Carbon Dioxide as a Contrast Agent to Guide Vascular Interventional Procedures

OBJECTIVE. The purpose of this study was to assess the value and limitations of carbon dioxide (CO$_2$) as a contrast agent to guide vascular interventional procedures.

SUBJECTS AND METHODS. Twenty-two adults underwent 26 vascular interventional procedures (21 arterial, five venous). We aimed to use only CO$_2$ if possible because these patients had renal insufficiency (n = 21; mean creatinine level, 2.8 mg/dl) or were allergic to contrast material (n = 1). Arterial procedures performed included renal angioplasty or stent (n = 6), iliac angioplasty or stent (n = 5), infrainguinal angioplasty (n = 5), arterial bypass graft angioplasty (n = 3), and thrombolysis (n = 2). Venous procedures included transjugular intrahepatic portosystemic shunt recanalization (n = 3), angioplasty of the venous anastomosis of a thigh dialysis graft (n = 1), and angioplasty of the inferior vena cava (n = 1).

RESULTS. Twenty-five of the 26 procedures were successfully performed. Of the 26 procedures, eight required no iodinated contrast material and 11 required less than or equal to 20 ml of contrast material. CO$_2$ proved to be adequate for the remaining seven procedures. Iliac artery angioplasty or stent placement required an average of 9 ml of iodinated contrast material; infrainguinal angioplasty required an average of 22 ml of iodinated contrast material.

CONCLUSION. CO$_2$ can be successfully used as a contrast agent in a variety of vascular interventional procedures. Such procedures can usually be performed in the iliac and infrainguinal arteries using minimal supplemental iodinated contrast material. However, CO$_2$ failed to provide satisfactory guidance in half of the intraabdominal procedures in our study.

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tion to iodinated contrast material and was undergoing hemodialysis. Seven (32%) of the 22 patients had diabetes mellitus.

**Arterial Interventions**

Twenty-one arterial interventional procedures were performed in 18 patients, including stent placement in the iliac artery \( (n = 4) \) (Fig. 1), stent placement in the renal artery \( (n = 3) \), angioplasty of the renal artery \( (n = 3) \), angioplasty of a femoropopliteal artery \( (n = 3) \), angioplasty of an infragenual vein bypass graft \( (n = 2) \) (Fig. 2), angioplasty of an intrapopliteal artery \( (n = 2) \), intimal thrombolyis in a bypass graft \( (n = 2) \), and angioplasty of an iliac artery \( (n = 1) \). One patient underwent angioplasty of a new vein graft stenosis 5 months after angioplasty of a different stenosis in the same bypass graft; these procedures are listed separately above. Another patient underwent thrombolysis of a vein bypass graft, angiography after urokinase infusion in conjunction with angioplasty of several vein bypass graft stenoses, and stent placement in the contralateral iliac artery over 2 days; these are listed above as three separate procedures. Multiple lesions within one arterial segment were also treated during the same procedure in the patient who underwent angioplasty of the iliac artery, in a patient who underwent angioplasty of the femoropopliteal arteries, and in two patients who underwent angioplasty of infrapopliteal arteries.

 Fifteen patients had previous diagnostic studies that showed stenoses greater than or equal to 50% of the cross-sectional diameter of the vessel. These studies included eight MR arteriograms, three arteriograms using iodinated contrast material, three Doppler sonographic examinations, and one arteriogram using CO\(_2\) as contrast material. The three patients who underwent diagnostic arteriography with iodinated contrast material experienced increases in serum creatinine levels from 2.0 to 5.9, from 2.3 to 2.7, and from 1.2 to 1.6 mg/dL, respectively. The serum creatinine level returned to near baseline before the interventional procedure in the first two patients, whereas the third had a progressive slight increase in serum creatinine level. In the four patients without previous diagnostic examinations and in those patients with MR arteriograms or sonographic examinations, arteriography using CO\(_2\) was performed before the interventional procedure to confirm that the diameter of the stenosis was more than 50% of the vessel diameter.

 Fifteen lower extremity interventional procedures were performed in 13 limbs of 12 patients. The indications included nonhealing ischemic foot ulcers in eight limbs, graft thrombosis with rest pain in two, half-block claudication in one, rest pain in one, and two different stenoses in a vein graft detected on separate sonographic surveillance examinations in an asymptomatic patient. The patient who underwent three separate arterial interventional procedures had rest pain attributed to vein graft thrombosis in the left leg and a nonhealing ischemic ulcer on the right foot. Six unilateral angioplasties, stent placement procedures, or both in the renal arteries were performed for poorly controlled hypertension and progressive renal insufficiency.

**Venous Interventions**

Five interventional procedures were performed in the venous systems of four patients. Three procedures were done after transjugular intrahepatic portosystemic shunt (TIPS) placement in two patients. One patient underwent angioplasty of a hepatic vein. Another patient underwent thrombolysis, thrombectomy, and angioplasty of the shunt after Doppler sonography showed stent occlusion. This same patient later underwent thrombolysis and stent placement in the shunt. Two TIPS revisions were performed without diagnostic imaging studies because of reaccumulation of ascites. Transjugular transhepatic portography was performed during these three procedures using CO\(_2\) as contrast material initially.

The two additional venous procedures were angioplasty of the inferior vena cava in a patient 21 months after an orthotopic liver transplant and angioplasty of the venous anastomosis of a thigh dialysis graft in a patient who had not taken oral steroid preparation because of a previous severe reaction to iodinated contrast material. The patient who underwent angioplasty of the inferior vena cava had diagnostic sonographic and MR examinations that showed occlusion of the intrapopliteal inferior vena cava. The patient who underwent angioplasty of a dialysis graft had a fistulogram after an intraoperative graft thrombectomy. Both patients underwent diagnostic studies using CO\(_2\) before the interventional procedure was performed.

**Techniques**

Using instrument-grade CO\(_2\), which is 99.99% pure, angiography was performed using rapid hand-injections of the gas. A 60-ml syringe was used for acroangiography, venacavography, or portal venography; and a 20-ml syringe was used for selective pelvic, lower extremity, or renal arteriography. To prevent air contamination, the syringes were filled with CO\(_2\) in a sterile fashion through a stopcock and were purged three times each before they were finally filled with CO\(_2\) and the stopcock closed. The time between filling the syringes and injecting the gas was minimized to prevent diffusion. The catheter was initially primed with CO\(_2\) to limit the explosive delivery of the gas. Images were acquired using digital subtraction technic on a DFS 4100 Plus system-Version 11E (ADAC Laboratories, Milpitas, CA) at a rate of three or four images per second on a 512 x 512 matrix. In most cases, a 5-French sizing pigtail or straight catheter (Cook, Bloomington, IN) was used to calculate the diameter of the treated artery. Six patients had prior conventional arteriograms or calcifications in the arterial wall visible on a scout radiograph, which were used to determine the diameter of the treated segment. In the three patients undergoing TIPS revi-

![Fig. 1.—75-year-old man who presented with diminished right common femoral artery pulse, ankle-brachial index of 0.51, and nonhealing ulcer on right foot. Serum creatinine level was 2.8 mg/dL. A, Arteriogram obtained with carbon dioxide (CO\(_2\)) as contrast agent shows short 60-80% stenosis (straight arrow) of distal right common iliac artery. Sizing pigtail catheter (curved arrow) was used to determine vessel diameter. B, Arteriogram obtained with CO\(_2\) as contrast agent after successful deployment of Palmaz 2006 stent (Johnson and Johnson, Warren, NJ) arrowed across stenosis, which was localized using only CO\(_2\) as contrast agent. Placement of stent was successful: no translesion pressure gradient at rest or with distal augmentation using intraarterial nitroglycerin was found. After sheath removal, patient had strong pulse in right common femoral artery. Foot ulcer subsequently healed.](image-url)
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Eight (31%) of 26 procedures were performed without using iodinated contrast material: stent placement in an iliac artery (n = 4), angioplasty of a renal artery (n = 1), and angioplasty of several lesions in the superficial femoral and popliteal arteries (n = 1), angioplasty of a vein graft (n = 1), and angioplasty of a dialysis graft (n = 1). In seven procedures (27%), CO₂ was the only contrast agent administered.

The patient undergoing angioplasty of the renal artery had a small amount of gadopentetate dimeglumine injected.

Eleven (42%) of 26 procedures were performed using less than or equal to 20 ml of full-strength equivalent iodinated contrast material: stent placement in a renal artery (n = 2), angioplasty of a femoropopliteal artery (n = 2), initiation of bypass graft thrombolysis (n = 2), angioplasty of a vein bypass graft (n = 2), angioplasty of infrapopliteal arteries (n = 1), recanalization of a TIPS (n = 1), and angioplasty of the inferior vena cava (n = 1).

The range of full-strength equivalent iodinated contrast material administered was 5-20 ml, with a mean and median of 14 ml. Iodinated contrast material injections were administered to confirm appropriate positioning before vascular intervention or to improve the quality of angiography after the procedure.

Follow-Up

Serum creatinine levels were measured after 1 or 2 days after 21 procedures. Multiple serum creatinine levels were measured for more than 2 days after 19 of these procedures. Serum creatinine levels were not measured after five procedures performed with only CO₂; one of these patients was already regularly undergoing hemodialysis. A 25% increase in serum creatinine to a level of at least 2 mg/dl was considered significant after the administration of iodinated contrast material [3]. Hospital and physician office records were reviewed to assess for sequelae of these procedures. Patients were monitored clinically until stenosis or occlusion at the intervention site recurred or until death.

Analysis

The patients were retrospectively divided into three groups to assess the adequacy of CO₂ to guide vascular interventional procedures. The three groups included patients in whom no iodinated contrast material was required to adequately perform the procedure, in whom less than or equal to 20 ml of full-strength equivalent (76% iodine concentration) contrast material was required, and in whom more than 20 ml of full-strength equivalent contrast material was required. When diluted contrast material was injected, the volume was reduced for the sake of comparison with the equivalent amount of 76% iodine contrast material. The volume of contrast material was calculated to include the injections both for imaging and for fluoroscopic observation. In one patient, two intraarterial hand injections (<20 ml) of diluted gadopentetate dimeglumine (Magnevist; Berlex, Imaging, Wayne, NJ) were substituted for iodinated contrast material after angioplasty of the renal artery [15]. The mean volumes of iodinated contrast material administered during angioplasty or stent placement of a renal artery, angioplasty or stent placement of an iliac artery, angioplasty of an infrapopliteal artery, and angioplasty of a bypass graft were calculated.

Results

Twenty-five (96%) of 26 interventional procedures were technically successful. Success was defined as a residual stenosis of less than or equal to 30% and no significant pressure gradient, if measured. A significant pressure gradient was considered to be less than or equal to a resting systolic gradient of 10 mm Hg in the arterial system and a portosystemic gradient of less than or equal to 12 mm Hg in patients undergoing TIPS revisions.
Seven (27%) of 26 procedures required more than 20 ml of full-strength equivalent iodinated contrast material: revision of a TIPS (n = 2), angioplasty of a renal artery (n = 2), stent placement in a renal artery (n = 1), angioplasty of separate common and external iliac artery stenoses (n = 1), and angioplasty of infrapopliteal arteries (n = 1). The range of iodinated contrast material administered was 35–350 ml, with a mean of 120 ml and a median of 80 ml.

Five (50%) of the 10 intraabdominal procedures required more than 20 ml of iodinated contrast material, whereas only two (13%) of the 16 extraabdominal procedures required more than 20 ml of iodinated contrast material (p = .051). The average volume of iodinated contrast material administered for the six angioplasty or stent procedures in a renal artery was 107 ml. In comparison, a mean of 215 ml of iodinated contrast material was required for angioplasty or stent placement in the renal artery in patients at our institution over the past 2 years when CO₂ was not used. In this study, an average of 9 ml of iodinated contrast material was required for the five angioplasty or stent procedures of the iliac arteries, and an average of 22 ml was required for the eight angioplasties of infrapopliteal arteries (including vein bypass graft). When the two angioplasties of infrapopliteal arteries are excluded, an average of only 10 ml of iodinated contrast material was required for the angioplasties of the femoropopliteal arteries and the bypass grafts. Our average contrast material volumes for arterial interventions in the iliac or infrapopliteal arteries of patients without compromised renal function cannot be compared with these results because these procedures are usually accompanied by complete diagnostic arteriography.

After 16 procedures in which iodinated contrast material was administered, three patients had a significant increase in serum creatinine levels; two of these patients were diabetic. One patient who received 15 ml of iodinated contrast material had a 0.7 mg/dl increase in serum creatinine level (30% greater than baseline). The level returned to baseline within a week. Two patients who received 45 and 350 ml of iodinated contrast material, respectively, had increases in their respective serum creatinine levels of 0.8 mg/dl (42%) and 1.8 mg/dl (55%). The first patient had partial recovery of renal function. The serum creatinine level of the other patient remained elevated, but to date this patient has not required dialysis. No patient had any other apparent reason for renal compromise such as hypotensive event, sepsis, cholesterol embolization, or administration of aminoglycosides or additional iodinated contrast material.

Eleven (61%) of 18 patients had a slight decrease in their serum creatinine levels after the administration of iodinated contrast material. Three patients had stable serum creatinine levels. One patient who received 15 ml of iodinated contrast material had an increase of 0.4 mg/dl (24%) in serum creatinine level, which returned to baseline after 1 week.

Complications

One procedure was not successful. Angioplasty was successfully performed for stenoses in the tibioperoneal trunk and proximal peroneal artery. However, angioplasty of an additional stenosis in the mid peroneal artery produced a 2-cm-long occlusion. Intraarterial urokinase was infused for several hours, but progressive pericatheter thrombosis occurred in the peroneal artery despite systemic anticoagulation. The patient was not considered a candidate for prolonged thrombolysis. The foot was not threatened, and a bypass graft to the dorsalis pedis artery was performed 1 week later for the nonhealing ulcer. This complication was not considered attributable to the use of CO₂.

A patient who underwent diagnostic pelvic and lower extremity arteriography using CO₂ before angioplasty of the superficial femoral artery experienced abdominal pain several hours later. Mesenteric arteriography using iodinated contrast material showed two small filling defects representing emboli or intraluminal injuries in the proximal left colic artery. The patient's symptoms resolved after systemic anticoagulation; no sequelae occurred, and the serum creatinine level did not increase after arteriography using iodinated contrast material. During attempts to selectively catheterize the left common iliac artery without injecting iodinated contrast material, the guidewire was inadvertently advanced into the inferior mesenteric artery several times, which presumably caused this complication. This complication may have been prevented with the use of iodinated contrast material.

Another patient had a decrease from 30 to 0 mm Hg in the systolic transesophageal gradient after angioplasty of a renal artery. The angioplasty site appeared patent using CO₂ and gadopentetate dimeglumine, and the procedure was considered successful based on the pressure measurements. Because this patient had a continuing increase in serum creatinine level from 3.9 mg/dl to 6.3 mg/dl, conventional arteriography using iodinated contrast material was performed 4 days later. This showed a large intimal flap at the angioplasty site and a short occlusion near the origin of the contralateral renal artery that was not identified previously using CO₂ aortography. Bilateral renal artery Palmaz stent placement was performed; pressure measurements were not repeated across the angioplasty site before stent placement. This patient required hemodialysis for 7 months after the procedure. Dialysis was not necessary over the following 9 months, but because of progressive renal failure, this patient now requires dialysis again.

After antegrade puncture for angioplasty of the superficial femoral artery, a small pseudoaneurysm of the distal external iliac artery developed in one patient. This complication was not considered to be related to the use of CO₂ and was successfully treated by sonographically guided compression.

Follow-Up

Because a variety of procedures were performed on a heterogeneous group of patients, overall patency data are not reported. Follow-up of 20 patients ranged from 7 days to 54 months (mean, 9 months; median, 6 months) from the time of their last procedure.

In 10 of 12 patients who underwent peripheral arterial interventional procedures, follow-up ranged from 7 days to 13 months (mean, 5 months; median, 3 months). Four patients are currently asymptomatic. One patient died of multiorgan system failure unrelated to the interventional procedure. Because their symptoms recurred or progressed, the other two patients underwent a bypass graft and two patients had an amputation. Two of these patients died postoperatively, and the other two were subsequently lost to follow-up and likely also died. Both patients who had undergone angioplasty of a vein bypass graft were monitored using Doppler sonography and arteriography. The angioplasty site was patent in one patient after 6 months. In the other patient, stenosis of the vein graft angioplasty sites recurred, but the contralateral iliac artery stent was patent; the patient died shortly thereafter of congestive heart failure. No other imaging was performed of these intervention sites.

Six of six patients who underwent renal artery interventional procedures are alive a mean of 7.5 months (median, 6 months; range, 1–16 months) after the procedures. None have experienced worsening of hypertension, although all still require medication for blood pressure control, dosages were decreased. Four have never required dialysis. One patient required dialysis for 7 months after angioplasty and subsequent placement of bilateral renal artery
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patients when CO₂ refluxed into the cerebral arteries. Three of these patients presumably had reflux of CO₂ into a vertebral artery from an upper extremity dialysis graft during outflow occlusion to visualize the arterial anastomosis [17] 22; therefore, we do not perform arterial CO₂ injections above the diaphragm. A recent case report attributes livedo reticularis, rhadomyolysis, massive intestinal infarction, and death to CO₂ arteriography in one patient without pathologic confirmation of atheroemboli [23]. To our knowledge, this complication has not been reported by others.

The literature describing CO₂ use in interventional procedures is limited. The use of CO₂ as a contrast agent has been described for venacavography before filter placement [16, 24] and for fluoroscopic guidance during placement of peripherally inserted central catheters [25, 26]. Rees et al. [27] have performed three TIPS procedures using only CO₂, and several authors describe angiography using CO₂ to guide angioplasties of the renal, iliac, or femoropopliteal arteries [16, 20, 21, 28-30]. Frankhouse et al. [31] reported findings similar to those of this study in 26 patients undergoing angioplasty of the renal, iliac, femoropopliteal, or infrapopliteal arteries. Eight procedures were performed using only CO₂, whereas 19 required supplementation with a mean of 39 ml of iohexol contrast material. Twenty-five (93%) of these 27 procedures were technically successful, and a transient increase in serum creatinine level was found in only two patients, who had received 60 and 70 ml of iohexol contrast material, respectively.

As our familiarity with CO₂ delivery and our confidence regarding image interpretation increased, we began to use CO₂ more frequently for diagnostic and interventional procedures in patients with azotemia or previous severe reaction to iohexol contrast material. Twenty-three (88%) of these 26 procedures were performed within the last 2 years of the 4.5-year study period. In 19 (73%) of 26 cases, the interventional procedure was successfully guided using CO₂ and a small amount of iohexol contrast material if necessary. Iohexol contrast material was used to confirm lesion location before intervention and to improve contrast resolution for better digital imaging after the procedure. CO₂ allowed angioplasty or stent placement in an iliac artery and angioplasty of an infrapopliteal artery or bypass graft to be performed using minimal amounts of iohexol contrast material.

Five of the seven procedures that required more than 20 ml of iohexol contrast material were infraabdominal. CO₂ visualization was limited by overlying bowel gas or respiratory motion during imaging for lesion localization. IV glucagon (Eli Lilly, Indianapolis, IN) injections may be helpful to reduce bowel gas artifacts. The inability to rapidly deliver a large bolus of CO₂ by hand injection into the aorta or portal vein may also have contributed to inadequate imaging before or after these interventional procedures. The commercial availability of a CO₂ injector may improve image quality and thereby further reduce the amount of iohexol contrast material required. Improved digital imaging systems with faster acquisition and 1024 × 1024 matrix may also enable better visualization of CO₂ in the abdomen. CO₂ angiography as described in this report may decrease the volume of iohexol contrast material necessary to perform renal artery interventional procedures, but half of these patients required substantial doses of contrast material.

Controversy exists regarding the risk factors for diminished renal function after the administration of iohexol contrast material [2-14]. Some authors have shown that the incidence and severity of renal insufficiency after iohexol contrast material administration are related to how much contrast material is used and to degree of renal compromise before the procedure [2, 4-10]. Because of the small number of patients in this study, we cannot show that the incidence of azotemia was reduced as a result of using CO₂ instead of iohexol contrast material.

In conclusion, this study shows that CO₂ may replace iohexol contrast material to guide vascular interventional procedures in patients with azotemia or previous severe reaction to contrast material. Seventy-three percent of procedures were successfully performed with no more than 20 ml of iohexol contrast material. CO₂ guidance was particularly useful for limiting the dose of iohexol contrast material in interventional procedures in the iliac and infrapopliteal arteries. CO₂ use can decrease the volume of iohexol contrast material required for some interventional procedures, but inadequate visualization with CO₂ required substantial doses of iohexol contrast material in half of the interventional procedures in this study. Improvements in CO₂ delivery systems may further reduce the amount of iohexol contrast material needed for these procedures.

References
Eschelman et al.