



CKJ REVIEW

Venous air embolism related to the use of central catheters revisited: with emphasis on dialysis catheters

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Abstract

Venous air embolism is a dreaded condition particularly relevant to the field of nephrology. In the face of a favourable, air-to-blood pressure gradient and an abnormal communication between the atmosphere and the veins, air entrance into the circulation is common and can bring about venous air embolism. These air emboli can migrate to different areas through three major routes: pulmonary circulation, paradoxical embolism and retrograde ascension to the cerebral venous system. The frequent undesirable outcome of this disease entity, despite timely and aggressive treatment, signifies the importance of understanding the underlying pathophysiological mechanism and of the implementation of various preventive measures. The not-that-uncommon occurrence of venous air embolism, often precipitated by improper patient positioning during cervical catheter procedures, suggests that awareness of this procedure-related complication among health care workers is not universal. This review aims to update the pathophysiology of venous air embolism and to emphasize the importance of observing the necessary precautionary measures during central catheter use in hopes of eliminating this unfortunate but easily avoidable mishap in nephrology practice.

Key words: air embolism, catheter, central vein, haemodialysis, retrograde pathway

Introduction

Air embolism is a rare but potentially catastrophic malady and can often be fatal. Rather than being a natural-occurring pathology, it is mostly the consequence of an iatrogenic error related to various clinical, blood vessel-related procedures [1, 2]. The entrance of air into the systemic veins causes venous air embolism, whereas its entrance into the pulmonary veins or systemic arteries results in arterial air embolism [3]. Because of the unique anatomy and physiology involving veins, the behaviour and complications of venous air emboli can be different from

those of their arterial counterparts. The notoriously dismal outcome of venous air embolism despite aggressive treatment emphasizes the importance of proper preventive measures. In a tertiary centre specialized in managing venous air embolism, the long-term data revealed a mortality of 25% for the affected patients, with about half of the survivors suffering from neurological sequelae [4].

The emphasis on venous air embolism is especially relevant to the field of nephrology, since this ailment is a potential complication of haemodialysis and the use of central venous

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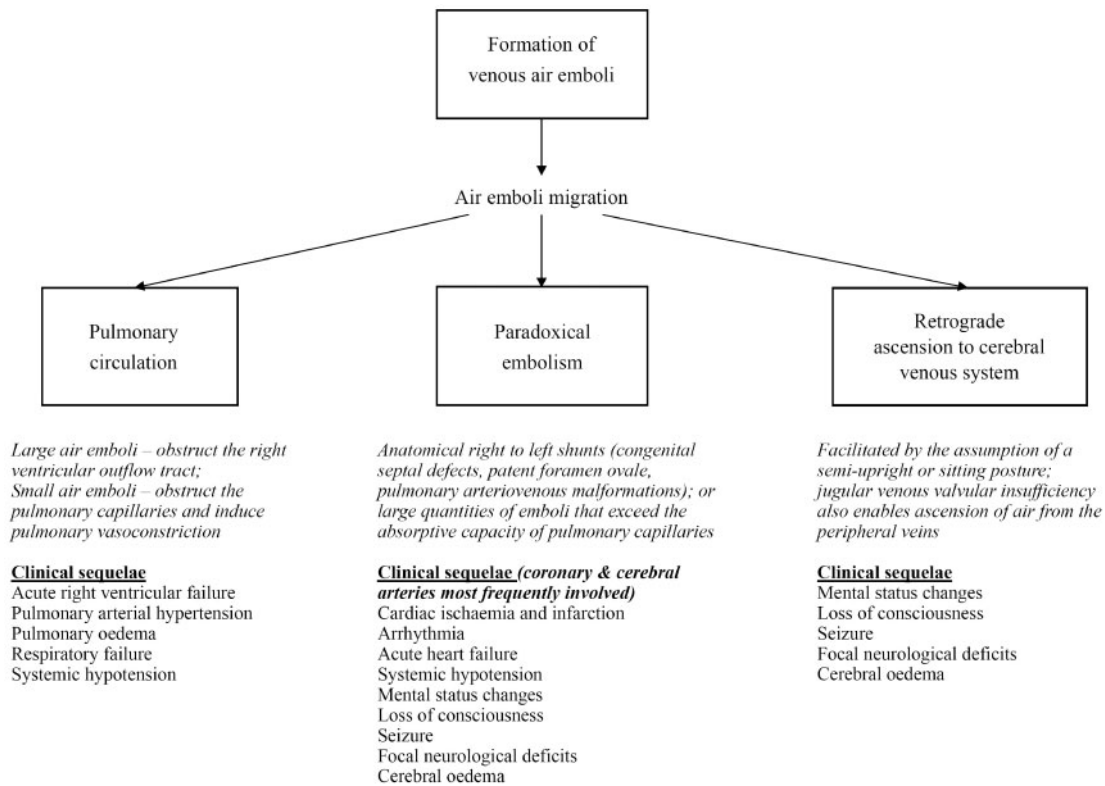


Fig. 1. Pathways of venous air emboli migration and their clinical sequelae. There are overlaps in the manifestations of emboli travelling along these pathways.

catheters [5, 6]. It is disheartening to realize that ever since the first fatal case of catheter-related air embolism was reported in 1969 [7], such a tragic but easily avoidable complication still often raises its ugly head almost half a century later, probably because of a general deficiency in knowledge of this clinically important entity among health care workers.

As there have been great advances in the understanding of venous air embolism over the last decade, we are updating the pathophysiology and preventive strategies pertaining to central catheter use in an attempt to increase the awareness of this iatrogenic complication among individuals who provide patient care.

Pathophysiology and clinical manifestations

Formation of venous air emboli

To generate venous air emboli, three essential elements are required: a source of air (i.e. the atmosphere), the connection between a vein and the source (i.e. the catheter) and a pressure gradient that favours air migration into the vein [8]. This latter gradient is readily established in circumstances in which the central venous pressure (CVP) is lower than the pressure of the atmosphere. Common conditions fostering such a favourable gradient include deep inspiration, hypovolaemia [9] and assumption of a semi-upright, sitting or upright posture that leads to hydrostatic pressure changes in the venous system because of the effect of gravity [10].

Migration of venous air emboli

Once atmospheric air enters a vein during catheter-related procedures, the air bubbles generated can migrate along three major pathways to produce various clinical problems (Figure 1).

Pulmonary circulation

The venous air emboli can be carried along by blood to the right heart before migrating to the pulmonary artery, especially if a patient happens to lie on his or her right side [11]. In the right ventricle, the trapped air produces a classic 'millwheel' murmur, which is described as a loud, churning sound [12]. The resulting clinical manifestations depend on the amount of air introduced, the rate of air entrance, as well as the position of the subject [12]. A lethal dose of air for humans has been estimated to be ~100 mL/sec; such entry is possible in the presence of a 5 cm H₂O pressure gradient created via a 14-gauge needle [13]. If a larger volume of air is introduced rapidly, an intracardiac airlock effect as a result of foam formation can be produced, causing obstruction of the blood flow through the right ventricular outflow tract. The pulmonary blood flow and venous return to the left heart are thus compromised, bringing about hypotension and eventually circulatory collapse [14]. A subject's position can also affect the outcome; however, with the assumption of a left lateral position (the 'Durant's position') the obstructive air at the outflow tract of the right ventricle can shift to the ventricular apex by its own buoyancy [12, 15]. A slower infusion of a smaller amount of air can also allow its migration into the pulmonary artery, leading to increased pulmonary arterial pressure and reduced systemic vascular resistance. These events will trigger a compensatory increase in cardiac output in an attempt to maintain the normalcy of systemic haemodynamics [14]. The pulmonary hypertension is also exacerbated by the intense pulmonary vasoconstriction in response to the presence of air bubbles in the pulmonary arterioles, a finding that has been demonstrated in both animal and human studies [16, 17]. Furthermore, aggregation of neutrophils, in particular, contributes to an increase in vascular permeability and the development of pulmonary oedema by the release of toxic

oxygen metabolites [18, 19]. Subsequently, the airway resistance is increased and lung compliance impaired, ushering in hypoxaemia and respiratory failure [20].

Paradoxical embolism

The migration of venous emboli into the arterial circulation defines paradoxical embolism. The latter typically involves the existence of an intracardiac right to left shunt in the form of a congenital septal defect or a patent foramen ovale. The presence of pulmonary arteriovenous malformations can also act as a conduit for air passage. Patent foramen ovale is not that uncommon, with an estimated prevalence of ~30% [21]. Even in the absence of an anatomical shunt, paradoxical embolism can still occur in the face of a large quantity of air. Under normal circumstances, air bubbles in the pulmonary microcirculation can be completely trapped and eliminated by the solution of air into the blood [22]. However, such a filtering capacity can be overwhelmed if the rate of air introduction exceeds that of the absorption threshold, thus enabling a spillover into the arterial circulation [23]. Traveling in systemic arteries, the air bubbles can occlude blood vessels to cause ischaemic end-organ damage. Furthermore, the systemic inflammatory response syndrome has also been reported as a result of the interaction between air emboli and arterial endothelium [24].

Retrograde ascension of air into the cerebral venous system

Nephrologists are probably among the first clinicians who were aware of the characteristic posture-dependent flow of air bubbles in the venous system. As early as the 1970s, it was observed that air could backflow to the cerebral veins if the patient is sitting or if the head is elevated with respect to the level of the heart. He or she might become aware of the rushing sound produced by the emboli traveling through the neck vessels [11, 25]. In contrast, air bubbles tend to move to the right heart if the patient is in a recumbent position [11]. However, this important observation was overlooked and catheter-related cerebral air embolism was mostly considered to be solely a consequence of paradoxical embolism. In 1991, this phenomenon of retrograde movement of venous air emboli in the direction of the brain was eventually recognized, when a massive accumulation of air was found exclusively in the cerebral veins of a patient who had a disconnected subclavian catheter but who did not have an intracardiac shunt [26]. This finding was also echoed by a later study that showed frequent transient passage of air to the upper region of the venous system of the head and neck after peripheral radiocontrast injection [27]. However, it was not until a decade later that this theory of a 'retrograde pathway' finally received well-deserved attention. In a landmark *in vitro* experiment, a silicone tube with adjustable diameter was placed vertically to simulate the superior vena cava, while a pump was employed to maintain the downward flow of citrated pig blood through the upper end of the tube. This pump was adjusted to provide different levels of blood flow, simulating the variable venous returns flowing downwards via the superior vena cava. Air bubbles of different sizes were introduced through a 16-gauge catheter inserted into the lower part of the tube. It was observed that air bubbles could rise upwards depending on their size, the diameter of the tube and the downward blood flow rate against which the air bubbles had to struggle [28]. These experimental findings lent strong support to the ascension potential of air emboli towards the brain against the caudally flowing blood in the cervical vein of a patient who assumes a vertical head-up position. A re-evaluation of the brain images in the published reports of 'paradoxical embolism' also failed to detect

the presence of air in the cranially directed arteries, suggesting that the retrograde venous pathway is the true portal of cerebral air embolism in affected patients. The behaviour of air bubbles in different inclination angles of the catheter mimicking various patient positions in clinical settings, from supine to upright, was then studied in another experiment. The upstream movement of air bubbles was not observed until the inclination angle was $>45^\circ$, and was most obvious when the angle reached 90° [29].

Among the published cases of cerebral venous air embolism related to central catheter use, air was most frequently demonstrated in the cortical veins [30–33] and the cavernous sinuses [33–36]. Moreover, air emboli involving the cavernous sinuses [37–40] and the jugular veins [39, 40] have also been reported after peripheral bloodline manipulations. Normally the valves in the jugular vein ensure unidirectional blood flow towards the heart. In the presence of valvular insufficiency, such a protective mechanism is impaired, allowing peripheral venous air emboli to pass through the jugular veins to reach the cerebral venous circulation [37]. As compared with the paradoxical pathway, patients affected by the retrograde migration of air often have much worse clinical outcomes [33]. In this regard, it is noteworthy that the marked increase in venous outflow resistance in the cerebral vessels as a result of the presence of venous emboli can bring about cortical tissue damage [41].

Clinical manifestations

The symptoms and signs of venous air embolism closely correlate with the above pathophysiologic processes. The migration of air emboli to the pulmonary circulation will lead to predominantly cardiopulmonary manifestations, whereas those of paradoxical air emboli (now becoming arterial in nature) will depend on the site of end-organ involvement. For the paradoxical variety, the cerebral arteries are most often the involved sites. Cerebral air embolism resulting from the paradoxical or retrograde pathway can have similar clinical features, including those of focal neurological deficits, mental status changes and seizures [33, 42], and death can occur. When a patient is suspected of having a venous air embolism, diagnostic tests to locate the air bubbles should be carried out immediately. Diagnosis can be confirmed when air emboli are demonstrated by echocardiogram, computed tomography or magnetic resonance imaging of involved organs. However, it is notable that cerebral air embolism cannot be ruled out even if one fails to demonstrate the presence of air on brain imaging, because rapid absorption of air bubbles can take place within a period of a few hours [43]. This observation emphasizes the importance of having a high index of suspicion and a timely arrangement of relevant workup for the affected patients.

Management

When venous air embolism is suspected, appropriate management must be started promptly while waiting for the results of diagnostic tests. It is paramount to locate the source of air entrance in order to stop further emboli generation. Intensive supportive care should be initiated at once in a closely monitored setting. Most often the affected patients are critically ill and thus adequate oxygenation by high-flow oxygen is essential, with consideration of mechanical ventilation in the case of life-threatening respiratory failure. Aggressive fluid resuscitation and vasopressor administration are often needed to maintain haemodynamic stability. Once the diagnosis of venous air

embolism is confirmed, more definitive therapy can be considered, especially if the patient is haemodynamically unstable or complicated by end-organ damage. However, apart from the above supportive measures, specific recommendations pertaining to the management of established venous air embolism still have not been firmly established [44, 45].

In the case of embolic obstruction at the right ventricular outflow tract, an assumption of the 'Durant's position' together with a head-down inclination has been suggested as the initial management step [5, 15]. However, the ideal position assumed by an affected patient remains controversial, as recent animal studies have demonstrated a lack of clinical improvement despite relocating air bubbles to the apex of the right ventricle by means of postural changes [46, 47]. It has been suggested that if a patient is in the Trendelenburg position at the time when air is in the systemic venous system, the buoyant air emboli can migrate to the veins of the lower extremities, causing peripheral venous obstruction and tissue ischaemia. As a consequence, cyanosis, numbness and pain can occur [41]. However, the outcome of this complication may not be life- or limb-threatening if the peripheral circulation is still in good order [41]. In order to remove the trapped air, intracardiac aspiration has been recommended [5, 48, 49]. However, the effectiveness of this option is questionable, since evaluation of this aspiration procedure has been carried out mostly in animal and laboratory studies. In humans, attempts to aspirate air in haemodynamically compromised subjects have often yielded disappointing results [17, 50].

The management consideration for cerebral air embolism, involving a retrograde or paradoxical pathway, is different. The affected patient should be placed flat and supine [3], rather than in a Trendelenburg position, to avoid potential exacerbation of any cerebral oedema. Moreover, in the case of paradoxical cerebral air embolism, a head-down inclination is ineffectual in preventing the air bubbles from being propelled into the cerebral vasculature [3]. Among all of the proposed therapeutic options, however, hyperbaric oxygen treatment is probably the only one that has been proven to be effective for both venous and arterial air embolism, particularly in patients with cerebral involvement [51]. The high barometric pressure reduces the volume of air emboli and maintains a high oxygen content in the blood to optimize oxygenation of ischaemic tissues. As a result, cerebral oedema can be alleviated with a resultant reduction in intracranial pressure [52]. If the treatment is started within 1–6 h, a more favourable outcome has been observed [51, 52]. In addition, when an affected patient develops seizures, anticonvulsant therapy is indicated.

Because of the paucity of evidence-based data for the treatment of venous air embolism, the role of preventive measures in avoiding iatrogenic venous air embolism has assumed much greater importance.

Prevention of venous air embolism—a nephrologist's perspective

Potential complications of air embolism have been well-recognized since the heydays of haemodialysis [53]. The negative pressure created by the blood pump can promote air entry into the extracorporeal circuit [54]. With improvements in dialysis technology, however, this risk has been greatly reduced, although sporadic cases of cerebral air embolism during haemodialysis are still being reported [55, 56] (Figure 2). Today, it is largely the improper care of central venous catheters that is



Fig. 2. Computed tomography of a patient suffering from cerebral venous air emboli. Air emboli in the bridging veins of the right cerebral hemisphere (white arrows) and the dural sinus (black arrow). Reprinted with permission from Elsevier [56].

instrumental in bringing about this complication in nephrology practice. When inserting a catheter into the internal jugular vein, most clinicians are aware of the importance of adopting the Trendelenburg position in an effort to facilitate the cannulation process by engorging the vein and to curb air entry through the resultant higher venous pressure [57, 58]. In particular, a number of cautionary measures against air embolism during catheter placement and maintenance have been suggested [59] (Table 1).

For the procedure of cervical catheter removal, in contrast, there is a relative lack of acknowledgement of important measures that prevent the CVP from becoming lower than the pressure of the ambient air. The maintenance of such a positive blood-to-air gradient is an integral step in discouraging the entry of air into the blood. These include assumption of the Trendelenburg position [61–66] and strict avoidance of talking, coughing or inspiration during the removal process. Appropriate breathing instructions should be provided at the moment of catheter removal. For cooperative patients, performing the Valsalva manoeuvre achieves the highest CVP and can offer the greatest protection against air emboli generation [67]. Temporary breath holding after full inspiration is another acceptable alternative. This has the advantage of preventing further inspiration should the patient fail to hold his or her breath any longer. On the other hand, performing the removal procedure during an expiratory phase possesses the risk of inadvertent inspiration if the patient is adversely agitated or 'shocked' by rapid catheter withdrawal [60]. Adequate haemostasis should be ensured by means of heparin avoidance on the day of catheter removal and application of a prolonged pressure onto the removal site [68, 69] in order to minimize the chance of air entry into the bloodstream. An air-occlusive dressing should also be applied for at least 24 h, because air embolism can still occur even though several hours might have elapsed following catheter removal [64]. Also, it should be noted that after the removal procedure, a patent subcutaneous tract may be left behind [60]. Such a tract, at times just a fibrin sheath, has been found to be a portal of air entry for fatal air embolism [70]. As a result, suturing of the subcutaneous tract after removal of a tunneled catheter has been recommended to seal off any remnant tract [71]. Recently, a novel technique has also been proposed to reduce the risk of air embolism related to the procedure of tunneled catheter exchange via a guidewire. In contrast to the conventional method of making an incision in the catheter for

Table 1. Cautionary measures against air embolism during the placement and maintenance of a cervical catheter^a

During catheter placement:

1. Correction of risk factors (such as dehydration, hypovolaemia, systemic vasodilatation), resulting in a reduced CVP whenever possible, to minimize the risk of ambient air entry into the bloodstream along a positive air-to-blood pressure gradient.
2. Assumption of the Trendelenburg position. If assumption of the latter position is not possible, elevation of the lower extremities using pillows can help.
3. Proper occlusion of the needle hub and the catheter at appropriate moments.

Care and maintenance of cervical catheters:

1. Ensure that all the connections are kept tight and all unused hubs are closed and locked when the catheter is not in use.
2. Regular inspection of the catheter and all connections for cracks or broken seals.
3. Fully prime and expel air from all syringes to be connected to the catheter upon its use.
4. Be cautious during patient transfer or movement to prevent accidental pulling of the catheter. In the case of a break in the closed system, together with a reduction in the CVP that is related to the repositioning of the patient from a recumbent posture to an upright one, the risk of venous air emboli generation is remarkably increased.

^aModified from Feil [59] and Brockmeyer et al. [60].

Table 2. Preventive strategies of venous air embolism related to cervical catheter removal^a

1. As in the placement of a catheter, risk factors resulting in a reduced CVP should be corrected whenever possible.
2. Avoid heparin use on the day of catheter removal; administer protamine prior to removal if heparin use is unavoidable.
3. Assumption of the Trendelenburg position to increase the CVP to a level higher than the pressure of ambient air so that air will be prevented from entering the blood.
4. Two approaches to breathing instructions upon catheter removal:
 - i. Valsalva manoeuvre—preferable if patient is cooperative.
 - ii. Full inspiration and then hold the breath.
 As it is difficult for patients to observe any of the above breathing requirements for a long period of time, the catheter removal procedure should be conducted quickly.
5. Strict avoidance of coughing and talking during the procedure.
6. A positive end-expiratory pressure should be applied for those patients being treated with mechanical ventilation.
7. Immediate coverage of the catheter removal site with an impermeable dressing such as a piece of gauze generously impregnated with an antibiotic cream.
8. Local pressure for at least 10 min to achieve adequate haemostasis after catheter removal.
9. Observe the patient for at least 30 min for any bleeding.
10. Application of air-occlusive dressing for 24 h.
11. Establishment of a catheter removal protocol/checklist.
12. Regular training for the health care workers responsible for catheter removal; ensure strict adherence to the protocol/checklist.

^aModified from Feil [59], Brockmeyer et al. [60], Pronovost et al. [64], and Boer and Hené [68].

guidewire introduction, an introducer needle is used to puncture a small hole through the catheter first at a site proximal to the subcutaneous tunnel. This approach creates a much smaller conduit for the purpose of guidewire insertion, resulting in a greatly diminished exposure of venous blood to atmospheric air and thus minimizing the risk of air embolism [72].

To conclude, removal of a central venous catheter should not be taken lightly and must be regarded as a major health care-related undertaking. The procedure should not be delegated to inexperienced personnel. Establishment of a protocol along with its strict adherence is essential (Table 2). The best practice can be achieved by assigning two independent individuals to carry out the procedure, with consideration of a pre-procedural safety briefing, similar in principle to the widely adopted practice of double-checking, which can help reduce medication errors as well as mishaps incurred in the surgical operating room [73, 74]. We are aware of instances in which removal of cervical catheters was carried out by untrained personnel without heeding the required precautionary measures. The patients involved tragically died soon after catheter removal, probably of air embolism. The unfortunate events were promptly reported by the media, with great damage to the

reputation of the involved institutions and their health care workers as well as the subsequent exposure to legal challenges. With a greater understanding of the underlying pathophysiology and an improved global awareness of air embolism relating to the use of central venous catheters [44], we hope that this unfortunate but avoidable complication can be eliminated in the near future.

Conflict of interest statement

None declared.

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