Endovascular aortic aneurysm repair with carbon dioxide-guided angiography in patients with renal insufficiency

Enrique Criado, MD, Gilbert R. Upchurch Jr, MD, Kate Young, MSRS, John E. Rectenwald, MD, Dawn M. Coleman, MD, Jonathon L. Eliason, MD, and Guillermo A. Escobar, MD, Ann Arbor, Mich

Objective: Renal dysfunction following endovascular abdominal aortic aneurysm repair (EVAR) remains a significant source of morbidity and mortality. We studied the use of carbon dioxide (CO₂) as a non-nephrotoxic contrast agent for EVAR.

Methods: Recorded data from 114 consecutive patients who underwent EVAR with CO₂ as the contrast agent over 44 months were retrospectively analyzed. CO₂ was used exclusively in 72 patients and in an additional 42 patients iodinated contrast (IC) was given (mean, 37 mL). Renal and hypogastric artery localization and completion angiography were done with CO₂ in all patients, including additional arterial embolization in 16 cases. Preoperative National Kidney Foundation glomerular filtration rate (GFR) classification was normal in 16 patients, mildly decreased in 52, moderate to severely decreased in 44, and two patients were on dialysis.

Results: All graft deployments were successful with no surgical conversions. CO₂ angiography identified 20 endoleaks (two type 1, 16 type 2, and two type 4) and three unintentionally covered arteries. Additional use of IC in 42 patients did not modify the procedure in any case. When compared with a cohort of patients who underwent EVAR using exclusively IC, the operative time was shorter with CO₂ (177 vs 194 minutes; \( P = .01 \)); fluoroscopy time was less (21 vs 28 minutes; \( P = .002 \)), and volume of IC was lower (37 vs 106 mL; \( P < .001 \)). Postoperatively, there were two deaths, two instances of renal failure requiring dialysis, and no complications related to CO₂ use. Among patients with moderate to severely decreased GFR, those undergoing EVAR with IC had a 12.7% greater decrease in GFR compared with the CO₂ EVAR group (\( P = .004 \)). At 1, 6, and 12-month follow-up, computed tomography angiography showed well-positioned endografts with the expected patent renal and hypogastric arteries in all patients and no difference in endoleak detection compared with the IC EVAR group. During follow-up, eight transluminal interventions and one open conversion were required, and no aneurysm-related deaths occurred.

Conclusions: CO₂-guided EVAR is technically feasible and safe; it eliminates or reduces the need for IC use, may expedite the procedure, and avoids deterioration in renal function in patients with pre-existing renal insufficiency. A prospective trial comparing CO₂ with IC during EVAR is warranted. (J Vasc Surg 2012;55:1570-6.)

The amount of iodinated contrast (IC) media injected during catheter-based procedures involving the renal arteries has been shown to have a strong correlation with a decrease in creatinine clearance following intervention in prospective, randomized trials. The perioperative use of IC agents is likely an important cause of renal dysfunction following endovascular abdominal aortic aneurysm repair (EVAR). Therefore, its avoidance should be beneficial in patients with pre-existing renal insufficiency and possibly in any patient undergoing EVAR. Carbon dioxide (CO₂) has no known nephrotoxicity and has a proven record of safety and technical viability as an alternative to IC agents during all types of vascular intervention. Encouraged by our initial experience with CO₂ angiography with a novel technique for EVAR, we expanded the use of CO₂ in our EVAR practice. This study describes the technical results and effects on renal function on 114 consecutive patients who underwent EVAR with CO₂ as a contrast agent and a comparison with a cohort of EVAR cases performed exclusively with IC.

METHODS

During a 44-month period, 114 consecutive patients (mean age, 72 years; range, 49-93 years; 94 males; mean aneurysm diameter, 58 mm) underwent EVAR using CO₂ as the intended contrast agent for angiographic localization of the aortic and iliac landing zones for endograft deployment, for guidance of additional endovascular procedures, and for completion angiography. These were consecutive patients and were not preselected for CO₂ angiography. One hundred ten cases were elective repairs and four were ruptured, emergency cases that have been the subject of a previous report. Two patients on dialysis underwent EVAR with CO₂ because it is the first author’s (E.C.) standard technique for EVAR in all cases, regardless of renal..
function. These two cases were used for technical comparisons but not for estimation of changes in renal function. CO2 was used exclusively in 72 patients, and in an additional 42 patients Iodixanol 270 (Visipaque; GE Healthcare, Princeton, NJ) was used as a contrast agent at the discretion of the attending surgeon (mean, 37 mL per case; range, 3-103 mL). In 31 patients, additional procedures were performed, including 23 endoluminal procedures (12 hypogastic artery embolizations, six iliac transluminal angioplasties or recanalizations, three inferior mesenteric artery embolizations, one accessory renal artery embolization, and one superior mesenteric artery stenting) and eight open procedures (five femoro-femoral bypasses and three femoral endarterectomies).

Patients were followed with physical examination and enhanced computerized tomography (CT) at 1, 6, and 12 months, and yearly thereafter. Patients with renal insufficiency were followed with ultrasound and CT without contrast. Estimation of glomerular filtration rate (eGFR) was expressed in mL/min/1.73 m² and calculated based on the formula recommended by the National Kidney Foundation (NKF) Practice Guidelines (186 x (plasma creatinine) -1.154 x (age) -0.203 x (0.742 if female) x (1.210 if African American)).

Preoperative renal function and IC allergy status. Mean preoperative eGFR and creatinine levels were 65 mL/min (range, 8-133 mL/min) and 1.4 mg/dL (range, 0.5-8.5 mg/dL), respectively. Before surgery, according to the NKF classification for chronic kidney disease based on eGFR, 16 patients had normal eGFR (≥90 mL/min), 52 had mildly decreased eGFR (60-89 mL/min), 40 had moderately decreased eGFR (30-59 mL/min), four had severely decreased eGFR (15-29 mL/min), and two were in kidney failure and on dialysis. In addition, 22 patients were diabetics, six had a single kidney, and two had a renal transplant. A severe contrast allergy was documented in nine patients. The patients on dialysis were not included in the statistical comparisons.

Cohorts of patients undergoing EVAR exclusively with IC. A contemporary cohort of 22 comparable patients undergoing EVAR exclusively with IC was used to record the operative time (193 ± 10 min, mean ± standard deviation [SD]), total fluoroscopy time (28 min, SD ± 1 min), total volume of IC used (106 ± 6 mL, mean ± SD), and postoperative endoleak detection. A separate cohort of 50 patients with pre-existing moderately decreased eGFR (30-59 mL/min) to severely decreased eGFR (15-29 mL/min) with a mean eGFR of 39 ± 12.4 mL/min, mean ± SD) was used to compare the postoperative changes in eGFR (−2.3 ± 29 mL/min, mean ± SD) with that of the CO2 EVAR group.

Preprocedural imaging and endograft selection. Thin-slice CT scanning and three-dimensional reconstruction (3D-CT) of the abdominal aortoiliac segment was done preoperatively in all patients, except in the ruptured cases that were evaluated without 3D reconstructions. In six patients with significant renal insufficiency, a CT scan without contrast followed by intraoperative CO2 angiography was done for endograft selection. Based on the CT information, endografts were selected for implantation based on the patient’s anatomy and the surgeon’s preference, including 97 Zenith Flex aortic endografts (Cook Medical Inc, Bloomington, Ind), 10 AneuRx (Medtronic Inc, Minneapolis, Minn), five Excluder (W. L. Gore & Associates Inc, Flagstaff, Ariz), and two Aortofix (Lombard, Sunnyvale, Calif).

Interventional technique. All endograft placements were done with fixed C-arm fluoroscopic imaging (AXIOM Artis dTA; Siemens AG, München, Germany). In 62 cases, we used a previously described technique for endograft deployment injecting CO2 though the endograft delivery sheath, and in 52, the procedure was done with an end-hole catheter or angiographic catheter for CO2 injection using the following technique.

The femoral arteries were exposed through bilateral short, oblique incisions placed just caudal to the inguinal ligaments. Stiff shaft guidewires (Terumo Medical Co, Somerset, NJ) were advanced into the suprarenal aorta under fluoroscopic guidance from both femoral sides, and 9-F, 11-cm-long sheaths were placed over the wire, and the guidewire was exchanged for a Lunderquist Extra Stiff Guidewire (Cook Medical Inc) or similar wire, and its tip placed in the proximal descending thoracic aorta from the side selected for main body deployment. The patient was given systemic heparin. From the contralateral side, a 5-F, 65-cm-long angled tip glide catheter was placed over the wire at the level of the first lumbar vertebral body. The endograft main body was ad-
vanced over the extra-stiff wire, until the proximal stent was in the perirenal aorta (Fig 1). A 60-mL Luer-lock syringe connected to the CO₂ delivery system (Angio Flush III Contrast Management System; Angio Dynamics Inc, Queensbury, NY) was used for all CO₂ hand injections. Catheters were purged with 5 to 10 mL of CO₂ prior to bolus injections. This purging maneuver facilitates smooth, nonexplosive CO₂ delivery during intravascular angiographic injection. Ventilation motion was held and, using the CO₂ subtraction settings, an aortogram was obtained using 40 mL of CO₂ hand-injected over approximately 2 seconds. The renal arteries were visualized, and the optimal subtraction image is stored for guidance during endograft deployment (Fig 2). The main body of the graft was deployed based on this angiogram. If a renal artery was not visualized, the table was tilted to elevate the kidney, which facilitates passage of CO₂ into the renal artery. It is important to bear in mind that the CO₂ bubble is highly buoyant and accumulates in the most superior portion of the arterial segment. Next, the contralateral docking limb was cannulated in a retrograde fashion. A retrograde angiogram was obtained using 30 mL of CO₂ in the anterior oblique projection (Fig 3). The contralateral limb of the graft was then deployed proximal to the origin of the hypogastric artery. The ipsilateral hypogastric artery was localized by retrograde injection of 30 mL of CO₂ in the anterior oblique projection (Fig 4), and the ipsilateral limb was deployed. Once the endograft was shaped with a compliant balloon, a completion angiogram was done through the 5-F angled glide, end-hole catheter, injecting 40 mL of CO₂ and including the renal and hypogastric artery origins in the field. The subtraction sequence was held to allow late opacification of the lumbar and inferior mesenteric arteries (Fig 5). Additional injections were obtained with the catheter in different positions or in different projections, if there was any suggestion of endoleak or other potential problem (Fig 6). Once a satisfactory angiogram was obtained, the procedure was completed in a standard fashion.

**Statistical analysis.** Statistical analysis was performed using PASW 18 software (SPSS, Chicago, Ill). Continuous variables between two groups were compared using Student’s *t*-test and comparisons between categorical values were performed using χ² analysis. Any comparisons between two or more groups were performed with one-way analysis of variance. All data are presented as the mean value ± the standard error of the mean, unless otherwise stated. Comparisons with *P* values <.05 were considered significant.

**RESULTS**

During a 44-month period, 114 consecutive patients underwent EVAR using CO₂ as the intended contrast
agent. All cases were technically successful without any conversions to open repair. The mean volume of CO₂ used for EVAR in 114 patients was 395 mL (range, 80-780 mL) with a mean number of 11 CO₂ angiographic runs per intervention. The mean total procedural time was 177 minutes. In 72 patients, the EVAR and all ancillary transluminal procedures were completed using exclusively CO₂ as the contrast agent (mean, 389 ± 17 mL of CO₂ per case) with a mean fluoroscopy time of 21 ± 1.2 minutes and a mean total procedural time of 165 ± 6 minutes. In 42 patients, where the attending surgeon deemed it necessary to use IC (mean, 37 ± 3.7 mL per case; range, 3-103 mL) in addition to CO₂ (mean, 430 ± 29 mL per case), the mean fluoroscopy time was 32 ± 3.2 minutes, and the total procedural time was 193 ± 9 minutes. The reasons for the use of additional IC were to visualize renal arteries or other branches not well seen with CO₂ alone, or to confirm the presence of endoleak suspected by CO₂ angiography.

Intraoperatively, three arteries were unintentionally covered by the endograft; this included one hypogastric and two renal arteries. One of the renal arteries was re-opened by applying traction on the body of the endograft, but this vessel thrombosed within 24 hours. The other two vessels were left covered. The coverage of these vessels was not due to inadequate visualization. It was due to short infrarenal necks in case of the renal arteries, and to a miscalculation of graft length in the case of the hypogastric. Completion CO₂ angiography identified 20 endoleaks (two type 1, 16 type 2, and two type 4). No additional endoleaks were detected with the intraoperative use of IC. At 1 month of follow-up, no additional type 1 or type 3 endoleaks were detected by CT or ultrasound.

When compared with the cohort of 22 patients who underwent EVAR exclusively with IC, the operative time was shorter in the CO₂ group (177 ± 7 min vs 193 ± 10 min; \( P = .01 \)), fluoroscopy time was less (21 ± 1 min vs 28 ± 1 min; \( P = .002 \)), and the volume of IC used was less (37 ± 4 mL vs 106 ± 7 mL; \( P < .001 \)).

Four patients returned to the operating room within 24 hours: two for femoral artery thrombosis, one for a type 1 endoleak identified intraoperatively, and one for a renal artery thrombosis secondary to encroachment of the orifice by the endograft. There were two postoperative deaths, resulting in a 1.7% 30-day mortality: one patient with advanced congestive heart failure who refused further treatment, and the second patient with a preoperative creatinine clearance of 17 mL/min, who required dialysis following surgery, and opted for hospice care.

During follow-up at 1 to 39 months, eight transluminal interventions and one open conversion were required, with
follow-up period. One patient had polycystic kidney disease. Two patients developed dialysis requirements during the immediate postoperative period. One of them had a preoperative GFR of 17 mL. The second patient required dialysis after going into acute heart failure on the second postoperative day.

Preoperatively, there was no severe renal insufficiency. In patients with pre-existing renal insufficiency or severe allergy to IC, it is advisable, if not mandatory, to use alternative, non-nephrotoxic or nonallergenic guiding methods for EVAR. As such, intravascular ultrasound (IVUS) and transabdominal ultrasound have been technically successful and have also suggested that reducing the amount of IC use during EVAR decreases the deterioration in renal function following intervention. However, IVUS has failed to gain popularity perhaps due to its technical complexity, cost, and limited availability in many surgical centers.

Our experience using CO₂ as a contrast agent for EVAR in unselected patients resulted in no intraprocedural mortality, no conversions to open repair, no failures to identify type 1 or type 3 endoleaks, a very low number of immediate reoperations, and a low reintervention rate during follow-up. Our results are comparable with those reported in large trials using IC and performed under optimal conditions in well-selected patients. Furthermore, it is important to note that our experience includes the learning curve of several surgeons using the CO₂ technique, which implies that our results could be im-

**DISCUSSION**

Renal failure following EVAR remains a source of morbidity and mortality in the immediate postoperative period and during long-term follow-up of these patients. Progression of renal dysfunction following EVAR appears to be related to multiple factors, including the use of IC media in the perioperative and postoperative period. The administration of IC media to patients undergoing EVAR is perhaps the only factor contributing to renal dysfunction that could be completely avoided, simply by avoiding its use. The purpose of an intravascular contrast agent during EVAR is to localize the major branches of the aorta and iliac arteries to allow precise deployment of the endograft, and upon completion, to identify significant endoleaks and ascertain patency of the graft, renal arteries, and outflow vessels.

CO₂, as a contrast agent, provides all this information, with the advantages that it has no known renal or systemic toxicity, is not allergenic, is widely available in the hospital environment at an extremely low cost, and when used with the adequate knowledge and technique is an extremely safe negative contrast agent. The technical suitability of CO₂ angiography for EVAR and its beneficial effect on preservation of renal function have been suggested during the last decade in several publications. However, the use of CO₂ for EVAR guidance remains anecdotal considering the large number of cases annually performed.

Vascular surgeons have traditionally been trained exclusively in the use of IC media for transluminal intervention, and very few are familiar with the use of alternative contrast agents. This is most likely the reason for the notable paucity of publications in which CO₂ angiography was used for EVAR guidance.

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Our experience using CO₂ as a contrast agent for EVAR in unselected patients resulted in no intraoperative mortality, no conversions to open repair, no failures to identify type 1 or type 3 endoleaks, a very low number of immediate reoperations, and a low reintervention rate during follow-up. Our results are comparable with those reported in large trials using IC and performed under optimal conditions in well-selected patients. Furthermore, it is important to note that our experience includes the learning curve of several surgeons using the CO₂ technique, which implies that our results could be im-

**Fig 6.** An additional oblique projection shows all the visceral vessels, a stenosis in the left renal stent, and retrograde opacification of the inferior mesenteric artery via the left colic and superior hemorrhoidal arteries, but without passage of carbon dioxide (CO₂) into the aneurysmal sac. The postoperative computerized tomography (CT) scan confirmed the absence of endoleaks in this patient.
proved with more experience. The shorter operative time for CO2-guided EVAR compared with EVAR done with IC may be a result of the avoidance of power injection, which may shorten the overall duration of the procedure, as hand injection of CO2 is faster compared with power injection. This difference, however, may just represent individual practice because the majority of the CO2 EVAR cases were done by the more experienced surgeons in the group. Our experience demonstrates that EVAR can be done safely, with technical results comparable with those obtainable with IC.

The degree and rate of deterioration in renal function following EVAR remains poorly defined. A large EVAR study showed a concerning 10% average decrease in creatinine clearance during the first year following surgery. However, another sizable study revealed a slight recovery in renal function during the second year following surgery, but without return to preoperative levels. A recent subanalysis of the EVAR I and II trials suggests that the rate of decrease in GFR following EVAR is slow, and that the increased rate in deterioration in renal function following EVAR is associated with endograft complications. A plausible explanation for this association may be the administration of IC required for the additional imaging and endovascular procedures required for the management of such complications. This may be yet another compelling reason to avoid IC in EVAR patients. Interestingly, these three referenced studies suggest that the presence of renal insufficiency prior to EVAR is not associated with an increased risk of long-term renal dysfunction. This finding is counterintuitive, since pre-existing renal insufficiency is a major predictor of postoperative renal failure in patients undergoing EVAR, and renal failure itself is associated with a significant increase in hospital mortality.

Our data suggest that CO2-guided EVAR in patients with pre-existing moderate to severe renal dysfunction (class 3 and 4 of the NKF classification) was associated with no change in GFR, while patients undergoing EVAR with IC sustained a significant postoperative reduction in GFR. This is an observation that we have not found described in the literature and that strongly suggests that CO2 eliminates the renal toxicity associated with IC in EVAR patients. A significant weakness of our study is that our patients were not routinely followed long term with eGFR measurements, so we cannot evaluate the duration of renal protection following CO2-guided EVAR. Unfortunately, the long-term renal protective effects of IC avoidance during EVAR may be counteracted by the large number of contrast-enhanced diagnostic and interventional procedures that these patients endure during long-term follow-up. The ideal renal protection policy would therefore have to include not only the avoidance of intraoperative IC but also the use of noncontrast methods for surveillance, such as ultrasound or unenhanced CT. The following rhetorical question may serve as an appropriate closing statement: If the technical success, morbidity-mortality, and follow-up results of CO2-guided EVAR are comparable with those obtained using IC, why should we continue to use the nephrotoxic agent?

**AUTHOR CONTRIBUTIONS**

Conception and design: EC
Analysis and interpretation: EC, JR
Data collection: KY, JE, GE, DC
Writing the article: EC
Critical revision of the article: EC, GU, KY, JR, JE, DC, GE
Final approval of the article: EC, GU, KY, JR, JE, DC, GE
Statistical analysis: JR, EC
Obtained funding: EC
Overall responsibility: EC

**REFERENCES**