Original Report

Kenneth P. Moresco[1]
Nilesh H. Patel
Yan Namyslowski
Himanshu Shah
Matthew S. Johnson
Scott O. Trerotola

Carbon Dioxide Angiography of the Transplanted Kidney: Technical Considerations and Imaging Findings

OBJECTIVE. We evaluated the usefulness of carbon dioxide as the primary contrast material for renal transplant arteriography.

CONCLUSION. Carbon dioxide accurately showed artery pathology including anastomotic and intrarenal stenoses, arteriovenous shunting, and diffuse arterial disease from chronic transplant rejection. Using carbon dioxide as a contrast agent reduced the volume of iodinated contrast material that needed to be used. There was no procedure-associated nephrotoxicity.

Renal transplantation is the definitive therapy for patients with end-stage renal disease. After successful transplantation, renal artery stenosis is a significant cause of patient morbidity and of transplant graft loss [1]. Noninvasive assessment of the organ vasculature by sonography, MR imaging, CT, and radionuclide studies have yielded mixed results with regard to diagnostic accuracy [2]. Thus, contrast-enhanced arteriography remains the standard technique for examination of patients with renal graft arterial disease [1]. Although diagnostic arteriography can be performed safely with a low incidence of complication [3], contrast material reaction and nephrotoxicity are associated risks [4, 5]. In fact, the risk of nephrotoxicity is magnified in this patient population.

Carbon dioxide (CO_2) arteriography has been used extensively to examine patients affected by peripheral artery occlusive disease, poorly controlled hypertension, and renal insufficiency; it is also used to examine patients after renal artery bypass surgery [6–9]. CO_2 offers the advantages of low cost and a decreased risk of contrast material reaction, nephrotoxicity, or both [10, 11].

We report on the usefulness of CO_2 as a contrast agent for obtaining images of patients with suspected renal artery disease after renal transplantation.

Subjects and Methods

Six patients (three women; age range, 33–53 years; mean age, 41 years) were referred for examination of their renal allograft. The cause of their renal disease was hypertension ($n = 2$), preeclampsia-induced renal failure ($n = 1$), systemic lupus nephritis ($n = 1$), and polycystic kidney disease ($n = 1$). Indication for arteriography was elevation in serum creatinine level ($n = 3$), new-onset or poorly controlled hypertension ($n = 1$), or both ($n = 2$). The amount of time since transplantation ranged from 110 days to 13 years (mean, 5 years 3 months). From reviewing operative reports, we learned that five patients had received cadaveric renal transplants and that one had received a transplant from a living related donor. A single artery ($n = 4$) or multiple arteries ($n = 2$) constituted the renal transplant: One patient with multiple arteries had a single anastomosis using a Carrel patch spanning the common and external iliac artery; the remaining five patients had their anastomosis to either the external iliac artery ($n = 4$) or the internal iliac artery ($n = 1$). The type of anastomosis used was either end-to-side ($n = 5$) or end-to-end ($n = 1$).

All procedures were performed on a state-of-the-art digital angiography unit (DFP-2000A; Toshiba Medical Systems, Tochigi, Japan). The X-ray control unit (automatic exposure control) determined the

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[1]All authors: Department of Radiology, Indiana University Medical Center, 550 N. University Blvd., Rm. UH0279, Indianapolis, IN 46202-5253. Address correspondence to K. P. Moresco.

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optimum imaging parameters (kilovoltage, current, and pulse width) for each digital angiogram. Maximum values for kilovoltage and pulse width were set at 100 (kilovoltage and milliseconds, respectively). A 14-inch-diameter image intensifier was used. The auto focus mode selected the focal spot size (i.e., small, medium, or large) on the basis of exposure parameters. Image acquisition was set at a rate of 10–15 frames per second with a 1024^2 matrix for image storage.

The system for CO_2 delivery is shown in Figure 1. In the closed system, a pair of three-way stopcocks was placed between the injection syringe and the catheter. The CO_2 source was connected to one of the three-way stopcocks; the second three-way stopcock was connected to a 10-ml syringe used for catheter flushing. CO_2 was drawn into the injection syringe while both stopcocks were in the "off" position to prevent inadvertent delivery of CO_2 to the patient.

Using this system, the operator performed hand-injected runs while in the room behind a movable shield. For nonselective renal arteriograms, the CO_2 was drawn into a 60-ml syringe. The volume was decreased to 20 ml for selective injection of the renal artery. Before each injection, the injection catheter was cleared using CO_2 from the flush syringe. If the patient subsequently underwent imaging with iodinated or gadolinium-based contrast material, then the CO_2 injection system was broken down, and the catheter was secured with a single check-flow valve.

Images were first obtained while the patient was in the supine position. A 5-French, multiple-side-hole sizing catheter (Royal Flush II; Cook, Bloomington, IN) was used with the side holes at the approximate level of the arterial anastomosis. The patient was then turned anteriorly between 30° and 45° so that the transplanted kidney was placed in the nondependent position (i.e., 45° left anterior oblique for a left iliac fossa transplant). The degree of obliquity that provided the best visualization of the arterial anastomosis varied among patients, so we performed a CO_2 study to determine the optimum degree for each patient. To further improve visualization of the main renal or intraparenchymal artery, we performed selective catheterization of the renal artery as needed. The patient was then returned to the supine position after each injection. Because of the location of the transplant in the iliac fossa, IV glucagon (0.5–1.0 mg) was administered to limit bowel peristalsis.

Image postprocessing was performed using the digital angiography system image-stacking software (DPP-2000, version 2.24; Toshiba Medical Systems, Tochigi, Japan). First, each subtracted CO_2 arteriogram was reviewed, and the best image was mask-selected. Each run was then sectioned so that only those image frames in which the desired vessel or vessels were opacified with CO_2 were included. A functional (summed-static) image was then constructed using the stored data and the contrast medium time–density curve. Background tissue motion was further suppressed by adjusting the threshold image density.

Image findings using CO_2 were confirmed with subsequent imaging using either nonionic iodinated contrast material (iohexol, 300 mg I/ml, Omnipaque 300; Nycomed, Princeton, NJ) or gadolinium-based contrast material (gadopentetate dimeglumine, Magnevist; Berlex Laboratories, Wayne, NJ). Contrast material imaging was performed in the projection that best showed the artery anatomy when using CO_2. In patients requiring intervention, gadolinium-based contrast material, iodinated contrast material, or CO_2 arteriography was performed to document the result.

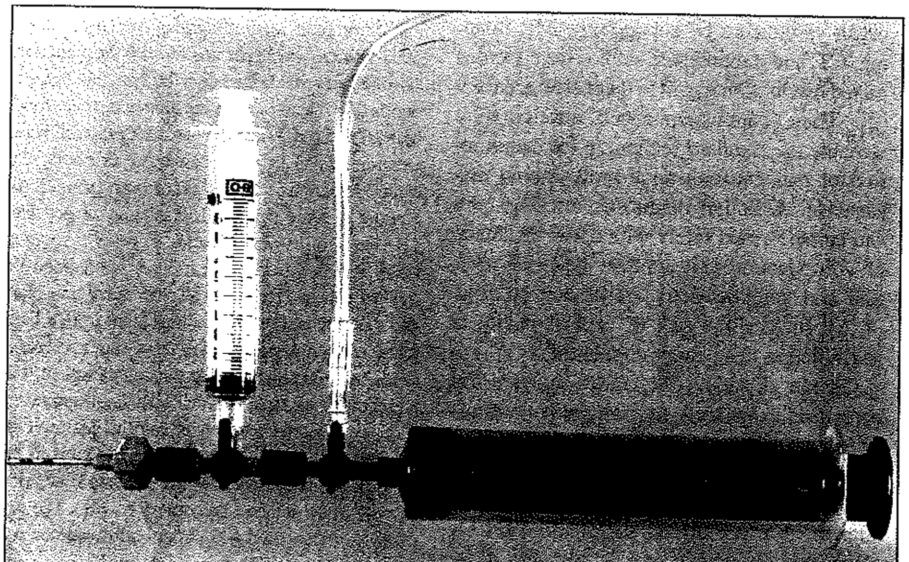

Fig. 1.—In carbon dioxide delivery system, carbon dioxide source is connected to distal three-way stopcock to which injection syringe is also connected (60 ml). Flush syringe (10 ml) and angiographic catheter are connected to proximal three-way stopcock. Note that operator must use caution when filling injection syringe so that carbon dioxide is not inadvertently administered to patient under high pressure.

Results

A total of eight arteries were examined in six patients. CO_2 arteriography was able to show the best projection for imaging the transplant artery anastomosis, main renal artery, and the segmental arteries (Fig. 2). The imaging quality beyond the level of the segmental arteries varied (Figs. 2 and 3A). This variability was most evident in the patient with chronic rejection (Fig. 3), in whom the renal vasculature showed a marked "pruned tree" appearance—a poor visualization beyond the main segmental arteries.

In all patients, CO_2 showed the native artery to the level of the graft anastomosis to be normal. Two anastomotic stenoses were identified using CO_2: One showed a 50% diameter reduction, and the second showed a 95% reduction. In the first patient, the narrowing involved an upper pole accessory artery and was not deemed hemodynamically significant. In the second patient, the anastomotic stenosis was successfully treated with balloon angioplasty. An upper pole segmental artery stenosis (Fig. 4) was found in a third patient and was also successfully treated with balloon angioplasty.

In one patient, CO_2 arteriography documented early opacification of the renal vein (Figs. 5A and 5B) during the arterial phase, thus indicating the presence of an atrioventricular fistula. The patient had undergone a percutaneous renal biopsy 12 days earlier; this procedure was the presumed cause of the atrioventricular fistula. During the same examination (Figs. 5C and 5D), the fistula was not identified using either gadolinium or nonionic iodinated contrast material. Embolotherapy was offered but was declined by the referring physicians.

In this series, confirmatory imaging was performed in all patients. The total volume of iodinated contrast material used ranged from 0 (n = 1) to 50 ml (mean, 18.3 ml; SD, ±16.8 ml). The patient who did not receive iodinated contrast material had confirmatory imaging performed using gadolinium-based contrast material. In another patient, a larger volume of contrast material was used (50 ml) because a malfunction in the room hardware required that the contrast material be reinjected several times both before and after angioplasty.

No significant change, which was defined as a 25% increase in the baseline serum creatinine level [3, 4], from the preprocedure to the immediate postprocedure serum creatinine level was seen in any of the patients. However, one patient did later require hemodialysis, and she received a total of 12 ml of nonionic contrast material. This patient was the one in whom angiographic evidence of chronic rejection was seen earlier. The creatinine level was 4.2 mg/dl on the day of

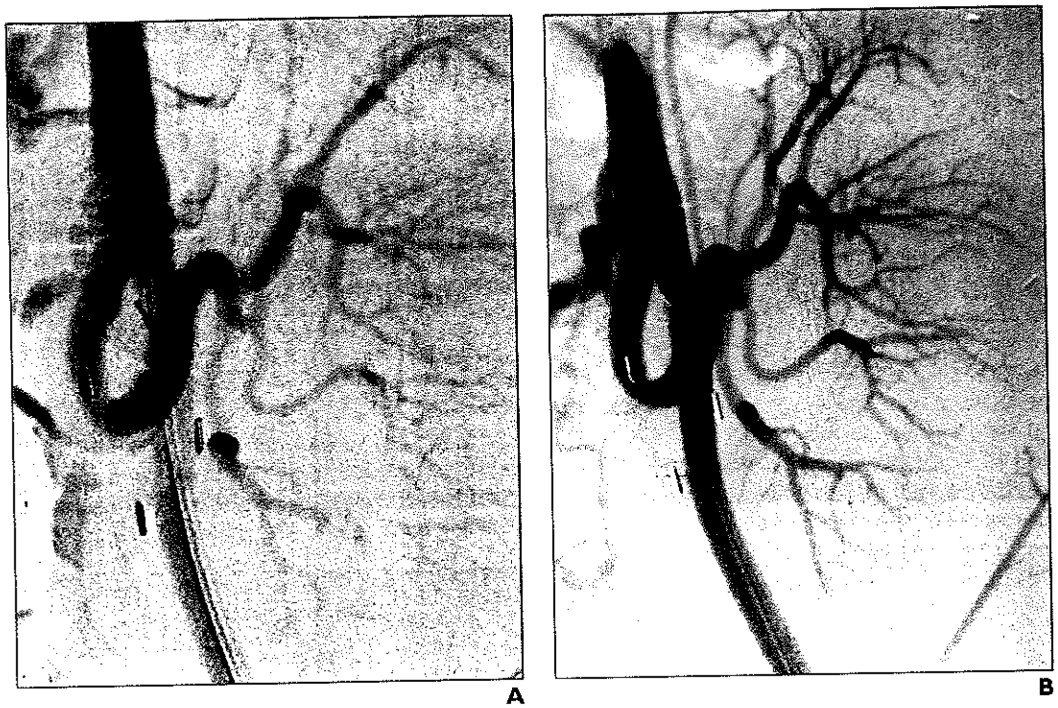

Fig. 2.—33-year-old woman with hypertension and mild elevation in serum creatinine level.
A, Renal transplant arteriogram in which carbon dioxide was used as contrast material. Injection of carbon dioxide to common iliac artery shows transplant anastomosis to be patent. First-, second-, and third-order branching of transplanted renal artery can be easily seen using carbon dioxide. Findings were confirmed using iodinated contrast material.
B, Renal transplant arteriogram in which iodinated contrast material was used.

the procedure and was 4.6 mg/dl on postprocedure day 1. Despite aggressive antirejection therapy, the creatinine level continued to rise to a level of 6.0 mg/dl on postprocedure day 7. Because of worsening azotemia, she ultimately resumed hemodialysis.

Discussion

Renal arteriography is the gold standard for the diagnosis of graft artery stenosis [1]. Depending on the associated risk factors and the definition used for contrast-induced renal failure, nephrotoxicity has been reported to occur after arteriography in 5.5–41.7% of the patients [4, 5]. The patients who are at highest risk are those with either preexisting renal insufficiency or diabetes. In kidney transplant recipients, worsening renal function is a major indication for graft examination. These patients may also have significant microvascular disease resulting from ongoing transplant rejection, hypertension, or both.

In our study group, CO_2, when combined with iodinated or gadolinium-based contrast material, proved safe in the examination of the renal transplant. CO_2 was most beneficial because it allowed the operator to determine the best projection in which to see the transplant artery anatomy without the usual risk of contrast agent–induced injury to the kidney. When confirmatory imaging was performed, the overall volume of the contrast material was limited to the absolute minimum needed to obtain representative images. The only patient who showed deterioration in renal function had angiography findings consistent with advanced, chronic transplant rejection. The patient had no significant change in creatinine level on postprocedure day 1. Despite aggressive medical therapy for graft rejection, renal function further deteriorated to the point that she required hemodialysis. The graft failure was thought to be caused by chronic rejection rather than the procedure itself.

The effect of CO_2 on the kidney has been evaluated experimentally in a dog model [10].

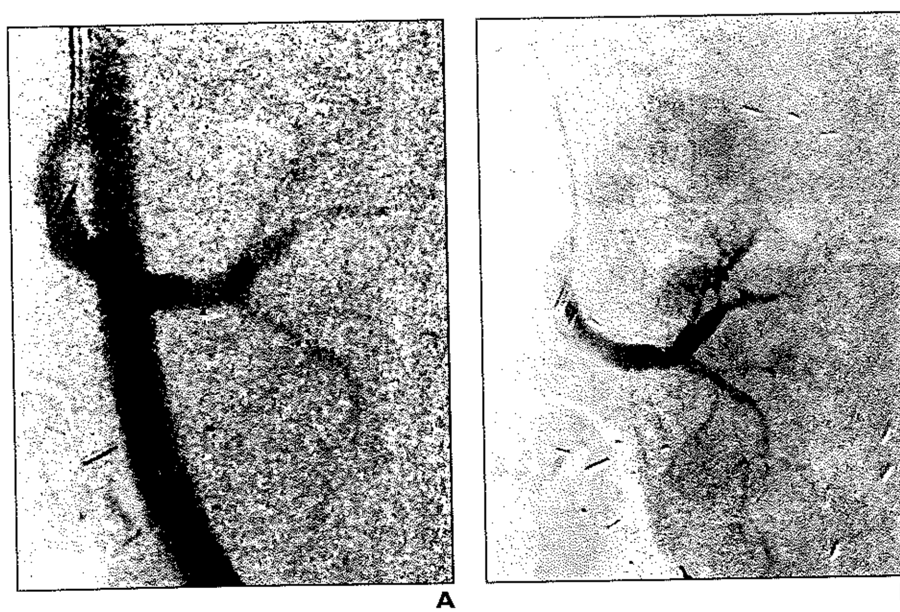

Fig. 3.—36-year-old woman who had undergone cadaveric renal transplantation 13 years earlier presented with rising creatinine level. Carbon dioxide and iodinated contrast material arteriography of left iliac fossa transplanted kidney.
A, Renal transplant arteriogram in which carbon dioxide was used as contrast material. Selective carbon dioxide injection of transplant kidney shows "pruned tree" appearance with poor opacification beyond second-order branching. Note brisk reflux into left common iliac artery.
B, Renal transplant arteriogram in which iodinated contrast material was used. Selective iodinated contrast material renal arteriography again showed "pruned tree" appearance along with multiple stenoses in distal artery branches. These findings are consistent with advanced, chronic vascular rejection.

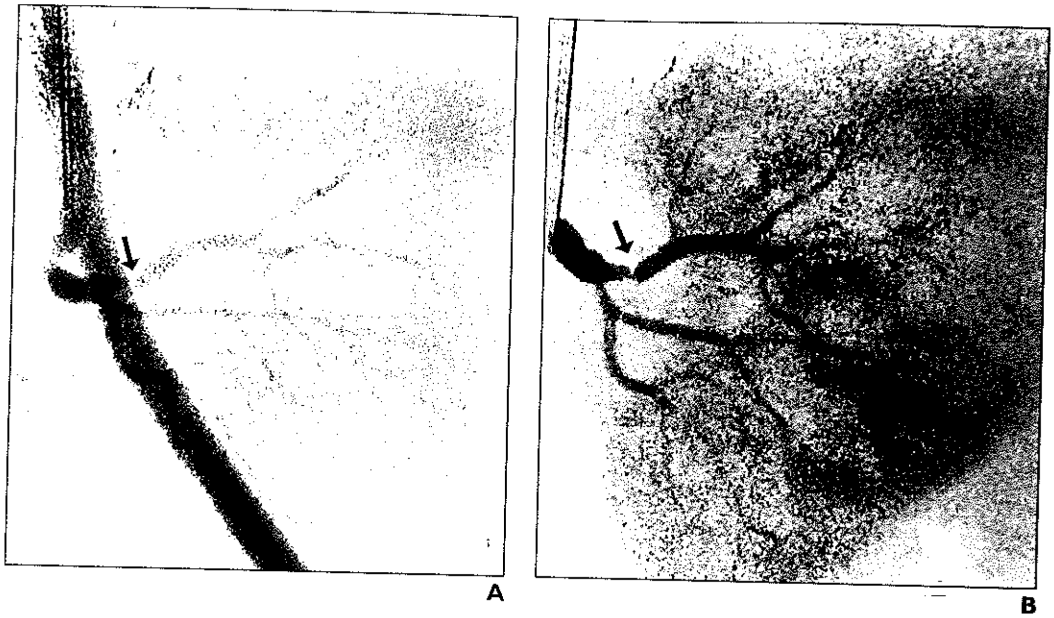

Fig. 4.—53-year-old man who had undergone cadaveric renal transplantation 10 months earlier and presented with hypertension.
A, Arteriogram of transplant artery stenosis using carbon dioxide as contrast material. Selective carbon dioxide injection of left iliac fossa transplanted kidney shows high-grade stenosis of upper pole segmental artery (*arrow*).
B, Arteriogram of transplant artery stenosis using iodinated contrast material. Stenosis (*arrow*) was confirmed using iodinated contrast material injection.

Fig. 5.—38-year-old man who had undergone cadaveric renal transplantation 4 months earlier. Transplant arteriography was performed 12 days after percutaneous renal biopsy for hypertension and rising creatinine level.
A–B, Arteriograms using carbon dioxide early (**A**) in arterial phase and late (**B**) in arterial phase show opacification of renal vein (*arrowhead*), indicating arteriovenous fistula.
C–D, Arteriogram using gadolinium-based contrast material (**C**) and using iodinated contrast material (**D**) performed as part of same study failed to show fistula. Main and lower pole accessory arteries are patent.

Blood flow measurements obtained after selective arteriography showed a transient decrease in renal blood flow that returned to normal within 24 hr. Light microscopy showed evidence of acute tubular necrosis in one animal. The necrosis was believed to have resulted from gas trapping caused by prolonged positioning of the kidney in the nondependent position. Despite the use of large volumes of CO_2, scanning electron microscopy showed no evidence of either endothelium damage or another abnormality. In clinical practice, renal function after CO_2 abdominal aortography and selective CO_2 renal arteriography showed no deleterious effect [11]. In the study by Harward et al., CO_2 was used to avoid the risk of nephrotoxicity in the acute follow-up examination of patients undergoing renal artery bypass surgery [11].

In our patients, no procedure-related injury to the kidney occurred. However, Hawkins [6] described parenchyma extravasation after CO_2 had been injected into a balloon-occluded renal artery. The mechanism by which this injury occurred was the explosive nature of the injection that resulted from forceful compression and subsequent rapid reexpansion in a closed system or a vascular bed. Although this technique may aid in the examination of selective or distal arteries, we believe its routine use should be avoided. To further limit the risk, we used a smaller volume of CO_2 on selective injection of the kidney, and we recommend careful clearing of blood from the catheter before injection to decrease catheter resistance, thus reducing the compressive force needed to expel CO_2 from the catheter.

CO_2 arteriography allowed accurate examination of the artery segments of interest. When compared with standard arteriography, the CO_2 arteriography was found to be highly correlated. In those patients requiring intervention, findings were confirmed not only for documentation, but also for sizing of the vessel before intervention. Although CO_2 has been used to guide percutaneous interventions [7, 12, 13], to our knowledge no study formally addresses the ability of CO_2 to accurately measure vessel diameter. Retrospective image evaluation showed a high correlation between vessel diameter measurements made using CO_2 and those made using iodinated contrast material. If CO_2 can be shown to be accurate, a confirmatory arteriogram using standard contrast material may not be needed. In addition, the arteriovenous fistula diagnosed in one patient after biopsy was seen only when performing imaging with CO_2. This finding has been previously described [14]. When compared with iodinated contrast material, the superior visualization provided by CO_2 is thought to result from the low viscosity of CO_2 that allows it to flow freely across arteriovenous shunts.

The benefits of CO_2 arteriography have been seen in clinical practice. Seeger et al. [7] compared CO_2 with iodinated contrast material for evaluation of peripheral vascular disease. These researchers found agreement between the contrast agents in 95% of patients, with accuracy in therapeutic plans using CO_2 alone in 92% of patients. CO_2 has also been compared with standard contrast material in the examination of patients with suspected renal artery stenosis [12]. CO_2 had a sensitivity of 83%, specificity of 99%, positive predictive value of 94%, and negative predictive value of 98%; a similar kappa value for CO_2 and standard contrast material was also found.

Because of the fluid properties of CO_2, opacification of the peripheral artery branches may be difficult; it is best accomplished if CO_2 is injected into a tight bolus. Bolus delivery of CO_2 is best achieved by using a dedicated CO_2 injector. An injector delivers a specified volume of CO_2 to the patient while avoiding the risk of air contamination. Unfortunately, dedicated CO_2 injectors are costly and, more important, are not currently approved for use by the Food and Drug Administration. The CO_2 delivery system [15] that is commercially available functions as a closed system with a CO_2 bag reservoir and a series of one-way check valves. Despite these advantages, the system can be time-consuming to assemble and cumbersome to use; it also lacks a detector for air contamination.

In our series, we used a system that was easy to assemble and that added little to the cost of the procedure. CO_2 can be drawn directly from a CO_2 canister or a similar reservoir that will limit the risk of air contamination. If CO_2 injectors are directly connected to the CO_2 canister, then extra caution must be taken when filling the syringe to avoid accidental delivery of CO_2 under high pressure. The operator must ensure that all connections between the patient and the CO_2 source are in the "off" position while filling the injection syringes.

Unlike liquid contrast agents, CO_2 must completely displace the blood pool to adequately opacify the vessel. Unless large volumes of CO_2 are used, blood displacement and vessel filling will be inadequate, and column fragmentation will occur. Inadequate vessel filling or vessel tortuosity can be compensated for with software that can stack or summate multiple images. In our patients, such image manipulation allowed improved visualization of the intraparenchymal vessels. Remasking and multiple-mask averaging can be used to improve image quality and suppress degradation caused by motion artifact. Because of the location of the renal transplant in the iliac fossa, motion artifact caused by bowel motion is also a significant concern. Although postprocessing may help minimize the effect of bowel motion, administration of glucagon before image acquisition may be most beneficial in preventing loss of image quality.

In the patient with chronic transplant rejection, the CO_2 was not well visualized beyond the central segmental vessels. The CO_2 was noted to rapidly reflux back to the native artery even on selective injections. We believe that this reflux was caused by the combination of high peripheral resistance and the fluid properties of CO_2—that is, a buoyant gas will follow the path of least resistance. Thus, despite proper patient and catheter positioning, the forward flow of the CO_2 was limited. This finding may signify a diffuse nature to the vascular pathology like that found in the patient from our series and was confirmed when iodinated contrast material was used to obtain images of the kidney.

Obtaining images of the distal vessels in the setting of proximal arterial occlusive disease may be difficult. In addition, poor filling may occur in the setting of vessel origins from the dependent portion of the vessel wall. By positioning the origin of the artery in the nondependent position, better peripheral opacification will result. In many instances, by placing the patient in Trendelenburg's position at a 20–30° angle vessel opacification will be further improved. However, caution should be taken to avoid renal ischemia when such positioning is used. If vertically oriented, the kidney requires approximately 2 min to clear the CO_2 from the cortex [7]. By contrast, if the kidney is returned to the horizontal position, CO_2 clears in approximately 30 sec. Thus, to prevent gas trapping–induced renal ischemia, the patient should be returned to the supine position between injections. Because of the risk of so-called vapor-lock, such serial injections should be separated by at least 2 min [9].

In conclusion, CO_2 may be the ideal contrast agent for the evaluation of renal transplant dysfunction because of the absence of associated nephrotoxicity. This contrast agent requires careful administration to avoid the risk of air contamination or vapor-lock–induced renal ischemia. Image quality can be optimized by adherence to proper technique combined with image postprocessing. We found that CO_2 was effective if used as the primary contrast agent for evaluation of the transplanted kidney: CO_2 was able to guide subsequent imaging with iodinated contrast material, thus limiting the overall volume of iodinated contrast material used. CO_2 may be better suited to show various transplant abnormalities such as arteriovenous fistulas.

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