From the Society for Vascular Surgery

The optimal operative protocol to accomplish CO_2-EVAR resulting from a prospective interventional multicenter study

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ABSTRACT

Objectives: Carbon dioxide (CO_2) angiography for endovascular aortic repair (CO_2-EVAR) is used to treat abdominal aortic aneurysms (AAAs), especially in patients with chronic kidney disease or allergy to iodinated contrast medium (ICM). However, some technical issues regarding the visualization of the lowest renal artery (LoRA) and the best quality image through angiographies performed from pigtail or introducer sheath are still unsolved. The aim of this study was to analyze different steps of CO_2-EVAR to create an operative standardized protocol.

Methods: Patients undergoing CO_2-EVAR were prospectively enrolled in five European centers from 2019 to 2021. CO_2-EVAR was performed using an automated injector (pressure, 600 mmHg; volume, 100 cc); a small amount of ICM was injected in case of difficulty in LoRA visualization. LoRA visualization and image quality (1 = low, 2 = sufficient, 3 = good, 4 = excellent) were analyzed at different procedure steps: preoperative CO_2 angiography from pigtail and femoral introducer sheath (first step), angiographies from pigtail at 0%, 50%, and 100% of proximal main body deployment (second step), contralateral hypogastric artery (CHA) visualization with CO_2 injection from femoral introducer sheath (third step), and completion angiogram from pigtail and femoral introducer sheath (fourth step). Intraoperative and postoperative CO_2-related adverse events were also evaluated. χ^2 and Wilcoxon tests were used for statistical analysis.

Results: In the considered period, 65 patients undergoing CO_2-EVAR were enrolled (55/65 [84.5%] male; median age, 75 years [interquartile range (IQR), 11.5 years]). The median ICM injected was 17 cc (IQR, 51 cc); 19 (29.2%) of 65 procedures were performed with 0 cc ICM. Fifty-five (84.2%) of 65 patients underwent general anesthesia. In the first step, median image quality was significantly higher with CO_2 injected from femoral introducer (pigtail, 2 [IQR, 3] vs introducer, 3 [IQR, 3]; $P = .008$). In the second step, LoRA was more frequently detected at 50% (93% vs 73.2%; $P = .002$) and 100% (94.1% vs 78.4%; $P = .01$) of proximal main body deployment compared with first angiography from pigtail; similarly, image quality was significantly higher at 50% (3 [IQR, 3] vs 2 [IQR, 3]; $P \leq .001$) and 100% (4 [IQR, 3] vs 2 [IQR, 3]; $P = .001$) of proximal main body deployment. CHA was detected in 93% cases (third step). The mean image quality was significantly higher when final angiogram (fourth step) was performed from introducer (pigtail, 2.6 ± 1.1 vs introducer, 3.1 ± 0.9; $P \leq .001$). The intraoperative (7.7%) and postoperative (12.5%) adverse events (pain, vomiting, diarrhea) were all transient and clinically mild.

Conclusions: Preimplant CO_2 angiography should be performed from femoral introducer sheath. Gas flow impediment created by proximal main body deployment can improve image quality and LoRA visualization with CO_2. CHA can be satisfactorily visualized with CO_2 alone. Completion CO_2 angiogram should be performed from femoral introducer sheath. This operative protocol allows performance of CO_2-EVAR with 0 cc or minimal ICM, with a low rate of mild temporary complications. (J Vasc Surg 2023;■:1-8.)

Keywords: Abdominal aortic aneurysm; Carbon dioxide; CO_2-angiography; Endovascular aortic repair

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Acute kidney injury (AKI), as defined by the Kidney Disease Improving Global Outcomes (KIDGO),[1] can occur after standard endovascular aortic repair (EVAR) procedures in up to 20% of patients treated for abdominal aortic aneurysm (AAA) and is related with a high risk of all-cause mortality and late cardiovascular morbidity.[2-4] The most widely recognized risk factor for AKI is the delivery of iodinated contrast medium (ICM) during the procedure.[5] Therefore, it is of paramount importance to minimize the use of ICM during EVAR, particularly in patients with preoperative chronic kidney disease.

Carbon dioxide (CO_2) has been proposed as an alternative to ICM during digital subtraction angiographies, due to its own non-nephrotoxic and non-allergenic properties.[6] These satisfactory premises led to use CO_2 in EVAR procedures starting from 2007[7]; however, in the first case series published in the literature, the gas injection was performed manually with temporary intraoperative and postoperative adverse events, such as abdominal pain, nausea, vomiting, hypotension, and no chance to set and standardize injection pressures and volumes.[8-10] For this reason, in the most recent experiences with CO_2-EVAR, the injections were performed through an automatic device, with the purpose of precisely setting gas volumes and pressures and improve patients' tolerance.

Nevertheless, the currently available case series with automated CO_2-EVAR showed inconsistent standardization of the technique, which is currently still defective. In fact, some issues regarding the visualization of the lowest renal artery (LoRA) – obviously crucial for a precise endograft main body deployment – or the preferred route of CO_2 injection – either through the pigtail or the introducer sheath – are still unsolved and do not always allow to accomplish zero iodine procedures.[11,12]

The aim of this study was to analyze the steps of CO_2-EVAR procedures steps in terms of LoRA and hypogastric artery (HA) visualization as well as image quality assessment, to create an operative protocol to standardize the procedure and to assess the safety of the technique.

METHODS

This was a prospective, European, multicenter, interventional, non-randomized study. Patients undergoing standard CO_2-EVAR procedures were prospectively enrolled in different European centers between 2019 and 2021. The five European centers involved were Vascular Surgery, IRCCS, University Hospital Policlinico S. Orsola-Malpighi, Bologna (Italy), (Principal Investigator), Vascular Center, Skåne University, Hospital of Malmö (Sweden), Clinic for Vascular Surgery, St. Franziskus Hospital of Münster (Germany), Vascular Surgery, University Hospital of Münster (Germany), and Vascular Surgery, Athens Medical Group, Kifisia Athens (Greece).

ARTICLE HIGHLIGHTS

- **Type of Research:** Multicenter prospective interventional study
- **Key Findings:** Sixty-five patients treated with carbon dioxide (CO_2) angiography for endovascular aortic repair (CO_2-EVAR) for abdominal aortic aneurysm. Preimplant ($P = .008$) and postimplant ($P < .001$) aortography better image quality if CO_2 injected from introducer sheath than from pigtail. Image quality and lower renal artery detection significantly improved when CO_2 was injected at 50% and 100% of proximal main body deployment.
- **Take Home Message:** CO_2-EVAR can be successfully accomplished with preimplant and postimplant CO_2 angiographies performed from introducer sheath, and the impediment to gas flow created by proximal main body deployment can be used to improve image quality and lowest renal artery visualization.

Standard EVAR was defined as an infrarenal aorto-bi-common-iliac implant, with either suprarenal or infrarenal fixation, following the endoprosthesis manufacturer instructions for use.

The inclusion criteria were age >18 years, indication for standard endovascular treatment of AAA (diameter ≥ 5.5 cm for males and ≥ 5 cm for females), and informed consent achievement. The exclusion criteria were severe chronic obstructive pulmonary disease, known atrium-or ventricular septal defect with right-left shunt, severe renal arteries atherosclerosis, and ruptured AAA.

The study protocol and all the accompanying documentation was approved by each local ethical committee. Every patient signed a dedicated consent form to be recruited in the study. Moreover, the study was registered in ClinicalTrials.gov with the identifier NCT04721951.

Patients' data were collected and inserted in a dedicated database.

Preoperative clinical and anatomical characteristics.

All preoperative demographics and clinical characteristics of the patients were evaluated. Hypertension was defined as blood pressure ≥ 140/90 mmHg; only active smoking was considered as a preoperative risk factor; dyslipidemia was defined as blood cholesterol ≥ 240 mg/dL, diabetes mellitus was defined as ≥ 126 mg/dL at blood glucose test or patients in chronic therapy for those conditions. Anemia was defined as a hemoglobin value <13 g/dL in male and <11 g/dL in female patients. Congestive heart failure was diagnosed in case of ≥ stage C following the New York Heart Association Classification. Coronary artery disease was defined in case of history of acute coronary syndrome, angina, coronary artery bypass, or percutaneous coronary intervention. Chronic obstructive pulmonary disease was diagnosed for stage 1 or 2 following the GOLD classification (patients with stages ≥ 3 were excluded from enrollment).

Peripheral artery disease was defined as a Rutherford category ≥ 3[13] and cerebrovascular insufficiency as a history of ischemic stroke or transient ischemic attack. Preoperative renal function was assessed evaluating chronic kidney disease in hemodialytic treatment, estimated glomular filtration rate (eGFR) (mL/min) and creatininemia (mg/dL). The KDIGO classification was used to stratify the different stages of chronic kidney disease (CKD).[14] pCO_2 (mmHg) and tCO_2 (mEq/L) were also evaluated by hemogas analysis. The anesthesiologic risk was stratified using the American Society of Anesthesiology (ASA 1, 2, 3, and 4) classification.

The proximal neck of the AAA was evaluated with preoperative angio computed tomography (CT) scan in terms of diameter (mm) and length (mm). Each patient underwent preoperative thoracoabdominal angio CT scan, and a similar amount of ICM was used. The ostium of the LoRA artery was considered anterior if between 9.01 and 2.59 at clock position.

Patients preparation. To minimize air in the bowel and improve image quality of CO_2 injections, patients were prepared with a low-residue diet and activated carbon (Simethicone 80 mg, two tablets after every meal) administrated the day before the procedure whenever possible. The type of anesthesia used, whether general, spinal, or local, was also reported.

The technique and procedure steps. CO_2-EVAR was performed using the Angiodroid (San Lazzaro, Bologna, Italy) automated CO_2 injector, which was preoperatively connected to the diagnostic pigtail together with the ICM injector. After bilateral femoral puncture, an 8 or 10F short introducer sheath (11 cm long) was bilaterally inserted and a Lunderquist guidewire bilaterally advanced in the thoracic aorta. The 5F diagnostic pigtail connected to both CO_2 and ICM was positioned between the renal arteries and the superior mesenteric artery (according to the bone landmarks preoperative evaluation at CT scan) to obtain the images. All CO_2 angiographies were performed using digital subtraction angiography (DSA) with patient in apnea to improve image quality. Then, the procedure was carried on as follows:

- Step 1: Detection of LoRA and image quality assessment before endograft deployment. The first CO_2 injection (suggested volume = 100 cc; pressure = 600 mmHg) was performed from the pigtail and the second (suggested volume = 100 cc; pressure = 600 mmHg) from the 8/10 F introducer sheath to compare different image qualities. The first phase of each injection with the automated injector included a flushing of CO_2 into catheter or introducer to avoid any kind of air embolization. If the LoRA was not detected with the first two angiographies, a double-injection technique was used, one CO_2 injection (suggested volume = 50 cc; pressure = 250 mmHg) without DSA/fluoroscopy to fill the aorta with gas, followed immediately by another CO_2 injection (suggested volume = 100 cc; pressure = 600 mmHg) under DSA.
- Step 2: Detection of LoRA and image quality assessment at different steps (0%, 50%, or 100%) of proximal main body deployment, as shown in Fig, with CO_2 angiography performed from pigtail (volume = 100 cc; pressure = 600 mmHg).
- Step 3: Detection of HA contralateral to the main body delivery side to deploy the contralateral leg and image quality evaluation with CO_2 injection performed from contralateral 8/10F introducer sheath (suggested volume = 100 cc; Ppressure = 600 mmHg).
- Step 4: Completion angiogram after aorto-bi-iliac implant to assess possible endoleaks, and the number of renal and hypogastric arteries visualized. The first injection was performed from pigtail (suggested volume = 100 cc; pressure = 600 mmHg) and the second from 8/10 F introducer sheath (suggested volume = 100 cc; pressure = 600 mmHg).

The intraoperative image quality with CO_2 was judged by the operators as 1 = low, 2 = sufficient, 3 = good, and 4 = excellent.

Additional procedure details. Other procedure details were evaluated (ie, the endografts used [Cook, Gore, Medtronic, Jotec, Endologix]) depending on each center choice; the overall number of CO_2 and ICM injections and the overall volume of CO_2 and ICM (cc), as well as the number of procedures accomplished with 0 cc of ICM (0-iodine). The total radiation dose area product (DAP) in Gy/cm^2, the fluoroscopy DAP and DSA DAP were also recorded.

The intraprocedural adverse events (IntraOP AEs) possibly related to CO_2 injections were considered, such as severe hypotension (drop of systolic blood pressure >50 mmHg), pain, vomit, and diarrhea.

Postoperative outcome. Postoperative mortality was evaluated together with the presence of endoleaks at duplex ultrasound (DUS), contrast-enhanced ultrasound (CEUS), or CT scan, and the postoperative eGFR (mL/min) before discharge and creatinine (mg/dL) were compared with the preoperative values. The renal function worsening requiring postoperative hemodialysis was also reported as well as the postoperative pCO_2 (mmHg) and tCO_2 (mEq/l) at hemogas analysis.

Possible postoperative CO_2-related adverse events (PostOP AEs) were also evaluated, similarly to the intraoperative ones (hypotension [drop of systolic blood pressure >50 mmHg], pain, vomiting, and diarrhea).

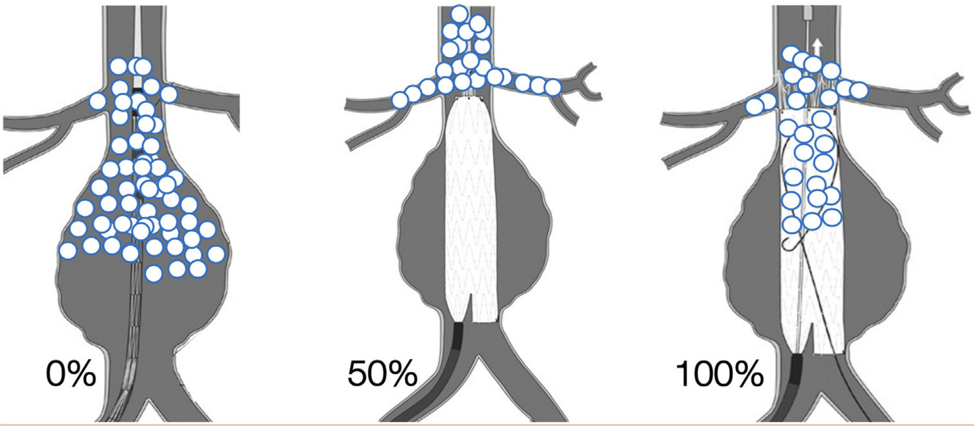

Fig. Carbon dioxide (CO_2) angiography at 0%, 50%, and 100% of proximal main body deployment.

Endoleaks detection. The endoleaks detected at final CO_2 angiogram were compared with those detected with DUS or CEUS or CT scan (performed before discharge) to verify the sensitivity of CO_2 angiographies on endoleak diagnosis.

Statistical analysis. Categorical variables were expressed with number (%); continuous variables were expressed with median and interquartile range (IQR). Statistical significance was reached for a P value $< .05$. χ^2 analysis was performed to compare categorical variables, and the Wilcoxon median test and the Student t test were used to compare continuous variables. Cox binary regression was used for multivariate analysis (95% confidence interval) for those variables with $P < .10$ at univariate analysis. The statistical analysis was performed with SPSS 25.0 for Apple (SPSS Inc, Chicago, IL).

RESULTS

In the considered period (2019-2021), 65 patients were enrolled in the study. Two patients (3.1%) were recruited by the Vascular Surgery of Athens, 22 (33.8%) by Bologna, 25 (38.5%) by Malmö, 2 (3.1%) by the St. Franziskus Hospital Münster, and 14 (21.5%) by the University Hospital Münster.

Preoperative clinical and anatomical characteristics. Patients' clinical and anatomical characteristics, such as proximal neck and LoRA ostium position, are reported in Table I.

Patients preparation. Twenty (30.8%) of 65 patients were prepared for CO_2-EVAR with low-residue diet, and 17 (26.2%) of 65 patients received activated carbon the day before the procedure. The procedure was performed under general anesthesia in 55 (84.6%) of 65 cases, spinal in nine (13.8%) of 65 cases, and local anesthesia in one (1.5%) of 65 cases.

Procedural steps analysis. Step 1 (first preimplant CO_2 injection) of the procedure showed a significantly better image quality when the angiography was performed from the femoral introducer rather than from the pigtail (median image quality: pigtail, 2 [IQR, 3] vs introducer, 3 [IQR, 3]; $P = .008$]. These data are reported in Table II.

In step 2 (CO_2 angiographies at different main body deployment phases), image quality ($P \leq .001$) and LoRA detection ($P \leq .001$) were significantly higher at 50% and 100% of proximal main body deployment compared with 0% as shown in Table III.

Furthermore, the LoRA visualization was significantly better at 50% (LoRA visualization step 1, 75.3% vs 50% MB deployment step 2, 92.3%; $P = .002$) and at 100% (LoRA visualization step 1, 75.3% vs 100% MB deployment step 2, 93.8%; $P = .01$) of proximal main body deployment compared with the first angiography from pigtail in Step 1. Similarly, the image quality was significantly higher at 50% (median image quality: first step 2 [IQR, 3] vs 50% MB deployment step 2, 3 [IQR, 3]; $P \leq .001$) and at 100% (median image quality: first step 2 [IQR, 3] vs 100% MB deployment step 2, 4 [IQR, 3]; $P = .001$) of proximal main body deployment compared with the first angiography from pigtail in step 1.

In step 3 (CO_2 injection performed from the contralateral femoral introducer sheath), the contralateral hypogastric artery was correctly visualized in 61 (93.8%) of 65 cases. The median quality image was 3 (IQR, 1).

In step 4 – CO_2 final angiogram performed from pigtail and from introducer sheath – the image quality was significantly better from the femoral introducer compared with the injection from pigtail (median image quality: pigtail, 2 [IQR, 2] vs introducer, 3 [IQR, 1]; $P \leq .001$), as reported in Table IV.

Additional procedure details. The median amount of CO_2 injected during the procedure was 990 cc (IQR, 481 cc), whereas the median ICM was 17 (IQR, 51), and the median procedural DAP was 161.3 Gy/cm^2 (IQR,

Table I. Patients' preoperative characteristics

	Total (n = 65)
Age, years	75 (11)
Male sex	55 (84.5)
Hypertension	43 (66.2)
Active smoker	15 (23.1)
Dyslipidemia	34 (52.3)
Diabetes	11 (17)
Anemia	4 (6.2)
Congestive heart failure	4 (6.2)
Coronary artery disease	23 (35.4)
Chronic obstructive pulmonary disease	11 (17)
Peripheral artery occlusive disease	8 (12.3)
Iodine allergy	4 (6.2)
Cerebrovascular insufficiency (stroke − TIA)	8 (12.3)
Preoperative creatinine, mg/dL	1.05 (0.5)
Preoperative eGFR, mL/min	65 (30)
Stage 1 CKD (eGFR ≥ 90 mL/min)	6 (9.2)
Stage 2 CKD (eGFR = 60-89 mL/min)	33 (50.8)
Stage 3 CKD (eGFR = 30-59 mL/min)	24 (37)
Stage 4 CKD (eGFR = 15-29 mL/min)	2 (3)
Stage 5 CKD - hemodialysis	0
Preoperative pCO_2, mmHg	31 (7)
Preoperative tCO_2, mEq/L	27 (5)
ASA score	3 (1)
Aortic diameter at the renal ostia, mm	22 (4)
Proximal neck length, mm	25 (10)
Anterior LoRA (9.01-2.59 clock position)	30 (46.2)

ASA, American Society of Anesthesiologists; *CKD*, chronic kidney disease; *eGFR*, estimated glomular filtration rate; *LORA*, lowest renal artery; *pCO_2*, pressure of carbon dioxide; *tCO_2*, total carbon dioxide; *TIA*, transient ischemic attack.
Data are presented as number (%) or median (interquartile range).

384.7 Gy/cm^2), as shown in Supplementary Table I (online only). Intraoperative CO_2-related adverse events occurred in five (7.7%) of 65 patients; however, if calculated on the number of patients (n = 10) who received spinal/local anesthesia, the rate is much higher (50%; 5/10). One patient had only a transient abdominal pain possibly due to CO_2 injection, two patients experienced abdominal pain and vomiting, and two patients reported nausea and vomiting. All these CO_2-related events had no intraoperative or postoperative consequences on patients. There were no inadvertent coverages of renal or hypogastric arteries.

Table II. Step 1 (first preimplant carbon dioxide [CO_2] injection): comparison between pigtail and introducer injections

	Pigtail injection	Introducer injection	*P* value
Injection pressure, mmHg	600 (150)	600 (150)	.31
Injection volume, cc	100 (1)	100 (1)	.31
LoRA detection	49 (75.3)	47 (72.3)	.47
Image quality	2 (3)	3 (3)	.008[a]

LoRA, Lowest renal artery.
Data are presented as number (%) or median (interquartile range).
[a] $P < .05$.

Postoperative outcome. Postoperative mortality rate was 0% with 0 mg/dL (IQR, 0.08 mg/dL) of median creatinine increase and 0 mL/min (IQR, 6.5 mL/min) of median eGFR decrease. There were eight (12.3%) of 65 cases of postoperative CO_2 possibly related adverse events. Three patients had pain, three had vomiting, and three had diarrhea by the first 24 hours after surgery. There were no other consequences of these symptoms, which were all temporary (resolved within 24 hours) during the hospitalization. All postoperative data are reported in Supplementary Table II (online only).

Endoleak detection. The analysis of different endoleaks was performed comparing completion CO_2 injections (step 4) from pigtail and introducer with DUS, CEUS, or CT scan performed before discharge.

All types of endoleaks (endoleak: final pigtail angiogram, 18 [27.7%] of 65 vs postoperative, 10 [15.4%]; $P = .04$), and in particular, type II endoleaks (type II endoleak: final pigtail angiogram, 15 [23%] vs postoperative, 7 [10.8%]; $P = .04$) were detected significantly more often with completion CO_2 injected from pigtail compared with the pre-discharge imaging DUS/CEUS/CT scan.

Safety assessment. All possible preoperative and procedural risk factors related to the occurrence of intraoperative CO_2 adverse events at univariate analysis were analyzed. The only significant predictor was the use of spinal/local anesthesia (spinal/local anesthesia: no IntraOP AE, 5 [8.3%] vs IntraOP AE, 5 (100%); $P \leq .001$). The multivariate analysis was not performed due to the small number of events (n = 5).

At univariate analysis, the only significant risk factor for postoperative CO_2-related adverse events occurrence was diabetes mellitus (diabetes mellitus: no PostOP AE, 4 [12.3%] vs PostOP AE, 4 [50%]; $P = .02$). At multivariate analysis, diabetes mellitus was confirmed as an independent risk factor for postoperative adverse events (6 [IQR, 0.9-37.7], $P = .04$); the CO_2 volume was a protective for postoperative adverse events occurrence (1.20 [IQR, 1-1.55]; $P = .02$).

Table III. Step 2: comparison between injections at 0%, 50%, and 100% of proximal main body deployment

	0% MB deployment	50% MB deployment	Tot MB deployment	*P* value
Injection pressure, mmHg	600 (150)	600 (150)	600 (150)	1
Injection volume, cc	100 (1)	100 (20)	100 (1)	1
LoRA detection	78.4%	92.3%	93.8%	<.001[a]
Image quality	3 (3)	3 (3)	4 (3)	<.001[a]

LoRA, Lowest renal artery; *MB*, main body.
Data are presented as number (%) or median (interquartile range).
[a] *P*<.05.

Finally, a comparison between pCO_2 and tCO_2 before and after the procedure was performed to assess the possible consequences of CO_2 injections on hemogasanalysis. The median preoperative and postoperative pCO_2 were not statistically different (median preoperative pCO_2 40 mmHg [IQR, 8 mmHg] vs postoperative pCO_2, 40 mmHg [IQR, 5 mmHg]; $P = .41$), as well as the tCO_2 (median preoperative tCO_2, 27.2 mEq/L [IQR, 4.6 mEq/L] vs postoperative tCO_2, 26.1 mEq/L [IQR, 4 mEq/L]; $P = .6$).

0-Iodine procedure analysis. Nineteen (29.2%) of 65 of procedures were performed with 0-iodine at all, as reported in Supplementary Table I (online only). At univariate analysis, the possible risk factors related to the possibility to achieve a 0-iodine procedure were LoRA detection with the preimplant angiography from pigtail in step 1 (LoRA detection first step pigtail: no-0-iodine EVAR, 30 [66.7%] vs 0-iodine EVAR, 18 [94.7%]; $P = .02$), LoRA detection with the preimplant angiography from introducer in step 1 (LoRA detection first step introducer: no-0-iodine EVAR, 23 [59%] vs 0-iodine EVAR, 19 [100%]; $P = .001$) and its image quality (median image quality first step introducer: no-0-iodine EVAR, 3 [IQR, 2] vs 0-iodine EVAR, 4 [IQR, 1]; $P = .03$). At multivariate analysis, though, there were no independent predictors of 0-iodine CO_2-EVAR procedure.

DISCUSSION

The present study represents the first European multicenter experience with CO_2-EVAR procedures. The population group of 65 patients submitted to CO_2-EVAR compares well with the most numerous experiences in the literature.[8,9,12,15]

We have divided the analysis in different steps to precisely evaluate the performance of CO_2 injections. In step 1 analysis, the LoRA, which is obviously crucial for a precise main body deployment, was similarly detected independently from the route of CO_2 injection (ie from pigtail and femoral introducer); however, the latter provided better images (median image quality: pigtail, 2 [IQR, 3] vs introducer, 3 [IQR, 3]; $P = .008$]. This is possibly due to the order of injections, with the one from the introducer being performed after the one from the pigtail, thus improving the image quality through the presence of a residual amount of gas in the aortoiliac axis; however no similar analysis is available in the literature. Moreover, the introducer sheath is a single lumen catheter, and the pigtail is multiple side hole; therefore, the gas is probably dispersed more with the pigtail due to the different holes compared with the introducer, which allows a straighter gas delivery.

Table IV. Step 4 (final angiogram): comparison between pigtail and introducer injections

	Pigtail injection	Introducer injection	*P* value
Injection pressure, mmHg	600 (150)	600 (150)	.31
Injection volume, cc	100 (0)	100 (0)	.31
Renal arteries detected	2 (1)	2 (1)	.13
Hypogastric arteries detected	2 (0)	2 (0)	.31
Image quality (1-4)	2 (2)	3 (1)	<.001[a]
Endoleak detection	18 (27.7)	17 (26.2)	.32

Data are presented as number (%) or mean ± standard deviation.
[a] *P*<.05.

In step 2, there were significantly better results in terms of LoRA visualization and image quality during the 50% and 100% of proximal main body deployment compared with the first CO_2 angiogram and with the 0% of proximal main body deployment. These data confirm the initial hypothesis about carbon dioxide distribution during the procedure; if the main body of the endograft is in the infrarenal aorta, it impedes the flow of the gas to the lower limb during the angiographies from pigtail and facilitates the flow to the renal arteries. This impediment at 50% of proximal main body deployment is due to incomplete opening of the tubular graft, whereas at 100% is probably due to incomplete opening of the ipsilateral leg; both mechanisms contribute to reduce gas dispersion in the sac and consequently to improve renal arteries enhancement with CO_2. This aspect has not been investigated before.

In step 3, the visualization of the contralateral hypogastric artery was 93% with a median good image quality. In our previous experiences,[11,12] the contralateral hypogastric artery was visualized in all cases without any

Table V. Standard protocol for carbon dioxide (*CO_2*) angiography for endovascular aortic repair (EVAR)

Step 1	CO_2 aortography from femoral introducer sheath before main body endograft insertion, to check the LoRA correct position	Injection parameters: Volume, 100 cc Pressure, 600 mmHg
Step 2	Insertion and deployment of the main body. CO_2 aortographies to be performed from pigtail, when the proximal main body is deployed at 50% and 100%, to double-check the LoRA position	Injection parameters: Volume, 100 cc Pressure, 600 mmHg
Step 3	CO_2 injection from contralateral femoral introducer to detect CHA and consequently deploy the contralateral leg	Injection parameters: Volume, 100 cc Pressure, 600 mmHg
Step 4	Once aorto-bi-iliac implant completed, final CO_2 angiogram from femoral introducer. Optional: extra CO_2 angiogram from pigtail (more sensitive for endoleak detection)	Injection parameters: Volume, 100 cc Pressure, 600 mmHg

CHA, Contralateral hypogastric artery; *LoRA*, lowest renal artery.
General anesthesia is recommended to reduce intraoperative gastrointestinal side effects. All CO_2 injections should be performed in DSA modality with patient in apnea

necessity of ICM injections; the present results confirm this finding.

In step 4, the completion CO_2 angiogram provided better images when the injection was performed from the femoral introducer sheath. Again, this result could be misread, because the CO_2 from the introducer was injected after the pigtail injection; the gas still present in the aorta could possibly improve image quality.

Beside these technical findings, the most relevant result of our study is that CO_2-EVAR procedures can be completed with a very minimal amount of iodine injection (median, 17 cc [IQR, 51 cc]), similarly to the case series of Fujihara et al[9] and significantly lower compared with our previous experience.[12]

The postoperative outcome in terms of mortality (0%) and renal function (0 mg/dL [IQR, 0.08 mg/dL] of median creatinine increase and 0 mL/min [IQR, 6.5 mL/min] of median eGFR decrease) was excellent. As reported before by Fujihara et al[9] and our group,[12] CO_2-EVAR with restrictive use of iodine can guarantee an almost zero impact on patients' renal function. Consequently, it could be used in all patients and particularly in those with CKD, but still should be further investigated in similar studies with larger populations.

Moreover, the endoleak analysis showed that the final CO_2 angiogram has a high sensitivity for endoleaks (endoleak: final pigtail angiogram, 18/65 (27.7%) vs postoperative, 10 [15.4%]; $P = .04$) and particularly type II endoleaks (type II endoleak: final pigtail angiogram, 15 [23%] vs postoperative, 7 [10.8%]; $P = .04$). Mascoli et al[16] reported similar results with three type II endoleaks detected by CO_2 and not by CEUS; differently, Huang et al[15] showed that ICM is superior to CO_2-DSA in detecting endoleaks, with an acceptable sensitivity for detecting any endoleak and sensitivity and specificity for detecting type I endoleaks using CO_2-DSA. Undoubtedly, intraoperative angiogram, DUS, CEUS, and CT scan are all different endoleak detection methods. In addition, it is important to underline that many type II endoleaks visualized during the procedure tend to spontaneously thrombose before the pre-discharge imaging. Therefore, these results should be corroborated with more specific and dedicated clinical studies.

The rates of intraoperative and postoperative CO_2-related adverse events were 7.7% and 12.3%, respectively, in the overall population; the rate of intraoperative CO_2-related adverse events, though, should be counted on patients who received spinal/local anesthesia (10 patients), and from this perspective, this rate is 50% (5/10 patients). These complications were all mild — abdominal pain, vomiting, and diarrhea — and transient with no consequences for patients; their limited clinical significance is probably related to the automated injections, which significantly reduces any air contamination and counterbalances the high pressure and volume of CO_2 delivered. As reported by Fujihara et al[9] and De Angelis et al,[10] who had similar events, CO_2 might cause a transient pain due to blood flow blockage into anterior vessels, such as the superior and inferior mesenteric arteries. However, in our analysis, the volume of CO_2 injected was not a risk factor for the occurrence of intraoperative gastrointestinal adverse events at univariate analysis; the preset volume of CO_2 (100 cc for each injection), in fact, was the one suggested by the injector company (Angiodroid, San Lazzaro, Bologna, Italy) for the abdominal aorta. The only significant predictor for intraoperative adverse events was a spinal/local anesthesia ($P \leq .001$); the problem could therefore be solved using general anesthesia as much as possible to reduce patients' discomfort.

Diabetes mellitus was confirmed as an independent risk factor for postoperative adverse events (n = 6 [IQR, 0.9-37.7]; $P = .04$). This aspect has never been reported before, but indeed, diabetic patients are more prone to have gastrointestinal symptoms such as nausea, diarrhea, and abdominal pain compared with the overall population[17]; as a possible explanation, it should be noted that these symptoms are sometimes triggered by CO_2 injection. Moreover, the CO_2 volume was surprisingly protective for postoperative adverse events occurrence (0.99 [IQR, 0.98-1]; $P = .03$); this aspect has not been investigated in the literature, but it strengthens the concept that high volumes of CO_2 injected in the aorta are safe for the patients using the automated CO_2 injector.

Finally, the 0-iodine analysis did not identify any independent predictor of feasibility of no-contrast EVAR; at univariate analysis, the detection of the LoRA in the first step by CO_2 a high image quality were all significantly related to the achievement of 0-iodine procedure. These aspects underline the importance of this CO_2-EVAR protocol.

The standard CO_2-EVAR procedure protocol with automated injector could be summarized in Table V following the results.

The study has several limitations. The population of 65 patients is relatively small, thus reducing the statistical power of the results. The image quality was evaluated by different operators, different equipment, and different imaging presets with no unique standard of measure; the subjectivity in images' evaluation is therefore a major limitation of the study. The visualization of the ipsilateral internal iliac artery was not specifically studied in the protocol. The gas injection parameters were suggested by the Angiodroid company, but not corroborated by dedicated clinical trials.

CONCLUSION

This experience allowed us to define a CO_2-EVAR operative protocol, in which the best image quality at pre- and postimplant aortography was obtained when the gas was injected from femoral introducer sheath; the proximal main body deployment creates an impediment to gas flow, which improves the image quality and the detection of LoRA with CO_2-angiography performed from pigtail.

This protocol enabled all involved centers to accomplish EVAR procedures using 0 or minimal iodine injections; however, the present results should be strengthened by other studies with larger populations. The CO_2 automated injector guaranteed patients' safety, in terms of intraoperative and postoperative complications, which were all transient and clinically mild.

AUTHOR CONTRIBUTIONS

Conception and design: AV
Analysis and interpretation: AV, GF
Data collection: AV, RV, ND, MA, MU, AO, JS, TB, NP, SP, MG
Writing the article: AV
Critical revision of the article: GF, RV, ND, MA, MU, AO, JS, TB, NP, SP, MG
Final approval of the article: AV, GF, RV, ND, MA, MU, AO, JS, TB, NP, SP, MG
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Additional material for this article may be found online at www.jvascsurg.org.

Supplementary Table I (online only). Procedure details

	Total (n = 65)
Endograft manufacturer	
Cook	32 (49.2)
Gore	16 (24.6)
Medtronic	12 (18.5)
Endologix	3 (4.6)
Jotec	2 (3)
CO_2 injections	9 (4)
Volume of CO_2 injected	990 (481)
ICM injections	1 (3)
Volume of ICM injected	17 (51)
0-iodine EVAR	19 (29.2)
Fluoroscopy radiation dose DAP, Gy/cm^2	29.7 (103.5)
DSA radiation dose DAP, Gy/cm^2	160.9 (322.4)
Total radiation dose DAP, Gy/cm^2	161.3 (384.7)
Intraoperative severe hypotension	0
Intraoperative abdominal pain	3 (4.6)
Intraoperative vomiting	4 (6.2)
Intraoperative diarrhea	0
Intraoperative adverse events	5 (7.7)

CO_2, Carbon dioxide; *DAP*, dose area product; *DSA*, digital subtraction angiography; *EVAR*, endovascular aneurysm repair; *ICM*, iodinated contrast medium.
Data are presented as number (%) or median (interquartile range).

Supplementary Table II (online only). Postoperative outcome

	Total (n = 65)
Death	0
Endoleak at DUS/CEUS/CT scan	10 (15.4)
Postoperative creatinine, mg/dL	1.02 (0.5)
Postoperative eGFR, mL/min	66 (32.5)
Creatinine increase, mg/dL	0 (.08)
eGFR decrease, mL/min	0 (6.5)
Renal function worsening requiring hemodialysis	0
Median postoperative pCO_2	41 (7)
Median postoperative tCO_2	26 (4)
Postoperative severe hypotension	0
Postoperative abdominal pain	3 (4.6)
Postoperative vomiting	3 (4.6)
Postoperative diarrhea	2 (3.1)
Postoperative adverse events	8 (12.3)

CEUS, Contrast-enhanced ultrasound; *CT*, computed tomography; *DUS*, duplex ultrasound; *eGFR*, Estimated glomular filtration rate; *pCO_2*, pressure of carbon dioxide; *tCO_2*, total carbon dioxide.