Carbon Dioxide Digital Subtraction Angiography for Renal Artery Stent Placement[1]

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Abbreviations: DSA = digital subtraction angiography, PTA = percutaneous transluminal angioplasty

PURPOSE: To determine the efficacy of renal artery stent placement with use of carbon dioxide as the primary contrast agent.

MATERIALS AND METHODS: Seventeen hypertensive patients with renal ostial stenosis were evaluated and underwent stent placement with use of CO_2 digital subtraction angiography (DSA). Besides hypertension, 11 patients had decreased renal function, three had iodinated contrast material allergy, one patient had both, and two had neither. Supplemental iodinated contrast material (25 mL or less) was used in five patients. Preprocedure and postprocedure serum creatinine levels were obtained to evaluate the effect of CO_2 on renal function. Arteriography was used to evaluate stent positioning.

RESULTS: Twenty-three Palmaz stents were placed in 17 patients. Six placements were bilateral, with a total of nine right and 14 left. No additional stents were required to correct malposition. One patient had a mildly significant, yet transient, rise in the postprocedure creatinine level. This patient received 10 mL of iodinated contrast material in addition to CO_2. There were no allergic reactions.

CONCLUSION: The utilization of CO_2 DSA facilitates the accurate placement of renal artery stents by eliminating the concern for contrast material—associated nephropathy and allergy. These attributes, coupled with the benefit of low viscosity, permit unrestricted imaging, guidance, and precise positioning not afforded by iodinated contrast material.

HYPERTENSION is a common disease affecting 10%–15% of the adult population in the United States (1,2). In approximately 1%–5% of cases, hypertension is the result of renovascular disease (1,3,4) and, therefore, is potentially treatable. Correctable disease, specifically renal artery stenosis, can also be responsible for renal insufficiency. Previously, both renovascular hypertension and renal insufficiency were treated with either medical therapy or surgical intervention. More recently, management with percutaneous transluminal angioplasty (PTA) has been utilized with varied success (5–7). Because some renal artery stenoses may be resistant to PTA, primary stent placement has been recommended as an alternative mode of therapy (4,8,9).

Many patients who require treatment for renal artery stenosis also have underlying renal insufficiency (9–12). This places a potential limitation on the volume of iodinated contrast material that can be safely administered without jeopardizing the patient's tenuous renal status. Unfortunately, multiple injections of contrast material are often required to avoid the complications associated with stent malposition.

Theoretically, the lack of carbon dioxide nephrotoxicity coupled with

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its extremely low viscosity would allow more precise stent placement without compromising the patient's renal status. To reduce the limitations of the procedure associated with iodinated contrast material, and to enhance the accuracy of renal stent positioning, we evaluated the use of CO_2 as either the exclusive or primary contrast agent.

MATERIALS AND METHODS

From January 1997 to June 1998, 17 consecutive patients with renal artery ostial stenoses underwent primary renal artery stent placement. All were initially examined and, subsequently, underwent stent placement with use of medical-grade CO_2 (Custom Medical Devices, Gainesville, FL) as the primary or exclusive contrast agent. The Institutional Review Board approved the use of CO_2 as a vascular contrast agent, and informed consent was obtained from all patients. These patients were referred to the division of interventional and vascular radiology after they were determined by the vascular surgery or cardiology service to have clinical or imaging evidence of renovascular hypertension. There were nine men and eight women, ranging in age from 50 to 76 years of age. Eleven of the patients also had renal compromise, three had allergy to iodinated contrast material, one had a combination of both, and two had neither. Five patients also had diabetes.

The laboratory at our institution recognizes a creatinine of greater than 1.2 mg/dL (106 μmol/L) as abnormal. Typically, when performing contrast-enhanced computed tomography (CT), 150 mL of nonionic contrast material is administered with a creatinine up to 2.0 mg/dL (177 μmol/L). For CT, no contrast material is employed in patients with a creatinine in excess of 2.0 mg/dL (177 μmol/L). Because diagnostic and interventional angiography can be much more variable and demanding regarding total dose of contrast material, we utilize CO_2 whenever the creatinine exceeds 1.2 mg/dL (106 μmol/L) or when we deem its advantages useful to the procedure.

All of the patients were evaluated with intraarterial CO_2 DSA using either a Toshiba Angioflex DFE-60A (Toshiba America Medical System, Tustin, CA) or Phillips LU (Phillips Medical System, Shelton, CT) angiographic unit to determine the presence and severity of renal artery stenosis. The Phillips unit had been upgraded with a Camtronics digital system (Camtronics Medical Systems, Hartland, WI). CO_2 was administered via a previously described method (13), which uses a converted fluid management system (AngioDynamics, Glens Falls, NY). If CO_2 images were considered suboptimal, supplemental images were obtained for confirmation using a small amount of dilute Visapaque (Nycomed, Princeton, NJ). However, Visapaque was not administered to patients with a history of iodinated contrast allergy.

Diagnostic images included an aortogram in the anterior-posterior and bilateral oblique projections obtained with use of a 4-F pigtail catheter (AngioDynamics). If the renal ostia was not well seen, the patient was placed in the appropriate oblique or decubitus position, which elevated the poorly visualized artery. This was performed to take advantage of the buoyancy of CO_2. The aortogram images were obtained with a CO_2 injection of 35 mL in 1–2 seconds. Subsequently, selective renal artery images were obtained with a 4-F hook catheter (AngioDynamics) using 10–20 mL of CO_2 injected during 1–2 seconds. A stenosis was considered significant if it was greater than 50% arteriographically and demonstrated an aortic to poststenotic renal arterial pressure gradient of 20 mm Hg or greater.

Ostial lesions with these parameters were primarily treated with stents using the following method, which evolved during the previous 2-year period and was finally formalized in January 1997. Initially, a 35-cm, Cordis 8-F sheath (Johnson & Johnson Interventional Systems, Warren, NJ) was placed at the access site. A 4-F hook catheter was then negotiated past the renal artery stenosis using either an 0.035-inch Glidewire (Medi-tech/Boston Scientific, Watertown, MA) or an 0.018-inch Nitinol wire (Microvena Corporation, White Bear Lake, MN). Once this catheter was beyond the stenosis, the initial wire was exchanged for a Rosen wire (Cook, Bloomington, IN) to enhance purchase. If it appeared that the severity of the stenosis would preclude traversal by an 8-F guide catheter, the stenosis was predilated to 4 mm. A balloon/stent/guide catheter system was subsequently prepared. This included a 6-mm × 2-cm diamond balloon (Medi-tech/Boston Scientific) placed entirely through a 50-cm, 8-F Cordis guide catheter connected to a Cook hemostatic valve. The balloon was then prepared by wiping it with a saline-soaked gauze. A medium-sized Palmaz stent (Johnson & Johnson Interventional Systems) of either 1.5 or 2 cm was then hand-crimped onto the balloon. This complex was then reinserted into the guide catheter, with the tip of the balloon extending just beyond the guide catheter to act as a taper.

The balloon/stent/guide catheter complex was then advanced into the renal artery using multiple CO_2 DSA runs as a guide for precise stent positioning. With use of a Tuohy-Borst, 5–10 mL of CO_2 could be hand injected either between the guide wire and balloon catheter or the guide catheter and the balloon. When the stent appeared to be in good position, the guide catheter was withdrawn to expose the stent. Additional confirmatory CO_2 DSA images were obtained and final adjustments made, if necessary. Once deployed, stent position was evaluated with use of 5–10 mL of CO_2 or, if necessary, dilute Visapaque. Again, CO_2 was delivered through one of the mechanisms discussed previously, including the selective catheter, guide catheter, or long 8-F sheath. A serum creatinine measurement was obtained prior to and the day after the examination. If the postexamination level demonstrated an elevation of greater than

0.5 mg/dL (44 μmol/L), additional serum creatinine levels were obtained.

RESULTS

Twenty-three ostial Palmaz stents (21 type 154 stents; two type 204 stents) were placed in 17 patients. Six patients had bilateral stents placed. Nine of the stents were right-sided, and 14 were on the left. The amount of CO_2 necessary for each procedure ranged from a minimum of 100 mL to a maximum of 200 mL, with an average of 129 mL. Iodinated contrast material was used in five patients and volumes ranged from 7 to 25 mL, with an average of 15 mL. Postprocedure angiography demonstrated dilatation of the offending stenosis by the underlying stent in all cases. No additional stents were necessary to remedy poor positioning.

Serum creatinine levels in our laboratory have a latitude of up to 10%. Follow-up creatinine levels demonstrated no change in five patients. A postprocedure decrease in serum creatinine level was seen in five patients, averaging 0.33 mg/dL (29 μmol/L), while seven patients had an increase averaging 0.29 mg/dL (26 μmol/L). Only one patient had a follow-up creatinine level that increased greater than 0.5 mg/dL (44 μmol/L) after angiography. This patient had an initial serum creatinine level of 3.1 mg/dL (274 μmol/L), which increased to 3.9 mg/dL (345 μmol/L). During arteriography, he received 130 mL of CO_2 and 10 mL of Visapaque. A serum creatinine level obtained 1 week after the procedure returned to baseline. Of the five patients who received small amounts of iodinated contrast material in addition to CO_2, the baseline creatinine ranged from 1.4 to 3.2 mg/dL (124–283 μmol/L), with a mean of 2.4 mg/dL (212 μmol/L). In these five individuals, the creatinine level increased in one patient (previously described), remained the same in two patients, and decreased in the other two patients. Of the 12 patients receiving only CO_2, the baseline creatinine levels ranged from 0.7 to 4.6 mg/dL (62–407 μmol/L), with a mean of 2.1 mg/dL (186 μmol/L). Four of these patients demonstrated a decrease in serum creatinine level averaging 0.38 mg/dL (34 μmol/L), three patients had no change in serum creatinine level, and five patients had an increase averaging 0.2 mg/dL (18 μmol/L).

There was no evidence of an allergic reaction in any of the 17 patients. There were no reports of pain, nausea, or bowel cramping, which sometimes is attributed to the use of CO_2. Furthermore, none of the procedures resulted in major or minor complications that interfered with discharge or added to the cost or duration of hospitalization.

DISCUSSION

According to the U.S. National Health Examination Survey, nearly 10%–15% of the adult population (approximately 23 million people) are afflicted with hypertension (1,2). Renal artery stenosis is the underlying etiology in approximately 1%–5% of these individuals (1,3,4), as well as 10%–15% of those with renal insufficiency (4). In the past, surgery was the only definitive option to alleviate the underlying renal artery stenosis in either condition. However, since Andreas Gruntzig's article in 1978 (14), percutaneous methods such as angioplasty and stent placement have evolved and proven to be viable alternatives (4–7,9–17).

Although renal PTA can successfully dilate many lesions, there are certain instances in which stent placement may be warranted. These circumstances include occluding dissections as a result of PTA, recurrent stenosis, elastic recoil, and resistant ostial lesions. Because most ostial stenoses represent adjacent bulky, aortic plaque as opposed to circumferential renal artery disease, they are commonly unyielding to the mechanism of PTA (18). Consequently, some authors have discussed the merit of primarily placing stents in ostial lesions (4,8,9).

Whereas renal artery stent placement has alleviated some of the potential deficiencies of PTA, there are inherent technical difficulties with this procedure, including the necessity for precise stent deployment. A malpositioned stent, especially near the renal hilum, may preclude future surgical reconstruction. Less acutely, the placement of additional stents to rectify malposition may stimulate needless intimal hyperplasia and precipitate premature failure. Consequently, iodinated contrast material has been utilized to optimize stent positioning. This, however, is self-limited because many of these patients have underlying renal insufficiency. According to Lautin, the two factors that most consistently correlate with contrast material—associated nephropathy include underlying renal insufficiency and diabetes (19), both of which are common in patients with renal artery stenosis. More significantly, the likelihood of contrast-associated nephropathy is reported to be even greater as the injection of iodinated contrast material approximates or enters the renal artery (20,21). Unfortunately, precise stent placement often requires multiple close proximity or selective renal artery injections because respiratory motion commonly precludes effective road mapping.

An analysis of several major renal artery stent placement series suggests that 33.3%–60.3% of patients had some degree of renal insufficiency prior to intervention (9–12). Therefore, the indiscriminate use of iodinated contrast material places many of these patients at risk for contrast-associated nephropathy. This complication is not trivial, as evidenced in an article by Shusterman et al (22). They reported that hospital-acquired acute renal failure had an extremely poor prognosis manifested by both a sixfold increase in the risk of death, as well as a doubling in the duration of hospitalization.

An additional disadvantage of iodinated contrast material, especially nonionic, is that it is extremely viscous. It is at least 400 times more viscous than CO_2. This property inhibits optimal imaging

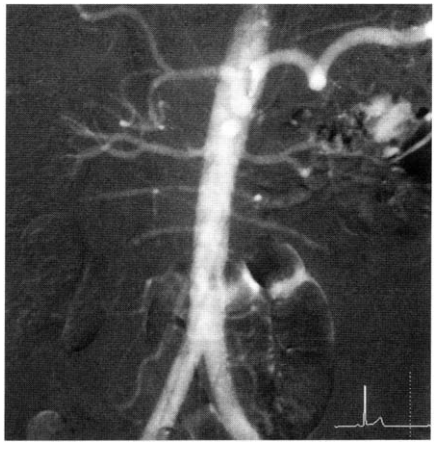


Figure 1. Diagnostic CO_2 digital subtraction aortogram to evaluate for renal artery stenosis.

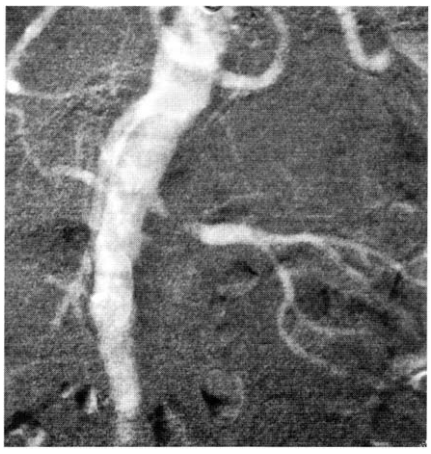


Figure 2. CO_2 digital subtraction aortogram obtained with the left side elevated to improve visualization of the left renal artery.

with iodinated contrast material by restricting its injection through coaxial systems, which house wires, stents, balloons, or other catheters. Also, because iodinated contrast material does not reflux proximally from selected arterial catheters, it is frequently difficult to adequately visualize the renal artery orifice and stenosis. Considering these drawbacks, it is understandable that several series using iodinated contrast material as a guide for renal stent placement had a 10%–20% incidence of malposition (13,15,23).

To address the potential difficulties of renal artery stent placement, we implemented the techniques described in the Materials and Methods section. We begin with a diagnostic CO_2 DSA aortogram **(Fig 1)**. If necessary, using the same CO_2 volume and injection rate, the patient may be placed in the partial or complete decubitus position to better visualize the nondependent renal artery **(Fig 2)**. This maneuver utilizes the buoyancy property of CO_2 (24) and is often successful for imaging poorly visualized renal arteries. Subsequently, a selective catheter is placed within the renal artery and CO_2 (5–10 mL) is administered. Unlike conventional liquid contrast material, CO_2 refluxes proximally and consistently defines the ostium and its relationship to the aorta **(Fig 3)**. Throughout much of the remainder of the procedure, CO_2 is administered either through the balloon or guiding catheter by using techniques set forth by Hawkins and colleagues (24–26). The low viscosity of CO_2 permits the facile injection through coaxial catheters and wires. This obviates the removal of the inner device to acquire optimal images. Consequently, with use of a Tuohy-Borst adapter, sufficient CO_2 can be administered through coaxial systems to render an adequate image without repetitive exchanges or the risk of losing access. For example, during stent placement, CO_2 can be injected through a balloon catheter around a wire with a matching outer diameter, or through a guiding catheter, while retaining the balloon catheter and stent **(Fig 4)**. This eliminates the need to place a smaller outer-diameter (usually tenuous) wire through the balloon to acquire an image with the more viscous iodinated contrast material.

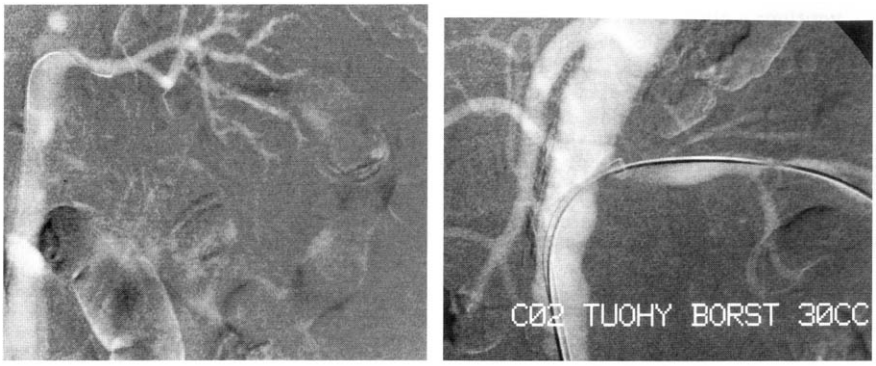
A 25-mL syringe is utilized, and all catheters are purged with CO_2 prior to the definitive injection for imaging. This permits a controlled, nonexplosive delivery. To purge the balloon catheter requires a more prolonged compression of the syringe because the outer diameter of the wire is in close apposition to the internal diameter of the catheter. When using CO_2, a larger syringe (20-mL or greater) is necessary to generate higher pressure for purging. If a larger syringe is not used, the smaller volume of gas will simply compress within the syringe and not be expelled.

Applying these methods, multiple images are obtained as the balloon/stent complex approaches and crosses the stenosis. Repeated visualization is essential because the relative position of the renal artery stenosis changes when cannulated by the wire, balloon, or guiding catheter. For precise positioning, constant monitoring is key.

Once the stent appropriately covers the stenosis, the guiding catheter is withdrawn and a confirmatory CO_2 DSA run is performed **(Fig 5)**. To be absolutely certain that the stent is positioned precisely, we perform a CO_2 injection after each adjustment. Because CO_2 rapidly dissolves in blood and is eliminated by the lungs, there should be no limitation in the number injections as long as 1–2 minutes elapse between injections (during any phase of the procedure) and there is no evidence of trapping (25). Trapping refers to the situation where a nondependent structure becomes persistently filled with gas, creating a vapor lock and, if severe enough, can result in ischemia. Ultimately, when positioning is optimal, the stent is deployed. Postprocedure images are obtained with CO_2 DSA. If necessary, at any time during the procedure, small amounts of dilute iodinated contrast material are administered. These techniques permitted us to treat 23 ostial stenoses with use of 23 stents without malposition or additional stents.

Because of our small population of patients (n = 17) and, for many, the short duration of follow-up, we have not yet evaluated the long-term effect of renal stent placement on hypertension or renal insufficiency. This study was done to confirm CO_2 DSA as a safe, accurate method for deploying renal artery stents without compromising renal function.

In this group of patients, multiple injections of iodinated contrast material would be ill-advised be-



a. b.

Figure 3. **(a)** Demonstrates reflux from a selective catheter into the proximal renal artery and aorta. **(b)** Demonstrates reflux from the guide catheter.

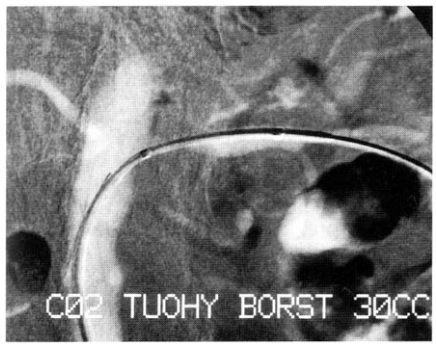


Figure 4. Ten milliliters CO_2 delivered via balloon to re-evaluate the position of the stenosis.

cause of their propensity for renal compromise. Prior to the initial examination, 65% of our patients had varying degrees of renal insufficiency. Because these patients were most susceptible to contrast-associated nephropathy, we compared their preprocedure and postprocedure serum creatinine levels to determine the effect of intravascular CO_2 on renal function.

According to Lautin et al, serum creatinine level is the most practical method for determining contrast-associated nephropathy (19). However, there is a difference of opinion regarding the alteration in creatinine that defines this (19,27). We chose the commonly used definition described by Solomon et al (28) (ie, an increase in the baseline serum creatinine concentration of at least 0.5 mg/dL [44 μmol/L] within 48 hours after the injection of radiocontrast agents). With use of this

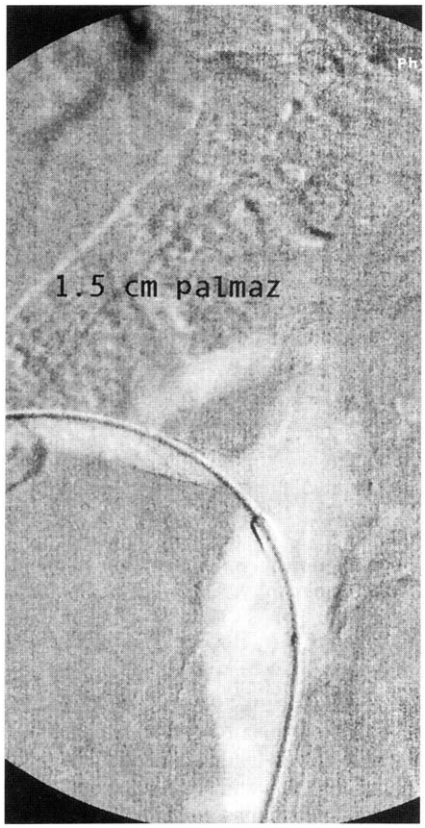


Figure 5. Postprocedure CO_2 DSA run through the balloon catheter with guide wire maintaining position.

interpretation, there was no evidence of contrast-associated nephropathy in any of the patients who received exclusively CO_2. Only one patient had a transient increase in serum creatinine greater than 0.5 mg/dL (44 μmol/L), but this returned to baseline within 1 week. Since this patient's initial creatinine was 3.1 mg/dL (274 μmol/L), the brief elevation was barely greater than our accepted laboratory variation. Furthermore, this individual also received 10 mL of iodinated contrast material, which may have contributed to the mild, transient rise. Occasionally, small amounts of dilute iodinated contrast material are indeed helpful when CO_2 imaging is hampered by excess bowel gas or uncontrolled respiratory motion. Alternatively, dilute gadolinium-based contrast agents could be administered in these circumstances (29); however, similar to iodinated contrast material, its maximum dose is limited. In addition, when CO_2 is used as the primary contrast agent, the small amount of liquid contrast material required may not warrant the expense of gadolinium.

Our experience suggests that CO_2 can be used exclusively or in conjunction with iodinated contrast material to optimize renal artery stent placement. As an imaging agent, CO_2 can facilitate the accurate placement of renal artery stents by eliminating the concern for both contrast-material—associated nephropathy and allergy. These attributes, along with the benefits of low CO_2 viscosity, permit unrestricted imaging, guidance, and precise stent positioning not afforded by iodinated contrast material. We believe the benefits of CO_2 make it an ideal imaging agent for renal artery stent placement and suggest that its use should not be exclusive to high-risk patients.

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