CO₂ Angiography in Interventional Oncology

CO₂ angiography not only helps prevent undesired complications, but it can also assist in the performance of interventional oncologic procedures.

BY JAMES CARIDI, MD, FSIR; JEFFREY D. VOGEL, MD; DARREN POSTOAK, MD; SCOTT PETERSON, MD; BRIAN S. GELLER, MD; IRVIN HAWKINS, MD; AND SEAN WILEY, RPA

n the early 1900s, carbon dioxide (CO_2) 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 CO_2 as a vascular imaging agent. Because of the poor imaging technology at the time, the effectiveness of CO_2 for vascular imaging was delayed. However, with the development of digital subtraction angiography (DSA), improved imaging systems, tilting tables, and safe, reliable delivery systems, CO_2 eventually became a viable vascular imaging agent.

CO₂ VERSUS LIQUID CONTRAST

As opposed to liquid contrast, CO_2 is a nontoxic, invisible, highly compressible, nonviscous, buoyant, and rapidly absorbable gas. Compared to oxygen, CO_2 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, CO_2 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.⁶⁻⁹

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

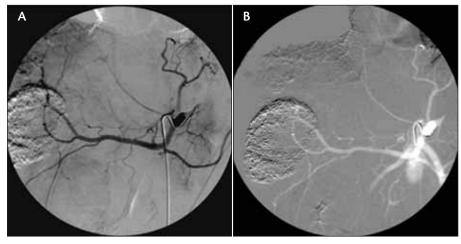


Figure 1. An iodinated contrast image of the celiac axis (A). Comparative anatomic detail using CO₂ DSA (B).

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).¹⁰

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 sub-

jected to one or more high-volume contrast procedures, potentially jeopardizing their renal function. The most valuable role of CO_2 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, CO_2 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).



Figure 2. CO_2 pelvic DSA showing both uterine arteries and hypervascularity present in a uterine leiomyoma.



Figure 3. Twenty mL of CO_2 is delivered into the hepatic parenchyma using a 22-gauge needle. The portal and hepatic veins are visualized due to the migration of CO_2 into the sinusoids and veins.

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 CO_2 angiography (Figure 2). The entire procedure can be performed using CO_2 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.11 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. ¹² Many of these patients are elderly and have a solitary, partially functioning kidney. In these susceptible individuals, CO_2 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 healthyappearing, young patients with fibroid-induced menorrhagia can present with volume depletion and acute renal failure, which has been described after UFE.13 Volume depletion is particularly prevalent in hepatocellular carcinoma patients who have concomitant liver insufficiency and ascites. 14 The post-transarterial hepatic chemoembolization incidence of acute renal failure is between 3% and 8%. 15-17 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, CO_2 angiography is useful in interventional

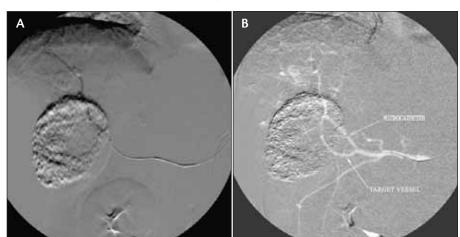


Figure 4. A hand injection into a microcatheter using iodinated contrast to confirm catheter position before delivery of drug-eluting beads (A). The target is not identified. A CO₂ hand injection into the same microcatheter (B). CO₂ refluxes centrally and subsequently shows the correct target and the necessity to move the catheter. Arrows delineate the microcatheter tip and the target vessel.

oncology because of its extremely low viscosity. This offers a number of advantages over iodinated contrast. One particularly valuable scenario is in portal vein embolization before extended hepatectomy. Portal vein access can oftentimes be difficult and extend the duration of the procedure. Accessing a peripheral portal vein radical can reduce bleeding, avoid transgressing tumor, permit easier catheter manipulation, and reduce nontarget embolization. The procedure entails placing a 22-gauge needle directly into the hepatic parenchyma and administering approximately 20 mL of CO₂ (Figure 3). Because of its low viscosity, CO₂ traverses the sinusoids and opacifies the portal vein and its branches. These images can be used as a target for optimal access.

Another advantage of low viscosity is the facile delivery of CO_2 through microcatheters. With the small internal diameters of microcatheters, iodinated contrast visualization of peripheral anatomy is often difficult unless a power injector is used. This impediment is removed with the use of hand injections of CO_2 .

The low viscosity of CO_2 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 CO_2 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, CO_2 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 when iodinated contrast adds significant risk when it is contraindicated or unsuccessful at fulfilling the appropriate treatment, but it also offers technical advantages not available with liquid contrast.

James Caridi, MD, FSIR, is Associate Professor of Radiology and Pediatrics and Chief of Vascular and Interventional Radiology at the University of Florida College of Medicine in Gainesville, Florida. He has disclosed that he holds no financial interest in any product or manufacturer mentioned

herein. Dr. Caridi may be reached at (352) 219-8965; caridj@radiology.ufl.edu.

Jeffrey D. Vogel, MD, is with the University of Florida College of Medicine in Gainesville, Florida. Dr. Vogel has disclosed that he holds no financial interest in any product or manufacturer mentioned herein.

Darren Postoak, MD, is with the University of Florida College of Medicine in Gainesville, Florida. Dr. Postoak has disclosed that he holds no financial interest in any product or manufacturer mentioned herein.

Scott Peterson, MD, is with the University of Florida College of Medicine in Gainesville, Florida. Dr. Peterson has disclosed that he holds no financial interest in any product or manufacturer mentioned herein.

Brian S. Geller, MD, is with the University of Florida College of Medicine in Gainesville, Florida. Dr. Geller has disclosed that he holds no financial interest in any product or manufacturer mentioned herein.

Irvin Hawkins, MD, is with the University of Florida College of Medicine in Gainesville, Florida. Dr. Hawkins has disclosed that he holds no financial interest in any product or manufacturer mentioned herein.

Sean Wiley, RPA, is with the University of Florida College of Medicine in Gainesville, Florida. Mr. Wiley has disclosed that he holds no financial interest in any product or manufacturer mentioned herein.

- Rautenberg E. Rontgenphotographie der Leber, der Milz, und des Zwerchfells. Deutsch Med Wschr. 1994;40:1205.
- Rosenstein P. Pneumoradiology of kidney position—a new technique for the radiological representation of the kidneys and neighboring organs (suprarenal gland, spleen, liver). J Urol. 1921;15:447.
- Paul RE, Durant TM, Oppenheiner MJ, et al. Intravenous carbon dioxide for intracardiac gas contrast in the roentgen diagnosis of pericardial effusion and thickening. AJR. 1957;78:224-225
 Phillips JH, Burch GE, Hellinger R. The use of intracardiac carbon dioxide in the diagnosis of pericardial disease. AJR. 1966;97:342-349.
- Hawkins IF. Carbon dioxide digital subtraction angiography. AJR. 1982;139:19-24.
- 6. Caridi JG, Hawkins IF, Klioze SD, et al. Carbon dioxide digital subtraction angiography: the practical approach. Tech Vasc Interv Radiol. 2001;4:57-65.
- 7. Hawkins IF, Caridi JG, Klioze SD, et al. Modified plastic bag system with 0-ring fitting connection for carbon dioxide angiography. AJR. 2001;176:229-232.
- Caridi JG, Hawkins IF. CO2 digital subtraction angiography: potential complications and their prevention. J Vasc Interv Radiol. 1997; 8:383-391.
- Weaver FA, Pentecost MJ, Yellin AE, et al. Clinical applications of carbon dioxide/digital subtraction arteriography. J Vasc Surg. 1991;13:266-272.
- Lang EV, Gossler AA, Fick LJ, et al. Carbon dioxide angiography: effect of injection parameters on bolus configuration. J Vasc Inter Rad. 1999;10:41-49.
- 11. Walsh SR, Tang TY, Boyle J. Renal consequences of endovascular abdominal aortic aneurysm repair. J Endovasc Ther. 2008;15:73-82.
- 12. Mazer MJ, Baltaxe HA, Wolfe GL. Therapeutic embolization of the renal artery with Gianturco coils: limitations and technical pitfalls. Radiology. 1981;138:37-46.
- 13. Rastogi, S, Wu YH, Shlansky-Goldberg RD, et al. Acute renal failure after uterine artery embolization. Cardiovasc Intervent Radiol. 2004;27:549-650.
- Kim Mj, Lee SW, Kim GA, et al. Acute renal failure after transarterial chemoembolization progressing to chronic renal failure in hepatocellular carcinoma.
 Nephrol Dial Transplant. 2000;15:741-742.
- Yamazaki H, Oi H, Matshushita M, et al. Renal cortical retention of contrast medium on delayed CT and nephropathy following TACE in patients with high serum creatinine level. Br J Rad. 2002;75:874-878.
- Huo TI, Wu JC, Kee PC, et al. Incidence and risk factors for acute renal failure in patients with HCC undergoing TACE: a prospective study. Liver International. 2004;24:210-215.
- Jang BK, Lee SH, Chung WJ, et al. Incidence and risk factors of acute renal failure after transcatheter arterial chemoembolization for hepatocellular carcinoma. Korean J Hepatol. 2008;14:168-77.