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Retrograde Blood Flow in the Brachial and Axillary Arteries during Routine Radial Arterial Catheter Flushing

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Background: **Flushing of radial arterial catheters may be associated with retrograde embolization of air or thrombus into the cerebral circulation. For embolization into the central circulation to occur, sufficient pressure must be generated during the flushing process to reverse antegrade blood flow in the arterial blood vessels of the upper extremity. This ultrasound study was designed to examine whether routine radial catheter flushing practices produce retrograde blood flow patterns in the brachial and proximal axillary arteries.**

Methods: **Duplex ultrasound examinations of the brachial and axillary arteries were conducted in 100 surgical patients to quantify direction and velocity of blood flow during catheter flushing. After obtaining Doppler spectral images of brachial and axillary arterial flow patterns, manual flushing was performed by injecting 10 ml flush solution using a syringe at a rate reflecting standard clinical practices. The flow-regulating device on the pressurized (300 mmHg) arterial flushing–sampling system was then opened for 10 s to deliver a rapid bolus of fluid (flush valve opening).**

Results: **The rate of manual flush solution injection through the radial arterial catheter was related to the probability of retrograde flow in the axillary artery (P < 0.001). Reversed arterial flow was noted in the majority of subjects (33 of 51) at a manual flush rate of less than 9 s and in no subjects (0 of 48) at a rate 9 s or greater. Retrograde flow was observed less frequently during flush valve opening (2 of 99 patients; P < 0.001 *vs.* manual flushing).**

Conclusions: **Rapid manual flushing of radial arterial catheters at rates faster than 1 ml/s produces retrograde flow in the proximal axillary artery.**

THE placement of invasive arterial catheters is an essential component of cardiovascular monitoring in critically ill patients. Invasive arterial pressure monitoring allows for continuous assessment of systemic blood pressures and repeated arterial blood sampling. In the United States, approximately 8 million catheters are placed in the operating room and intensive care unit settings each year.[1] The radial artery is the most common site for arterial cannulation because of the presence of collateral circulation in the hand and the superficial location of the artery at the wrist. Several large studies have reported a low risk of serious complications during and after radial artery catheter use.[2–4]

A rare but recognized complication of indwelling radial artery pressure monitoring is retrograde embolization of air or thrombus during catheter flushing. The incidence of acute neurologic events directly related to flushing of radial artery pressure monitoring systems is unknown. However, several recent case reports of intracerebral gas embolization and severe neurologic injury after the placement and flushing of radial arterial catheters illustrate a significant risk of routine invasive arterial pressure monitoring systems.[5-7]

Arterial pressure monitoring systems are flushed to prevent clotting and subsequent loss of catheter patency and to return blood in the pressure tubing after arterial blood gas sampling. Two flushing systems are in common use. A manual flush system uses a syringe incorporated within the pressure tubing. After withdrawal of blood into the system, the plunger on the syringe is compressed to return unused arterial blood. After manual flushing, a flow-regulating device connected to a pressurized volume system is opened to deliver a rapid bolus of fluid to clear the pressure line and cannula of blood ("flush valve opening"). Retrograde embolization of flush solution, air, and thrombus is possible with both types of flushing systems. Studies in neonates and infants have demonstrated retrograde arterial flow of saline solution into the central circulation during rapid manual flushing and opening of flush valves (documented by the presence of microbubbles on ultrasound examination).[8,9] However, a similar ultrasound investigation in adult surgical patients was unable to observe microbubbles in the carotid arteries during rapid manual flushing.[10] Although standard reviews in anesthesiology and critical care state that radial artery catheters should be flushed slowly to reduce the risk cerebral embolization,[11–16] there is insufficient evidence to define safe practices related to radial artery flushing in adults.

For air or thrombus to reach the central circulation and cerebral arteries, sufficient pressure must be generated during the flushing process to reverse blood flow in the brachial and axillary arteries. The aim of the current investigation was to determine whether routine flushing of radial artery catheters results in retrograde arterial flow in the brachial and proximal axillary arteries. Direction and velocity of blood flow can be accurately quantified using Doppler ultrasound techniques. Therefore, duplex ultrasonography examinations of both arteries were performed during both manual flushing and flush valve opening to determine the presence or absence of retrograde arterial flow. An additional objective of the study was to obtain quantitative data regarding the rates of manual flushing that might produce reversal of arterial blood patterns in the peripheral

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circulation. We also sought differences in demographic characteristics, hemodynamic data, and manual flush rates between patients in whom retrograde flow was observed after radial arterial flushing and those in whom retrograde flow was not observed.

Materials and Methods

This study was approved by the institutional review board of Evanston Northwestern Healthcare (Evanston, Illinois), and written informed consent was obtained from all subjects. One hundred patients presenting for elective cardiac, orthopedic, vascular, or general surgical procedures requiring invasive radial artery catheterization were enrolled. Exclusion criteria included emergency procedures, the presence of known upper extremity vascular disease or vascular grafts, or the need for brachial or femoral arterial cannulation. A duplex ultrasound examination was performed on the brachial artery to determine the presence or absence of retrograde blood flow during a manual flushing and flush valve opening of a radial catheter. The process was repeated in an identical manner but with duplex imaging of the axillary artery.

Radial artery catheterization was performed with local anesthesia before induction of anesthesia. The selection of site (right or left side) was at the discretion of the managing anesthesia care team. If radial artery harvesting for coronary artery bypass grafting was anticipated, the catheterization was performed in the dominant hand. A 20-gauge, 4.45-cm-long catheter (Arrow International Radial Artery Catheterization Set; Reading, PA) was used in all subjects. The catheter was connected to a closed arterial flushing-sampling system (Single Kit Flush Device; Abbott Laboratories, North Chicago, IL) that incorporates a 12-ml syringe within the pressure tubing and a flush valve adjacent to the pressure transducer. The system was carefully primed with 0.9% normal saline solution to remove all air bubbles and was then pressurized to 300 mmHg.

Anesthesia was induced with either thiopental (2–4 mg/kg) or propofol (1–2 mg/kg) and maintained with either isoflurane (0.4–2.0%) or sevoflurane (0.4–2.5%). All ultrasound examinations were conducted during the time interval between anesthetic induction and surgical incision. Systolic blood pressure was maintained within 25% of baseline values during the study period using phenylephrine boluses (50–100 μg), if required.

Duplex ultrasound examinations of the brachial and axillary arteries were conducted in each subject during manual flushing and flush valve opening. Duplex ultrasound uses high-resolution B-mode imaging to visualize anatomic components of the vessel and pulsed-wave Doppler to quantify direction and velocity of blood flow. Doppler data were exhibited on the Doppler spectral display, with velocity data on the y-axis, time on the x-axis, and direction of flow indicated as above or below the zero baseline (the transducer was oriented so that flow toward the Doppler beam was displayed above the zero baseline; fig. 1). The brachial artery was located by placing a 7-MHz linear array transducer (Accuson, Mountain View, CA) approximately 5 cm above the antecubital fossa. The artery was identified by the pulsatile motion of the walls with B-mode imaging, the lack of compressibility of the vessel with the transducer, and the detection of characteristic flow patterns with color-flow Doppler. After obtaining a high-quality longitudinal view of the brachial artery, the Doppler sample volume (1.5 mm) was positioned within the center of the vessel. Angle correction was performed by aligning the Doppler angle indicator parallel to the direction of flow in order to obtain accurate velocity data. Acute Doppler angles of 60° or less were maintained to minimize measurement error. A characteristic triphasic flow pattern was observed on the Doppler spectral display. This consisted of forward flow during systole, followed by a brief period of flow reversal during diastole, then a return of low-velocity forward flow during the remainder of diastole (fig. 1). After obtaining and recording brachial artery ultrasound examinations during catheter flushing, the axillary artery was identified. The transducer was positioned in the axilla, and the artery was identified as described above. The proximal axillary artery was visualized by sliding the transducer in a series of overlapping increments toward the chest wall. The most proximal portion of the axillary artery visualized on B-mode imaging was then used for the pulsed-wave Doppler examination. The Doppler study of the axillary artery was conducted as described for the brachial artery.

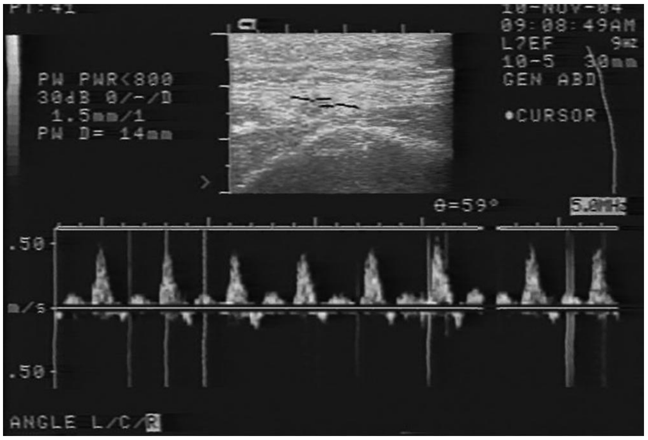

Fig. 1. Duplex ultrasound examination of the proximal axillary artery during an 11-s manual flush with a syringe. All blood flow is directed in an antegrade direction toward the ultrasound transducer (above the zero baseline on the Doppler spectral display).

After an adequate triphasic signal on the Doppler spectral display was obtained from the brachial artery, a manual flush was performed. Ten milliliters of flush

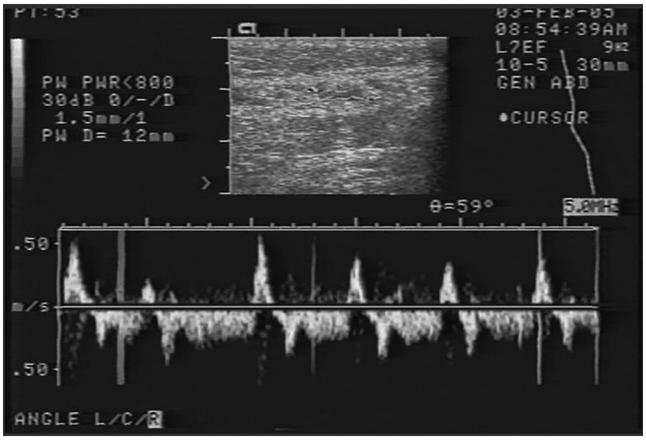

Fig. 2. Duplex ultrasound examination of the proximal axillary artery during a 4-s manual flush with a syringe. Reversal of arterial blood flow in the vessel is observed during the manual flushing process (sustained high-velocity flow below the zero baseline on the Doppler spectral display).

solution (saline solution and blood) was withdrawn into the syringe within the arterial flushing–sampling system. Clinicians were then instructed to compress the plunger on the syringe at a rate that reflected standard manual flushing practices. The rate of manual flushing was recorded by an independent observer. Approximately 10–15 s after manual flushing, the flush valve on the transducer system was opened for 10 s. At a system pressure of 300 mmHg, a 10-s flush valve opening is required to clear the pressure tubing of blood. Duplex ultrasound images of the brachial artery were continuously recorded onto videotape starting immediately before the manual flushing and concluding 10 s after flush valve opening was completed. The ultrasound transducer was repositioned over the axillary artery, and the manual flush and flush valve opening was repeated and recorded as previously described. The duration of manual flushing and flush valve opening were the same as those used for the brachial artery. All ultrasound images were analyzed off-line by a blinded echocardiographer to determine the presence or absence of retrograde flow. Retrograde arterial blood flow was defined as sustained high-velocity flow below the zero baseline on the Doppler spectral display persisting for the duration of the flushing process (fig. 2).

Demographic data (age, sex, height, weight, surgical procedure, preexisting medical conditions, and American Society of Anesthesiologists physical status) were obtained from preoperative anesthetic notes. Hemodynamic data were collected at the time of each flushing. Systolic blood pressure, diastolic blood pressure, mean arterial blood pressure, and heart rate were recorded immediately before each flushing process.

Statistical Analysis

Based on previous clinical and experimental models, we hypothesized that retrograde blood flow would not be observed in the axillary arteries of at least 97% of patients after manual flushing. To test this hypothesis, we proposed studying 100 subjects with the expectation that no retrograde flow would be detected in any patients. According to the "rule of three," if no retrograde flow was detected in any of the patients, there is a 95% confidence that the true risk of reversal of arterial blood flow is between 0% and 3%.[17]

The demographic characteristics, hemodynamic data, and manual flush rates of patients in whom retrograde flow was observed after radial arterial flushing were compared with those of patients in whom retrograde flow was not observed using the Fisher exact probability test for nominal data and the Mann–Whitney rank sum test for ordinal and continuous data (which were found to be nonnormally distributed). The Wilcoxon signed rank test was used to compare the incidence of retrograde flow under the two flush conditions and at the two arteries.

The only variable that differed between patients in whom retrograde flow was observed after radial arterial flushing and patients in whom retrograde flow was not observed was the duration of manual flush. The relation of the occurrence of retrograde flow to the duration of manual flush was sought using simple logistic regression analysis.

The criterion for rejection of the null hypothesis was $P < 0.05$, with the Bonferroni correction for multiple applications to the same data where applicable.

Results

High-quality triphasic Doppler signals of the brachial and axillary arteries were obtained in 99 patients. In one subject, poor visualization of the upper extremity arteries resulted in inadequate Doppler spectral images. This patient was excluded from further data analysis. Baseline patient demographic data and type of surgical procedure are presented in table 1.

Doppler ultrasound brachial arterial flow data during radial catheter flushing are presented in tables 2 and 3. Retrograde flow was observed more frequently during manual flushing (57% of patients) than during flush valve opening (9% of patients; $P < 0.001$). The incidence of retrograde flow decreased as the rate of manual flushing increased (3 of 3 patients during a 3-s flush, 4 of 6 patients during an 8-s flush, 2 of 13 patients during a 12-s flush, and 0 of 3 patients during a 15-s flush). The time to inject 10 ml flush solution manually (the flush duration) of patients in whom retrograde brachial arterial flow was observed was significantly less than those of patients in whom it was not ($P < 0.001$ for median values 6 s and 10 s, respectively). The probability of retrograde brachial arterial flow after manual radial arterial flushing was determined by simple logistic regression analysis to be

Table 1. Patient Characteristics

	Study Group
Sample size	99
Sex, M/F	56/43
Age, yr	70 ± 13
Weight, kg	79.8 ± 20.6
Height, cm	170.4 ± 9.0
Smoking history	31
Use of ethanol	51
ASA PS, II/III/IV	18/37/44
Preexisting diseases	
Hypertension	64
Myocardial infarction	16
Congestive heart failure	17
Chronic obstructive pulmonary disease	9
Asthma	5
Sleep apnea	7
Liver disease	2
Chronic renal insufficiency	7
Chronic renal failure	1
Diabetes mellitus	14
Thyroid disease	13
Cerebral vascular accident	3
Operative procedures	
Cardiac	64
Vascular	8
General	19
Orthopedic	8

Data are mean ± SD or number of patients.

ASA PS = American Society of Anesthesiologists physical status.

related to the manual radial arterial flush duration ($P < 0.001$; table 4).

The results of Doppler studies of the axillary artery during catheter flushing are presented in tables 2 and 3. Retrograde flow was more frequent during manual flushing (33% of patients) compared with flush valve opening (2% of patients; $P < 0.001$). Retrograde flow was noted in all (3 of 3) subjects at a 3-s manual flush, 10 of 13 subjects at a 5-s flush, 2 of 7 subjects during an 8-s flush, and in none of the 48 subjects in whom flushing was conducted over 9 s or greater. The time to inject 10 ml flush solution manually (the flush duration) of patients in whom retrograde axillary arterial flow was observed was significantly less than those of patients in whom it was not ($P < 0.001$ for median values 5 and 10 s, respectively). The probability of retrograde axillary arterial flow after manual radial arterial flushing was also found to be related to the manual radial arterial flush duration ($P < 0.001$; table 4).

Table 2. Evidence of Retrograde Arterial Flow during Manual Flushing

Flush Rate, s	Brachial Artery, Positive Response/Number of Patients	Axillary Artery, Positive Response/Number of Patients
3	3/3	3/3
4	5/6	5/6
5	12/13	10/13
6	13/14	10/14
7	8/8	3/8
8	4/6	2/7
9	3/7	0/7
10	5/20	0/18
11	0/1	0/1
12	2/13	0/14
13	1/1	0/1
14	0/4	0/5
15	0/3	0/2

Table 3. Evidence of Retrograde Arterial Flow during Flush Valve Opening

Flush Rate, s	Brachial Artery, Positive Response/Number of Patients	Axillary Artery, Positive Response/Number of Patients
10	9/99	2/99

Patient demographic data and intraoperative hemodynamic data were analyzed to determine factors potentially associated with the risk of retrograde blood flow. No associations were observed between any preoperative demographic variable and the observation of retrograde flow. In addition, no association was observed between any measured hemodynamic variable (systolic blood pressure, diastolic blood pressure, mean blood pressure, heart rate) and the occurrence of retrograde flow in either the brachial artery or axillary artery. The only difference found between patients in whom retrograde flow was observed after radial arterial flushing and those in whom retrograde flow was not observed was in the duration of manual flush, as noted above.

Discussion

In this investigation, we assessed the risk of producing retrograde arterial blood flow in the brachial and axillary arteries using two standard arterial flush techniques in adult surgical patients. We observed evidence of reversed blood flow in the proximal axillary artery when manual flushing of radial arterial catheters was conducted at rates faster than 1 ml/s. In addition, a small incidence (2%) of retrograde blood flow was detected during flush valve opening at a system pressure of 300 mmHg.

Arterial line placement is one of the most frequently performed procedures by anesthesiologists and critical care physicians. Approximately 33–50% of all patients admitted to an intensive care unit will have an indwelling arterial catheter placed.[2,13] The radial artery is the most common site for arterial cannulation because the risk of serious complications related to this site is low.[1] A recent review of complications of invasive radial arterial catheters, which included 19,617 patients from 27 studies, reported a low risk (< 1%) of major adverse events (permanent ischemic damage, sepsis, local infection, pseudoaneurysm, and bleeding).[1] Another infre-

Table 4. Simple Logistic Regression Model Analyzing the Relation between Duration of Manual Flush and Presence or Absence of Retrograde Arterial Flow

Artery	Variable	Coefficient	SE	Wald Statistic	*P* Value	Odds Ratio	95% CI
Brachial	Constant	5.903	1.129	—	—	—	—
	Time	−0.654	0.125	27.597	< 0.001	0.520	0.407–0.664
Axillary	Constant	6.818	1.466	—	—	—	—
	Time	−1.053	0.221	22.592	< 0.001	0.349	0.226–0.539

quent complication of radial catheter placement and maintenance is neurologic injury due to retrograde embolization of air or thrombus during catheter flushing. The incidence central nervous system embolization during flushing has not been established. Gronbeck and Miller[18] observed one neurologic event in a series of 500 arterial catheter insertions. Other case series examining the safety of invasive arterial catheters, involving 1,000–4,932 patients, reported no clinical evidence of central nervous system embolization.[2–4] Several case reports, however, have described the occurrence of transient and permanent neurologic events immediately after flushing of radial catheters,[19,20] with a diagnoses of cerebral air embolization confirmed by computed tomography scanning and magnetic resonance imaging.[5–7] These case reports suggest that arterial flushing systems carry the risk of producing retrograde embolization into the central circulation.

During manual flushing of arterial pressure monitoring systems with a syringe, the primary factors determining the risk for retrograde embolization are the volume of injectate and the rate at which the volume is returned to the patient.[6,9,20] In neonates and infants, evidence of retrograde blood flow in the central circulation has been documented when small volumes of flush solution are injected rapidly. Butt *et al.*[8] observed microbubbles in the aortic arch and common carotid arteries in all neonates when a 0.5- or 1.0-ml bolus volume of saline was administered over 1 s through a radial arterial catheter. No microbubbles were noted on ultrasound examinations when manual flushing was conducted over 5 s. Other pediatric studies have confirmed that manual flush volumes as small as 0.3 ml can reach central arterial circulation when injected rapidly.[21] Only two clinical investigations have examined the safety of manual flushing practices in adult patients. Lowenstein *et al.*[20] administered tagged saline from a syringe directly connected to radial catheter at a rate of 12–15 ml/s. Saline was detected at the junction of the subclavian and vertebral arteries when an average volume of 6.6 ml was injected. Murphy *et al.*[10] examined the common carotid arteries and aortic arch for the presence of microbubbles in 100 adult surgical patients during manual radial arterial catheter flushing with 10 ml saline and blood. No evidence of retrograde passage of microbubbles was observed in any subject when syringe flushing was conducted over 4–20 s.

In the current investigation, a standard manual flush volume of 10 ml was used in all subjects. The rate of injection was determined by clinicians providing patient care. Based on the results of our previous study,[10] we hypothesized that retrograde blood flow would not be detected in the proximal axillary artery of any subjects during rapid or slow manual flushing. Unexpectedly, we observed a clear association between rate of manual injection and the demonstration of reversed arterial flow in the axillary artery. Retrograde blood flow was noted in all subjects (3 of 3) when flushing was performed at maximal rates (10 ml in 3 s). The percentage of patients with evidence of reversed axillary blood flow decreased as the duration of manual flushing increased: 83% of subjects (5 of 6) during a 4-s flush, 71% subjects (10 of 14) during a 6-s flush, and 29% of subjects (2 of 7) during an 8-s flush. When the duration of manual flushing exceeded 8 s, no retrograde flow was observed in the axillary artery of any subject (0 of 48 patients).

After diagnostic blood sampling, the flush valve on the pressure transducer is opened to purge the arterial line of blood. Fluid kinetics differ significantly between a syringe flush (volume limited/pressure unlimited) and flush valve opening (volume unlimited/pressure limited). The volume and velocity of flush delivery during valve opening is determined by several factors, which include infusion bag pressure, driving pressure (infusion bag pressure minus mean arterial pressure), diameter of the arterial cannula, duration of the flushing process, and type of flow-regulating device.[9,22,23] *In vitro* and *in vivo* investigations have reported flow rates of 0.61–5.7 ml/s after opening of flush valves.[22–24] Only one clinical investigation has examined patients for evidence of retrograde arterial blood flow during flush valve opening. Microbubbles were detected in the carotid artery of four of six neonates and infants after a 2-second flush valve opening at an infusion bag pressure of 300 mmHg.[9] No microbubbles were observed during flushing at a system pressure of 100 mmHg. In our study, retrograde arterial flow was detected in the brachial artery in nine subjects and the axillary artery in two subjects during flush valve opening. We also observed a significantly lower incidence of retrograde flow in the axillary artery during flush valve opening (2%) compared with manual flushing (33%; $P < 0.001$). Difference in peak pressure generation during flushing likely account for these findings. Proximal delivery pressures as high as 2,372 mmHg have been measured during rapid administration of a 2.5-ml syringe bolus through an arterial cannula (compared with peak pressures of 320 mmHg during flush valve opening).[25] As noted in pediatric studies, higher driving pressures in an arterial pressure monitoring system are more likely to produce retrograde flow and cerebral embolization.

Experimental and clinical investigations suggest that several factors other than rate, volume, and pressure of flush solution administration may increase the risk of retrograde embolization. These factors include patient size, patient position, and hemodynamic status.[20,22,25] Lowenstein *et al.*[20] observed a positive correlation between patient height and the volume of manual flush solution required to reach the vertebral arteries. Hypotension during the flushing process may also facilitate the passage of air or clot into the central circulation by reducing the gradient between proximal flushing pressures and central aortic pressures. Larger volumes of flush solution are delivered after flush valve opening when mean arterial pressure is low.[22] In the current investigation, we observed no association between patient height or blood pressure and the detection of retrograde flow. However, we attempted to maintain systemic blood pressure within 25% of baseline values during the period of time ultrasound measurements were obtained. Therefore, no data were collected during periods of profound hypotension.

In conclusion, our findings demonstrate that flushing of radial arterial catheters with a syringe at rates faster than 1 ml/s generates enough pressure to reverse blood flow in the brachial and proximal axillary arteries. The incidence of retrograde arterial flow is significantly lower during flush valve opening than during manual flushing. Our findings suggest that rapid manual flushing of arterial flushing–sampling systems frequently produces reversal of blood flow in the axillary artery. However, adverse clinical outcomes related to radial arterial catheter flushing are rare, and our previous investigation was unable to document the passage of microbubbles into the central circulation during the flushing process.[10] Further clinical studies examining the effect of rapid catheter flushing on cerebral blood flow and hemodynamics may help to define safe flushing practices in adult patients.

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