Comparison of Diagnostic Accuracy with Carbon Dioxide versus Iodinated Contrast Material in the Imaging of Hemodialysis Access Fistulas[1]

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Abbreviations: AV = arteriovenous, PTFE = polytetrafluoroethylene

PURPOSE: Imaging of dialysis fistulas was performed with use of carbon dioxide and iodinated contrast material. Images were then compared to assess the quality and accuracy of CO_2 as a contrast agent.
PATIENTS AND METHODS: Thirty-two patients underwent digital subtraction imaging of the fistulas performed with both iodinated contrast material and CO_2 to evaluate the venous anastomosis. The images were blinded and the degree of stenosis was graded in 10% increments by two physicians. Statistical analysis including sensitivity, specificity, and accuracy of CO_2 images was performed.
RESULTS: There was no significant difference in physician ratings of the degree of venous stenosis ($P > .30$). Estimation of the degree of stenosis was significantly higher with CO_2 than with ionic contrast material ($P = .0001$). When iodinated contrast material is used as the gold standard, the sensitivity, specificity, and accuracy of CO_2 were 94%, 58%, and 75%, respectively.
CONCLUSIONS: CO_2 has a role as a contrast agent in the imaging of dialysis access grafts when the use of iodinated contrast material is of concern. CO_2 is safe for venous injections; however, it should not be used to evaluate the arterial anastomosis with the "reflux technique."

Currently, there are more than 450,000 patients receiving dialysis worldwide, with the vast majority of these patients requiring hemodialysis. This mode of renal replacement therapy, however, continues to be plagued by the lack of a trouble-free permanent venous access. The Scribner arteriovenous (AV) shunt, developed in 1960, provided the first reliable "permanent" hemodialysis venous access. This development was followed by the Cimino AV fistula and finally the prosthetic AV graft (1). The prosthetic graft, most commonly composed of polytetrafluoroethylene (PTFE), currently reigns as the most popular choice for a permanent hemodialysis access.

Unfortunately, the PTFE graft is not without problems of its own. The most costly of these problems, both in terms of patient morbidity and healthcare dollars, is graft failure. Graft failures are most commonly due to venous anastomotic stenosis or intragraft stenoses (presumably due to neointimal hyperplasia secondary to recurrent needle cannulation) with resultant thrombosis, pseudoaneurysms, or infection (2).

Mechanisms for access salvage now involve both the surgical and radiologic fields. Procedures such as surgical thrombectomy and revision, pharmacologic thrombolysis, angioplasty, and atherectomy are increasingly common (3–7). The common denominator in all of these procedures is the use of a fistulo-

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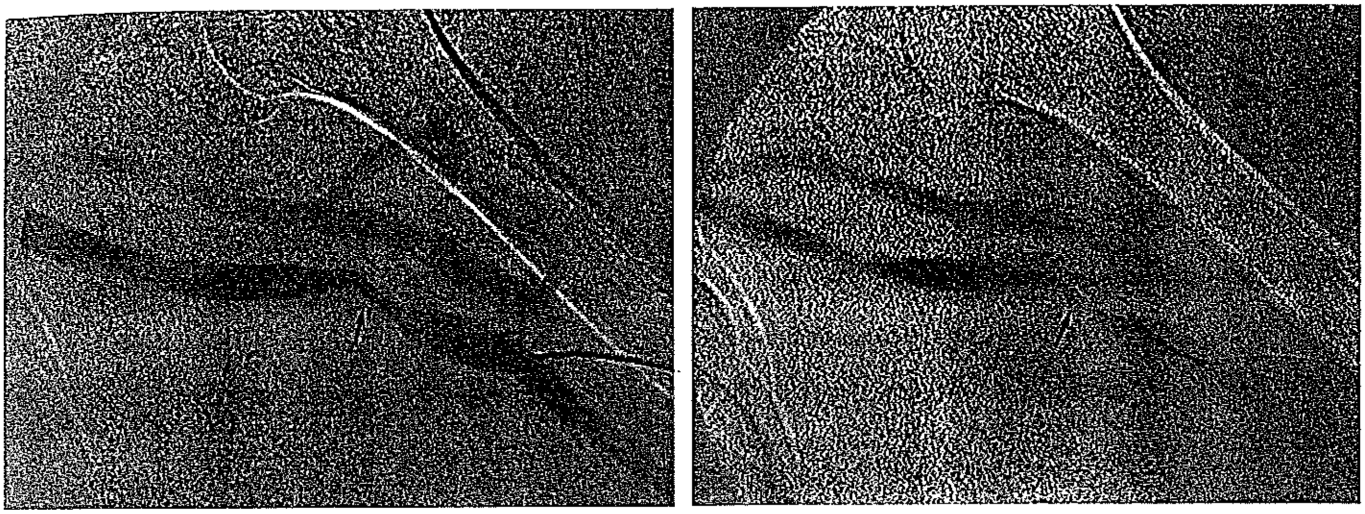


a. b.

Figure 1. (a) Straight upper arm PTFE graft visualized with iodinated contrast material. Arrow denotes venous anastomotic stenosis. (b) Same graft seen with use of CO_2. Arrow denotes venous anastomotic stenosis.

gram as a "roadmap" for any access revision.

In the past, images of the hemodialysis fistula were obtained with use of iodinated intravascular contrast agents. These agents, however, are associated with nephrotoxicity, further robbing the patient of residual renal function (8,9). The use of the newer nonionic contrast agents, while minimizing any allergic reactions, may not have any advantage over older ionic agents in terms of minimizing nephrotoxicity (10). The nonionic contrast agents are also significantly more expensive than ionic agents. A relatively inexpensive contrast agent that minimizes the risk for allergic reactions is needed.

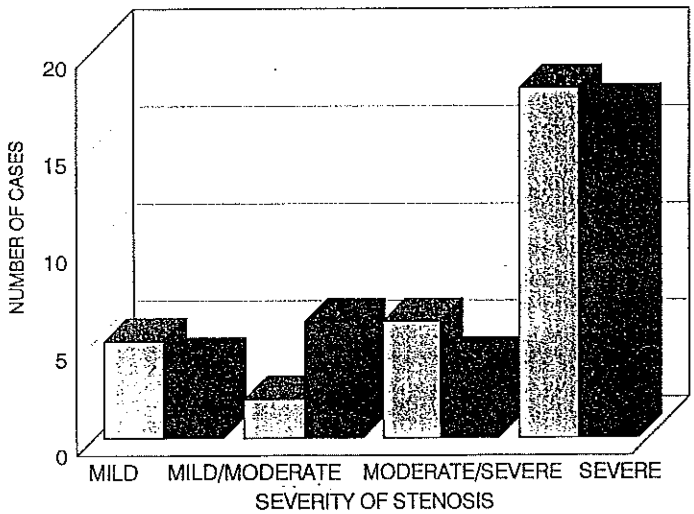
In the past few years, in part through work by Hawkins et al (11), carbon dioxide has gained increasing acceptance as a contrast agent. This compound is exceedingly inexpensive. In addition, allergic or significant nephrotoxic reactions have not been documented in humans to our knowledge. For these reasons, we designed a study to evaluate the diagnostic accuracy of CO_2 versus iodinated contrast material in the diagnosis of PTFE graft stenoses in hemodialysis accesses.

PATIENTS AND METHODS

Thirty-two patients were selected for this study. Twenty-eight of these patients had been selected by virtue of their inclusion in another study. These 28 patients had been scheduled for routine imaging of the fistula 3 months following the placement of a PTFE graft. An additional four patients were selected as they were scheduled for imaging due to access malfunction (indications included increased recirculation time and previous thrombosis).

The patient population consisted of 16 women and 16 men. The mean age of the patients was 59.1 years and their mean time on dialysis was 9.2 months. Causes of renal failure included diabetes mellitus ($n = 16$), hypertension ($n = 10$), glomerulonephritis ($n = 3$), systemic lupus erythematosus ($n = 1$), familial nephritis ($n = 1$), and autosomal dominant polycystic kidney disease ($n = 1$). All accesses were upper arm PTFE grafts (Impra, Tempe, Arizona).

Diagnostic imaging of the fistulas was performed after percutaneous placement of a 4-F, 65-cm-long vertebral angle 1 (Mallinckrodt, St Louis, Mo) catheter in the graft. The tip of the catheter was placed just proximal to the venous anastomosis. Ten milliliters of Isovue 300 (iopamidol; Squibb Diagnostic, Princeton, NJ) was injected manually for the iodinated studies and 40 mL of CO_2 was delivered manually for the CO_2 studies. All injections were boluses. The patients were in supine position with their arm at their side. All images were obtained with digital subtraction angiography. Acquisition rates of 2 frames per second for iodinated contrast studies and 6–15 frames per second for the CO_2 studies were used. The venous anastomosis was examined by using the identical projection for both contrast media (Fig 1). The venous anastomosis was chosen for specific evaluation due to its aforementioned association with graft thrombosis and the ability to compare independent evaluators' interpretations of degree of stenosis. The entire fistula (arterial anastomosis and central veins) was evaluated with iodinated contrast material to complete the examination. An independent person then blinded the pairings (CO_2 and iodinated contrast material) for each patient and two vascular radiologists (K.O.E. and G.M.G.) randomly



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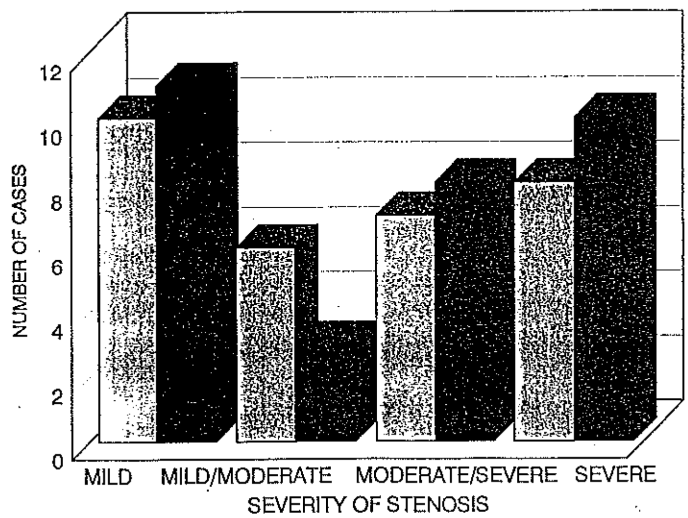

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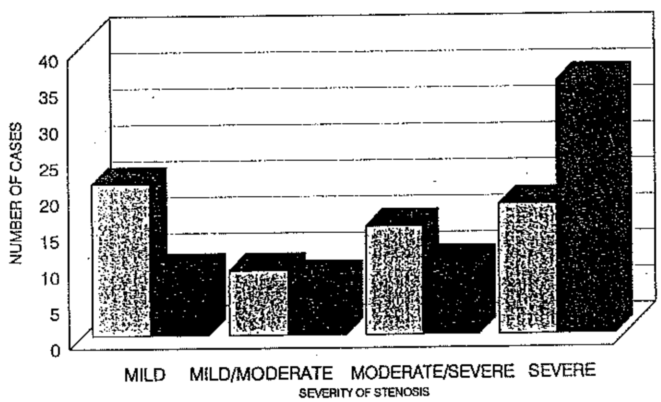

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Figures 2–4. Distribution of severity ratings by physician for (2) CO_2 and (3) nonionic contrast medium. In 2 and 3, light bars indicate rating by G.M.G.; dark bars indicate K.O.E. (4) Distribution of severity ratings by contrast medium. Light bars indicate nonionic media, and dark bars indicate CO_2.

evaluated the films. The percentage stenosis at the venous anastomosis was estimated based on visual inspection and grouped by 10% increments (0–10%, 11%–20%, etc). These were then defined as the physician ratings. The analysis of these data consisted of four parts. First, descriptive statistics were computed for the ratings given by the two radiologists. Second, a paired *t* test was performed to determine whether the observed difference in the ratings of CO_2 and iodinated contrast material for each patient was statistically significant. Third, an analysis of variance and Wilcoxon rank test were performed to determine whether the observed difference in the patient ratings were physician related. Fourth, the sensitivity, specificity, and accuracy of CO_2 as a contrast agent were computed with use of iodinated contrast material ratings as the gold standard.

RESULTS

Analysis of the data shows that little variability existed between the physicians' severity ratings (Figs 2, 3). The Wilcoxon rank test showed no significant difference in the physician ratings regardless of whether CO_2 or iodinated contrast material was used ($P > .30$). When corresponding ratings of the venous anastomotic stenoses with the different contrast agents are compared, significant differences are seen, however. The paired *t* test indicated that the degree of stenosis as determined with CO_2 fistulography is significantly higher on average than the ionic ratings ($P = .0001$). The percentage stenosis seen on the CO_2 images, on average, was judged 16% higher than the stenosis on the corresponding iodinated images. The distribution of severity ratings by contrast medium indicated that there are almost twice as many severe stenoses diagnosed when CO_2 is used compared with iodinated contrast material (Fig 4). Thus, use of CO_2 results in an overestimation of the number of severe cases. It is this unequal distribution of cases that results in an overall significant difference in the correlation between the two agents. After combining the mild and mild-moderate categories as "no treatment" and the moderate-severe and severe categories as "treatment required," the sensitivity, specificity, and accuracy ratings obtained with use of CO_2 as a contrast agent were 94%, 58%, and 75%, respectively. The positive predictive value was 69%, and the negative predictive value was 89%. The data also showed that there was no significant improvement in the correlation of ratings if two views of the venous anastomosis were available for physician grading. Finally, all patients underwent physiologic monitoring, including pulse oximetry and electrocardiography, and no adverse events occurred due to CO_2 in this study.

DISCUSSION

CO_2 is a nontoxic, nonallergenic gas that is rapidly absorbed and then excreted by the lungs. Its use as an angiographic contrast agent was first described by Dotter and Judkins in 1964 (12). Since that time, only a few reports have described the clinical utility of CO_2 for this purpose (11,13). Weaver et al in particular found CO_2 angiography provided diagnostic value in peripheral vascular disease (14). The advantages of using CO_2 as a contrast agent include its lack of nephrotoxicity or hyperosmolality. This combination of advantages is especially important in the population with end-stage renal disease in whom cardiovascular and renal impairment frequently coexist. In addition to these considerations, preservation of residual renal function is an advantage not to be ignored. The development of mechanisms for kinetic modeling have allowed physicians to objectively measure the adequacy of the dialysis prescription. These models have shown that residual renal function frequently contributes significantly to overall clearances (15,16). The use of potential nephrotoxins then becomes something to avoid. Finally, the minimal expense of CO_2 ($20/tank) makes it even more attractive as an intravascular contrast agent.

Despite the advantages of CO_2, the concern has been whether the image quality obtained with CO_2 was high enough to make diagnostic and therapeutic decisions. We chose to address this question by studying a specific population, the hemodialysis patient with end-stage renal disease. Specifically, we examined hemodialysis access (PTFE graft) fistulograms. Hemodialysis patients frequently require repeated radiologic examinations, as dictated by access failure. It was our hope that, by showing the reliability of CO_2 fistulograms, angiographers could feel confident about using the agent when avoidance of iodinated contrast material in high-risk patients is necessary. As outlined above, the degree of venous anastomotic stenosis—the most common site of intragraft stenosis—was consistently overestimated slightly with CO_2. This peculiarity of CO_2 makes this test highly sensitive but only moderately specific. This is important when a treatment decision is made based on the findings on a CO_2 fistulogram.

Several inherent properties of CO_2 may limit the accuracy of images obtained with this agent. The compressibility of the gas makes delivery in an even bolus difficult and results in an "explosive" injection. To lessen this effect, we cleared the catheter of blood by injecting 10 mL of CO_2 prior to the bolus. However, the use of a dedicated CO_2 injector would more reliably solve this problem. Unfortunately, we did not have access to this at our institution. The buoyancy of CO_2 has been a important consideration in acquiring consistent vascular images. With the patient supine, the gas layers anteriorly. To optimize filling of the arm fistula, it may be helpful in the future to elevate the arm or place the patient in the Trendelenburg position. Also advanced digital capabilities such as increased matrices, faster frame rates, and stacking of images may have improved our results with CO_2.

After the study was terminated, we had the opportunity to use CO_2 to image entire grafts including the central veins and arterial anastomosis. Like the venous anastomosis, CO_2 could be used safely and adequately for evaluation of the central veins; however, problems arose when we attempted to evaluate the arterial anastomosis with a "reflux" technique. In three of five patients in which this was attempted, there were significant, though transient, neurologic sequelae. After injection of CO_2 into the arterial anastomosis by compressing the venous limb of the graft just proximal to the catheter tip, two patients experienced seizures and a third patient experienced loss of consciousness with an associated 30-second respiratory arrest. We assume CO_2 refluxed retrograde into the brachial artery back to the subclavian and vertebral artery. Animal studies have supported the hazards of CO_2 in the cerebral circulation (17). Our current recommendation is to use CO_2 fistulography in patients with a known severe allergic reaction to nonionic contrast medium or in other high-risk patients such as those with congestive heart failure. If the arterial anastomosis needs to be evaluated, extreme caution should be used. Arm positioning and injection of small amounts of CO_2 may lessen the chance of reflux into the cerebral circulation.

CONCLUSION

While iodinated contrast medium remains the standard in the evaluation of vascular structures, this study indicates the feasibility of CO_2 as a contrast agent for upper extremity fistulography. The image quality in the majority of cases was sufficient to make therapeutic decisions, however, the accuracy may be improved with better delivery, patient positioning, and refinements in digital capabilities. Limitations and dangers remain and should be considered when CO_2 is used.

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