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RAPID COMMUNICATION

Prospective evaluation of carbon dioxide as a contrast medium in pacemakers or defibrillators carriers for venous angiography (SPARKLING pilot study)

Alberto Spadotto [1,2], Maria Carelli [1], Giulia Massaro [1,2], Cristian Martignani [1], Matteo Ziacchi [1], Mauro Biffi [1], and Igor Diemberger [1,2]*

[1]Cardiology Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Via Massarenti 9, Bologna 40138, Italy; and [2]Institute of Cardiology, Department of Medical and Surgical Sciences, University of Bologna, Via Massarenti 9, Bologna 40138, Italy

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Introduction

Venography continues to be a valuable tool during cardiac implantable electronic device (CIED) procedures, particularly in complex scenarios like device upgrades or lead extractions, despite the widespread use of ultrasound-guided access.[1–4] Carbon dioxide (CO_2) has emerged as a potential alternative to iodinated contrast media (ICM), especially in patients at risk for contrast-induced nephropathy (CIN) or with ICM allergies, though evidence evaluating its use in venous angiography in CIED procedures is limited to one small study.[5]

To address this gap, this study aimed to compare CO_2 and ICM venography in CIED-related interventions and assess the safety of CO_2.

Materials and methods

Study design and endpoints

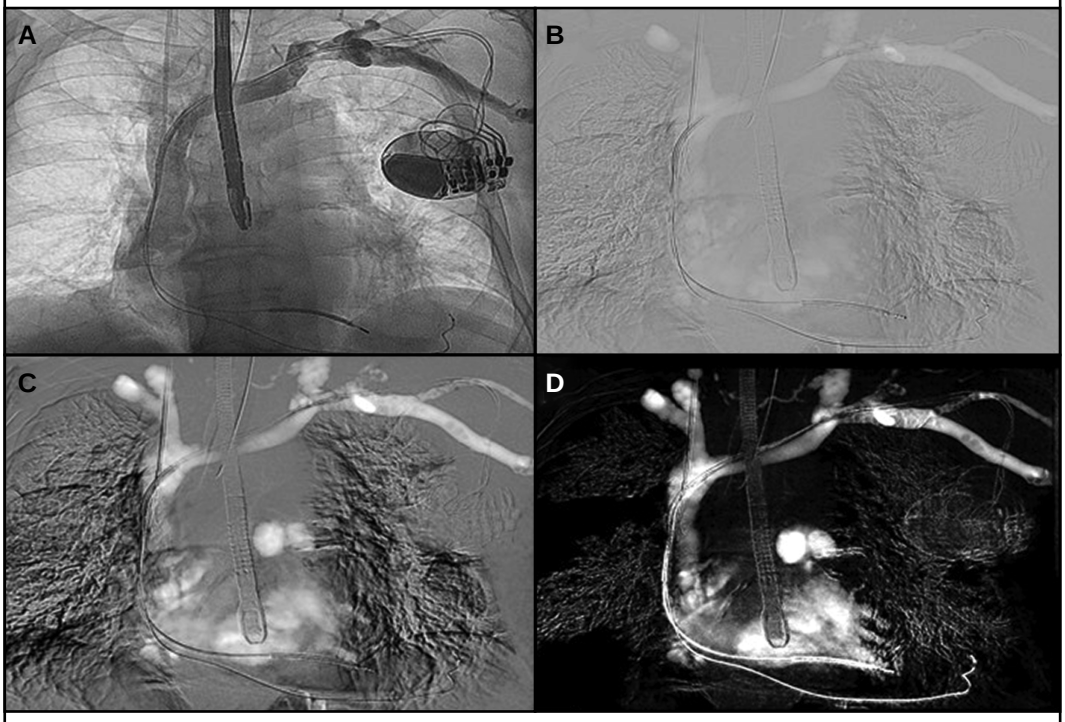
This prospective, single-centre randomized crossover study compared CO_2 and ICM venous angiography during CIED procedures. Patients presenting right-to-left shunt (evaluated via pre-procedural echocardiography with bubble test), pulmonary hypertension, lung failure, or known allergy to ICM were excluded.

The sequence of imaging techniques was randomized. Carbon dioxide angiography was performed using an automated system, delivering a 50 mL CO_2 bolus at 300 mmHg, preceded by a 10 mL flush, and images were enhanced with digital subtraction angiography (DSA) and stacking techniques. Digital subtraction angiography subtracts pre- and post-contrast images to isolate contrast-enhanced structures, while stacking overlays multiple frames to improve image clarity. Two stacking tools were used: default stacking (DS) integrated in current X-ray system and a custom-made software (CS) approach, requiring image upload into a specific software (*Figure 1, panel 1*).

Two experienced radiology technicians, blind to the study, independently assessed image quality for multiple venous segments (e.g. axillary, subclavian; see *Figure 1, panel 2*). The primary endpoint was vessel visualization evaluated by patency visibility and optimal visualization, defined as a lumen-to-background contrast enabling measurement of vessel diameter and degree of stenosis for each modality [with/without stacking (WoS)]. The secondary endpoint was to evaluate the incidence of adverse events.

* Corresponding author. Tel: +39 0512143598. *E-mail address:* igor.diemberger@unibo.it

Panel 1
Venography images acquired prior to a biventricular ICD extraction. Image A was obtained using iodinated contrast medium. Images B, C, and D were captured using CO_2 contrast processed and digital subtraction angiography without stacking, postprocessed using the default stacking and the custom-made software, respectively.



Panel 2
Visibility of venous segments with different techniques (ICM, CO_2, WoS and postprocessed with DS or CS). Inter-method comparison was assessed usin Pearson's X^2 test.

	ICM	CO_2			*P* WoS vs. ICM	*P* DS vs. ICM	*P* CS vs. ICM
		WoS	DS	CS			
Axillary	98.3%	82.9%	86.5%	92.5%	0.004	0.02	n.s.
Subclavian	97.5%	91.0%	95.1%	96.7%	n.s.	n.s.	n.s.
Innominate	96.4%	84.0%	91.1%	95.4%	0.02	n.s.	n.s.
Superior vena cava	79.8%	75.7%	85.3%	88.9%	n.s.	n.s.	n.s.
Cephalic	63.9%	40.0%	44.2%	47.9%	0.009	0.003	n.s.
Jugular	28.9%	36.2%	38.8%	56.4%	n.s.	n.s.	0.002
Cont. innominate	26.0%	46.9%	61.3%	68.4%	0.02	<0.001	<0.001

Panel 3
Optimal visualization of venous techniques (ICM, CO_2, WoS and postprocessed with DS or CS). Inter-method comparison using Pearson's X^2 test.

	ICM	CO_2			*P* WoS vs. ICM	*P* DS vs. ICM	*P* CS vs. ICM
		WoS	DS	CS			
Axillary	91.8%	57.4%	63.9%	83.6%	<0.001	<0.001	n.s.
Subclavian	70.5%	50.8%	73.8%	91.8%	0.002	n.s.	<0.001
Innominate	47.5%	32.8%	49.2%	70.5%	0.02	n.s.	<0.001
Superior vena cava	18.0%	16.4%	24.6%	36.1%	n.s.	n.s.	0.002
Cephalic	50.8%	29.5%	36.1%	36.1%	0.001	0.02	0.02
Jugular	14.7%	11.5%	14.7%	31.1%	n.s.	n.s.	0.003
Cont. innominate	0.0%	14.7%	18.0%	19.7%	<0.001	<0.001	<0.001

CO_2, carbon dioxide; Cont., contralateral; CS, custom-made stacking; DS, default stacking; ICM, iodinated contrast media; WoS, without stacking.

Figure 1. Comparison of iodinated contrast media and carbon dioxide venography in CIED-related interventions.

All patients provided written informed consent, and the study was approved by the Institutional Review Boards and conducted following the Declaration of Helsinki.

Statistical analysis

Continuous variables were summarized as mean ± standard deviation or median and interquartile range, based on their distribution. Group differences were assessed using the Student's *t*-test. Inter-operator agreement and intra-method variability were assessed by comparing the standard deviation of measurement differences.

Analyses were conducted using STATA (v.18.0, StataCorp LLC, College Station, USA).

Results

Study population

Among the 62 patients screened, two were excluded (one due to a patent foramen ovale with a right-to-left shunt and the other due to severe pulmonary hypertension). Sixty patients were included (76.7% male, mean age of 72.6 ± 13.1 years, and a mean creatinine 1.3 ± 0.7 mg/dL).

Vein visualization

Visibility rates, defined as the percentage of veins in which the patency can be determined, are reported in *Figure 1, panel 2*. The proportion of veins with optimal visualization is reported in *Figure 1, panel 3*.

Inter-operator agreement for image quality classification (i.e. non-visible, patency visibility, optimal visualization) was good across all venous segments. Intra-method variability, measured by the standard deviation of differences between the two operators' measurements, was lower with CO_2 than with ICM (ICM: 2.41; CO_2 WoS: 2.02; DS: 1.98; CS: 1.96). The reduction was statistically significant for both WoS ($P = 0.03$) and stacking techniques (DS: $P = 0.02$; CS: $P = 0.01$).

Three venous stenoses > 75% were identified with both ICM and CO_2, regardless of post-processing techniques: one in the axillary and two in the subclavian veins.

Safety

Four patients (6.7%) experienced CIN, defined as a 25% relative increase or a 0.5 mg/dL absolute increase in serum creatinine. No acute adverse events were reported in either imaging group.

Discussion

This study compared ICM and CO_2 venography for evaluating major thoracic veins in CIED candidates. Carbon dioxide venography WoS visualized subclavian vein patency in over 90% of cases, with results comparable to ICM. Patency visualization of the axillary and innominate veins was slightly lower but remained above 80%. Carbon dioxide venography WoS proved suitable for CIED procedures, offering almost real-time imaging without the need for time-consuming post-processing. Stacking techniques further enhanced image quality in most venous districts, allowing for clearer delineation of vessel size and morphology. This may provide a significant advantage in complex cases where precise anatomical assessment is critical.

These results are consistent with two smaller non-randomized studies that compared CO_2 venography with ICM venography outside the CIED context[6,7] and are further supported by evidence from interventional procedures involving CO_2 upper limb venous system venography.[8]

Winters *et al.*[5] previously evaluated CO_2 venography in 23 patients undergoing revision of existing pacemaker or ICD systems, though without ICM comparison. Additionally, Okubo *et al.*[9] reported two successful cases of CO_2 coronary sinus angiography in patients undergoing cardiac resynchronization therapy. Despite the challenges associated with DSA techniques and severe motion artefacts, instructing breath-hold to the patient enabled image acquisition sufficient for catheter guidance. Thanks to its unique properties, CO_2 enables safe, efficient delivery of large, undiluted boluses, enhancing the visualization of high-capacity central veins often sub-optimally assessed by ICM. This may be particularly valuable in CIED procedures, especially in complex cases requiring precise periprocedural planning for contralateral implantations.

In this study, 6.7% of patients developed CIN despite guidelines prophylactic hydration. No CO_2-related adverse events were observed in this study. The most common CO_2-related complication reported in literature is brief injection-site pain, attributed to the explosive delivery of compressed gas; however, the use of an automated injection system in this study likely mitigated this and automated delivery minimizes the risk of air contamination, gas embolism, and intrapulmonary vapour lock.[10]

Study limitation

This study is limited by its single-centre design and moderate sample size, which may restrict the generalizability of the findings. A larger cohort and a parallel-group design would be necessary to more rigorously assess safety outcomes. Moreover, image interpretation was performed by two expert electrophysiology technicians, potentially introducing reviewer bias.

Conclusions

Carbon dioxide venography represents a feasible and safe alternative to ICM in CIED procedures, with post-processing stacking software further enhancing image quality.

Further studies are warranted to validate its broader clinical applications, such as coronary sinus imaging, identify patient populations that may benefit most, and evaluate its potential for reducing CIN.

Conflict of interest: none declared.

Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

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