Carbon dioxide (CO₂) angiography as an option for endovascular abdominal aortic aneurysm repair (EVAR) in patients with chronic kidney disease (CKD)

Chiara De Angelis1 · Francesco Sardanelli2,3 · Matteo Perego4 · Marco Ali5 · Francesco Casilli6 · Luigi Inglese7 · Giovanni Mauri2,8

Abstract To assess feasibility, efficacy and safety of carbon dioxide (CO₂) digital subtraction angiography (DSA) to guide endovascular aneurysm repair (EVAR) in a cohort of patients with chronic kidney disease (CKD). After Ethical Committee approval, the records of 13 patients (all male, mean age 74.6 ± 8.0 years) with CKD, who underwent EVAR to exclude an abdominal aortic aneurysm (AAA) under CO₂ angiography guidance, were reviewed. The AAA to be excluded had a mean diameter of 52.0 ± 8.0 mm. CO₂ angiography was performed by automatic (n = 7) or hand (n = 6) injection. The endograft was correctly placed and the AAA was excluded in all cases, without any surgical conversions. Two patients (15.4%) had an endoleak: one type-Ia, detected by CO₂-DSA and effectively treated with prosthesis dilatation; one type-III, detected by CO₂-DSA, confirmed using 10 ml of ICM, and conservatively managed. In one patient, CO₂ angiograms were considered of too low quality for guiding the procedure and 200 ml of ICM were administered. Overall, 11 patients (84.6%) underwent a successful EVAR under the guidance of the sole CO₂ angiography. No patients suffered from major complications, including those typically CO₂-related. Two patients suffered from abdominal pain during the procedure secondary to a transient splanchnic perfusion’s reduction due to CO₂, and one patient had a worsening of renal function probably caused by a cholesterol embolization during the procedure. In patients with CKD, EVAR under CO₂ angiography guidance is feasible, effective, and safe.
Introduction

Endovascular aneurysm repair (EVAR) has become the treatment of choice for abdominal aortic aneurysms (AAA) in patients with suitable anatomy, especially in elderly patients with comorbidities because it is less invasive than open surgery [1, 2]. The standard endovascular procedure implies the use of iodinated contrast material (ICM) to guide digital subtraction angiography (DSA), but risks of nephrotoxicity and allergic reaction may represent a contraindication to their administration [3]. Notably, the incidence of chronic kidney disease (CKD) in EVAR patients has been reported to be about 7–25% [4, 5] and acute kidney injury after EVAR 2–16%. Mortality in patients with acute kidney injury after EVAR can be as high as 30–50% [6]. Thus, finding an alternative method to guide an EVAR procedure, allowing for avoiding or reducing the amount of administered ICM, would be extremely helpful.

Carbon dioxide (CO₂) is a gas with chemical and physical properties that makes it a theoretical ideal contrast material for angiography in this setting. It has specific advantages because it is not allergenic and not toxic, 20-fold more soluble than O₂ in blood and 400-fold less viscous than ICMs. Moreover, it is very cheap and does not necessarily require dedicated hardware. Gaseous CO₂ can be used as a negative intra-arterial contrast material below the diaphragm instead of ICM and CO₂-DSA can be considered a good alternative to ICM-DSA in patients at risk of contrast nephrotoxicity or with previous known allergic reactions to ICM [1, 7, 8]. In particular, CO₂ is indicated in patients with reduced renal function (serum creatinine >1.5 g/dl) that should undergo diagnostic or therapeutic DSA, because ICM may induce nephropathy [9]. It may also be used in combination with ICM, in order to reduce its amount during the procedures [8, 10, 11]. Moreover, CO₂ can be safely used as a contrast material in the pediatric age, especially in case of contraindications to ICM such as renal transplant [12]. The CO₂-DSA has been reported to be feasible and safe in small series of patients for diagnostic and interventional endovascular procedures under the diaphragm, in patients with contraindications to ICM [1–3, 7, 13–15].

The aim of this study was to assess feasibility, safety and efficacy of CO₂-DSA to guide EVAR procedures for AAA in patients with CKD.

Materials and methods

Study population

The Institutional Review Board approved this study (Ethical Committee of the BLINDED; authorization number BLINDED on DATE BLINDED). It was retrospectively evaluated clinical data and DSA images in a consecutive series of 13 patients, all male (mean age 74.6 ± 8.0 years), with CKD as a contraindication to ICM (none of the treated patients had allergy) who underwent EVAR procedures for the treatment of an AAA at our Institution between 2010 and 2015.

In order to avoid the administration of ICM, patients were studied before the procedure with ultrasound and unenhanced computed tomography (CT) or magnetic resonance imaging (MRI) for planning the EVAR. The type of endoprosthesis was chosen according to the patient’s characteristics and size of the AAA and of the landing zone.

Procedure

Before the procedure, the anesthesiologist performed firstly a spinal anesthesia. Sedation was avoided, as respiratory depression and hypotension caused by air contamination could be mistaken for adverse effects of sedatives and/or analgesics. For these reasons, patient’s vital signs (heart and respiratory rates, electrocardiogram) were monitored: relevant changes should be considered as a possible sign of excessive CO₂ dose or air contamination.

Then, the patient was positioned on a standard angiographic table in Trendelenburg position. No specific preparation was required. No hydration was needed in patients with renal impairment treated using only CO₂; instead, patients had to be hydrated with intravenous isotonic saline solution before the procedure in case of use of ICM, to preserve renal function [8]. Sedation was avoided, as respiratory depression and hypotension caused by air contamination could be mistaken for adverse effects of sedatives and/or analgesics. For these reasons, patient’s vital signs (heart and respiratory rates, electrocardiogram) were monitored: relevant changes should be considered as a possible sign of excessive CO₂ dose or air contamination.

All patients were punctured from bilateral femoral access. An angiographic catheter was positioned in the appropriate location and was connected to a manual or automatic injection system (see below), taking care of preventing an “explosive” delivery by initially filling it with a small amount of CO₂ (90% of CO₂ is injected in the last 0.5 s during a 4 s injection) [16]. Considering the risk of injecting high CO₂ volumes, the catheter was not directly connected to the CO₂ cylinder containing a large gas volume at a very high pressure. CO₂ was delivered into the
vessel by using a handheld syringe or by a plastic bag system. In case of doubt at DSA images obtained with CO₂, or if the operator judged the CO₂ images inadequate for the correct performance of the EVAR procedure, ICM administration was performed.

The manual injection system used was “home-made” and composed by three Luer-lock syringes linked together forming a “reservoir”, connected to another 20-ml syringe for diagnostic injection and to a disposable gas cylinder filled with 99% laboratory-grade CO₂ through a filter (Fig. 1). The CO₂ canister (cylinder) is medical grade. The filter (0.2 µm) was necessary to hold big particles (such as air) and purify the injected CO₂. Moreover, the filter prevented CO₂ emission into the room, that could be toxic and undetectable by the operators.

The automatic apparatus for the injection of CO₂ (Grupo Grifols, S.A., Parets del Valles, Spain) was composed by a Luer-lock syringe connected with a CO₂ delivery system from a gas cylinder. The injection was guided by a monitor that displayed injection parameters (dose, pressure and slope). Before the procedure, in order to remove air from the circuit and the catheter, an injection test was performed into sterile saline solution, outside the patient (Fig. 2). An intravenous bolus of 0.5–1 mg of glucagon was administered to decrease the effects of bowel gas motion [10, 17].

Another available plastic bag system is produced by Merit Medical system, Inc (South Jordan, Utah, USA) [18]. Another recently introduced, FDA-approved portable CO₂ delivery system is the CO₂mmander with Angio-Assist (PMDA, LLC, Ft.Myers, FL, USA). It allows for the delivery of CO₂ at a low pressure to any reservoir such as the plastic bag or a large syringe with the Luer-lock fitting. The AngioAssist is a unique stopcock system with valves that control direction of gas flow, allowing gas delivery in a non-explosive fashion using a 60 cc reservoir syringe and a 30 cc injection syringe.

During the procedure, angiographic images documented the positioning of the prosthesis. Modern equipment for image quality and processing system, with 1024×1024 matrix and rapid data manipulation, greatly increased the ability to utilize CO₂ as a contrast material. Acquisition programs had a high frame rate (>6 frames/s), as the gas propagated quickly into the vessels, and a high kilo-voltage to lower the skin dose but keep the contrast discrimination [1, 8].

The CO₂ injection was performed using automatic delivery system in seven patients and manual delivery system in the remaining six patients (Figs. 1, 2).

**Image and data analysis**

Angiographic images and clinical records of the patients were evaluated to determine the EVAR technical success and rate of major and minor complications related to the CO₂-DSA procedure. Also, clinical results of EVAR procedure were assessed.

The angiographic procedure was considered completely successful if no use of ICM was required, and partially successful if less than 20 ml of ICM were necessary to complete the EVAR placement.

---

**Fig. 1** Manual CO₂ injection system. This figure illustrates the manual system for CO₂ injection, composed by: three luer lock syringes connected in series (asterisk, a) that represent a “reservoir”, connected to another syringe (arrow, a) used for diagnostic injection and connected, through a filter (F, a), to a disposable gas cylinder (B, b).
The EVAR procedure was considered completely successful if the aneurysm was correctly excluded, the graft correctly placed and no endoleak was caused. Complications were evaluated and categorized as major or minor according to the SIR guidelines [19].

Statistical analysis

Descriptive statistics tests were used. The distribution was reported as percent and 95% confidential interval (95% CI).

Results

In all thirteen patients it was possible to correctly identify the anatomical landmarks (aortic and iliac landing zones) for a successful graft deployment with CO₂. All grafts were finally correctly placed and the AAA excluded with no need of surgical conversions. The mean diameter of AAA in the 13 patients was 52.0 ± 8.0 mm (mean ± standard deviation).

A successful case is shown in Fig. 3.

CO₂-DSA was performed by automatic (n = 7) or hand (n = 6) injection. In one of the first patients treated, the quality of CO₂ images was considered insufficient to correctly visualize the procedure, and 200 ml of ICM was administered. However, in this case no further information changing the strategy were finally derived from the ICM-DSA images.

One patient developed a type-Ia endoleak, caused by incomplete attachment of the proximal portion of the prosthesis immediately after the EVAR deployment; this endoleak was detected by CO₂-DSA and effectively treated with prosthesis dilatation. A second patient developed a type-III endoleak immediately after the EVAR deployment, caused by a graft defect or a graft module disconnection; this endoleak was detected by CO₂-DSA. However, as this might be a critical clinical decision whether to treat or not to treat such endoleak, in this case a conventional DSA with 10 ml of ICM was performed. The findings of conventional DSA confirmed the diagnosis obtained with CO₂-DSA and the endoleak.
was conservatively managed. Follow-up is ongoing with unenhanced CT and MR (Fig. 4).

Thus, 11/13 patients (84.6%, 95% CI 55–98) in this study underwent a completely successful EVAR with the guidance of the sole CO₂ angiography, one patient had a partially successful CO₂-guided EVAR and one patient did not benefit from CO₂-DSA as >20 ml of ICM were used.

No patients suffered from major complications. Two patients (15.4%, 95% CI 2–45) suffered from abdominal pain during the procedure secondary to a transient splanchnic perfusion reduction due to CO₂, and one patient (7.7%, 95% CI 0–36) had a transient worsening of renal function after the procedure.

Discussion

The results demonstrate that CO₂-DSA can be safely and effectively used for guiding EVAR in patients with CKD. In each patient it was always possible to guide the EVAR procedure with CO₂-DSA, with both manual or automatic systems, without any problem related to the CO₂ administration. Only in two cases it was needed to administer ICM. In one early case, findings demonstrated with CO₂-DSA were followed by conventional ICM-angiography. Notably, the findings of conventional ICM-angiography did not provide any further information changing the therapeutic approach. In a second case, ICM was administered, as CO₂-DSA demonstrated a type III endoleak. Again, the ICM-DSA confirmed the findings of CO₂-DSA. Thus, probably with a higher experience in the use of CO₂-DSA, even a larger proportion of cases could be managed without any use of ICM.

Complications related to CO₂ administration were all regarded as minor, and limited in time and self-limited. Two patients experienced moderate pain during the procedure. Being CO₂ a gas, it tends to float above the blood flow, and may concentrate in the superior part of the blood vessels. Thus, it might cause a transient pain due to blood flow blockage into anterior vessels, such as superior and inferior mesenteric artery. Simply rotating the patient or applying a gentle pressure on the abdomen might be enough to fully restore the blood flow, and to resolve the symptoms. However, caution has to be made and at least few minutes should be waited in between one CO₂ administration and the other. One patient experienced a transient decrease in renal function. As no ICM were administered, and the patient had severe atherosclerosis of the aortic wall, this complication was thought to be related to a minimal embolization into a renal artery during the procedure.
Although the use of CO₂-DSA was first reported by Hawkins in 1982 [20], since then CO₂ has been described as a possible alternative to ICM for angiography in few reports [1, 2, 7, 20].

Different delivery systems can be used. Automatic injection implies a closed system with a fast learning curve. It is self-priming, easily adjustable and does not cause explosive delivery nor air contamination. Hand injection implies an open or semi-open system implying a moderate risk of explosive delivery and possible air contamination; moreover, gas delivery is less precise and the learning curve might be longer. Thus, if available, automatic injection systems should be preferred. On the other hand, the manual injection systems are extremely simple and cheap, and in our experience not burdened by any complication. This system could be thus considered in case an automatic system is not available. Digital subtraction is particularly helpful, due to the low CO₂ density [20].

Theoretically, unlimited amounts of CO₂ may be administered for CO₂-DSA because the gas is effectively eliminated by means of respiration, keeping in mind to allow sufficient time for its clearance (i.e., 2–3 min between subsequent injections) [10]. Using CO₂ in combination with ICM reduce the amount of ICM administered [8, 10], thus being helpful to reduce the renal damage related to ICM administration. Other advantages of CO₂ arteriography include avoidance of fluid overload, use of thinner catheters, visualization of stents and costs lower than ICM procedures.

The use of CO₂ has no absolute contraindications. A relative contraindication does exist in patients with an atrial or ventricular septal defect (CO₂ bubbles may enter the systemic circulation via the patent foramen ovale or ventricular septal defects) or a pulmonary arteriovenous malformation because of the possibility of paradoxical gas embolism. The CO₂ should be used with caution in patients with pulmonary insufficiency or pulmonary hypertension because a diagnostic dose of CO₂ may cause an increase in pulmonary arterial pressure [14]. Seizures, loss of consciousness, brief respiratory arrest, or some combination of these complications have been reported in some patients when CO₂ reached the cerebral arteries.

![Fig. 4 Endovascular abdominal aortic aneurysm repair. The patient was a 71 year-old man suffering from arterial hypertension, dyslipidemia, and stage III chronic kidney disease (plasma creatinine 2.97 mg/dl). Infrarenal abdominal aortic aneurysm was detected by ultrasound and CT scans (not shown), with evidence of an increasing size. Baseline aortography is shown in image (a), iliac arteries angiographic study in image (b), both performed with repeated boluses of CO₂. Image (c) shows the positioning of the endovascular prosthesis to exclude the aortic aneurysm. Image (d) shows the proximal sealing optimization by elastomeric balloon dilatation. Final CO₂ angiography (e, f) showed successful angiographic patency and correct position of prosthetic elements, the absence of proximal endoleak, and the presence of type III endoleak at the level of left prosthetic elements overlap (arrow). No treatment was performed; further controls demonstrated the endoleak resolution. The presence of type III endoleak at the level of left prosthetic elements overlap was demonstrated with CO₂-DSA (arrow, g) and confirmed with C-DSA after 10 ml of ICM (arrow, h).](image-url)
Therefore, arterial CO₂ injections should be not performed above the diaphragm [8, 10]. Other complications resulting from intravascular CO₂ injection may be severe, but are generally rare [10]. They often relate to an incorrect application of technique that may result in air contamination and cause serious complications (vapor lock in the pulmonary artery with consequent hypotension), or to an inadvertent injection of excessive volumes of CO₂.

Overall, CO₂-DSA is a good alternative choice to perform diagnostic or therapeutic interventional procedures in patients with contraindications to ICM, i.e. allergy or CKD. Of note, patients with AAA requiring EVAR are frequently in the elderly and have comorbidities which imply contraindications not only to surgery but also to ICM injection (CKD and allergy to ICM). The CO₂ seems to be the favorite alternative option for these patients, and EVAR procedures guided by CO₂-DSA allow to treat a larger number of patients.

This study agrees with some other previously published studies. In particular, in 2012 Criado et al. [7] published their experience of CO₂ angiography as the preferred angiographic contrast agent for EVAR in 114 consecutive patients. They concluded that CO₂-guided EVAR is technically feasible and safe, eliminating or reducing the need for ICM [7]. In 2015, Sueyoshi et al. [2] found that CO₂-DSA is reliable for the detection of endoleaks in the EVAR procedures.

In a wider framework, this work should be thought as one of the ways to be run for reducing contrast administration (and, whenever possible also X-ray radiation) to EVAR patients, a need that is absolutely important for their follow-up. One possible way in that direction is to use non-contrast MRI [22, 23].

This study has some limitations. First, the small number of patients. However, these 13 patients are the entire consecutive series treated with CO₂-DSA-guided EVAR at our center from 2010 to 2015. Second, it is a retrospective study, as it frequently happens for procedures alternative to conventional methods to be used in a small proportions of patients.

In conclusion, this study confirm that CO₂ angiography is feasible, effective and safe to guide EVAR procedure in patients with CKD, using both manual or automatic delivery systems. This approach can allow for treating patients preventing ICM-nephropathy in case of CKD.

An open issue to be investigated is the possibility to use CO₂-DSAs not only in special subgroups of patients but as a standard approach for infra-diaphragmatic interventional procedures. Thus, the majority of patients could benefit from avoidance or minimal use of ICM. This way should be explored with large randomized controlled trials. First reported results from two trials seem highly promising [3, 24]. In the current era of patient-centered medicine, more efforts should be dedicated to this approach.

References


