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 CO_2 via microcatheters which would lessen the risk of arterial injury. CO_2 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 cm^3 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 cm^3 of CO_2 into the right atrium for detection of pericardial effusion was established as a safe procedure [1–6], I proceeded to use CO_2 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 cm^3/sec for a total of 50–60 cm^3 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. CO_2 injected via very small catheters using digital subtraction systems should further reduce the hazard of angiographic procedures. My interest in CO_2 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 CO_2 injected intraarterially involves 20 patients aged 10–83 years. Digital subtraction imaging was used in 17 and conventional filming in three. Intraarterial 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 cm^3 plastic syringes that were filled from a small medical grade CO_2 tank using a standard oxygen regulator. The syringe was flushed with CO_2 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

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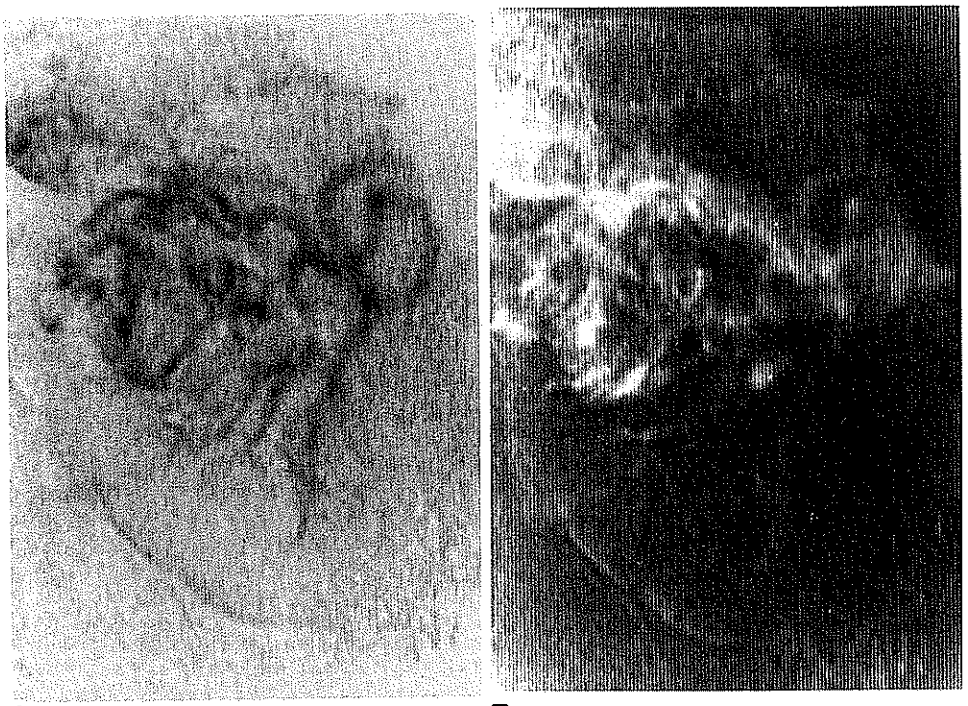

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Fig. 6.—Selective right renal CO_2 arteriogram injecting 15 cm^3/sec for a total of 80 cm^3 with patient in steep left posterior oblique projection (side of interest up). **A**, Electronically reversed arterial-capillary phase. Two hypervascular masses in upper pole and middle of right kidney which proved to be hypernephroma. Faint capillary blush in normal lower pole. **B**, Capillary-venous phase with veins draining tumor area.

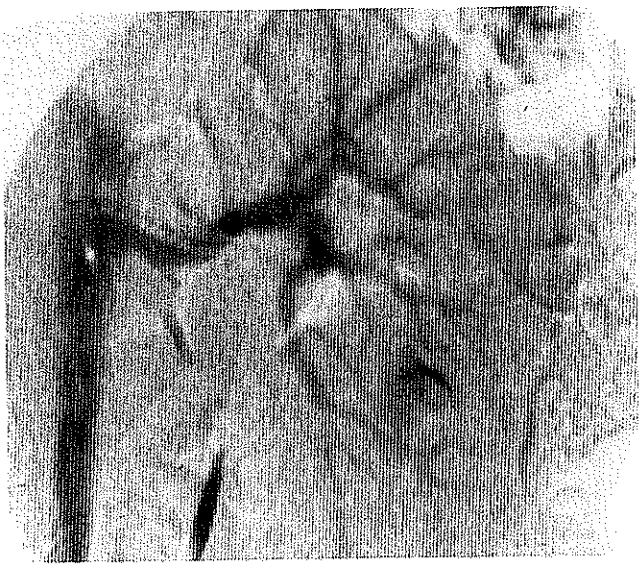

Fig. 7.—Renal arteriogram. Selective hand injection of 20 cm^3 of CO_2 into left renal artery in AP projection. Marked reflux into abdominal aorta. Distal renal arteries not perfused since distal branches were lower than injection site.

was positioned higher than the injection site. Since an injection rate of 25 cm^3/sec filled the superior mesenteric artery without reflux even without selective injection, the selective injections should be well over 25 cm^3/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 CO_2 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 ×3 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 CO_2, 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 CO_2 (total 600 cm^3) and four contrast injections. The aortic injections with 3 cm^3/sec of Renografin 76, for a total of 9 cm^3, 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 CO_2 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

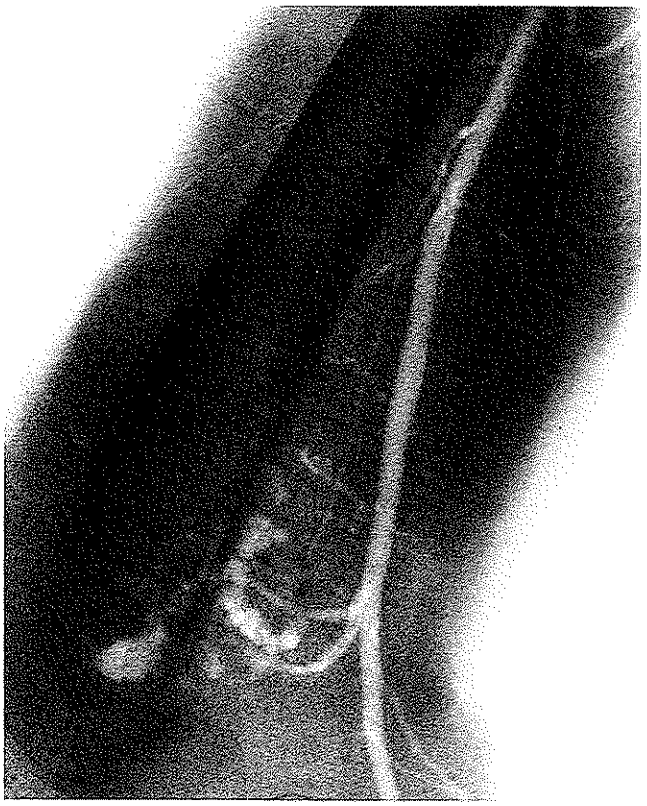

Fig. 8.—Osteosarcoma of the distal femur. Images obtained with *standard subtraction filming* injecting by hand 20 cm^3 of CO_2.

discomfort during the CO_2 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 CO_2 than with the standard contrast mixed with Xylocaine; however, the CO_2 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 cm^3/kg in about 30 sec) [9], but CO_2 has been proven to be safe since its solubility in serum is about 20 times that of O_2 [1, 4, 10] and because it combines with alkaline blood buffers facilitating its disappearance from the gaseous state [1]. Intravenous medical grade CO_2 (50–100 cm^3) 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 cm^3/kg every 15 min for as many as eight injections) [10], it resulted in only minimal change in P_{CO_2} (up to 2.9 vol/%), P_{O_2} (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 cm^3/min for a total of 10,000 cm^3, no demonstrable effects were noted [13]. Bendib et al. [14] reported injections of 200 cm^3 of CO_2 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 CO_2 being absorbed before returning to the right atrium.

Although animal experimentation has shown rapid elimination of CO_2, if large volumes of CO_2 are required in patients, pH, P_{CO_2}, P_{O_2}, etc. should be closely monitored during these procedures, especially in patients with respiratory disease.

The apparent absence of toxicity of CO_2 would be very advantageous in arch and cerebral arteriography; however, additional experimental studies should be undertaken before CO_2 is used in the cerebral or coronary circulation.

Oppenheimer et al. [10] believed that CO_2 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 CO_2 resulted in very rapid absorption. While such blocks may occur, recent experience with arterially injected CO_2 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 CO_2 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 cm^3/sec during aortography, higher aortic injection rates should be required to achieve better arterial filling. However, I have been reluctant to increase CO_2 injection rates above 50 cm^3/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 cm^3 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 CO_2 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 CO_2 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 CO_2 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 CO_2 bolus progressed in a

distal direction rapidly. However, when the artery would dip to a lower level, the CO_2 bolus would occasionally be trapped in the higher segment of the artery and the blood would apparently flow under the CO_2 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 CO_2 (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 CO_2 injection.

Although intravenous injections of CO_2 for arterial opacification would not be feasible since most of the CO_2 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 CO_2 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 CO_2 delivery, one recent case demonstrates excellent resolution (fig. 8). However, in an additional two cases, CO_2 produced very poor arterial visualization.

Many aspects of CO_2 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 current imaging systems makes the CO_2 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 CO_2 as a contrast agent in the coronary or cerebral circulations.

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