

# Clinical applications of carbon dioxide/digital subtraction arteriography

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During an 18-month period 33 patients in whom there were contraindications to the use of iodinated contrast arteriography underwent 40 carbon dioxide/digital subtraction arteriograms for lower extremity ischemia (19), severe hypertension and renal insufficiency (12), or arterial aneurysm (2). Contraindications to iodinated contrast agents included renal insufficiency, congestive heart failure, and contrast hypersensitivity. Sixteen aortic, 15 iliac-femoral-popliteal-tibial, five aorta-iliac-femoral and four aorta-iliac-femoral-popliteal-tibial carbon dioxide/digital subtraction arteriography studies were performed. In 11 studies, imaging of selected arterial segments required the addition of 10 to 60 ml of dilute nonionic contrast. Guided by carbon dioxide/digital subtraction arteriography studies four femoral-tibial bypasses, three aneurysmorrhaphies, two aorto-renal bypasses, one aortofemoral bypass and one femoral-femoral bypass were successfully performed in 11 patients. In addition, carbon dioxide/digital subtraction arteriography directed angioplasties of the common iliac (4), superficial femoral (6), popliteal (3), or tibio-peroneal trunk (1) were performed in 10 patients. Complications of carbon dioxide/digital subtraction arteriography included transient deterioration in renal function in three patients in whom 20 ml of nonionic contrast was used, a nonfatal myocardial infarction after a popliteal percutaneous transluminal angioplasty in one patient, and transient tachypnea and tachycardia during a carbon dioxide/digital subtraction arteriography study in one patient. Diagnostic arteriograms are obtainable using carbon dioxide as the contrast agent. Carbon dioxide/digital subtraction arteriography permits patients with symptomatic arterial disease at high risk for contrast related complications to safely undergo arteriography and subsequent arterial reconstruction or endovascular intervention. (J VASC SURG 1991;13:266-73.)

Advances in vascular surgery have expanded the indications for operative and endovascular intervention to an elderly patient population that frequently has coexisting renal, cardiac, or other medical illnesses. Surgical morbidity has, in parallel, been dramatically reduced by innovations in modern anesthesia and critical care, thus permitting complex interventions to be safely performed in these compromised patients. However, the nephrotoxicity, high osmolality, and allergic potential of presently available intravascular contrast agents remains significant, and thus for many patients the performance of preoperative arteriography now represents the

greatest hazard of a proposed vascular reconstruction.<sup>1-4</sup> Carbon dioxide (CO<sub>2</sub>), a nontoxic, injectable, rapidly absorbed gas is a potential alternative to standard contrast and may increase the safety of arteriography in the patient at high risk.<sup>5-10</sup>

Carbon dioxide has several properties that make it an attractive alternative to standard agents. It is nonallergenic, eliminating the possibility of fatal hypersensitivity reactions. It is not nephrotoxic or hyperosmolar, which eliminates the need for prearteriography hydration in patients in whom cardiac and renal dysfunction coexist. It can be used for sequential studies on consecutive days without increasing the risk of renal failure. It is cost effective; one tank of CO<sub>2</sub> gas costs approximately 20 dollars, whereas nonionic contrast costs 1 dollar/ml.

Hawkins<sup>11</sup> in 1982 described the first use of CO<sub>2</sub> as an arterial contrast agent. By use of CO<sub>2</sub> and digital subtraction technique, high-quality arteriographic images of the abdominal aorta, visceral arteries, renal arteries, and lower extremity arterial tree were obtained. The issue of whether such studies were of sufficient quality and accuracy to guide the manage-

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ment of patients with arterial disease was not addressed.

During the past 18 months CO<sub>2</sub>/digital subtraction arteriography (CO<sub>2</sub>/DSA) has been used at our institution to assess the extent and pattern of arterial disease in a select group of patients at high risk. Subsequent arterial reconstruction, endovascular intervention, or nonoperative management was based solely on these diagnostic studies. From this experience specific information concerning the diagnostic value, limitations, and complications of CO<sub>2</sub>/DSA in the patient with arterial disease has been accrued. This report outlines this experience, details the technical aspects of CO<sub>2</sub>/DSA, and summarizes the clinical context in which we have found this technique to be of value.

## PATIENTS

Between December 1988 and May 1989, 33 patients have undergone 40 arteriograms in which CO<sub>2</sub> gas was used as a contrast agent. Seventeen patients were women; 16 were men. Their mean age was 61 years (range 27 to 81 years). Associated medical illnesses included renal insufficiency not requiring dialysis in 22 (67%), hypertension in 18 (56%), diabetes in 16 (50%), cardiac disease in 13 (41%), cerebrovascular disease in six (19%), and chronic obstructive pulmonary disease in five (16%). Diagnostic arteriography was indicated for the evaluation of severe lower extremity ischemia manifested by rest pain, forefoot gangrene, nonhealing digital amputation, or ulceration in 19 (60%) patients; severe hypertension and renal insufficiency in 12 (34%); and arterial aneurysms in two (6%) patients. Relative contraindications to iodinated contrast arteriography included: elevated serum creatinine,  $\geq 1.7$  mg/dl, in 22 patients (mean serum creatinine = 2.7 mg/dl); congestive heart failure in 12, contrast hypersensitivity in two.

## METHODS

All CO<sub>2</sub>/DSA procedures were performed via either a femoral or axillary artery puncture. When using a femoral puncture the use of an antegrade or retrograde approach was dependent on the arterial segments of interest. Catheters, 5 to 5.5F, were used in each patient. For abdominal and pelvic arteriography a pigtail catheter was used. Antegrade or retrograde studies of the femoral, popliteal, and tibial vessels were performed with a preshaped endhole catheter or dilator. Immediately before injection the catheter and attached tubing were flushed with 5 to 10 cc of CO<sub>2</sub>. Fifty cc of CO<sub>2</sub> gas in a plastic syringe was then

rapidly injected intraarterially by hand before imaging. Up to 15, 50 cc injections of CO<sub>2</sub>, spaced 2 minutes apart, were used in any single study. Digital subtraction technology was the sole method of imaging with imaging speed at 3 to 6 exposures/sec. When arterial segments were not adequately visualized by CO<sub>2</sub>/DSA a small volume of nonionic contrast (10 to 20 cc) mixed 1:1 with normal saline was used to delineate the arterial anatomy. This was necessary in 11 studies. Analgesia was administered as necessary. Baseline and postprocedural peripheral arterial blood gas samples were obtained in nine studies.

In 19 patients with lower extremity ischemia the arterial segments for CO<sub>2</sub>/DSA were selected according to the anatomic location of the occlusive lesion. Twenty-three studies were performed in these 19 patients, 10 in conjunction with percutaneous transluminal angioplasty (PTA). Carbon dioxide/digital subtraction arteriography was confined to the iliac-femoral-popliteal-tibial segments in 15 studies, aorta-iliac-femoral segments in four, and aorta-iliac-femoral-popliteal-tibial segments in four. The lower extremity was elevated to enhance the quality of the arterial image by taking advantage of the lower density of CO<sub>2</sub> as compared to blood.

In 10 of 19 patients with limb ischemia, PTA directed by CO<sub>2</sub> was performed. Before performing PTA, CO<sub>2</sub> was used to image the arterial segment of interest, and CO<sub>2</sub>/DSA roadmap images were obtained. Dilute nonionic contrast was used to inflate the angioplasty balloon. Resolution of the waist of the balloon was observed fluoroscopically. Successful PTA end points included fluoroscopic resolution of the balloon waist, equalization of intraarterial pressures proximal and distal to the lesion, or repeat CO<sub>2</sub>/DSA demonstrating a <50% residual stenosis.

Fifteen studies were performed in 12 patients to investigate renovascular disease. Eleven patients had severe hypertension plus renal insufficiency, and one had hypertension only. Intraaortic injection of CO<sub>2</sub> was used in all studies. Selective renal artery injections were performed in one patient. The iliac and femoral arteries were studied as well by CO<sub>2</sub>/DSA in three patients with an abdominal aortic aneurysm, one with aortoiliac occlusive disease, and one with a renal transplant. Renal artery imaging by CO<sub>2</sub>/DSA was enhanced by placing the patient in a prone, oblique, or lateral decubitus position such that the renal artery of interest was nondependent.

The iliac and femoral arteries were studied in one patient with a pulsatile inguinal mass after a cardiac catheterization, and the abdominal aorta was studied



Fig. 1. CO<sub>2</sub>/DSA of the infrageniculate popliteal artery. The anterior tibial artery is occluded at its origin. The peroneal (P) and posterior tibial (PT) arteries are patent proximally, but contain extensive occlusive disease. The inability of CO<sub>2</sub>/DSA to image the distal reconstitution of the infrapopliteal arteries necessitated the use of (non-ionic) contrast.

by CO<sub>2</sub>-DSA in a single patient with a mycotic abdominal aortic aneurysm involving the renal and visceral arteries.

## RESULTS

The partial pressure of CO<sub>2</sub> (P<sub>CO<sub>2</sub></sub>) in peripheral arterial blood gas samples obtained after CO<sub>2</sub>/DSA was unchanged from baseline determinations. Although pain from the procedure was less than that with ionic contrast agents, some patients did experience enough discomfort to require mild parenteral

analgesia. The CO<sub>2</sub>/DSA studies performed are summarized with respect to indication, location, contrast agent, and treatment in Table I.

In patients with lower extremity ischemia, all arterial segments in continuity were satisfactorily imaged by use of only CO<sub>2</sub> as the contrast agent. However, visualization of the arterial anatomy and collateral pathways distal to an occlusion or high-grade (>90%) stenosis was occasionally suboptimal because of fragmentation of the CO<sub>2</sub> contrast column by the stenosing lesion (Fig. 1). This limitation in CO<sub>2</sub>/DSA was most pronounced when an infrapopliteal arterial segment was involved by severe occlusive disease. This necessitated the addition of 10 to 20 ml of dilute nonionic contrast in six patients. In two other patients severe tortuosity of the common and external iliac artery resulted in poor visualization because of sequestration of CO<sub>2</sub> within these segments. Forty milliliters of dilute nonionic contrast demonstrated tortuous iliac vessels in both patients and a 50% common iliac stenosis in one.

With the diagnostic information obtained entirely from these CO<sub>2</sub>/DSA studies, PTA of stenotic or occluded arterial segments was performed in 10 patients and arterial reconstruction in six. One of these patients underwent both a PTA and arterial reconstruction. Three of the remaining patients were managed nonoperatively, and one patient underwent a Symes amputation.

Percutaneous transluminal angioplasty procedures involved lesions of the common iliac (4), superficial femoral (6), popliteal (3), and tibioperoneal trunk (1). In seven patients the PTA was performed at the time of the initial diagnostic study. Carbon dioxide was the only contrast agent used to guide the angioplasty in seven patients (9 lesions). In one patient a PTA of a tibioperoneal trunk stenosis was complicated by spasm and arterial thrombosis. Sixty milliliters of dilute nonionic contrast, intraarterial urokinase, and nitroglycerin were required to restore patency. One patient had a successful common iliac PTA guided by CO<sub>2</sub> but required 10 ml of nonionic contrast to guide angioplasty of a 3 cm occlusion of the superficial femoral artery. One patient had a superficial femoral artery PTA guided by CO<sub>2</sub> only, but poor visualization of a distal popliteal lesion by CO<sub>2</sub> necessitated 10 ml of nonionic contrast for PTA. After PTA, restoration of pulses distal to the dilation occurred in five patients, the ankle/brachial Doppler index improved in four, and no observable hemodynamic change was documented in one.

Reconstructive procedures included four femoral-tibial bypasses, one femoral-femoral bypass,



Fig. 2. CO<sub>2</sub>/DSA arteriogram demonstrates the left renal artery (R), superior mesenteric artery (S), and celiac axis (C).

Table I. CO<sub>2</sub>/DSA diagnostic and therapeutic studies

Indication	Location	Patients	Studies	Contrast		Treatment	
				CO <sub>2</sub>	CO <sub>2</sub> + nonionic	PTA	Arterial reconstruction
Limb ischemia	A-I-F	4	4	3	1	2	2
	I-F-P-T	11	15	8	7	7	2
	A-I-F-P-T	4	4	1	3	1	2
Renovascular Aneurysm	A-R	12	15	15	0	0	3
	A	1	1	1	0	0	1
	F	1	1	1	0	0	1
Total		33	40	29	11	10	11

A, Aorta; F, femoral; I, iliac; P, popliteal; R, renal; T, tibial.

and one aorta-femoral bypass. In all patients undergoing arterial reconstruction the CO<sub>2</sub>/DSA study correlated well with the intraoperative findings, allowing the completion of the planned operative procedure. Primary graft patency of these reconstructions is 100% with a mean follow-up of 7 months (range 1 to 15 months).

Renovascular disease was evaluated by 15 CO<sub>2</sub>/DSA studies in 12 patients. Carbon dioxide was the only contrast agent used in these studies. The main renal artery and proximal segmental branches were reliably visualized, but imaging of the intraparenchymal arterial architecture was erratic. Proximal and primary branch points of the celiac and superior mesenteric arteries were also well imaged (Fig. 2). An associated infrarenal abdominal aortic aneurysm was present in three patients. Although in

all three the proximal portion of the aneurysm was successfully imaged, the distal aorta and iliac arteries could not be imaged with CO<sub>2</sub>/DSA. In one patient, associated severe aortoiliac occlusive disease was well demonstrated by the CO<sub>2</sub>/DSA.

In eight patients, the renal arteries were imaged bilaterally and were free of significant occlusive disease. A widely patent transplant renal artery was demonstrated in another patient (Fig. 3). Occlusive bilateral main renal artery disease was demonstrated in the remaining three patients (Fig. 4). Findings included two renal artery occlusions, two high-grade (>90%) stenoses, and two moderate (>50%) stenoses. Based on these studies, three patients have undergone arterial reconstruction, one patient is awaiting renal revascularization, and eight are being managed nonoperatively. Arterial reconstructions



Fig. 3. CO<sub>2</sub>/DSA of renal transplant demonstrates a widely patent main renal artery (*arrow*) arising from the external iliac artery with visualization of segmental and tertiary renal branches. A proximal external iliac stenosis is also demonstrated.

have included an aortofemoral-unilateral aortorenal bypass, an aortorenal bypass, and an abdominal aortic aneurysm resection. In all instances operative findings corroborated those demonstrated by CO<sub>2</sub>/DSA. The two patients undergoing renal revascularization have been followed for 1 and 8 months. Hypertension and renal function have improved in both. One patient, at 4 and 8 months after surgery, has had follow-up CO<sub>2</sub>/DSA studies demonstrating patency of the aortorenal graft and distal renal artery.

Common femoral and suprarenal aortic false aneurysms have been successfully imaged in two patients by use of CO<sub>2</sub>/DSA (Fig. 5). The CO<sub>2</sub>/DSA images provided accurate localization of the arterial disease. Both aneurysms were successfully repaired.

Complications of CO<sub>2</sub>/DSA have been limited to a transient deterioration in renal function (increase in serum creatinine >0.5 mg/dl) in three patients in whom 20 ml of nonionic contrast were necessary and a nonfatal subendocardial myocardial infarction in one patient after a popliteal PTA guided by CO<sub>2</sub>/DSA. One patient with chronic obstructive pulmonary disease, developed tachypnea, tachycardia, and hypertension after the fifteenth CO<sub>2</sub> injection. This rapidly resolved. This is the only morbidity that may be attributable to the use of CO<sub>2</sub> as a contrast agent.



Fig. 4. CO<sub>2</sub>/DSA aortogram with occlusion of left renal artery (*arrow*) and contralateral severe proximal stenosis of the right renal artery. The superimposed density overlying the aorta represents the superior mesenteric artery. This patient underwent a left aortorenal bypass followed by a subsequent right aortorenal bypass. Significant improvement in hypertension and renal function has occurred.

## DISCUSSION

The 33 patients who have undergone 40 CO<sub>2</sub>/DSA studies represent only a small fraction of the 2500 patients who have undergone diagnostic arteriography at our institution during the period of this study. In this highly selected group, only eight diagnostic studies and three PTA procedures performed with CO<sub>2</sub>/DSA had to be supplanted with (nonionic) contrast. Inadequate imaging of collateral pathways and the arterial tree distal to an area of severe lower extremity occlusive disease was predominant reason for the use of contrast. Nevertheless, the volume of contrast required to complete a full diagnostic study was markedly reduced. The benefit of CO<sub>2</sub> in this group of patients at high risk is exemplified by the three patients in whom even a small nonionic contrast load induced a transient, biochemical deterioration in renal function. Conventional contrast arteriograms would likely have resulted in acute renal failure.

As a gas CO<sub>2</sub> has a lower density and layers anteriorly with the patient supine. This property and the spatial relationship of various arterial segments must be considered in maximizing CO<sub>2</sub> arterial im-

*W. A.*

aging. In tortuous or aneurysmal arteries excessive sequestration of CO<sub>2</sub> in the nondependent segments limited the quality of the arterial image in three patients and prevented effective imaging altogether in two. Altering patient position to take advantage of the buoyancy of CO<sub>2</sub> is thus an important element in CO<sub>2</sub> arterial imaging. Elevation of the lower extremities increases flow of CO<sub>2</sub> into distal segments of the arterial tree; the prone or decubitus position takes advantage of the posterior location and posterolateral aortic origin of the renal arteries in renal artery imaging. The supine position enhances the imaging of the visceral arteries.

Although the medical status of patients in this study precluded extensive comparison of CO<sub>2</sub> images with standard contrast studies, a few general observations concerning the quality and accuracy of CO<sub>2</sub>/DSA can be made. First, in those few instances where both contrast and CO<sub>2</sub> images were available, arterial architecture was similar, and although overall vessel enhancement was greater with nonionic contrast, this was not of practical significance. The validity of CO<sub>2</sub> images when compared to standard contrast arteriograms was also reported by Hawkins<sup>11</sup> in his original study. Second, CO<sub>2</sub>/DSA findings correlated very well with the findings at operation. The patency rate of the arterial reconstructions performed lends support to the accuracy of these images. Finally, the positive hemodynamic benefit demonstrated in 9 of 10 patients after PTA attests to the ability of CO<sub>2</sub>/DSA to accurately image critical arterial disease.

The use of CO<sub>2</sub> to successfully image the PTA of a critical arterial lesions permits the endovascular intervention when the risk standard contrast is prohibitive. It is of interest that the potential benefits of a gaseous contrast agent in transluminal dilation was first mentioned by Dotter and Judkins<sup>12</sup> in their classic article on transluminal angioplasty. Other endovascular interventions such as atherectomy may also be possible by use of only CO<sub>2</sub> as contrast.

Severe bilateral renal artery occlusive disease or unilateral disease in a solitary kidney can be present in up to one third of patients with coexisting hypertension and azotemia.<sup>13</sup> The identification of those patients who could be benefited by surgical correction has been hampered by the inaccuracy of available noninvasive screening tests and the nephrotoxicity associated with iodinated contrast arteriograms. We found that CO<sub>2</sub>/DSA facilitated screening arteriography in this patient population and provided sufficient anatomic detail on which revascularization



Fig. 5. Lateral CO<sub>2</sub>/DSA aortogram demonstrates a false aneurysm (arrow) of the juxtarenal aorta. The superior mesenteric artery (S) is imaged anterior to the aorta (A).

could be based. Carbon dioxide/digital subtraction angiography was also of diagnostic value in a single investigation for transplant renal artery stenosis. Its wide application in this ever enlarging patient population deserves further study.

Complications were rare. The one patient in whom tachypnea and tachycardia developed may have had CO<sub>2</sub> pulmonary emboli or hypercarbia caused by inefficient respiratory excretion of CO<sub>2</sub>. Silverman et al.<sup>14</sup> have reported the occurrence of femoral vein bubbles after the rapid insufflation of CO<sub>2</sub> during arterial angiography in canines. Deleterious consequences were not observed in these animals. Prevention of such an occurrence in man can be accomplished by spacing CO<sub>2</sub> injections at least 2 minutes apart and possibly longer in those patients with known pulmonary disease.

This study of 33 patients with diverse patterns of arterial disease confirms the safety and clinical usefulness of CO<sub>2</sub>/DSA. In patients at risk for contrast related complications, pathologic processes involving the abdominal aorta, visceral and renal arteries, and lower extremity arterial tree were accurately assessed and then corrected by use of CO<sub>2</sub>/DSA images as a guide. Even when tortuosity or severe occlusive dis-

case precluded effective CO<sub>2</sub>/DSA imaging, a complete study was possible with minimal nonionic contrast. Future refinements and experience with this technique should result in wider and more varied applications in the areas of renal transplantation, endovascular intervention, and combined diagnostic and therapeutic vascular procedures.

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#### DISCUSSION

Dr. Ernest Ring (San Francisco, Calif.). Several advances over the past few years have made arteriography a safer and much better tolerated procedure. In particular, the introduction of low osmolar contrast media has markedly reduced the severe pain that formerly accompanied arteriographic injections and led to approximately a sixfold reduction in the incidence of major allergic reactions. Unfortunately, as was pointed out, these new contrast agents have done little to reduce renal toxicity, which is far and away the most common serious complication of intraarterial contrast administration. They also cost about \$1/ml and add at least \$100 to \$200 to the cost of most procedures and millions of dollars to the cost of healthcare in the United States.

For several years CO<sub>2</sub> has been enthusiastically advocated by Hawkins as an inexpensive, nontoxic contrast agent for arteriography. However, like other somewhat eccentric sounding new ideas, this recommendation has been rather consistently ignored by most of the rest of established medicine, myself included. Furthermore, since CO<sub>2</sub> costs practically nothing, it has no champion industry to fund the necessary supporting research or to supply a sales force that would create a market for its use.

It is reassuring to find that even with these kinds of

obstacles, a new method that has merit will eventually find its way into clinical practice.

I do have one technical question for Dr. Weaver. Being a gas, CO<sub>2</sub> is compressible, and when injected by hand through a syringe, it releases in a fairly uncontrolled short burst, rather like a belch. Have you looked at any alternative injection methods that might better control the flow of the gas so that it injects more like the liquid agents?

Dr. Weaver. Dr. Ring, concerning the cost of CO<sub>2</sub>, we are still using the same CO<sub>2</sub> tank that we started with. It does go a long way and is therefore very cost effective.

From a technical standpoint, the issue that you bring up is an important one. One of the initial difficulties with these procedures was obtaining a smooth, rapid, and even injection of CO<sub>2</sub>. We have found that if the catheter is cleared of all blood by CO<sub>2</sub> gas just before the injection, then the CO<sub>2</sub> injection was improved. But it is certainly not an optimal system, and presently Hawkins, at the University of Florida, is in the process of developing an automated injection device for CO<sub>2</sub> much like what is available for iodine-containing contrast agents. If in fact that can be developed, I think that the indications for CO<sub>2</sub> contrast in arteriography will be broadened.

Dr. James Seeger (Gainesville, Fla.). Over the past 8 years at the University of Florida, approximately 600 pa-

tients have undergone CO<sub>2</sub> angiography under the direction of Dr. Irwin Hawkins. The findings from that fairly large number of patients have indicated several things that I think are worth emphasizing. In addition, I have a couple of questions for the authors.

We have found that fairly good quality images of the renal arteries, the aorta, and the infrainguinal vessels down to the level of the knee can routinely be obtained by use of CO<sub>2</sub> angiography. The advantages of this technique are (1) improved imaging of tumors and arteriovenous fistulas, (2) absence of allergic complications, (3) ease in delivery through very small catheters, which makes outpatient angiography easier, (4) minimal cost, and (5) lack of pain in most patients. In addition, in very complex diagnostic procedures, large volumes of gas can be used for multiple injections because CO<sub>2</sub> is rapidly cleared by the lungs. Measurement of pH and pCO<sub>2</sub> in patients, even those with pulmonary disease, shows minimal problems. Finally, preliminary results from our laboratory have shown that CO<sub>2</sub> may be a good blood displacement agent for PTA.

However, there are some problems, and I wonder if the authors have seen any of these. To start with, delivery can be difficult, and in some patients it seems virtually impossible to get an adequate study. I would like to know what variability you have seen from patient to patient in your ability to get adequate studies using CO<sub>2</sub> angiography. Second, we have seen a couple of patients in whom there was an increase in ischemia after CO<sub>2</sub> gas injection. This appeared to be associated with leg elevation to im-

prove distal delivery of the CO<sub>2</sub> gas; we have not seen this problem since this practice was discontinued. I wonder if this problem has been seen by the authors. Finally, as you mentioned, there are problems with delivery, and explosive delivery can occur with hand injection. The CO<sub>2</sub> injector that Dr. Hawkins is developing works some days and does not work some days. So a reliable delivery system is still a little bit away.

**Dr. Weaver.** Dr. Seeger, the experience at the University of Florida is obviously far greater than what we have had to date.

Initially, we did have a moderate amount of variability in the quality of our studies. In large part, this was due to not maximizing changes in patient position to take into account the buoyancy of CO<sub>2</sub>. With greater attention to this technical point, the quality of our studies has markedly improved.

As far as the problem with the injection of CO<sub>2</sub> is concerned, as I mentioned in answering Dr. Ring's question, we find that displacing all the blood in the catheter by CO<sub>2</sub> before injection makes a big difference and eliminates the explosive effect you describe. This has also made the resolution of our studies much better.

With regard to increased ischemia: no, we have not had that occur. What we have had occur and I have no plausible explanation for it, is marked symptomatic improvement in lower extremity rest pain of two patients after the CO<sub>2</sub> arteriogram.