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First experimental study of carbon dioxide digital subtraction lymphangiography

P.B. Dimakakos[1], M. Papasavva[1], T. Stefanopoulos[2], D. Mourikis[2], G. Kostopanagiotou[3], A. Doufas[4]

[1] Vascular Department of the 2nd Surgical Clinic, Medical School, University of Athens, Athens, Greece
[2] X-Ray Department, Medical School, University of Athens, Athens, Greece
[3] Experimental Department, Medical School, University of Athens, Athens, Greece
[4] The Anesthesiological Department, Medical School, University of Athens, Athens, Greece

Abstract. Fourteen pigs with an average weight of 17 kg were used in this study. Under general anesthesia and magnification 1–3 ccm/kg of carbon dioxide were administered in the lymph vessels of the front and rear legs. Imaging of the peripheral lymph vessels, lymph nodes and the thoracic duct was achieved with digital subtraction angiography. The quality of lymphangiography was satisfactory and comparable with that of the standard non-ionic contrast agent. It is anticipated that further technical evolution will permit the application of CO_2/DSA lymphangiography to man. Carbon dioxide is non-nephrotoxic and is non-allergic; it is inexpensive, can be administered in unlimited quantity and is quickly eliminated via the pulmonary system.

Key words: Carbon dioxide – Lymphangiography – Digital subtraction angiography

The administration of ordinary contrast material to patients with renal diseases or a history of allergies is usually contraindicated and creates a diagnostic problem [1–3].

Kerns and Hawkins [4] have reported approximately 20% of patients either with renal insufficiency or a history of a previous reaction to iodinated contrast material.

Carbon dioxide is non-nephrotoxic, does not produce allergic reactions, it is an rapidly injectable absorbed gas with low viscosity quickly eliminated from the lungs.

The use of CO_2 as an intravascular contrast agent during digital subtraction angiography (DSA) allows accurate imaging and provides an alternative method with little risk [4, 5].

Extended experimental and clinical investigations as well as the development of new injection equipment have established CO_2/DSA angiography as an exact, reliable imaging method of the arterial and venous system [4–10].

Correspondence to: P. Dimakakos, 27–29 Alopekis Street, GR-106 75 Athens, Greece

Despite the advantages which CO_2 possesses as an intraluminal imaging agent, it has not been used for imaging of the lymphovascular system.

The present study presents to the first experimental efforts using CO_2 in combination with digital subtraction angiography lymphovascular imaging.

Material and methods

Fourteen pigs which, as is known, possess an anatomically well-developed lymphovascular system and weighing an average of 17 kg were used.

The study was carried out according to the international rules for experimental research.

Following a 24-h period fasting from food and water ad libitum the pigs received 0.4 mg/kg of body weight Midazolan IM. A #22 guage venous catheter was placed in an ear vein and 5 mg/kg thiopental sodium was given as induction to anesthesia and following intubation of the trachea, 1 mg/kg/h was administered for maintenance of anesthesia. Analgesia was secured by 5 mg/kg/h of fentanyl and muscular relaxation with 0.1 mg/kg/h of IV pancuronium. The animals were ventilated with a mixture of oxygen/air (F_1,O_2: 0.4–0.5). The inhaled air volume was 15 ml/kg and respiratory periodicity approximately 10 min, so that PCO_2 at 30–40 mmHg could be achieved. The low CO_2 (1/400 of that of iodine contrast agents) viscosity allowed its administration via very thin catheters.

Catheters for lymphangiography with a needle gauge of 30 G were used placed on a flexible transparent catheter (Mccarthy's Surgical). A 2-way stopcock was placed on the other end of the catheter.

After intracutaneous administration of methylene blue and magnification, the lymph vessels in the periphery were exposed, both in the anterior and posterior ends. The position of the extremities was elevated to 20 degrees.

Administration of CO_2 was done via a 10 cm plastic syringe which was filled from an oxygen tank via an adapted gauge for gas transfusion.

In order to avoid admixture of atmospheric air and thrombosis of the lumen of the needle the catheter was filled with heparinized normal saline (5000 IU lt of normal saline). A 3 cm syringe filled with CO_2 was used to inject the heparinized serum into the vessel under direct observation. When all the heparinized serum was replaced by the gas then the 10 cm syringe with the CO_2 was applied to the stop-cock in order to commence infusion. In this way the explosive administration due to high degree of CO_2 pressure

was avoided, when an amply long fluid column of mercury has to be propelled.

The administration of CO_2 to the vessel was done manually, slowly and stable, under fluorescopic guidance. For the next infusion the same filling procedure of the catheter with heparinized serum was followed. The mean dose was 2 ccm/kg of body weight. Imaging of the lymphatic vessels was carried out using digital subtraction angiography.

For the comparative control following with CO_2 ionized water soluble imaging material (Imagopaque®) was administered and lymphangiography was repeated.

Results

Not one of the experimental animals showed any hemodynamic disturbances. The experimental animals No. 7 and 8 were allergic to Imagopaque, this resulted in exanthema, tachycardia, fall of blood pressure and death.

During the initial attempts at imaging of the lymphovascular system, extravasation occurred, probably due to the higher pressure and the low CO_2 viscosity, this could be avoided by lowering of pressure in the experiments that followed. Thus, the following digital subtraction angiography demonstrated good visualization of the lymph vessels and lymph nodes at the anterior and posterior extremities as well as of the thoracic duct (Figs. 1–4).

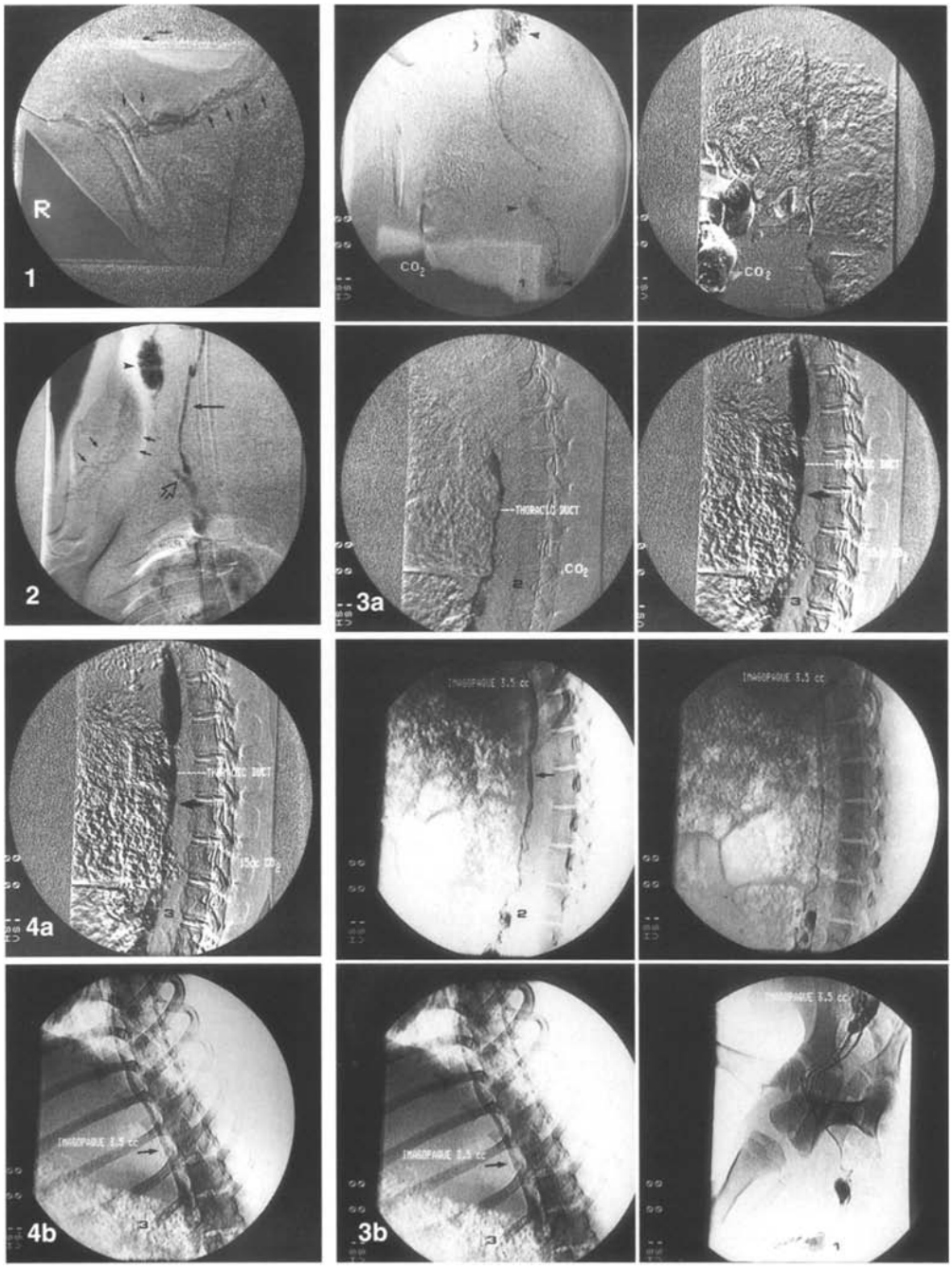

Fig. 1. Images the lymph vessels of the foreleg with CO_2

Fig. 2. Images the lymph vessels of the foreleg with neck node and part of the jugular vein system

Fig. 3a, b. Provides comparative images of lymph vessels and nodes in cross section of the rear leg (*1*), para-aortal, and the thoracic duct (*2* and *3*) with CO_2 (**a**) and the classic agent imagopaque (**b**)

Fig. 4a, b. Images the comparison between the thoracic duct in magnitude with CO_2 (**a**) and the classic agent imagopaque (**b**)

Table 1. Data on lymphangiography in 14 pigs

No	Weight	Leg	Number of injections	Total amount of CO_2 (cm^3)
1	15	Front	3	25
2	21	Front	4	40
3	16	Front	2	20
4	23	Back	5	50
5	18	Back	3	40
6	20	Back	4	45
7[a]	14	Back	2	25
8[a]	19	Front	4	45
9	23	Back	5	60
10	18	Front	3	35
11	17	Front	4	40
12	15	Back	3	30
13	15	Back	3	30
14	18	Front	4	35

[a] death of

These figures are comparable to those which were taken with the non-ionized water soluble contrast agent.

Discussion

Carbon dioxide was tested in detail, both in the arterial and venous system, during the experiment before it was administered to man [11].

Moore and Braselton [12] in 1940 had administered significant quantities of CO_2 to the veins of cats without any bad effects.

Oppenheimer et al. injected CO_2 into the carotid arteries of dogs without ill effects. Hipona [13] carried out roentgenologic visualization of the portal circulation and Goldenber of the hepatic veins [14].

The first clinical applications were imaging of the cardiac cavities of the valves and diagnosis of pericardial fluid [15–18].

Hawkins et al. [6] have been systematically doing pioneer work related to imaging of the arterial system below the diaphragm since 1982. Sullivan recently applied the above procedure for the imaging of the venous system of the upper extremities and the superior and inferior vena cava [2].

Carbon dioxide has not been widely accepted by radiologists because it is invisible and very difficult to deliver because of its compressibility [19].

The low density of CO_2 requires digital subtraction angiography. We have been using the model DVT-S of the Philips company.

The best angiographic imaging is achieved when the dose of the drug, the pressure of administration and the time of contact with the blood harmonizes with the diameter and flow speed. For each vessel there is an optimum dose which, if surpassed, does not mean better imaging [20]. The higher dose and pressure in our first experiments led to extravasation, probably due to the low CO_2 viscosity.

The reported disadvantages of the drug have been in intraaortic infusion, nausea and slight pain [21], as well as diarrhea due to the administration of a great quantity in a short time interval [4].

The value of CO_2 as a contrast agent, in imaging of the vessels of the central nervous system [22–23], is in an experimental stage and is still ambiguous.

The advantages of CO_2, in association with DSA as a contrast agent, 24 being non-allergic, non-nephrotoxic, relatively painless (10% have mild to moderate discomfort), the unlimited administration with free intervals (<100 ml injection every 3–4 min), the low viscosity (1/800 of non-ionic contrast), the administration via thin catheters and the minimal economic cost [19] attract the interest for a larger application of CO_2 in the future.

For the lymphovascular system more experimental studies will be required, defining more exact technical parameters which will also permit its application in man.

References

1. Cavo JJ, Trindade E, McGregor M (1991) The risks of death and of severe non-fatal reactions with high versus low osmolarity contrast media: a metaanalysis. AJR 156:825–832
2. Sullivan KL, Bonn J, Shapiro MJ, Gardiner A (1995) Venography with carbon dioxide as a contrast agent. Cardiovasc Intervent Radiol 18:141–145
3. Seeger JM, Self S, Harward TRS et al. (1993) Carbon dioxide gas as an arterial contrast agent. Ann Surg 217:688–698
4. Kerns SR, Hawkins IF Jr (1995) Carbon dioxide digital subtraction angiography. Expanding applications and technical evolution. Am J Radiol 164:735–741
5. Kerns SR, Hawkins IF Jr, Sabatelli FW (1995) Current status of carbon dioxide angiography. Radiol Clin North Am 33: 15–29
6. Hawkins IW (1982) Carbon dioxide digital subtraction arteriography. Am J Roentgenol 139:19–24
7. Krasny R, Hollmann JP, Guenther W (1987) Erste Erfahrungen mit CO_2 als gasförmiges Kontrastmittel in der DSA. Fortschr Roentgenstr 146:450–455
8. Weaver FA, Pentecost MJ, Yellin AE et al. (1991) Clinical applications of carbon dioxide/digital subtraction arteriography. J Vasc Surg 13:266–273
9. Bettmann MA, D'Agostino R, Juravsky LI (1994) Carbon dioxide as an angiographic contrast agent. Invest Radiol 29: 545–546
10. Hahn ST, Pfamatter T, Cho KJ (1955) Carbon dioxide gas as a venous contrast agent to guide upper-arm insertion of central venous catheters. Cardiovasc Intervent Radiol 18:146–149
11. Oppenheimer MJ, Durant DM, Stauffer H et al (1956) Cardiovascular respiratory effects and associated changes in blood chemistry. Am J Physiol 186:325–334
12. Moore RM, Braselton CW (1940) Injections of air and carbon dioxide into a pulmonary vein. Ann Surg 112:212–218
13. Hipona FA, Park WM (1967) Capnosplenoportography: assessment of portal vein patency in dogs with carbon dioxide gas. AJR 99:606–611
14. Gordenberg DB, Brogton BG (1967) Hepatic venography with carbon dioxide. Maryland State Med J 17:79–80
15. Bendib MBT, Toumi M, Boudjellab AH (1977) Carboxyangiographic et carboxyangiographic clargi en cardiologic. Ann Radiol 20: 673–686
16. Stauffer HM, Durantt M, Oppenheimer MJ (1956) Gas embolism: roentgenologic considerations including the experimen-

tal use of carbon dioxide as an intracardiac contrast material. Radiology 66:686–692
17. Durant TM, Stauffer HM, Oppenheimer MJ, Paul RE (1957) The safety of intravascular carbon dioxide and its use for roentgenologic visualization of intracardiac structures. Ann Intern Med 47:191–201
18. Scatliff JH, Kummer AJ, Janzen AH (1959) The diagnosis of pericardial effusion with intracardiac carbon dioxide. Radiology 73:871–874
19. Hawkins IF, Caridi JG, Weingarten KE (1996) Carbon dioxide digital subtraction angiography versus iodinated contrast imaging. 5th Internal Course on Vascular and Interventional Radiology as Therapeutic Alternative, Las Palmas – Spain p 145–175
20. Schmitz-Rode T, Alzen G, Gunther RW, Pott H (1993) CO_2 controlled injection system experiments in dogs. Cardiovasc Intervent Radiol 16:297–302
21. Miller FJ, Mineau DE, Koehler PR et al (1983) Clinical intraarterial digital subtraction imaging. Radiology 148:273–278
22. Coffey R, Quisling RG, Mickle JP et al. (1984) The cerebrovascular effects of intraarterial CO_2 in quantities required for diagnostic imaging. Radiology 151:405–410
23. Shifrin S, Plich WB, Verstandig AG, Gomori M (1990) Cerebral angiography with gaseous carbon dioxide CO_2. J Cardiovasc Surg 31:603–606
24. Harward IF, Smith S, Hawkins RVT, Seeger JM (1993) Follow-up evaluation after renal artery bypass surgery with use of carbon dioxide arteriography and color-flow duplex scanning. J Vasc Surg 18:23–30