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End-tidal Nitrogen Provides an Early Warning of Slow, Ongoing, Venous Air Embolism

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VENOUS air embolism (VAE) occurs in a variety of clinical situations. In a conscious patient, the presence of signs and symptoms facilitate the diagnosis,[1] but during anesthesia, recognition of VAE may be delayed, usually after cardiovascular compromise has occurred. Therefore, monitoring plays a vital role in diagnosing VAE during anesthesia.

Ideal monitoring for VAE should detect air entrainment early. Because air bubbles exit the venous circulation *via* the alveoli,[2] the sudden appearance of end-tidal nitrogen (ETN_2) during anesthesia should be a very early indicator of VAE, provided that air is not used as an anesthetic carrier gas.

We present two cases of intraoperative VAE of unknown origin. In both cases, ETN_2 concentrations increased abruptly long before any hemodynamic changes occurred, suggesting that air was entrained long before causing clinical problems.

Case Reports

Patient #1

A 61-yr-old woman was admitted for an elective repair of an infrarenal aortic aneurysm. She had a history of chronic hypertension, and, although asymptomatic, a preoperative transthoracic echocardiogram was consistent with hypertrophic cardiomyopathy.

Intravenous, radial-artery, and right internal jugular pulmonary artery catheters were placed. Anesthesia was maintained with fentanyl, isoflurane, and a mixture of oxygen and nitrous oxide. A transesophageal echocardiographic (TEE) probe was inserted after induction of anesthesia. Surgery proceeded with no unusual venous bleeding or injury. The aorta was cross-clamped distal to the renal arteries, and the subsequent 35 min were uneventful. During this period, the end-tidal carbon dioxide ($ETCO_2$) gradually decreased from 33 mmHg to 28 mmHg, although the minute ventilation was unchanged.

Abruptly, the blood pressure decreased from 140/76 mmHg to 80/55 mmHg, the oxyhemoglobin saturation (by pulse oximetry) decreased from 96% to 85%, and the $ETCO_2$ decreased from 28 mmHg to 9 mmHg (fig. 1). The pulmonary artery pressure increased from 32/22 mmHg to 53/34 mmHg, and the central venous pressure from 19 mmHg to 27 mmHg. The ETN_2 was 3.4% (26 mmHg), but, simultaneously with hypotension, decreased to 0.8% (6 mmHg) (fig. 1). Transesophageal echocardiography revealed a large air bubble lodged anteriorly in the main pulmonary artery just distal to the pulmonary valve, which showered microemboli with each cardiac contraction (fig. 2). No further air entrainment was detected with TEE.

Nitrous oxide was promptly substituted with 100% oxygen. All infusions were immediately stopped, but no air was found in the fluid administration tubing and no infusion bags were empty. Before this event, no cardiac output measurements or interventions occurred that could have led to an acute intravenous injection of air. During the next several minutes, the oxyhemoglobin saturation remained at 85-92%, and the patient's lungs were ventilated manually with 100% oxygen. Respiratory system compliance appeared grossly unaffected, and auscultation revealed bilaterally symmetric breath sounds without wheezing.

Immediately after TEE visualization of air in the pulmonary artery, 25 ml air was aspirated from the side, central venous, and pulmonary artery ports. Immediately, the patient's blood pressure increased to 145/65 mmHg, the oxyhemoglobin saturation increased to 100%, and the $ETCO_2$ increased from 11 mmHg to 24 mmHg, but the ETN_2 remained at 0.8% (6 mmHg) for the next 20 min (fig. 1). Continuous TEE documented the slow dissipation of the air bubble (which now measured 1.5 cm) from the pulmonary artery (fig. 2). During this pulmonary air microembolization, no hemodynamic problems were encountered, the $ETCO_2$ remained approximately 24 mmHg, and the ETN_2 stayed between 0.4% and 0.8% (3-6 mmHg). Soon after the air bubble was no longer visible on TEE, the $ETCO_2$ increased from 25 mmHg to 33 mmHg, and the ETN_2 decreased to 0%.

Review of the stored hemodynamic data indicated that approximately 50 min before the acute decrease in blood pressure, the ETN_2 concentration had suddenly increased to 3.4% (26 mmHg), whereas the $ETCO_2$ had decreased from 33 to 28 mmHg. This suggests that air was gradually entering the venous system for at least 50 min

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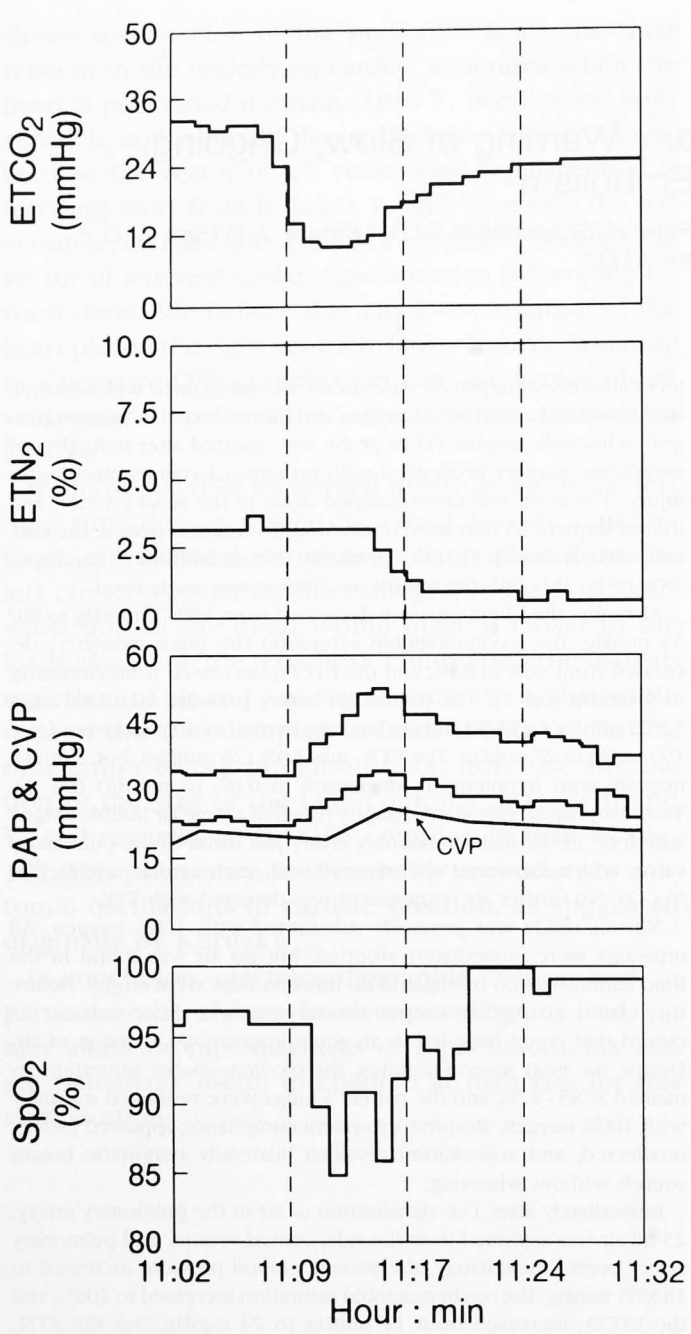

Fig. 1. Sequence of changes in end-tidal carbon dioxide ($ETCO_2$) end-tidal nitrogen (ETN_2), pulmonary artery pressures (PAP, systolic and diastolic), central venous pressure (CVP), and oxyhemoglobin saturation (SpO_2) in response to air embolus. The increase in ETN_2 occurred before acute changes in other parameters, and the maximal decrease in $ETCO_2$ preceded maximal increase in PAP and CVP.

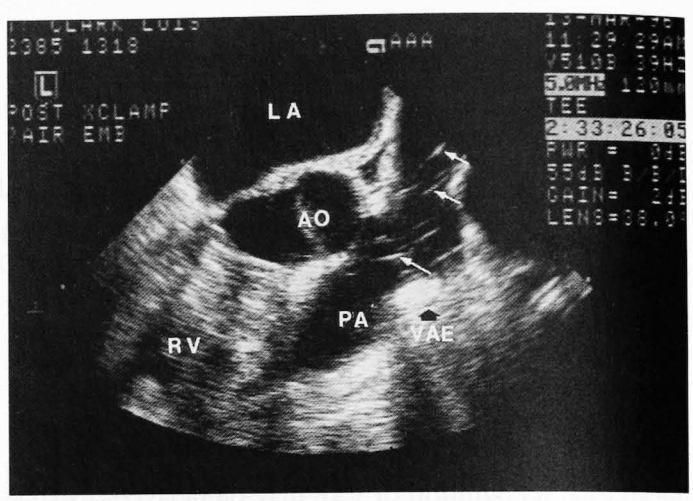

Fig. 2. Right ventricular outflow tract revealed an air bubble lodged anteriorly in the main pulmonary artery just distal to the pulmonary valve. The air bubble (VAE) was dissipating a shower of air microemboli (white arrows) distally during systole. AO = aorta; LA = left atrium; PA = pulmonary artery; RV = right ventricle.

before its discovery, culminating in an air bubble in the pulmonary artery, causing hemodynamic compromise.

The remainder of the surgery and anesthesia were uneventful. The postoperative electrocardiogram results were unchanged. Results of a postoperative chest roentgenogram were consistent with moderate pulmonary venous congestion and interstitial edema, which may be encountered after clinically significant VAE.[3,4]

Patient #2

An otherwise healthy, 31-yr-old woman was admitted for a partial thyroidectomy. Standard monitoring was applied. Anesthesia was maintained with fentanyl, isoflurane, and a mixture of oxygen and nitrous oxide. The patient was placed in the 15° reverse Trendelenburg's position for surgery. The first 45 min after induction of anesthesia were uneventful.

Suddenly, her blood pressure decreased from 115/55 mmHg to 63/35 mmHg, her oxyhemoglobin saturation decreased to 85%, and her $ETCO_2$ decreased from 25 mmHg to 14 mmHg, and ETN_2 was noted to be 5.6% (43 mmHg), but soon thereafter decreased to 0.4% (3 mmHg). The electrocardiogram demonstrated ventricular bigeminy followed by multifocal ventricular ectopy and a 20-s episode of ventricular tachycardia. Occasional sinus beats showed deep ST-segment depression. Oxygen (100%) was promptly substituted for nitrous oxide, and isoflurane was discontinued. All infusion tubes and bags were immediately inspected for the presence of air, but none was found. The patient was placed in steep Trendelenburg position, and the neck wound was covered and compressed to prevent air from entering through the incision. Arterial and central venous catheters were inserted. Hypotension and ventricular ectopy persisted for the next 15 min, despite treatment with fluid infusions, phenylephrine, and lidocaine. After blood pressure returned to normal and dysrhythmias resolved, ETN_2 still remained near 0.4% (3 mmHg), while $ETCO_2$ was 26 mmHg. Transesophageal echocardiography of the right ven-

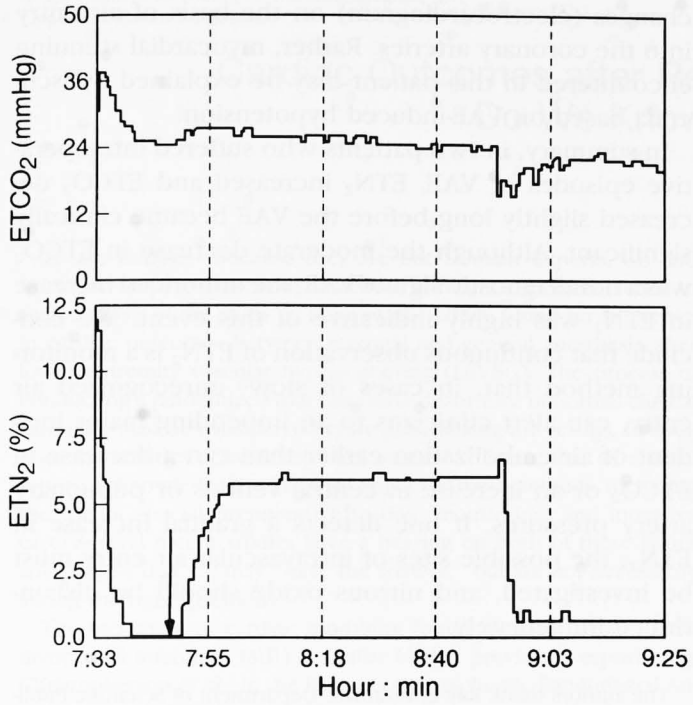

Fig. 3. Sequence of changes in end-tidal carbon dioxide ($ETCO_2$) and end-tidal nitrogen (ETN_2) before and during air embolus. It is evident that increase in ETN_2 started immediately after the skin incision (arrow) and almost 1 h before the cardiovascular collapse and decreases in $ETCO_2$ and ETN_2.

tricular outflow tract was performed shortly after the dysrhythmia had resolved and revealed no air in the right heart chambers or in the main pulmonary artery. The base and middle segments of all the walls of the left ventricle were either severely hypokinetic or akinetic, whereas the function of the apical segments was normal. An intraoperative chest roentgenogram was normal. The remainder of the anesthetic was uneventful. Postoperative electrocardiograms were normal, and the patient denied having cardiac symptoms.

Creatine phosphokinase concentration 8 h after surgery was 281 U/l, with a 9% MB isoenzyme fraction. Cardiac catheterization revealed an ejection fraction of 45%, but the coronary arteries were patent and normal. A basilar segment of the inferior lateral and posterior wall remained severely hypokinetic, whereas the distal myocardial segments and apex had normal contractility.

Review of the ETN_2 data revealed a gradual increase from 0 to 5.2% (40 mmHg) soon after incision (fig. 3, arrow), stayed at that level for 45 min, and then acutely peaked at 7% (53 mmHg) immediately before cardiovascular collapse. This suggests air entrainment shortly after neck incision. Simultaneously with cardiovascular collapse, the ETN_2 concentration acutely decreased (fig. 3).

Discussion

Although VAE frequently occurs due to acute entrainment of air into the venous circulation, it may enter gradually.[5,6] During slow air entrainment, clinical presentation with cardiovascular collapse may be a relatively late event in the VAE syndrome. This appears to have happened in these patients. In both patients, the ETN_2 concentration increased long before it was detected, and the embolic event was suspected only after $ETCO_2$ and blood pressure acutely decreased.

Early detection can reduce the morbidity of VAE.[7] Transesophageal echocardiography and precordial Doppler ultrasonography are considered the best methods to detect VAE.[8] Transesophageal echocardiography allows quick visualization of the air, but requires skill in interpretation as well as continuous monitoring. In our first patient, who had hypertrophic cardiomyopathy, the TEE probe was not oriented to monitor the right ventricular outflow tract, so we missed the entry of air into the right ventricle and pulmonary artery. Once the diagnosis of VAE was clinically suspected, TEE quickly confirmed the diagnosis. Lacking TEE, a clinician can rely on end-tidal gas measurements to diagnose VAE. Matjasko *et al.*[9] found that ETN_2 concentration increases before $ETCO_2$ decreases, especially during bolus injections but also after slower (1 ml/kg/min) intravenous air infusions. The ETN_2 concentration is more specific and sensitive than is $ETCO_2$ for diagnosing VAE. This is because nitrogen is the only component in expired gas that is not present in inhaled gas (provided air is not the carrier gas), and because either the cardiac output must significantly decrease or the pulmonary artery must become significantly occluded with air before the $ETCO_2$ concentration decreases. Also, due to the multifactorial etiology of a reduced $ETCO_2$, an increase in the ETN_2 can be considered more specific for VAE.

In patient #1, air entry started approximately 50 min before the patient became hypotensive. In patient #2, the ETN_2 concentration increased soon after neck incision, but cardiovascular collapse occurred 1 h later. There is a possibility that the slow expansion of air bubbles over time, due to nitrous oxide, contributed to the delayed manifestation of VAE.

Adornato *et al.*[6] demonstrated that during slow intravenous infusion of air, central venous and pulmonary artery pressure abruptly increased, systemic vascular resistance progressively decreased, and blood pressure decreased moderately until the ability of the cardiac output to compensate was exceeded, and then it decreased sharply. In contrast, a bolus injection of air caused an immediate increase in central venous pressure and decreases in pulmonary artery and systemic pressures. The pattern of hemodynamic changes in patient #1 (fig. 1) corresponded to that described with

slow intravenous air injection.[6] Dramatic changes in pulmonary artery pressure, central venous pressure, and $ETCO_2$ occurred only seconds before hypotension occurred. These are all late signs of VAE and in no way were useful in predicting the impending cardiovascular collapse.

Contrary to the findings of Matjasko *et al.*,[9] in our patient #1, the $ETCO_2$ nadir preceded the peak of pulmonary artery pressure (fig. 1). English *et al.*[10] demonstrated that the pulmonary artery pressure and $ETCO_2$ concentrations remained altered longest after the air injection, findings consistent with our observations in patient #1 (fig. 1). This patient had a moderately elevated pulmonary artery pressure, a decreased $ETCO_2$, and an increased ETN_2 for 20 min after the severe clinical manifestations of VAE resolved. This timing also corresponds to the dissemination of the large air bubble from the pulmonary artery, as visualized by TEE. During this entire period, the patient was hemodynamically stable, and, without TEE, we never would have attributed this process to a subclinical course of VAE. Therefore, moderate increases in pulmonary artery pressure and central venous pressure and a decrease in $ETCO_2$ concentrations are nonspecific signs and are diagnostic of VAE only in the presence of other signs and symptoms and/or more advanced monitoring tools such as TEE.

Of interest, in both patients, after the sudden decrease in $ETCO_2$ (which presumably indicates a large amount of air/nitrogen delivered to the pulmonary circulation), the ETN_2 paradoxically decreased. Matjasko *et al.*[9] attributed this paradoxical decrease in ETN_2 to hypotension, low cardiac output, and an increased number of ventilated but not perfused alveoli. This may reduce gas exchange from venous blood into the alveoli. Therefore, less nitrogen is excreted by ventilation and detected in the end-tidal gases.[9]

In patient #2, the clinical presentation was characterized by severe hypotension and life-threatening cardiac dysrhythmias. The electrocardiogram in VAE typically demonstrates right heart strain, myocardial ischemia, conduction blocks, and ventricular fibrillation.‡[6] Transesophageal echocardiography and cardiac catheterization in our patient excluded the presence of a patent foramen ovale. If present, it would have helped explain the myocardial stunning (TEE) and myocardial ischemic changes (electrocardiogram) on the basis of air entry into the coronary arteries. Rather, myocardial stunning encountered in this patient may be explained by ischemia based on VAE-induced hypotension.

In summary, in two patients who suffered intraoperative episodes of VAE, ETN_2 increased and $ETCO_2$ decreased slightly long before the VAE became clinically significant. Although the moderate decrease in $ETCO_2$ was a nondiagnostic sign of VAE, the unnoticed increase in ETN_2 was highly indicative of this event. We conclude that continuous observation of ETN_2 is a monitoring method that, in cases of slow, unrecognized air entry, can alert clinicians to an impending major incident of air embolization earlier than can a decrease in $ETCO_2$ or an increase in central venous or pulmonary artery pressures. If one detects a gradual increase in ETN_2, the possible sites of intravascular air entry must be investigated, and nitrous oxide should be discontinued immediately.

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