direct toxic effect of oxygen on the lens [91].

Risk factors

Risk factors like previous biliary interventions, hepatobiliary surgery, portosystemic shunts, percutaneous transhepatic biliary drainage, liver abscess, blunt trauma to the liver, gastric ulcer, bilio-venous fistula, Billroth II or Roux-en-Y, should alert the endoscopist for possible air embolism during or after ERCP if they notice any signs or symptoms [34,49,92,93]. Sphincterotomy during ERCP can disrupt the gastrointestinal mucosal barrier and it can result in shunts between the veins in duodenal wall and intestinal cavity [94]. In patients with blunt hepatic trauma causing bile leak and lacerated hepatic veins, air/CO_2 insufflation during ERCP can potentially cause gas to enter into the IVC from the lacerated hepatic veins, although this is extremely rare in clinical practice [34]. Air embolism can travel into the right ventricle from the IVC and to the lungs leading to impaired gas exchange and cardiac failure. Budd-Chiari syndrome causes chronic inflammation from biliary strictures which potentially leads to bilio-venous fistula [49]. The risk of air embolism is increased during ERCP with preexisting bilio-venous fistula from air insufflation and sphincterotomy. Also, in patients with difficult cannulation during ERCP for obstructive jaundice who undergo percutaneous transhepatic cholangiography (PTC) are more prone to bilio-venous fistula which could be a risk factor for air embolism [93]. Cholangitis from biliary stones can lead to focal weakening of bile duct wall and adhesions with adjacent structures and are more prone to develop bilio-venous fistula, a high risk for air embolism [95]. According to Afreen *et al*, the incidence of air embolism is more in ERCP involving stent removal with replacement and cholangioscopy [96]. Cholangioscopy is sometimes used when there are equivocal ERCP findings to evaluate the extent of cholangiocarcinoma before surgery, biliary stones not identified by routine cholangiography, treatment of difficult bile duct stones and for evaluation of indeterminate biliary strictures [97,98]. Biliary stones and strictures cause inflammation which could lead to bilio-venous fistula and hence they are more prone to air embolism during cholangioscopy.

Prophylactic measures

Use of ERCP only when appropriately indicated can minimize the risk of air embolism. Air insufflation into the portal vein can occur during sphincterotomy and use of CO_2 can minimize air embolism but more studies need to be done to standardize use of CO_2 [99]. As ERCP is sometimes a lengthy procedure, the use of CO_2 has an advantage of being rapidly absorbed into the intestinal mucosa with greater elimination through expiration, thereby helping deflate the bowel quickly [100,101]. Use of CO_2 not only decreases bowel residual gas volume but also decreases abdominal discomfort and nausea after the procedure [100]. Endotracheal intubation with capnography during ERCP can play an important role in the early recognition of air embolism. When there is decrease in cardiac output from air embolism, capnography reveals a fall in etCO$_2$ [30]. Although it is not well studied if endotracheal intubation with capnography should be routinely offered to all patients who undergo ERCP but patients with risk factors can benefit from capnography for early recognition of air embolism. Use of precordial Doppler ultrasound can be beneficial in patients with risk factors to detect early air embolism during ERCP. The role of routine preprocedural evaluation for PFO in patients with risk factors who undergo ERCP is unclear and is not performed in routine practice. However, when ERCP is indicated in patients with PFO and risk factors, consideration of placement of CVC for evacuation of air from right atrium should be anticipated to prevent the complications from air

embolism. Also, in patients who undergo repeat ERCP after PTC and if a fresh blood clot is noticed at the ampulla site which could be a sign of bilio-venous fistula, sphincterotomy should potentially be deferred to avoid air embolism and PTC drain should be left in place until the stent is placed [93]. Gastroscopes with distinct controls to infuse CO_2 and saline with limits on rates of infusion can minimize the risk of air embolism.

The differential diagnosis of acute coronary syndrome (ACS), acute stroke, PE and cardiogenic shock should also be considered. ACS can be non-ST elevation myocardial infarction (NSTEMI) or ST elevation myocardial infarction (STEMI). ECG shows ST elevation in STEMI and emergency catheterization is warranted. However, in NSTEMI ECG shows non-specific ST and T wave changes or ST depression with elevated troponin. Treatment of NSTEMI includes antiplatelet agents like aspirin, clopidogrel, statin and anticoagulation with heparin or low molecular weight heparin if there are no contraindications. Cardiogenic shock can be from any acute cause of severe left ventricular or right ventricular dysfunction. Common causes include acute myocardial infarction like STEMI or NSTEMI or PE. Diagnosis is confirmed when there is hypotension (systolic blood pressure <90 mmHg), cardiac index (<1.8 L/min per m^2), hypoperfusion and elevated pulmonary capillary wedge pressure (>15 mmHg) [102]. Coronary angiography is recommended in patients with acute myocardial infarction for reperfusion. Echocardiogram shows severely depressed right ventricle or left ventricle or both. Acute stroke can present with signs and symptoms of acute change in mental status during or after the procedure, failure to regain consciousness after the procedure, focal neurological deficits like hemiparesis, paraplegia and quadriparesis. MRI is diagnostic, and it shows acute infarcts if there is stroke.

Concluding remarks

Although air embolism is rare, diagnosis is critical in the management to prevent severe morbidity and mortality. High risk factors should alert the endoscopist to anticipate air embolism so that it can be treated early. At the discretion of endoscopist and anesthesiologist, intubation with continuous end tidal capnography should be considered especially in patients with high risk factors undergoing ERCP, as fall in $etCO_2$ levels can often be the first clue in the diagnosis of air embolism. CO_2 insufflation seems to be a better option than air to prevent air embolism, however more prospective studies are needed to show the benefit. Precordial Doppler ultrasound can often diagnose air embolism, although TEE is more sensitive. Supportive treatment and prompt use of HBOT in cerebral air embolism can improve the outcome. PE should always be considered in the differential diagnosis especially with hemodynamic instability. Multidisciplinary team involving endoscopist, anesthesiologist, radiologist, intensivist, surgeon, cardiologist and the ancillary staff is key in the management of air embolism.

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