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AUTHOR NUMBER:	**1**
First Name	Kyung
Middle Initital	J.
Last Name	Cho
Suffix (Jr., III, etc.)	
Degrees	MD
Email address	kyungcho@med.umich.edu
Fax	
Phone	
Affiliation	
Title	
Department	Radiology
Institution	University of Michigan Medical Center
Street Address	
City	Ann Arbor
State or Province	Michigan, USA
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CO_2 as a Venous Contrast Agent: Safety and Tolerance

Kyung J. Cho
Department of Radiology, University of Michigan, Ann Arbor, Michigan, U.S.A.

INTRODUCTION

CO_2 has been used increasingly as a contrast agent in both the arterial and venous circulations, particularly in patients with hypersensitivity to iodinated contrast material and renal insufficiency. CO_2 can be used as a contrast agent for upper extremity venography, wedged hepatic venography, fine-needle transjugular intrahepatic portosystemic shunt (TIPS), and splenoportography (1–6). With the advent of the plastic bag system (7), the safety and ease of gas delivery has been improved, allowing multiple injections from the CO_2 bag.

GAS FLOW DYNAMICS

The unique physical properties of CO_2 affect the flow dynamics of the gas in venous circulation. The low viscosity of CO_2 allows its injection through a small catheter or needle as small as 27 gauge. When injected into a vein, CO_2 flows through the venous system and into the central veins rapidly, usually faster than contrast material. From the right atrium, the gas bubbles pass through the right ventricle into the pulmonary artery. In the supine position, the gas bubble is trapped in the pulmonary outflow tract (Fig. 1A). In the left lateral decubitus position, the bubble is trapped in the right atrium (Fig. 1B), allowing the blood to flow underneath the bubbles. In the Trendelenburg position and in the presence of elevated right heart pressure, the gas bubble may reflux into the hepatic vein from the right atrium (Fig. 2).

In general, the gas flow in small veins depends on the injection pressure. The injection pressure (explosive delivery) is the force used to push gas bubbles through the veins. In the larger veins, venous pressure and the flow of blood push the gas into the heart. The luminal gas filling depends on the size of the vessels injected. In small veins, the percent luminal gas filling should exceed 80%, whereas in the large veins, such as the vena cava, luminal gas filling is about 60% to 80% due to its buoyancy.

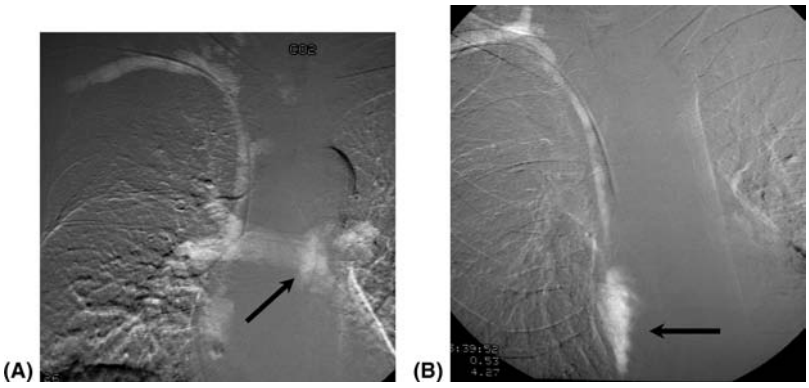

Figure 1 Right central venograms in the supine (**A**) and left lateral decubitus (**B**) positions following injections of CO_2 into a right arm vein. In the supine position, CO_2 flows promptly into the pulmonary artery (*arrow*). In the lateral decubitus position (right side up), CO_2 bubbles are trapped in the right atrium (*arrow*).

EFFECTS OF CO_2 ON THE CARDIOPULMONARY FUNCTION

Although CO_2 was used as an intravenous contrast agent as early as the 1950s for the diagnosis of pericardial effusion (8–10), little is known about the effects of bolus central venous injections of the gas on the hemodynamic and ventilatory functions. We, therefore, evaluated the effects of single intracaval injections of increasing amounts of CO_2 on the hemodynamic and ventilatory parameters in order to determine the safety and tolerance of the gas, and the adequacy of the routine monitors used during the use of CO_2 as a venous contrast agent.

The cardiopulmonary effects of the intracaval administration of increasing amounts of CO_2 (0.2–6.4 cc/kg body weight) were studied in 15 pigs (25–38 kg body wt) placed in the supine, left, or right lateral decubitus position. One animal from the

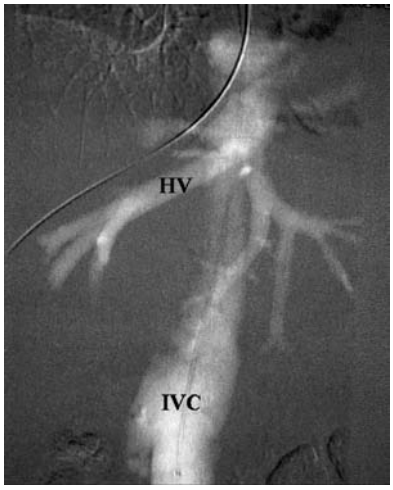

Figure 2 CO_2 injection into the right hepatic vein in a patient with pulmonary hypertension. CO_2 injected into the right HV, has refluxed into the middle and left HVs, and the IVC. *Abbreviations*: HV, hepatic vein; IVC, inferior vena cava.

left-side-up group died upon the intracaval injection of 6.4 cc CO_2/kg, apparently from a gas embolism. All of the other animals survived the intracaval injections of CO_2 in doses increasing to 6.4 cc/kg body weight. All of the animals showed no significant changes in their vital signs when administered 0.2–1.6 cc CO_2/kg. The systemic and pulmonary arterial pressure responses to incremental increases of CO_2 volumes in swine placed in the supine position is shown in Figure 3. A significant drop in the systemic blood pressure started to occur at the dose of 3.2 cc CO_2/kg, regardless of the body positions (Fig. 4). Pulmonary arterial pressure increased with the injection CO_2 at a dose of 0.4–3.2 cc/kg (Fig. 5). Despite the significant fall in the blood pressure after the injection of CO_2, SaO_2 remained above 90% (Fig. 6).

In summary, CO_2 given in diagnostic quantities is safe and causes no significant cardiopulmonary effects. Because CO_2 increases pulmonary arterial pressure, the gas should be used cautiously in patients with pulmonary hypertension. Blood pressure monitoring and capnography provide the earliest signs of a potentially life-threatening venous gas embolism. The body position has no influence on the severity of cardiopulmonary responses to CO_2. However, in the event of an accidental injection of an excessive amount of CO_2, placing the patient in the right-side-up position will help trap the gas bubbles in the right atrium, allowing continued blood flow underneath the gas bubbles.

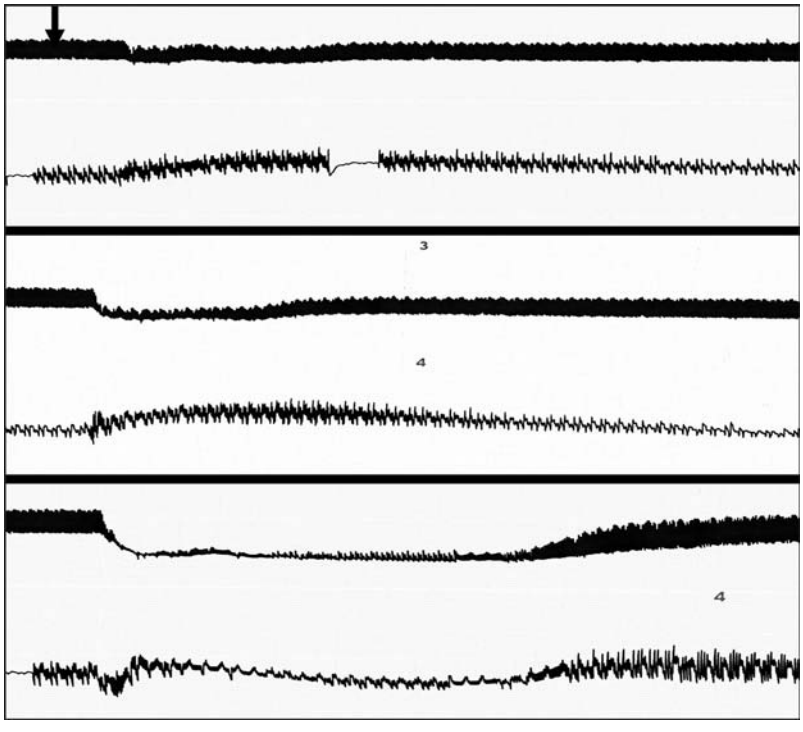

Figure 3 Polygraph tracings of the systemic (SBP, upper record) and pulmonary (MPAP, lower record) arterial pressures following intracaval injections of CO_2 at 1.6 cc/kg (**A**), 3.2 cc/kg (**B**), and 6.4 cc/kg (**C**) in swine placed in the supine position during CO_2 injection. At 1.6 cc/kg, SBP decreased 6% and MPAP increased 25%. At 3.2 cc/kg, SBP decreased 24% and MPAP increased 32%. At 6.4 cc/kg, SBP decreased 74% but pulmonary arterial pressure changed slightly. *Arrow* = Time of CO_2 injection.

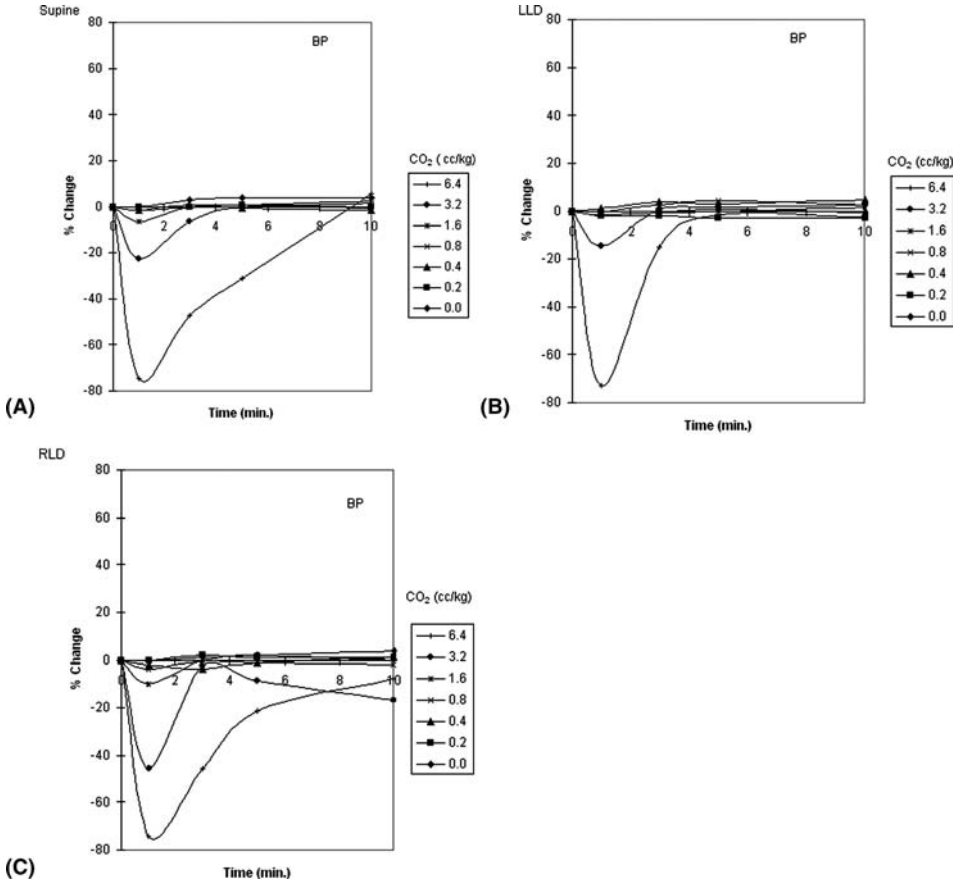

Figure 4 Average per cent changes in systemic blood pressure following intracaval injections of ascending doses of CO_2 in swine placed in the supine (**A**), left lateral decubitus (**B**), and right lateral decubitus (**C**) positions. At the doses of 3.2cc/kg, systemic blood pressure started to fall significantly, regardless of the body position. The hemodynamic response to the intracaval injections of large amounts of CO_2 was greater when the animals were placed in the right lateral decubitus position.

CLINICAL APPLICATIONS

Carbon dioxide has been generally used as an alternative venous contrast agent in patients with renal failure or a history of contrast allergies. At our institution, CO_2 is the contrast agent of choice for a variety of venous studies, including subclavian venography, wedged hepatic venography, percutaneous splenoportography, and inferior vena cavography prior to filter placement in patients with renal failure or contrast allergy and fine-needle TIPS. CO_2 is a useful contrast agent during venous interventions including catheter-directed thrombolysis, hepatic vein stent placement, inferior vena caval stent placement, and visualization of collateral veins.

Since CO_2 is visible fluoroscopically, it can be used to opacify target veins for percutaneous acces, such as the basilic vein for PICC placement and the subclavian vein for Hickman placement.

There are no absolute contraindications to the use of CO_2 in venous circulation. The only possible contraindication to CO_2 injection is a history of intracardiac shunts.

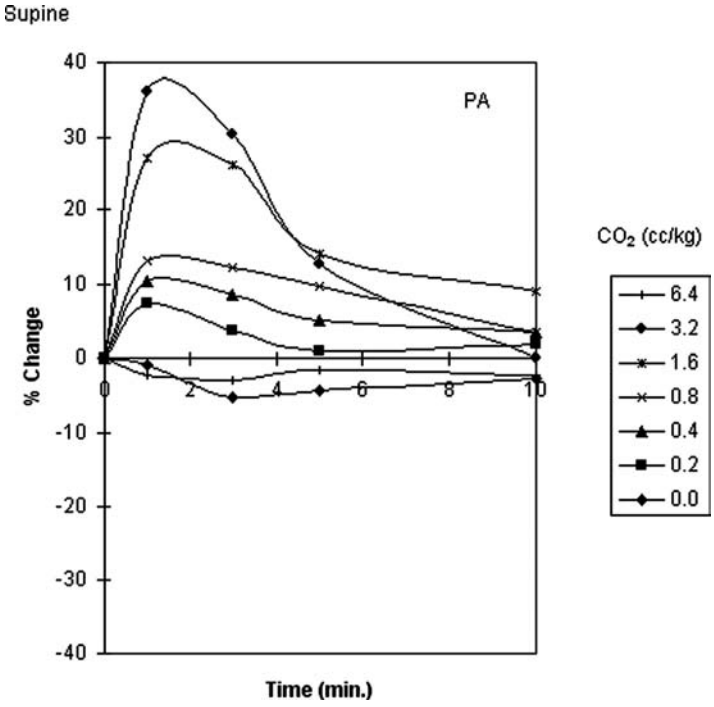

Figure 5 Average percent changes in pulmonary arterial pressure with ascending doses of CO_2 (0.2–6.4 cc/kg) in swine in the supine position. Pulmonary arterial pressure started to rise in 10–15 seconds following injection of 0.2 cc/kg CO_2. The degree of the rise in pulmonary arterial pressure increases with ascending doses of CO_2 up to 3.2 cc/kg.

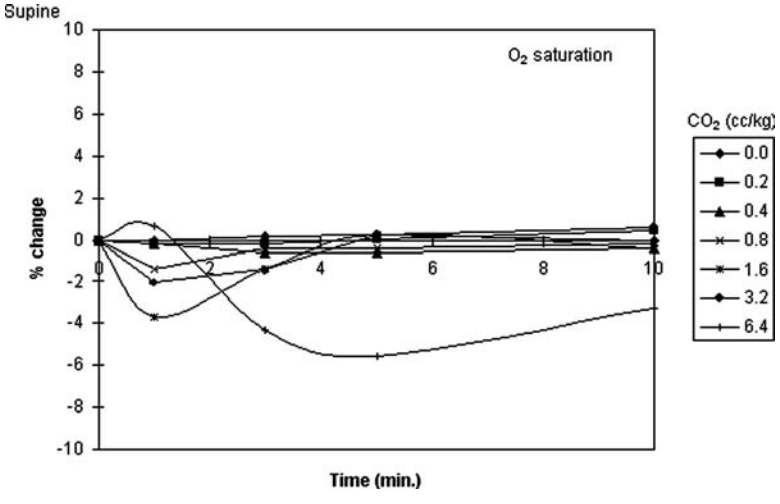

Figure 6 Average changes in SaO_2 following intracaval injection of increasing doses of CO_2 in a supine pig. There were minimal changes in SaO_2 despite significant fall in the systemic blood pressure and ET-CO_2.

Because CO_2 can increase pulmonary arterial pressure by 30% to 40%, the gas should be used cautiously in patients with severe pulmonary hypertension. We have not encountered a single incidence of a clinically significant paradoxical gas embolism in hundreds of patients who had undergone venous CO_2 injection studies. It is generally known that a patent foramen ovale is present in 10% to 15% of the population. This suggests that the CO_2 from the intravenous injection does cross the patent foramen ovale into the left atrium, or that small amounts of CO_2 entering the left heart cause no clinically significant systemic gas embolism. The known clinical signs for gas embolism of the coronary artery are bradycardia, hypotension, and an abnormal electrocardio gram (ECG).

SAFETY

The bolus administration of CO_2 into either the peripheral vein or the central vein in quantities of 30–50 cc, required for diagnostic imaging, causes no change in vital signs. Any significant change in vital signs after the intravenous injection of CO_2 should raise suspicion of a possible air contamination or paradoxical embolism. CO_2 injection should be stopped and vital signs should be re-evaluated. Then fluoroscopy should be performed over the lung and mediastinum in search for a retained gas bubble. If the gas bubble is visible in the pulmonary artery over 30 seconds after the injection, air contamination has occurred.

There is no simple method for distinguishing CO_2 from air. We have used either the digital subtraction technique or fluoroscopy to detect air contamination during CO_2 venous studies (Fig. 7). Our experimental study has shown that 45cc of CO_2 trapped in the right atrium dissolves completely in 70 sec (45–90 sec). If CO_2 is injected in the supine position, the gas bubble trapped in the main pulmonary artery should disappear within 15–20 seconds. If air contamination has occurred, the bubble will remain visible one minute after the injection. F7

There is no dedicated CO_2 injector in the U.S. Currently the hand-held syringe and the plastic bag system are used for CO_2 delivery. The hand-held syringe is a simple method for CO_2 delivery. This is inconvenient when multiple injections are required. When filling the syringe with CO_2, it should be filled and emptied three times before filling for injecting into the catheter. Once the syringe has been filled with CO_2, the tip of the syringe should be closed using a one-way stopcock. When the syringe is open to the ambient air, CO_2 in the syringe is rapidly replaced by air through gas diffusion because of the difference in the partial pressure of CO_2 between the syringe and the air. A gas chromatographic study has shown that 43% of the CO_2 in a 20-mL syringe will be replaced by air in 30 minutes. Although CO_2 is heavier than air, we found that the speed of air contamination is not affected by the syringe position.

The Plastic Bag system (AngioFlush 111 Fluid Management System, AngioDynamics, Queensbury, New York, U.S.A.) is quite useful when multiple CO_2 injections are needed. We routinely use this system for our venous CO_2 studies. It is comprised of the fluid collection bag and fluid management system. The check valves of the system have eliminated the need for the use of a stopcock and all connections are air tight. The residual air in the bag is removed by filling and emptying it three times. Once the bag has been filled with CO_2, it is connected to the side arm port of the fluid management system. A 60 mL luer-lock syringe is connected to the injection port of the system. Once all connections have been made, the stopcock between the bag and the CO_2 fluid management system is closed before aspirating the syringe to check for an air leak.

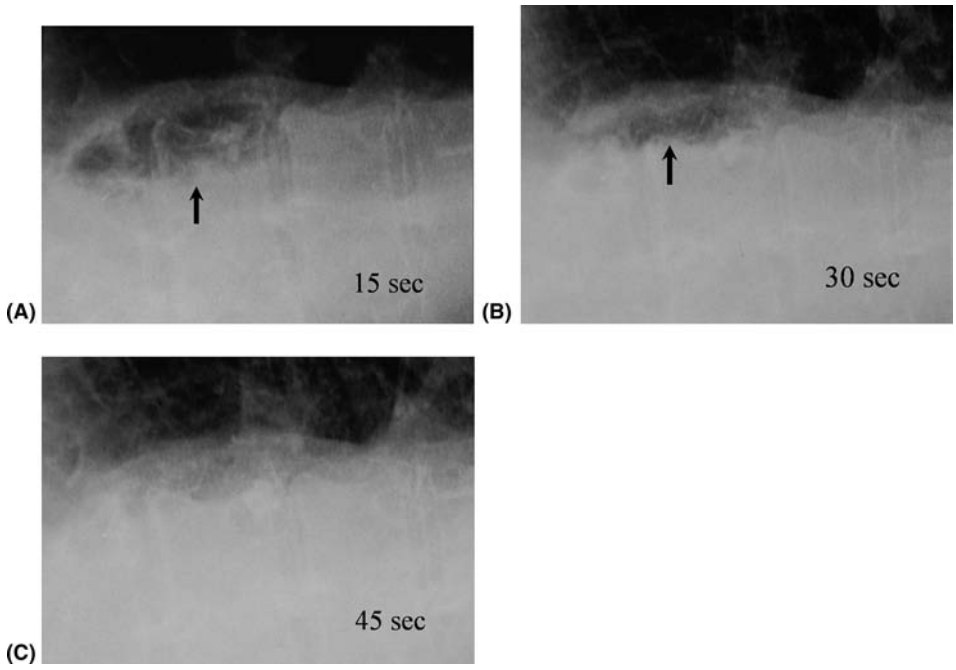

Figure 7 Absorption of CO_2 bubbles trapped in the right atrium in the left lateral decubitus position at 15 seconds (**A**), 30 sec (**B**), and 45 sec (**C**) following peripheral IV injection. The gas bubbles (*arrows*) trapped in the right atrium have completely absorbed by 45 seconds.

PREVENTION AND MANAGEMENT OF AIR EMBOLISM

When CO_2 is used as a venous contrast agent, air contamination precautions should be taken, regardless of the type of delivery system used. Since early detection of air contamination can prevent serious or even fatal accidents, we check blood pressure one minute after CO_2 injection and check the pulmonary artery for a persistent gas bubble fluoroscopically. Any significant fall in blood pressure after CO_2 injection may be due to air contamination, and the gas delivery system should be checked for an air leak. Capnography provides both the hemodynamic and ventilatory information in a real time manner. We found it to be an effective monitor for CO_2 venous studies. Heavy sedation should be avoided before CO_2 delivery because the hemodynamic and ventilatory responses to the sedation may mimic an air embolism. For upper extremity venography or inferior vena cavography we generally perform the procedure without conscious sedation.

When the patient develops significant hemodynamic and ventilatory abnormalities following the injection of gas, he/she should be placed in the lateral decubitus and in the Trendelenburg position to trap the gas in the right ventricle and atrium so that the blood continues to flow underneath the gas bubbles. Oxygen should be administered by mask. If possible, catheter aspiration may be performed.

CONCLUSION

Carbon dioxide is a safe and useful venous contrast agent. There should be no significant changes in vital signs following the intravenous injection of CO_2 in quantities used

for diagnostic CO_2 imaging. The gas should be used whenever possible, even in patients with or without normal renal function. Because of the low viscosity, the gas can be injected using a small catheter or needle, and it visualizes the central veins well. The current CO_2 delivery system must be used correctly to prevent air contamination. Excessive doses of sedatives and narcotics should be avoided because it can result in respiratory depression and hypotension. These side effects can mimic the side effects of the inadvertent administration of large amounts of CO_2 and air contamination. All patients who receive CO_2 should be awake and alert. When repeated doses of CO_2 are administered, sufficient time must be allowed for the gas to be absorbed completely. In the event of accidental injection of large amounts of CO_2 or an inadvertent injection of air, the maximal derangement in the cardiopulmonary functions will occur within one minute after the injection. CO_2 should be used with caution in patients with severe pulmonary hypertension since CO_2 causes a transient rise in the pulmonary arterial pressure.

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