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Retrograde Air Embolization during Routine Radial Artery Catheter Flushing in Adult Cardiac Surgical Patients

An Ultrasound Study

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Background: **Rapid flushing of radial artery catheters may result in retrograde embolization of air into the cerebral circulation. This study examined the incidence of central air embolization during and after flushing of an arterial pressure monitoring system.**

Methods: **One hundred adult patients undergoing cardiac surgical procedures were enrolled in this study. Ten ml of saline and blood were withdrawn into a syringe in the arterial flushing-sampling pressure system and then readministered to the patient through a 20-gauge radial artery catheter over 3–12 s. The right carotid artery, left carotid artery, and aortic arch were visualized using ultrasound imaging techniques during three manual flushes of the system. The left and right common carotid arteries were examined for the presence of macrobubbles or microbubbles using a linear array ultrasound transducer. The aortic arch was imaged using transesophageal echocardiography to detect retrograde air emboli. The severity of air embolization was quantified using a modification of an established grading system.**

Results: **A total of 298 ultrasound studies in 100 patients were recorded and analyzed after radial artery catheter flushing. Two aortic arch images were not obtained because of an inability to place the probe. Most clinicians (54%) returned flush solution to patients at near-maximal injection rates (2–3 ml per second). No air emboli (macrobubbles or microbubbles) were detected in the carotid arteries or aortic arch of any subject.**

Conclusion: **Retrograde air embolization is a rare event after routine radial artery catheter flushing in adult patients with stable hemodynamic conditions.**

FLUSHING of arterial catheters with fluid may be associated with embolization of air or thrombus. Reference texts in anesthesiology[1–5] and critical care medicine[6–10] describe the potential risk of retrograde passage of air into the cerebral circulation during manual flushing of the arterial pressure system. The risk of cerebral air embolization in adult patients during routine invasive radial arterial pressure monitoring remains largely unknown. Only one case report of an apparent cerebral air embolus has been published.[11] The rapid injection (12–15 ml per second) of saline directly into a radial artery catheter *via* a syringe can produce retrograde flow into the central arterial circulation.[12] The use of an arterial flushing-sampling pressure system appears to limit the rate and volume of flush solution administration and minimize the risk of cerebral air embolization.[12]

During routine clinical use, approximately 5–10 ml of blood and saline is withdrawn into a syringe whenever an arterial blood sample is collected. Clinicians frequently return this "waste" solution to the patient through the arterial pressure tubing. Closed arterial pressure monitoring systems, which are designed with a syringe incorporated within the arterial pressure tubing, necessitate the return of withdrawn blood and saline through the arterial catheter. The rapid withdrawal of a saline-blood mixture into a syringe and subsequent injection into a patient can potentially produce two types of air emboli. Large air bubbles (macrobubbles) can be visualized in the arterial pressure tubing during the manual flushing process.[4,11] In addition, the withdrawal and administration of 5–10 ml of saline and blood from a syringe results in the generation of numerous microbubbles (as observed during a contrast echocardiography study).[13] The presence of macrobubbles or microbubbles in the central circulation can be detected accurately using ultrasound imaging techniques. The aim of this clinical investigation is to determine the incidence of retrograde air embolization into the carotid arteries and aortic arch during routine manual flushing of an arterial pressure monitoring system in adult patients.

Materials and Methods

A pilot study was performed to confirm that a closed arterial flushing-sampling pressure system (Single Kit Flush Device, Abbott Laboratories, North Chicago, IL) produces microbubbles in a manner similar to a diagnostic contrast echocardiography examination. In a series of six patients, the arterial pressure system was attached to a 20-gauge, 48-mm cannula that was inserted into a vein at the level of the wrist. Withdrawal of 10 ml of a saline-blood mixture into a syringe and readministration to the patient was conducted as described in the protocol below. Using transesophageal echocardiography (TEE), a midesophageal four-chamber view was obtained to visualize air in the right side of the heart. In all six patients, nearly complete opacification of the right heart chambers with microbubbles was observed within 3–5 s of injection (fig. 1).

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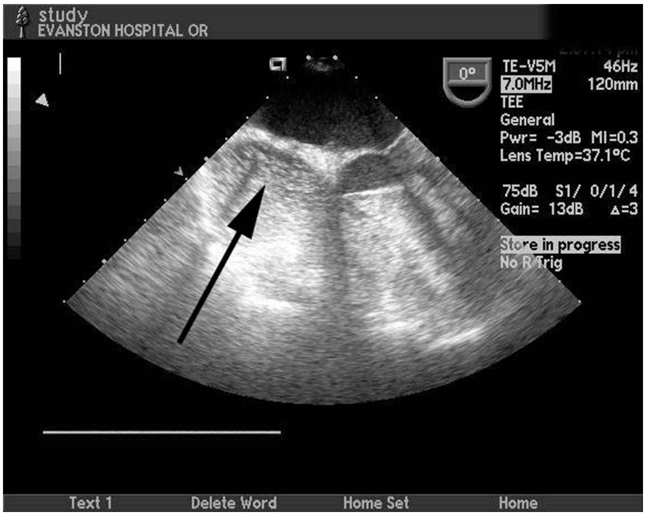

Fig. 1. Demonstration of numerous air bubbles in the right atrium with transesophageal echocardiography. The bubbles were generated by the administration of 10 ml of a blood/saline solution from a flushing-sampling arterial pressure system into a vein at the level of the wrist.

This prospective study was approved by the Evanston Northwestern Healthcare Institutional Review Board, and written informed consent was obtained from all subjects. One hundred adult patients presenting for cardiac surgical procedures were recruited over an 11-month period. Exclusion criteria included inability to place a radial artery catheter, morbid obesity (which could result in poor-quality images of the carotid arteries), or the presence of contraindications to TEE probe placement (esophageal or cervical spine disease).

Intravenous and radial artery catheters (20-gauge) were placed under local anesthesia. If radial artery harvesting was anticipated, the radial artery catheter was inserted in the dominant hand. Otherwise, the catheter was introduced into the radial artery with the strongest palpable pulse. Central access was established before induction of anesthesia, and TEE probe placement occurred after tracheal intubation.

Anesthesia was induced with fentanyl (5–10 μg/kg), midazolam (2–5 mg), and thiopental (1–3 mg/kg), or etomidate (0.1–0.3 mg/kg). Neuromuscular blockade was achieved with rocuronium (0.6–1.0 mg/kg).

All measurements were obtained during a period of stable hemodynamics between tracheal intubation and surgical incision. Heart rate and blood pressure were maintained within 20–25% of baseline values by adjusting the depth of anesthesia or through the administration of vasoactive drugs (phenylephrine or esmolol). The right carotid artery, the left carotid artery, and then the aortic arch were imaged with ultrasound during three manual flushes of the pressure line. A closed arterial flushing-sampling pressure monitoring system with a 12-ml syringe incorporated within the pressure tubing was used in all subjects. The system was attached to a pressurized (300 mm Hg) 500-ml bag of normal saline and carefully primed to remove all air. A total of 10 ml of saline and blood was withdrawn into the syringe over 5–10 s. After a 5-s pause, the plunger on the syringe was compressed to return the flush solution to the patient. The rate at which the withdrawn sample was returned through the radial artery catheter was determined by a member of the anesthesia care team and measured by an independent observer. Clinicians were instructed to compress the syringe at a rate that reflected their usual clinical practice and to perform all three flushes at approximately the same rate. The presence or absence of air in the pressure tubing during the flushing process was recorded. No intravenous fluids were administered during the measurement periods.

The right and left common carotid arteries were imaged using a 7 MHz linear array transducer (Accuson, Mountain View, CA). The probe was positioned on the surface of the neck so that a longitudinal view of the lumen of the common carotid artery was obtained (fig. 2). Depth and gain settings were adjusted to optimize two-dimensional imaging. The carotid artery was identified by demonstrating appropriate flow with color Doppler imaging, lack of compressibility of the vessel with the probe, and the presence of pulsations with cardiac contractions. The aortic arch was imaged from the upper esophageal aortic arch long-axis view using a multiplane TEE probe (Accuson, Mountain View, CA). Two-dimensional images were collected using high-frequency settings (5 or 7 MHz). Ultrasound examinations were performed by one of three cardiac anesthesiologists certified in perioperative TEE. All images were recorded onto videotape and analyzed offline. Echocardiographic data were collected for 30–40 s after each arterial line flushing and stored. An echocardiologist blinded to all information regarding patient demographics and intraoperative events reviewed the carotid artery and aortic arch studies. The severity of air embolization was quan-

Fig. 2. Image of the common carotid artery obtained with a 7 MHz linear array transducer.

Table 1. Grading Scale For Central Air Embolization

Grade	Definition
0	No air emboli
1	The presence of a few microbubbles
2	A shower of microbubbles filling the vessel
3	The presence of macrobubbles (bubbles >1 mm diameter)
4	A mixture of microbubbles and macrobubbles

Modified from criteria established by Parmet[14] and Kato.[15]

tified using a modification of previously established grading systems for central embolization[14,15] (table 1).

Hemodynamic data were recorded at the time of each flushing. Systolic and diastolic blood pressures were measured from the radial artery catheter. Thermodilution cardiac output was performed in triplicate at the time of the final catheter flushing (during imaging of the aortic arch).

To determine if rapid syringe compression increased the risk of central air embolization, the time from the start to the completion of the flushing process was recorded. No previous studies have defined the rate of flush solution administration that constitutes "rapid" arterial flushing. The maximal rate that flush solution could be returned to the patient through a 45-mm, 20-gauge catheter was 2–3 ml/s (determined clinically by the authors). Therefore, we defined "rapid" flushing as the return of 10 ml of fluid in the syringe in 5 s or less.

Statistical Analysis

The purpose of clinical trial was to test the hypothesis that no air would be detected in the central arterial circulation of at least 97% of patients after arterial catheter flushing. To test this hypothesis, we proposed studying 100 patients with the expectation that no air would be detected in any of the study subjects. According to the "rule of three," if no air was observed in any of the patients, there is a 95% confidence that the true risk of retrograde air embolization is between 0% and 3%.[16]

The 95% confidence interval for the proportion of subjects in whom there was evidence of central air embolization was calculated based on the single proportion Wilson score method (NCSS, Kaysville, UT).[17] Because the proportion was 0, the true proportion cannot be less than 0 and only the upper confidence interval can be calculated. When a 95% confidence interval is calculated in the usual way, there is an equal 2.5% chance that the true proportion is higher or lower than the upper or lower limit, respectively. As a result, when a 95% confidence interval for a 0 proportion is calculated in the usual way, it is actually a 97.5% confidence interval. Therefore, to provide the true 95% confidence interval for the 0 proportion, it was necessary to compute a 90% confidence interval in the usual way.§

Table 2. Patient Characteristics

	Study Group
Sample Size	100
Gender (M/F)	85/15
Age (yr)	68.7 ± 10.8
Weight (kg)	83.5 ± 15.8
Height (cm)	173.5 ± 10.7
Cardiac Output (l/min)	4.8 ± 1.2
Smoking History	30
Use of Ethanol	45
ASA physical status (III/IV)	39/61
Preexisting Diseases	
Chronic Obstructive Pulmonary Disease	30
Congestive Heart Failure	10
Myocardial Infarction	14
Hypertension	21
Diabetes Mellitus	34
Stroke/Cerebral Vascular Accident	2
CEA	3
Chronic Renal Insufficiency/ Renal Failure	1
Operative Procedures	
CABG	63
Valve	12
Combined CABG and Valve	3
Redo CABG	4
Redo Valve	12
Redo Combined CABG and Valve	1
Outpatient CABG	1
Other	4

Data are mean (± SD) or number of patients.

ASA = American Society of Anesthesiologists; CABG = coronary artery bypass graft; CEA = carotid endarterectomy; Redo = Reoperative.

Arterial blood pressure measurements at the times of each of the three injections were compared with Friedman analysis of variance on ranks with all *post hoc* pairwise multiple comparisons made with Dunn's method. The criterion for rejection of the null hypothesis was $P < 0.05$.

Results

A total of 298 ultrasound studies were recorded and analyzed after radial artery catheter flushing. High-quality images of the left and right common carotid arteries were obtained in all 100 subjects. Two aortic arch images were not obtained because of an inability to place the transesophageal echocardiography probe. The aortic arch was clearly visualized in the remaining 98 patients. Patient demographic data are presented in table 2. Right-sided radial artery catheters were placed in 68 patients, and left-sided catheters were inserted in the remaining 32 patients.

The readministration of flush solution in the syringe to

§ The Prism guide to interpreting statistical results: The confidence interval of a proportion. Available at: http://graphpad.com/articles/interpret/contingency/conf_int_proportion.htm. Accessed April 7, 2004.

Table 3. Systolic and Diastolic Blood Pressures at the Times of Flushing

	Flush 1	Flush 2	Flush 3
Systolic Blood Pressure (mm Hg)	122* (84–210)	115 (78–188)	110 (82–184)
Diastolic Blood Pressure (mm Hg)	64* (40–112)	60 (34–98)	60 (40–88)

Data are median (range).

* $P < 0.05$ versus the other two flushes.

patients was performed rapidly (≤5 s) in 54 subjects and slowly (>5 s) in 46 subjects. In only 26 of the 100 study patients was flushing conducted in 10 s or more. Air bubbles (macrobubbles) passing through the arterial pressure tubing into the radial artery catheter were observed in 22 patients. Hemodynamics remained stable during all measurement periods (table 3).

No evidence of central air embolization was observed in this clinical trial. Offline analysis of the 298 ultrasound studies conducted in 100 subjects was performed to determine the presence or absence of macrobubbles or microbubbles in the carotid arteries or aortic arch. No microbubbles were detected in any of the ultrasound studies. In addition, no larger air bubbles were observed in either common carotid artery or in the aortic arch during rapid and slow flushing of radial artery catheters. Thus, given the absence of evidence of central air embolization observed in the 100 subjects included in this clinical trial, there is 95% confidence that the true risk of retrograde air embolization is between 0% and 2.63%.

Discussion

Cerebral air embolization has been reported during the placement, flushing, and removal of invasive arterial and venous catheters. Acute neurologic events have been observed immediately after the flushing of dialysis[18,19] and temporal artery catheters.[20] Neurologic manifestations of intracerebral air have also been described in patients with central venous lines[21,22] and intraaortic balloon pumps.[23] In each of these case reports, the suspected cause of acute neurologic deterioration was air embolization to the brain. In adult patients, only one clinical case of an apparent retrograde air embolization from a radial artery catheter has been published.[11] A seizure was witnessed in this postoperative patient immediately after the pressure monitor system was flushed. Air was seen filling the line from a stopcock adjacent to the transducer, and a computed tomographic scan performed after the event demonstrated intracerebral air.

Two small experimental investigations have examined risk factors for retrograde passage of air into the central circulation during flushing of radial artery catheters. Lowenstein *et al.* studied 10 postoperative patients to determine a safe volume of flush solution.[12] Saline was labeled with a γ-emitting isotope (sodium pertechnetate) and a γ-ray detector was placed at the subclavian-vertebral artery junction. The solution was injected directly into the radial artery catheter through a syringe at an estimated rate of 12–15 ml/s. The isotope was detected in the central circulation after an average of 6.6 ml of flush solution was administered. A correlation between patient height and volume of flush solution needed to produce a positive result was noted. When the experiment was repeated using an arterial pressure system that limited the volume and rate of injection, no retrograde movement of flush solution was detected. Chang *et al.* injected a mixture of ^{133}Xe and air into the left radial artery of four macaques monkeys (approximately 7 kg weight) to determine the volume of air required to produce cerebral air embolization.[11] Air bubbles were seen in the brain when more than 2.0 ml of air/^{133}Xe were injected or flushed through the arterial line system. These studies suggest that retrograde air embolization is possible under certain circumstances (extremely rapid flushing or when large volumes of air are introduced into the radial artery).

Arterial flushing-sampling pressure monitoring systems in current use are designed to limit the risk of air embolization. Closed systems may reduce air entrainment by incorporating a syringe within the pressure tubing and by eliminating three-way stopcocks in the pressure line. These systems also prevent clinicians from administering excessively large flush volumes and rates. In the current investigation, we examined the risk of retrograde air embolization during routine flushing of a closed pressure monitoring system. No air was detected in the central circulation after nearly 300 flushes of radial artery catheters in 100 individuals.

Despite advances in system design, air bubbles are still present within the pressure tubing and syringe. Microbubbles are generated when saline is withdrawn into a syringe, and the concentration of microbubbles can be increased significantly if blood is added to an agitated saline solution.[13,24] In our pilot study, an image nearly identical to a contrast echocardiography study (opacification of right heart structures with microbubbles) was observed in all subjects after venous injection. This finding suggests that numerous microbubbles are present in the flush solution that is returned to the patient from the syringe. In addition, a careful examination of the pressure tubing during the flushing process revealed the presence of air (macrobubbles) in 22 patients. It is likely that small or large air bubbles were introduced into the radial artery of the majority of patients in this study. However, retrograde passage of these air emboli into the aortic arch and carotid vessels was not observed, presumably because of the absence of retrograde flow resulting from relatively slow injection permitted by the arterial flushing-sampling pressure monitoring system and the small volume of air entrained by the system.

Ultrasound is a highly sensitive tool for the clinical diagnosis of intracardiac or intravascular air. Air bubbles with a diameter as small as 5–10 μm can be visualized with ultrasound transducers.[25] We used a high-frequency linear array probe to detect air in the left and right common carotid arteries. No previous investigations have utilized two-dimensional ultrasound to visualize retrograde air embolization during invasive catheter flushing in adult subjects. However, this imaging modality has been used to measure the presence of microbubbles within the lumen of the carotid artery during various diagnostic studies.[26,27] In the presence of right-to-left intracardiac shunting, microbubbles can be observed in the carotid artery with a linear array ultrasound transducer after an intravenous injection of agitated saline.[26] During equivocal carotid bifurcation ultrasound studies, the administration of contrast microbubbles can provide complete visualization of the lumen of the vessel.[27] We have also observed the passage of air bubbles in the carotids after cardiopulmonary bypass using the methodology described in this study. Transesophageal echocardiography was used to image the aortic arch, as TEE is the most sensitive monitor available to detect air in the heart and great vessels.[28] Retained air and microbubbles in the left ventricle and aortic arch are frequently observed with TEE after cardiopulmonary bypass.[29,30] Ultrasound imaging techniques offer a unique method of detecting air emboli in real time. We were unable to document any evidence of air bubbles in the central circulation of our study population using two different, highly sensitive, ultrasound imaging modalities.

Risk factors for retrograde air embolization during radial artery catheter flushing in adult patients have been described in the literature. These risk factors include small patient size (short arm length reduces the distance between the radial and subclavian arteries), patient position (risk is increased in the sitting position), rate of injection, and volume of flush solution.[11,12] Cerebral embolization of air may also be more likely if right-sided catheters are used because air bubbles must pass all the great vessels supplying the brain before they are cleared to a more innocuous distal site.[5] Although relatively large flush volumes (10 ml) and rapid injection rates (as fast as 3 ml/s) were used in this investigation, no evidence of retrograde movement of air bubbles was observed. Furthermore, no air emboli were detected in smaller patients enrolled in the study or when right-sided radial artery catheters were flushed.

Some methodological limitations of this study that merit comment. First, we did not examine the vertebral arteries for air during catheter flushing. Air bubbles traveling in a retrograde manner in the subclavian artery would reach the vertebral artery before the common carotid artery. There is a close anatomic relationship between the origins of the vertebral and common carotid artery, particularly on the right side. Therefore, it is likely that air emboli would enter both vessels during the flushing process. Second, the rate of catheter flushing was not defined or controlled in our experimental protocol. In the initial study design, patients were randomized to receive either a rapid (≤5 s) or slow (>5 s) administration of 10 ml of flush solution. Our Institutional Review Board did not approve our initial proposal because of "the risk of cerebral air embolization during rapid flushing." Our protocol was therefore revised from a randomized, controlled trial to an observational study using standard clinical flush practices. We observed that the majority of clinicians readministered the solution in the syringe at a near-maximal rate despite admonitions in the literature against rapid flushing of catheters. Third, we only examined patients for central air embolization during manual flushing of the arterial system. We did not determine the pressures generated during manual flushing of the catheter nor did we assess the risk of air embolization after opening of the flush valve on the pressurized system. Finally, all examinations were conducted on adult patients using a closed flushing-sampling pressure system. The risk of cerebral air embolization may be increased if certain patient-specific or system-specific factors are altered. The potential for retrograde air embolization is significant in neonates and infants during rapid catheter flushing. Several case reports of acute cerebral events have been described in pediatric patients in association with invasive arterial catheter use.[20,31] In addition, evidence of central air embolization has been observed in infants after the flushing of arterial pressure tubing[32,33] Using high-frequency ultrasonic probes, these investigators detected air bubbles in the common carotid arteries of the majority of pediatric patients after the administration of a fast flush bolus volume through the radial catheter.[32,33] In both adult and pediatric patients, the incidence of this complication may be increased when 1) larger arterial catheters are placed, 2) more proximal arteries (brachial and axillary) are cannulated, 3) alternate arterial flushing-sampling pressure systems are used, 4) larger volumes or higher pressures of flush solution are administered (a "power flush"), and 5) flushing is conducted during periods of severe hypotension or shock.

The belief that ". . .the potential for retrograde embolization of air or thrombus is quite high during intraarterial pressure monitoring" persists in the literature.[5] We conclude that cerebral embolization of air is a rare event in adult cardiac surgical patients during routine flushing of a blood-conserving arterial pressure line system. Although large and small air bubbles were generated during the withdrawal and readministration of saline and blood from a syringe, no macrobubbles or microbubbles were seen in the central arterial circulation. Vigilance in detecting air in the pressure tubing and syringe is still required, as retrograde embolization may occur during periods of severe hypotension or if large volumes of air are introduced into the radial artery.

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