

Air embolism secondary to endoscopy in hospitalized patients: results from the National Inpatient Sample (1998-2013)

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Abstract

Background Air embolism is a rare, but potentially catastrophic complication of endoscopic procedures. We herein evaluated the overall incidence of air embolism after endoscopy. We also measured mortality outcomes after air embolism.

Methods Patients who underwent endoscopy as an index procedure during hospitalization were selected from the National Inpatient Sample from 1998-2013. The primary outcome of interest was the incidence of air embolism after endoscopy. All-cause mortality after endoscopy was measured as a secondary outcome and the Charlson Comorbidity Index was calculated. Binary logistic regression was used to explore the effect of air embolism on inpatient mortality, using $P < 0.05$ as level of significance.

Results A total of 2,245,291 patients met the inclusion criteria. Mean age at the time of procedure was 62.5 years. Esophagogastroduodenoscopy (EGD) was the most common endoscopic procedure, accounting for 80% of endoscopic procedures. Air embolism occurred in 13 cases, giving a rate of 0.57 per 100,000 endoscopic procedures. Air embolism was most common after endoscopic retrograde cholangiopancreatography (ERCP), occurring in 3.32 per 100,000 procedures, compared with 0.44 and 0.38 per 100,000 procedures for EGD and colonoscopy, respectively. The case fatality rate for post endoscopic air embolism was 15.4%. After adjusting for covariates, air embolism after endoscopy was independently associated with higher odds of inpatient mortality: odds ratio 10.35, 95% confidence interval 1.21-88.03 ($P < 0.03$).

Conclusions Air embolism is most common after ERCP. It is frequently associated with disorders involving a breach to the gastrointestinal mucosa or vasculature. Though rare, it is an independent predictor of inpatient mortality.

Keywords Air embolism, endoscopy, mortality

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Introduction

Air embolism occurs during endoscopic procedures when air is inadvertently introduced into the vasculature. Air embolism rarely complicates endoscopy; however, it entails

a high risk of leading to severe or even fatal outcomes if not diagnosed and treated promptly, and death can occur even with aggressive interventions to treat this problem [1,2]. Though most commonly associated with endoscopic retrograde cholangiopancreatography (ERCP), air embolism can complicate any endoscopic procedure [3-5].

Plausible mechanisms for air embolism following endoscopic procedures include, but are not limited to the following: insufflated air under pressure entering into an exposed vessel through a compromised mucosal barrier; mechanical manipulation of the bile ducts; the presence of biliary venous shunts; direct passage of air into the portal venous system during biliary manipulation; and inability of the pulmonary circulation to remove air emboli [6]. The risk of post-endoscopic air embolism appears to be increased by the following factors: a) biliary interventions; b) portosystemic shunts; c) hepatobiliary tumors; d) blunt/penetrating trauma to the liver; e) high pressure insufflation; and f) inflammatory lesions, including hepatic abscess, inflammatory bowel disease, and mesenteric ischemia [7-10].

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The true incidence of air embolism is difficult to ascertain. Most studies of air embolism in the literature are case reports and there is a paucity of data on the incidence of post-endoscopic air embolism, especially in hospitalized patients. The aim of this study was to describe the incidence and outcomes of air embolism after inpatient endoscopic procedures in the United States during the 16-year period from 1998-2013, using a large national database: the National Inpatient Sample (NIS).

Patients and methods

Data source

Study data were obtained from the NIS database, the largest publicly available all-payer inpatient healthcare database in the United States. It has a weighted national estimate in excess of 35 million admissions annually. Its large sample size is ideal for developing national and regional estimates, and enables analyses of rare conditions, uncommon treatments, and special populations [11]. It has been used and validated in several studies to report reliable estimates of the burden and outcomes of gastrointestinal diseases [12-15].

Study sample

We queried the database for all endoscopic procedures using the International Classification of Diseases, 9th revision, Clinical Modification (ICD-9-CM) coding system. ICD-9-CM codes used to extract relevant data are listed in Supplementary Table 1.

Diagnosis of post-endoscopic air embolism

There is no ICD-CM-9 code that specifically applies to air embolism secondary to endoscopy. Therefore, we adopted a retrospective cohort design to identify cases. This methodology has been utilized/validated by other studies referencing the NIS to study the incidence of procedure-related gastrointestinal disorders [12,16]. After ICD-CM-9 codes 999.1 (air embolism to any site following infusion, perfusion, or transfusion) and 958.0 (traumatic air embolism) had been used to identify preliminary cases, the selection was refined by including only cases that had an endoscopy as an index procedure during hospitalization. For the purposes of this study, post-endoscopic air embolism was defined as an ICD-CM-9 code for a diagnosis of air embolism that occurred in cases with an endoscopy as the index procedure during hospitalization.

Other study variables

For each record, an estimate of premorbid condition was calculated using the Charlson Comorbidity Index [17]. This is a

Table 1 Population baseline characteristics and type of endoscopy

Characteristics	(n)	(%)
Gender		
Male	979775	43.6
Female	1264471	56.3
Race		
White	1279653	57.0
African American	398212	17.7
Hispanic	283154	12.6
Asia-Pacific	207911	9.2
Others	76361	3.4
Age (M (SD) years)	62.5 (19.4)	
Endoscopy		
EGD	1804899	80.4
Colonoscopy	263114	11.7
Sigmoidoscopy	56736	2.5
ERCP	120542	5.4
Admission type		
Non-elective	2040970	90.9
Elective	204321	9.1
Hospital location		
Urban	1998309	88.9
Rural	246983	11.1
Hospital region		
North East	435586	19.4
Midwest	520908	23.2
Southern	902607	40.2
West	386190	17.2

SD, standard deviation; ERCP, endoscopic retrograde cholangiopancreatography; EGD, esophagogastroduodenoscopy

scoring system for predicting mortality by weighting comorbid conditions; it has been used in several studies to measure the burden of disease [18-20].

Study outcomes

Our primary outcome of interest was the incidence of air embolism after endoscopy. All-cause inpatient mortality after endoscopy was measured as a secondary outcome.

Statistical analysis

Categorical and continuous variables were expressed using frequencies, proportions, measures of central tendency as well as standard deviation. We used the chi-square test to assess differences between categorical variables. Effect sizes

were quantified using odds ratios (OR) with 95% confidence intervals (CI). Binary logistic regression was used to explore the effect of air embolism on inpatient mortality after controlling for covariates. Missing cases were excluded from analysis. The level of significance for all tests was $P < 0.05$. All analyses were performed using SPSS software (IBM Corp. Released 2017. IBM Statistics for Macintosh, Version 25.0. Armonk, NY).

Results

Patient demographics and hospital characteristics

We identified 2,245,291 endoscopies that were performed as index procedures on hospitalized patients in the United States between 1998 and 2013. A total of 1,264,471 patients (56%) were female and 1,279,653 (57%) were Caucasians. Mean age at the time of procedure was 62.5 years. Nearly all hospitalizations were non-elective admissions (91%). Similarly, most hospitalizations/endoscopic procedures (89%) occurred in urban hospitals. Most patients were treated in the South (35%) and Midwest (20%) regions (Table 1).

Endoscopic procedures

EGD was the most common endoscopic procedure, accounting for 80% of endoscopic procedures. Colonoscopy, ERCP and sigmoidoscopy accounted for 12%, 5.5%, and 2.5% of procedures, respectively. A higher proportion of lower gastrointestinal procedures—i.e., sigmoidoscopy (67.5%) and colonoscopy (69.7%)—occurred in patients older than 60 years of age compared to ERCP and EGD.

Post-endoscopic air embolism

Post-endoscopic air embolism occurred in 13 cases, producing a rate of 0.57 per 100,000 endoscopic procedures. Per procedure, air embolism was most common after ERCP, occurring in 3.32 per 100,000 procedures, compared with 0.44 and 0.38 per 100,000 procedures for EGD and colonoscopy, respectively ($P < 0.05$). We recorded no cases of air embolism after sigmoidoscopy. The mean age of patients with air embolism was 49.5 ± 20.5 years. The primary diagnoses in cases that developed post-endoscopic air embolism are presented in Table 2. On bivariate analysis, ERCP was the only endoscopic procedure significantly associated with post-endoscopic air embolism (OR 7.45, 95%CI 2.25-24.86; $P < 0.001$) (Table 3).

Inpatient mortality

Inpatient mortality after endoscopy was 1.4%. Patient and hospital characteristics were significantly associated with inpatient mortality included age, sex, race, comorbid status and payer type (Table 4).

For patients who had an air embolism after endoscopy, the case fatality rate was 15.4%. On bivariate analysis, post-endoscopic air embolism was significantly associated with greater odds of inpatient mortality (OR 12.85, 95%CI 2.85-58.01; $P = 0.01$). After adjusting for covariates, the occurrence of air embolism after endoscopy was an independent predictor of inpatient mortality (OR 10.35, 95%CI 1.21-88.03; $P < 0.03$) (Table 4).

Discussion

Air embolism is usually an iatrogenic phenomenon. In some cases, it runs a subclinical course and is probably

Table 2 Diagnosis and demographics for air embolism cases

	Diagnosis	Sex	Age	Procedure type	Admission to procedure (days)	Outcome
1	Internal hemorrhoids with complicated NEC	M	73	Colonoscopy	5	Alive
2	Dyskinesia of esophagus	M	38	EGD	0	Alive
3	Crohn's disease	F	31	EGD	7	Alive
4	Obstruction of biliary duct	F	59	ERCP	0	Alive
5	Obstruction of biliary duct	M	28	ERCP	13	Alive
6	Poisoning by other medications/drugs	M	60	EGD	0	Alive
7	Chronic gastric ulcer with hemorrhage	M	83	EGD	6	Alive
8	Choledocholithiasis with obstruction	F	42	ERCP	1	Deceased
9	Hepatic laceration	F	32	ERCP	5	Deceased
10	Complications of lung transplant	F	33	EGD	*	Alive
11	Foreign body in stomach	F	87	EGD	4	Alive
12	Gastritis	M	39	EGD	1	Alive
13	Unspecified chest pain	F	39	EGD	0	Alive

NEC, necrotizing enterocolitis; EGD, esophagogastroduodenoscopy; ERCP, endoscopic retrograde cholangiopancreatography

underdiagnosed [4,21]. However, severe cases often manifest with cardiopulmonary and cerebrovascular symptoms and are associated with high morbidity and mortality outcomes. While neurologic sequelae appear to be more common, cases with cardiopulmonary symptoms are at a greater risk of death [22].

Table 3 Odds of air embolism by endoscopy type

Endoscopy type	Odds ratio	95%CI		P-value
EGD	0.39	0.13	1.19	0.15
Colonoscopy	0.86	0.11	6.86	0.88
ERCP	7.46	2.25	24.86	0.001
Sigmoidoscopy*				

*No recorded cases of air embolism

CI, confidence interval; ERCP, endoscopic retrograde cholangiopancreatography

Studies show mortality rates due to air embolism range from 12-30%, comparable to our finding of 15.4%. More than half of these patients die within the first 48 h [22,23].

In comparison to surgical or endovascular interventions, air embolism rarely complicates endoscopy. McCarthy *et al* observed that endoscopy accounted for only 2 of 67 cases of air embolism over a 25-year period of hospital records [22]. Likewise in this study, we observed that air embolism complicated approximately 1 in 175,000 endoscopic procedures. The risk for air embolism was, however, higher in ERCP procedures, being 7.5- and 8.8-fold greater compared to EGD and colonoscopy, respectively. Furthermore, ERCP was the only endoscopic procedure significantly associated with developing an air embolism (OR 7.45, 95%CI 2.25-24.86; P<0.001). This finding is well described in the literature, and may be explained by air entering the arterial or venous system of the liver during ERCP maneuvers [4].

Table 4 Logistic regression estimating the effect of air embolism on inpatient mortality

Variable	Odds Ratios	95%CI		P-value
Sex				
Female	1			
Male	1.43	1.39	1.47	0.001
Race				
White	1			
Non-White	1.06	1.03	1.09	0.001
Charlson score				
0	1			
1	1.13	1.08	1.17	0.001
2+	2.14	2.07	2.20	0.001
Age (continuous)				
Admission type				
Elective	1			
Emergent	0.97	0.92	1.02	0.29
Hospital location				
Urban	1			
Rural	1.03	0.99	1.08	0.94
Hospital region				
North-East	1			
North-East	0.77	0.74	0.81	0.001
South	0.89	0.86	0.92	0.001
West	0.96	0.92	1.01	0.12
Insurance type				
Private	1			
Non-private	1.16	1.11	1.21	0.001
Air embolism				
No	1			
Yes	10.35	1.21	88.03	0.03

CI, confidence interval

Compared to diagnostic ERCP, therapeutic ERCPs involve more invasive and aggressive instrumentation of the biliary system and entail a higher risk for air embolism [24]. It is believed that a combination of high pressure from air insufflation and mechanical trauma to the bile ducts by instruments during therapeutic ERCP could potentiate entry of air into the circulation through the biliary tree.

Albert *et al* observed that the use of small-diameter endoscopes and air insufflation for direct intraductal biliary endoscopy promotes the development of air embolism [25]. The authors strongly recommended that only CO₂ be used for insufflation during intraductal biliary endoscopy.

Though air embolism even with CO₂ has been documented, CO₂ has been shown to have an overall better safety profile as compared to room air [4,8,26]. CO₂ was also recommended in a recent report by the American Society for Gastrointestinal Endoscopy's technology committee [27].

Air embolism can occur even with an intact mucosal barrier [28]. However, a pre-existing breach in the gastrointestinal mucosa is a commonly implicated factor in developing air embolism after endoscopy. The first reported case of endoscopy-related cerebral air embolism occurred during an EGD and involved a patient with a duodenal ulcer and duodenocaval fistula [29]. Other reported cases of air embolism after endoscopy include perforated gastric ulcer, esophageal biopsy, Crohn's disease with fistulas and erosive esophagitis [8,30-32]. Similarly, in our study we demonstrate that most cases of air embolism after endoscopy occurred in relation to gastrointestinal disorders involving a breach to the gastrointestinal mucosa or vasculature (Table 2). Therefore, it is imperative for endoscopists to maintain a high index of suspicion for air embolism when performing endoscopy involving these gastrointestinal disorders.

In this study, we report an all-cause inpatient mortality rate of 1.4%. In addition, we observed that the risk of inpatient mortality was much higher in patients with more comorbidities. The case fatality rate after air embolism was 15.4%. After controlling for comorbidities amongst other relevant factors, we observed that air embolism after endoscopy independently increased the risk of inpatient mortality. This finding underscores the need for increased awareness of air embolism during endoscopy and the prompt implementation of appropriate therapeutic measures when air embolism is diagnosed.

Air embolism can be considered in the differential diagnosis when patients experience unexpected, sudden and significant hemodynamic instability during endoscopy. Prompt supportive treatment, including resuscitation and high-flow oxygen (if not already being delivered) and cardiopulmonary support as needed, should be implemented, even before air embolism is confirmed if the level of suspicion is high. Fluid resuscitation increases central venous pressure and may prevent further entry of air into the venous system. Hyperbaric oxygen therapy may improve outcomes in patients with cerebral air embolism [33].

Our study has several limitations, most of which are inherent to the administrative nature of the NIS database. While the NIS is an established database used in many published analyses, it is subject to data misclassification, incomplete documentation,

and other coding difficulties. Furthermore, the NIS applies only to an inpatient population and our findings cannot be generalized to the overall population. The NIS lacks data on the severity of gastrointestinal disease and we could therefore not include this in our analysis. However, despite these limitations, most of our study findings are consistent with the previous literature.

In conclusion, air embolism after endoscopy is rare. However, it has a high potential for adverse outcomes and its occurrence independently predicts patient mortality. Endoscopists should maintain increased awareness for air embolism, especially in patients undergoing high-risk procedures like therapeutic ERCP. Larger studies are needed to quantify the risk of post-endoscopic air embolism, especially in disorders that involve a breach in the gastrointestinal mucosa.

Summary Box

What is already known:

- Air embolism is most commonly associated with endoscopic retrograde cholangiopancreatography (ERCP) procedures
- Patients who have air embolism are at very high risk of death
- Disorders with a breach to the gastrointestinal mucosa predispose to post-endoscopic air embolism

What the new findings are:

- Post-endoscopic air embolism occurs in approximately 0.57 per 100,000 endoscopic procedures
- ERCP is the only endoscopic procedure significantly associated with developing post-endoscopic air embolism
- Air embolism is an independent predictor of mortality, irrespective of comorbid status

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Supplementary Table

Supplementary Table 1 Procedures and ICD-9-CM codes used for data selection

Procedure	Code
Flexible fiber optic colonoscopy	45.23
Flexible sigmoidoscopy	45.24
Esophagogastroduodenoscopy (EGD)	45.13
Closed [endoscopic] biopsy of small intestine (brushing or washing for specimen collection)	45.14
EGD with closed biopsy	45.16
Endoscopic retrograde cholangiography	51.11
Endoscopic retrograde cholangiopancreatography	51.10
Endoscopic retrograde pancreatography	52.13
Endoscopic biopsy of biliary duct or sphincter of Oddi	51.14
Pressure measurement of sphincter of Oddi	51.15
Endoscopic biopsy of pancreatic duct	52.14
Cannulation of pancreatic duct	52.92
Endoscopic dilation of ampulla and biliary duct	51.84
Endoscopic insertion of nasobiliary drainage tube	51.86
Endoscopic removal of stone from biliary tract	51.88
Endoscopic insertion of nasopancreatic drainage tube	52.97
Endoscopic insertion of stent into pancreatic duct	52.93
Endoscopic sphincterotomy and papillotomy	51.85
Endoscopic excision or destruction of lesion of biliary ducts or sphincter of Oddi	51.64
Endoscopic excision or destruction of lesion or tissue of pancreatic duct	52.21
Excision of other bile duct	51.69
Endoscopic insertion of stent into bile duct	51.87
Endoscopic removal of stone from pancreatic duct	52.94
Endoscopic dilation of pancreatic duct	52.98