

Accuracy and Safety of Carbon Dioxide Inferior Vena Cavography¹

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Index terms: Carbon dioxide • Venae cavae, angiography

JVIR 1999; 10:1183-1189

Abbreviations: CO₂ = carbon dioxide, DSA = digital subtraction angiography, IVC = inferior vena cava

PURPOSE: The purpose of this study was to assess the accuracy of carbon dioxide compared to iodinated contrast material for determining inferior vena cava (IVC) diameter prior to filter placement, and to assess the safety of CO₂ when used for this purpose.

PATIENTS AND METHODS: Consecutive patients undergoing inferior vena cavography prior to filter placement were prospectively evaluated with use of both CO₂ and iodinated contrast material. The diameter of the IVC was measured and compared in the same four locations in each patient for both agents. The diameter was corrected for magnification and pin-cushion distortion. The ability of CO₂ to correctly classify IVC diameter as ≤ 28 mm or > 28 mm, based on the IVC diameter with iodinated contrast material, was determined. A consensus panel assessed renal vein visualization with CO₂ and iodinated contrast material. Blood pressure and arterial oxygen saturation were measured immediately before and after CO₂ injection.

RESULTS: Among 30 patients, there was no significant difference in the measured diameter of the IVC with CO₂ versus iodinated contrast material after correction for magnification and pin-cushion distortion. One of 30 patients (3.3%) in this study was misclassified as having an IVC ≤ 28 mm with CO₂ when, in fact, the IVC diameter was > 28 mm based on iodinated contrast material. This could be clinically significant for certain IVC filters. Forty-seven percent of renal veins identified on contrast venography were identified by CO₂ vena cavography. There was no significant difference in the blood pressure or oxygen saturation values measured before and after CO₂ injection. However, one patient with pulmonary artery hypertension did experience transient, symptomatic hypotension after CO₂ injection.

CONCLUSIONS: In most patients, CO₂ vena cavography accurately evaluated IVC diameter prior to filter placement. In 3.3% of patients, the discrepancy in measurements between CO₂ and iodinated contrast material could be clinically significant, depending on the type of filter placed. CO₂ was less accurate than iodinated contrast material in identifying renal veins. Although CO₂ vena cavography is safe in the majority of patients, it should be used with caution in patients with pulmonary hypertension.

IODINATED contrast material has traditionally been used for imaging of the inferior vena cava (IVC) prior to filter placement. Vena cavography of the IVC is performed prior to filter placement for four reasons: (i) measuring the IVC diameter, (ii) determining renal vein location, (iii)

diagnosing intracaval thrombus, and (iv) identifying venous anomalies. This information guides the location and type of filter placed. Accurate evaluation and sizing of the IVC is important to prevent filter malposition or migration.

During the past decade, the use

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of CO₂ as a contrast agent for diagnostic arterial and venous imaging has become well-established (1–8). Recently, CO₂ has been used for inferior vena cavography in patients with contraindications to contrast agents. Compared to nonionic iodinated contrast material, CO₂ is less expensive and without the risk of anaphylactoid reaction. It is also without the risk of renal injury, except possibly in the case of repeated injections into the renal artery. Concerns remain, however, regarding the accuracy of CO₂ angiography for vessel sizing (4,6). In a previous report, poor opacification with CO₂ prior to filter placement led to underestimation of IVC diameter compared to that obtained with use of iodinated contrast material (6). This study assesses the safety and the accuracy of CO₂ venography in determining IVC diameter prior to filter placement.

PATIENTS AND METHODS

This was a prospective trial. All patients undergoing IVC venography prior to filter placement at a single, tertiary care medical center between 5/15/94 and 8/25/95 were offered the opportunity to participate. All enrolled patients underwent inferior vena cavography with use of both CO₂ and iodinated contrast material. The Institutional Review Board approved the protocol. Informed consent was obtained from all patients. Exclusion criteria included patients who were unable to receive iodinated contrast material because of renal insufficiency or severe contrast material allergy, or because of the inability of the patient to give their own informed consent. Patients who were not enrolled, but who underwent CO₂ vena cavography, were assessed for filter migration by comparing the level of fluoroscopically guided deployment to an abdominal radiograph obtained after filter placement. Nineteen men and 11 women were enrolled in the study, who ranged in age from 24 to 85 years.

CO₂ was hand-injected as a 50–60-mL bolus via a 60-mL syringe as

rapidly as possible. All syringes were flushed with CO₂ several times before use via a three-way stopcock to purge the syringe of room air. Syringes were filled with the positive pressure in the CO₂ cylinder, not by active withdrawal of the syringe plunger. To achieve this, the valve of the cylinder was only partially opened, as exposure of the syringe to the full pressure in the cylinder resulted in rapid expulsion of the plunger from the syringe. At no time was the tubing from the CO₂ cylinder connected directly to the patient, or to a stopcock connected to the patient. This precaution was taken to avoid the possibility of inadvertent injection of large volumes of CO₂ into the patient. The carbon dioxide used was instrument grade, 99.99% pure CO₂ (Keystone Airgas, Radnor, PA).

Because CO₂ is a compressible gas, an uncertainty with this method of CO₂ injection is the exact amount (ie, number of moles) of CO₂ in the syringe and injected into the patient at atmospheric pressure. There is some variability in the pressure used to fill the syringe, resulting in different amounts of gas. However, the maximum pressure in the syringe, and therefore the maximum amount of gas that could be injected, is determined by the pressure required to displace the plunger out of the syringe. Knowledge of this pressure limit permits a calculation of the ratio of moles of CO₂ at ambient pressure to that at the pressure that displaces the plunger from the syringe. Because $PV = nRT$ (where P = pressure, V = volume, n = number of moles, R = universal gas constant, and T = temperature) by Boyles Law, and the volume (V) of the syringe is constant, the number of moles at maximum syringe pressure (N_p)/number of moles at ambient pressure (N_a) = maximum syringe pressure (P_p)/ambient pressure (P_a). This pressure limit, P_p was determined experimentally. The syringe pressure was monitored while it was filled with CO₂ in the routine fashion until the plunger was expelled from the syringe. The pressure required to expel the plunger

was recorded. This procedure was repeated three times and the average of the three pressures used to determine P_p .

The vena cavogram was obtained with use of a 5-F calibrated pigtail catheter (Cook, Bloomington, IN). The pigtail was placed near the confluence of the iliac veins (Fig 1). The iodinated contrast material study was performed before the CO₂ study. CO₂ vena cavography was performed using digital subtraction angiography (DSA), with a filming rate of three frames per second. For iodinated contrast material, the choice of using DSA versus film screen was at the discretion of the attending interventional radiologist. For film screen technique, the injection rate of contrast material was generally 25 mL per second (mL/sec) for a total of 50 mL. For DSA, 20 mL/sec for a total of 40 mL was typically injected. All studies were performed in the posteroanterior projection with the patient in the supine position. Image acquisition for both film screen and DSA was generally at three frames per second. The studies were performed in two angiography suites, one room with a 9-inch image intensifier and the other with a 14-inch image intensifier.

The patient's oxygen saturation was monitored with pulse oximetry (Nellcor; Puritan Bennett, Pleasanton, CA) and the blood pressure with an automated blood pressure cuff (Dinamap; Criticon, Tampa, FL). These values were measured immediately before and after CO₂ injection. The safety of CO₂ vena cavography was determined by comparing pre- and post-CO₂ injection blood pressure and oxygen saturation.

• Image Analysis

A single image that best opacified the IVC was chosen for all imaging analysis.

The same reference point was chosen for both the CO₂ and iodinated contrast material vena cavograms. Using this reference point as a guide, the same four infrarenal measurement points were

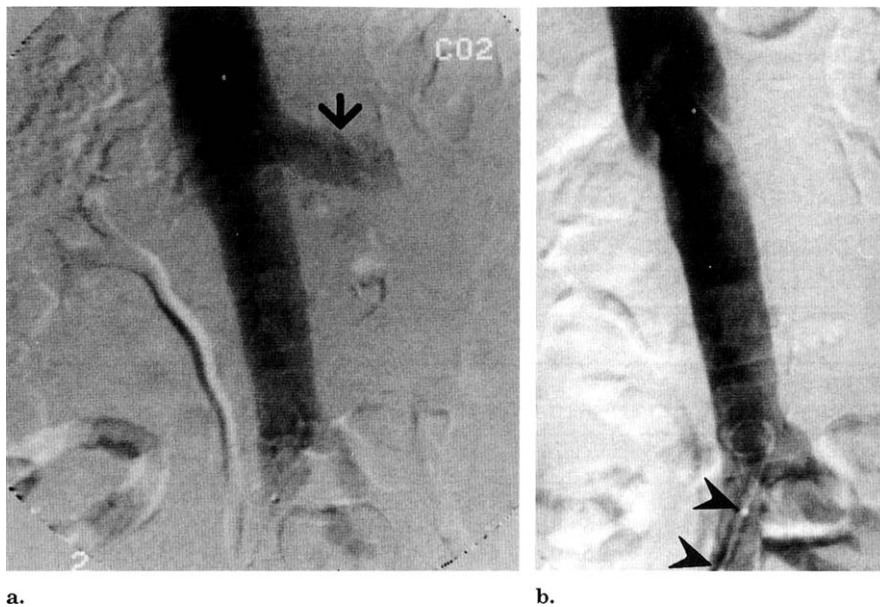


Figure 1. (a) CO₂ inferior vena cavogram. The left renal vein was well opacified in this patient (arrow). (b) Iodinated contrast material inferior vena cavogram in the same patient as (a). Note radiopaque calibration markers on the catheter (arrowheads). The markers located on the shaft of the catheter were typically in the periphery of the image, while the infrarenal IVC was in the center of the image.

chosen 2 cm apart for both the iodinated contrast material and CO₂ vena cavograms. An electronic caliper with a resolution of 0.01 mm (Digimatic, Mitutoyo, Japan) was used to measure the IVC diameter at the four points.

A consensus panel of three interventional radiologists reviewed each CO₂ and contrast material veno cavogram separately for visualization of the right and left renal veins using routine clinical criteria. This included actual opacification of the renal vein, as well as inflow of unopacified blood from a renal vein (Fig 1). The patient's name was obscured to prevent comparison of contrast agents.

Correction factors for magnification and pincushion distortion were determined. All IVC diameter measurements were corrected for magnification, which was calculated from the calibrated catheter. Digital subtraction images were corrected for pincushion distortion. Because the calibration markers for the inferior vena cavograms were routinely at the periphery of the image, whereas the infrarenal IVC mea-

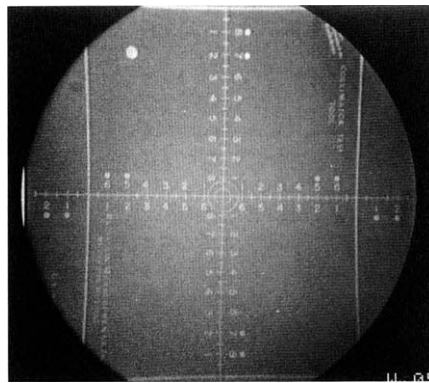


Figure 2. Grid phantom imaged with 14-inch image intensifier. The scale is in centimeters. Note distortion and magnification near the periphery of the grid relative to the center.

surement points were at the center of the image (Fig 2), correction was made for pincushion distortion. This was calculated from a 1-cm grid phantom by determining the ratio of the same unit of measurement at the edge versus the center of the grid phantom (Fig 2). The correction factor for the 14-inch image intensifier was 1.23 and for the

9-inch image intensifier was 1.37. This was applied to all digital images, except in two patients. Both of these patients were accessed from an internal jugular approach and the markers on the sizing catheter were in the middle of the field, obviating the need for this correction.

• Data Analysis

Differences in the IVC diameters between CO₂ and iodinated contrast material were analyzed using the paired *t* test, with and without correction for pincushion distortion. All of the latter images were corrected for magnification. A separate analysis with the paired *t* test was performed comparing CO₂ and iodinated contrast material IVC diameters for patients in whom DSA was used to image the iodinated contrast material vena cavogram. These images were corrected for magnification, but not pincushion distortion.

The differences in pre- and postinjection oxygen saturation and blood pressure were analyzed using the paired *t* test. Significance was defined as $P < .05$.

A large IVC was defined as having a diameter greater than 28 mm on the iodinated contrast material study. A normal IVC was defined as less than or equal to 28 mm in diameter on the iodinated contrast material study. The percentage of patients undersized by CO₂ was calculated as those with a large IVC as determined with use of iodinated contrast material, but classified as normal as determined by CO₂/total number of patients in study ($N = 30$) $\times 100$.

RESULTS

During the study period, a total of 110 inferior vena cavograms were performed prior to filter placement. Eighty of 110 patients were not enrolled (30 refused, 32 were unable to give their own consent, 14 had contraindications to iodinated contrast material, and four for miscellaneous reasons including DSA malfunction). A total of 30 patients

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were enrolled. For iodinated contrast material, film screen technique was performed in 20 patients and DSA was performed in the other 10 patients. Twenty-five Greenfield filters and five Bird's Nest filters were placed. The Greenfield filter was placed preferentially. At the time of this study, prior to the availability of the over-the-wire stainless-steel Greenfield filter, the Bird's Nest filter was preferred for left sided insertion by some operators. The Bird's Nest filter was placed because of operator preference (one) and insertion via left common femoral vein (four).

The maximum pressures required to expel the plunger from the syringe were 318, 323, and 323 mm Hg above ambient pressure (mean, 321 mm Hg). Using Boyle's Law, the amount of CO₂ in the syringe at this maximum pressure was calculated: $N_p/N_a = P_p/P_a = 760 + 321/760 = 1.42$ (atmospheric pressure is 760 mm Hg). Therefore, when injecting 60 mL of CO₂ in the syringe used in this study, up to $1.42 \times 60 \text{ mL} = 85.2 \text{ mL}$ of ambient pressure CO₂ was injected into the patient.

There was no statistically significant difference in the blood pressure or oxygen saturation measured before and after CO₂ injection (**Table 1**). The mean systolic blood pressure before injection was 129 ± 17 (range, 105–157), compared to 124 ± 20 (range, 92–158), after injection $P = .65$. The mean diastolic blood pressure before CO₂ was 66 ± 12 (range, 44–85), compared to a mean of 63 ± 10 (range, 38–73) $P = .9$ after CO₂ injection. The mean oxygen saturation was $100\% \pm 1$ (range, 94–100) before CO₂ injection and $99\% \pm 2$ (range, 94–100) after injection $P = .79$.

One patient with a history of scleroderma and severe pulmonary artery hypertension had a 14 mm Hg decrease (130/65 to 116/65) in systolic blood pressure immediately after CO₂ injection. The patient tolerated the contrast material venogram earlier without evidence of adverse reaction or change in hemodynamics. Shortly thereafter, during filter insertion, the patient

Table 1
Cardiopulmonary Sequelae

	Pre CO ₂	Post CO ₂	P Value
Systolic BP (range)	129 ± 17 (105–157)	124 ± 20 (92–158)	.65
Diastolic BP (range)	66 ± 12 (44–85)	63 ± 10 (38–73)	.90
O ₂ Saturation (range)	100 ± 1 (94–100)	99 ± 2 (94–100)	.79

Table 2
Diameters without Correction for Pincushion Distortion

Measurement Point	CO ₂	IC	P value
A*	16.16 ± 2.77	18.66 ± 3.12	.0026
B*	15.65 ± 3.22	17.97 ± 3.45	.0027
C*	15.70 ± 3.44	18.35 ± 2.91	.0023
D*	17.84 ± 4.11	19.45 ± 3.37	.0035
Overall	16.34 ± 3.50	18.61 ± 3.23	$P < .0001$ overall

* A is most cephalad, with B–D progressively more caudal.

became obtunded. These symptoms were likely multifactorial in origin because the patient also received one unit of fresh frozen plasma and intravenous sedation, but were likely in part related to the CO₂ injection. She recovered without sequelae. The systolic blood pressure of four other patients decreased by more than 10 mm Hg immediately after injection of the CO₂ but they remained stable and otherwise asymptomatic. None of these patients had a history of pulmonary hypertension, although one was asthmatic. Other than the patient with scleroderma described previously, no other patient experienced symptoms related to the injection of CO₂.

Without correction for pincushion distortion, the IVC diameters at the four points of measurement with CO₂ were significantly less than with iodinated contrast material (**Table 2**). However, when CO₂ was compared to only those iodinated contrast material images produced with DSA, there was no significant difference in the IVC diameter (mean for all points measured 17.69 ± 3.12 for iodinated contrast material vs. 17.14 ± 3.59 for CO₂; $P = .23$). This suggested that the

difference was imaging, not contrast dependent, which lead to estimation of the pincushion distortion in the digital imaging systems with the grid phantom. After correction for pincushion distortion, the IVC diameter measured with CO₂ was not statistically different from iodinated contrast material (**Table 3**). Application of the correction factor for pincushion distortion can overcorrect and cause an overestimation of the IVC diameter. This overcorrection is due to the method of calculating the correction factor. The correction is calculated from the size ratio of a fixed length at the periphery and center of the image. If the catheter calibration markers are more central rather than at the extreme periphery of the image field, or if the point of IVC measurement is slightly off center, the correction factor will then overestimate the IVC diameter. This probably accounts for the fact that, in some cases, the IVC diameter was larger with CO₂ than with iodinated contrast material. Because this correction was applied to all CO₂ vena cavograms and only the DSA iodinated contrast material cavograms, there was a greater increase in caval diameter after correction for

Table 3
Diameters with Correction for Pincushion Distortion

Measurement Point	CO ₂	IC	P value
A*	20.15 ± 3.32	20.00 ± 3.34	.77
B*	19.45 ± 3.38	19.31 ± 3.96	.83
C*	19.56 ± 3.92	19.73 ± 5.53	.76
D*	22.28 ± 5.10	20.93 ± 4.39	.07
Overall	20.36 ± 4.1	19.99 ± 3.83	.24

* A is most cephalad, with B–D progressively more caudal.

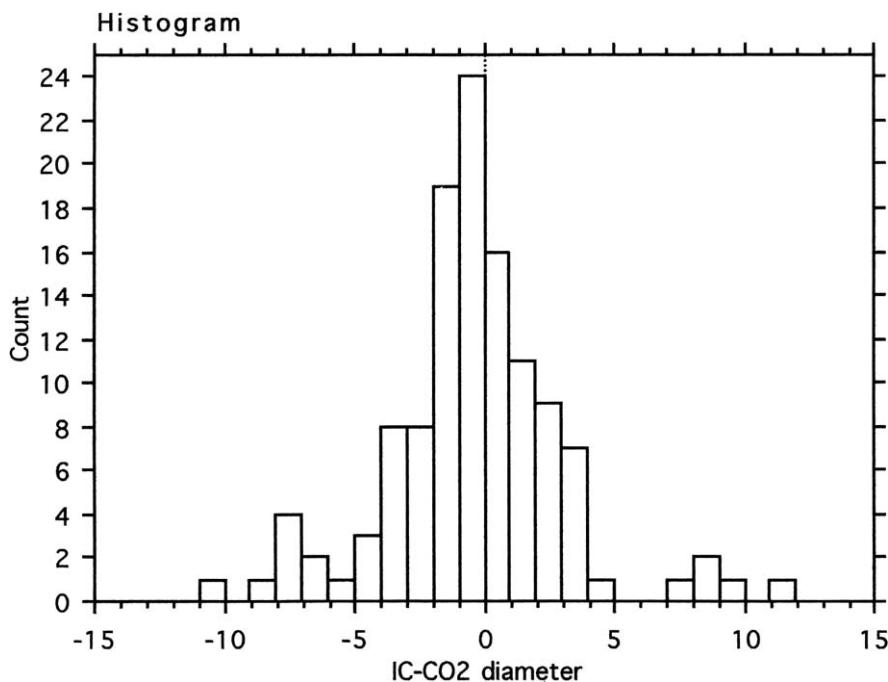


Figure 3. Distribution of the differences in diameters (mm) as measured with CO₂ and iodinated contrast material, calculated by iodinated contrast-CO₂.

pincushion distortion in the CO₂ cavograms than with the iodinated contrast material studies. The distribution of differences between the IVC diameter as measured by iodinated contrast material and CO₂ are displayed in **Figure 3** (this graph contains 30 patients × four measurements/patient = 120 measurements). The mean was -0.37 , with a standard deviation of 3.43 .

The consensus panel review of iodinated contrast material vena cavograms identified two renal veins in 25 patients and one renal vein in five patients. Thus, all patients had at least one renal vein identified with iodinated contrast material. On the CO₂ vena

cavogram, the panel identified 26 of the 55 (47%) renal veins seen on the contrast material vena cavogram, with 16 of 30 patients having at least one renal vein identified. No accessory renal veins were identified on either the contrast material or CO₂ vena cavography. No routine attempt was made to selectively catheterize the renal veins. The panel identified a filling defect on a film screen iodinated contrast material vena cavogram but not on the CO₂ vena cavogram in one patient. After review by the panel, this discrepancy was further investigated by reviewing the final dictated report, and all available images from the inferior vena

cavograms. The official report of this patient noted that filling defect changed in appearance and, therefore, was not believed to represent a thrombus. The consensus panel agreed with this interpretation.

Sixty patients not enrolled in the study had IVC filters placed with use of CO₂ only. There were no immediate filter migrations in any of these patients.

Two patients had large IVCs. One had a diameter of 35.85 mm as determined with use of iodinated contrast material, and was incorrectly classified as normal with a diameter of 27.45 mm as determined with use of CO₂. The second had a diameter of 30.44 mm as determined with use of iodinated contrast material, and was correctly classified as large with a diameter of 31.71 mm as determined with use of CO₂. Therefore, one of 30 (3.3%) patients in the study had large IVCs that were incorrectly classified as normal by CO₂.

DISCUSSION

• Accuracy

To accurately image a vessel, CO₂ must replace all or most of the blood volume. Unlike iodinated contrast material, once CO₂ dissolves in blood, its ability to act as a contrast agent is lost. With an inadequate volume of CO₂ and/or too slow a rate of injection, the buoyant property of CO₂ will cause it to layer along the nondependent surface of the vessel. The full diameter of the vessel could, therefore, be underestimated or the intraluminal pathology could be unrecognized. The method of CO₂ injection in the current study introduces operator-dependent variability in injection rate. Controlled bolus injections with a dedicated CO₂ injector may minimize this problem. Such an injector was not available during the current study.

Nonetheless, this study demonstrates that with correction for magnification and pincushion distortion, the diameters obtained with CO₂ and iodinated contrast mate-

rial were quite close in most cases. Pincushion distortion is an artifact inherent to digital imaging not seen in flat film-screen geometry (9). The convex image intensifier input screen causes pincushion distortion, with objects near the edge of the screen being more magnified than objects near the center. A grid phantom was used to measure the pincushion distortion of the two image intensifiers used in this study, and a pincushion distortion correction factor was calculated for each image intensifier. This is not a perfect correction because not all of the IVC measurements were directly in the center of the field. In addition, not all of the calibration markers were at the extreme periphery of the images. However, it is a close approximation because the infrarenal IVC was always placed at the center of the image, and the catheter was placed with the pigtail at the iliac vein-IVC confluence. This positioned the calibration markers of the catheter near the periphery of the image. Without correction of pincushion distortion, there was significant underestimation in the IVC diameter as measured on DSA. Correction for pincushion distortion reduced the difference in the measured diameters between CO₂ and iodinated contrast material.

This information can be applied to clinical practice. If the calibration object is near the periphery of a digital subtraction image, and the vessel to be measured is near the center of the image, this inherent distortion should be corrected. This problem exists whether the contrast agent is CO₂ or iodinated contrast material. One method of correction is that used in this study. This requires the use of a grid phantom and calculation of the pincushion distortion for each image intensifier. Another way to compensate for this distortion is to place the calibration object near the point of measurement. When placing a filter from the jugular approach, the calibration markers will be in the infrarenal IVC near the point of filter placement. When placing the filter from the common femoral vein, a method of compensation for this dis-

ortion is to advance the calibration markers to the point of vessel measurement, and obtain a digital radiograph with all other parameters unchanged from the digital subtraction vena cavogram. This single radiograph can be used for calibration, and the digital subtraction vena cavogram can be used for vessel measurement. This technique was not used in the current study because the degree of pincushion was not appreciated until after the study was completed and the data were analyzed.

However, some caution should be exercised when using CO₂ to measure IVC diameter. Although diameters measured with CO₂ and iodinated contrast material did not differ significantly after correction for pincushion distortion, 3.3% of patients in this study were misclassified as having normal-sized IVCs with CO₂ (<28 mm), when, in fact, the IVC diameter was larger than 28 mm when determined with use of iodinated contrast material. Because of this inaccuracy, CO₂ cannot be recommended for routine evaluation of the IVC prior to filter placement. In cases in which iodinated contrast material represents a significant risk, CO₂ may play a role. For the purpose of IVC filter placement, overestimation of IVC diameter does not pose a clinical risk. However, underestimation of IVC diameter could result in migration of an undersized filter. Thus, when the IVC diameter measured with CO₂ is close to the maximum for a particular filter, it is advisable to confirm the measurement by another means, such as iodinated contrast material or intravascular ultrasound. Alternatively, a filter with a greater maximum diameter could be selected in these circumstances.

This study was not designed to assess diagnostic accuracy; the population size did not provide a sufficient number of abnormal studies. Nevertheless, some observations can be made. The ability of a panel of radiologists to identify normal anatomy could be assessed. Of 55 renal veins identified on iodinated contrast material venography, only 26 were identified on review of the

CO₂ venograms. Thus, it is possible that renal vein anomalies could be missed with CO₂ inferior vena cavography. However, this can occur with iodinated contrast material, and some advocate selective renal venography to detect renal vein anomalies (10). When using CO₂ alone for evaluation of the IVC prior to filter placement, selective renal venography could be performed. Despite this limitation, 60 IVC filters were safely placed with CO₂-guided imaging alone without routine renal venography. During our experience, we noted that the level of renal vein inflow is often easier to identify on cine viewing of the digital subtraction angiogram, rather than the final static images. However, only static images were available for review by the consensus panel.

• Safety

CO₂ is 20 times more soluble in blood than oxygen, permitting rapid dissolution and expiration of the gas during the first pass through the lungs (11). Despite this, imaging during upper extremity venography often demonstrates CO₂ in the right atrium, ventricle, and pulmonary artery (6). This suggests its presence is well tolerated in most patients. Previous studies have shown the safety of intravenous injections of large amounts of CO₂, initially performed for evaluation of pericardial effusions (11–13). Unlike the current study, however, evaluation of pericardial effusions involved trapping CO₂ in the right atrium by placing the patient in the left lateral decubitus position. This could have added a margin of safety, permitting dissolution of CO₂ into blood before entry into the pulmonary artery and allowing for blood flow underneath the trapped gas into the right ventricle. With the patient in a supine position, large volumes of CO₂ may accumulate in the anteriorly positioned pulmonary artery, causing vapor lock and resulting in right ventricular overload with pump failure. Cardiovascular collapse has been reported from embolism of a large volume of CO₂

during laparoscopic surgery (14). In the current study, one patient with a history of severe pulmonary artery hypertension developed delayed transient systemic hypotension after, and likely in part related to, the CO₂ injection. The underlying pulmonary hypertension and compromised right ventricular function likely made her more susceptible to hemodynamic compromise from the CO₂ injection. There was no significant compromise in blood pressure or oxygen saturation in any other patient in the current study. Based on this experience, intravenous CO₂ injections of the volume used in this study should be performed with caution in patients with a significant history of pulmonary hypertension or right-sided heart failure. In any patient, the risk of significant gas trapping depends on the volume of CO₂ injected and the time interval over which it is injected. If multiple large injections are required, fluoroscopy over the chest should be done to evaluate clearance of the CO₂ from the right atrium, right ventricle, and main pulmonary arteries between injections.

There are a number of limitations of this study. The consensus panel reviewed only static images. In practice, renal vein inflow and reflux are seen intermittently and are better appreciated on cine review of digital images, suggesting that the panel review of this study may underestimate the ability of both contrast material and CO₂ venography to identify renal veins. Another factor, which complicated the study, was the use of both film screen and DSA to image the iodinated contrast material cavograms. The degree to which pincushion distortion would alter the measurements was not appreciated at the outset of the study. However, this

finding serves as a reminder to account for this distortion when making measurements with DSA. The lack of abnormal IVCs was also a limitation of this study. It was not possible to assess the ability of CO₂ to accurately diagnose the range of abnormalities possible in the IVC.

CONCLUSION

CO₂ inferior vena cavography is safe and adequate to evaluate the IVC diameter in most cases. However, some restrictions should be placed on its use. CO₂ vena cavography is not as accurate as iodinated contrast material vena cavography for identification of the renal veins and additional maneuvers, such as selective renal venography, may be required. In 3.3% of patients in this study, the discrepancy in IVC diameter between iodinated contrast material and CO₂ could potentially be of clinical importance when placing filters with a maximum IVC diameter of 28 mm. Caution is advised when injecting intravenous CO₂ into patients with pulmonary artery hypertension.

Acknowledgment: The authors wish to thank Andrew Maidment, PhD, for calculating the pincushion distortion correction factors.

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