

CO₂ Digital Subtraction Angiography: Potential Complications and Their Prevention¹

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Index terms: Angiography, contrast media • Carbon dioxide • Contrast media, complications • Digital subtraction angiography, complications

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Abbreviations: AAA = abdominal aortic aneurysm, DSA = digital subtraction angiography, IMA = inferior mesenteric artery, SMA = superior mesenteric artery, TIPS = transjugular intrahepatic portosystemic shunt

THE use of CO₂ as a radiographic imaging agent dates back to 1914 when Rautenberg insufflated the peritoneum for visualization of the intraabdominal viscera (1). Subsequently, in the 1920s, it was also used to evaluate retroperitoneal structures (2,3) and later in the 1950s and 1960s, it was employed intravenously to delineate hepatic veins and diagnose pericardial effusion (4-9). The infrequency of untoward events associated with these procedures illustrated the safety of CO₂ (10). Arguably, there are reports of gas embolism, sometimes fatal, with the use of CO₂ for insufflation during laparoscopy, but the reported incidence is exceedingly rare (15 per 113,253) and is associated with peritoneal cavity administration of CO₂ at 1-3 L/min under high pressure (11-13). These volumes far exceed those necessary for intravascular diagnostic or therapeutic purposes.

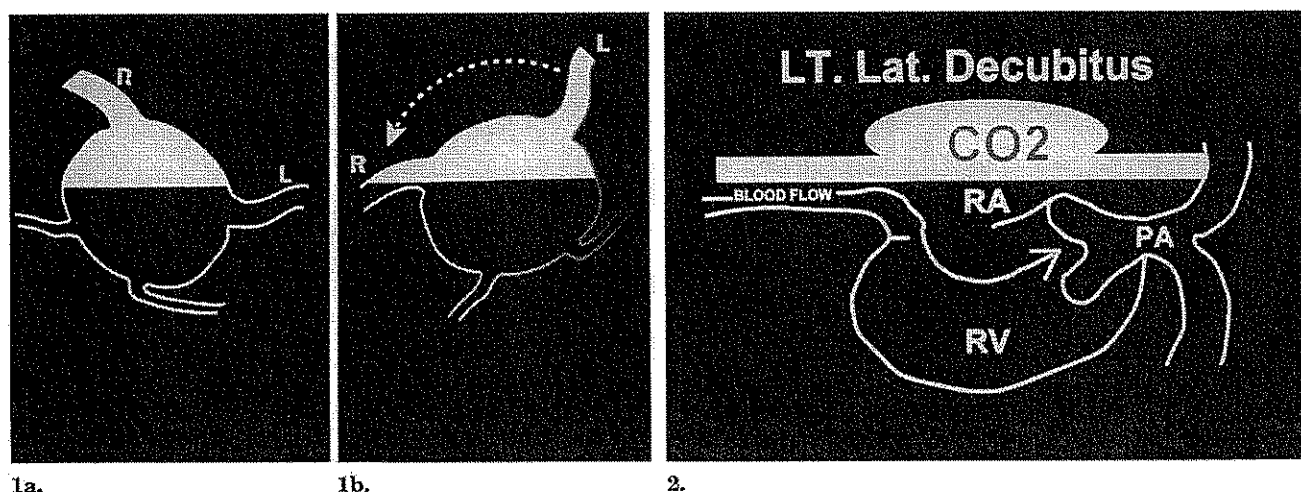
In the 1970s, Hawkins pioneered the use of intraarterial CO₂ for diagnostic arteriography (14). With the advent of digital subtraction angiography (DSA), stacking software, and tilting examining tables, CO₂ angiography became a viable alternative, offering multiple advantages when compared with iodinated contrast material (15-17). CO₂ has no allergic potential and, when used appropriately, lacks renal toxicity. However, as Hawkins demonstrated in 14 canines (18), one animal did demonstrate transient acute tubular necrosis, but this was subsequent to repetitive selective renal artery boluses of CO₂ while the kidney was in the

vertical position. Normally, the renal arteries are positioned posteriorly and this scenario is highly unlikely unless the patient were to remain in the decubitus position and multiple selective injections were made without a delay. Frankhaus (17) and Weaver (19) reported diagnostic and interventional procedures in high-risk patients with use of both pure CO₂ and CO₂ in addition to a small amount of contrast material. In the patients who received pure CO₂, there was no abnormal elevation of creatinine level. In addition to this lack of renal toxicity, we are presently investigating the low viscosity of CO₂, which appears to be beneficial in both diagnostic and interventional procedures. Finally, CO₂ DSA may offer this variety of benefits without inflating, and possibly reducing, cost. We believe these benefits, along with the previously described technological advancements, have led to an increase in the interest in and proliferation of the use of CO₂ DSA (15). However, we also believe that prior to performing CO₂ DSA, an understanding of CO₂ and its unique physical properties is imperative to prevent rare, yet potential, untoward events not seen with liquid contrast material. Our long CO₂ experience at the University of Florida, which includes more than 100 animals and 1,200 patients resulted in seven major untoward events. Based on this and others' experiences, we examined the etiologies and prevention of potential CO₂ DSA complications.

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Figures 1, 2. (1) CO₂ buoyancy. (a) When blood is not totally displaced (eg, in an older patient with counterclockwise rotation of the aorta), only the nondependent right renal artery (R) fills with CO₂ (white). (b) The left renal artery (L) can be filled and visualized if the patient's left side is elevated. (2) Intentional trapping of CO₂ in the right atrium (RA). In the left lateral decubitus position, CO₂ traps in the nondependent portion of the right atrium allowing blood to flow unimpeded into the right ventricle (RV) and pulmonary artery (PA).

UNIQUE PROPERTIES OF CO₂ AND THEIR RARE BUT POTENTIAL ADVERSE EFFECT

Unlike traditional vascular imaging agents, CO₂ is a nontoxic, noncombustible, odorless, and colorless gas. As a gas, it is buoyant, invisible, highly compressible, nonviscous, and heavier than air. These unique features differentiate it from liquid contrast material and define how it can be used as a safe and efficacious vascular imaging agent.

As opposed to liquid contrast material, CO₂ does not mix with blood. Consequently, to render a diagnostically accurate image, it must displace blood from the vessel being examined. Greater displacement yields a higher quality and more accurate image. This in part relates to the buoyancy of CO₂, which causes it to float and assume a nondependent position. If an insufficient amount of blood is displaced, only the anterior or non-gravity-dependent portion of the vessel will be visualized and its contrast will be diminished.

In some instances, such as large vessels, incomplete displacement is common. However, if one is aware

of the buoyancy factor, this can be used as an advantage. For instance, during an aortic injection, CO₂ assumes a nondependent position and fills the superior mesenteric and celiac arteries, yielding excellent images of their origins. Conversely, when trying to improve the image of a more posterior structure, the patient or the table can be rotated to maneuver the area of interest into the nondependent position (Fig 1).

Alternatively, because it is buoyant, CO₂ also has the potential to become trapped in nondependent structures. Normally, intravascular CO₂ is eliminated rapidly in one of two ways. When injected intravenously, it is removed by the lungs (presumably after cardiac churning and rapid dissolution in the blood) in approximately 12–15 seconds. Likewise, after an intraarterial injection, it dissolves within a finite period as long as a sufficient CO₂–blood interface is present. Consequently, CO₂ will be eliminated rapidly as long as both of these processes are unimpeded.

The problem arises when trapped CO₂ cannot be eliminated and obstructs normal blood flow causing a vapor lock. This is more likely to

occur when excessive doses are administered or the blood–CO₂ interface is reduced. It is important to realize, however, that an excessive dose is specific to the patient and varies depending on the patient's anatomy. Because of this, an excessive dose cannot be defined by a specific volume alone. As a general rule, extrapolated from our experience, we do not exceed 100 cm³ per injection. However, in the anesthesia literature, angiocardiology with doses of CO₂ as large as 7.5 mL/kg have been well tolerated (13). Again, individual doses of that magnitude are unnecessary for our purposes. Yet, it is also important to realize that a compromising dose can result from either one large bolus or multiple smaller ones performed in rapid succession. Regardless of the reason, the consequences of trapping are dependent on the location and rapidity of elimination. The most susceptible sites are the main pulmonary artery, inferior mesenteric artery, and the abdominal aorta in patients with an aneurysm.

Concerning the pulmonary arteries, CO₂ has been used safely in a large number of patients in the 1960s and 1970s for the detection of

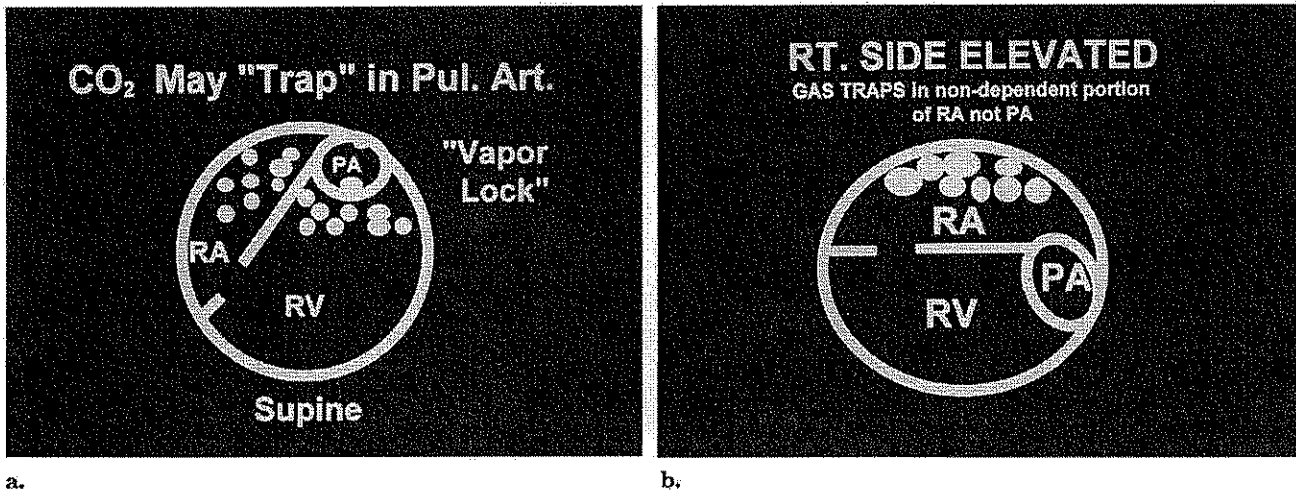


Figure 3. Trapping in the pulmonary artery. (a) If a patient is in the supine position and a relatively large amount of CO₂ (white) is injected into the venous system, CO₂ may trap anteriorly in the pulmonary artery (PA). (b) If the right side is elevated, the gas is released from the pulmonary artery (PA) and resides in the nondependent right atrium (RA) without obstruction. RV = right ventricle.

pericardial effusion. Bendib et al reported 1,600 cases in which 200 cm³ were injected intravenously without significant complications (10). However, many of these injections were performed in the left lateral decubitus position. In this position, CO₂ is trapped in the nondependent portion of the right atrium, which leaves enough space for blood to flow beneath the CO₂ into the right ventricle (Fig 2). Subsequently, it enters the pulmonary artery and is eliminated by the pulmonary circulation. Presently, most intravenous injections of CO₂ are performed with the patient in the supine position. In this position, the pulmonary artery is mostly anterior. Therefore, rather than the CO₂ trapping in the right atrium, it can be trapped in the pulmonary artery (Fig 3).

If CO₂ flows rapidly into the peripheral pulmonary arteries and dissolves quickly, no hemodynamic changes have been noted. If large volumes are injected or if a smaller amount of gas (possible air contamination) does not quickly dissolve, the pulmonary outflow tract can be blocked (vapor lock) resulting in electrocardiographic changes of coronary ischemia (elevated S-T segment), bradycardia, hypotension, and if uncorrected, death. This

appears to have been the etiology for complications that arose in two of our patients. Preceding our current methods of delivery, CO₂ was administered directly from its cylinder through a series of stopcocks. In this instance, while performing CO₂ portography during a transjugular intrahepatic portosystemic shunt (TIPS) procedure, one of the stopcocks was inadvertently turned the wrong way and was open to the patient. Because CO₂ is compressed in the cylinder, it flowed directly from the cylinder into the patient at a rate of 20–50 cm³/sec for more than 60 seconds (Fig 4). Ultimately, at least 1,200–3,000 cm³ were delivered. Such a large volume could not be eliminated by the lungs and became trapped in the main pulmonary artery. The entire right heart and pulmonary outflow tract filled with CO₂ and resulted in a "vapor lock phenomena," which prevented perfusion of the coronary arteries. As a consequence, during the time course, which we estimated to be 5 minutes, there was S-T segment elevation, bradycardia, and hypotension. However, because of its excellent solubility and placement of the patient in the left lateral decubitus position, CO₂ rapidly dissolved and cardiac function

returned to normal within 1 minute. Extrapolating from our past experience with three animals, had the flow continued for several more minutes or had the regulator been set at a higher rate, the patient probably would not have survived.

The other complication was very similar in that the same clinical manifestations occurred during another TIPS procedure, but only 20 cm³ was administered. After thorough review, it was discovered that the CO₂ syringe with 20 cm³ had been in a horizontal position for an extended period of time prior to injection. If the stopcock was in the incorrect position, the CO₂ may have been replaced with room air. This would explain why such a limited volume could cause a similar effect. When this became clinically apparent (the duration of the trapped gas was not known), the patient was placed in the left lateral decubitus position, allowing blood to flow into the right ventricle and pulmonary artery below the trapped right atrial gas (Fig 2). Afterward, the patient's status rapidly returned to baseline within 1 minute.

Likewise, because of their anterior location in the aorta, the celiac, superior mesenteric (SMA), and

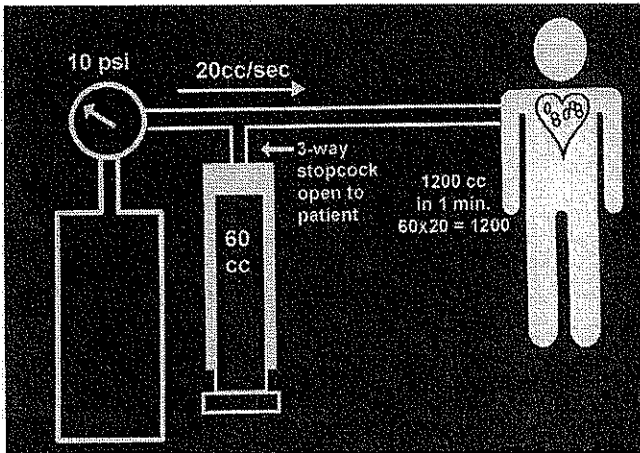


Figure 4. Avoiding excessive CO₂ delivery. Excessive intravascular volumes can be delivered if the CO₂ cylinder is connected directly to the patient and the three-way stopcock is inadvertently malpositioned. Even with the regulator functioning properly and set at low pressure (10 psi), it is estimated that 20 cm³/sec can be delivered through a 5-F catheter, which equals 1,200 cm³ in 1 minute.



Figure 5. CT scan obtained 24 hours after CO₂ injection demonstrates gas in anterior AAA.

inferior mesenteric arteries (IMA) are also predisposed to trapping. The IMA is, however, most susceptible because it is located in the lower abdominal aorta where aneurysms are more likely to occur. Because of their flow dynamics and shape, aneurysms tend to trap gas anteriorly and can result in a vapor lock of the IMA. Normally, CO₂ is rapidly dissolved (20× more soluble than O₂) and does not cause significant ischemia. However, if the CO₂ load is too great or if an aneurysm is present and the interface with blood is decreased, CO₂ cannot dissolve efficiently and ischemia can ensue. Clinically, this is manifested by abdominal pain, cramping, and diarrhea. In addition, because of partial pressure differences, if CO₂ persists for an extended duration, it has the potential of being replaced by O₂ and N₂. When this occurs, O₂ and N₂ can enter the IMA and, because of their decreased solubility, compared with CO₂, persist for a longer period of time potentially causing significant ischemia and, if uncorrected, infarction. Although this has never been reported, on two occasions abdominal computed tomography (CT) performed 24 hours subsequent to a CO₂ DSA

procedure (300–500 cm³ with dedicated injector over 1 hour) demonstrated residual gas anteriorly in an aneurysm (Fig 5). By this time, CO₂ should have been dissolved and this most likely represented less soluble O₂ and N₂.

In another instance, multiple large boluses of CO₂ were administered in rapid sequence into the abdominal aorta (2,000 cm³ total in less than 1 hour). Augmented by the presence of an abdominal aortic aneurysm (AAA), CO₂ trapped anteriorly. Because of the reduced blood–gas interface and the rapid administration of CO₂, it could not be dissolved quickly enough and an apparent vapor lock ensued. Although a stagnant column of CO₂ was not visualized, it was speculated that the nondependent IMA distal branches had stasis and remained filled with CO₂. Unlike the usual occlusive vascular disease where collateral flow develops distally, when a vessel is filled with trapped CO₂, we believe the pressure of the gas prevents collateral flow from entering (extrapolated from our experience with CO₂ angiography) (20). This apparently resulted in ischemia manifested by diarrhea, abdominal pain, and

cramping. Immediate endoscopy suggested ischemia, however, a mucosal biopsy performed at the time was normal and when aortic bifemoral graft surgery was performed 3 weeks later, the bowel was normal.

CO₂ is also invisible, permitting inadvertent undetected contamination. This is most commonly due to either the CO₂ source or room air. Early in our experience, we examined CO₂ cylinders acquired from hospital stores and found that in addition to CO₂, many contained H₂O, particulate matter, and rust. These contaminants are not readily visible and, if undetected, could be inadvertently administered. Consequently, a pure source of CO₂ is mandatory (CMD, Gainesville, FL). However, this does not eliminate the other possibility of room air contamination. Because both CO₂ and room air are invisible, contamination is impossible to detect and may result in a potentially fatal air embolism. The original method of CO₂ delivery, still used by many, is to fill a large syringe and deliver it directly into the angiographic catheter. With use of this method, if the stopcock remains open, CO₂ will exit as it is replaced by room air at approximately 0.2 cm³/sec. Therefore, a closed system is preferred, but residual room air and the components of this system must be purged and stop cocks, if present,

must remain in the appropriate position to avoid contamination.

The diffusion and convection of CO₂ are extremely important as possible etiologies of air contamination, which we have previously not appreciated. Because of the high partial pressures of CO₂ in the syringe (100%) and very low partial pressures (.03%) in the surrounding room air, the gas is rapidly exchanged to create an equilibrium. With use of Fick's first law, we have calculated a diffusivity of air-CO₂ at .2 cm³/sec. The time required to completely replace CO₂ with air in a 20-cm³ syringe is calculated to be approximately 72 minutes. We are presently using gas chromatography to actually measure the amount of contamination in the syringe with an open stopcock in different positions.

Another dual-edged CO₂ attribute is that of low viscosity. Although this may be helpful in circumstances such as detection of gastrointestinal bleeding, it also has the potential of causing dissection or extravasation. We know of no cases of dissection, however, CO₂ was used in the 1960s for coronary endarterectomy (21). This was accomplished by placing the needle between the intima and media prior to a forceful injection. Theoretically, a similar situation could also occur inadvertently and result in a serious dissection or perforation.

We have experienced three cases of peritoneal extravasation without sequelae during CO₂ wedged-hepatic venography for the visualization of the portal vein for TIPS procedures. This most commonly resulted from peripheral catheter placement in combination with the low viscosity and explosive delivery of CO₂. A similar experience was reported by Semba et al, but resulted in liver laceration, subcapsular hematoma and, eventually, multiple system failure and death (22).

An additional serious potential complication is neurotoxicity. Whether this is a true concern at

this time is uncertain. However, our rat studies suggest caution should be taken to avoid intracranial CO₂ delivery. Our preliminary studies involved 20 rats in which CO₂ was injected directly into the carotid artery with a tuberculin syringe (23). This resulted in neurologic deficit and disruption of the blood brain barrier in all rats. On the contrary, however, our investigation of CO₂ in the aortic arch and carotid and vertebral arteries of canines yielded no neurologic deficit. Similarly, Shifrin et al reported on 14 canines that received large amounts of CO₂ directly into the ascending aorta or common carotid arteries and demonstrated no neurologic deficit or EEG changes (24). Nevertheless, there is a report referring to transient unconsciousness and seizure-like activity after suspected inadvertent CO₂ delivery into the cerebral circulation, occurring during the evaluation of dialysis shunts (25). We believe the compressibility of CO₂ often leads to explosive delivery, which can result in counter-current reflux into the cerebral circulation.

Our first and only known encounter with cerebral exposure occurred in a patient with a right axillary-femoral, femoral-posterior tibial artery graft in addition to an occluded left carotid and stenotic right brachiocephalic artery. Because of the patient's symptoms of claudication and elevated creatinine level, CO₂ was chosen to evaluate the integrity of this graft. After several diagnostic injections, the patient inadvertently raised his head, developed dizziness, and subsequently became unconscious. Once his head was lowered, he immediately regained consciousness and later demonstrated no neurologic deficit. It was postulated that when the patient elevated his head, the buoyancy of CO₂ caused a large volume present in the graft to travel in a counter-current direction toward the cerebral circulation. The assumption is that this large bolus of CO₂ temporarily impeded normal blood flow, resulting in transient

symptoms until the CO₂ rapidly dissolved. Room air contamination would offer an alternative explanation, however, a dedicated closed system that delivers pure CO₂ was utilized and room air would have resulted in more serious consequences. Regardless, the lack of a permanent deficit with CO₂ in this case does not exclude the potential for neurotoxicity. In addition, it is uncertain whether these untoward effects are truly secondary to CO₂, its explosive delivery, or possibly air contamination. Because of this uncertainty, we avoid intraarterial CO₂ delivery into the cerebral circulation or when this potential exists, such as in dialysis grafts.

Finally, pain, nausea, vomiting, and the urge to defecate are less severe, possible complications, but in inexperienced hands are more likely to occur. Although rare, these most commonly occurred (<10%) with large (>100 cm³) explosive injections into the abdominal aorta. Similarly, extremity pain occasionally resulted from selective injections in which greater than 20 cm³ was delivered explosively. Each of these is significant in that they not only cause patient discomfort but also lead to patient motion, often resulting in degraded, worthless images. Probably, the least common pathway for these symptoms is trapping, which may lead to ischemia and subsequently pain. Another remote possibility, because these occurred while we were using disposable cylinders of pure CO₂, is contamination from old tanks. More likely is the scenario in which CO₂, because of its compressibility, is delivered in an explosive manner, resulting in rapid distention of the vasculature.

Notably, our experience with 1,200 patients resulted in only seven potentially serious complications. This is a reflection of the safety of CO₂, which has also been corroborated by other authors (26-28). However, our experience also suggests that, albeit small, there are potentially dangerous complications, including death, that can be avoided when CO₂ DSA is performed appropriately.

PREVENTION

Averting unlikely untoward consequences of CO₂ DSA is simple once its unique properties and their effects are understood. Trapping, which is a result of buoyancy and/or excessive volumes as well as patient and vessel position, can be eliminated by a few simple steps. Because excessive volume is by far the most serious complication, a large, rapid intravascular CO₂ burden should be avoided. The compressibility of CO₂ results in considerable difficulty in the operator knowing the exact volume of CO₂ that is being injected. For medical application, the source of CO₂ is always a CO₂ cylinder containing a large volume under very high pressure (actually, CO₂ is in a liquid state). A gas regulator is used to decrease the pressure for delivery and the pressure per square inch (psi) is indicated on the regulator. The indicator reads above the ambient atmospheric pressure (14.7 psi at sea level). That is, when the pressure gauge indicator is set at 14.7 psi (1 atmosphere), pressure is actually set at 2 atmospheres. According to Boyle's Law, if a 100-cm³ syringe is filled at 4 atmospheres (44.1 psi on indicator), it will not contain 100 cm³, but 400 cm³ when injected into a container at atmospheric pressure (Fig 6).

The volume injected into the vascular system also is dependent on the pressure of the vascular system. However, the variation in delivered volume is much less important. The volume for an intravenous injection (10 mm Hg [760 mm + 10 mm = 770 mm Hg] venous pressure) compared to that for a patient with severe arterial hypertension (250 mm Hg [760 mm + 250 mm = 1,010 mm Hg]) only varies by 25%. Therefore, if a known quantity of CO₂ is injected in a "nonexplosive" manner, the subsequent injection can be tailored for the size, flow, and pressure of the vascular system to optimize vascular filling.

Because the CO₂ cylinder contains more than 3 million cm³, the angiographic catheter should never be connected directly to the CO₂

BOYLE'S LAW

Volume of gas varies inversely to pressure

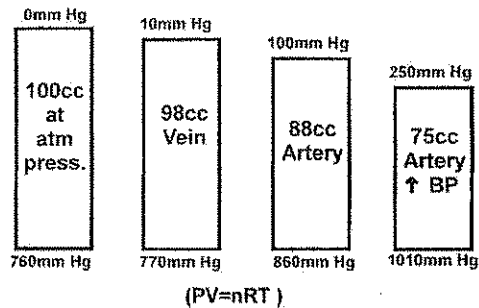


Figure 6. Boyle's law: volume of injected gas changes only minimally with variation of patient's systemic blood pressure.

cylinder. This eliminates the possibility of regulator malfunction or incorrect stopcock direction. Either of these errors can result in the inadvertent delivery of excessive volumes of CO₂. To circumvent this problem, we suggest the use of a closed system that delivers a controlled volume of CO₂. This does not include a syringe or contrast power injector, which we have previously advocated. With their use, CO₂ may present in its compressed state and the true volume injected is not apparent unless calculated using the volume of the syringe and accurate regulator measurements (Fig 7). We recommend the use of either a dedicated CO₂ injector or a closed plastic bag delivery system. One dedicated injector, developed by AngioDynamics (Queensbury, NY), has multiple transducers that constantly monitor pressure. If the pressure becomes excessive, there are five failsafe mechanisms responsible for terminating the injection. Likewise, the plastic bag delivery system utilizes a 1,500-cm³ reservoir that is kept flaccid to prevent compression of CO₂. When aspirated from this noncompressed state, only the aspirated volume can be injected and inadvertent large-volume administrations are eliminated.

If the volume per bolus is controlled and enough time lapses between injections for CO₂ to dissolve, an unlimited volume can be

delivered. Presently, we do not exceed 100 cm³ per injection (arterial or venous) and we wait approximately 90–120 seconds before proceeding with the next run. The time between injections is proportional to the volume delivered. This allows CO₂ to dissolve or be eliminated by the lungs. In addition, when either one venous or several arterial injections (in which an arteriovenous shunt may be present) are made, fluoroscopy or DSA of the heart and pulmonary circulation can be performed to evaluate for any trapped CO₂. The same is true for AAA. Consequently, if trapping is identified either by this method or by patient symptomatology, it can be reduced by changing the patient's position. This change should be made to reorient the nondependent position, causing dissipation of CO₂ and, at the same time, reestablishing blood flow. For example, if there is main pulmonary artery trapping, the patient is placed in the left lateral decubitus position causing CO₂ to rise in the right atrium, thereby allowing blood to flow beneath the trapped CO₂ into the right atrium and ventricle and subsequently the pulmonary circulation (Fig 3). Likewise, if trapping is noted in an AAA, IMA, or other visceral artery, it can be reduced by rotating the patient from one decubitus position to the other. If it occurs in the lower extremities, simply lowering the legs can allevi-

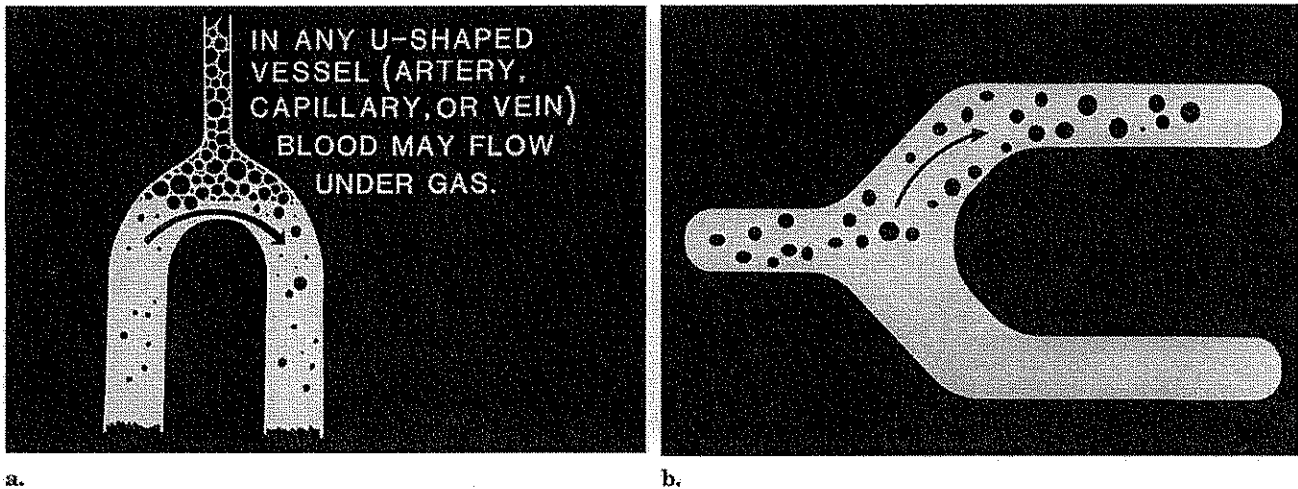


Figure 7. (a) Trapping of CO₂ in inverted U-shaped structures. Although many believe that gas blocks capillaries, we believe that the gas will trap in the apex of any U-shaped vessel (artery, capillary, vein). (b) If the position is changed, the buoyancy of the gas frees the trapped bubbles.

ate the problem (Fig 7). Therefore, the awareness of trapping and how to eliminate it helps avert potentially harmful sequela.

To prevent contamination, a pure disposable source of CO₂ should be used (CMD, Gainesville, FL). This eliminates the possibility of injecting contaminants from an old CO₂ cylinder. Likewise, room air contamination must also be avoided. Although not recommended, if a simple syringe is used for angiographic catheter delivery, a stopcock must be used and kept in the off position during transport and after venting to prevent diffusion with room air. A better method of precluding air contamination is to use a dedicated closed system in which room air is first purged and then prevented from entering. The dedicated CO₂ injector, already described, is ideal and satisfies these requirements. However, it is not currently available in the United States.

Because this injector was designed to be failsafe, transducers originally would abort any low- or high-pressure conditions. This precluded its use for high- or low-pressure procedures such as TIPS, and precipitated the development of a closed plastic bag, hand delivery system by converting a setup routinely used for liquid waste man-

agement (AngioDynamics) (29). Briefly, once the system is purged of room air, the use of glued connections and one-way "check" valves, traditionally used for pulse-spray thrombolysis, prevent air contamination by removing the risk of incorrect stopcock direction. In addition, the glued connectors eliminate the possibility of contamination from the Venturi effect, which can occur in any connection or with stopcocks. Because we are dealing with invisible gases, it is imperative to use one of these methods to avoid the inadvertent intravascular injection of room air.

Preventing neurotoxicity is relatively simple. To begin with, intra-arterial injections are never made above the diaphragm or when the patient's head is elevated. Both of these will avoid exposure of CO₂ to the cerebral circulation as long as reflux does not occur. To prevent reflux, the explosive delivery potential of CO₂ must be eliminated and this relates to the compressibility of the gas. Normally, if CO₂ is present in a syringe and the plunger is advanced, the gas will compress as the very viscous liquid is being forced from the catheter. At the instant the fluid is cleared from the catheter, CO₂ expands in an explosive manner into the vessel. In fact, during a 4-second injection, 95% of

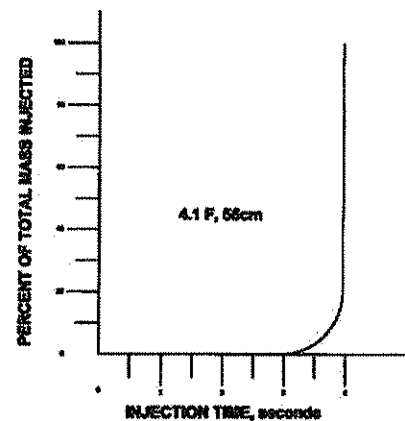


Figure 8. Graph plotting time against total mass injection with a 4.1-F catheter. Ninety-five percent of the CO₂ is delivered in the last 0.5 second during a 4-second injection.

CO₂ is delivered in the last 0.5 second of the injection (Fig 8). This results in very high flow rates and, as a result, possible reflux.

To eliminate this, the angiographic catheter is first purged of saline or blood prior to the definitive CO₂ injection. With the dedicated injector this is done automatically. When a hand delivery system such as the one described previously is used, a small amount of CO₂ is delivered by a smaller "purge syringe" utilizing a small

finite volume of CO₂, usually 3–5 cm³. Once saline or blood is purged from the catheter, reflux of blood is prevented by the one-way check valves. Therefore, a more controlled, nonexplosive, diagnostic delivery can be performed with use of a larger delivery syringe, markedly reducing the possibility of reflux and neurotoxicity. The smaller 3-mL syringe is not absolutely necessary because the same purging function can be performed by the larger delivery syringe. However, it does provide a constant reminder for those with or without CO₂ experience that purging is necessary and requires only a small volume of gas.

Possible "jet effect" and dissection injury of CO₂ can be reduced by avoiding single end-hole catheters and eliminating hepatic wedge injections close to the liver capsule. The low viscosity of CO₂ easily allows the gas to travel along tissue planes (coronary artery and endarterectomy experience) (21). If the catheter is wedged, there is a definite possibility of dissection. This can be reduced by using a catheter with at least one side hole that serves as a safety valve. Experimentally, with use of a gelatin vascular model, CO₂ was injected up to 200 cm³/sec with a multiple-side-hole catheter without injury. Comparison injection with use of the same catheter and "fragile" model, injecting 12 mL/sec of iodinated contrast material produced extensive damage (Hawkins IF, unpublished data, 1990).

CO₂ hepatic wedged portograms have been extremely helpful in visualizing the portal vein for TIPS procedures. Extravasations can be reduced by injecting less forcefully or, if this is inadequate, an occlusion balloon catheter can be placed in a major hepatic vein and a more vigorous injection performed (30). Presently, we have abandoned wedge injections in favor of advancing the TIPS needle into the suspected location of the portal vein (31). CO₂ apparently flows through the sinusoids into the portal vein without causing extravasation. In an ongoing experimental rabbit study, direct injection into the liver

parenchyma produced no evidence of hepatic injury.

Another concern, but as of yet not a problem in our patients, is the use of CO₂ in individuals with chronic obstructive pulmonary disease. To date, we have not had any complications relating to this phenomena. This may relate to our awareness of this potential and conservative use of CO₂ in these patients. In addition, similar to Weaver et al (19) and Frankhouse et al (17), when utilizing CO₂ in these patients, we increase the time between injections to greater than 2 minutes. Of note, however, are studies by Weaver and Bettman demonstrating no change in the partial pressure of CO₂ (PCO₂) in peripheral arterial blood/gas samples after CO₂ DSA when compared to baseline values. This includes five patients in Weaver's study who were noted to have chronic obstructive pulmonary disease.

Finally, pain, nausea, vomiting, and the urge to defecate can be precluded by utilizing some of the techniques already described. In our experience, these symptoms have been more common when an explosive-type delivery is used. Support for this theory is the finding that these untoward effects have been virtually eliminated by limiting the frequency and volume of injections while employing a controlled, non-explosive delivery. Smaller volume injections have been made possible by stacking software, which superimposes multiple frames yielding a composite image. As a consequence, there is no sensation, or, at most, very little patient discomfort, which equates with less patient motion and an excellent quality examination (26,32). By employing these techniques with either the dedicated injector or closed plastic bag delivery system, we have reduced our minor side effects from approximately 10% to less than 1%.

CONCLUSION

When compared with traditional intravascular contrast agents, CO₂

has demonstrated many advantages. It is nonallergic and lacks renal toxicity. Its low viscosity allows the use of smaller catheters that potentially reduce procedural complications. This property is also currently under investigation for its usefulness in diagnostic and interventional procedures, including gastrointestinal hemorrhage. Furthermore, CO₂ DSA may be able to provide these benefits at a reduced cost. Presently, the closed plastic bag delivery system costs \$43, and a 3,000,000-cm³ tank of CO₂, approximately \$300. Most procedures require roughly 400 cm³, or 4¢ of CO₂. This reduction is in addition to the elimination of costly complications that may result from allergic reactions or renal toxicity when iodinated contrast material is used. Finally, when used appropriately, CO₂ can be administered in unlimited quantities with minimal or no discomfort.

It is these advantages in addition to the recent acceptance of CO₂ DSA as a viable alternative that have led to a recent increase in interest and utilization. However, commensurate with this should be the awareness of CO₂ and its unique properties. While these provide many advantages, an incomplete comprehension of the effects of buoyancy, compressibility, and invisibility could potentially result in a unique set of untoward effects. Although extremely rare, a few serious complications from the unguided use of CO₂ could bias its usefulness and inhibit its evolution into a more commonly employed agent.

ADDENDUM

We recently had another experience with pulmonary artery gas embolism during a TIPS procedure. After reviewing the details of the case, the embolism occurred secondary to a technical error in which the delivery syringe was placed at the purge syringe site. Twenty cubic centimeters of room air was inadvertently delivered. After the appropriate maneuvers, the patient re-

covered without sequela. However, during our review, we revisited the literature and discovered an adverse effect potentiating gas embolism when NO anesthesia is used in the presence of intravascular room air or CO₂ (we typically use general anesthesia for TIPS). According to Steffey et al (33), in the presence of intravascular room air or CO₂, NO diffuses from the soft tissues into the gas bubble intensifying it and diluting its contents. As a result, the bubble becomes larger and lasts longer than if it was pure CO₂. In the presence of NO anesthesia, it takes 5.5 times less venous CO₂ to cause an adverse hemodynamic pulmonary response than CO₂ alone. We therefore strongly recommend an alternative to NO if general anesthesia is to be used during a procedure employing intravascular CO₂.

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