Carbon-Dioxide-Guided Vascular Interventions: Technique and Pitfalls

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Abstract

Purpose: To evaluate the usefulness of carbon dioxide (CO₂) angiography to guide vascular interventions.

Methods: A prospective study was carried out of 50 procedures (angioplasty, stenting, stent-grafting and embolization) using CO₂ angiography. Indications for using CO₂ were renal impairment, cardiac failure, previous reaction to conventional iodinated contrast, or likelihood of needing high doses of conventional contrast. CO₂ was intended to be the sole contrast agent. The use of additional conventional contrast or gadolinium was recorded, as were procedural complications. Radiation dose was compared with similar procedures using conventional contrast.

Results: Angiographic quality was satisfactory in 44 (88%) procedures and CO₂ guidance was all that was required; in 6 (12%) cases adjunctive use of conventional contrast or gadolinium was necessary. Contrast doses were significantly reduced and there was a trend toward decreased radiation doses with CO₂. There were two significant complications but only one related to the use of CO₂.

Conclusion: CO₂ angiography is well tolerated and can be successfully used to guide even complex vascular interventions. High-risk patients can be spared the risks of conventional contrast agents.

Key words: Digital subtraction angiography—Carbon dioxide—Arteries, transluminal angioplasty—Stents and prostheses—Arteries, therapeutic embolization

Intravenous injection of carbon dioxide (CO₂) was used for many years to detect pericardial effusion [1]. Hawkins [2] first described the use of gas as an arterial contrast agent, when he inadvertently injected air into the celiac axis. CO₂ is a much safer intravascular contrast than air as it is 20 times more soluble in blood [3]. The low intrinsic contrast of CO₂ limited its use until the advent of digital subtraction angiography (DSA). Early DSA units produced CO₂ images inferior to those obtained with conventional angiographic contrast and the technique was largely confined to a few patients with major contraindications to iodinated contrast. Recent improvements in the quality of angiographic equipment, particularly digital data acquisition and manipulation, have improved the quality of DSA images considerably and expanded the use of CO₂ as a diagnostic tool. Our experience with diagnostic CO₂ angiography using contemporary software with image summation has encouraged us to pursue its use in intervention in high-risk patients. The aim of the present study was to assess the efficacy and safety of CO₂ angiography to guide vascular interventional procedures in patients at significant risk of adverse events from conventional iodinated contrast.

Materials and Methods

Patients

A prospective study of CO₂-guided vascular interventional procedures in all patients at significant risk of complication from the use of conventional iodinated contrast. Local approval had been obtained to use CO₂ for angiography and intervention. The study group comprised 38 consecutive patients undergoing a total of 50 interventions, between March 10, 1999 and March 15, 2000. There were 28 men and 10 women with a median age of 75.6 years (range 57–89 years). The control group was derived from the most recent patients undergoing comparable procedures with conventional contrast: 40 procedures in 39 patients (30 men, 9 women) having a median age of 74.7 years (range 35–86 years). All procedures were performed by consultant vascular radiologists (D.O.K., L.R., I.V.P.) experienced in vascular intervention and diagnostic CO₂ angiography. Indications for using CO₂ were renal impairment, cardiac failure, previous reaction to conventional iodinated contrast, or likelihood of needing high doses of conventional contrast; some patients had more than one risk factor (Table 1). Impaired renal function (serum creatinine (Cr) > 1.5 g/dl) was the most common indication, present in 23 (61%) of patients. Patients undergoing endovascular aortic aneurysm repair were elderly and in addition to

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renal impairment frequently had medical conditions placing them at increased risk of contrast reaction and nephrotoxicity. Thirteen of the 15 patients (87%) had a risk factor for iodinated contrast in addition to the anticipated contrast load.

Prior to intervention a variety of diagnostic studies had been performed including ultrasound, magnetic resonance angiography, computed tomography, and carbon dioxide and conventional angiography. Iodinated contrast was avoided whenever possible in patients at risk of contrast nephrotoxicity or contrast reaction. Patients with renal impairment were hydrated with intravenous normal saline before the procedure in case iodinated contrast was needed.

Images were acquired using a Siemens Multistar TOPS system or proprietary iopamidol software. Detailed informed consent regarding the procedures and including the use of CO₂ was obtained from every patient. Patients were warned that CO₂ sometimes causes discomfort during injection. The apparatus used for drawing up CO₂ has been described elsewhere [4] and consisted of passing medical-grade CO₂, via low-pressure connectors, sequentially through a particle filter and three-way tap into an underwater seal. Luer lock syringes fitted with sliding caps were then allowed to fill under pressure of the CO₂ via the three-way tap. The contents of the syringe were discarded three times to ensure they contained CO₂ uncontaminated by room air. Hand injections of 20–60 ml of medical-grade CO₂ were used for each run. Volumes of CO₂ injected were kept to 100 ml every 2 min to allow the gas to dissolve and be excreted. Radiation doses were calculated from Dose-Area-Product meter readings from the angiography unit and were a total of the screen and image acquisition dose. These arc routinely recorded for all procedures performed in the angiography suite and were subsequently compared with the 10 most recent comparable cases in each category performed with conventional iodinated contrast (Ultrasound 300 Iopromide, Schering, Germany).

**Procedure**

The types of procedure ranged from simple superficial femoral artery (SFA) angioplasty to complex cases of endovascular aortic aneurysm repair (Table 2). Only embolization cases suitable for coil occlusion were attempted with CO₂ guidance. Nine of the embolization procedures were of the inferior mesenteric, lumbar or internal iliac artery performed electively prior to aortic aneurysm repair, the other two procedures were treatment for type II endoleaks. Angioplasty and stenting were performed in the conventional manner but all pre-, per- and post-procedural angiography was performed with CO₂. Twelve patients had more than one procedure, nine had aortic stent-grafting preceded by inferior mesenteric, lumbar or internal iliac artery embolization, and three had bilateral lower limb or bilateral renal artery intervention. In keeping with our normal practice the bowel was paralyzed prior to angiography of the abdomen or pelvis.

**Assessment**

The principal outcome measure was whether the procedure could be successfully completed using CO₂ angiography. During angioplasty identification of the stenosis and the runoff were considered mandatory (Fig. 1). For endovascular aneurysm repair and stenting demonstration of the target deployment site was essential to allow accurate positioning (Fig. 2). Completion angiography was scrutinized for endoleaks. If any additional contrast was used the reason for this was noted and the volume recorded. Complications were also documented and an attempt was made to evaluate whether the use of CO₂ was a contributory factor. Conventional contrast was either useful in clarifying appearances seen on CO₂ angiography or considered essential for performing the procedure (Table 3).

Statistical analysis was performed using a two-sided Mann–Whitney U-test.

**Results**

**Technical Success**

Of the 50 procedures performed, 48 were successfully completed with CO₂ guidance (Table 3). Angioplasty of the superficial femoral artery could not be performed with CO₂ guidance in one patient due to severe pain during CO₂ injection. Embolization was easy to perform with CO₂ guidance but it was difficult to demonstrate occlusion of the target vessel. If flow persisted coils were placed until the operator judged that thrombosis would occur (Fig. 3). In all patients undergoing elective embolization prior to aneurysm repair, thrombosis of the target vessel was confirmed at the time of endovascular repair (Fig. 4). Lumbar embolization proved impossible in one patient using CO₂ due to the buoyancy of the gas. Endoleaks were well shown and the appearances correlated with conventional angiography (Fig. 5).

**Contrast Dose.** CO₂ angiography significantly reduced the volume of conventional contrast used for all procedures (Table 4). Conventional contrast was deemed to be useful in four cases as it increased confidence in the interpretation of

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**Table 1. Indications for using CO₂ angiography**

<table>
<thead>
<tr>
<th>Indication for using CO₂</th>
<th>No. of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal impairment (Cr &gt; 1.5 g/dl)</td>
<td>23 (61)</td>
</tr>
<tr>
<td>Cardiac failure</td>
<td>9 (24)</td>
</tr>
<tr>
<td>Previous contrast reaction</td>
<td>2 (5)</td>
</tr>
<tr>
<td>Anticipated high contrast load</td>
<td>13 (40)</td>
</tr>
</tbody>
</table>

Cr, serum creatinine.

*Some patients had more than one indication for avoiding conventional contrast.

**Table 2. Procedures performed with CO₂ angiography**

<table>
<thead>
<tr>
<th>Procedure</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral arterial angioplasty/ stenting</td>
<td>10</td>
</tr>
<tr>
<td>Renal artery angioplasty/stenting</td>
<td>13</td>
</tr>
<tr>
<td>Fistuloplasty</td>
<td>1</td>
</tr>
<tr>
<td>Endovascular aortic aneurysm repair</td>
<td>15</td>
</tr>
<tr>
<td>Embolization</td>
<td>13*</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
</tr>
</tbody>
</table>

*Patients undergoing aneurysm repair often had embolization of the inferior mesenteric artery (IMA), lumbar arteries and an internal iliac artery. Internal iliac artery embolization was counted as a separate procedure from IMA and lumbar artery embolization (counted as a single procedure).
findings seen on CO₂ angiography. Conventional contrast was helpful in two cases of endovascular repair; in one it helped localize a type III endoleak which was readily apparent with CO₂, in the other case it confirmed occlusion of the superior mesenteric artery which had occurred in the interval between assessment and stent-grafting. Contrast was also useful in two cases of renal stenting to demonstrate the intrarenal vessels; in one case it confirmed renal emboli.

Conventional contrast was essential in two cases to allow completion of the procedure.

**Radiation Doses.** Radiation doses varied according to the complexity of the case but there was a tendency toward reduction compared with those for equivalent procedures performed using conventional iodinated contrast (Table 4).
Complications Related to CO₂

Pain. A single angioplasty could not be performed due to leg pain during CO₂ injection. The patient undergoing fistuloplasty experienced arm pain during CO₂ injections; this proved tolerable when the injection volume was kept low.

Malpositioning. A single complication was directly attributable to the use of CO₂ guidance. During endovascular aneurysm repair the graft appeared to cover the renal ostia (Fig. 6). The graft was moved caudally; repeat angiography showed that it was now too distal, and this required the placement of an additional extension cuff. Retrospective review of the images showed that the catheter tip was directed toward the celiac axis, and preferential filling of this vessel led us to assume mistakenly that the graft had been placed above the renal arteries. The initial placement had been correct and, rather than moving the graft, the angiographic catheter should have been moved and a repeat angiogram obtained.

Gas Buoyancy. In some patients the internal iliac artery did not fill in the supine position. In these cases a catheter was placed more selectively, which always allowed the internal iliac artery to be visualized. The lumbar arteries could not be visualized in one patient, necessitating the use of conventional contrast to perform the procedure. Gas trapping was seen in the patients with abdominal aortic aneurysm; there were no cases of abdominal pain and there was no evidence of mesenteric ischemia. To prevent the possibility of cerebral CO₂ embolization when the patient sat up, residual CO₂ was simply aspirated through a conventional angiographic catheter.

Complications Unrelated to CO₂

In a patient with high-grade stenosis in a solitary kidney there was renal artery thrombosis complicated by microembolization requiring thrombolysis. Both the renal artery occlusion and abnormal intrarenal flow were apparent with CO₂ angiography; conventional contrast subsequently confirmed the peripheral emboli. Renal perfusion was restored with no loss of renal function. This problem appeared related to difficulty with catheterization rather than the use of CO₂.

Discussion

CO₂ is established as a safe alternative contrast agent in patients with significant renal impairment [5–8] or other contraindications to conventional iodinated contrast media [9]. However, limitations in image quality secondary to the low inherent contrast of CO₂ and difficulties with bolus fragmentation have meant that it has never gained widespread acceptance and its use has been confined to a small number of enthusiasts.

Modern digital angiographic equipment with 1024 × 1024 matrix and rapid digital data manipulation has greatly increased the ability to utilize CO₂ as a contrast agent. High acquisition frame rates are generally recommended when using CO₂ and this has led to concern about radiation dose to the patient. In practice, contemporary image summation software integrates several frames, thereby minimizing the effects of breakup of the gas bolus and permitting the use of standard frame rates (2 frames/second) with satisfactory results. With the use of an unfamiliar technique for guiding interventions an initial increase in the radiation dose may be anticipated. In fact, with our current technique there has been a tendency toward a reduction in radiation dose when CO₂ is used. This is most evident for renal angioplasty and aortic stent grafting; the reason for this is uncertain. One of the limitations of the current study has been the use of historical controls; it may be argued that with prospective data collection in the study group there may have been a tendency on the part of the operators to try to keep screening times to a minimum. However, no significant difference in the screening times between the study and control groups was identified (Table 4). In addition, the recording of radiation doses for procedures was not exceptional to the study period, being routine and available for all procedures performed in the angiography suite. Rapid delivery of a large volume of gas,
Fig. 4. A, B. Completion CO₂ angiography after endovascular aortic aneurysm repair. A Early phase shows no endoleak. Coils are noted in the inferior mesenteric artery (IMA) (black arrows). B Late phase. The marginal branch of the IMA has filled retrogradely from the superior mesenteric artery; CO₂ reaches the coil nest (white arrow) but does not fill the aneurysm sac.

Fig. 5. A–D. Endoleaks demonstrated with CO₂ angiography. A Perigraft (type I) endoleak (white arrows). B Lumbar collaterals and inferior mesenteric artery (black arrows) with type II endoleak (white arrows). C Graft defect (type III endoleak) (white arrow). D Diffuse opacification due to transfemoral porosity, type IV endoleak (white arrows), retrograde filling of the marginal branch of the inferior mesenteric artery (black arrow).

Gamma expansion and bolus fragmentation tend to lead to shorter image acquisitions with CO₂. It is likely that the major source of reduction in radiation dose is a decrease in the number of frames acquired during each angiographic run. Increased experience with newer techniques may have contributed to dose reduction but this is considered unlikely, as all operators were experienced in the procedures performed in both the control and the study groups.

There have been surprisingly few reports detailing the use of CO₂ to guide vascular intervention. CO₂ readily passes through the hepatic sinusoids and has been used to opacify the portal vein during transjugular intrahepatic portosystemic shunt (TIPS) procedures [10, 11]. The documented experience with arterial intervention is limited; in 1991 Weaver et al. [12] reported 10 peripheral angioplasties under CO₂ guidance. Eschelman et al. [13] performed a variety of procedures in 26 patients. CO₂ alone was used in just over one quarter of the patients, and a similar proportion requiring more than 20 ml of contrast. Iliac angioplasty/stenting was the only procedure in which the majority of cases (4 of 5) were performed without conventional contrast. Frankhouse et al. [9] reported similar results in a series of 26 patients; supplemental contrast was needed in 73%. We have been able to demonstrate that many arterial interventions can be
Table 4. Comparison of volumes of conventional contrast used, radiation doses and screening times for comparable procedures using CO₂ and conventional contrast.

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Volume of conventional contrast (ml)</th>
<th>Range (mean)</th>
<th>CO₂ angiography</th>
<th>Conventional angiography</th>
<th>p value</th>
<th>Radiation dose (cGy/cm²)</th>
<th>Range (mean)</th>
<th>CO₂ angiography</th>
<th>Conventional angiography</th>
<th>p value</th>
<th>Screening time (min)</th>
<th>Range (mean)</th>
<th>CO₂ angiography</th>
<th>Conventional angiography</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral PTA/</td>
<td>0-35 (3.2)</td>
<td></td>
<td>CO₂ angiography</td>
<td></td>
<td>&lt;0.0001</td>
<td>260-18 672 (4726)</td>
<td>174-22 615 (9110)</td>
<td>0.3494</td>
<td></td>
<td>2.5-50.2 (11.7)</td>
<td>2.6-31.9 (10.3)</td>
<td>0.4679</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal PTA/</td>
<td>0-100 (9.7)</td>
<td>50-350 (150)</td>
<td>CO₂ angiography</td>
<td></td>
<td>&lt;0.0001</td>
<td>2415-17 509 (8879)</td>
<td>5952-47 854 (15 409)</td>
<td>0.0688</td>
<td></td>
<td>9.5-26.7 (14.4)</td>
<td>6.9-96.8 (26.4)</td>
<td>0.1712</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stent-grafting</td>
<td>120 (13.3)</td>
<td>150-400 (270)</td>
<td>CO₂ angiography</td>
<td></td>
<td>&lt;0.0001</td>
<td>7161-24 903 (14 041)</td>
<td>6493-32 557 (20 096)</td>
<td>0.1775</td>
<td></td>
<td>13.0-37.7 (31.8)</td>
<td>9.7-74.8 (28.7)</td>
<td>0.2609</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Embolization</td>
<td>0-120 (10.5)</td>
<td>100-400 (215)</td>
<td>CO₂ angiography</td>
<td></td>
<td>&lt;0.0001</td>
<td>6538-46 128 (14 215)</td>
<td>4951-36 821 (15 833)</td>
<td>0.07045</td>
<td></td>
<td>8.5-43.3 (27.7)</td>
<td>7.6-83.6 (37.2)</td>
<td>0.6539</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Initial diagnostic angiogram of at least three views with a catheter in the aorta performed prior to intervention in all patients.

Fig. 6. A Initial CO₂ angiogram showing the renal artery origins (white arrows). B CO₂ angiogram following initial positioning of the graft (black arrows). Neither renal artery is visible. C Angiogram following repositioning. The graft is too low (black arrowheads). Renal artery origins are shown (white arrows).

successfully performed using only CO₂ angiography. In simple procedures such as peripheral angioplasty and stenting demonstration of the arterial anatomy was straightforward. Completion views of the arterial runoff were considered a vital component of the procedure and were always of sufficient quality to exclude distal embolization.

The utility of carbon dioxide angiography to guide complex procedures might be limited by poor image quality and gas buoyancy. Gas buoyancy is an advantage when it is necessary to display the anterior visceral vessels but is theoretically disadvantageous for posterior vessels such as the renal and internal iliac arteries. Our experience with CO₂ renal and peripheral angiography suggested that this would not be the case. When posterior vessels do not fill during a flush injection they will normally be demonstrated by placing a selective catheter close to their origin. We have not found it necessary or helpful to use postural maneuvers such as elevation of the legs during peripheral angiography or decubitus views to show the renal arteries. We suspect that this is largely due to improvements in image quality with modern angiographic equipment.

Endovascular treatment of renal artery stenosis is an obvious indication for CO₂-guided intervention. The use of even small volumes of non-ionic contrast can be associated with a significant deterioration in renal function in patients with chronic renal impairment [14]. In Kan et al.’s [15] small series treating 11 renal arteries in 10 patients, nine (82%) required additional contrast (10-110 ml, mean 36 ml). Caridi et al. [16] performed 29 renal angioplasties in 21 high-risk patients using CO₂. The majority of the lesions were non-ostial and stents were not used. Small additional volumes of conventional contrast were used in six (29%)
patients and decubitus views were frequently necessary. We were concerned that it might not be possible to demonstrate and catheterize posterior renal arteries, but this has not been a problem and decubitus views were never required. CO₂ clearly demonstrated abnormal intrarenal flow in the patient with renal artery thrombosis and microembolization, as was confirmed by injection of conventional contrast. We used CO₂ alone in 85% (n = 11) of patients undergoing renal angioplasty with or without stenting and in only two (15%) of the cases was the contrast judged to have provided additional useful information.

Endovascular stent-grafting also proved surprisingly easy to perform with CO₂ alone. The only complication that we directly attribute to the use of CO₂ was misplacement of an aortic stent-graft early in our experience. Despite having clearly demonstrated the position of the renal arteries on the preliminary run they were not seen when the graft was partially deployed. In view of this our current practice is to use conventional contrast if there is any doubt as to the position of the renal arteries. Endoleaks and graft porosity were readily apparent and responded to conventional management.

Embolization procedures were slightly more problematic as it was very difficult to demonstrate satisfactory occlusion of the target vessel with CO₂. When flow persisted operator experience was used to decide when sufficient coils had been deployed to occlude the vessel. This proved to be satisfactory as all embolized vessels were occluded at the time of stent-grafting. Clearly CO₂ can only be used to guide coil embolization and would be inappropriate when injecting particulate or liquid embolic agents.

We have found that CO₂-guided interventions have been very well tolerated by patients, with only one procedure (2%) being abandoned (procedure completed with conventional contrast) due to pain. Injection of CO₂ can cause pain secondary to adventitial distension from large gas volumes and possibly contamination of the gas with rust particles and acid due to corrosion in the gas cylinder. Using disposable gas cylinders and passing the gas through a blood filter before filling the syringes minimizes these effects. In our experience, most patients reported minimal if any discomfort during injection and none required sedation or analgesia.

CO₂ is not a panacea and can have significant physiologic effects. The effects of CO₂ on the circulation are complex [17, 18]. In the canine renal artery CO₂ causes vasoconstriction and a small decrease in renal perfusion, which normalizes within 24 hr [19]. CO₂ affects cerebral blood flow and has been shown to be neurotoxic in animals and humans causing anesthesia and convulsions [20, 21]. For this reason it is not used for supradiaphragmatic arterial injection. Other potential problems relate to the buoyancy of the gas; there have been reports of gas trapping occurring in the abdominal aorta [22] and pulmonary artery [23]. Excess CO₂ trapped in the apex of an aneurysm should be simply removed by aspiration via the angiographic catheter. In our experience of using CO₂ angiographic guidance in 15 endovascular aneurysm repairs and 11 associated embolization procedures there have been no episodes of visceral ischemia.

Conclusion

With modern angiographic hardware and software CO₂ can be safely and simply used to guide many arterial interventions. It is particularly useful where there is a contraindication to conventional contrast. Image quality and patient and operator acceptability are sufficiently high to warrant its use in other circumstances. CO₂ is now our first-choice contrast agent for renovascular intervention and stent-grafting. It must be remembered that CO₂ is not suitable for all angiography: it cannot be used above the diaphragm or for liquid and particulate embolization.

References