



# Intraoperative venous air embolism in the non-cardiac surgery—the role of perioperative echocardiography in a case series report

Jingjing Ji<sup>1,2</sup>, Yali Tian<sup>1,2</sup>, Luning Chen<sup>1,2</sup>, Bingbing Li<sup>1</sup>

<sup>1</sup>Department of Anesthesia, Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School, Nanjing 210008, China;

<sup>2</sup>Graduate School of Nanjing University Medical School, Nanjing 210008, China

*Correspondence to:* Bingbing Li. Department of Anesthesia, Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School, Nanjing 210008, China. Email: icccolor@163.com.

**Abstract:** Venous air embolism (VAE) is commonly one of the iatrogenic complications associated with divergent high-risk surgeries. In this case-series report, we presented a series of VAE cases in our institute during the last 6 consecutive years. There were total of nine cases suspected to be VAE according the clinical symptom and signs, of which seven cases were definitively diagnosed VAE using transthoracic echocardiography (TTE). We also reported two presumptive cases of paradoxical VAE during hepatectomy in this case series, furthermore, the cause, complications and hazards secondary to paradoxical VAE were discussed as well. All cases had an uneventful recovery from VAE with the assistance of TTE as well as other therapeutic management of VAE, except one neurosurgical patient died from postoperative hemorrhagic stroke per se. Therefore, VAE or paradoxical air embolism can occur during various non-cardiac operations and the significance of perioperative ultrasound should be emphasized in the treatment of VAE.

**Keywords:** Venous air embolism (VAE); ultrasound; non-cardiac surgery; anesthetic management; case series

Submitted Jan 09, 2020. Accepted for publication Apr 29, 2020.

doi: 10.21037/atm-20-497

**View this article at:** <http://dx.doi.org/10.21037/atm-20-497>

## Introduction

Venous air embolism (VAE) is commonly iatrogenic due to infusion of bubbles adhering to the intravenous (IV) infusion set, residual air in drug-filled syringes, or ambient air intruding into the venous system in diverse surgical procedures (1). In previous reports, this incidence of VAE in neurosurgery conducted in the sitting position varies with a wide range from 4.9% to 76% (2,3). The prevalence of this adverse event during the laparoscopic surgery is less than 0.6%, while as high as 10–50% in hysteroscopic endometrial ablation procedure (4,5). The severity of VAE and its hazards to patients depend not only on the solubility of certain gas in blood, the rate and amount of gas entering the vein, but also the ability to eliminate the air via the lungs (6). Massive air or gas (3–5 mL/kg) entrained in the main pulmonary artery trunk, owing to the air-lock effect, results in acute right ventricle outflow tract

(RVOT) obstruction and severe hypoxia, which is a leading cause contributory to cardiac arrest in operation room (1). In some scenarios, VAE was refractory to the routine ACLS (advanced cardiovascular life support intervention), requiring extracorporeal circulation support to achieve the return of spontaneous circulation (7).

Herein, we reported this case serials of VAE in recent 6 years in our department. Albeit VAE has the features of sudden onset, rapid development, and intractable management, the mortality or morbidity remains relatively low if standardized management are strictly implemented in the operation theatre including scrutinizing the patients prior to high-risk surgery, vigilance to the early signs of VAE, timely ceasing the surgical manipulation, as well as meticulous titration of vasoactive agents under the guidance of echocardiography. We present the following case series in accordance with the GARE reporting checklist.

**Table 1** Demographics and surgical management of patients

Patients	Demographics			Surgical management	
	Sex, age (y)	ASA status	Comorbidities	Operation	Position
1	F, 42	III	History of laparoscopic examination and abdominal nodule biopsy, PFO	Radical resection of gallbladder cancer	Supine
2	M, 62	III	History of LC, mild anemia	Radical resection of gallbladder cancer	Supine
3	M, 65	III	Hypertension	Transurethral resection of the prostate	Lithotomy
4	M, 78	III	Hypertension, previous history of prostatic puncture and biopsy	Robot assisted laparoscopic radical prostatectomy	Trendelenburg position
5	F, 36	II	History of induced abortion, mild anemia	Hysteroscopic resection of uterine myoma	Lithotomy
6	M, 69	III	Atrial fibrillation, mild anemia	Resection of intracranial aneurysm	Supine
7	M, 72	III	Hypertension, sinus tachycardia	Laparoscopic right hemihepatectomy + LC	Reverse Trendelenburg position
8	M, 55	III	Myocardial bridge in the middle and distal part of left anterior descending branch	Laparoscopic right hemihepatectomy + LC	Reverse Trendelenburg position
9	F, 12	II	–	Posterior spinal fusion with allogeneic bone graft	Prone

PFO, patent foramen ovale; LC, laparoscopic cholecystectomy.

## Case presentation

The demographic characteristics and surgical data of all patients are listed in *Table 1*. Once the patients arriving at the operating room, the IV access was established. The routine monitors including electrocardiogram (ECG), heart rate (HR), blood pressure (BP), pulse oximeter (SpO<sub>2</sub>), end-tidal carbon dioxide pressure (P<sub>ET</sub>CO<sub>2</sub>) were applied before general anesthesia induction. The invasive BP (IBP) monitor was established via left radial arterial catheterization, which is also facilitated in blood gas sample collection. Except femoral vein catheterization in case 6, the deep venous catheters were placed in the right internal jugular vein for monitoring central venous pressure (CVP) monitoring in other eight patients. Anesthesia was induced with dose of midazolam (0.05 mg/kg), 1% propofol (1–2 mg/kg), sufentanil (0.25–0.5 µg/kg) and vecuronium (0.1 mg/kg). Endotracheal tube was intubated and secured at the incisors 21–23 cm from tip of the tube. The ventilator was set to volume-controlled ventilation mode (tidal volume at 8–12 mL/kg, respiratory rate at 12 times/min, inspiration and expiration ratio at 1:2) after confirming that the endotracheal tube was in place. The P<sub>ET</sub>CO<sub>2</sub> was maintained between 35 and 45 mmHg via adjusting the tidal

volume. Anesthesia was maintained with 2% propofol (50–100 µg/kg/min), remifentanyl (0.1 µg/kg/min), cisatracurium (2 µg/kg/min), and dexmedetomidine (0.1–0.2 µg/kg/h). *Table 2* summarized the additional information about intraoperative conditions.

In the case 1 undergoing an open surgery of resection of gallbladder cancer, we noticed the patient promptly developed tachycardia over 120 bpm with decrease of end-tidal CO<sub>2</sub> when the surgeons were manipulating the bleeding of hepatic vein minor approximate to retrohepatic inferior vena cava (RIVC). We promptly performed the transesophageal echocardiography (TEE) scanning within 2 minutes after onset of end-tidal CO<sub>2</sub> drop. TEE explicitly showed air bubbles in left side of heart chambers (*Videos 1,2*). Unexpectedly, we couldn't detect any air in the right-side heart in this patient with paradoxical air embolism all time. The patient did have the patent foramen ovale (PFO) identified by intraoperative TEE and postoperative agitated saline test with transthoracic echocardiography (TTE), and there existed the prerequisite of intracardiac defects contributory to paradoxical air embolism. However, the source of venous air of this was still undetermined yet. The bleed from hepatic vein was

**Table 2** Intra- and postoperative situation

Patients	Intraoperative situation		Postoperative outcomes		
	Initial clinical observations	Other manifestations	Abnormal results of postoperative auxiliary examination	In-hospital complications	Postoperative length of stay (d)
1	HR ↑ , P <sub>ET</sub> CO <sub>2</sub> ↓	Bubbles in the left cardiac cavities (Videos 1,2)	Abnormal myocardial enzyme	Severe abdominal infection	21
2	P <sub>ET</sub> CO <sub>2</sub> ↓ , IBP	Bubbles in the right cardiac cavity	Abnormal myocardial enzyme	–	14
3	P <sub>ET</sub> CO <sub>2</sub> ↓ , SpO <sub>2</sub> ↓	Bubbles in the right cardiac cavity, the right ventricle size was dilated with reduced contractility, moderate tricuspid regurgitation	–	Pulmonary edema	6
4	BP ↓ , SpO <sub>2</sub> ↓	Bubbles in the right cardiac cavity	BNP ↑	Systemic infection symptoms, pulmonary edema	14
5	P <sub>ET</sub> CO <sub>2</sub> ↓ , IBP ↓	Jugular venous distension, subcutaneous emphysema	–	–	2
6	P <sub>ET</sub> CO <sub>2</sub> ↓ , IBP ↓	Numerous bubbles in the right cardiac cavity	–	Died after suffering a hemorrhagic shock	–
7	P <sub>ET</sub> CO <sub>2</sub> ↓ , SpO <sub>2</sub> ↓	Bubbles in the right cardiac cavity	Abnormal myocardial enzyme	–	12
8	HR ↑ , P <sub>ET</sub> CO <sub>2</sub> ↑ , SpO <sub>2</sub> ↓	Millwheel murmur, subcutaneous emphysema, bubbles in both ventricular cavities (Video 3)	–	Pulmonary edema	22
9	HR ↑ , IBP ↓	Subcutaneous emphysema	–	–	16

↑, increase; ↓, decrease. HR, heart rate; P<sub>ET</sub>CO<sub>2</sub>, end-tidal carbon dioxide pressure; IBP, invasive blood pressure; SpO<sub>2</sub>, pulse oximeter; BNP, brain natriuretic peptide.

tackled with anastomosis without any difficulty and the surgical field was soaked with saline gauzes. Meanwhile, the patient was placed on the Trendelenburg position. The air lodged in systemic circulation lasted approximately 30 mins with no obvious hemodynamic parameters fluctuation and deterioration in oxygenation. TEE examination showed that there is no evident regional wall motion abnormality of left ventricle (LV) or global LV decompensation secondary to coronary artery air embolism. Therefore, the surgery was resumed and accomplished uneventfully. The patient, fortunately, had a smooth recovery with no sign of ischemia stroke complicated with systemic air embolism. In the case 8 undergoing laparoscopic hepatectomy, when the surgeons were manipulating the right hepatic vein approximating second hepatic hilar (portal visceral), the patient was manifested by tachycardia with gradual decrease in SpO<sub>2</sub> to

96% on 100% oxygen ventilation. The surgical intervention was suspended and pneumoperitoneum was discontinued instantly after the confirmation of the mill-wheel murmur on the left chest. Bed-side ultrasound showed numerous bubbles in both ventricular cavities on Apical Four-Chambers View (Video 3). The preoperative cardiac ultrasonography did not show any significant intracardiac right-to-left shunt and there is no evidence of pulmonary arteriovenous fistula from chest computer-tomography (CT) in this case. The vital signs of the patient returned to normal following the rapid infusion of Lactated Ringer's solution concomitant with norepinephrine infusion at 0.05 µg/kg/min. The patient recovered uneventfully without any sign of neurologic deficit from general anesthesia.

The patient 4 undergoing robot-assisted prostate resection, developed severe hypotension and hypoxia

when position of the patient returned to supine from deep Trendelenburg position at the end of surgery. The hypotension was refractory to the conventional fluid infusion and vasoconstrictor treatment for 30 min. The point of care ultrasound was used to assess the cause of the circulatory decompensation. The size of right ventricle moderately dilated with slight shift of intraventricular septum towards the LV. The quantitative analysis of the right ventricle systolic pressure via the peak flow velocity of tricuspid valve regurgitation and tricuspid annular plane systolic excursion (TAPSE) with M modality indicated that the right ventricle contractility was moderately depressed due to elevated pulmonary arterial pressure. The TTE also showed that the well-filled LV squeezed quite well without regional wall motion abnormality. Therefore, the infusion of norepinephrine started at 0.1 µg/kg/min and the BP gradually improved. The patient was subject to moderate pulmonary infiltration in bilateral lower lobes on post-operation of day (POD) 2–3. The patient 8 also had pulmonary edema leading to moderate hypoxia after surgery. The pathogenesis of gas embolism-induced pulmonary edema is complex. Air bubbles-induced turbulent flow activates platelet which leads to the release of inflammatory cytokine or chemokine, recruitment of neutrophils resulting in a series of inflammatory reactions to pulmonary arteriole endothelium (8). The interstitial pulmonary edema was completely dissipated under the PEEP treatment. The recovery of these two patients were uneventful thereafter.

Other postoperative informations were described in *Table 2*.

## Discussion

VAE is a rare but potentially catastrophic complication in non-cardiac surgery. In this 6-year case series, there are 7 cases eventually diagnosed with VAE with echocardiography, two “presumptive” cases incapable to be proved with echocardiography due to poor image quality. It has been proved that the incidence of VAE varies according to the type of medical interventions or surgical operation. Consistent with the previous reports (3,9,10), the hepatic surgery (2/9), neurosurgery (1/9), as well as laparoscopic surgery (5/9) remains the high-risk procedure contributing to VAE in this study. The prognostic outcome of these patients was encouraging, and all patients were discharged uneventfully from hospital without any neurologic sequelae except one neurosurgical case who

died of postoperative hemorrhagic stroke complicated from cerebral vascular anastomosis per se.

## Diagnosis of VAE

The tachycardia with ST-T segment changes is commonly prominent manifestation in patients with mild to moderate volume of air embolism. However, this sign lacks of high specificity during general anesthesia. Generally, the case with abrupt drop in  $P_{ET}CO_2$  and pulse saturation concomitant with the exaggerated difference between  $PaCO_2$  and  $P_{ET}CO_2$  over 10 mmHg (normal range of 4–5 mmHg) are highly presumptive of VAE. In line with the previous reports (11–13), the early signs of VAE cases in this series were tachycardia and eminent drop in  $P_{ET}CO_2$ . In the laparoscopic procedure, although the value of  $P_{ET}CO_2$  is not decreased to such an extent as lower as in other procedures due to carbonate dioxide pneumoperitoneum, the gradient between  $PaCO_2$  and  $P_{ET}CO_2$  remains widened (>10 mmHg). With the extensive use of ultrasound technique in the operation theatres recently, it offers a rapid, precise, and real-time approach in detecting VAE (14). TEE has the advantage over transthoracic echo because it provides a high-quality image to delineate the pathophysiological changes of the patient (15). TEE, therefore, has been a promising tool to aid in diagnosis of perioperative VAE, especially in evaluation of the coexisting intracardiac defect, the cause of circulatory collapse as well as improving the prognostic outcome of patients with VAE. The transthoracic echo, as an alternative monitoring modality, is relatively noninvasive, less time-consuming and atraumatic to patient with broader indications compared with TEE. In this study, 6 out of 9 cases were diagnosed with TTE, only one with TEE. We can obtain the images without difficulty from Apical Four-Chamber View to make the diagnosis of VAE with superficial ultrasound except that two patients (2/9) complicated with subcutaneous emphysema.

## Paradoxical VAE

According to the criteria of Johnson (16), paradoxical VAE must be considered “proved” when the embolus was found lodged in the abnormal communication between the systemic arterial and venous system, while the presumptive case is considered: (I) embolus in systemic venous circulation, (II) abnormal communication between left and right circulation, (III) arterial system embolization

with no evidence of the source of embolus in the left side of heart. In this 6-year case series, there were two cases presumptive to be paradoxical VAE, accounting for 22% (2/9) of all cases with VAE. These two cases, albeit the bubbles were explicitly detected in the left heart chambers, are not conformed to the criteria of the “proved” case for we didn’t see any air traveling through the intracardiac or any transpulmonary communications. Although the case 1 complicated with tiny PFO, the only chambers we can detect the air are the left atrium and LV in an open surgery. We still couldn’t explain the source of these air in the systemic circulation without any evidence of air in the right heart. According to Aboyans’s study (17), only 16 out of 40 cases were identified to have venous and arterial system embolus simultaneously in pulmonary embolism cases, whereas 7% of cases having arterial system embolism solitarily. In case 8, although we can detect the air bubbles in left and right ventricles simultaneously, we still couldn’t uncover the communication between left and right heart. A meta-analysis conducted in 2014 (18) indicated that TEE had a sensitivity of 89.2% and a specificity of 91.4% in detection of PFO. It is difficult to differentiate PFO from pulmonary arteriovenous malformation (PAVM) and the accepted echocardiographic criteria relies on a delay of 3 to 8 cardiac cycles or 2 to 5 s of agitated saline bubbles to appear in the left atrium. Nonetheless, whether the time of bubble appearance can be used as a basis for distinguishing the location of the shunt point is still controversial (19,20). Despite no detectable intracardiac defect existing in some circumstances, pulmonary embolism frequently resulted in the increased right heart pressures that set the stage for right-to-left shunting via a functional PFO, which might account for the occurrence of paradoxical VAE in patients with intact intra-atrial or ventricular septum in the percutaneous nephrolithotomy (PCNL) or hepatectomy surgeries (21,22). The actual passage leading to paradoxical VAE lacks supportive evidence and is still in debate in those patients.

One of the most common complications associated with paradoxical air embolism is postoperative stroke secondary to cerebral vascular embolization. The predominant clinical presentations are paralysis, altered mental status, and coma (23). Hyperbaric oxygen therapy (HBOT) leads to the reduction in the volume of bubbles, aids removal of nitrogen, and improves the oxygenation of potentially hypoxic tissue (24). The air embolization in coronary arteries, its definitive diagnosis based on fluoroscopy or Coronary Arterial angiography, is relatively

rare but life-threatening if extensive coronary circulation involved (25). The TTE or TEE, as the frontline screening tool in the operation theatre, can be used to assess the involved coronary artery manifestation of the regional wall motion abnormality via Four-Chamber and LV Short Axis View at mid-papillary muscle plane. The deterioration in hemodynamic conditions after coronary air embolism should be stabilized with inotropic support, coronary vasodilators, and an intra-aortic balloon pump. Cardiopulmonary resuscitation may be necessary in the presence of ventricular arrhythmias or severe LV dysfunction. Fortunately, the two cases in this study didn’t develop coronary arterial air embolism leading to acute LV decompensation, which was identified under direct real-time view via echocardiography.

### *Treatment of VAE*

Prevention is far superior to the treatment of VAE. The hazards of high pneumoperitoneum pressure (>14 cmH<sub>2</sub>O), severe hypovolemic status, steep reverse Trendelenburg position, should be highlighted. The routine management of perioperative VAE comprises of abrupt cessation of surgical manipulation and pneumoperitoneum, the surgical field soaked with saline solution. All patient susceptible to air embolism were placed at Trendelenburg position immediately following suspending the surgical procedure in this study. The cessation of air-oxygen mixture was implemented and high FiO<sub>2</sub> is mandatory in this scenario (26,27).

The circulatory collapse complicated with VAE is not uncommon. There are 3 cases in this series (3/9) subject to refractory hypotension, which was ultimately tackled with inotropic support by norepinephrine and dobutamine infusion under the guidance of echocardiography. In patient with sluggish circulation after air embolism, the right heart function plays a pivotal role in maintaining the stability of systemic circulation. The goal of adjustment of hemodynamic parameters is enhancing the contractility of right heart and ensuring the adequate right coronary artery blood perfusion by increasing the systemic vascular resistance. TTE provides invaluable information of LV myocardial contractility, valvular stenosis or insufficiency, the volume status, right heart function as well as the exclusion of the obstructive factors comprising of tamponade, pleural effusion, or pneumothorax. In case 3, the right ventricle size was dilated with reduced contractility and moderate tricuspid regurgitation indicating elevated pulmonary arterial pressure posterior to air lock in



RVOT. The commencement of norepinephrine infusion contributed to reversal of circulatory depression.

## Conclusions

In addition to improving the detection of VAE, echocardiography has a pivotal role in assessment of the right ventricle dysfunction in massive PE and guiding the pharmacotherapy in refractory hypotension after VAE (28). The presumptive case of paradoxical air embolism is not infrequent to encounter if routine monitor with the echocardiography is implemented in this case-series. The assessment of coronary artery occlusion and regional wall motion abnormality is of paramount importance post air embolism. Therefore, point-of-care ultrasound is not only facilitated in the diagnosis of VAE but also tailoring the treatment of VAE complicated the severe cardiovascular decompensation.

## Acknowledgments

**Funding:** This research was supported by the Nanjing Science and Technology Development Foundation, No. QRX17013; the Six Talent Summit Project of Jiangsu Province, No. WSN-147; the Nanjing Health Commission of Nanjing Municipal Government, No. YKK17084.

## Footnote

**Provenance and Peer Review:** This article was commissioned by the Guest Editors (Glenn Hernández and Guo-Wei Tu) for the series “Hemodynamic monitoring in critically ill patients” published in *Annals of Translational Medicine*. The article was sent for external peer review organized by the Guest Editors and the editorial office.

**Conflicts of Interest:** All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/atm-20-497>). The series “Hemodynamic monitoring in critically ill patients” was commissioned by the editorial office without any funding or sponsorship. The authors have no other conflicts of interest to declare.

**Ethical Statement:** The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Written informed consent was obtained

from the patient for publication of this study and any accompanying images.

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**Cite this article as:** Ji J, Tian Y, Chen L, Li B. Intraoperative venous air embolism in the non-cardiac surgery-the role of perioperative echocardiography in a case series report. *Ann Transl Med* 2020;8(12):798. doi: 10.21037/atm-20-497