Carbon Dioxide in Angiography to Reduce the Risk of Contrast-Induced Nephropathy

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KEYWORDS

- Digital subtraction angiography • Carbon dioxide
- Plastic bag delivery system • Arteries
- Transluminal angioplasty • Stents • EVAR veins
- Angioplasty • Inferior vena cava filters [Q7]
- Embolization • Bleeding • Tumors • Uterine artery

Carbon dioxide (CO_2) is a nontoxic, invisible gas that is highly compressible, nonviscous, buoyant, and rapidly absorbed. It is 20 times more soluble than oxygen. CO_2 is not only rapidly dissolved in the blood but, when delivered intravenously, is eliminated by one pass through the lungs. Most importantly, CO_2, as an intravascular imaging agent, lacks both allergic potential and renal toxicity. Moreover, its low viscosity (1/400 that of iodinated contrast) provides unique qualities useful in both angiographic diagnosis and intervention.

Currently, CO_2 has been used as an intravascular alternative to iodinated contrast material for over three decades. Although it is dissimilar to routine contrast and requires a unique delivery system, it has been routinely used successfully as an adjunct to liquid contrast in patients in renal failure and those allergic to contrast. It is not the quintessential contrast agent and often requires more meticulous manipulation to produce the desired images. In the past, fool-proof, safe delivery of CO_2 was very difficult. However, a converted fluid management plastic bag delivery [Q8] system has now been used for the last 14 years, and is both faster and easier than injecting iodinated contrast. More importantly, the delivery system is almost completely fail-safe.[1]

With the advent of MR angiography and CT angiography, the diagnostic use of CO_2 digital subtraction angiography (DSA) has declined significantly. Recently, however, there has been resurgence because of gadolinium-induced nephrogenic systemic fibrosis (NSF) in patients with advanced reduction in renal function.[2] Therefore, if an angiographic examination is necessary in patients with renal impairment, the choices may potentiate either NSF from the gadolinium- or contrast-induced nephropathy from iodinated contrast. Alternatively, CO_2 DSA can be used safely in many of these cases. Additionally, intravascular CO_2 use has also increased because of the recent discoveries of more useful applications, as well as the increasing complexity of cases requiring greater contrast doses. CO_2 can be used in unlimited doses without jeopardizing the kidney.

UNIQUE PROPERTIES OF CO_2

CO_2 is invisible, buoyant, compressible, and nonviscous. These unique properties can provide

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distinct advantages and disadvantages in angiographic procedures. As an endogenous gas, it is nonallergic, nonnephrotoxic, and its viscosity is 1/400 that of iodinated contrast and, therefore, can disseminate more readily than liquid contrast. Because it is a gas, CO_2 is invisible, and air contamination must be avoided. Moreover, even without contamination, administration of the gas into the cerebral vessels is an absolute contraindication.

As opposed to liquid contrast, CO_2 does not mix with blood. It is buoyant and will rise to the nondependent portion of a large diameter vessel. Therefore, to assure accurate representation of a vascular structure the entirety of blood in the imaged vessel should be displaced. Incomplete displacement can lead to spurious imaging (i.e. smaller vessels or larger percentage stenoses).

Because CO_2 is compressible, steps must be taken to avoid excessive volumes and explosive delivery. If compressed, a 20-cc syringe can hold 200 ccs of CO_2. This exposes the patient to possible excessive and explosive delivery, which can lead to undesired reflux and rapid expansion of vessels, which could cause untoward symptoms, such as pain, nausea, and vomiting following CO_2 injection into the abdominal aorta, celiac, or superior mesenteric artery. Advantages [Q9] and disadvantages of CO_2 are presented in **Box 1**.

Box 1
Advantage and disadvantages of CO_2

Advantages

Nonallergic

Nonneprhotoxic

Low viscosity—easily delivered via microcatheter, between catheter and guidewire, flows readily into bleeding sites and from paremchymal injections into the venous system

Can inject larger volumes via small catheter with reflux resulting in CO_2 filling of proximal vessels

Cost

Disadvantages

Invisible, allowing potential for undetected contamination

Requires a unique delivery system

Gas is compressible

Contraindicated in the cerebral and coronary circulation and thoracic aorta

Bowel gas and motion can reduce or eliminate image quality

Obtaining quality diagnostic images may be more labor intense

WHY SHOULD I LEARN HOW TO USE CO_2?

Presently, with advances in delivery and imaging systems, CO_2 can be safely used in patients at risk for adverse reactions to iodine- or gadolinium-based contrast agents for most diagnostic and interventional procedures. In addition, CO_2 has definite advantages for many interventional procedures. The authors' 38-year experience in over 6,000 patients and review of the literature have shown that CO_2 is the only safe angiographic contrast for patients with a history of serious allergic reactions to iodinated contrast media and in patients with renal failure. Contrast-induced nephropathy (CIN) and NSF are serious complications that should be avoided. As discussed in detail elsewhere in this issue of *The Clinics*, these complications are associated with marked increase in morbidity and mortality of the affected patients.

LACK OF RENAL TOXICITY OF CO_2

Animal studies in canines showed that selective CO_2 injection in renal arteries had no significant effect on renal function or histology, with the exception of one dog that sustained a minimal degree of acute tubular necrosis. This animal endured multiple selective renal CO_2 injections while the dog's kidney was positioned above the injection catheter, resulting in trapped CO_2 and minimal ischemia.[3] A more recent study in rats[4] comparing renal cortical and medullary blood flow with CO_2 versus ioxaglate showed that the marked decrease in medullary flow with ioxaglate was absent with CO_2.

As far as the authors are aware, there are no reports in the published literature of CO_2 causing CIN. The authors' clinical experience in using CO_2 for angiography in patients with renal failure and renal transplant patients (over 100 patients)[5] has been extremely encouraging, with no technical complications or important deterioration in renal function. In renal transplant patients, CO_2 angiography is more effective because of the anterior position of the transplanted kidney, which allows good filling of the renal arteries with CO_2, much better than in the native kidney, which has a posterior-oriented position.

The right renal artery always fills with aortic injections; however, the more posterior located left renal artery occasionally is difficult to image. Using the plastic bag system injecting smaller volumes (30 cc) of CO_2 with nonexplosive delivery and an end-hole catheter, the left renal artery is much more frequently seen (**Fig. 1**). If, after one or two abdominal injections, the left renal artery is not seen, the authors either selectively catheterize this artery or elevate the left side of the patient. If these maneuvers are not successful, placing the patient in the right lateral decubitus position always results in filling the left renal artery with CO_2 if it is patent.

IMPORTANT FEATURES OF CO_2

Low Viscosity

The low viscosity of CO_2 increases its sensitivity in detecting acute hemorrhage, arteriovenous shunting, collateral vessels, and arteriovenous shunting in tumors. The low viscosity also allows easy administration of CO_2 into microcatheters and permits injection between the catheter and guidewire, eliminating the need to remove the guidewire from the target organ after intervention. This makes CO_2 an ideal contrast agent for interventional procedures, such as angioplasty and stent placement and verifying the exact position of the needle or catheter before a larger catheter or device is placed in a potentially dangerous location. With wedged hepatic and splenic arterial injection and injection into the hepatic parenchyma and splenic pulp, the low viscosity facilitates visualization of the portal veins without causing histologic damage.

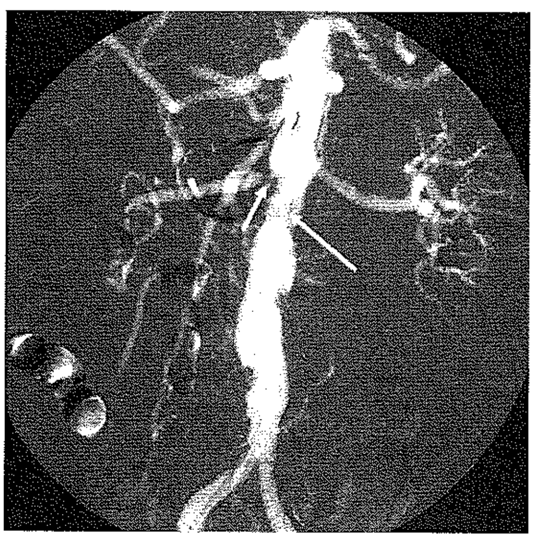

Fig. 1. Atherosclerosis of the abdominal aorta. Abdominal aortogram (DSA technique) with 30 cc of CO_2 shows markedly irregular wall and narrowing (*long arrow*) of the infrarenal aorta. There is a severe stenosis at origin of the right renal artery (*short arrow*). The left renal artery is patent, with good distal perfusion.

Reflux

The gaseous property of CO_2 results in central reflux from the point of administration. This permits central assessment of the feeding vessels without the need for catheter withdrawal to improve central visualization that might be required with iodinated contrast agents. This is exemplified by the placement of renal stents and the need to identify the appropriate position of the ostium and stenosis. Using CO_2 injection through the sheath with the stent-mounted balloon catheter in place, and between the balloon catheter and guide wire, the location of the more central stenosis can be assessed and the stent positioned with precision.

POTENTIAL COMPLICATIONS OF CO_2

Excessive Volumes

Injecting excessive volumes of CO_2 is probably one of the most serious potential complications and might lead to drop in blood pressure, bradycardia, and elevation of the ST segments in EKG. The authors experienced this complication only once with one patient after inadvertently injecting over 3,000 cc of CO_2 during a transjugular intrahepatic portosystemic shunt (TIPS) procedure. The patient was placed in the left lateral decubitus position with immediate normalization of vital signs and EKG. With the right side elevated, the buoyant gas shifted to the higher right atrium and the blood flew under the gas to perfuse the pulmonary artery. The patient's survival can be attributed to the extreme solubility of CO_2. In another patient, after injection over 2,000 cc of CO_2 into an abdominal aortic aneurysm (AAA), the patient developed severe diarrhea, with follow-up endoscopy demonstrating colonic ischemia. The trapped CO_2 prevented flow into the inferior mesenteric artery (IMA) for over 1 hour and the gas, which does not mix with blood, produced a barrier preventing normal collateral blood flow. Fortunately, the colon was found to be normal 2 weeks later during the AAA surgery.

More recently, the authors have performed an extensive venous study in 20 swine,[6] injecting the equivalent of 50 cc to 600 cc of CO_2 in man. There were no untoward events and little or no changes in blood gases, pH, or pulmonary or arterial blood pressure when the equivalent of 100 cc was injected. However, when an amount comparable to 600 cc was injected, there was one death. It was noted that as the volume of CO_2 was increased, the pulmonary pressure increased incrementally. Although the authors have not experienced any cerebral complications, theoretically, if the pulmonary pressure increases markedly, a potentially patent foramen ovale may open and the CO_2 could flow into the left atrium and subsequently into the aortic arch.

To prevent any possibility of injecting excessive volumes of CO_2, the patient should never be connected directly to the CO_2 cylinder. The cylinder typically contains over 3 million cc of compressed gas at very high pressure. If a stopcock is turned in the wrong direction, the cylinder can unload directly into the vascular system. Even a syringe connected directly to a cylinder can contain an excessive volume. Because of Boyle's law, the volume of CO_2 decreases with increased pressure. If the cylinder's CO_2 regulator is set at a high psi, a hand syringe will be filled with a higher volume of CO_2. If a finite-volume plastic bag delivery system is used, there is no possibility of injecting excessive or inaccurate volumes. When the CO_2 source (plastic bag) is at atmospheric pressure (flaccid plastic bag), whatever volume is aspirated from the source will be the exact volume in the syringe.

AIR CONTAMINATION

An uncompromised closed-delivery system is crucially important to avoid air contamination. [Q10] Cho and colleagues[7] have shown that if the stopcock of a syringe remains open, the extremely diffusible CO_2 in the syringe is quickly replaced with room air, regardless of the syringe's position. The differential in partial pressure between CO_2 in the syringe and in the room air causes room air to diffuse into the syringe with the open stopcock at a rate of 0.2 cc per second, with air replacing the majority of the CO_2 within 20 minutes. Thus, it is very important to use a leak-proof closed system to prevent potential lethal air complications.

Indications of CO_2 Angiography

CO_2 is used primarily for angiography, with the exception of the cerebral or coronary circulations in patients with iodinated contrast allergy and renal failure. It permits multiple, safe injections for renal transplant evaluation and intervention. CO_2 is also very beneficial in complex interventional procedures, where it can be used alone or in combination with iodinated contrast to minimize the risk of renal complications and volume-overload problems in patients with congestive heart failure. Because of the rapid dissolution and one-pass elimination by the lungs, there is no maximum CO_2 dose when less than 100 cc is injected every 2 minutes. In addition, using the closed plastic bag [Q11] delivery system, CO_2 can be very expediently injected as a contrast agent in any luminal structure, such as the biliary tree, urinary tract, abscess cavity, and fistula.

The very low-viscosity of CO_2 can occasionally provide additional information, otherwise not obtainable with iodinated contrast. In addition to the previously mentioned advantages of the low viscosity of CO_2, the authors have noted that when CO_2 was used during embolization the tumors have appeared totally ablated with liquid contrast but were only partially embolized, as noted with subsequent CO_2 injections. Because embolization procedures alone can exacerbate renal failure and many are high risk,[8] the authors are routinely using the many unique properties of CO_2 for most oncologic procedures. For TIPS procedures (**Fig. 2**),[9] evaluation of portal

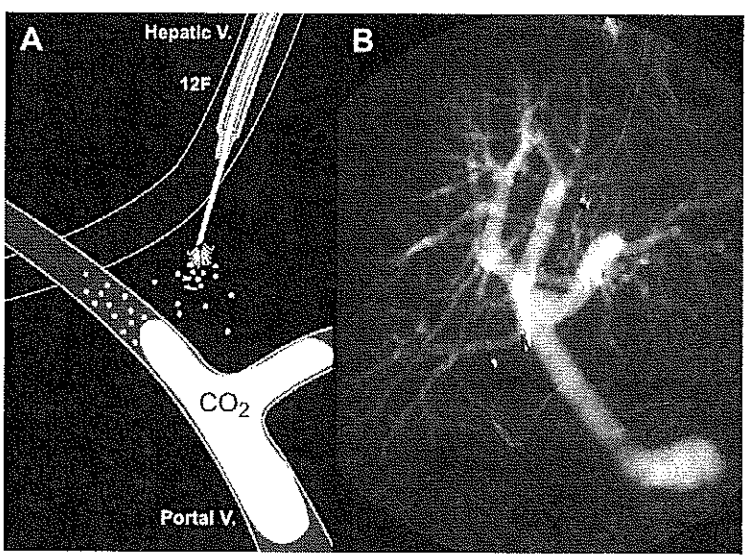

Fig. 2. CO_2 prenchymal hepatic injection with fine needle for TIPS. (*A*) Diagram of portal vein targeting: 21-gauge needle advanced 1 cm through hepatic vein into parenchyma, injecting 30 cc of CO_2 forcefully. (*B*) Entire portal system filled, including extra hepatic portal vein.

hypertension and occlusion, and portal vein embolization, the low-viscosity also permits filling of the portal system much more reliably than iodinated contrast, either by wedged hepatic vein injections, direct injections into the parenchyma of the liver, or via a fine-needle in the splenic pulp[10] and injection into peripheral hepatic arteries. CO_2 passes very easily through the sinusoids into the portal system against the direction of blood flow. CO_2 is also ideal for the filling of central veins from distal injection sites (25-gauge needle in hand vein) and frequently, in patients with venous thrombosis, it is the only contrast that will opacify the more central system, permitting accurate assessment and successful intervention (**Fig. 3**). It can be used effectively for inferior vena cava (IVC) filter placement, even at the bedside.[11] There is a recent report of CO_2 use for intraosseous venography in percutaneous vertebroplasty.[12]

Recently, CO_2 has been used in high-risk endovascular aneurysm repair procedures to reduce CIN and has been effective in demonstrating endoleaks.[13–15] This was underscored in a case where a covered stent was placed to repair a lacerated superficial femoral artery (**Fig. 4**). The leak was detected only after CO_2 was employed.

ABSOLUTE CONTRAINDICATIONS

Studies of CO_2 carotid injections in rats, dogs, and rabbits[16,17] have suggested that CO_2 could be neurotoxic. Because of possible neurotoxicity and cardiac ischemia,[18] the cerebral and coronary arterial circulation should never be exposed to CO_2. The authors never inject CO_2 in the prone position because the buoyancy will fill spinal arteries and may cause spinal cord ischemia. Never administer CO_2 with the patient's head in an elevated position because the buoyant CO_2 can flow countercurrent and cause possible reflux into the cerebral circulation. Because of the possibility of central reflux into the cerebral circulation, CO_2 should not be used to evaluate the arterial

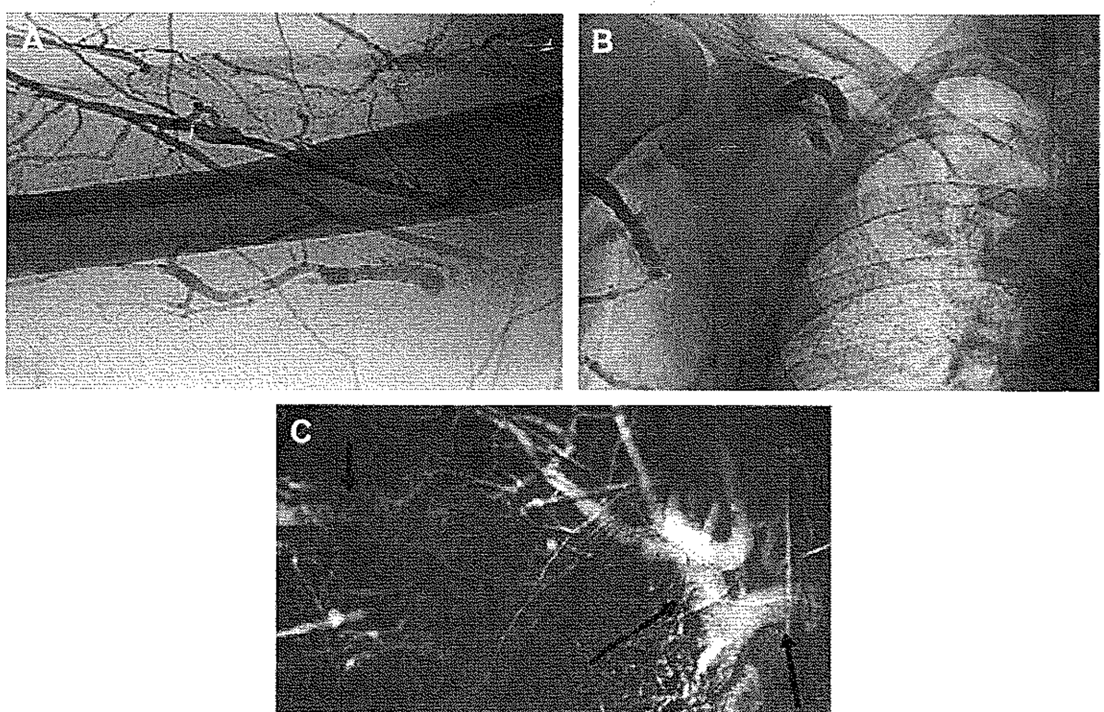

Fig. 3. Right axillosubclavian vein thrombosis in a 31-year-old man with right arm swelling and recent pulmonary embolism. (*A*) Right arm venogram with iodinated contrast shows no filling of the brachial or axillary veins secondary to thrombosis. (*B*) Only a few isolated veins are filled in the shoulder and axilla. (*C*) CO_2 venogram again shows occlusion of the axillary and subsubclavian veins with acute thrombus in cephalic vein (*shorter arrow*). There is excellent filling of the right and left innominate veins (*long arrows*) and the superior vena cava (SVC) secondary to the low viscosity of CO_2, which guided a successful catheter-directed fibrinolysis.

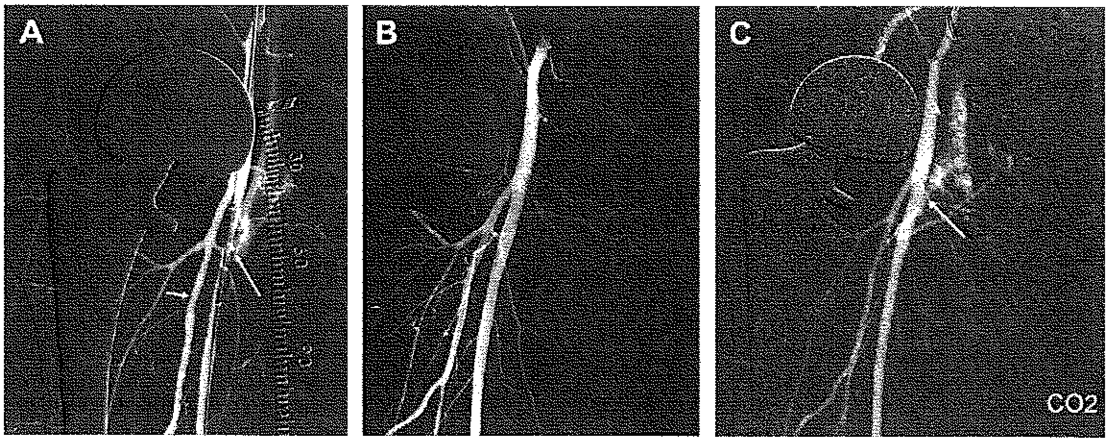

Fig. 4. Endoleak seen only with CO_2 in a patient with a lacerated femoral artery. (*A*) Injection of 10 cc of CO_2 as the covered stent catheter was positioned at the bleeding site of a superficial femoral artery laceration with shunting into the femoral vein (*longer arrow*). After the stent was deployed, the hemorrhage stopped. Note the irregular wall along the deep femoral artery (*shorter arrow*) representing stationary arterial wave. (*B*) One day after stent placement, the patient clinically was massively bleeding; however, injection of 20 cc of iodinated contrast showed no evidence of extravasation. (*C*) Injection of 10 cc of CO_2 immediately after the iodinated injection showed type one endoleak (*arrow*), which was treated successfully by over-dilating the stent graft.

limb of dialysis fistula. It can, however, be used cautiously for evaluating the venous limb.

RELATIVE CONTRAINDICATIONS

The authors do not use CO_2 in conjunction with nitrous oxide anesthesia during CO_2 studies, because in animals it has been found that partial pressure differentials of the nitrous oxide saturated in the soft tissues will diffuse into the CO_2 bubble, increasing its volume by approximately six times. The CO_2 bubble may increase from 100 cc of injected CO_2 to 600 cc, which in the venous system may cause significant problems (vapor lock of the pulmonary artery). If only small volumes of CO_2 are required, nitrous oxide could be used safely if there is no alternative contrast available.

The authors have used CO_2 in hundreds of patients with pulmonary compromise without complications; however, the volumes are reduced and a greater delay between injections allows more time for the CO_2 to be absorbed.

In patients who present with intestinal ischemia or an AAA, the authors reduce the number of injections and volumes and allow more time between injections, permitting absorption of the CO_2. If the gas remains trapped in the aneurysm, the patient's position is changed to free the gas.

CO_2 DELIVERY

The delivery of CO_2 has evolved over the past 38 years. It has included many different manual delivery systems, with or without manifolds, as well as more than five dedicated automated controlled systems. Many of these were not user friendly and never approved by the Food and Drug Administration. Previously, during bench testing of these devices, the authors discovered multiple potential complications but experienced a few clinical complications, which were short-lived.

After more than 20 years of experimenting with many different systems, the authors introduced a plastic bag system, as well as a technique of [Q12]
delivery extrapolated from their experience with computer-controlled injectors. The plastic bag system has proven to be very user friendly and actually much faster and easier than liquid angiographic injectors or hand delivery systems. If assembled correctly, its only disadvantage is the ease of making rapid injections in regions where ischemia could occur if injections are made more frequently, without time for the CO_2 to reabsorb.

Because the plastic bag, which only contains 1,500 cc at atmospheric pressure (if it is not distended), there is no possibility of inadvertently injecting excessive volumes and virtually no probability of air contamination if one uses the system properly. The authors have used this system for over 12 years without complications. In the last 8 years, improvements have been instituted that further reduce the probability of air contamination (**Fig. 5**).[1]

The authors feel that it is extremely important to employ a disposable aluminum cylinder containing United States Pharmacopeia (USP) grade

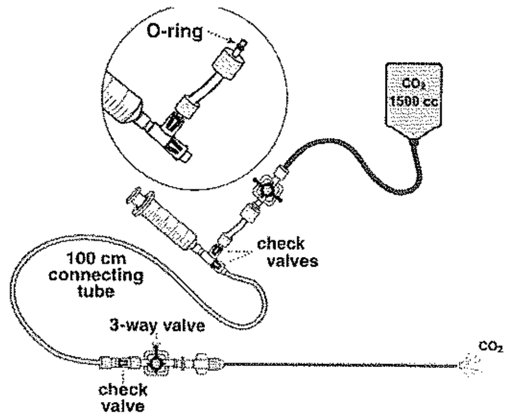

Fig. 5. Current plastic bag delivery system showing details of the O-ring gas fitting, which prevents air aspiration during delivery syringe filling. The one-way check valves eliminate stopcock manipulation and prevent back bleeding into the angiographic catheter. The distal three-way stopcock is used to clear the air from the distal fittings and inject drugs or iodinated contrast, keeping the system closed at all times. The authors now flush the catheter every 3 to 5 minutes with CO_2 instead of saline.

[Q13] (99.99%) CO_2 with high purity gas fittings and regulators. The cylinder is supplied with a special spring-loaded push-button valve. These disposable cylinders are individually checked for CO_2 [Q14] purity. The authors also use a 0.2-micron filter to eliminate any particulate or microbial contaminates. This filter is attached to the spring-loaded push-button valve. The bag will only fill when the button is depressed. If a cylinder is used without this spring valve, which closes automatically, the cylinder may empty in a few hours if the main valve is inadvertently left partially open.

The present system is very user-friendly, requiring less than 3 minutes to fill and flush the CO_2 bag. The bag is filled and emptied three times via a short sterile connecting tube and a standard three-way valve connected to the submicron filter. Sterility is maintained by keeping the bag on the angiographic table to be sure the delivery component is securely connected to the plastic bag. It is recommended to initially overfill the bag one time, manually squeezing to check for a gas leaks. The bag is connected to the delivery system, which has an O-ring gas fitting and multiple one-way check flow valves, which obviate stopcock manipulation. The distal check valve inhibits blood from filling the angiographic catheter. Repeated injections can be made very rapidly simply by aspirating and injecting. All the connections are glued by the manufacture with a 100-cm connecting tube between the delivery syringe and the distal high-pressure three-way stopcock. The extension tube permits the operator to stand behind a protective radiation barrier during the injections. The distal high-pressure three-way stopcock, which is connected to the angiographic catheter, is used to remove air from the stopcock by back-bleeding the angiographic catheter and then closing the stopcock to the patient and flushing the stopcock with CO_2 three times, resulting in a pure CO_2-blood interface. After a forceful injection of 5 cc of CO_2 is made to clear the blood from the catheter, the system is ready for multiple nonexplosive CO_2 injections and imaging. The high-pressure three-way stopcock can also be used to administer drugs or inject iodinated contrast, either by hand or angiographic injector. It can also be used to discharge excess CO_2 from the delivery syringe, maintaining a closed system without chance of air contamination at all times. The distal three-way stopcock is never used for CO_2 delivery because if the port closest to the plastic bag is open, air will be aspirated as the syringe is filled. This is the only way air can be inadvertently injected.

The system can also be used for interventional procedures if a specialized side-arm O-ring fitting is attached. This permits injection of the low- [Q15] viscosity CO_2 between the guidewire and the catheter, or guidewire and any size needle. Injection of relatively large amounts of CO_2 between the guidewire and catheter permits accurate visualization of vascular anatomy before, during, and after interventional procedures (balloon dilatation, stent placement, or placement of larger potentially dangerous catheters, and so forth). A large syringe and considerable force is required to purge the liquid from the small space between the catheter and the guidewire or needle. There is a prolonged delay of many seconds; however, when the liquid is cleared, the syringe's plunger moves forward easily and subsequent injections can be made rapidly with little effort.

Hospital stores can provide a CO_2 cylinder that is filled with pure USP grade gas; however, frequently the tanks are cast iron and may contain rust and other contaminates. Again, the authors strongly suggest obtaining a disposable cylinder, with gas-type fittings, that has been individually tested for purity. When a new cylinder is delivered, 15 cc to 20 cc of CO_2 should be injected into the venous system imaging the pulmonary artery, to be absolutely sure that there is no air contamination. The CO_2 will trap in the anterior-located main pulmonary artery and will absorb within 15 to 20 seconds. It is easily seen with routine fluoroscopy; however, the pulmonary artery can be more accurately visualized with DSA (**Fig. 6**). If it remains longer, there is a possibility of air contamination.

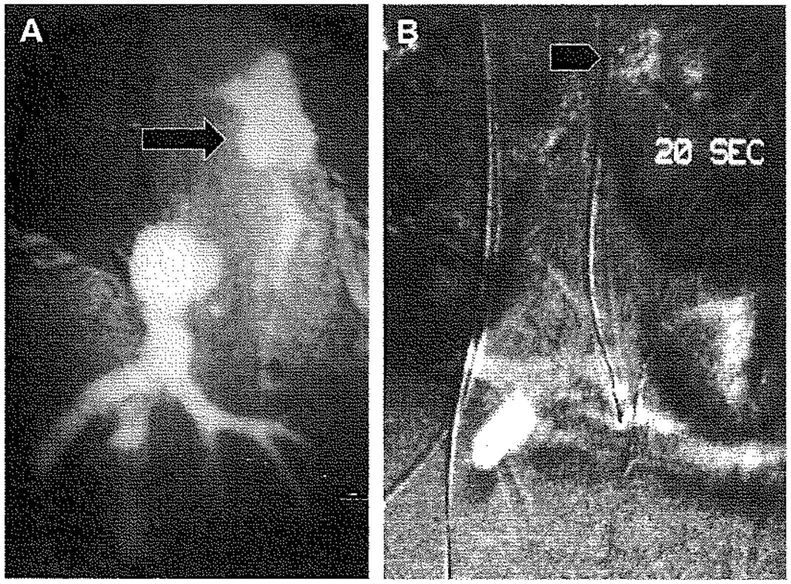

Fig. 6. Method to detect possible air contamination of CO_2. (*A*) For TIPS procedure or any venous study when multiple injections are anticipated, a hepatic vein or any vein is injected imaging the pulmonary artery. Initially CO_2 traps in most anterior main pulmonary artery (*arrow*). (*B*) After 15 to 20 seconds, the majority of CO_2 will dissolve because of extreme solubility of CO_2 in blood (*arrowhead*). If CO_2 remains longer than 20 seconds, one should suspect air contamination.

A closed system without any possibility of valves connecting to the exterior is absolutely necessary to prevent air contamination. With the present plastic bag system, it is extremely important to connect the bag to the delivery system properly. A 30 cc to 60 cc Luer-lock delivery syringe is connected to the end where the O-ring gas fitting is attached. A label stating delivery port is attached. After the plastic bag is filled, the delivery system is also flushed three times. Do not add stopcocks and never connect the delivery system to the CO_2 cylinder. There is never a need to refill the plastic bag (1,500 cc is always more than enough). To be sure there are no leaks in the delivery connections, the one-way bag's stopcock is closed and the delivery syringe is forcefully aspirated. If there is a leak in the tubing or the fittings, the syringe will fill with room air. If the system is sealed, the operator is able to only retract the syringe's plunger a short distance.

During the last 12 years the authors have not flushed the catheter with saline because CO_2 plus water produces carbonic acid and discomfort. The catheter is flushed every 2 to 5 minutes with CO_2.

General principles for CO_2 delivery are as follows:

Be absolutely sure that you are using a pure source of CO_2 USP (99.9%). CO_2 may be used to fill the cylinder; however, the cylinder itself may be contaminated with rust, bacteria, methane or some other contaminate. It is recommended to use a disposable cylinder individually tested for purity.

Use a delivery system where there is no possibility of injecting excessive volumes of CO_2. The flaccid plastic bag prevents inaccurate and inadvertent injections of excessive volumes.

Use a closed system to prevent air contamination. The CO_2 cylinder, which contains over 3,000,000 cc, should never be connected to the closed system. Always maintain the closed integrity of the system. Never use additional stopcocks. When using the plastic bag delivery system, be sure that all ports are closed and that the delivery syringe is attached adjacent to the gas-fitting port for the plastic bag.

Prevent explosive delivery. Purging liquid (blood or saline) from the angiographic catheter prior to CO_2 delivery results in a more consistent delivery, with less discomfort and less breakup into small bubbles.

Initially inject small volumes of CO_2 (30 cc for aortograpy and 5 cc to 10 cc for most selective injections) and increase or [Q16] decrease the injection rate and volume depending upon the vascular bed that is being imaged.

Wait 2 minutes between injections, depending upon the volume injected and ischemic tolerance of the vascular bed. In high-risk areas, such as abdominal aneurysms, intestinal ischemia, or severe pulmonary compromise, the authors suggest waiting approximately 5 minutes between injections.

In poor flow conditions, elevate the area of interest (legs 10° to 15°, renal arteries 30° to 45°), and if the renal arteries cannot be filled, use the cross-table decubitus position. Alternatively, placing the catheter's tip close to the area of interest will also improve filling.

Injecting vasodilators (nitroglycerin 100 mcg [Q17] to 250 mcg) intra-arterially into the vascular bed prior to CO_2 delivery improves filling considerably.

Any type radio-opaque-tipped catheter can be used; however, a single end-hole catheter causes less breakup into small bubbles.

DSA imaging: Use a 1,024 × 1,024 high-resolution system with a high-framing rate (4–6 frames per second). Most equipment manufacturers provide a software package that increases photon flux to improve visualization of this low-negative contrast agent, and a stacking program, which integrates multiple frames to produce a single diagnostic composite image.

If the operator has not used the delivery system previously, the following recommendations are suggested:

Assemble the bag and delivery system and practice injecting the CO_2 via a catheter into a container filled with water. Inject both with the angiographic catheter and, for interventional procedures between the guidewire and the catheter, between the needle and a guidewire using a specialized [Q18] side-arm O-ring fitting.

The integrity of the connection to the bag should be tested frequently by closing the stopcock to the plastic bag and forcefully aspirating.

After one feels comfortable with the system's setup and the delivery technique, the DSA imaging should be tested with the injection of 20 cc of CO_2 into an iliac or a peripheral vein. If the images demonstrate poor contrast (gray), the angiographic equipment applications person should be contacted to change the acquisition parameters. Do not perform your first procedure when iodinated contrast cannot be used.

Furthermore, to ensure the purity of every new CO_2 cylinder, the authors suggest making a venous injection (SVC, IVC, right atrium, or even a peripheral vein) and imaging the pulmonary artery to see if the trapped CO_2 disappears from the pulmonary artery within 15 to 20 seconds. If it remains longer, air contamination is a possibility. Injection of 20 cc of room air is not lethal; however, multiple large volume injections may be disastrous.

Current procedural parameters are as follows:

Runoff (pelvis and lower extremity)

a. Initially, obtain both leg runoffs with the catheter in the distal aorta.
b. Inject 20 cc to 40 cc in 1 second.
c. Elevate the feet 10° to 15° for optimal filling and obtain images of pelvis, thigh, knee, lower legs, and feet.
d. If the IMA is filled and the patient experiences pain, urge to defecate, or has symptoms of intestinal ischemia, the injections should be aborted or the injections should be made more distally in either femoral artery, where the IMA will not be filled.
e. If there is no stacking program, a longer injection (approximately 60 cc over 2 to 3 seconds) is necessary.

Single leg runoff with selective common iliac or more distal femoral arterial injections produce better filling and are unlikely to cause intestinal ischemia. This is the authors' presently preferred method.

a. Perform a selective (antegrade is preferable) injection of the common femoral or more distal arteries. Positioning can be either "over-the-hill" or antegrade placement of a 4 French catheter in the contralateral extremity. If distal filling is suboptimal, a microcatheter can be passed through the antegrade catheter and advanced as distally as possible (**Fig. 7**). For ipsilateral vessels, retract the catheter to the distal external iliac artery.
b. With stacking, inject 20 cc in 2 seconds. If filling remains poor, inject 20 cc to 40 cc over 3 to 4 seconds. [Q19]
c. Without stacking, begin with 20 cc to 40 cc over 3 to 4 seconds.
d. Intra-arterial nitroglycerine, 100 Fg to 150 Fg prior to injection.

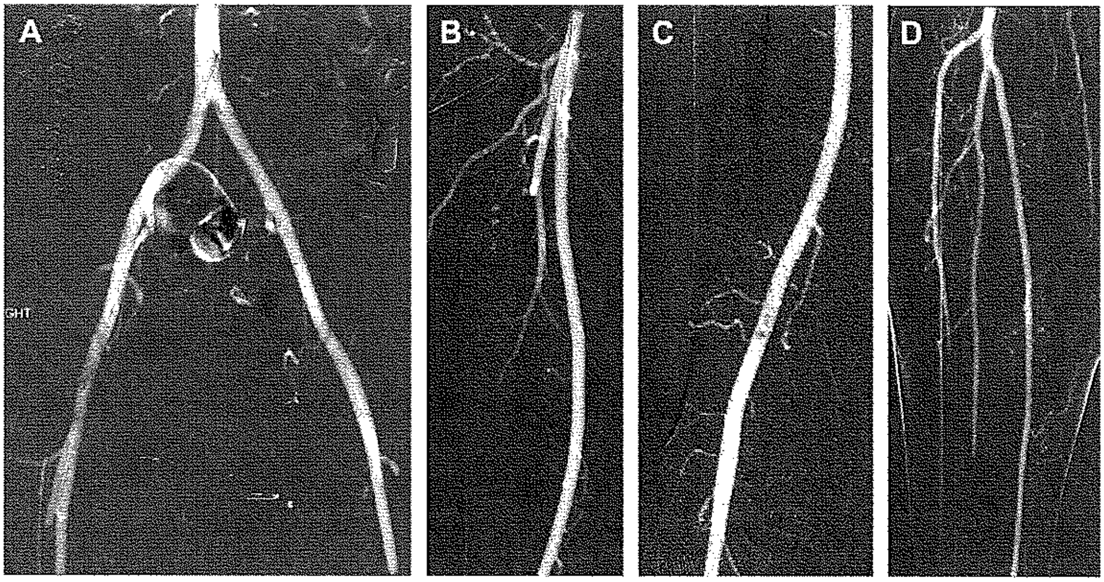

Fig. 7. Coaxial catheterization for preoperative lower extremity arteriogram in a 48-year-old man with ameloblastom of the mandible. [Q23] (*A*) Normal CO_2 pelvic arteriogram using an end-hoe catheter (shepherd's hook catheter). (*B*) Right superficial femoral arteriogram was performed with the shepherd's hook catheter positioned in the proximal superficial femoral artery. (*C*) The 3-French microcatheter was passed coaxially for the popliteal arteriogram. The popliteal artery is normal. (*D*) The popliteal artery and its trifurcation branches are normal. Both tibial and peroneal arteries are patent. The volume of CO_2 injected, ranged from 20 cc to 30 cc every 2 seconds.

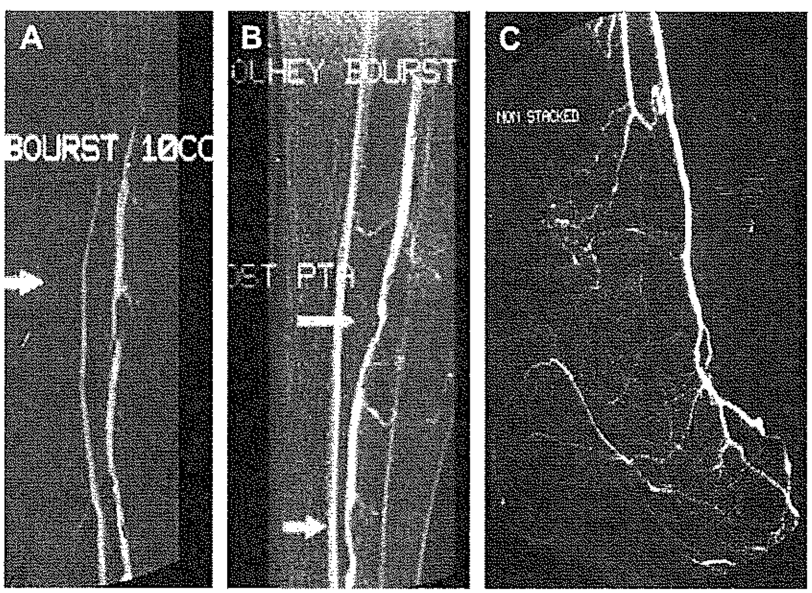

Fig. 8. CO_2-guided anterior tibial angioplasty via the contralateral approach. (*A*) A 10-cc CO_2 injection via a 300-cm [Q24] coronary angioplasty catheter demonstrates a 99% stenosis of the mid-anterior tibial artery and 50% stenosis of its [Q25] lower one-third. (*B*) With a specialized side-arm O-ring fitting multiple CO_2, injections were made with the 0.018-inch guidewire positioned distal to the lesions. Postangioplasty image shows only very minimal residual stenosis (*arrows*). (*C*) Good filling of the foot and of dorsalis pedis artery and other unnamed collaterals, again injecting between the guidewire and the balloon catheter. No vasodilators or stacking was required. If iodinated contrast were used, very large amounts of contrast for each injection would have been required via a large guiding catheter at the aortic bifurcation.

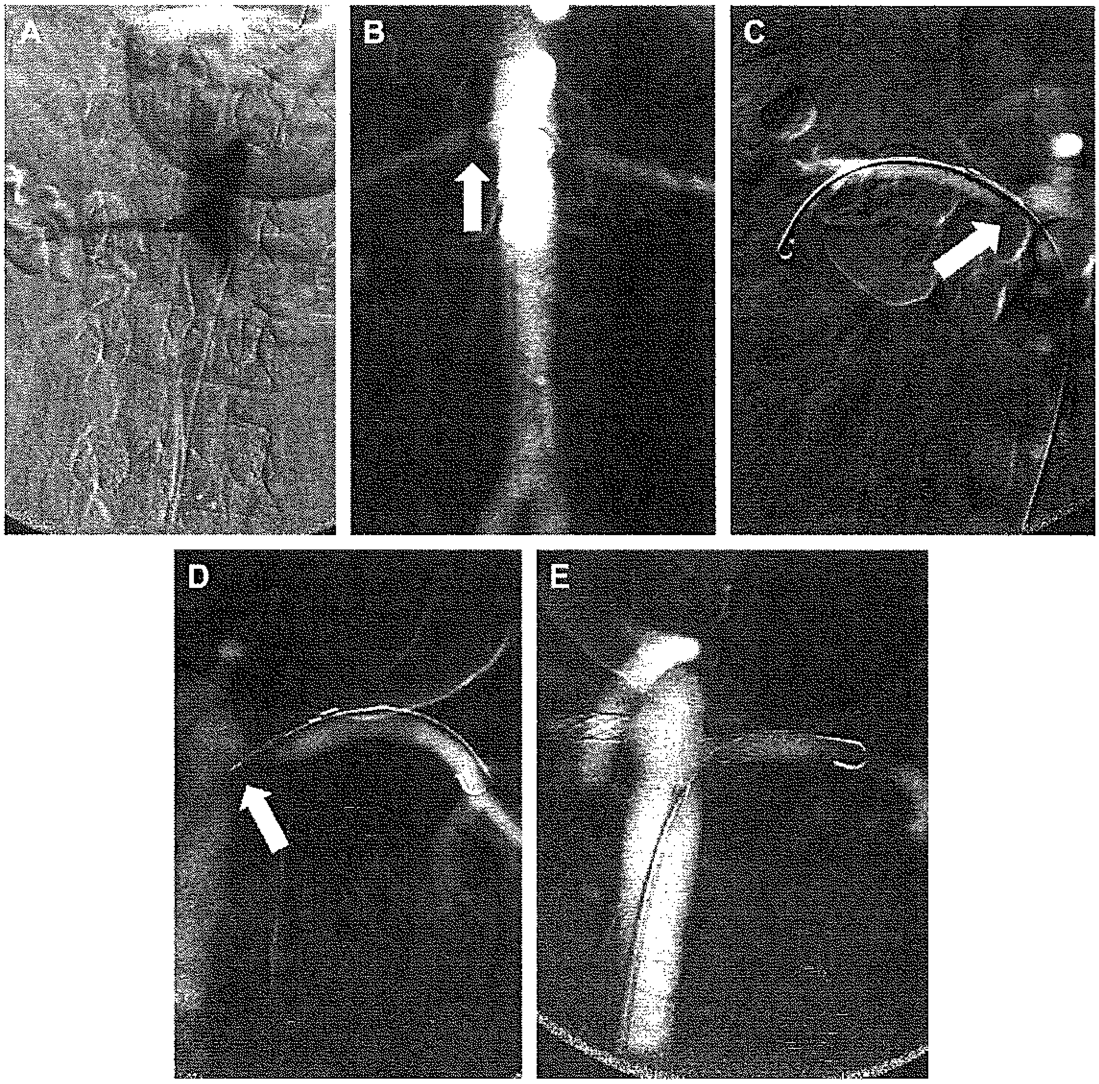

Fig. 9. Bilateral renal stent placement. (*A*) Selective iodinated contrast injection of the right renal artery shows a tight stenosis without any filling of the distal renal arteries. (*B*) A similar injection of 20 cc of CO_2 shows the tight stenosis plus more distal filling of the right renal artery and a 50% stenosis of the origin of the left renal [Q26] artery. (*C*) Injection between the stent catheter and the Rosen wire with reflux into the aorta demonstrates that the stent has advanced too distally (*arrow*). (*D*) Injection between the Rosen wire and the stent catheter demonstrating that the stent has been advanced several millimeters too distally into the left renal artery (*arrow*). (*E*) Final CO_2 injection between the guiding catheter and the Rosen wire showing excellent position and patency of both stents.

Aortogram

a. Twenty years ago, the authors injected 200 cc in 2 seconds with a computer-controlled injector, with occasional nausea, abdominal discomfort, urge to defecate, and more nausea when glucagon was used.
b. During the last 14 years, with the nonexplosive plastic bag system the authors have reduced the volume to 30 cc in half a second with less nausea, and if bowel gas obscures the image glucagon may be used.
c. The left renal artery is more difficult to image and may be better visualized by elevating that side. If necessary, a selective injection with a shepherd hook catheter (10 cc–20 cc CO2 in 1 second) can be performed. Do not inject with patient in the prone position because the lumbar arteries will always fill with potential unknown neurotoxic effects.

d. Selective injections of the visceral arteries commonly require 5 cc to 30 cc in 1 to 2 seconds.

Venous: always image the pulmonary artery after the first injection to rule out air contamination (persistent gas). Normally, CO_2 should disappear after 10 to 20 seconds.

a. SVC and IVC: 20 cc to 50 cc in 1 to 2 seconds.
b. Subclavian: 20 cc to 40 cc in 1 to 2 seconds.
c. Peripheral veins: 15 cc to 25 cc, 4 to 8 seconds, usually with 22-gauge Angiocatheter. Rapid injection precipitates pain.

Interventional procedures

a. Using a specialized side-arm O-ring fitting, CO_2 can be injected between the guidewire and needle or catheter
b. Use a 20 cc to 50 cc Luer-locked syringe. With a smaller syringe, CO_2 will simply compress without injecting.
c. Wait 5 to 10 seconds for CO_2 to exit the catheter. CO_2 will compress as it purges fluid from the catheter.
d. After purging, subsequent injections require less pressure and delay.

For angioplasty, stent placement, and fibrolysis (renal, superior mesenteric artery, iliac) over the aortic bifurcation with distal intervention (**Fig. 8**), CO_2 can be injected between the guidewire and the stent catheter to verify its exact position before the stent is deployed. For renal stent placement, the extreme buoyancy of the gas always results in reflux into the aorta, which visualizes the exact positions of the renal artery ostium (**Fig. 9**).

TIPS: Using any needle, inject 30 cc of CO_2 into the hepatic parenchyma for visualization of the portal vein throughout the various steps of the procedure. With the guidewire in place, CO_2 can be injected between the needle and the guidewire to verify the needle entry site and determine stent positioning.

SUMMARY

Clinical experience with the use of CO_2 as a contrast agent has shown that it is safe, and in patients with renal impairment can prevent CIN and the associated morbidity and mortality of this complication. In addition, CO_2 contrast-enhanced examinations may offer more diagnostic information than standard techniques with iodine-based contrast agents in several clinical applications. Equipment advances and competence in using CO_2 delivery systems made imaging with CO_2 a reliable technique for diagnostic and interventional procedures. Utilization of both CO_2 and liquid contrast also increases the safety and efficacy of many procedures.

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