Clinical Investigation

JOURNAL OF ENDOVASCULAR THERAPY
A SAGE Publication
An official publication of the ISEVS

Journal of Endovascular Therapy
1–11

DOI: 10.1177/15266028261440717
www.jevt.org
Mary Ann Liebert
A Part of Sage

Inter-Center Radiation Variability in CO_2-Guided EVAR: Lessons From the Zero Iodine Contrast Multicenter Prospective Study

Emiliano Chisci, MD[1], Emanuele Ferrero, MD[2], Michele Antonello, MD[3], Luca Mezzetto, MD[4], Raffaele Pulli, MD[5], Gioele Simonte, MD[6], Mauro Gargiulo, MD[7], Giovanni Pratesi, MD[8], Luca Bertoglio, MD[9], and Tommaso Lazzarotto, MD[1]; on behalf of The Zero Iodine Contrast Evar Collaborative Study Group*

Abstract

Introduction: Current diagnostic reference levels (DRLs) for endovascular aortic repair (EVAR), based on iodinated contrast media (ICM) protocols, range from 100 to 200 Gy·cm^2. As CO_2 is a negative contrast agent requiring digital subtraction angiography (DSA) for visualization, it may be associated with increased radiation exposure. This multicenter study presents the largest prospective data set to date evaluating radiation dose during EVAR using CO_2 angiography alone with an automated injector. **Methods:** A prospective, multicenter, nationwide, nonrandomized, investigator-initiated observational study of dosimetry recorded during EVAR procedures with CO_2 as exclusive contrast medium was conducted. Primary endpoints included dose-area product (DAP) and reference air kerma (K_{ar}) measurements across all participating centers. Secondary objectives focused on evaluating optimization strategies to reduce radiation exposure for both patients and operators at a single investigational site. **Results:** A total of 293 patients were enrolled across 10 centers, between January 2023 and January 2024, median DAP and K_{ar} were 189 Gy·cm^2 (interquartile range [IQR] 107-285) and 626.5 mGy (IQR 145.5-1373.5), respectively, with significant inter-center variability (all $p<0.001$). Newer angiographic systems demonstrated markedly lower DAP (median: 90 Gy·cm^2, IQR 71-153) vs older systems (191 Gy·cm^2, IQR 111-409; $p<0.001$). Through sequential optimization, we achieved progressive dose reductions: 38.5% via low-dose protocols, 52.3% with modern equipment, culminating in a 56% overall reduction ($p<0.001$) with synchronized CO_2-DSA—yielding a final median DAP of 28.5 Gy·cm^2. **Conclusions:** CO_2-guided EVAR exhibits substantial radiation dose variability, driven by angiographic system generation, software, and synchronization protocols. Modern systems with optimized low-dose protocols and CO_2-DSA synchronization reduce radiation exposure to levels comparable to ICM-based EVAR.

Clinical Impact

This large multicenter prospective study establishes a reliable radiation dose benchmarks for CO_2-guided endovascular aortic repair (EVAR), showing that modern angiographic systems with optimized low-dose protocols and synchronized CO_2-digital subtraction angiography achieve median dose-area product values comparable with conventional iodinated contrast media EVAR, thereby dispelling concerns about excessive radiation exposure with CO_2-guided EVAR.

Keywords

EVAR, CO_2 angiography, multicentre, prospective, radiation, dosimetry

Introduction

Endovascular aortic repair (EVAR) is a well-established treatment for abdominal aortic aneurysm (AAA).[1] Current diagnostic reference levels (DRLs) for EVAR (dose-area product; DAP values range 100-200 Gy·cm^2 in Europe)[2–11] and radiation safety guidelines—including the 2023 European Society for Vascular Surgery updates[12,13]—are based solely on iodinated contrast media (ICM) protocols.

This oversight is critical, as lifelong surveillance exposes EVAR patients to cumulative radiation risks,[14] necessitating dose-reduction strategies at all care stages. Younger patients face heightened risks due to increased radiosensitivity and longer life expectancy.[15] CO_2 is a negative contrast agent with inherently low radiopacity compared with ICM, rendering it undetectable under conventional fluoroscopy. Its visualization requires digital subtraction angiography (DSA), which typically involves higher frame rates and longer exposure times than standard fluoroscopy. Consequently, CO_2 angiography may be associated with increased radiation exposure compared to conventional ICM angiography, due to the technical requirements necessary to obtain diagnostic image quality.[16–18] Despite increasing adoption, data on CO_2-guided EVAR dosimetry remain limited and inconsistent, with studies identifying elevated radiation exposure as a major challenge. Reported DAP values range from 161 to 925 Gy·cm^2.[19–23]—significantly exceeding recommended ICM-EVAR ranges.[2–11,24]

This study analyzes radiation data from a prospective multicenter zero iodine contrast EVAR study,[25] where EVAR was performed exclusively with CO_2 angiography. A secondary aim was to identify best practices for minimizing radiation exposure in CO_2-EVAR for both patients and operators.

Materials and Methods

Study Design

This was a prospective, multicenter, nationwide, nonrandomized, investigator-initiated observational study of dosimetry recorded during EVAR procedures with CO_2 as exclusive contrast medium. An automatic CO_2 injector (Angiodroid SpA, San Lazzaro di Savena, Italy) was used for standardized imaging. All participating centers had at least 2 years of experience with CO_2 angiography and had performed a minimum of 30 EVAR procedures using this technique prior to study inclusion. Structured proctoring and dedicated training workshops were implemented to promote protocol standardization and to minimize inter-center variability, ensuring consistent application of the CO_2 angiography technique across all sites. With the purpose to protect both the patient and the operator, all operators were trained in ALARA principles[26] with a focus on constantly minimizing fluoroscopy time, narrowing X-ray exposure area by maximizing collimation, adequate positioning of anti-radiation shields, and reducing radiation in extreme angulations as much as possible. In addition, fusion imaging technology was routinely employed during EVAR procedures and had been standard practice in all centers prior to the study, ensuring consistent use throughout the trial. The inclusion and exclusion criteria of the trial have been already published.[22] The brand and model of angiography equipment used, the type of dosimetry protocol employed, and whether the protocol accounted for patient body mass index (BMI) were recorded. Devices were classified as old (installed $\geq$5 years ago) or new ($<$5 years ago): old devices included the Siemens Artis Zee, Philips Allura FD20, Allura Clarity IQ FD20, and Ziehm RDF 3D, while new devices comprised the Philips Azurion 7 M20 Clarity IQ, Siemens Artis Pheno, Artis ZeeGO, and General Electric IGS 740. In newer-generation angiographic systems, acquisition parameters were optimized to reduce

[1]Department of Surgery, Vascular and Endovascular Surgery Unit, USL Toscana Centro, "San Giovanni di Dio" Hospital, Florence, Italy
[2]Vascular and Endovascular Surgery Unit, Mauriziano Umberto I Hospital, Turin, Italy
[3]Division of Vascular and Endovascular Surgery, Department of Cardiac, Thoracic Vascular Sciences and Public Health, School of Medicine, University of Padua, Padua, Italy
[4]Department of Vascular Surgery, University and Hospital Trust of Verona, University of Verona – School of Medicine, Verona, Italy
[5]Section of Vascular Surgery, Department of Excellence of Experimental and Clinical Medicine, University of Florence, Florence, Italy
[6]Unit of Vascular and Endovascular Surgery, Santa Maria della Misericordia Hospital, Perugia, Italy
[7]Vascular Surgery, University of Bologna – DIMEC, Bologna, Italy
[8]Clinic of Vascular and Vascular Surgery, IRCCS Ospedale Policlinico San Martino, University of Genoa, Genoa, Italy
[9]Division of Vascular Surgery, Department of Experimental and Clinical Sciences, University of Brescia School of Medicine, Spedali Civili di Brescia, Brescia, Italy
[10]Vascular Surgery Unit, IRCCS University Hospital Policlinico S. Orsola, Bologna, Italy
[11]Vascular and Endovascular Surgery – Department of Emergency and Organs Transplantation, "Aldo Moro" University of Bari School of Medicine, Bari, Italy

*__THE ZERO IODINE CONTRAST EVAR COLLABORATIVE STUDY GROUP:__ Emiliano Chisci, MD,[1] Emanuele Ferrero, MD,[2] Michele Antonello, MD,[3] Luca Mezzetto, MD,[4] Raffaele Pulli, MD,[5] Gioele Simonte, MD,[6] Mauro Gargiulo, MD,[7] Giovanni Pratesi, MD,[8] Luca Bertoglio, MD,[9] Tommaso Lazzarotto, MD,[1] Simone Panci, RT,[1] Azzurra Guidotti, MD,[1] Cecilia Fenelli, MD,[1] Sara Simongini, MD,[1] Lorenza Chiera, MD,[2] Michelangelo Ferri, MD,[2] Andrea Gaggiano, MD,[2] Simona Marrocco, MD,[3] Elda Chiara Colacchio, MD,[3] Michele Piazza, MD,[3] Franco Grego, MD,[3] Lorenzo Grosso, MD,[4] Gian Franco Veraldi, MD,[4] Sara Speziali, MD,[5] Roberto Falso, MD,[5] Giacomo Isernia, MD,[6] Gianbattista Parlani, MD,[6] Massimo Lenti, MD,[6] Enrico Gallitto, MD,[7] Chiara Mascoli, MD,[10] Caterina Melani, MD,[8] Sergio Zacà, MD,[11] Lucia Di Stefano, MD,[11] Domenico Angiletta, MD,[11] Stefano Bonardelli, MD,[9] Apollonia Verrengia, MD,[9] and Stefano Michelagnoli, MD[1].

Corresponding Author:
Emiliano Chisci, Department of Surgery, Vascular and Endovascular Surgery Unit, USL Toscana Centro, "San Giovanni di Dio" Hospital, Via Torregalli, 3, Florence 50124, Italy.
Email: e.chisci@gmail.com

radiation exposure. The frame rate ranged from 2 to 4 frames per second, compared with 4 to 6 frames per second in older systems. Furthermore, the detector dose per frame was reduced relative to earlier angiographic platforms. Detailed angiographic parameters for the new and old devices are reported in Supplemental Table 1. Each center applied its own standardized acquisition protocol. Local Ethics Committees (Approval No. 23085, December 30, 2022) approved the study and patients provided informed consent before the procedure and during follow-up. Inclusion in the computerized database required patient consent.

Dosimetric Data

The collected dosimetric data to estimate DRLs were:[27]

Fluoroscopy time (FT): It is often used as a first approximation as an indicator of the complexity of the procedure or the experience of the operator; taken alone, it cannot be used as a descriptor of patient dose.

Kerma (kinetic energy released per unit mass) product in air-area (KAP): It is expressed in Gy·cm^2, mGy·cm^2, cGy·cm^2 or μGy·cm^2, indicated in this study as DAP. It is an important indicator of the dose to the patient as it is correlated with the stochastic effects of radiation. In this study, the unit of measure reported was Gy·cm^2.

Reference air kerma (K_{ar}) or cumulative air kerma, at the interventional reference point (IRP): It is expressed in mGy, it is used to monitor the dose to the patient in real time as it provides an indication of the possible maximum skin dose. The IRP is placed on the axis of the X-ray beam 15 cm from the isocenter of the C-arm toward the X-ray tube. This quantity is also commonly used to define the alert levels (trigger levels) useful for warning the operator that the procedure is imparting skin dose values to the patient above the thresholds for radiation skin damage.

Operative Technique and Carbon Dioxide Protocol

All procedures were performed in an angio suite or hybrid room equipped with a C-arm according to a standardized protocol which included 3 main CO_2 angiographies. The first angiography represents the iliac field (hypogastric bifurcation of both sides, iliac bifurcation) and is performed by connecting the Angiodroid system to the 11 F (11 cm) femoral introducer sheath where the main body of the graft was to be deployed. The second angiography represents the renal field and is performed by connecting the Angiodroid to a long contralateral sheath $>$ 6F (45-55 cm) close to L1 to L2 vertebrae.

Fusion of preoperative computed tomography (CT) images with live fluoroscopy was used to provide an overlay or smartmask to facilitate endovascular navigation.

Radiographers were also able to optimize the image obtained through post-processing software, including the use of re-masking and stacking software, and the creation of a reference imaging overlay or drawing markers for the target vessels like the lowest renal artery or hypogastric artery to safely deliver the graft or limbs without the need for additional angiography, provided that the target vessels are clearly visualized.

At the end of the procedure, the third and final angiogram was performed through 1 of the 11 F femoral sheaths. This angiogram was aimed at evaluating graft, iliac, and renal patency, and the absence of high flow endoleaks. Each of 3 major angiographies was performed with a CO_2 volume of 100 mL and a pressure of 650 mmHg in all 10 centers. To avoid gas fragmentation, the catheter was flushed each time it was connected to a sheath, and an interval of 120 seconds was observed between 2 injections to avoid excessive CO_2 administration into the aorta, which could cause possible complications (abdominal pain, nausea, and vapor lock). The zero iodine contrast EVAR study recommends using 5 consecutive steps in case of difficulty in visualizing the target vessels, as already published.[25] All patients were placed on a specialized low-residue diet for 7 days preoperatively to minimize intestinal gas formation (see Supplemental Table 2).

Best Practice Evaluation

One of the participating centers introduced some structured protocol modifications to minimize radiation exposure, with the goal of identifying optimal practices for dose optimization. The angiographic system was upgraded during the study period, enabling intra-trial comparison of old vs new devices under consistent EVAR protocols with unchanged operating personnel. In the initial phase of the study, this center used a ceiling-mounted angiography system (Artis Zee dTA, Siemens) for both stationary and fluoroscopic acquisitions. First group (group A) included patients treated with the Artis Zee dTA (Siemens) and a standard CO_2 protocol, while second group (group B) comprised patients treated with the same angiographic system but under a low-dose CO_2 protocol. Later, the center transitioned to a new hybrid room (Azurion7 M20 with Clarity, Philips). The patients of this last group (group C) were then treated with a standard CO_2 protocol but with an updated new angiographic system. In addition, a synchronization system was introduced. The synchronization mechanism utilized a direct cable connection between the angiographic system and the automated CO_2 injector, ensuring precise coordination between DSA and CO_2 delivery. After testing, the delay between X-ray emission and CO_2 injection was fixed at 2.5 seconds. Supplemental Table 3 summarizes the technical characteristics of the dosimetric protocols over time, comparing the 2 angiographic systems and protocol settings at this center.

Endpoints

Procedural technical success was defined as the ability to deploy the endoprosthesis without the use of ICM, ensuring the patency of the endoprosthesis, and the renal and visceral vessels, in the absence of surgical conversion or mortality, and type I or III endoleaks. The primary objective was to determine the median kerma-area product (KAP) and air kerma values across all participating centers. A secondary objective was to establish best practices for optimizing radiation exposure for both patients and operators when using CO_2 angiography. Image quality assessment—defined by adequate contrast and spatial resolution—was evaluated post-procedure using operator-completed questionnaires with 6 key criteria (see Supplemental Table 4). This protocol was implemented at the center designated for best practice investigation. Image quality assessment was self-reported by the operating physician immediately after image acquisition. Any additional angiographic runs, when required, were performed in accordance with the standardized protocol.[25] The image quality score ranged from 6 to 30, with scores >28 defined as clinically appropriate. Cases scoring ≤ 28 underwent structured review to identify contributing factors, focusing on performance comparisons between upgraded and old C-arm system, variations in imaging protocols, and efficacy of CO_2 injection synchronized with DSA.

Statistical Analysis

Patient data were collected using the ARGOS-Dedalus Digital Medical Record System (Florence, Italy). Normality and homogeneity of variance were assessed using the Kolmogorov-Smirnov and Levene's tests, respectively. Continuous data are presented as mean $\pm$ standard deviation (SD) or median (interquartile range [IQR]), while categorical variables are reported as absolute frequencies and percentages (%). Non-normally distributed data were analyzed using the Kruskal-Wallis test, with post hoc pairwise comparisons performed using the Dunn-Bonferroni test to identify significant differences between groups in the center where best practices were examined. Monotonic relationships between fluoroscopy time, BMI, and dosimetric values (DAP and K_{ar}) were evaluated using Spearman's rank correlation coefficient (ρ). A 2-tailed p-value <0.05 was considered statistically significant. All analyses were conducted using SPSS (version 24.0; SPSS Inc., Chicago, Illinois)

Results

A total of 293 patients were enrolled across 10 centers, between January 2023 and January 2024 with a median age of 78 years (IQR 72-83), of whom 256 (87%) were male. Technical success was achieved in 99.7% of cases (1 limb occlusion). The overall median procedure time, fluoroscopy time, and injected CO_2 volume were 90 minutes (IQR 65-125), 15 minutes (IQR 10-22), and 600 mL (IQR 400-800), respectively. Dosimetric data showed a non-parametric distribution. Across all centers, the median DAP and K_{ar} for the entire cohort were 189 Gy·cm^2 (IQR 107-285) and 626.5 mGy (IQR 145.5-1373.5), respectively. Table 1 summarizes the dosimetric data stratified by center and angiograph system type. A comparison between older and newer angiograph systems revealed significantly lower DAP values for newer systems (median: 90 Gy·cm^2, IQR 71-153) compared with older systems (median: 191 Gy·cm^2, IQR 111-409; $p<0.001$). Figure 1 illustrates the median, IQR, and range of DAP values across centers, with significant inter-center variability ($p\leq 0.001$). Similarly, Figure 2 depicts the median, IQR, and range of K_{ar} per center, showing a statistically significant difference ($p<0.0001$). No significant correlations were observed between radiation metrics and procedural factors: neither DAP (fluoroscopy time: $\rho=0.52$, $p=0.13$; BMI: $\rho=0.28$, $p=0.43$) nor K_{ar} (fluoroscopy time: $\rho=0.60$, $p=0.07$; BMI: $\rho=0.07$, $p=0.84$) demonstrated statistically significant associations. Furthermore, patients with multiple comorbidities—particularly those with impaired renal function or reduced ejection fraction—did not require modifications of the procedural workflow, additional radiation time, or increased radiation exposure. Dosimetric parameters remained comparable across these subgroups.

Results of Best Practice Implementation in a Single Center

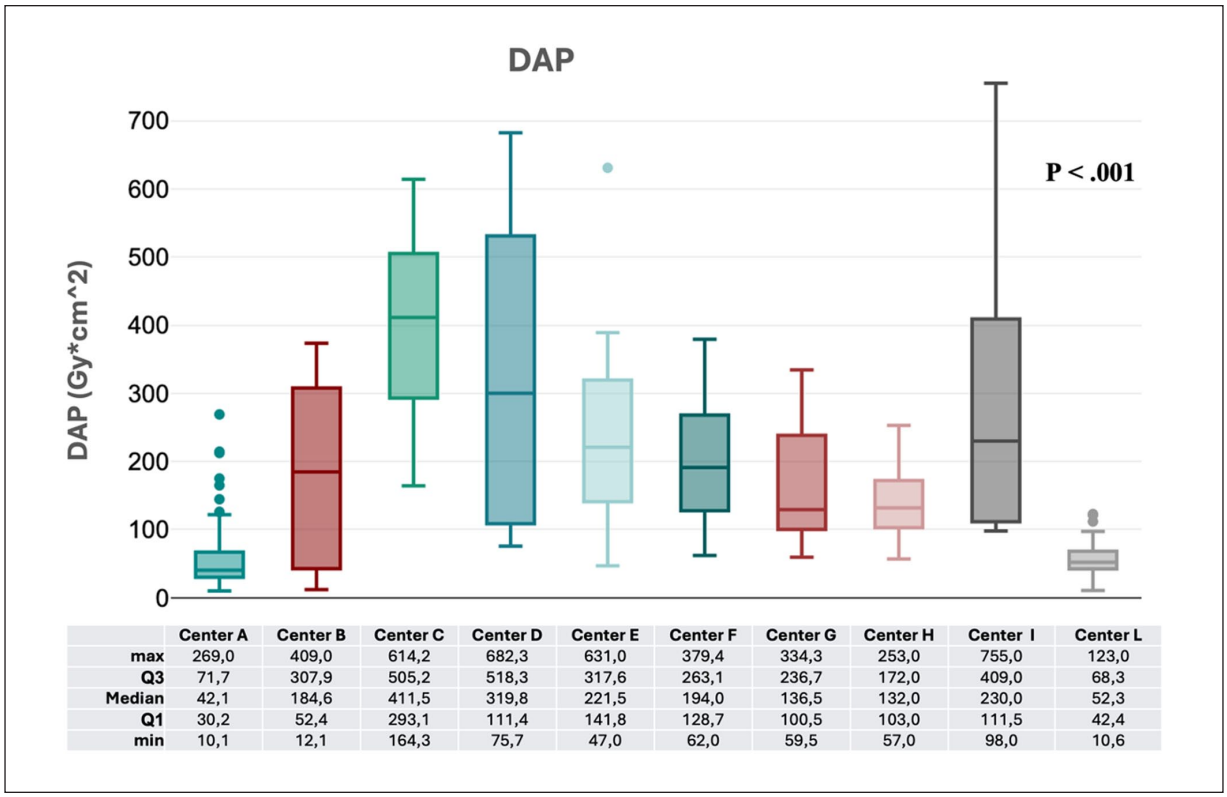
The reference center investigating best practices reported a median DAP of 28 Gy·cm^2 (IQR 16-59) for 150 conventional consecutive ICM-guided EVAR procedures, which were not included in this multicenter study. In their CO_2-guided EVAR cohort of 93 patients evenly distributed across 3 groups, significant dose reductions were observed as reported in Figure 3. Group A (n=30) had median DAP and K_{ar} values of 65 Gy·cm^2 (IQR 36-102) and 425 mGy (IQR 216-798), respectively, while group B (n=31) showed improved values of 40 Gy·cm^2 (IQR 20-64) and 314 mGy (IQR 188-491). Group C (n=32) demonstrated the lowest exposures at 31 Gy·cm^2 (IQR 15-38) and 133 mGy (IQR 56-148), with all intergroup comparisons being statistically significant ($p<0.001$). Fluoroscopy times were consistent across groups at a median of 11.4 minutes (IQR 9.1-17.2).

The progressive implementation of low-dose protocols first on older equipment and subsequently with new angiographic systems yielded substantial radiation reductions without compromising image quality or technical success, which remained at 100% throughout. Compared to baseline, the first implementation achieved a 38.5% dose reduction, increasing to 52.3% with the second implementation, while group C showed a 22.5% reduction vs group B. In a

Table 1. Dosimetric Data Stratified by Center and Angiograph System Type.

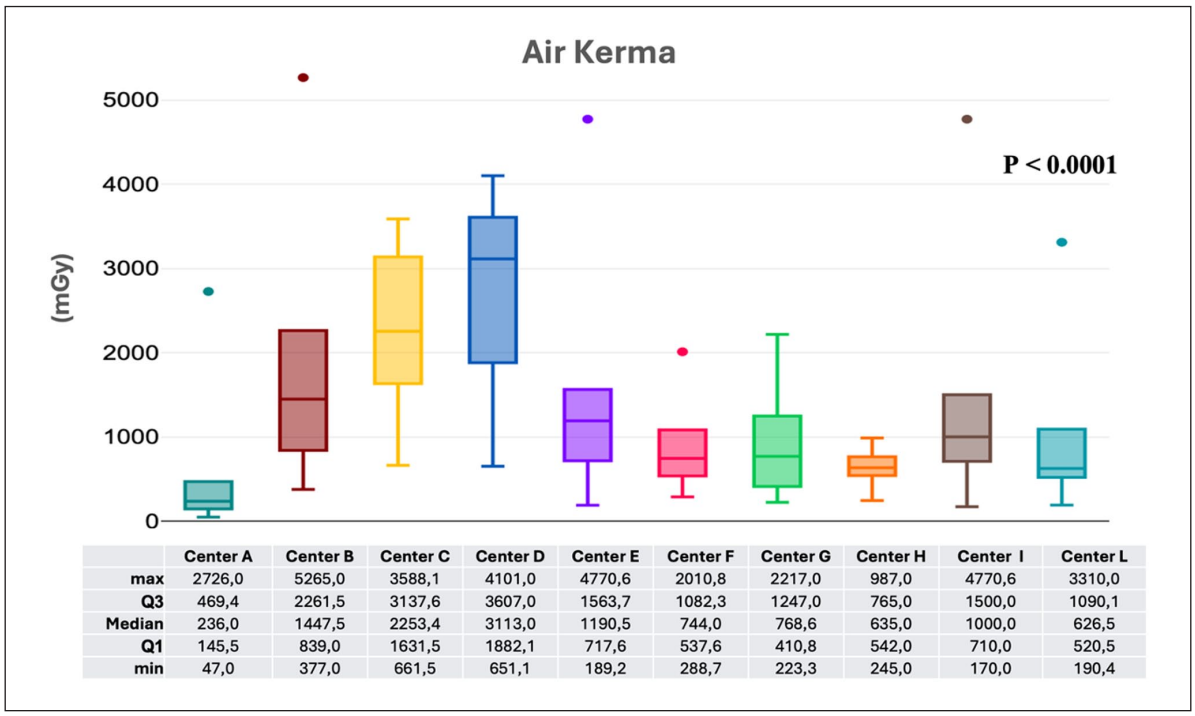
	Brand angiographic system	Model (OLD device: O NEW device: N)	DAP ($Gy \cdot cm^2$) median (IQR)	K_{ar} (mGy) median (IQR)	K_{ar} normalized by the time of procedure (mGy/s) median (IQR)	Fluoroscopy time (minutes) median (IQR)	BMI median (IQR)
Center A (n=93)	Siemens Philips	Artis Zee (O) Azurion 7 M20 ClarityIQ (N)	42.1 (30.2-71.7)	235 (145.5-469.4)	20.5 (11.9-31.9)	13.0 (10.0-17.1)	25 (18-33)
Center B (n=9)	Siemens	Artis Zee (O)	184.6 (52.4-307.9)	1477.5 (839-2261.5)	69 (44.0-96.2)	24.0 (10.0-39.0)	25 (20-28)
Center C (n=11)	Philips	Allura FD20 (O)	411.5 (293.1-505.2)	2253.4 (1631.5-3137.6)	54.6 (47.8-93.5)	26.3 (24.7-37.9)	29 (24-34)
Center D (n=10)	Siemens	Artis Pheno (N)	319.8 (111.4-518.3)	3113 (1882-3607)	44.5 (34.6-60.2)	39.8 (32.8-47.4)	27 (23-32)
Center E (n=16)	Philips	Allura ClarityIQ FD 20 (O)	221.5 (141.8-317.6)	1190.5 (717.6-1563.7)	56.6 (32.1-83.6)	19.0 (16.8-24.3)	25 (20-35)
Center F (n=12)	Philips	Allura Clarity ClarityIQ FD (O)	194.0 (128.7-263.1)	744 (537.6-1082.3)	50.9 (39.0-80.3)	14.0 (9.7-19.7)	27 (24-33)
Center G (n=81)	Siemens	Artis ZeeGO (N)	136.5 (100.5-236.7)	768.6 (410.8-1247)	52.2 (42.4-68.4)	13.7 (11.2-17.1)	27 (17-41)
Center H (n=28)	Siemens	Artis Pheno (N)	132.0 (103.0-172.0)	635 (542-765)	37.6 (27.9-49.3)	16.5 (14.9-24.1)	27 (20-34)
Center I (n=22)	Ziehm	RDF 3D (O)	230.0 (111.5-409.0)	1000 (710-1500)	32.5 (26.5-36.4)	21.0 (18.0-25.0)	27 (20-34)
Center L (n=11)	General Electric	IGS 740 (N)	52.3 (42.4-68.3)	626.5 (520.5-1090)	52.2 (42.4 -68.4)	31.0 (24.0-42.5)	28 (21-33)
p-value	-	-	0.0004	< 0.0001	0.0032	0.0007	0.19

Abbreviations: BMI, body mass index; DAP, dose-area product; K_{ar}, reference air kerma.



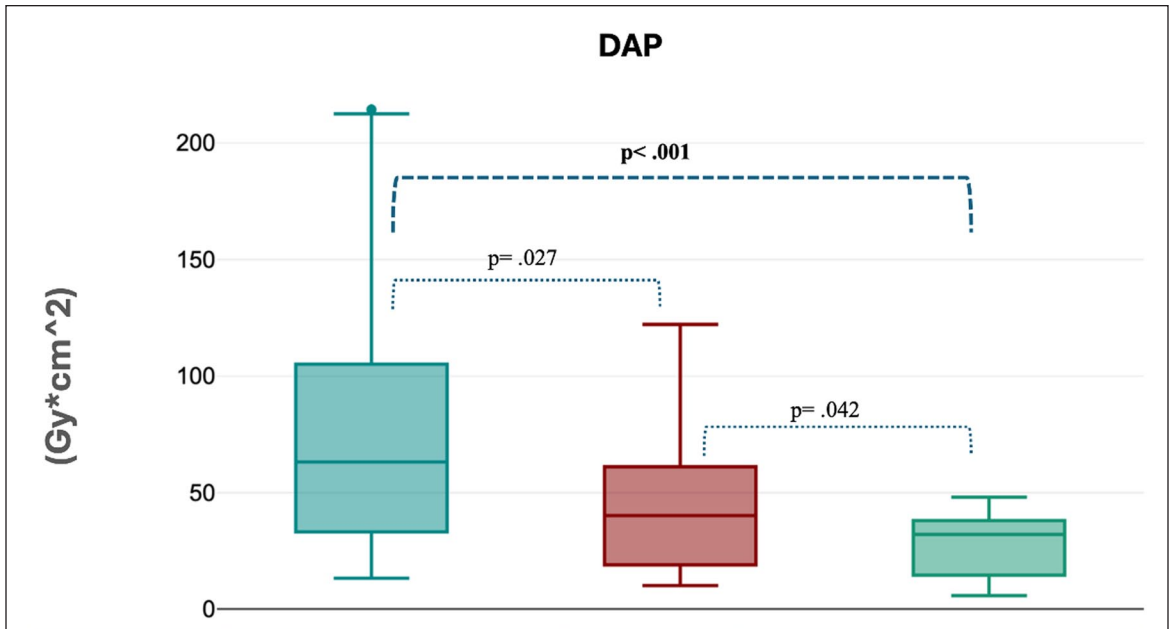
	Center A	Center B	Center C	Center D	Center E	Center F	Center G	Center H	Center I	Center L
max	269,0	409,0	614,2	682,3	631,0	379,4	334,3	253,0	755,0	123,0
Q3	71,7	307,9	505,2	518,3	317,6	263,1	236,7	172,0	409,0	68,3
Median	42,1	184,6	411,5	319,8	221,5	194,0	136,5	132,0	230,0	52,3
Q1	30,2	52,4	293,1	111,4	141,8	128,7	100,5	103,0	111,5	42,4
min	10,1	12,1	164,3	75,7	47,0	62,0	59,5	57,0	98,0	10,6

Figure 1. Dose area product (DAP) values across centers. Median, IQR, and range values are showed.



	Center A	Center B	Center C	Center D	Center E	Center F	Center G	Center H	Center I	Center L
max	2726,0	5265,0	3588,1	4101,0	4770,6	2010,8	2217,0	987,0	4770,6	3310,0
Q3	469,4	2261,5	3137,6	3607,0	1563,7	1082,3	1247,0	765,0	1500,0	1090,1
Median	236,0	1447,5	2253,4	3113,0	1190,5	744,0	768,6	635,0	1000,0	626,5
Q1	145,5	839,0	1631,5	1882,1	717,6	537,6	410,8	542,0	710,0	520,5
min	47,0	377,0	661,5	651,1	189,2	288,7	223,3	245,0	170,0	190,4

Figure 2. Reference air kerma (K_{ar}) values across centers. Median, IQR, and range values are showed.



	Group A Normal Dose OLD DEVICE (1.8 microGy/fr) Siemens Artis Zee	Group B Low dose OLD DEVICE (0.8 micro Gy/fr) Siemens Artis Zee	Group C NEW DEVICE (0.8 micro Gy/fr) Philips Azurion7 M20-clarity
max	214.30	122,13	48,01
Q3	101,43	63,95	37,45
Median	65	40	31
Q1	36,15	19,51	15,23
min	13,23	10,09	5,79
Fluoroscopy time	12	16	11

Figure 3. Results of best practice implementation in a single center. Dose Area Product (DAP) values in the three different groups. Median, IQR, and range values are showed. First group (Group A) included patients treated with the Artis Zee dTA (Siemens) and a standard CO_2 protocol, while second group (Group B) comprised patients treated with the same angiographic system but under a low-dose CO_2 protocol. Group C were treated in a new hybrid room (Azurion7 M20 with Clarity, Philips) with a standard CO_2 protocol but with an updated new angiographic system.

subgroup analysis of group C, synchronized CO_2 injection in 15 patients provided an additional 12% DAP reduction compared with 17 non-synchronized cases (28.5 vs 32.5 Gy·cm^2, p=0.23), attributed to reduced latency in CO_2 delivery. Following the step-by-step implementation, a total DAP reduction of 56% was attained compared with the baseline measurements. Image quality remained clinically appropriate across all groups, with mean scores of 29.5, 29.1, and 29.3, respectively (p=0.45), with only 2 suboptimal cases (both in patients with BMI>33). Following study completion, the center adopted a new low-dose CO_2 protocol (frame rate of 2-3 frames per second, detector dose of 0.72 µGy per frame, pulse rate of 7.5 pulses/s, and copper [Cu] filtration of 0.4 mm) for the upgraded device as standard practice, achieving a further 60% reduction in DAP per DSA shot—equivalent to a 2.6-fold decrease in radiation exposure. The accompanying Figure 4A and B challenges readers to identify which DSA image was acquired using the optimized low-dose protocol with the new device (Philips, Azurion 7 M20 Clarity).

Discussion

This study represents the largest multicenter analysis to date on radiation dosimetry in CO_2 guided EVAR. While national and international guidelines define DRLs for EVAR procedures, these benchmarks are currently validated only for ICM. In Europe, standard DRLs for EVAR range from 100 to 200 Gy·cm^2, whereas previously reported DAP values for CO_2-based procedures have varied widely, from 161 to 925 Gy·cm^2.[2–12,19–24] The median DAP recorded in this study was 189 Gy·cm^2, aligning with European DRLs, though certain centers reported significantly higher exposures.

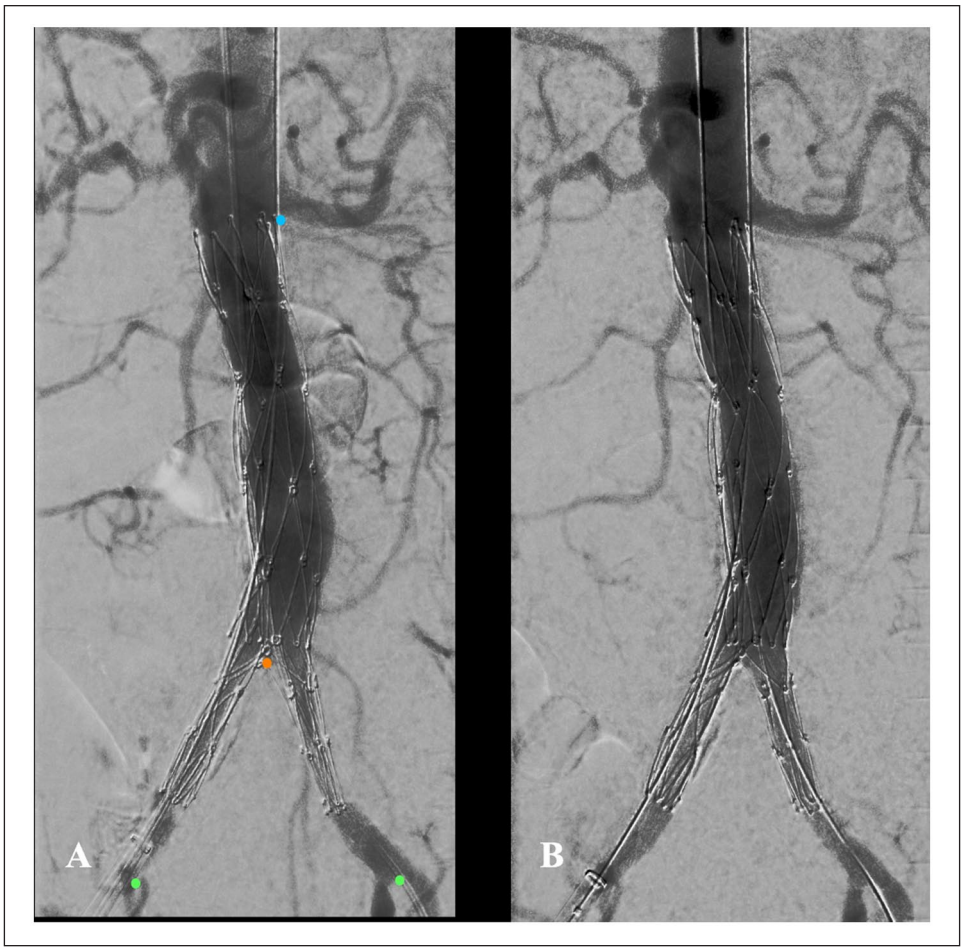


Figure 4. Completion CO_2 angiography performed on the same patient using both standard and low-dose protocols on the same Philips Azurion 7 M20 Clarity system. Image A (CO_2 standard dose protocol) demonstrated: DAP: 3,196 Gy·cm² ; DAP/Fr: 0.133 Gy·cm²/Fr; K_{ar}: 19.4 mGy; K_{ar}/Fr: 0.80 mGy/Fr while on Image B (CO_2 low-dose protocol) demonstrated: DAP: 1.221Gy·cm² ; DAP/Fr: 0.071Gy·cm²/Fr; K_{ar}: 7.38mGy; K_{ar}/Fr: 0.43 mGy/Fr. The achieved dose reduction did not compromise diagnostic image quality, with all anatomical structures remaining clearly visualized.

A key finding is the pronounced sensitivity of CO_2 dosimetry to the specific angiographic equipment and imaging protocols used—more so than for ICM. Significant variability was observed across different manufacturers' systems. Older-generation angiographic systems and standard-dose protocols were associated with substantially higher radiation doses for both patients and operators. In contrast, modern angiographic platforms reduced acquisition dose by 53%, and low-dose protocols on the same systems yielded an additional 38.5% reduction. Synchronization techniques contributed a further 12% decrease in total radiation exposure (with same device and protocol). Following the step-by-step implementation, a total DAP reduction of 56% vs the baseline measurements was attained. The final radiation for each patient is influenced by the necessity to perform additional angiographies beyond the 3 scheduled acquisitions, as well. As previously reported, the need for supplementary angiographies is primarily related to anatomical factors—such as the clock position of the lowest renal artery (particularly between 3 and 9 o'clock) or large aneurysm—which may impair optimal visualization with CO_2.[25] The anticipation of potential difficulties in target vessel visualization may help mitigate radiation exposure. Technical adjustments—such as pre-emptive table tilting prior to angiography or selective catheterization of the target vessel followed by selective CO_2 injection—can reduce the need for repeated acquisitions and therefore limit radiation dose. Conversely, inadequate or difficult target vessel visualization inevitably results in additional imaging runs and consequently increases radiation exposure.

Some studies[28,29] showed that new imaging technology in the hybrid operating room suite can significantly reduce radiation dose for both patients and staff, without changing standard ways of working. These findings underscore the critical role of equipment optimization and protocol standardization in reducing radiation exposure during CO_2-guided EVAR. Older angiographic systems, which lack

advanced dose-reduction features, tend to generate higher scatter radiation and require longer fluoroscopy times due to the inherently lower radiopacity of CO_2. In contrast, modern systems equipped with pulsed fluoroscopy, noise reduction, frame rate reduction, dose-to-detector control, and dynamic collimation can achieve radiation doses comparable with those seen with ICM. The absence of standardized protocols for CO_2 angiography remains a significant barrier to wider adoption. Training initiatives are urgently needed to overcome the technical learning curve of CO_2 angiography, raise operator awareness of radiation dosimetry, and promote best practices for minimizing exposure. Notably, procedural efficiency has improved significantly compared with early CO_2 EVAR experiences. Criado,[30] a pioneer in the field, reported average procedure times of 177 minutes with 21 minutes of fluoroscopy. In this study, these metrics improved markedly, likely due to the use of automated CO_2 injectors, standardized workflows that reduce redundant diagnostic angiography, and the integration of 3D image fusion.[13,24] This technique aligns preoperative CT data with real-time fluoroscopy using bony landmarks for accurate co-registration, thereby eliminating the need for repeated DSA and reducing radiation exposure by up to 70% in both standard and complex aortic procedures.[24] In addition, comprehensive pre-procedural planning—including axial imaging, multiplanar reconstructions, and 3D modeling—enables precise selection of optimal projection angles for target vessel visualization. This improves workflow efficiency and contributes to further reductions in ionizing radiation.[24,31]

Implementing a pre-procedural gas-reducing diet along with trained radiology technologists who have completed the learning curve allows for optimized image post-processing. Advanced algorithms enable multiplanar transformations—including zooming, windowing, distance measurement, and contrast enhancement—while specialized CO_2-DSA tools, such as re-masking (selecting pre-CO_2 arrival frames as masks), 4-directional pixel shift for motion correction, and stacking software to compensate for CO_2 fragmentation, further enhance diagnostic image quality. Moreover, substantial differences were observed in acquisition parameters, particularly in frame rate and detector dose per frame, which are among the most influential determinants of radiation exposure. Radiation dose parameters must be locally validated to ensure an appropriate balance between image quality and patient safety.

Future angiographic systems should incorporate artificial intelligence to standardize these post-processing workflows. By combining best practices—including a low-dose protocol, new imaging equipment, and synchronization—the study achieved a 56% reduction in DAP, reaching a final DAP value comparable with the center's reference for ICM (median 28.5 Gy·cm^2 for CO_2 vs 28 Gy·cm^2 for ICM). Synchronization provides a clear benefit by precisely controlling the delay before starting DSA, reducing total radiation exposure and minimizing motion artifacts, which also simplifies post-processing. The European Directive on Basic Safety Standards for Protection from the Hazards of Radiation requires EU Member States to enhance radiation safety for both patients and health care professionals.[7] Occupational exposure during X-ray-guided procedures is closely linked to patient exposure, making it essential to manage both through an integrated approach.[32] Health care workers repeatedly exposed to low-dose radiation have a 20% increased risk of developing cancer compared with non-exposed colleagues.[33,34] At the same time, the use of iodine as a contrast medium in medicine faces growing environmental and supply chain challenges. Global iodine demand is increasing steadily—by about 8% annually—driven by an aging population requiring more diagnostic procedures and by expanding clinical applications. Currently, ~90% of global ICM supply originates from just 2 countries: China (60%-70%) and Japan (30%), creating significant vulnerabilities in long-term availability as highlighted by regulatory agencies.[35] The direct environmental impact of medical CO_2 use is negligible. However, indirect effects are associated with the energy required for CO_2 capture (typically as an industrial by-product), purification, compression, and transport, as well as with the manufacturing and distribution of steel cylinders. The CO_2 cylinder used with the automatic injector system contains 2 L of gas, typically sufficient for approximately 2 years of activity (≈500 EVAR procedures) in a high-volume vascular center. As the cylinder is refillable and reused, its embodied environmental impact is distributed over prolonged clinical use, thereby reducing its relative contribution to the overall environmental burden. In contrast, iodinated contrast agents must be disposed of as special waste, with each vial discarded even if partially unused.[36,37] Modern low-dose EVAR imaging protocols incorporate dynamic dose adjustment capabilities, allowing selective escalation to higher-dose settings when critical procedural tasks demand enhanced resolution—particularly during device deployment and complication assessment (type I/III endoleaks, branch vessel patency). This adaptive approach mirrors the "as low as reasonably achievable" (ALARA) principle, strategically balancing minimal radiation exposure with diagnostic certainty—analogous to adjusting vehicle speed for safe navigation in critical visibility conditions. Ongoing collaboration with industry partners is essential for systematically evaluating and refining imaging technologies to optimize both image quality and radiation dose. These partnerships are key to advancing low-dose protocols, synchronization algorithms, and next-generation angiographic systems tailored to CO_2-based procedures. This synergy between clinical research and technological innovation is vital to ensure reproducible, dose-efficient CO_2 EVAR implementations across varied clinical environments.

This study has several limitations that should be acknowledged. First, despite efforts to standardize the protocol across centers, differences in angiographic equipment, imaging platforms, local protocol implementation, and acquisition settings likely contributed to inter-center variability in radiation dose and limited the comparability of dosimetric data. Second, substantial variability in patient enrollment across centers (range 9-93 patients per center) was observed. This heterogeneity reflected differences in the timing of ethical committee approval, adherence to device-specific instructions for use (IFU), and local selection criteria for AAA management (open vs endovascular repair). Such variability may have contributed to differences in the reported dosimetric outcomes. Third, the analysis was conducted at the center level rather than at the individual operator level. Radiation exposure data were therefore aggregated per center and not stratified according to operator experience or technique. This approach does not allow assessment of inter-operator variability. Although the technique had been standardized across participating centers and was implemented only after completion of the learning-curve phase, residual variability among operators cannot be entirely excluded. Furthermore, the study was not designed as a randomized controlled trial. As increasingly emphasized in the literature, a properly designed randomized study is warranted to comprehensively evaluate not only radiation dosimetry, but also procedural parameters, clinical outcomes, renal function, safety endpoints, and long-term results of EVAR performed with CO_2 compared with ICM. Finally, a formal cost analysis addressing the economic impact of implementing new devices and standardized CO_2 protocols was not performed.

Conclusions

This study highlights considerable variability in radiation dosimetry during CO_2-guided EVAR, largely influenced by differences in angiographic equipment, imaging software, and the application of synchronization technique. To effectively minimize radiation exposure, we strongly recommend 3 core strategies: first, the adoption of modern angiographic systems equipped with dose-reduction technologies; second, the implementation of optimized low-dose imaging protocols; and third, the routine integration of CO_2-DSA synchronization to enhance procedural efficiency and reduce unnecessary exposure. When consistently applied, these measures can lower radiation doses to levels comparable with those observed in ICM-based EVAR. Future multicenter prospective studies should utilize standardized imaging platforms and protocols to optimize DLRs.

ORCID iDs

Emiliano Chisci https://orcid.org/0000-0002-4701-9855
Luca Mezzetto https://orcid.org/0000-0002-6284-1740
Gioele Simonte https://orcid.org/0000-0002-2268-9166
Luca Bertoglio https://orcid.org/0000-0001-6871-2176
Tommaso Lazzarotto https://orcid.org/0000-0002-3841-209X

Author Contributions

E.C., S.M., E.F., A.G., M.F., M.G., L.B., and S.P. contributed to study design. E.C., E.F., E.C.C., L.M., R.F., G.S., C.M., G.P., D.A., L.B., S.S., S.P., T.L., L.C., MF, AG, SM, M.A., M.P., F.G., L.G., G.F.V., S.S., R.P., G.I., G.P., M.L., E.G., M.G., C.M., S.Z., L.D.S., S.B., A.V., and S.M. contributed to data collection. EC, SM, EF, AG, MF, MG, LB, SP, SS, and TL contributed to data analysis. E.C., E.F., E.C.C., L.M., R.F., G.S., C.M., G.P., D.A., L.B., S.S., S.P., T.L., L.C., M.F., A.G., S.M., M.A., M.P., F.G., L.G., G.F.V., S.S., R.P., G.I., G.P., M.L., E.G., M.G., C.M., S.Z., L.D.S., S.B., A.V., and S.M. contributed to writing.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Supplemental Material

Supplemental material for this article is available online.

References

1. Wanhainen A, Van Herzeele I, Bastos Goncalves F, et al. Editor's choice—European Society for Vascular Surgery (ESVS) 2024 clinical practice guidelines on the management of abdominal aorto-iliac artery aneurysms. *Eur J Vasc Endovasc Surg*. 2024;67(2):192–331.
2. Medical exposure to ionising radiation. National Diagnostic Reference Levels (DRLs) for fluoroscopy and fluoroscopically guided interventions. https://www.hiqa.ie/sites/default/files/2022-10/National-diagnostic-reference-levels-(DRLs)for-fluoroscopy-and-fluoroscopically-guided-interventions-(FGIs).pdf. Accessed April 2025.
3. Schegerer A, Loose R, Heuser LJ, et al. Diagnostic reference levels for diagnostic and interventional X-ray procedures in Germany: update and handling. *Rofo*. 2019;191:739–751.
4. Tuthill E, O'Hora L, O'Donohoe M, et al. Investigation of reference levels and radiation dose associated with abdominal EVAR (endovascular aneurysm repair) procedures across several European centres. *Eur Radiol*. 2017;27(11):4846–4856.
5. Rial R, Vañó E, Del Río-Solá ML, et al. National diagnostic reference levels for endovascular aneurysm repair and optimisation strategies. *Eur J Vasc Endovasc Surg*. 2020;60(6):837–842.
6. Rehani MM, Ciraj-Bjelac O, Vañó E, et al. ICRP Publication 117. Radiological protection in fluoroscopically guided procedures performed outside the imaging department. *Ann ICRP*. 2010;40(6):1–102.

7. Council Directive 2013/59/Euratom of 5 December 2013 laying down basic safety standards for protection against the dangers arising from exposure to ionising radiation, and repealing directives 89/618/Euratom, 90/641/Euratom, 96/29/Euratom, 97/43/Euratom and 2003/122/Euratom. https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=OJ%3AL%3A2014%3A013%3ATOC. Accessed April 2025.
8. ICRP Publication 60. 1990 recommendations of the international commission on radiological protection. *Ann ICRP*. 1991;21:1–201.
9. ICRP Publication 103. The 2007 recommendations of the international commission on radiological protection. *Ann ICRP*. 2007;37:1–328.
10. ICRP Publication 135. Diagnostic reference levels in medical imaging. *Ann ICRP*. 2017;46:1–143.
11. ICRP Publication 147. Use of dose quantities in radiological protection. *Ann ICRP*. 2021;50:9–82.
12. Weiss S, Van Herzeele I; European Vascular Surgeons in Training (EVST) and the ESVS academy. Radiation protection training for vascular surgeons in twenty-one European countries. *Eur J Vasc Endovasc Surg*. 2020;59(4):512–513.
13. Modarai B, Haulon S, Ainsbury E, et al. Editor's choice—European Society for Vascular Surgery (ESVS) 2023 clinical practice guidelines on radiation safety. *Eur J Vasc Endovasc Surg*. 2023;65(2):171–222.
14. Motaganahalli R, Martin A, Feliciano B, et al. Estimating the risk of solid organ malignancy in patients undergoing routine computed tomography scans after endovascular aneurysm repair. *J Vasc Surg*. 2012;56:929–937.
15. National Research Council. *Health Risks From Exposure to Low Levels of Ionizing Radiation: BEIR VII Phase2*. Washington, DC: National Academies Press; 2006.
16. Sharafuddin MJ, Marjan AE. Current status of carbon dioxide angiography. *J Vasc Surg*. 2017;66:618–637.
17. Cho KJ. Carbon dioxide angiography: scientific principles and practice. *Vasc Specialist Int*. 2015;31(3):67–80.
18. Ali F, Mangi MA, Rehman H, et al. Use of carbon dioxide as an intravascular contrast agent: a review of current literature. *World J Cardiol*. 2017;269:715–722.
19. Chao A, Major K, Kumar SR, et al. Carbon dioxide digital subtraction angiography-assisted endovascular aortic aneurysm repair in the azotemic patient. *J Vasc Surg*. 2007;45(3):451–458.
20. Tantawy TG, Seriki D, Rogers S, et al. Endovascular aneurysm repair assisted by CO2 digital subtraction angiography and intraoperative contrast-enhanced ultrasonography: single-center experience. *Ann Vasc Surg*. 2021;70:459–466.
21. Vacirca A, Faggioli G, Mascoli C, et al. CO2 automated angiography in endovascular aortic repair preserves renal function to a greater extent compared with iodinated contrast medium. *Ann Vasc Surg*. 2022;81:79–88.
22. Quaglino S, Ferrero E, Ferri M, et al. Safety, effectiveness and pitfalls of carbon dioxide routine use as a contrast agent for endovascular abdominal aortic repair. *Ann Vasc Surg*. 2023;101:120–126.
23. Vacirca A, Faggioli G, Vaccarino R, et al. The optimal operative protocol to accomplish CO2-EVAR resulting from a prospective interventional multicenter study. *J Vasc Surg*. 2023;77(5):1405–1412.
24. Hertault A, Maurel B, Midulla M, et al. Editor's choice—minimizing radiation exposure during endovascular procedures: basic knowledge, literature review, and reporting standards. *Eur J Vasc Endovasc Surg*. 2015;50(1):21–36.
25. Chisci E, Ferrero E, Antonello M, et al. Editor's choice—feasibility and safety of using carbon dioxide exclusively in regular endovascular aortic aneurysm repair: results of a multicentre, prospective, zero iodine contrast endovascular aneurysm repair study. *Eur J Vasc Endovasc Surg*. 2025;69(3):392–402.
26. National Council on Radiation Protection and Measurements. *Implementation of the Principle of as Low as Reasonably Achievable (ALARA) for Medical and Dental Personnel: Recommendations of the National Council on Radiation Protection and Measurements*. Bethesda, MD: The Council; 1990.
27. International Atomic Energy Agency. *Dosimetry in Diagnostic Radiology: An International Code of Practice* [Technical Reports Series No. 457]. Vienna: IAEA; 2007.
28. van den Haak RF, Hamans BC, Zuurmond K, et al. Significant radiation dose reduction in the hybrid operating room using a novel X-ray imaging technology. *Eur J Vasc Endovasc Surg*. 2015;50(4):480–486.
29. Rohlffs F, Spanos K, Debus ES, et al. Modern image acquisition system reduces radiation exposure to patients and staff during complex endovascular aortic repair. *Eur J Vasc Endovasc Surg*. 2020;59(2):295–300.
30. Criado E, Upchurch GR Jr, Young K, et al. Endovascular aortic aneurysm repair with carbon dioxide-guided angiography in patients with renal insufficiency. *J Vasc Surg*. 2012;55(6):1570–1575.
31. Stansfield T, Parker R, Masson N, et al. The endovascular preprocedural run through and brief: a simple intervention to reduce radiation dose and contrast load in endovascular aneurysm repair. *Vasc Endovascular Surg*. 2016;50(4):241–246.
32. ICRP Publication 139. Occupational radiological protection in interventional procedures. *Ann ICRP*. 2018;47:1–118.
33. Andreassi MG, Piccaluga E, Guagliumi G, et al. Occupational health risks in cardiac catheterization laboratory workers. *Circ Cardiovasc Interv*. 2016;9(4):e003273.
34. Wang JX, Zhang LA, Li BX, et al. Cancer incidence and risk estimation among medical x-ray workers in China, 1950e1995. *Health Phys*. 2002;82:455–466.
35. Zanardo M, Ambrogi F, Asmundo L, et al. The GREENWATER study: patients' green sensitivity and potential recovery of injected contrast agents. *Eur Radiol*. 2025;35(3):1205–1214.
36. Pepin EW, Unachukwu E, Schultz S, et al. Optimization of iodinated contrast media inventory management: effect of inventory diversification on waste reduction. *J Am Coll Radiol*. 2024;21(1):175–181.
37. Toia GV, Ananthakrishnan L. The environmental impact of iodinated contrast media: strategies for optimized use and recycling. *J Comput Assist Tomogr*. 2025;49:203–214.