CARBON DIOXIDE DIGITAL SUBTRACTION ANGIOGRAPHY

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Carbon dioxide (CO_2) was used in radiology as an imaging agent as early as 1914, for evaluating the retroperitoneum and later in the 1950's for the diagnosis of pericardial effusion (1-2). We pioneered in the 1970's the intraarterial use of CO_2 (3). With the development of high-resolution digital subtraction angiography(DSA), stacking software (adding multiple images), tilting tables and reliable delivery systems, CO_2 became viable as an angiographic imaging agent. With the advent of DSA, reliable imaging of "low-density" contrast became available (Fig. 1 and Fig. 2).

Unique Properties of CO_2:

CO_2 is a nontoxic, invisible gas that is highly compressible, nonviscous and buoyant. Most importantly, CO_2, as an intravascular imaging agent, lacks both allergic potential and renal toxicity. It is 20 times more soluble than O_2 and is rapidly dissolved in the blood.

Unlike iodinated contrast, CO_2 does not mix with blood but must displace it to render an image. Also, the buoyancy of CO_2 causes it to rise to the anterior, nondependent portion of the vessel. Therefore, in larger vessels (aorta and iliac arteries), if an insufficient volume is injected there will be incomplete displacement of blood, resulting in incomplete filling and potentially a spurious image. Normal vessels may appear smaller than their true caliber. To overcome this phenomenon, either a larger amount of CO_2 must be administered or, using the buoyancy principle, the area of interest should be placed in the nondependent position.

Indications:

CO_2 can be injected as a contrast agent in any luminal structure (arterial, venous, biliary tree, urinary tract, abscess cavity, fistula). We previously used CO_2 primarily in patients with iodinated contrast allergy and renal failure. However, its gaseous characteristics can occasionally provide additional information otherwise unattainable. Its very low viscosity permits detection of arterial bleeding, visualization of the portal system by hepatic parenchymal injection for TIPS procedures (Fig. 3), visualization of

small collaterals in ischemic disease and AV shunting in tumors. The very low viscosity also allows delivery via very small catheters and injections between the guidewire and the needle or catheter, making it ideal for interventional procedures such as angioplasty and stent placement (Fig. 4). Furthermore, there is no maximum dose if less than 100 cc are injected every 2 minutes because of its rapid dissolution and elimination from the lungs. This is of great benefit in complex interventional procedures where CO_2 can be used alone or in combination with iodinated contrast to minimize the risk of renal compromise.

Contraindications:

Our studies with rats (6) suggest that the safety of cerebral CO_2 is questionable. We, therefore, avoid any arterial injections above the diaphragm and never administer CO_2 with the patient's head in an elevated position.

CO_2 DSA has not been a problem in patients with chronic obstructive airway disease (COPD). However, in these patients, we do attempt to reduce the volume and allow more time between each injection. A recent evaluation by our laboratory using swine included the direct inferior vena cava (IVC) administration of CO_2 at different volumes. This resulted in no significant change in either PO_2 or pulmonary artery, central venous or systemic arterial pressure at an injection of 1.6 ml/kg. This is well below the individual dose required for diagnostic purposes. Use CO_2 very cautiously in patients with ischemic bowel or in situations where the gas may cause a "vapor lock."

Potential Complications and Precautions:

Because CO_2 is invisible, it is susceptible to contamination without detection. Our initial studies revealed water, rust and particulate matter within reusable sources. Therefore, a pure medical-grade source and disposable cylinder (Custom Medical Devices, Gainesville, FL) are mandatory. Furthermore, a closed delivery system is imperative to eliminate the additional possibility of room air contamination. Because of its extreme diffusivity, an open syringe containing CO_2 can be replaced with less soluble room air in approximately 72 minutes. In addition, a system employing stopcocks can be easily contaminated if they are inadvertently malpositioned or loose. In a closed system, one-way "check" valves and glued stopcocks can be utilized to reduce this possibility.

Another rare, yet potential, complication is "trapping." This occurs when an excessive volume of CO_2 is delivered or the blood-gas interface is reduced and interferes with normal dissolution. As a result, a bolus of gas can cause a vapor lock that can restrict blood flow and potentially cause ischemia. Abdominal aortic aneurysms,

pulmonary outflow tract, celiac, superior and inferior mesenteric arteries are most susceptible because of their nondependent location.

If trapping does occur, it can be reduced by positional maneuvers. For example, if trapping during an inadvertent excessively large volume injection occurs in the pulmonary artery, bradycardia hypotension and coronary ischemia can result. By placing the patient in the left lateral decubitus (Durants) position, CO_2 migrates to the nondependent portion of both the pulmonary artery and the right atrium. This allows blood flow to be reestablished beneath the residual CO_2. Similarly, trapping in an abdominal aortic aneurysm can be reduced by rolling the patient, first to one decubitus position and then to the other. As a precaution for trapping, fluoroscopy of susceptible sites can be performed between CO_2 injections. If persistent gas is visualized, positional changes can be instituted. For venous injections, fluoroscopy of the pulmonary artery will demonstrate dissolution of the gas within 10-30 sec. If the gas remains longer, the possibility of room air contamination must be considered.

Injection of excessive volumes (> 400 cc) is the most dangerous potential complication. Excessive doses are first and foremost avoided by ensuring that the CO_2 cylinder is never connected directly to the catheter. A CO_2 cylinder usually contains 3,000,000 cc of pressurized gas and can flood the low-resistance circulatory system if a stopcock is inadvertently malpositioned. Also, because it is compressible, a syringe loaded under pressure will have an indeterminate volume of CO_2 and potentially result in an excessive dose. It is suggested that a noncompressed, known volume (usually 30-50 cc, or less, depending on the site of evaluation) be administered via a dedicated injector or closed plastic bag system. Purging the catheter of saline or blood with a small volume of CO_2 should be performed prior to injection to eliminate compressed CO_2 and explosive delivery. We have also found that the elimination of explosive delivery reduces the subjective discomfort of pain, nausea and the urge to defecate. Moreover, if using CO_2 to evaluate permanent dialysis access, great care should be taken to avoid explosive delivery and reflux into the artery and possibly into the cerebral circulation (7).

CO_2 should be used cautiously with nitrous oxide anesthesia. In theory, nitrous oxide may diffuse from the soft tissue into the CO_2 "gas bubble" and cause a five-to-six fold increase in the occlusive effect (8). An innocuous 100 cc CO_2 injection may have the effect of 500-600 cc of gas and result in a "vapor lock" condition.

Delivery:

During the last 30 years we have tried many different delivery systems, including many hand delivery systems with manifolds and more than five dedicated mechanical and computer controlled systems. Most were potentially extremely dangerous; however, fortunately the complications that occurred were short lived. Others (including many with considerable experience) are using homemade systems with multiple stopcocks etc., which have resulted in severe complications. Most have occurred from air contamination with stopcocks placed incorrectly. Currently, there are two safe delivery mechanisms: the dedicated injector (9) and the closed plastic bag hand delivery system (10).

The dedicated computer-operated injector (Coject; Angiodynamics, Glens Falls, NY) is essentially fail-safe since there is no chance of delivering excessive volumes. The injector delivers CO_2 nonexplosively and is EKG-gated (injects more CO_2 during systole and more during diastole). It also has an automated saline flushing system. Since it is not approved by the U. S. Food and Drug Administration, we developed a plastic bag hand delivery system (Angioflush III fluid collection bag and Angioflush III fluid management system; AngioDynamics, Glens Falls, NY) from the principles learned by using the dedicated injector.

A disposable CO_2 cylinder containing laboratory grade 99.99% pure CO_2 is used to fill a plastic bag, which only contains 1500 cc at atmospheric pressure if it is not distended. There is no possibility of inadvertently injecting excessive volumes. The bag is connected to a delivery system, which uses multiple one-way check flow valves obviating stopcock manipulation. The system can also be used for interventional procedures if a specialized fitting (Tuohy-Borst) with O-rings is attached. This permits injection of the low viscosity CO_2 between the guidewire and the catheter, or guidewire and any size needle. Large amounts of CO_2 permit accurate visualization of vascular anatomy before and during interventional balloon dilatation, stent placement, or placement of larger potentially dangerous catheters.

General Delivery Principles:

1. Use a closed system (i.e., the plastic bag) or a dedicated CO_2 injector.
   a. Never connect the catheter directly to the CO_2 cylinder. This avoids the potential inadvertent delivery of excessive and possibly lethal volumes.
   b. Don't use additional stopcocks. Malpositioned stopcocks can result in room air contamination and air embolus.
2. Avoid explosive delivery. Purging fluid (blood or saline) from the angiographic catheter results in a more consistent delivery with less discomfort.
3. Initially, inject small volumes of CO_2. Increase or decrease volume as required for specific anatomy.

4. Wait 2-3 min. between injections to allow any potentially trapped CO_2 to dissolve. Wait 5 minutes in patients with possible intestinal ischemia.
5. Elevate area of interest in poor flow conditions (feet, 10-15°; renal artery, 30-45°).
6. Vasodilators (nitroglycerin 100-150 ug IA) can be used to improve filling.
7. Delivery catheter.
   a. Use radiopaque-tipped catheter.
   b. At least one sidehole is recommended for safety.
   c. Any flush catheter is acceptable; however, catheters with only an end hole and Halo catheters produce less gas "breakup."
8. DSA imaging.
   a. Three-to-four frames/sec. using a 60 ms pulse width with adequate penetration.
   b. Obtain frequent scouts. Correct exposure is difficult; however, extra effort results in good contrast and images comparable to iodinated contrast.
   c. When the CO_2 bolus is "broken up" (fragmented), use image stacking, if available.
   d. If imaging is consistently poor, consult an equipment applications specialist to optimize acquisition.

Specific Procedure:

1. Runoff
   a. Initially, obtain both leg runoffs with the catheter in the distal aorta. Perform aortogram after the runoff.
   b. Inject 20-40 cc in 1 second.
   c. Elevate the feet 10-15° for optimal filling and obtain images of pelvis, thigh, knee, lower legs and feet.
   d. If IMA is filled and patient experiences pain, urge to defecate or has symptoms of intestinal ischemia, multiple distal aortic injections should be keep to a minimum. Selective iliac or more distal injections produce better filling and are unlikely to cause intestinal ischemia.
   e. If there is no stacking program, a longer injection (~ 60 cc over 2-3 sec.) is necessary.
   f. Problem - poor filling of the lower leg and feet.
      - Perform a selective injection of the common femoral or more distal arteries. Most runoff exams are currently examined in this fashion.
      - With stacking, inject 10-20 cc in two sec. If filling remains poor, inject 20-40 cc over 3-4 sec.
      - Without stacking, begin with 20-40 cc over 3-4 sec.
      - Intraarterial nitroglycerine, 100-150 ug prior to injection.
      - When large volumes are required, discomfort may occur, precipitating patient motion and distorting images.

2. Aortogram
   a. Usually performed after the runoff. We believe this allows the patient to become acclimated to CO_2 and, as a result, less discomfort and nausea are experienced with larger aortic injections.
   b. Attempt to obtain the aortogram without glucagon. Our experience is that CO_2 and glucagon may cause nausea.
   c. Higher flow rates may be necessary (25-50 cc in 1/2 sec.).
   d. The left renal is more difficult to image and may be better visualized by elevating that side. If necessary, a selective injection with a shepherd hook catheter (10-20 cc CO_2 in 1 second) can be performed. The ostium is usually apparent secondary to CO_2 reflux. Also, cross-table DSA with the patient in the decubitus position always fills the renal. However, use low volumes since the lumbars will also fill better, which could cause spinal cord problems. Don't inject with patient prone. Spinal arteries will always fill with unknown effects.
   e. Selective injections of the visceral arteries commonly require 10-30 cc in 1-2 seconds.
3. Venous - always image the pulmonary artery after the first injection to rule out air contamination (persistent gas). Normally, CO_2 should disappear after 10-30 sec.
   a. SVC and IVC - 20-60 cc in 1-2 sec.
   b. Subclavian - 20-40 cc in 1-2 sec.
   c. Peripheral veins - 15-25 cc, 4-8 sec. Rapid injection precipitates pain.
4. Interventional Procedures.
   a. Using a Tuohy-Borst fitting, CO_2 can be injected between the guidewire and needle or catheter. Wires without coil wrap are better (glidewire, .018 torque wire).
   b. Use a 20-40 cc Luer-locked syringe. With a smaller syringe, CO_2 will simply compress without injecting.
   c. Wait 20-30 sec. for CO_2 to exit the catheter. CO_2 will compress, purge fluid from the catheter and inject.
   d. After purging, subsequent injections require less pressure and delay.
5. TIPS
   a. Using any needle, inject 20 cc of CO_2 into the hepatic parenchyma for visualization of the portal vein throughout the various steps of the procedure.
   b. With the guidewire in place, CO_2 can be used to verify the needle entry site and determine stent positioning.
6. Renal PTA and stent placement. CO_2 can be injected between the guidewire and the stent catheter to verify its exact position before the stent is deployed. The extreme buoyancy of the gas always results in reflux into the aorta, which visualizes the exact positions of the renal artery ostium.

References

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Figures

Figure 1: Closed Plastic Bag Delivery System.