

# Lower Extremity Arteriography with Use of Iodinated Contrast Material or Gadodiamide to Supplement CO<sub>2</sub> Angiography in Patients with Renal Insufficiency<sup>1</sup>

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**Abbreviations:** CO<sub>2</sub> = carbon dioxide, Cr = serum creatinine, CRI = chronic renal insufficiency, DSA = digital subtraction angiography, IA = intraarterially, PVD = peripheral vascular disease, SFA = superficial femoral artery

**PURPOSE:** To determine if the use of nonionic contrast material, as compared to the use of gadodiamide to supplement carbon dioxide angiography in patients with peripheral vascular disease (PVD) and chronic renal insufficiency (CRI), results in significant worsening of renal function.

**MATERIALS AND METHODS:** Lower extremity angiographic procedures (diagnostic and diagnostic/intervention) were performed in 40 patients with CRI (baseline serum creatinine [Cr] > 1.5 mg/dL) using CO<sub>2</sub> alone or CO<sub>2</sub> supplemented with the use of either nonionic contrast material or gadodiamide (up to 0.4 mmol/kg). Serum creatinine levels were obtained before the procedure and at 48 hours after the procedure. The peak Cr level was also determined for patients with a significant (> 0.5 mg/dL) Cr elevation.

**RESULTS:** Forty-two lower extremity angiographic procedures (19 diagnostic and 23 diagnostic/interventions) were performed in 40 consecutive patients from August 1997 to October 1998, with a mean preprocedure Cr of 2.2 mg/dL and a mean postprocedure Cr of 2.4 mg/dL. Twenty-five of the 40 patients (63%) had diabetes mellitus. Fifteen procedures, including six interventions, were performed utilizing CO<sub>2</sub> and nonionic contrast material in 15 patients. Six of these 15 patients (40%) demonstrated a Cr increase > 0.5 mg/dL at 48 hours. Seven procedures, including two interventions, were performed with CO<sub>2</sub> alone in seven patients. No patients in this group demonstrated an increase in serum creatinine of greater than 0.5 mg/dL at 48 hours. Twenty procedures, including 15 interventions, were performed with CO<sub>2</sub> and gadodiamide in 18 patients. In one of these 20 procedures (5%) there was an increase in Cr > 0.5 mg/dL at 48 hours. The difference in worsening renal function for the nonionic contrast group (six of 15) compared with the CO<sub>2</sub>/gadodiamide group (one of 20) was statistically significant ( $P = .03$ ). When comparing the use of CO<sub>2</sub> and nonionic contrast material versus CO<sub>2</sub> alone and with gadodiamide (six of 15 versus one of 27), the difference is also statistically significant ( $P < .01$ ). The average volume of supplemental contrast material was similar in the nonionic contrast material and gadodiamide groups, as was the average volume of supplemental nonionic contrast material in the six patients with an increased Cr.

**CONCLUSION:** The use of small volumes of nonionic contrast material to supplement CO<sub>2</sub> angiography in patients with PVD and CRI can be associated with a significant increased risk of worsening renal function when compared to angiography performed with CO<sub>2</sub> alone or CO<sub>2</sub> and gadodiamide.

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THE risk of contrast-material-induced nephropathy during angiography in patients with underlying chronic renal insufficiency (CRI) and peripheral vascular disease (PVD) is a serious concern. Many of these patients present with extensive disease, and endovascular and/or surgical treatment is frequently necessary to avoid amputation. Diagnostic angiography is currently the most reliable "road map" for treatment and is frequently performed with iodinated contrast material. The reported incidence of contrast-material-induced nephropathy in patients with CRI varies from 9% to 93% (1,2). This large disparity in incidence reflects the use of different criteria to determine when contrast nephropathy is present, different patient population studied, and different pre- and post-contrast treatment algorithms. Although most patients who develop contrast-induced nephropathy recover, prolonged hospitalization and delay in therapy may result (1,3).

Carbon dioxide has been reported to be non-nephrotoxic (4). Therefore, with improvements in digital subtraction angiography (DSA), CO<sub>2</sub> is being used more frequently as an alternative contrast agent to evaluate lower extremity anatomy in patients with CRI and PVD (4,5). However, angiograms obtained with use of CO<sub>2</sub> may result in an incomplete evaluation of lower extremity arterial anatomy in up to 50% of patients (6). In these patients, completion of the diagnostic angiogram, as well as portions of the interventional procedure, may require the use of small amounts of iodinated contrast material. Unfortunately, in some patients with pre-existing CRI, use of small amounts of iodinated contrast material has been associated with contrast-induced nephrotoxicity (7).

Reports of the use of gadolinium-based (gadodiamide) contrast agents administered intraarterially (IA) to perform angiographic diagnostic and interventional procedures in patients with CRI and PVD have recently appeared (8–12). We present a retrospective review of

the incidence of contrast-induced nephropathy in patients with CRI and PVD undergoing angiographic diagnostic and interventional procedures with the use of CO<sub>2</sub> alone, CO<sub>2</sub> supplemented with nonionic iodinated contrast, and CO<sub>2</sub> supplemented with gadodiamide.

## MATERIALS AND METHODS

Patients with CRI (baseline serum creatinine [Cr] > 1.5 mg/dL) with symptoms of advanced PVD (severe claudication, rest pain, and/or tissue loss) referred for lower extremity angiography were included in the study. In each patient, an attempt was made to perform the lower extremity angiography study of the symptomatic leg utilizing CO<sub>2</sub> alone. If, in the opinion of the interventional radiologist performing the study, a complete angiographic study of the symptomatic leg could not be completed with CO<sub>2</sub> alone, either Iohexol (Omnipaque; Nycomed, Princeton, NJ) or gadodiamide (Omniscan; Nycomed-Amersham, Princeton, NJ) was randomly selected by the interventional radiologist performing the study to complete the diagnostic examination. Gadodiamide or nonionic contrast material was used to guide the interventional procedure unless CO<sub>2</sub> images were unequivocal.

Just prior to the procedure, each patient was hydrated with 300–500 mL of normal saline. The diagnostic procedures were performed with use of either a 5-F, ultra-high-flow pigtail catheter (Mallinckrodt, St. Louis, MO) or a 5-F Sos Omni catheter with extra sideholes (Angiodynamics, Glens Falls, NY) for the aortogram and runoff studies. When selective angiograms were obtained, either the 5-F Omni catheter (Angiodynamics) or an endhole catheter was used. CO<sub>2</sub> angiograms were obtained with use of the plastic bag delivery system, as described by Hawkins et al (13). Hand injections of 20–40 mL of CO<sub>2</sub> in the abdominal aorta, and 20–30 mL in the iliac arteries and superficial femoral artery (SFA) were performed while acquiring DSA images over the ar-

teas of interest. The technique used to perform the lower extremity CO<sub>2</sub> angiography has been described elsewhere (14). Maneuvers including elevation of the extremity of interest, administration of IA boluses of 150 mcg of nitroglycerin, and placement of an endhole catheter into the distal SFA or popliteal artery whenever possible were performed to visualize the trifurcation and foot vessel.

If adequate CO<sub>2</sub> studies could not be obtained, hand injections of 5–10 mL of gadodiamide or nonionic contrast material were used with DSA to evaluate the arterial vessels from the knee to the foot. If the catheter could not be placed in the SFA, 30–40 mL of gadodiamide or 20–30 mL nonionic contrast were administered at a rate of 5–6 mL/sec into the common femoral artery with a power injector to evaluate the distal runoff. An attempt was made to obtain the images for only one station of the symptomatic leg. However, when evaluation of two lower stations was needed, an automated stepping technique (Perivision; Siemens Medical Systems, Iselin, NJ) was used to allow imaging of two stations with a single contrast material injection. Because unsubtracted images were usually suboptimal, adequate amounts of analgesic medication were administered to limit patient motion.

Endovascular interventions included percutaneous transluminal angioplasty, stent placement, and thrombolysis. These procedures were performed using standard techniques as previously described (15,16). Progress of an endovascular intervention was monitored with hand injections of 10–20 mL of CO<sub>2</sub>, 5–10 mL of gadodiamide, or 4–8 mL of nonionic contrast material via an endhole catheter or vascular sheath during DSA image acquisition. Serum creatinine levels were obtained within 24 hours of initiating the procedure, and at 24 and 48 hours after the procedure in all patients. Additional Cr levels were obtained as clinically indicated.

## • Statistical Analysis

Two  $\times$  two contingency tables displaying numbers of patients with or without a rise in creatinine of more than 0.5 mg/dL were created. The Fisher exact test was used to compare the treatment groups.

## RESULTS

Forty-two procedures were performed in 40 consecutive patients (27 men, 13 women), with a mean age of 67 years (range, 53–82 years). Twenty-five of the 40 patients (63%) had diabetes mellitus. The mean preprocedure Cr was 2.2 mg/dL (range, 1.6–3.6 mg/dL) and the mean postprocedure Cr was 2.4 mg/dL (range, 1.5–4.3 mg/dL). The patients were divided into three groups based on the contrast agent or agents used. In the group utilizing only CO<sub>2</sub> as the angiographic contrast agent, seven procedures were performed in seven patients (five men, two women; mean age, 64 years; range, 53–82 years). Diagnostic lower extremity angiography examinations were performed in all patients. Two of the seven patients underwent endovascular intervention. The mean preprocedure and postprocedure Cr level was 2.3 mg/dL (range, 1.6–3.1 mg/dL). In no patients in this group was there a rise in Cr greater than 0.5 mg/dL. Technical success was 100%. No periprocedural or postprocedural complications occurred.

In the group of patients receiving CO<sub>2</sub> supplemented with nonionic contrast material, 15 procedures were performed in 15 patients (nine men, six women; mean age, 69 years; range, 53–82 years). Lower extremity angiography examinations were performed in all patients. In 11 of the 15 patients (73%), nonionic contrast material was required to complete the diagnostic portion of the lower extremity examination, and in an additional four patients nonionic contrast material was required to complete the interventional study. Six of the 15 patients (40%) underwent endovascular intervention. Mean preprocedural Cr was 2.1 mg/dL (range,

**Table 1**  
Comparison of Procedures Resulting in a Rise in Cr of > 0.5 mg/dL at 48 hours in CO<sub>2</sub> + Nonionic contrast vs CO<sub>2</sub> + Gadodiamide

	CO <sub>2</sub> + NIC	CO <sub>2</sub> + Gd
Number of procedures resulting increase of serum Cr > 0.5 mg/dl at 48 hrs/Number of procedures	six of 15 (40%)	one of 20 (5%)
Mean preprocedure Cr (mg/dL)	2.2 (1.6–2.9)	3.3 (one patient)
Mean postprocedure Cr (mg/dL)	3.3 (2.5–3.6)	4.3 (one patient)
Average amount of supplemental contrast agent	51 mL (33–80 ml)	70 mL (one patient) (0.3 mmol/kg)

1.6–2.9 mg/dL). The mean 48 hour postprocedural Cr was 2.5 mg/dL (range, 1.7–3.6 mg/dL). The average amount of nonionic contrast material used to supplement CO<sub>2</sub> in this patient group was 53 mL (range, 33–100 mL). Six of the 15 patients (40%) in the CO<sub>2</sub>/nonionic contrast material group demonstrated a rise in Cr of greater than 0.5 mg/dL 48 hours after the procedure (Table 1). The mean preprocedural Cr in the six patients was 2.2 mg/dL (range, 1.6–2.9 mg/dL). The mean 48-hour postprocedural Cr in these six patients was 3.3 mg/dL (range, 2.5–3.6 mg/dL). The average volume of nonionic contrast material used to supplement CO<sub>2</sub> in the six patients was 51 mL (range, 33–80 mL). Technical success was 100%. No periprocedural complications occurred. One death occurred from multisystem organ failure 7 days after below-the-knee amputation and 18 days after lower extremity angiography. This patient had a rise in serum creatinine of 1.3 mg/dL at 48 hours and a peak Cr rise of 1.6 mg/dL prior to starting dialysis. In the remaining five patients with an elevated Cr of greater than 0.5 mg/dL at 48 hours, discharge or surgical treatment was delayed an additional 2 days until the Cr stabilized.

In the group of patients receiving CO<sub>2</sub> supplemented with gadodiamide, 20 procedures were performed in 18 patients (13 men, five women; average age, 67 years; range, 53–82 years). In 10 of the 20 procedures (50%), gadodiamide was needed to supplement CO<sub>2</sub> to complete the lower extremity angiography stud-

ies. In the remaining 10 patients, gadodiamide was used to supplement the CO<sub>2</sub> to complete the endovascular interventions. Endovascular intervention was performed in 15 of the 20 (75%) procedures. The mean preprocedural Cr was 2.3 mg/dL (range, 1.6–3.6 mg/dL). The mean 48-hour postprocedural Cr was 2.3 mg/dL (range, 1.6–4.3 mg/dL). The average amount of gadodiamide used to supplement CO<sub>2</sub> in this group of patients was 55 mL (0.29 mmol/kg) (range, 20–100 mL; 0.13–0.40 mmol/kg). In the single patient in the CO<sub>2</sub> with gadodiamide group that experienced a rise in Cr of greater than 0.5 mg/dL, the preprocedural Cr was 3.3 mg/dL and the postprocedural Cr was 4.3 mg/dL (Table 1). The patient received 70 mL (0.3 mmol/kg) of gadodiamide. The technical success rate was 100%. One periprocedural complication resulted during recanalization of an occluded SFA segment. An embolus migrated distally into the proximal anterior tibial artery. The focal occlusion in the anterior tibial artery was successfully treated with use of thrombolysis and balloon angioplasty, with a good postangioplasty result.

The incidence of diabetes mellitus in each group was not significantly different: CO<sub>2</sub>, four of seven (57%); CO<sub>2</sub> + nonionic contrast, nine of 15 (60%); CO<sub>2</sub> + gadodiamide, 12 of 20 (67%) ( $P > .05$ ). The mean preprocedural Cr were not significantly different for each group (group I, Cr = 2.3 mg/dL;

group II, Cr = 2.1 mg/dL; group III, Cr = 2.3 mg/dL;  $P > .05$ ).

The number of procedures resulting in worsening renal function (six of 15) in the CO<sub>2</sub>/nonionic contrast group compared with the CO<sub>2</sub>/gadodiamide group (one of 20) and CO<sub>2</sub> + CO<sub>2</sub>/gadodiamide group (one of 27) was statistically significant (group II vs. group III,  $P = .03$ ; group II vs. group I + group III,  $P = .01$ ) (Table 2).

**DISCUSSION**

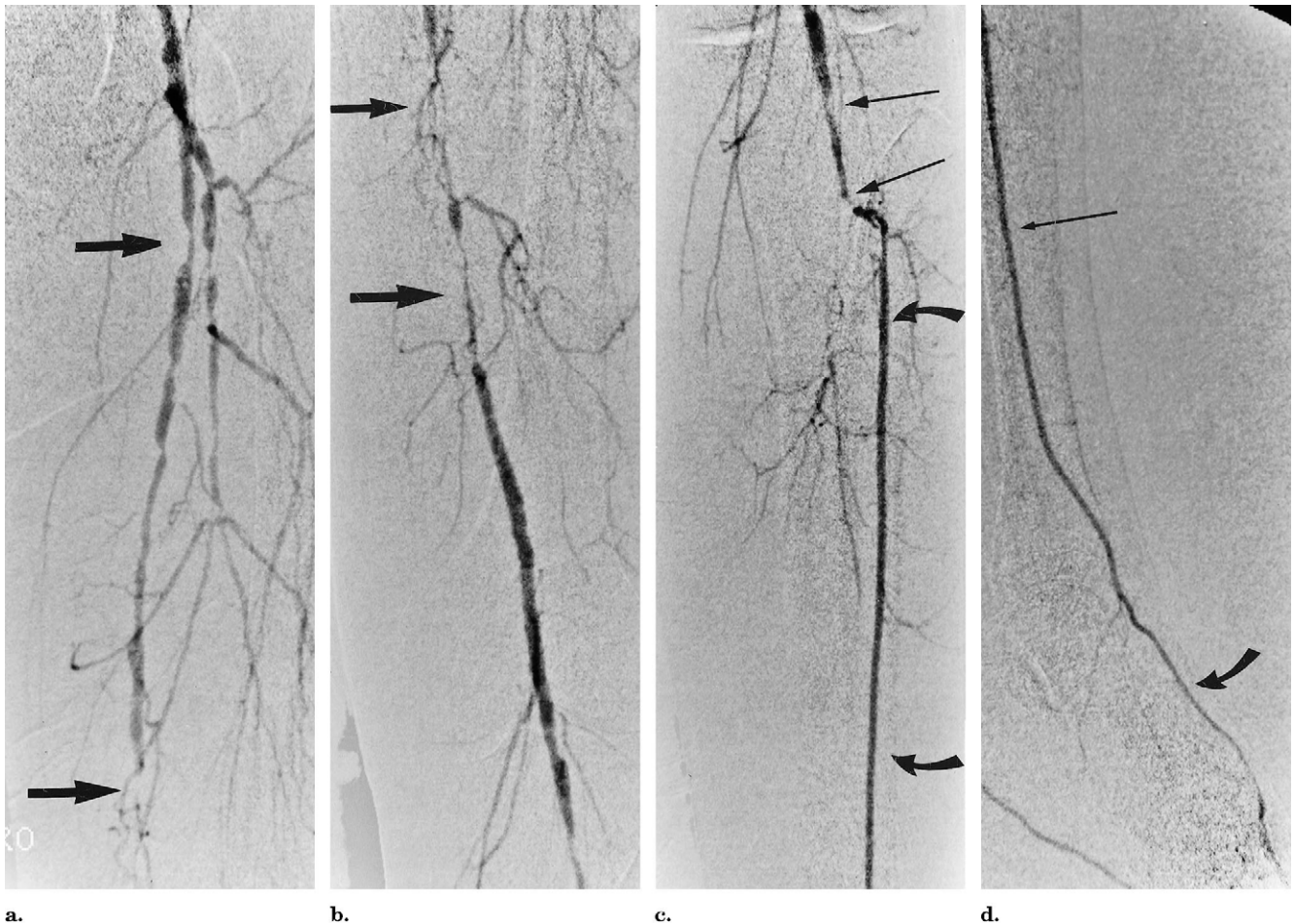
Although several risk factors for contrast-induced nephropathy have been described, only diabetes and underlying renal insufficiency have been consistently identified as risk factors for contrast-induced nephropathy (1,17). In patients with renal insufficiency and symptomatic PVD, a noninvasive diagnostic study for the evaluation of the lower extremity anatomy is desirable. Recently, promising reports of successful evaluation of the lower extremity arterial anatomy using Duplex sonography and magnetic resonance angiography have been described (18,19). However, at this time, neither of these methods have become widely accepted and, as a result, the majority of surgeons and interventional radiologists still require a lower extremity angiogram prior to undertaking surgical bypass or endovascular intervention. Ideally, it would be desirable to perform lower extremity arteriography and guide potential endovascular intervention with a non-nephrotoxic contrast agent.

CO<sub>2</sub> is considered to be non-nephrotoxic (20) and has become a realistic alternative to iodinated contrast material for angiographic procedures below the diaphragm due to recent improvements in CO<sub>2</sub> imaging capabilities and delivery systems. Seeger et al described excellent correlation of CO<sub>2</sub> angiograms of the lower extremity with studies performed using iodinated contrast material (14). In our series, CO<sub>2</sub> angiography was particularly useful in evaluating runoff below the knee in patients with SFA oc-

**Table 2**  
Breakdown of Studies Performed with CO<sub>2</sub>, CO<sub>2</sub> + NIC, and CO<sub>2</sub> + Gd

Group	Patient (M:F)	Mean Age (y)	No. of Procedures (Dx: Interventions)	No. of Diabetics	Mean Volume (mL) Contrast Supplemental	Mean Cr pre Cr	Mean post Cr	Percentage of Patients with an Increase in Cr > 0.5 mg at 48 hrs.	Percentage of Procedural Technical Success	P Value vs Group II (patients with an increase after Cr > 0.5 mg/dL)	Comments
I (CO <sub>2</sub> )	7 (5:2)	65 (53-82)	7 (5:2)	4 (57%)	2.3 (1.6-3.1)	2.3 (1.6-3.1)	2.3 (1.6-3.1)	0/7 (0%)	100%		
II (CO <sub>2</sub> + NIC)	15 (9:6)	69 (53-82)	15 (9:6)	9 (60%)	53.4 (33-100)	2.1 (1.6-2.9)	2.5 (1.7-3.6)	6/15 (40%)	100%		One death of a patient with elevated post Cr due to multiorgan failure
III (CO <sub>2</sub> + Gd)	18 (13:5)	67 (53-82)	20 (5:15)	12 (67%)	55.3 (20-100)	2.3 (1.5-3.6)	2.3 (1.6-4.3)	1/20 (5%)	100%	.03	Post SFA recanalization embolus to AT which was visualized with Gd and treated successfully with thrombolysis and PTA
IV (group I + group III)	25 (18:7)	67 (53-82)	27 (10:17)	16 (64%)	2.3 (1.5-3.6)	2.3 (1.6-4.3)	2.3 (1.6-4.3)	1/27 (3.7%)	100%	.01	

NIC = nonionic iodinated contrast; Gd = gadodiamide; SFA = superficial femoral artery; AT = anterior tibial artery. Note.—Numbers in parentheses are ranges.



**Figure 1.** Left lower extremity CO<sub>2</sub> angiograms provide adequate visualization of the arterial anatomy from the level of the left femoral head to the left foot. The study demonstrates the following levels of disease. (a) Patent proximal SFA with diffuse disease, including an area of focal occlusion with segments of reconstitution in the midsegment (arrows), (b) long segment of severe disease including focal occlusions and areas of reconstitution in the abductor canal segment (arrows), (c) focal areas of severe disease in the distal popliteal artery (arrows) and widely patent anterior tibial artery (curved arrows), and (d) widely patent anterior tibial artery to the foot (arrows) filling of patent dorsalis pedis artery (curved arrow).

clusion because of the propensity of the CO<sub>2</sub> to travel via collaterals into the distal vessels when the lower extremity is elevated and IA nitroglycerin administered. CO<sub>2</sub> “stacking” software was particularly helpful to produce a diagnostic image in these patients (Fig 1). However, Rolland et al reported only a 50% success rate for completing an entire lower extremity angiographic study with CO<sub>2</sub> in a small series of patients (6). In addition, in patients with poor tibial runoff, CO<sub>2</sub> tends to overestimate disease because of dissolution of the gas in the slow flow vessels (21). Indeed in our series, CO<sub>2</sub> alone provided a complete

lower extremity angiography examination in only 21 of 42 procedures (50%).

Therefore, to complete some lower extremity angiography examinations successfully, a supplemental contrast agent must be used to visualize those vessels not seen with CO<sub>2</sub> angiography (Fig 2). The use of small volumes of iodinated contrast material has been advocated for the completion of these examinations (21). However, even small amounts of iodinated contrast material have been shown to worsen renal function in some patients with underlying renal insufficiency (7). Unfortunately, we found

this to be the case in our small series of patients who received small amounts of iodinated contrast material to supplement the CO<sub>2</sub> angiograms. Forty percent (six of 15) of the patients receiving relatively small amounts of supplemental iodinated contrast material (mean, 51 mL of nonionic contrast) demonstrated a rise in Cr of greater than 0.5 mg/dl at 48 hours. All six of these patients remained in the hospital until their Cr returned to baseline (average, 5.2 days; range, 2–18 days). In the two patients who were not treated with endovascular therapy, surgery was delayed.

Gadolinium-based contrast



**Figure 2.** (a) CO<sub>2</sub> angiogram obtained at the trifurcation level with the catheter tip in the proximal SFA demonstrates poor visualization of the trifurcation vessels at the lower leg level. (b) Left lower leg angiogram obtained after the administration of 20 mL of nonionic contrast material with the catheter positioned in the proximal SFA demonstrates the arterial anatomy at the trifurcation and tibial vessel level in the lower leg. (c) Left foot angiogram obtained after the administration of 30 mL of nonionic contrast material with the catheter in the proximal SFA demonstrates no significant flow into the foot. Occluded anterior tibial (arrow) and posterior tibial (curved arrow) arteries are seen. The CO<sub>2</sub> angiogram was not interpretable.

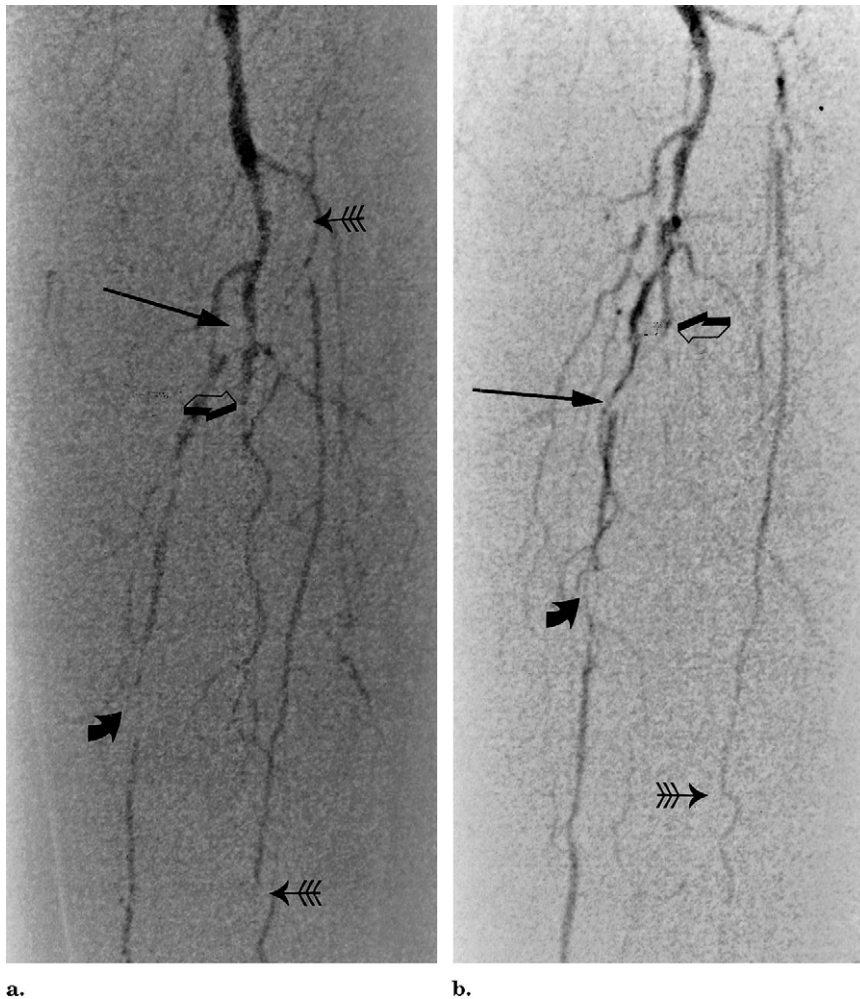
agents have been advocated as an alternative to iodinated contrast material in patients with renal insufficiency. Studies have shown that these agents do not worsen renal function when used intravenously in doses up to 0.4 mg/kg (22,23). Reports of IA use of gadolinium-based contrast agents in the patients with renal insufficiency have been promising (8,12). Gadodiamide provided visualization of the runoff vessels below the knee utilizing small volume (5–10 mL injections) from an endhole catheter positioned in the distal SFA or popliteal artery and utilizing larger injections (20–40 mL) delivered via an endhole catheter in the common femoral artery when the SFA was patent (**Fig 3**). In addition, gadodiamide was helpful for monitor-

ing the progress of endovascular intervention. In our study, dissection flaps and filling defects were not well visualized with CO<sub>2</sub> angiograms. The use of the liquid contrast agent gadodiamide also helped confirm or “clear” areas of stenosis seen with the CO<sub>2</sub> and helped to monitor progress of the intervention (**Fig 4**).

The injection of the low osmolar solution gadodiamide resulted in less pain when injected into the runoff vessels of the lower extremity compared with our previous experience after the injection of the ionic agent gadopentetate dimeglumine (Magnevist; Berlex Laboratories, Wayne, NJ). Less pain results in less motion and less image degradation. Subjectively, patient reports of pain or extremity motion

during contrast material injections were similar with use of gadodiamide and nonionic contrast material, but were more than with CO<sub>2</sub> unless gas trapping in the toes occurred. Dilution of the gadodiamide with saline prior to injection into the arterial system results in suboptimal images and is not recommended. In addition, the low concentration (0.5 mmol/mL) of gadolinium in the gadolinium-based contrast agents currently available in the United States results in suboptimal “native” (unsubtracted) images. Gadodiamide images were typically inferior to nonionic contrast images, but diagnostic.

To optimize imaging of gadolinium-based contrast agents with the lowest amount of radiation per exposure, images were obtained at



**Figure 3.** (a) CO<sub>2</sub> angiogram at the trifurcation level with the catheter positioned in the proximal SFA demonstrates focal occlusion of the proximal posterior tibial artery (arrow), severe disease in the midportion of the posterior tibial artery (curved arrow), occlusion of the peroneal artery (open arrow), and segments of the anterior tibial artery (hatched arrows). (b) Gadodiamide angiogram at the trifurcation level in the lateral position confirms the occlusion of the proximal portion of the posterior tibial artery (arrow), severe disease in the midportion of the posterior tibial artery (curved arrow), occlusion of the peroneal artery (open arrow), and focal occlusions of the anterior tibial artery (hatched arrows).

approximately 96 KVp because of the higher KeV (50.2) of gadolinium compared with that of iodine (33 KeV), resulting in less radiation per exposure at this KVp (24). Reducing the radiation per exposure is useful because it is usually necessary to increase the dose administered during imaging to reduce image noise (primarily due to quantum mottle) because of the low concentration of gadolinium. Gadolinium angiograms are usually obtained with use of a

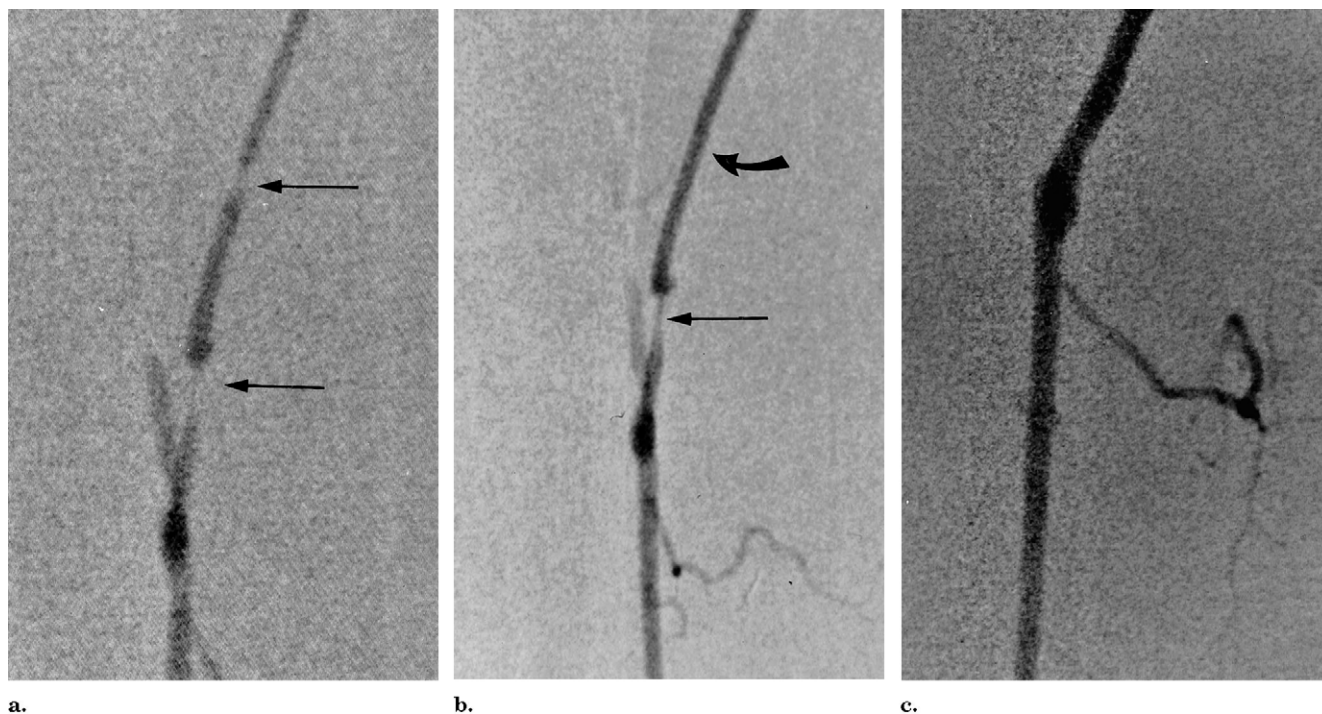
DSA program of two frames per second for 3 seconds followed by one frame per second for the remainder of the procedure.

It is important to note that gadolinium-based contrast agents cost 5–10 times as much per milliliter as nonionic iodinated agents. We believe that the difference in cost can be justified by a reduced hospital stay when contrast-induced nephropathy is avoided.

One patient in the CO<sub>2</sub>/gadodia-

mid group developed an increase in Cr greater than 0.5 mg/dl. Although atheroembolization could have caused this patient's worsening renal function, no clinical evidence of atheroembolization was found, and the rather quick return to baseline renal function is unusual with an atheroembolic episode. The increase in Cr in this patient suggests that contrast-induced renal failure can occur while using CO<sub>2</sub> and IA gadodiamide. Although the patient had several severe medical problems, including diabetes mellitus and a history of severe congestive heart failure, which occurred again 24 hours after the procedure, gadodiamide may have played a role in the patient's worsening renal function. Of interest is a recent report of presumed gadolinium-based contrast-induced nephrotoxicity in a patient undergoing lower extremity angiography (25). The IA dose of gadolinium-based contrast agent administered in this patient was equal to 0.44 mmol/kg. This report, as well as the single episode of worsening renal function in our series, suggests that, until a larger experience is gained using IA gadolinium-based contrast agents, the minimum dose necessary to complete the examination should be utilized.

This study has several limitations. The decision to supplement CO<sub>2</sub> angiograms with either gadodiamide or nonionic iodinated contrast material was based on the opinion of the angiographer at the time of the study that the study was either inadequate or did not completely depict the extent of vascular disease before intervention, after intervention, or during intervention. No attempt was made to reach a consensus regarding these images. No effort was made to address the selection bias in the study. Patients with varying cardiac function, which may effect both the quality of the angiograms and/or the effects of nonionic contrast or gadodiamide on renal function, were not identified. No attempt was made to determine if each patient was maximally hydrated. Rather, patients received a moderate fluid



**Figure 4.** (a) CO<sub>2</sub> angiogram obtained at the upper tibial level in this patient with a femoral-to-posterior tibial vein bypass graft, with the catheter positioned in the proximal portion of the graft, demonstrates a patent vein bypass graft with focal areas of “stenosis” (arrows). (b) Gadodiamide angiogram at the same level with the catheter positioned in the proximal portion of the graft demonstrates a single focal area of high-grade stenosis just above the distal anastomosis (arrow). The other area of high-grade stenosis in the more proximal portion of the graft is not present on the gadodiamide angiogram and represents an area of under-filling on the CO<sub>2</sub> angiogram (curved arrow). (c) Gadodiamide angiogram demonstrates improvement in the stenosis in the distal portion of the graft after balloon angioplasty.

bolus, which may have been inadequate in some.

In conclusion, the use of small volumes of nonionic contrast material to supplement CO<sub>2</sub> angiography in patients with PVD and CRI can be associated with a significant increased risk of worsening renal function when compared to angiograms obtained with use of CO<sub>2</sub> alone or with gadodiamide.

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