Current status of carbon dioxide angiography

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ABSTRACT

Objective: Unfamiliarity of endovascular surgeons with carbon dioxide (CO_2) angiography is one of the main reasons for its limited use. This review is intended to familiarize the reader with the principles and applications of that modality.

Methods: We conducted a comprehensive review of contemporary literature related to CO_2 angiography and its use in the field of vascular and endovascular surgery, including technical details and diagnostic and interventional applications.

Results: Cardinal physicochemical characteristics of CO_2 include buoyancy, ultralow viscosity, and nonmixing with blood. Because of the risk of neurotoxicity, intra-arterial CO_2 angiography should only be performed below the diaphragm. Venous CO_2 angiography can be performed anywhere in the torso and extremities. Ultralow viscosity enables intraprocedural imaging during vascular interventions without the need to exchange for an angiographic catheter. Benefits, advantages, and emerging applications of CO_2 angiography are listed. Potential complications and their avoidance and troubleshooting are discussed.

Conclusions: CO_2 holds promise as an effective and versatile angiographic contrast agent. It is also a valuable modality for the guidance of endovascular interventions. Current availability of easy to use, safe, and portable CO_2 delivery systems will likely expand the use of that modality even beyond the traditional indications of renal insufficiency and iodinated contrast allergy. (J Vasc Surg 2017;66:618-37.)

Since the discovery of x-rays, it became obvious that enhancement of the subtle differences in density is essential to delineate the borders of various soft tissue structures. The discovery of iodine as a safe contrast agent allowed research on iodinated contrast media (ICM) to begin, and in 1924, Brooks[1] described the first known clinical use of sodium iodine as a contrast agent in lower extremity angiograms, which was used to guide the level of amputation in patients with peripheral vascular disease. Over the years, contrast angiography evolved solely as a positive-contrast technique using almost exclusively ICM, a trend that continues to date.

The attributes of carbon dioxide (CO_2) as a negative contrast agent were recognized several decades ago.[2] Its wide availability, low cost, nontoxicity, and rapid tissue clearance rendered this agent a natural choice as a negative contrast agent in a variety of nonvascular imaging applications such as cisternography, peritoneography, and double-contrast gastrointestinal (GI) imaging. The safety of CO_2 over other gases is attributed to its much higher tissue solubility, virtually eliminating the risk of serious complications from inadvertent gas embolism.

Irvin F. Hawkins, widely acknowledged as a pioneer of modern CO_2 angiography, described how an error led him to the realize the potential of this technique when he inadvertently injected air into the celiac artery, luckily without ill consequences.[3] This experience, coupled with his knowledge of the safety of CO_2 as an intravenous contrast agent, led him to postulate CO_2 as a potential negative contrast agent in the arterial system. His early experience marked the beginning of this new approach for intravascular imaging, and since then, the work of Hawkins and many other pioneers has enabled the current status of CO_2 as a safe and highly versatile intravascular contrast agent.

The two obvious indications of CO_2 angiography are high-risk state for iodinated contrast-induced nephropathy (CIN) and iodinated contrast allergy. However, many other indications exist, including applications where CO_2 may outperform ICM.

Despite the recognized value of CO_2 angiography among interventional radiologists and angiographers, it has been slow to make its way into the toolbox of the vascular surgeon. This is likely a result of unfamiliarity, because CO_2 angiography is not a readily disseminated skill in vascular training programs. CO_2 angiography has not been standardized as a discipline, and the way it is performed varies depending on the operator and the application. There is also an exaggerated fear of complications and an unfounded assumption that it is time consuming and produces inferior-quality imaging.

This review is intended to better familiarize the reader with the technique of CO_2 angiography by introducing the key physical and chemical features contributing to the value of CO_2 as a contrast agent and how they can be used to optimize imaging in various applications. We will introduce the methods and approaches used

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for CO_2 angiography and define its indications, risks, benefits, and applications where it can be of value. We will introduce the current imaging and technical details that assist the operator in obtaining excellent image quality. We will also describe the value of CO_2 as a contrast agent during a growing number of interventional procedures and explore future trends and potential of CO_2 in a variety of imaging and interventional applications.

METHODS

A comprehensive search of the United States (U.S.) National Library of Medicine related to CO_2 angiography and its use in the field of vascular surgery was conducted via PubMed. To ensure that pertinent studies were not missed, broad search terms were used: "CO_2 angiography," "carbon dioxide angiography," and "non-contrast angiography." Other search terms were "risks of" and "contrast induced nephropathy." The publications ranged in date from 1924 to present, with most of the research published in the last 10 years. Selected publications included reviews, case studies, and clinical trials.

RESULTS

The search term "carbon dioxide angiography" yielded 817 publications. The search was further refined by selecting English language publications. Publications were selected based on their relevance to the topic of discussion and on the quality of the study.

The retrospective review and publication of clinical data on all patients in this report was approved by our Institutional Review Board.

DISCUSSION

CO_2 as an alternative ICM

The most recognized indication for the use of CO_2 as an alternative to ICM is in patients at high-risk of CIN. This serious complication is the third-leading cause of hospital-acquired renal failure[4] and carries a severalfold increase in short-term and long-term mortality. The incidence of CIN varies widely depending on the definition used, patient risk factors, route and rate of administration, and amount of contrast used. CIN usually manifests ~48 to 72 hours after administration of intravenous ICM. Suspected pathophysiology is generation of reactive oxygen species as a result of renal vasoconstriction/ischemia or direct tubular injury. Of the many approaches suggested to prevent CIN, current evidence seems to support only hydration as a protective countermeasure. The evidence for administration of N-acetylcysteine or bicarbonate infusions in the perioperative period has been less convincing, although many providers continue to use them in practice.

Established risk factors for CIN include pre-existing renal insufficiency, diabetes mellitus, dehydration, cardiovascular disease with congestive heart failure, smoking, current use of calcium channel blockers or diuretics, advanced age (≥70 years), multiple myeloma, hypertension, and hyperuricemia.[4] Vascular patients represent a population at high risk for developing CIN. Evidence from prospective clinical trials has consistently shown diabetes mellitus and baseline renal insufficiency are the most significant independent risk factors, both of which are highly prevalent in the vascular patient population.

Although the cutoff level of renal dysfunction to prompt the use of an alternative contrast medium is not uniformly defined, avoidance of extrinsic risk factors, such as use of nephrotoxic agents, in this high-risk population should be a high priority. This highlights the need for alternative non-nephrotoxic contrast media for diagnostic and interventional vascular applications. CO_2 can fulfill both roles, and some investigators have even advocated for its routine use during angiography.[5]

The second most common indication for CO_2 angiography is a known allergy to contrast media. Allergic contrast reactions range from mild rash to anaphylaxis. Pretreatment protocols have been developed to lower the incidence and severity of these reactions; however, there are many patients who would benefit from complete avoidance of ICM, especially in situations where immediate angiography is needed and in patients with history of anaphylaxis.

Another indication for CO_2 angiography is specific applications where CO_2 actually outperforms conventional ICM. As described under "Physical and chemical properties of CO_2," certain characteristics of CO_2 can allow better diagnostic information in certain specific applications. For example, improved demonstration of collateral pathways and reconstituted vessels distal to obstructions, demonstration of occult sites of GI bleeding, and visualization of portal-splanchnic veins can be attributed to the ultralow viscosity of CO_2, whereas enhanced vascular filling during central venography is attributed to nonmixing and volume displacement characteristics of CO_2.

Intraprocedural guidance during endovascular interventions is another often overlooked capability of CO_2 angiography, such as during balloon angioplasty and stenting of mesenteric and renal arteries, aortoiliac and lower extremity peripheral vascular occlusive disease, fine-needle transjugular intrahepatic portosystemic shunt (TIPS), embolization therapy, and endovascular abdominal aortic aneurysm (AAA) repair (EVAR).[6-9] The use of CO_2 during interventions allows unlimited on-demand intraprocedural angiographic guidance. In addition, CO_2 angiography allows accurate device positioning without the multiple exchanges by injecting CO_2 through the interventional sheath. This is possible owing to the low viscosity of CO_2, which enables it to be injected with little resistance through the small space around the guidewire or interventional device catheter.