In the early 1900s, carbon dioxide (CO2) was used as an imaging agent for visualization of the abdominal and retroperitoneal viscera. Subsequently, its gaseous attributes were also found to be useful in the evaluation of hepatic veins, as well as in the diagnosis of pericardial effusion. In the 1970s, Hawkins began studying the use of CO2 as a vascular imaging agent. Because of the poor imaging technology at the time, the effectiveness of CO2 for vascular imaging was delayed. However, with the development of digital subtraction angiography (DSA), improved imaging systems, tilting tables, and safe, reliable delivery systems, CO2 eventually became a viable vascular imaging agent.

**CO2 versus Liquid Contrast**

As opposed to liquid contrast, CO2 is a nontoxic, invisible, highly compressible, nonviscous, buoyant, and rapidly absorbable gas. Compared to oxygen, CO2 is 20 times more soluble. It is rapidly dissolved in the blood, and when delivered intravenously, it is also eliminated by a single pass through the lungs. Its viscosity is 1/400 that of iodinated contrast, resulting in unique diagnostic and interventional advantages. Additionally and more significantly, as an imaging agent, CO2 lacks both allergic potential and renal toxicity.

Because CO2 does not perform like a traditional liquid contrast, it is imperative that proceduralists familiarize themselves with its unique properties and how they affect safe, tolerable, and effective delivery. Specific details of these properties and safe administration are easily assimilated and have been well described in the literature.

**Advantages and Disadvantages of CO2 Angiography**

First, CO2 is not always the consummate vascular contrast agent, and there can be distinct disadvantages. It is invisible, requires a unique delivery system, is often more labor intensive, cannot be used in the cerebral circulation, and bowel gas and motion can significantly interfere with accurate imaging. However, there are many opportunities in which CO2 used alone or in conjunction with a small amount of iodinated contrast can offer unique attributes resulting in the safe, efficacious performance of a procedure that may have been precluded without it. It is, by far, the ideal imaging agent for patients with an iodinated contrast allergy or renal insufficiency. When administered appropriately, the acceptable volume of CO2 delivered during a procedure is unlimited. Therefore, it is a valuable agent in high-volume contrast procedures, either alone or as an adjunct to iodinated contrast. Diagnostically, its low viscosity can detect bleeding and fistulas overlooked by liquid contrast. Because of its low viscosity, hand injections are much more easily performed when using microcatheters. Finally, CO2 delivery normally refluxes and demonstrates not only the typical peripheral anatomy seen with traditional contrast but...
also opacifies centrally as well. This central visualization can be advantageous in identifying catheter position, anatomy, and pathology without repositioning of the catheter. Although mild reflux from a gentle administration may be helpful, excessive reflux with a forceful delivery should be avoided. Depending on the catheter position, the latter method could result in undesirable repetitive delivery to the cerebral or mesenteric circulation.

**ADVANTAGES OF CO₂ ANGIOGRAPHY FOR INTERVENTIONAL ONCOLOGY**

Considering the advantages of CO₂ angiography, there are some patients who are now afforded procedures that in the past were either precluded or precarious because of the patients’ comorbidities. Furthermore, these same advantages may permit more facile performance and information not provided by iodinated contrast. One arena in which these advantages play a crucial role is in interventional oncology. Typically, these patients are older, have a number of comorbidities, and often require a number of invasive procedures, some of which necessitate a high volume of contrast. Fortunately, most vessels requiring imaging in interventional oncology are typically 1 cm or less. Vessels of this size demonstrate the best anatomic and pathologic correlation when compared with iodinated contrast (Figure 1).  

Currently, most interventional oncology patients are evaluated in a clinic and then scheduled for their procedure. Although uncommon, some patients have such a severe iodinated contrast allergy that its administration is not an option. Other less severe but more common allergic scenarios may require preprocedure prophylaxis. Despite the best intentions, patients may present for their procedure without the necessary premedication for a variety of reasons. In these instances, rescheduling would appear to be the only safe recourse. Considering travel distance, emotional setback, and the potential cost of the prepared agent, this represents an extremely unfortunate option. When presented with this scenario, CO₂ angiography can easily be used to replace and avert the problems of iodinated contrast allergy.

Aside from allergy, interventional oncologic preprocedure assessment must include a thorough evaluation of the patient’s renal status. Many of these patients are often subjected to one or more high-volume contrast procedures, potentially jeopardizing their renal function. The most valuable role of CO₂ in interventional oncology is the fact that it is not nephrotoxic. In fact, it is the only vascular imaging agent that can state this claim. Regardless of the type of embolization procedure, CO₂ can replace iodinated contrast and offer patients life-prolonging or palliative procedures previously precluded because of renal insufficiency. This is exemplified by uterine fibroid embolization (UFE).

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**Figure 1.** An iodinated contrast image of the celiac axis (A). Comparative anatomic detail using CO₂ DSA (B).

**Figure 2.** CO₂ pelvic DSA showing both uterine arteries and hypervascularity present in a uterine leiomyoma.
A classic contraindication for this procedure is renal insufficiency; however, the size and anterior position of the uterine arteries make these vessels ideal candidates for CO2 angiography (Figure 2). The entire procedure can be performed using CO2 alone or with small amounts of contrast.

In addition to patients with obvious preexisting renal insufficiency in whom the use of CO2 angiography is intuitive, many interventional oncology patients with apparent normal renal function are at risk for contrast-induced nephropathy. One of the principal risks predisposing this group of patients to renal insufficiency is their age. Excluding those patients undergoing UFE, a preponderance of oncology patients are elderly. Despite near-normal creatinine values, patients older than 70 years have a > 30% chance of having an abnormally low glomerular filtration rate. Therefore, any insult to the kidneys in this group could result in significant renal insufficiency. One group that is especially vulnerable to renal compromise is that of patients with renal cell carcinoma who require embolization of the entire kidney or a subsequent renal cell carcinoma long-bone metastasis. Many of these patients are elderly and have a solitary, partially functioning kidney. In these susceptible individuals, CO2 can be used throughout the embolization procedure, significantly lowering if not eliminating the administration of iodinated contrast.

In addition to age, many interventional oncology patients also have a number of comorbidities that predispose to renal insufficiency. Diabetes and volume depletion are common in this group of patients. Even healthy-appearing, young patients with fibroid-induced menorrhagia can present with volume depletion and acute renal failure, which has been described after UFE. Volume depletion is particularly prevalent in hepatocellular carcinoma patients who have concomitant liver insufficiency and ascites. The post-transarterial hepatic chemoembolization incidence of acute renal failure is between 3% and 8%. If these patients progress to frank liver failure, they have an additional propensity for renal insufficiency. Also exacerbating volume depletion is the fact that interventional oncology procedures can precipitate nausea and vomiting from postembolization syndrome.

Finally, interventional oncology procedures can compromise the patient’s renal status with the use of periprocedural drugs that adversely affect the kidneys. One of the biggest offenders in the oncology arena is nonsteroidal anti-inflammatory drugs. Administered to reduce symptoms of postembolization syndrome, these drugs must be used with caution because they predispose the patient to acute renal failure through a variety of mechanisms.

In addition to preventing allergic sequelae and nephrotoxicity, CO2 angiography is useful in interventional

Figure 3. Twenty mL of CO2 is delivered into the hepatic parenchyma using a 22-gauge needle. The portal and hepatic veins are visualized due to the migration of CO2 into the sinusoids and veins.

Figure 4. A hand injection into a microcatheter using iodinated contrast to confirm catheter position before delivery of drug-eluting beads (A). The target is not identified. A CO2 hand injection into the same microcatheter (B). CO2 refluxes centrally and subsequently shows the correct target and the necessity to move the catheter. Arrows delineate the microcatheter tip and the target vessel.
Because of its low viscosity, CO₂ traverses the sinusoids not opacified by thicker iodinated contrast. The low viscosity of CO₂ is also useful in demonstrating arteriovenous shunting that may not be evident when using more viscous iodinated contrast. The appearance of an arteriovenous shunt can change the type and size of the chosen embolic agent thus avoiding nontarget embolization. Another less common advantage of low viscosity is in demonstrating obscure parasitized arteries not opacified by thicker iodinated contrast.

As previously stated, the tendency of CO₂ to reflux centrally when injected can assist in anatomic or pathologic vascular evaluation without removing the catheter from a position that was difficult to achieve (Figure 4). Unlike iodinated contrast, which opacifies peripherally, CO₂ is useful in that it demonstrates both peripheral and central anatomy.

**CONCLUSION**

In summary, interventional oncology patients are a unique group. They may require one or more high-volume contrast procedures, are usually older, and often have comorbidities. The presence or potential for renal insufficiency should not preclude a life-extending or palliative procedure. CO₂ angiography not only offers distinct benefits over iodinated contrast, which opacifies peripherally, CO₂ is useful in that it demonstrates both peripheral and central anatomy.

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