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Clinical Investigations

Venography with Carbon Dioxide as a Contrast Agent

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Abstract

Purpose: The purpose of this study was to evaluate the feasibility, safety, and potential role of carbon dioxide (CO_2) as a contrast agent for venography.

Methods: Consecutive patients with contraindications to iodinated contrast agents or with unsatisfactory iodinated contrast studies underwent CO_2 digital subtraction venography. The images were rated by three experienced angiographers. Image quality and complications were assessed.

Results: Over a 14-month period, 66 vein segments were studied in 21 patients. There was good correlation between experienced angiographers on CO_2 image quality ($R_i = 0.80$) and good agreement on diagnosis ($k = 0.62$). In 91% of the vein segments evaluated with CO_2 there was interobserver agreement on the diagnosis. Upper extremity veins were adequately imaged with CO_2 alone in all (6/6) patients with contraindications to iodinated contrast. Following suboptimal iodinated contrast studies in six patients, CO_2 produced significantly better quality upper extremity central vein images ($p < 0.05$). Pain following injection into peripheral veins was the only CO_2-related complication. Inferior vena cava (IVC) filters were successfully deployed with CO_2 alone in 78% (7/9) of patients; two required iodinated contrast.

Conclusion: Based upon initial experience, CO_2 venography can be recommended in patients with contraindications to iodinated contrast or unsatisfactory iodinated contrast studies.

Key words: Contrast media—Veins, extremities—Veins, innominate, subclavian—Vena cava filters—Venography, contrast—Catheters and catheterization

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Allergic reactions and renal failure secondary to iodinated contrast (IC) have prompted the search for safer angiographic methods. CO_2 has been studied as a contrast agent for arteriography [1, 2]. We report here our initial experience with CO_2 used as a contrast agent for venography, as assessed by agreement among three experienced angiographers (raters) on image quality and diagnosis, and by the success and complication rates of venous interventions performed in the veins imaged with CO_2.

Materials and Methods

Venous imaging with CO_2 during a 14-month period was reviewed retrospectively. Informed consent was obtained prior to each study. CO_2 upper-extremity venography was performed in 12 patients: for IC allergy in three, renal failure in three, and poor quality IC venograms in six. CO_2 was used to study the inferior vena cava (IVC) in nine patients: prior to filter placement because of renal failure in seven patients, due to contrast allergy in one patient, and due to cervical traction in one patient (patients in cervical traction would normally be given nonionic contrast to minimize nausea and vomiting and potential aspiration due to an inability to turn the head). The indications for upper extremity venograms were as follows: prior to central venous access in four studies, predialysis graft placement in three studies, arm edema in two studies, pain in one study, and uncertain in two studies. Patients ranged in age from 34 to 83 years, with a mean of 60 ± 16 years. There were 8 males and 13 females. All studies were performed at our institution between April 1992 and May 1993.

CO_2 was injected by hand from a 60-ml syringe, and images were produced with digital subtraction. Upper extremity venograms were performed by injecting 50 ml of CO_2 into a forearm or hand vein in a dependent position. The arm was placed on a horizontal arm board slightly lower than the shoulders and thorax, or was permitted to hang freely over the edge of the angiography table. IVC studies were performed by injecting 50 ml of CO_2 into a 5 Fr pigtail catheter; the pigtail was placed at the confluence of the iliac veins. Prior to placement of an IVC filter, the IVC diameter was measured with the aid of a calibrated catheter (Cook Inc., Bloomington IN, USA), or by correlation with catheter diameter. Radiographs of the abdomen were performed following filter placement to confirm filter position. Radiographs of the chest were obtained following central venous catheter placement to assess catheter position.

The CO_2 and IC images evaluated by the three raters were those produced as part of routine care. The studies were presented in random sequence so that CO_2 and IC studies from the same patient were not viewed sequentially unless by chance. The names of the patients were obscured from the raters. The cephalic, axillary, subclavian, and innominate veins and the suprarenal and infrarenal IVC were rated for quality. The raters were instructed to grade the veins from 0 (nonvisualized) to 6 (excellently visualized). Intraclass correlation (R_i) was used to measure the degree of agreement on quality among the three raters. The two-tailed, paired t-test was used to compare the quality ratings of veins evaluated with CO_2 vs IC.

The diagnoses of the CO_2 venograms from the reports of the radiologists performing the studies were reviewed. In addition, the raters classified the cephalic, axillary, subclavian, and axillary veins, and the supra- and infrarenal IVC as normal or abnormal. Agreement among the three raters was evaluated with Cohen's kappa (k) [3].

Twelve upper-extremity venograms were performed with CO_2, 6 of which also utilized IC, producing 48 upper-extremity vein segments evaluated with CO_2 and 24 with IC. Nine IVCs were studied with CO_2, 2 of which also used IC, yielding 18 vein segments evaluated with CO_2 and 4 with IC. Thus, a total of 66 vein segments were evaluated with CO_2, and 26 with IC.

The following scale was used to evaluate R_i and k; < 0.2 = poor, 0.21–0.4 = fair, 0.41–0.60 = moderate, 0.61–0.80 = good to very good, 0.81–1.00 = very good to excellent correlation or agreement.

The success and complications of venous interventions following preprocedure CO_2 venography were evaluated by reviewing inpatient and outpatient charts.

Results

Quality and Diagnosis

For all images (CO_2 and IC), there was good interobserver correlation on the evaluation of image quality, with $R_i = 0.84$, and good agreement on diagnosis, with $k = 0.64$. For CO_2 images only, the correlation among raters on quality was only slightly less, with $R_i = 0.80$. There was interobserver agreement on diagnosis in 91% of vein segments evaluated with CO_2, with $k = 0.62$.

The six CO_2 venograms performed for IC allergy or renal failure were considered of adequate quality by the radiologist performing the examination, and no IC was used. Among the six patients with poor quality IC upper-extremity venograms, the mean quality score and standard deviation in the subclavian vein were 1.5 ± 1.8 with IC, which was significantly lower than 4.6 ± 1.1 with CO_2 ($p < 0.05$). In the innominate vein, the mean score was 0.75 ± 1.4 with IC, which was significantly lower than 4.1 ± 1.9 with CO_2 ($p < 0.05$). There was no significant difference between CO_2 and IC in the cephalic or axillary veins.

Diagnoses from the radiologists performing the upper extremity CO_2 venograms were as follows: four normal, two pericatheter innominate vein thromboses, two innominate vein stenoses, two innominate vein occlusions, one axillary vein stenosis, and one stenosis at the thoracic outlet associated with thoracic outlet syndrome (Figs. 1, 2).

Interventions

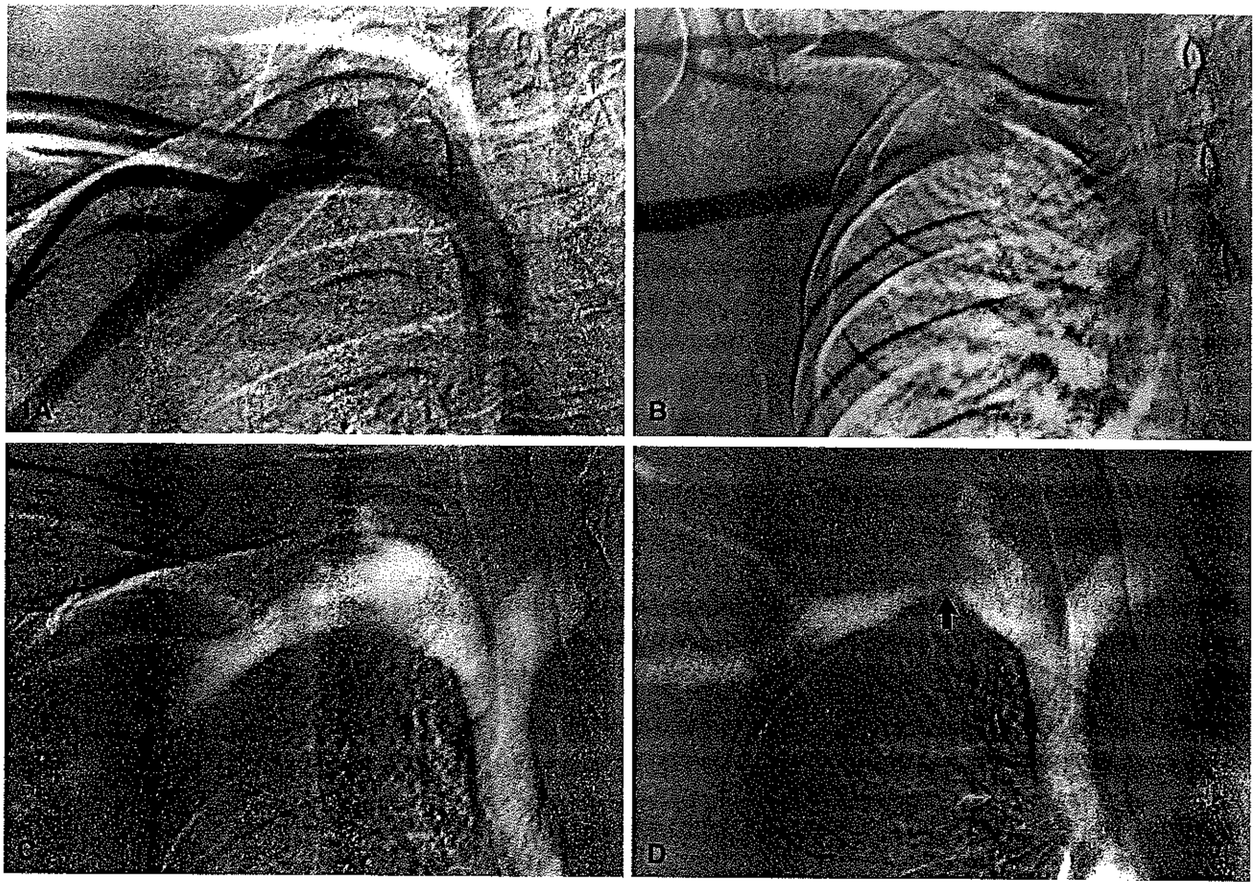
The outcome of seven studies in six patients who had CO_2 venograms prior to an intervention was evaluated. Four patients had central venous catheters placed. One patient had an innominate vein occlusion by CO_2 venography and had a central venous catheter placed on the contralateral side. In another patient, the central veins were normal, and a catheter was advanced into the superior vena cava. There was an innominate vein occlusion in a patient with well-developed collaterals, and a peripherally inserted central venous catheter was positioned in the subclavian vein. In another patient, an innominate vein stenosis was successfully traversed, permitting a peripheral port to be placed with the catheter tip in the superior vena cava. Two patients were evaluated prior to dialysis-access graft placement. Bilateral upper extremity venography was performed in one patient prior to a planned dialysis graft placement, but the graft was never placed. The veins were interpreted as normal in one upper extremity, but there was an innominate vein stenosis on the contralateral side. A second patient studied prior to dialysis access had a successfully placed graft in the arm interpreted as normal on CO_2 venography. Thus, all attempts to place central venous catheters or dialysis-access grafts were successful and without acute complications.

In seven of nine patients, an IVC filter was placed based upon the CO_2 study alone (Fig. 3). All seven were interpreted as normal by the radiologist performing the study. There were no complications related to filter placement in these patients. In two, IC was judged necessary. In one patient, opacification with CO_2 was too poor to evaluate the IVC. IC produced an IVC study of excellent quality in this patient, which was interpreted as normal. In another patient, an area of narrowing in the infrarenal IVC was judged to be inadequately characterized with CO_2, and an IC study was performed. The filling defect appeared extrinsic on the CO_2 vena cavagram, but intrinsic on the IC study. Intravascular ultrasound indicated that the filling defect was extrinsic. Based upon a history of malignancy, it probably represented lymphadenopathy.

In two patients, the diameter of the IVC determined by CO_2 could be compared to IC. In one patient, the corrected IVC diameter with IC was 17.3 mm, compared with 17 mm with CO_2. In the patient with poor opacification of the IVC with CO_2, the corrected diameter with CO_2 was 16 mm, compared with a corrected diameter of 26 mm with IC.

Complications

There were no major CO_2-related complications. Some patients did experience pain upon injection of CO_2 into



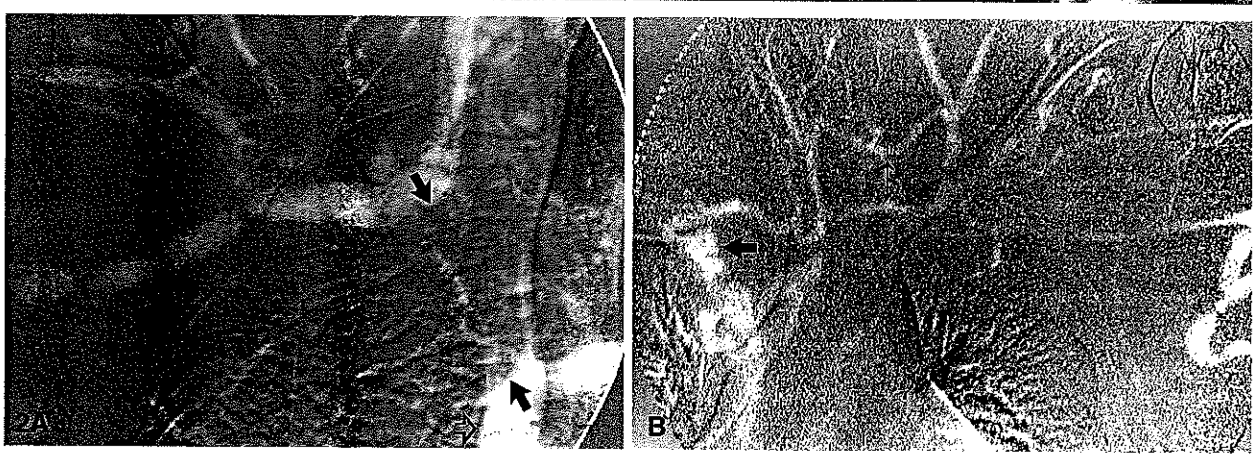


Fig. 1. A The right subclavian and innominate veins were poorly visualized with IC in this patient with thoracic outlet syndrome. **B** Abduction of the arm lead to even poorer opacification of these veins with IC. This radiograph was obtained 13.5 sec after contrast injection. Doppler ultrasound revealed slow axillary vein flow, especially with abduction of the arm. Subtraction artifact resulting from patient motion during the long image-acquisition sequence contributed to poor image quality. Slow flow probably diluted the IC, also contributing to the poor quality. **C** CO_2 venography demonstrated normal subclavian and innominate veins in the same patient with the arm adducted. The nonvisualized portions of the axillary and cephalic veins were normal on other images in this venogram. **D** CO_2 venography with the arm abducted revealed compression of the subclavian vein at the thoracic outlet (arrow). This image was obtained 2.5 sec after injection of CO_2.

Fig. 2. A CO_2-visualized reconstituted vessels. A nonvisualized right innominate vein (solid arrows) was confirmed to be occluded by retrograde flow into the ipsilateral internal jugular vein and opacification of the superior vena cava (hollow arrow) via collateral vessels. Note that the nonopacified areas in the axillary vein are due to segmentation of the contrast column. This was apparent on reviewing multiple sequential venogram images. **B** Collateral veins were imaged with CO_2. A left-arm injection of CO_2 opacified neck veins (double arrowhead), confirming occlusion of the left innominate, subclavian, and axillary veins. The right innominate vein was faintly opacified (arrow).

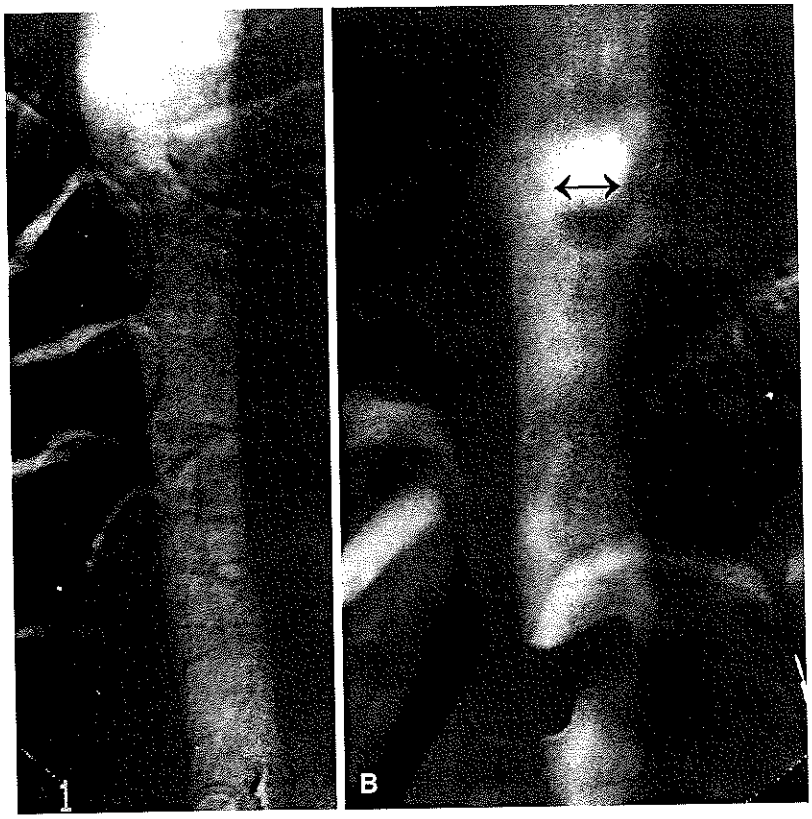


Fig. 3. A The IVC was well opacified in this CO_2 study. Neither of the renal veins was visualized. **B** Reflux into the renal veins (double arrowhead) is demonstrated in this CO_2 IVC study.

upper extremity veins, although this did not lead to termination of CO_2 use. There was no pain or sensation associated with CO_2 injection into the IVC. There were no signs or symptoms of compromise of the pulmonary circulation after CO_2 injection.

Discussion

Feasibility and Efficacy

There was good agreement among experienced radiologists evaluating the quality and diagnosis of CO_2 venograms, but such agreement is not sufficient to prove the accuracy of a contrast agent. However, it is a necessary condition for a contrast agent to be diagnostically useful. The best method of evaluating a diagnostic modality is by clinical or pathologic proof and follow-up data [4]. The ability to successfully and safely perform interventions based upon the information from CO_2 venograms is good evidence of the accuracy of this contrast agent.

In most patients with contraindications to IC, CO_2 permitted venous interventions to be performed without the use of IC. An initial attempt to image veins with CO_2 prior to interventions seems indicated in such patients. Some caution, however, is necessary when determining vessel diameter. There was good correlation of IVC diameter between CO_2 and IC in a single case where the inferior vena cavagram was of good quality. With poor opacification of the IVC by CO_2, vessel size was underestimated. This may be due to layering of the CO_2 along the nondependent surface of the vessel. With an inadequate volume of CO_2, the full diameter of the vessel may not be appreciated. Further evaluation is needed to assess the accuracy of CO_2 in measuring vessel diameter.

There are a number of diagnostic options for imaging veins. IC and CO_2 could not be directly compared because both agents were used in the same patients only when one produced an inadequate study. However, in patients with poor quality upper extremity IC venograms, CO_2 produced significantly better image quality in central veins. CO_2 can therefore be recommended in instances where there is poor opacification of the subclavian or innominate veins with IC. The improved opacification with CO_2 may be due to the ability of CO_2 to flow to a less dependent position independent of blood flow.

Poor quality IC images in this study may have been due in some cases to dilution of IC associated with slow flow. CO_2 traveled rapidly to the central veins, minimizing the dilution which probably occurred with IC.

The more rapid flow of CO_2 may also be responsible for less subtraction artifact due to less patient motion during the study. This, too, probably contributed to the superior quality of some of the CO_2 images compared with IC. One negative quality of CO_2 as a contrast agent is segmentation of the contrast column. Review of multiple sequential images generally resolves any uncertainty.

Safety

Pain was experienced by some patients during CO_2 injection. Gas compressed in the syringe prior to delivery could lead to rapid expansion of small peripheral veins, resulting in pain.

There have been reports of CO_2 emboli leading to cardiopulmonary collapse during laparoscopic surgery with CO_2 insufflation of the peritoneum [5–7]. One liter of CO_2 was inadvertently injected into a vein rather than the peritoneum in one reported case, leading to a cardiac murmur without hemodynamic compromise [7]. In another case, all or part of 3.5 L of CO_2 used to insufflate the peritoneum entered the venous system, leading to cardiovascular collapse [5]. However, in a series of 90 patients receiving intravenous injections of 50–60 ml of CO_2 during cineangiocardiography to evaluate pericardial disease, none experienced complications; this series included one patient with an atrial septal defect [8]. Unlike our patients, though, these patients were placed in the left lateral decubitus position to capture CO_2 in the right atrium. This maneuver probably permitted some CO_2 to dissolve prior to entering the pulmonary artery. Information on the volume of intravenous CO_2 needed to produce major complications is available from animal studies. Mice developed seizures after intravenous injection of 34.2 ml of CO_2/kg of body weight [9]. A 70-kg person would require 2.4 L of intravenous CO_2 to produce seizures at this dose.

None of the patients reported here experienced signs or symptoms of cardiovascular collapse. CO_2 is soluble in water, which may partly explain the lack of symptoms. However, dissolution was not rapid enough to prevent CO_2 from entering the pulmonary artery in the gaseous state. The pulmonary artery was visualized in some patients during upper extremity venography. The transient presence of CO_2 in the pulmonary artery appeared to be well tolerated.

Additional experience will be needed to determine the role of CO_2 in imaging veins of patients without contraindications to IC or suboptimal IC studies.

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