Digital Subtraction Angiography of the Abdominal Aorta and Lower Extremities: Carbon Dioxide versus Iodinated Contrast Material[1]

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PURPOSE: To compare the diagnostic value of carbon dioxide to that of iodinated contrast material for digital subtraction angiography of the abdominal aorta and lower extremities.

MATERIALS AND METHODS: Thirty-five patients underwent comparative CO_2 and iodinated contrast material arteriography of the abdominal aorta and lower extremities. For each contrast study, three independent observers evaluated the degree of opacification and percentage of stenosis of each vessel, the degree of certainty of their observations, and the overall quality of the study. Data of CO_2 and iodinated studies were compared using analysis of variance for repeated measures. Interobserver and intertechnique agreements were estimated with Cohen's kappa and intraclass correlation coefficient.

RESULTS: Iodine-based vascular opacification was superior to that with CO_2 in the central and distal arteries ($P = .02$). The degree of certainty and overall quality score were higher for iodine than for CO_2-based contrast studies ($P = .00001$). The interobserver agreement for categorizing stenoses was higher for iodine as compared to CO_2-based angiography. No significant difference was observed between the mean stenosis values obtained with CO_2 and iodine-based angiography in any segment. Intraclass correlation coefficient demonstrated a high degree of convergence of the two techniques for assessing the percentage of stenosis.

CONCLUSION: CO_2 can be used as an alternative to iodinated contrast material for obtaining arteriograms of the abdominal aorta and lower extremities for investigating atherosclerotic disease.

Index terms: Angiography, comparative studies • Angiography, contrast media • Arteries, extremities • Carbon dioxide • Contrast media, comparative studies.

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Abbreviations: ANOVA = analysis of variance, DSA = digital subtraction angiography

IODINATED contrast materials are widely used for peripheral angiography but toxicity problems remain in a number of patients. The utilization of steroids and nonionic contrast agents decreased, but not eliminated, the risk of hypersensitive reactions (1–5). In addition, renal toxicity occasionally leading to permanent renal dysfunction, cardiac toxicity, vascular and hematologic disturbances, and other systemic events represent other risks to be considered following iodinated contrast angiography (6–8).

Carbon dioxide has been used in the vascular system for over 30 years (9,10). It can be considered a good contrast agent for infradiaphragmatic angiography because it is nontoxic, nonallergenic, inexpensive, and is eliminated via the lungs in a single pass (11–17). The use of CO_2 has been limited in part, because it had been difficult to inject properly due to its compressibility,

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with a somewhat explosive delivery using either a handheld syringe or conventional injector (11–17). It is also recognized that the images obtained with CO_2 angiography can appear less sharp and well defined compared to images obtained with iodinated contrast. In addition, technical limitations with respect to filming have also impeded the propagation of this technique (11–17).

The purpose of this study is to evaluate the diagnostic performance of CO_2 digital subtraction angiography (DSA) of the abdominal aorta and lower extremities performed with a dedicated CO_2 injector (Angiodynamics, Glenn Falls, NY) in comparison to iodinated DSA.

MATERIALS AND METHODS

Over a period of 12 months, 35 consecutive patients (23 men and 12 women; age range, 45–83 years; mean age, 64.5 years) were prospectively and sequentially investigated via angiographic examination employing CO_2 (USP grade) and iodine-based (ioversol [Optiray 320]; Mallinckrodt Medical, St. Louis, MO) contrast agents in two centers. The order of contrast delivery (CO_2 followed by ioversol or ioversol followed by CO_2) was randomized. Seventeen patients were assigned to the CO_2-ioversol cohort and 18 to the ioversol-CO_2 group. One patient in the ioversol-CO_2 group did not complete the study secondary to a technical difficulty, inability to trigger the CO_2 injector, leaving 34 patients in the study population.

Subjects required infradiaphragmatic arteriography for lower extremity claudication (category I-1 to I-3 of the Society of Vascular Surgery and International Society of Cardiovascular Surgery) (18) and were willing and able to give fully informed consent prior to the start of the procedure. The exclusion criteria were as follows: refusal or inability to give consent, the presence of a systemic infection, severe pulmonary dysfunction, pregnancy, uncontrolled diabetes, utilization of contrast media during the preceding 7 days, medically unstable subjects, patients with rest pain, and patients with atrial septal defect, ventricular septal defect, or any suspected right to left shunt with the possibility of reflux into the cerebral circulation. Last, patients who received nitrous oxide anesthesia within the past year were also excluded (19). This was recommended by our sponsor (Angiodynamics, Glenn Falls, NY) due to the fact that nitrous oxide anesthesia enhances the risk associated with CO_2 administration by increasing the mean pulmonary arterial pressure. We wanted to be sure that any residual nitrous oxide from prior anesthesia was not present to eliminate the possibility of any untoward hemodynamic pulmonary event. This project was approved by the research and ethics committee in each institution.

Two radiologists (V.L.O., A.A.C.) performed the arteriography procedures below the diaphragm with 5-F catheters via a common femoral artery approach. For the purpose of the present study, the common and external iliac arteries are considered as one, and will be referred to as "iliac artery." The vascular region investigated varied depending on the clinical context: 16 patients underwent abdominal aortography and bilateral iliac arteriography; two patients underwent abdominal aortography, and bilateral iliac and femoropopliteal arteriography; two patients underwent abdominal aortography, femoropopliteal, profunda femoris, and runoff vessel arteriography; seven patients underwent evaluation of the femoropopliteal, profunda femoris, and runoff vessels; seven patients underwent femoropopliteal arteriography alone. Abdominal aortography and iliac arteriography were always performed with a 5-F pigtail catheter (Angiodynamics). Infrainguinal arterial evaluation was always performed unilaterally in the symptomatic limb using a 5-F cobra or Sos Omni catheter (Angiodynamics) introduced from the opposite common femoral artery across the aortic bifurcation and into the iliac artery of the symptomatic side. Diagnostic images were obtained with use of Digicon (Picker, Cleveland, OH) and arc-U (Philips Medical Systems, Eindhoven, The Netherlands) angiographic systems using the same projections in each patient with each contrast agent.

All CO_2 angiograms were obtained with a dedicated ECG-gated CO_2 injector (Angiodynamics) designed to deliver CO_2 in a consistent and safe manner. This CO_2 injector is connected to a closed system and uses high-quality medical-grade pure CO_2. An integrated 0.2-μm filter is used to remove bacteria and a continuous heparinized saline flush maintains catheter patency between injections. Multiple one-way valves prevent the retrograde blood flow and the system is purged prior to each use to avoid injecting room air.

Due to the buoyancy of CO_2, optimal arterial visualization was obtained by positioning the area of interest in a nondependent manner when possible. A dose of 20 mg of hyoscine butylbromide (Buscopan; Boehringer Ingelheim, Ontario, Canada) was administered intravenously prior to obtaining abdominal aortograms if active peristaltic activity was observed. The lower extremity evaluation was performed with a wedge that elevated the patient's limbs approximately 20°. A 2–3-minute wait between injections was performed to allow the CO_2 to dissolve, thus preventing any vapor lock phenomena. The diagnostic images of the CO_2 studies were reconstructed by summating several angiographic frames using stacking software (Adac; Picker), prior to filming. The maximum single injection dose of CO_2 was 200 mL, and the total procedural dose could not exceed 1,500 mL. Injection volumes are given in **Table 1**.

Iodinated arteriograms were obtained with ioversol and use of a conventional angiographic intravascular injector (Angiomat 6000; Leibel Flarsheim, Cincinnati, OH). The total procedural volume of contrast media could not exceed 250 mL. The injection regimens are given in **Table 1**. When angiography was technically unsatisfactory, it was repeated with a larger volume of iodinated contrast or CO_2. We must

Table 1
Injection Rates for CO_2 and Iodinated Arteriography

	Ioversol		CO_2	
Injection site	Rate (mL/sec)	Volume (mL)	Rate (mL/sec)	Volume (mL)
Aorta	20–25	40–50	40–60	80–120
Iliac artery	5–10	15–20	20–40	60–80
Femoral artery	4–6	12–20	20–40	60–80
Popliteal artery	4–6	12–20	20–40	60–80

Note.—CO_2 = carbon dioxide.

emphasize that image reconstruction of some CO_2 arteriograms could not be performed at the time of the examination due to technical limitations of the stacking software, hence image quality could not always be appreciated until the examination was processed for filming. The iodinated or CO_2 angiograms were photographed using the same technique.

The total number of vessels studied is as follows: aorta (n = 20), right renal (n = 20), left renal (n = 20), right iliac (n = 18), left iliac (n = 18), femoropopliteal (n = 18), profunda (n = 9), anterior tibial (n = 9), posterior tibial (n = 9), and peroneal (n = 9). The arterial segments were grouped into three categories as follows: segment A being the central vessels, includes the abdominal aorta, and renal and iliac arteries. The proximal vessels were evaluated in segment B and comprise the profunda femoris and femoropopliteal arteries. Last, segment C represents the distal vessels including the anterior tibial, posterior tibial, and peroneal arteries.

The diagnostic utility was evaluated via blind comparison of the CO_2 and iodinated angiographic studies separately by three radiologists (C.H., G.S., E.T.) who had not performed the arteriography procedures. A CO_2 or iodinated contrast study from each patient was randomly displayed on one of two multiviewers without placing both contrast studies from a given patient on the same multiviewer. The corresponding angiographic study was placed on the second multiviewer, hence, each multiviewer contained either a CO_2 or iodinated contrast study from a given patient while at the same time containing a mix of CO_2 and iodinated contrast studies from different patients. The studies on each multiviewer were read with a time interval of 2 months to avoid interpretation bias.

Vessel opacification was evaluated by using integer values from 0 to 2 according to the following definition: 0 = absent, 1 = partial, and 2 = satisfactory. The most severe stenosis of each satisfactorily opacified vessel (score of 2) was measured with precision microcalipers (General, Switzerland) and a magnifying lens. Vessels unsatisfactorily opacified with either CO_2 or iodine were excluded from the stenosis evaluation. The percentage of stenosis was obtained by comparing the diameter at the stenosis to that of a nearby area excluding any region of poststenotic dilation. The degree of stenosis was then categorized as follows: 1 = 0–29.9%, 2 = 30.0%–49.9%, 3 = 50.0%–69.9%, 4 = 70.0%–99.9%, 5 = complete occlusion. For each vessel studied, the level of radiologist certainty was evaluated using the following scoring system: 1 = low, 2 = moderate, 3 = high. In addition, each examination was scored for overall quality as follows: 1 = excellent, 2 = good, 3 = fair, 4 = poor, 5 = inadequate.

• Statistical Analysis

Mean opacification scores, mean percentage of stenosis, mean categorical stenosis, degree of certainty, and overall quality scores were first compared for iodinated and CO_2 arteriograms, using three-way analysis of variance (ANOVA) for repeated measures. The model included factors to investigate differences between the three observers and between the two contrast agents. A third factor was also introduced to reflect the type of segment evaluated (central, proximal, distal). Because few patients had all segments examined, this last factor was treated as a "between-subjects" factor. Interobserver and intertechnique agreements were estimated based on Cohen's kappa coefficient and intra-class correlation coefficient (20,21). An uncorrected alpha level of 0.05 was used for all analyses.

RESULTS

CO_2 adequately opacified (score of 2) 89% and iodinated contrast 99% of vessels, respectively. The number of inadequately opacified vessels is as follows: observer 1, iodinated contrast = 4, CO_2 = 21; observer 2, iodinated contrast = 0, CO_2 = 15; observer 3, iodinated contrast = 1, CO_2 = 14. ANOVA for repeated measures demonstrates that iodine-based vascular opacifaction is superior to CO_2 in the central arteries (aorta, renal, and iliac) **(Fig 1)** and distal arteries (anterior tibial, posterior tibial, and peroneal) **(Fig 2)** (P = .02, **Table 2**), regardless of the observer. The degree of opacification is similar in the proximal arteries (profunda femoris, superficial femoral, popliteal) **(Table 2)**.

There is no significant difference in the mean stenosis values obtained with CO_2 or iodine-based an-

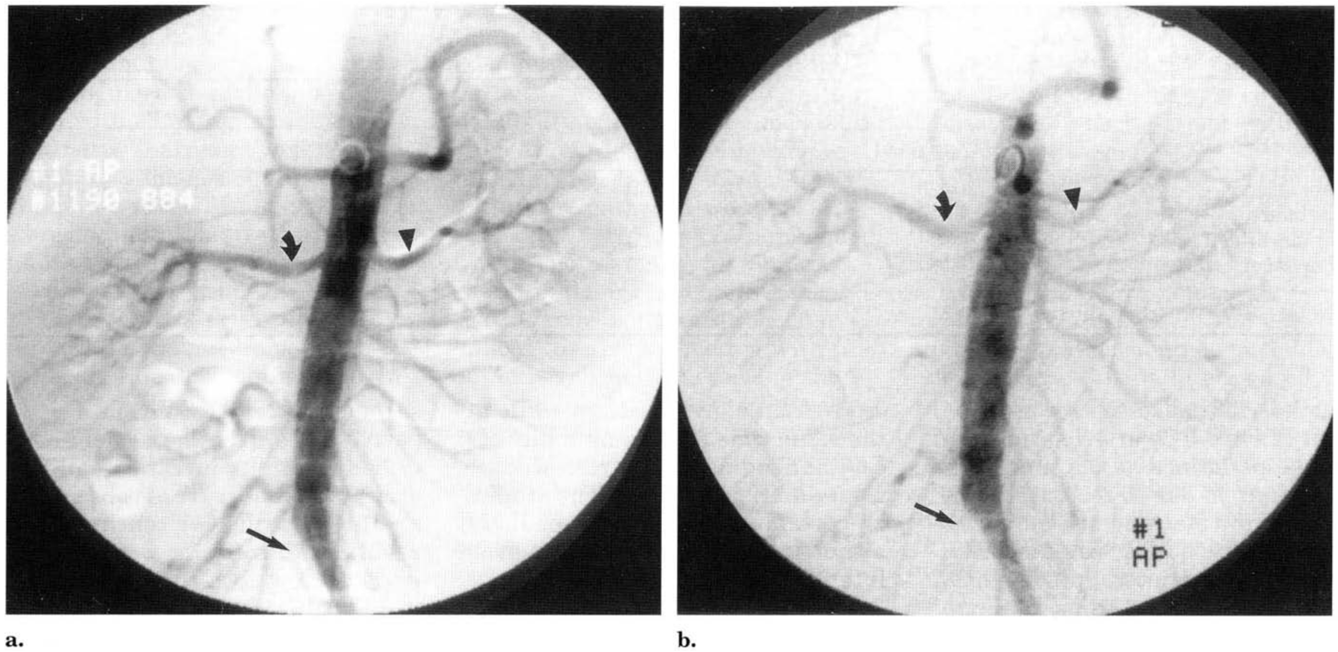


Figure 1. A 42-year-old patient with right hip claudication. **(a)** Abdominal aortogram obtained with iodinated contrast material. The right (curved arrow) and left (arrowhead) main renal arteries are free of stenosis. There is complete occlusion of the right common iliac artery (arrow). **(b)** Abdominal aortogram obtained with CO_2 in same technical conditions as in **(a)**. The clinically relevant information is present on this study with the occluded right iliac artery being well demonstrated (arrow). The renal arteries appear free of stenosis, but the left renal artery (arrowhead) is poorly opacified as compared to the right renal artery (curved arrow), probably because of its more posterior situation.

giography in any segment for any of the observers **(Fig 3)**. This result, obtained with ANOVA analysis, is present in both the mean percentage **(Table 3)** and categorical groups **(Table 4)**.

A significant difference in both measured percent stenosis and categorical groups is present between segment A versus B and C seen with both the CO_2 and iodine, due to the distribution of atherosclerotic disease **(Tables 3 and 4)**. A slight but nonetheless significant difference exists between observer 1 versus 2 and 3 for the observed mean percentage of stenosis with observer 1 being slightly more severe using both CO_2 and iodine (P = .03, **Table 3**). This interobserver effect is not present in the mean categorical analysis **(Table 4)**.

The interobserver agreement (kappa of Cohen) with respect to the category of stenosis was higher for iodinated contrast angiography as compared with CO_2 angiography **(Table 5)**.

Further statistical analysis utilizing intraclass correlation coefficients demonstrates a high degree of convergence between the mean percentage stenosis values obtained with CO_2 and iodine. The values obtained are 0.847, 0.975, and 0.824 for each of the three respective observers.

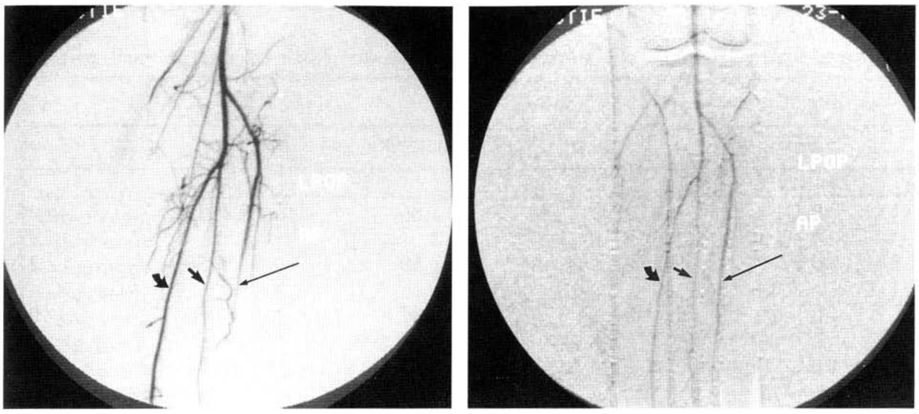
All three observers found a significantly greater degree of certainty and overall quality with iodine-based contrast studies compared to those utilizing CO_2 (P = .00001, **Tables 6, 7**).

• Adverse Events

In the ioversol-CO_2 group, a 68-year-old man with a history of angina, coronary artery disease, hypertension, cerebrovascular accident, and diabetes developed unstable angina pectoris immediately following the procedure. He received medical in-hospital treatment, and the episode resolved with no sequelae. Three other patients in this group experienced moderate adverse events: one had transient chest pain and two experienced urticaria following iodinated contrast administration. All episodes resolved uneventfully. There were no complications related to the use of CO_2.

DISCUSSION

The flow dynamics of CO_2 (gas/fluid) are different from those of iodinated contrast material (liquid/liquid), which mixes with blood and readily depicts any downstream vessel, given adequate iodine concentration (11). Considering that CO_2 is a gas, adequate visualization of the vasculature requires that a sufficient quantity of CO_2 be injected to completely displace the blood column in the vessel of interest. This is why larger volumes of CO_2 are required as compared to iodinated contrast to obtain angiographic images of diagnostic quality (11–17). The relative decrease in opacification with CO_2 in the cen-



a. b.

Figure 2. A 60-year-old patient with left lower extremity claudication. **(a)** Arteriogram of the proximal runoff vessels obtained with iodinated contrast material injected into the proximal superficial femoral artery. There is incomplete filling of the anterior tibial artery (long arrow), and both the peroneal (short arrow) and posterior tibial (curved arrow) arteries are normal. **(b)** CO_2 arteriogram obtained under the same conditions as in **(a)**. The vascular opacification is significantly less in the present study compared with the iodinated arteriogram shown in **(a)**. The anterior tibial artery (long arrow) appears occluded distally, which may account for the slow flow in this vessel on the iodinated study. Although no focal stenosis is identified, there is marked underfilling of both the peroneal (short arrow) and posterior tibial (curved arrow) arteries.

tral and distal arterial systems is due to different phenomena, some of which can be diminished if strict attention to technique is observed (11–17). The rate and total volume of injection determine the degree of opacification, as a slow rate or insufficient volume of contrast material will not be able to replace the blood column in the target vessel (11–13,15). Underfilling of a blood vessel with CO_2 will falsely demonstrate a vessel of diminished caliber (11). Lack of opacification in the central arteries (aorta, renal, and iliac) is probably caused in part by their large diameter, which makes them difficult to fill, given the intrinsic buoyant properties of CO_2 (11). Optimal vascular opacification with CO_2 also requires that the artery of interest be in a nondependent position relative to the injection site. This can be accomplished by properly positioning the patient for visceral studies and with the use of a tilting table to investigate the lower extremities (11,16). These maneuvers, however, are not fail proof, as shown by the lack of opacification occasionally observed in the central and distal vessels, despite optimal patient positioning. This suggests that the quality of CO_2 angiograms can be affected in situations where the target vessel is in a dependent position, too large or far from the injection site.

The observed difference in mean stenosis between segment A versus B and C reflects the distribution of disease in this population, with the femoral, popliteal, and tibial vessels being more diseased than the aorta or renal arteries. These differences in disease distribution were similarly demonstrated with both CO_2 and iodine-based angiography.

The decrease in kappa scores with CO_2-based angiography reflects a decrease in consistency of the stenotic measurements between the observers. This result is probably due to diminished vessel filling causing suboptimal delineation of the edge of the vessels when CO_2 is used. Interestingly, the intraclass correlation coefficient, which compares intertechnique numerical values, demonstrated a stronger correlation than the kappa values (21), thus confirming the convergence of the two techniques in terms of the percentage of stenosis.

The significantly greater degree of certainty and overall quality ($P = .00001$ for both tests) with the iodine examinations probably reflect two major factors. The difference in opacification may have played a large role. Furthermore, the radiologists who evaluated the studies are used to the high-contrast images provided by iodinated contrast material and likely possess an inherent bias. Although partly subjective, the preference for high-contrast images may limit the wide acceptance of CO_2 angiography.

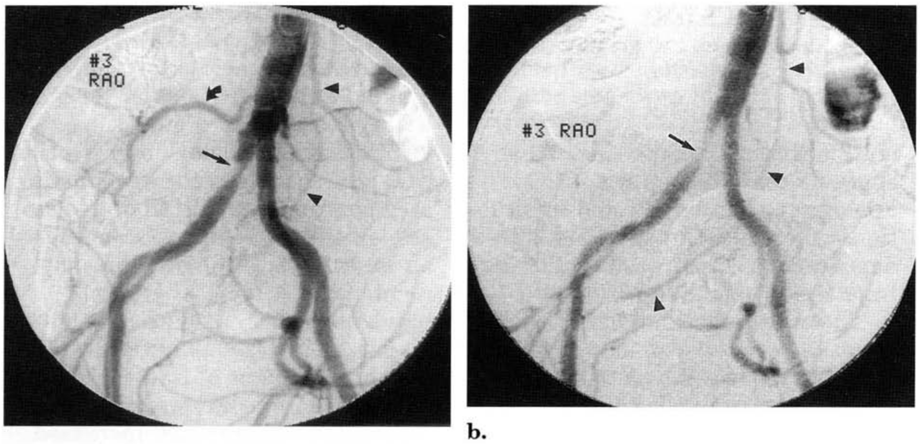
Very limited data are available regarding the accuracy of CO_2 in stenosis evaluation. Despite lower opacification scores obtained with CO_2 compared with iodinated DSA in our study, the stenosis measurements were comparable with both contrast agents. Our results bear certain similarities with the ones found by Black et al (22). They compared the accuracies of CO_2 and iodinated DSA densitometry for quantifying stenoses in a pulsatile ex vivo flow model. They observed that CO_2 was equally accurate as iodinated contrast for quantifying stenoses, except for eccentric stenoses in an intermediate range of hemodynamic significance, where CO_2 proved superior. As such, the lower viscosity of CO_2 may allow detection of subtle changes of luminal diameter that are masked with iodinated contrast. The presumed increased sensitivity of CO_2 to subtle variations of the vascular lumen may compensate for its weaker opacification, as found in our study.

The safety of CO_2 angiography has been proven in several studies with a 30-year history of use in the vascular system (9–12, 15). However, potential complications mandate extreme caution when this technique is used. Caridi and Hawkins reported a case of transitory (less than 24 hours) left colon ischemia from a suspected vapor lock phenomena that occurred in a patient who had an abdominal aortic aneurysm with a patent inferior mesenteric artery (11). The phenomenon of vapor lock has been fatal when massive amounts (1,500 mL) of CO_2 have been injected into

Table 2
Mean Opacification Scores

	Iodine			CO_2		
	Mean OS	SD	*n*	Mean OS	SD	*n*
Observer 1						
Segment A	1.99	0.1	96	1.85	0.35	96
Segment B	2	0	27	2	0	27
Segment C	1.93	0.27	27	1.59	0.56	27
Observer 2						
Segment A	2	0	96	1.87	0.36	96
Segment B	2	0	27	2	0	27
Segment C	2	0	27	1.74	0.53	27
Observer 3						
Segment A	2	0	96	1.83	0.45	96
Segment B	2	0	27	2	0	27
Segment C	2	0	27	1.85	0.46	27

Note.—OS = opacification score (scale of 0 to 2), SD = standard deviation, *n* = number of vessels. Scale: 0 = non opacification; 1 = partial opacification; 2 = satisfactory opacification. Opacification scores were significantly higher for iodine as compared to CO_2, especially for segments A and C ($P = .02$).



a.

b.

Figure 3. A 55-year-old patient with right leg claudication. **(a)** Pelvic arteriogram obtained with iodinated contrast material injected through a pigtail catheter. The obtained stenosis value of the right common iliac artery is 62% (arrow). An enlarged right lumbar artery is opacified (curved arrow). The inferior mesenteric artery is also well seen (arrowheads). **(b)** Pelvic arteriogram obtained with CO_2 under the same conditions as in **(a)**. The right iliac artery stenosis, measured at 65% (arrow), is in close agreement with that obtained using iodinated contrast. Note that the right lumbar artery that was opacified with iodinated contrast material is not filled with CO_2 because of posterior position. Conversely, the inferior mesenteric artery, which is anterior in position, fills more with CO_2 (arrowhead) than it did with iodinated contrast.

the central venous circulation in dogs placed and maintained in the right lateral decubitus position (11,15,16). This situation can occur in any vascular bed given the proper conditions (rapidly repeated large volume injections with no repositioning, thus preventing CO_2 from dissolving into adjacent blood). This can usually be eliminated in human adults by maintaining single injected volumes below 200 mL, allowing 2–3 minutes between injections, and repositioning the patient following injections to accelerate dissolving into adjacent blood (11,14–16). Transient mesenteric ischemia can still occur despite these precautions, as was reported in a female patient after CO_2 angiography of the abdominal aorta and iliac arteries (23). More dramatic complications of CO_2 angiography have also been reported. Rundback et al have described the development of livedo reticularis, rhabdomyolysis, massive intestinal infarction, and death following CO_2 angiography in a patient with congestive heart failure (24). At present, the use of CO_2 in the thoracic aorta, or coronary or carotid arterial system is contraindicated because the effects of intraarterial CO_2 on the brain are poorly understood with various conflicting studies in dogs and rats (25,26). Until definitive studies unequivocally demonstrate its safety, the use of intraarterial CO_2 should be limited to the abdominal aorta and lower extremities in addition to the venous system.

The degree of contrast-induced renal dysfunction has been elucidated by Hall et al whose group found that increases in baseline serum creatinine level occurred in 2%–62% of patients following iodine contrast angiography (27). This group also found that contrast-induced renal insufficiency occurred

Table 3
Mean Percentage of Stenosis after Exclusion of Unsatisfactorily Opacified Vessels

	Iodine			CO_2		
	Mean PS (%)	SD (%)	*n*	Mean PS (%)	SD (%)	*n*
Observer 1						
Segment A	20.4	30.0	76	21.8	30.9	76
Segment B	42.5	36.2	27	47.1	35.3	27
Segment C	41.0	41.1	16	39.5	44.0	16
Observer 2						
Segment A	17.2	28.6	76	18.5	31.4	76
Segment B	41.1	34.9	27	40.4	37.6	27
Segment C	39.8	42.1	16	40.0	44.2	16
Observer 3						
Segment A	17.3	28.5	76	19.0	30.5	76
Segment B	40.0	35.7	27	42.1	38.4	27
Segment C	38.9	41.8	16	41.8	42.4	16

Note.—PS = percentage of stenosis, SD = standard deviation, n = number of vessels, CO_2 = carbon dioxide. There was a statistically significant difference between the percentage of stenosis found in segment A versus segments B and C (P = .002). There was also a slight difference between observer 1 versus observers 2 and 3, with observer 1 being more severe (P = .03). No significant effect was demonstrated with respect to contrast material employed (contrast material (CM): P = .29; CM × observer: P = .35; CM × segment: P = .92; 3-way interaction: P = .50).

Table 4
Mean Category of Stenosis after Exclusion of Unsatisfactorily Opacified Vessels

	Iodine			CO_2		
	Mean CS	SD	*n*	Mean CS	SD	*n*
Observer 1						
Segment A	1.62	1.09	76	1.74	1.19	76
Segment B	2.48	1.40	27	2.70	1.44	27
Segment C	2.50	1.71	16	2.50	1.75	16
Observer 2						
Segment A	1.56	1.04	76	1.63	1.41	76
Segment B	2.41	1.27	27	2.48	1.48	27
Segment C	2.44	1.67	16	2.50	1.75	16
Observer 3						
Segment A	1.56	1.02	76	1.62	1.07	76
Segment B	2.44	1.34	27	2.48	1.40	27
Segment C	2.44	1.67	16	2.56	1.71	16

Note.—CS = category of stenosis, SD = standard deviation, n = number of vessels. Five categories of stenosis are employed: 1 = 0%–29.9%; 2 = 30.0%–49.9%; 3 = 50.0%–69.9%; 4 = 70.0%–99.9%; 5 = occlusion. There is a statistically significant difference between the category of stenosis found in segment A versus segments B and C (P = .001). No statistical effect is present for the contrast material or the observers with respect to category of stenosis in any segment (contrast material [CM]: P = .11; CM × observer: P = .79; CM × segment: P = .92; 3-way interaction: P = .62).

in 41.7% of patients with pre-existing renal dysfunction (27). Several solutions have been suggested to lower the risk of renal failure induced by iodinated contrast. Solomon et al showed that hydration with 0.45% saline for 12 hours before and 12 hours after angiography significantly reduces acute renal dysfunction in patients with chronic renal insufficiency (28). Dopamine infusion in renal doses has also been proven effective in preventing acute contrast-induced deterioration in renal function after angiography in patients with pre-existing renal insufficiency (29). The use of nonionic iodinated contrast material has diminished the incidence of minor reactions in comparison with high-osmolarity contrast agents. However, it has had no effect on the incidence of severe hypersensitivity reactions and death due to anaphylactic reactions (1–4).

In addition to virtually eliminating the risk of contrast-induced hy-

Table 5
Interobserver Agreements for Category of Stenosis after Exclusion of Unsatisfactorily Opacified Vessels

	Iodine			CO_2		
Observers	Kappa	95% CI	*n*	Kappa	95% CI	*n*
1 and 2	0.78	0.69–0.87	147	0.68	0.58–0.78	142
3 and 1	0.80	0.72–0.88	147	0.68	0.58–0.78	140
2 and 3	0.87	0.80–0.94	150	0.72	0.62–0.81	146

Note.—CI = confidence interval, *n* = number of vessels. Interobserver agreements are based on classification of stenoses into five categories. Categories: 1 = 0%–29.9%; 2 = 30.0%–49.9%; 3 = 50.0%–69.9%; 4 = 70.0%–99.9%; 5 = occlusion. Kappa value ranges: <0.4 = poor agreement; 0.4–0.75 = fair agreement; >0.75 = good agreement.

Table 6
Degree of Certainty

	Iodine		CO_2	
	Mean DC	SD	Mean DC	SD
All observers	2.89	0.23	2.55	0.51

Note.—DC = degree of certainty (scale of 1 to 3). These numbers are based on observations in 119 arterial segments.
Scale: 1-low; 2-moderate; 3-high.
The effect of contrast material used with respect to observer certainty is highly significant ($P < .00001$).

Table 7
Overall Quality Scores in 34 Patients

	Iodine		CO_2	
	Mean OQS	SD	Mean OQS	SD
Observer 1	1.85	0.56	2.88	1.04
Observer 2	1.47	0.62	3.01	1.03
Observer 3	1.47	0.56	2.76	0.70

Note.—OQS = overall quality score (scale: 1-excellent, 2-very good, 3-good, 4-fair, 5-unacceptable), SD = standard deviation.
The statistical effect with respect to contrast material utilized is highly significant ($P = .00001$).

persensitivity and nephrotoxicity, CO_2 angiography provides satisfactory information for planning of surgical or endovascular procedures (11,14–17,22,30). Furthermore, the low viscosity of CO_2 enables smaller sized catheters to be employed during diagnostic studies (11,14,15). Technically, CO_2 angiography is safe and very inexpensive on a per case basis compared to iodinated contrast studies (11,15). The explosive delivery problem previously encountered has been eliminated with the newer handheld and injector delivery systems (11). Furthermore, image stacking programs are now readily available on modern angiographic equipment and can help to deliver excellent diagnostic quality studies. These factors should help promote the diffusion of CO_2-based angiography. Our findings that no significant difference in the mean stenosis values is observed between the two techniques and that the interobserver agreement with respect to the category of stenosis is only marginally inferior for CO_2 angiography as compared to iodinated DSA further support the use of CO_2 when iodinated contrast material is contraindicated.

Despite the numerous advantages that CO_2 offers, its limitations should be considered when choosing a contrast agent for performing angiography. CO_2 angiography lacks the high-contrast images and accurate delineation of the vascular lumen. Subsequently, the observers' degree of certainty and the overall quality of the study are lower than those obtained with iodinated DSA. An additional consideration when using CO_2 is the added time needed to perform an angiographic study. It is likely that injections will be repeated due to inadequate vascular opacification more often than with iodinated contrast angiograms. Furthermore, a time lag is necessary between injections to prevent vapor lock. Lastly, an injector capable of injecting both CO_2 and iodinated contrast would also help promote this technique since the start-up costs are not insignificant if a dedicated CO_2 injector is required.

We must emphasize some limitations of our study. Although we have attempted to assess the diagnostic value of CO_2 angiography, the study was not designed to evaluate the impact on treatment strategies or clinical outcome. Also, we did not evaluate patients with more advanced lower limb ischemia (rest pain, tissue loss, or gangrene) who are likely to have more extensive atherosclerotic disease of the lower extremity arteries.

In summary, in the majority of patients, CO_2 angiography enables accurate depiction of vascular disease involving the abdominal aorta and arteries of the lower extremities compared with iodinated contrast angiography. Although the overall quality of CO_2 angiography remains inferior to that of iodinated contrast angiography, it can be useful in patients with a history of iodine hypersensitivity reactions and when the preservation of already diminished renal function is an objective.

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