Carbon Dioxide as a Venous Contrast Agent: Applications in Interventional Radiology

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Purpose: To evaluate the safety and usefulness of carbon dioxide (CO$_2$) as a venous contrast agent for upper-arm placement of peripherally inserted central venous catheter (PICC), vena caval filter placement, and for visualization of the portal vein in transjugular intrahepatic portosystemic shunt (TIPS).

Materials and Methods: About 20–30ml of CO$_2$ was used as an alternative to iodinated contrast material for digital subtraction angiography (DSA) and fluoroscopy to guide upper-arm placement of PICC in 46 patients, for inferior venacavogram before filter placement in five, and for visualization of the portal vein during TIPS in two. Vital signs, peripheral arterial oxygen saturation, and renal function were checked during and after delivery of CO$_2$.

Results: All CO$_2$ DSA for PICC placement clearly delineated patency or stenosis of the central veins. In 41 of 46 patients (89%), PICC placement with CO$_2$ guidance was successful. The mean number of venipunctures for PICC placement was 1.9, and the mean volume of CO$_2$ injected for venipuncture was 35ml. In five patients, Titanium Greenfield filters were successfully implanted into the inferior vena cava following CO$_2$ vena cavography. In two patients in whom hepatopetal portal flow was seen on indirect portography, the portal vein was visualized by CO$_2$-wedged hepatic venography. Injection of CO$_2$ into the splenic vein following TIPS placement revealed shunt patency. Vital signs and oxygen saturation did not change, and there was no evidence of renal toxicity following CO$_2$ injection.

Conclusion: CO$_2$ is a safe and useful alternative contrast agent for upper-arm placement of PICC, pre-filter placement cavography, and wedged hepatic venography and portography for TIPS.

Index Words: Carbon dioxide
Angiography, contrast media
Digital subtraction angiography
Venography
Veins, interventional procedure

During recent decades, the role of vascular/interventional radiology has increased and in various diseases it is now the preferred treatment.

In most diagnostic and interventional radiologic procedures, contrast material is required; although iodinated contrast media are only slightly toxic and are tolerated by the patient, their use is relatively contraindicated in patients with renal insufficiency and a history of contrast reaction. In the 1950s, CO$_2$ was used as an intravenous contrast medium to detect pericardial effusion (1, 2), and with the advent of digital subtraction angiography (DSA) in the 1980s, it has become a useful alternative to iodinated contrast...
medium for abdominal and peripheral arteriography (3). Because of its lack of renal toxicity and allergic reaction and the possibility of using large amounts, CO2 is thought to be an ideal contrast agent in vascular and interventional procedures. The utility of CO2 as a venous contrast agent is still not widely known, however.

We prospectively evaluated the safety and usefulness of CO2 as a venous contrast agent in upper-arm placement of peripherally inserted central venous catheter (PICC), in inferior vena cavography before filter placement, and in wedged hepatic venography and direct portography during transjugular intrahepatic portosystemic shunt (TIPS) procedure.

**Materials and Methods**

Between February 1994 and July 1994, CO2 was used to guide PICC placement in 46 patients, vena caval filter placement in five, and for visualization of the portal vein during TIPS in two. Because in some cases an intravenous CO2 injection is not definitely safe, patients with compromised pulmonary function, asthma and diabetes were excluded from this study.

**PICC placement**

Forty six patients, 20 men and 26 women, underwent CO2-guided PICC placement. Their ages ranged from 13 to 86 (mean, 50) years. Clinical indications were antibiotic therapy (n=18), pancreatitis, osteomyelitis and other infectious diseases), chemotherapy (n=9), lymphoma, leukemia and other malignancies), hyperalimentation (n=6), Crohn’s disease, deep vein thrombosis and pancreatitis), long-term intravenous hydration (n=1), chronic renal failure) and a combination of indications (n=12). Six patients were at increased risk with iodinated contrast medium, and ten were known to be allergic to this.

The technique for PICC placement has been previously described (4). In the supine position, the patient’s non-dominant arm was used for access, whenever possible. To minimize compression and explosive delivery of CO2, 5—10ml of the gas was injected just before delivery of a further 20—40ml for DSA of central veins to image patency of the subclavian and innominate veins, and the superior vena cava (Fig. 1). The upper arm was then prepared and draped in a sterile fashion; the puncture site in the middle one-third of the upper arm was selected under fluoroscopy during more peripheral injection of small quantities of CO2, and was anesthetized with 2% xylocaine. The target vein, usually basilic or brachial, was punctured with a 21-gauge needle (Micropuncture set, Cook Inc., Bloomington, U.S.A.) under fluoroscopic guidance during slow peripheral CO2 injection via an intravenous line at the wrist joint. When venous spasm developed during venipuncture, 100μg of nitroglycerine was injected into the vein. After the target vein was punctured, a 0.018inch, 60cm long, guidewire was introduced into the central vein. After removal of the needle, a 5.5 Fr peel-away sheath with dilator was inserted over the guidewire. Optimal PICC length was measured by passing the guidewire to the junction of the superior vena cava and right atrium, and the PICC was then cut to the length traversed by the guidewire. This and the dilator were then removed, and the PICC was introduced through the peel-away sheath; its tip was placed at the junction of the superior vena cava and right atrium. The sheath was then peeled away and the wings at the PICC hub were anchored to the skin with sutures. The PICC was then flushed with 10ml of normal saline containing 1,000 units of heparin, and was covered with an occlusive dressing. Finally, the optimal position of the PICC was confirmed by chest radiography (Fig. 1). The PICC kits used for this study were 5 Fr single lumen (Cook Inc., Bloomington, U.S.A.) or 4.5 Fr double lumen kits (HDC corporation, San Jose, U.S.A.). A 60-ml syringe, connected to a closed system—which included a manifold (Morse Manifold, NAMIC, Medical Production Division, NY, U.S.A.) for delivery of CO2, and a three-way high pressure stopcock for infusion of heparinized saline—was used to obtain CO2 from the CO2 cylinder (Airco Cylinder Operation, Ann Arbor, U.S.A.). Microfilters (effective for 0.2μm, Gelman, Ann Arbor, U.S.A.) were placed between the cylinder and syringe to ensure sterility of the gas. Vital signs including pulse rate, arterial oxygen saturation, blood pressure and ECG were monitored during the procedure. Post-procedural serum creatinine level was compared to its pre-procedural values.

The success rate of PICC placement, the number of venipunctures made to obtain venous access and the volume of CO2 for venipuncture were recorded. The quality of fluoroscopic CO2 images of the target veins and of CO2 DSA images of the central veins were evaluated by the authors. After completion of the procedure, the patients were asked about any discomfort or pain during CO2 injection.

**Inferior vena cavography**

Five patients underwent CO2 venacavography before filter placement; four were men and one was a woman, and their mean age was 51 (range 40—76)
years. In all five, deep vein thrombosis in the lower extremities was demonstrated or suspected on Doppler imaging, or clinically.

After puncturing the femoral vein, a 5 Fr pigtail catheter (Cook Inc., Bloomington, U.S.A.) was introduced with its tip at the bifurcation area of the inferior vena cava. Using DSA at 5 exposures/sec, and with an injection of 40ml CO₂, this vein was then examined in the supine position. After confirmation of caval patency and renal vein level, Titanium Greenfield filters (Meditech Inc., Watertown, U.S.A.) were implanted in the inferior vena cava under fluoroscopic guidance (Fig. 2).

CO₂ DSA was evaluated for caval patency, intraluminal thrombus and renal vein level.

**TIPS**

Wedged hepatic CO₂ venography was performed for visualization of the portal vein during TIPS procedure in two men with a history of obstinate gastroesophageal variceal bleeding. After puncture of the right internal jugular vein, the right hepatic vein was catheterized and wedged with a 5 Fr Torcon NB Advantage catheter (Cook Inc., Bloomington, U.S.A.). To evaluate the patency and anatomy of the portal vein, wedged DSA of the hepatic vein was then performed at an imaging speed at 5 exposures/sec to evaluate patency and anatomy of the portal vein; 20ml CO₂ was hand injected. After wedged hepatic venography, TIPS procedure was performed. To evaluate shunt patency, post-TIPS portography at the same imaging speed was performed; 40ml CO₂ was hand injected via a 5 Fr catheter (Fig. 3). Vital signs were monitored, and post-procedural serum creatinine level was compared to its pre-procedural value.

![Fig. 1. CO₂ guided placement of peripherally inserted central venous catheter (PICC) in 53 year-old man with metastatic colon cancer](image-url)

A. CO₂ DSA obtained with hand injection of 20ml CO₂ shows patent right subclavian (S) and innominate veins (RI) and superior vena cava (SVC). Note reflux of CO₂ into left innominate vein (LI).

B. A 105mm spot film was taken during peripheral injection of CO₂ before venipuncture at the level of middle one-third of upper arm. Note filling of the medial basilic vein with CO₂ (arrows).

C. Subclavian venogram with iodinated contrast material in a different patient who had undergone Hickman placement shows occluded left innominate vein (large arrow) and collateral circulation (small arrows).

D. CO₂ DSA (the same patient of C) also shows occlusion of left innominate vein.

E. Chest radiograph taken after PICC placement shows the tip of the PICC at the junction of the SVC and right atrium (arrow).
Results

**PICC placement**

In all patients, CO$_2$ DSA demonstrated the central veins; in three, stenosis of the innominate vein or thrombosis of the subclavian vein, and associated collateral veins were delineated; these findings correlated well with the contrast venograms(Fig. 1). In 41 of the 46 patients PICCs were successfully placed (89 %). The mean number of venipunctures needed to gain venous access was 1.9, and the mean volume of CO$_2$ injected to visualize the target vein during venipuncture was 35ml (range, 5−300 ml). There was no significant change in vital signs and arterial oxygen saturation during and after CO$_2$ delivery. Increased serum creatinine levels following the procedure were not seen in any patients (Table 1). Five patients in whom

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**Fig. 2.** CO$_2$ venacavogram for filter placement in 48 year-old man with extensive deep vein thrombosis of lower legs

A. Pre-placement CO$_2$ venacavography obtained with hand injection of 40mL. CO$_2$ shows caval patency and reflux of the gas into left renal vein (arrow). There is no reflux of CO$_2$ into right renal vein.

B. Post-placement radiograph shows optimal placement of the Titanium Greenfield filter with the nose at level of superior endplate of L2.

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**Fig. 3.** Wedged hepatic venogram with CO$_2$ in transjugular intrahepatic portosystemic shunt (TIPS) in 55 year-old woman with gastroesophageal bleeding history

A. CO$_2$ wedged hepatic venography shows filling of the right and left portal radicles (asterisks). Note filling of the recanalized umbilical vein with CO$_2$ (arrow).

B. Portography after TIPS placement shows patency of the shunt (S) and evidence of hepatopetal portal venous (P) flow.
venipuncture using CO₂ failed, subsequently underwent successful PICC placement using iodinated contrast material.

Fluoroscopic CO₂ images of the vein targeted for venipuncture were rated by the authors as excellent (complete filling of target veins of normal caliber) in 39 %, good (incomplete filling of target veins of normal caliber) in 50 % and poor (incomplete filling of target veins of small caliber) in 11 %. DSA images of the central veins were rated as excellent (complete image of the subclavian vein) in 52 %, good (adequate image of the subclavian vein, but with incomplete filling of the venous lumen) in 39 % and poor (inadequate image of the subclavian vein, with incomplete filling of the venous lumen) in 9 %. Possible reasons for the failure in five patients of PICC placement with CO₂ were small veins, venous spasm and technical failure. Four patients in whom the intravenous catheter had not been properly pre-filled with CO₂ complained of pain and discomfort when CO₂ bolus was injected. No procedure-related death or evidence of renal failure following the procedure was observed.

**Inferior vena cavaography**

In all five patients, CO₂ DSA of the inferior vena cava demonstrated caval patency and the level of the renal veins; Green-field filters were subsequently placed. Vital signs and oxygen saturation did not change during and after the injection of CO₂, and no patient developed complications or renal failure following the procedures.

**TIPS**

In the two patients involved, wedged CO₂ DSA of the hepatic vein showed the portal veins and TIPS was successfully performed. Post-TIPS CO₂ portography demonstrated patency of the created shunt and portal venous system. Vital signs and oxygen saturation did not change during and after the injection of CO₂, and these patients did not complain of abdominal discomfort or pain during CO₂ injection. Neither complication nor renal failure developed following the procedure.

**Discussion**

According to our earlier study and experience, the usual dose of low osmolar iodinated contrast media (iodine content 240mg/ml) used for PICC and caval filter placement was about 50ml. Considering that the reaction to intravenous iodinated contrast medium is partly associated with the dose of contrast given(5, 6), this amount does not assure absolute safety.

CO₂, an injectable and rapidly absorbed gas, has several properties that make it an attractive alternative to iodinated contrast materials. It is nonallergenic, and the possibility of fatal hypersensitivity reactions is thus eliminated. Because it has no known nephrotoxicity, large quantities can be used for sequential studies without the risk of renal failure. The low viscosity of the gas (1/400 of iodinated contrast material) permits the injection of a large volume via a small catheter or needle (3, 7). Unlike contrast material, CO₂ does not usually require pre-procedural preparation involving hydration.

CO₂ has been used for the diagnosis of pericardial disease, with an antecubital injection of 50 or 60ml of the gas over a 2–3 second interval (2). In 1982 Hawkins described the clinical use of CO₂ as an arterial contrast agent, and since then it has also been used in DSA as a contrast medium in multiple organs (3, 7). A canine study (8) showed that a right atrial bolus of CO₂ usually disappeared within 15–30 seconds of injection, and it has also been demonstrated in dogs that intravenous injections of CO₂ at a rate of 100ml/min for a total volume of 10,000ml caused no demonstrable adverse effects (9). Clinical and experimental studies have also revealed that a relatively large amount of CO₂ can enter the right heart and pulmonary circulation without producing clinically significant pulmonary gas embolism (2, 10, 11). Because CO₂ is 20 times more soluble in blood than oxygen or air (11), the gas is rapidly dissolved in blood and exhaled through the lungs.

In our study, fluoroscopic imaging of the target vein with CO₂ was sufficient to guide percutaneous puncture of the vein in 89 % (41 of 46) of the patients. In 83 % of these, venipuncture was achieved after two trials. According to our earlier study and experience, this number of venipunctures is comparable to that obtained with iodinated contrast media(12). We found that a magnified fluoroscopic view was helpful for venipuncture of a small target vein. Intravenous nitroglycerine injection is helpful in preventing venous spasm as well as in relieving spasm during venipuncture. The five failures of PICC placement using CO₂ occurred at the early stage of this study, and could be attributed to relatively unskilled technique. Overall, however, the ability of CO₂ to visualize the target vein on fluoroscopy was considered as good to excellent.

In caval filter placement, pre-placement demonstration of caval patency and level of the renal veins is important; the results of our study showed that CO₂ DSA could delineate caval patency and renal veins.

Our study also showed that CO₂ can be used as a
good contrast agent during TIPS. Wedged hepatic venography showed simultaneous delineation of the portal vein, and this helps to guide puncture of the portal vein. A post-TIPS splenoportogram clearly visualized patency of the created shunt and splenoportal venous anatomy. The above results indicate that for all or part of the process, CO₂ can be used as a contrast agent for PICC placement, in cavography for filter placement and in TIPS. By reducing the amount of iodinated contrast media needed, the risk of hypersensitive reaction and nephrotoxicity can thereby be minimized.

Depending on whether CO₂ or iodinated contrast material is used, the appearance of DSA imaging is somewhat different. When injected into a peripheral vein, CO₂ tends to break and form gas bubbles, the appearance of which varies according to the amount of gas injected and the size of the vessels. To improve DSA imaging, a stacked imaging technique is helpful. An image of this kind is created by integrating multiple images into a single composite image using a stacking software program (8).

When performing CO₂ DSA with a bolus injection of gas, compression of CO₂ frequently results. This occurs when the catheter is filled with fluid, and as a result, a large volume of CO₂ is suddenly injected. This explosive delivery may cause discomfort to the patient and unsatisfactory filling of vessels (13), and to avoid its occurrence, a specially designed injection system or technique is required (14). This involves the injection of 5—10ml CO₂ into the catheter immediately before a bolus injection of the gas.

When multiple injections of CO₂ are required, a period of 3—5 minutes should be allowed to elapse between each injection in order to allow absorption of the gas. To promote transportation of CO₂ by the blood, the patient’s postion should be changed, especially when pain is felt after CO₂ injection. To prevent thrombus formation resulting from reflux of blood into the catheter, this should be flushed with heparinized saline immediately after injection of a CO₂ bolus.

Our study demonstrated that CO₂ is a useful venous contrast agent for upper-arm placement of PICC, pre-filter placement cavography, and wedged hepatic venography and splenoportography in TIPS. It is not only a contrast medium of choice in patients with renal failure or hypersensitivity to an iodinated agent, but also a useful alternative in venography and interventional procedures. With further investigation, the utility of CO₂ in vascular/interventional radiology is likely to increase.

References
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정맥조영제로서의 이산화탄소: 중재적 시술에서의 응용

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목적: 상완말초정맥을 통한 중심정맥도관삽입술, 하대정맥혈틀삽입술 그리고 경경정맥간내문맥간정맥단락술을 시행할 때 이산화탄소의 정맥조영제로서의 유용성과 안전성을 알아보고자 한다.

대상 및 방법: 상완말초정맥을 통한 중심정맥도관삽입환자 46명, 하대정맥혈틀삽입환자 5명 그리고 경경정맥간내문맥간정맥단락술환자 2명 등 총 53명의 환자에 대하여 상기 시술에 필요한 정맥의 전산화감산정맥조영술 (digital subtraction angiography) 및 X선투시에 이산화탄소를 조영제로 사용하였다. 모든 예에서 20-40ml의 이산화탄소를 1회용주사기를 사용하여 손으로 주입하였다. 시술후 시술성공률 및 조영제로 사용한 이산화탄소의 효능을 평가하였으며, 이산화탄소주입전후의 활력증후, 동맥산소포화 및 신기능의 변화들을 관찰하였다.

결과: 중심정맥도관삽입술에 앞서 시행한 이산화탄소중심정맥조영술상 중심정맥의 개통성 혹은 폐쇄여부를 정확히 알 수 있었다. 중심정맥도관삽입술을 시행한 46명중 41명 (89%)에서는 도관을 성공적으로 삽입하였다. 도관삽입을 위한 말초정맥의 천자회수는 평균 1.9회이었고 천자를 위하여 사용된 이산화탄소의 양은 평균 35ml이었다.

하대정맥혈틀삽입술에 이산화탄소 하대정맥조영술을 시행하여 하대정맥의 개통성과 신정맥의 위치를 확인하였던 5명에서는 모두 성공적으로 하대정맥혈틀을 삽입하였다. 경경정맥간내문맥간정맥단락술을 시행하기 전에 얻은 폐기정맥조영술 (wedged hepatic venography)상 문맥이 잘 조영되었으며 단락술 시행후 얻은 문맥조영술상 단락의 개통이 잘 묘출되었다. 모든 예에서 이산화탄소의 주입으로 인한 활력증후나 신기능의 변화 등 합병증은 발생하지 않았다.

결론: 이산화탄소는 말초정맥을 통한 중심정맥삽입술, 하대정맥혈틀삽입술, 그리고 경경정맥간내문맥간정맥단락술을 시행할 때 필요한 X선투시 및 전산화 감산정맥조영술에 안전하고 유용하게 사용할 수 있는 조영제이다.
아시아 지역 방사선과 의사의 국내 수련병원 Fellowship 안내

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