Carbon Dioxide Digital Subtraction Arteriography

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Arterially injected carbon dioxide coupled with digital subtraction fluoroscopy consistently produced clinically useful images of arteries in 17 patients. Occasionally good parenchymal images and venograms were also obtained. The buoyancy of the gas requires that the area of interest be in a nondependent position to insure good arterial perfusion. The exceedingly low viscosity of gas should permit delivery of the CO₂ via microcatheters which would lessen the risk of arterial injury. CO₂ does not produce hypersensitivity reactions and, even in large volumes, should not produce the discomfort associated with iodinated contrast material.

In 1971, I inadvertently injected 70 cm³ of room air into a celiac artery with unexpectedly good negative contrast delineation of the arterial tree (Fig. 1) and surprisingly without untoward effects. Since injection of 50 cm³ of CO₂ into the right atrium for detection of pericardial effusion was established as a safe procedure [1–6], I proceeded to use CO₂ for abdominal, visceral, renal, and extremity arteriography in 10 selected patients, most of whom were hypersensitive to iodinated contrast material. Although intraarterial injection at rates of about 25 cm³/sec for a total of 50–60 cm³ caused no discomfort or untoward reactions, the gas produced suboptimal display of distal arteries (Fig. 2). No capillary or venous phase was imaged.

The advent of digital fluoroscopy with its subtraction and enhancement capabilities has greatly improved the imaging of contrast material of very low concentration [7]. Digital subtraction angiography permits arterial imaging with intravenous injections, but the dangers of large volumes of iodinated contrast material are still present. CO₂ injected via very small catheters using digital subtraction systems should further reduce the hazard of angiographic procedures. My interest in CO₂ arteriography has been renewed by the good images obtained with digital subtraction technique. By modifying injection rates and positioning, useful images can be obtained not only with a digital system but with conventional angiographic subtraction techniques as well.

Subjects and Methods

My recent experience with CO₂ injected intraarterially involves 20 patients aged 10–83 years. Digital subtraction imaging was used in 17 and conventional filming in three. Intravenous injections were made in the abdominal aorta (10 patients, including celiac and renal), hypogastric (two patients), and upper and lower extremity (eight patients) using standard 3 and 4.1 French straight, shepherd’s crook, and pigtail catheters. In the first five patients, hand injections were made with 35 or 60 cm³ plastic syringes that were filled from a small medical grade CO₂ tank using a standard oxygen regulator. The syringe was flushed with CO₂ four to six times and then attached to the catheter. The catheter’s stopcock was opened to allow blood to displace the air bubble before the catheter was attached to the syringe.

In subsequent patients, a standard mechanical injector has been used with two 3-way
was positioned higher than the injection site. Since an injection rate of 25 cm³/sec filled the superior mesenteric artery without reflux even without selective injection, the selective injections should be well over 25 cm³/sec and aortic injection considerably higher. In one case when injections were made into the celiac axis, the apparent diameter of the branches varied with the injection rate. The lower injection rate filled only the superior part of the vessels producing a spurious image of narrow arteries. Also occasionally I have seen CO₂ trapped in a segment of the artery that was positioned higher than the more distal vessels. After several seconds, the segment of gas would be pushed into the distal distribution. At no time were small (less than 0.5 cm segments) bubbles observed even in several cases with x3 magnification and standard filming.

In 10 patients (nine hypersensitive to contrast material and one with diabetes) in whom only a digital subtraction examination was performed with CO₂, no significant discomfort occurred during injections in eight and mild abdominal pain occurred in only two. Most of the patients experienced only a slight warm feeling in the abdomen during aortic injections. For the distal arterial run-off films, there was only a warm feeling in the lower extremities. Other patients have experienced a "pins and needles" sensation in their feet which lasts 5-10 sec. The diabetic patient slept throughout the 1½ hr study which involved eight injections with CO₂ (total 600 cm³) and four contrast injections. The aortic injections with 3 cm³/sec of Renografin 76, for a total of 9 cm³, also produced no discomfort as is usual using small amounts of contrast arterially for digital angiography.

Ten patients underwent standard abdominal and extremity angiography and, at the end of this study, were transported to the digital fluoroscopy unit for CO₂ angiography. All patients received 10-15 mg of Valium orally and 2-3 mg of Dilaudid intramuscularly about 1 hr before the initial standard angiographic procedure. In all the lower extremity studies, 2 mg of Xylocaine was mixed with each cubic centimeter of Renografin 76. In all except one case, the
discomfort during the CO₂ injection was only a fraction of that experienced with the standard large volume Renografin 76 studies. One patient had more discomfort (although still very minimal) with CO₂ than with the standard contrast mixed with Xylocaine; however, the CO₂ injection culminated a long procedure with the premedication having been given more than 4 hr earlier.

**Discussion**

In animals, intravenous air is lethal when injected in relatively large quantities (8 cm²/kg in about 30 sec) [9], but CO₂ has been proven to be safe since its solubility in serum is about 20 times that of O₂ [1, 4, 10] and because it combines with alkaline blood buffers facilitating its disappearance from the gaseous state [1]. Intravenous medical grade CO₂ (50–100 cm³) was used for many years for the detection of pericardial effusion [1–6] and recently as a contrast agent for sonography [11]. Before being used for pericardial effusion, it underwent extensive testing both intravenously and intraarterially. Pulmonary vein, left ventricle, and carotid artery injections [10, 12] were performed because of the possibility of left-to-right intracardiac shunts. Even when injected in huge volumes in dogs (7.5 cm³/kg every 15 min for as many as eight injections) [10], it resulted in only minimal change in Pco₂ (up to 2.9 vol/%), Po₂ (down 0.3 vol/%), pH (0.008), blood pressure, and cardiac function. The right atrial bolus usually disappeared in 15–30 sec. When intravenous injections were made in dogs at a rate of 100 cm³/min for a total of 10,000 cm³, no demonstrable effects were noted [13]. Bendib et al. [14] reported injections of 200 cm³ of CO₂ into the right heart in 1,000 patients without complications.

With the exception of coronary and cerebral injections, arterial injections should be considerably safer than intravenous injections, since the gas must pass through at least one capillary bed (two in the case of the celiac, superior mesenteric, and inferior mesenteric arteries) before it returns to the right atrium. This additional transit time should result in a large quantity of the CO₂ being absorbed before returning to the right atrium.

Although animal experimentation has shown rapid elimination of CO₂, if large volumes of CO₂ are required in patients, pH, Pco₂, Po₂, etc. should be closely monitored during these procedures, especially in patients with respiratory disease.

The apparent absence of toxicity of CO₂ would be very advantageous in arch and cerebral arteriography; however, additional experimental studies should be undertaken before CO₂ is used in the cerebral or coronary circulation.

Oppenheimer et al. [10] believed that CO₂ bubbles blocked the pulmonary capillary bed, resulting in an increased respiratory rate that lasted several minutes after the injection. The capillary block was transient and caused no significant problems because the solubility of CO₂ resulted in very rapid absorption. While such blocks may occur, recent experience with arterially injected CO₂ has demonstrated that at least in tumors it does not produce emboli but acts like liquid contrast medium (arterial washout time being the same and the venous phase being seen in three patients). The fact that the CO₂ bolus flows like liquid contrast material if the area of interest is in the nondependent position suggests that the capillaries are not blocked.

Since I have found that the superior mesenteric artery will accept 25 cm³/sec during aortography, higher aortic injection rates should be required to achieve better arterial filling. However, I have been reluctant to increase CO₂ injection rates above 50 cm³/sec before animal studies are performed to rule out intimal damage. Although I have not seen evidence of intimal damage, I did experience renal parenchymal carbon dioxide extravasations during a very rapid hand injection with a 6 cm³ syringe into a renal artery that was balloon occluded. A follow-up iodinated contrast arteriogram using ×3 geometric magnification demonstrated no apparent intimal damage.

The buoyancy of CO₂ has been an extremely important factor in achieving consistent and uniform arterial filling. If the area of interest was higher than the injection site, good perfusion of CO₂ was noted. Even in selective injections, if the catheter was positioned higher than the organ of interest (i.e., the renal parenchyma being lower than the aorta in the supine position), the buoyancy of the CO₂ resulted in most of the carbon dioxide refluxing into the abdominal aorta (fig. 7). Also in several extremity studies, even with the patient in the Trendelenburg position, the CO₂ bolus progressed in a
distal direction rapidly. However, when the artery would dip to a lower level, the CO₂ bolus would occasionally be trapped in the higher segment of the artery and the blood would apparently flow under the CO₂ not effectively pushing it distally. More recently, consistently good images have been obtained when the area of interest is elevated about 30° with our tilting-table digital system. Placing the patient supine, prone, or oblique has been effective for abdominal structures depending on the direction of the supplying arteries.

Although I have used “mini catheters” for the last 12 years [15], the very low viscosity of CO₂ (about 1/400th that of Renografin 76) will permit injections via even smaller catheters. Currently 0.021–0.035 inch (0.053–0.089 cm) catheters are being fabricated by bonding Teflon to the steel wrappings of a standard guide wire. By removing the mandril (core), a lumen is created. The small size would permit arterial punctures with as small as a 19–21 gauge needle and subsequently this maneuverable, radiopaque catheter could be advanced safely to the area (e.g., abdominal aorta, arch) for the desired CO₂ injection.

Although intravenous injections of CO₂ for arterial opacification would not be feasible since most of the CO₂ should be absorbed by blood and eliminated in the lungs, arterial entry with microcatheter would probably be no more invasive than the present intravenous digital technique involving large intravenous catheters and potentially dangerous contrast material. In this initial experience, arterially injected CO₂ has produced images superior to standard intravenous iodinated contrast digital angiography, and the selectivity of the arterial approach eliminates the difficulties of superimposition of vessels that occurs with the intravenous injections.

Although the present digital system enhances contrast imaging, its resolution is currently inferior to standard filming techniques. With standard subtraction and optimal CO₂ delivery, one recent case demonstrates excellent resolution (fig. 8). However, in an additional two cases, CO₂ produced very poor arterial visualization.

Many aspects of CO₂ require further research, but the potential advantages warrant this effort: (1) no hypersensitivity reactions; (2) no known toxicity, permitting multiple large volume injections; (3) very low viscosity, enabling injections of large volumes via very small catheters; and (4) minimal patient discomfort. The quality of the imaging systems makes the CO₂ technique very viable for hypersensitive patients. With further improvements in imaging and delivery systems, and after further studies regarding possible toxicity, this technique may challenge iodinated contrast material in other angiographic and interventional studies. It is also possible that further studies may encourage the use of CO₂ as a contrast agent in the coronary or cerebral circulations.

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REFERENCES