CARBON DIOXIDE

DIGITAL SUBTRACTION ANGIOGRAPHY & INTERVENTION

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DISCLOSURES

Intravascular CO₂ is not FDA approved
Reference:

Carbon Dioxide DSA: A comprehensive user guide for all operators

VASCULAR DISEASE MANAGEMENT
2014;11(10):E221-E256
Celiac axis cut film taken in 1971 during accidental injection of room air that lead to Dr. Hawkins investigating CO$_2$ as an imaging agent.
CO₂ ADVANTAGES

- Non-allergic
- Non-nephrotoxic (unlimited volumes)
- Rapidly absorbed (20 - 30X O₂)
- Low viscosity (1/400 iodinated contrast)
  - Easier to use with microcatheters
  - Can inject in-between catheter and wire
  - Better detection of bleeding, AVF
  - Portal vein visualization
- Central reflux
  - Ability to identify vessel (ostium) central to catheter tip
- Cost (100 cc = .03)
**CO₂ DISADVANTAGES**

1. Requires unique delivery system
2. Invisible – concern for undetected contamination
3. Cerebral vessels should be avoided
4. Bowel gas can interfere with abdominal images
5. Potentially more labor intensive
CO$_2$ UNIQUE PROPERTIES

- Endogenous gas
- Invisible
- Low viscosity
- Buoyant
- Compressible
CO₂ CONCERNS

- Contamination
- Excessive volumes
- Intracerebral exposure
- Compressive delivery
- COPD
- Nitrous oxide anesthesia
- Pulmonary HTN
INVISIBLE

? CONTAMINATION

1. Reusable CO$_2$ cylinder
   Rust, methane, H$_2$O, particulate matter,
carbonic acid found over time

2. Room air
   diffusivity with open syringe
   malpositioned stopcock
   inadequate flushing
An 20 cc open syringe containing pure CO₂ is replaced by room air in 16 min.
CO dissipates in ~ 20 secs in pulmonary artery during venous injections. If not one has to consider contamination.
PREVENT CONTAMINATION

1. Use a disposable source of medical grade CO₂
2. Use a closed delivery system
3. Eliminate stopcocks if possible
4. Glue connections
5. Flush system 2-3 times
CO₂ UNIQUE PROPERTIES
$\text{CO}_2 \text{ IS BOUYANT}$
BUOYANT

- CO₂ doesn’t mix with blood - it displaces it
- CO₂ rises to a non dependent position
- Anterior images easily visualized
- Posterior imaging depends upon displacement of blood
CO_{2} FLOW DYNAMICS

Buoyancy

30^0 inclination

CO2

Blood
Buoyancy of CO$_2$
Lack of total displacement potentiates spurious result
Advantage: can rotate area of interest to better demonstrate it

Supine: L renal not visualized

L side up: L renal fills
Renal Tx arteries arise anteriorly and are easier to opacify.
CO$_2$ in abdominal aortic aneurysms must be monitored
Lateral aortogram shows decreased CO$_2$ blood interface which decreases absorption
If left unabsorbed for a prolonged period more occlusive gases can replace CO2 over time.
### PHYSICAL PROPERTIES OF CO$_2$ AND PHYSIOLOGICALLY RELATED GASES

<table>
<thead>
<tr>
<th></th>
<th>CO$_2$</th>
<th>O2</th>
<th>N2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular wt</td>
<td>44</td>
<td>32</td>
<td>28</td>
</tr>
<tr>
<td>Solubility</td>
<td>0.87</td>
<td>0.03</td>
<td>0.016</td>
</tr>
</tbody>
</table>

Solubility of CO$_2$ is 29 x that of O$_2$
Very rare but potential “TRAPPING” and ischemia if CO2 is not absorbed

$\text{CO}_2$ does not mix with blood and pressure can prevent Collateral circulation

Wait for CO2 to absorb before another injection!
CO₂ – BUOYANCY

+ 

ABERRANT ANATOMY
OR EXCESSIVE VOLUME

↓

POTENTIAL “TRAPPING”

↓

POTENTIAL VAPOR LOCK

↓

ISCHEMIA
PREVENT TRAPPING

• Prevent excessive volumes

• Monitor with fluoroscopy

• Wait between injections

• Aspirate if necessary

• ** CHANGE THE PATIENT’ S POSITION**
Avoid excessive volumes
THE HEMODYNAMIC AND VENTILATORY RESPONSES TO INTRACAVAL ADMINISTRATION OF ASCENDING DOSES OF GASEOUS CARBON DIOXIDE: EXPERIMENTAL STUDY IN 20 SWINE – Kyung Cho

- **CO₂**: 0.2 - 6.4 cc/kg
- **Position in supine, LLD, RLD**
- **Monitoring:**
  - HR, RR, BP,
  - PA, SaO₂, pCO₂,
  - pO₂, pH, HCO₂,
  - ETCO₂ at 1,3,5, & 10 min post CO₂
CONCLUSIONS

• Higher volumes showed various changes in recorded parameters

• $CO_2$ in doses of 0.2-1.6 cc/kg (112 cc in 70Kg) caused no cardiopulmonary effects.

• Intravenous diagnostic $CO_2$ DSA may increase PA pressure, $CO_2$ should be used cautiously in patients with pulmonary hypertension.

• Giving appropriate doses and allowing absorption there is no total limit of $CO_2$
PREVENT EXCESSIVE VOLUMES

- Excessive Volume:
  - 1 large bolus exceeding recommendations
  - multiple small injections without delay

- NEVER connect directly to a CO₂ cylinder!!!!!!!!!!

- Deliver known volumes - non-compressed system

- Wait 1-2 min. between injections

- Limit volumes to < 100 cc’s / injection

- Use stacking software
• EXPLOSIVE DELIVERY
  Pain, N&V
  Reflux - potential trapping, neurotoxicity

• INDETERMINATE VOLUMES
  Compressed gas can lead to false volumes
  Can lead to accidental excessive volumes
PREVENT EXPLOSIVE DELIVERY

• Use a non-compressed closed system

• Purged to atmospheric pressure

• Purge catheter of saline or blood before definitive injection
OTHER POTENTIAL CONCERNS

• NEUROTOXICITY

• NITROUS OXIDE ANESTHESIA

• COPD

• Pulmonary HTN
INTRACEREBRAL EXPOSURE

• No definitive proof of neuro toxicity however prudent to:
  • Avoid direct or reflux exposure
  • Avoid arterial injections above the diaphragm or upper extremity (reflux)
COPD

- CO$_2$ endogenous production 250 cc/min
- No problem unless in respiratory failure
- Precaution: decrease volume and increase interval between delivery
NITROUS OXIDE ANESTHESIA

• $N_2$ can diffuse from soft tissue to $CO_2$ bubble

• $CO_2$ bubble becomes 5-6 X more occlusive

• Avoid nitrous oxide anesthesia with $CO_2$ procedure like TIPS
PULMONARY HTN

• Avoid high volume venous procedures if patient has known pulmonary HTN

• Potential PFO
CONTRAINDICATIONS

• Supra-diaphragmatic arterial injections (intracranial CO₂)

• Use with nitrous oxide anesthesia

• Known left to right shunts
INDICATIONS

- Iodinated contrast allergy
- Renal insufficiency
- High volume contrast procedures
- Detection of arterial bleeding
- Intervention
NON-NEPHROTOXIC
DEFINITION OF CIN
(contrast induced nephropathy)

• Rise in serum Cr > 0.5 mg/dl
• Rise of serum Cr > 25% baseline
• 2\textsuperscript{nd} or 3\textsuperscript{rd} most common cause of hospital acquired acute renal failure (behind shock and nephrotoxic drugs)

• The overall incidence of CIN is 7%

• Risk of CIN requiring dialysis is
  • 4\% with renal insufficiency
  • 3\% when undergoing percutaneous coronary intervention

Nash et al; Am Jour Kidney Dis. 
Dangas, G et al; AmJCardio. 95 2005:13-19

Lindsey, J et al; AmJCardio. 94 2004:786-789
CLASSIC CONTRAST INDUCED NEPHROPATHY RISKS:

- Diabetic nephropathy
- Myeloma
- Large volume contrast
- Intravascular volume depletion
OTHER RISK FACTORS

- Hypotension (SBP < 80 mmHg)
- Heart Failure (NYHA III/IV)
- Use of intra-aortic balloon pump (IABP)
- Preexisting renal dysfunction SC > 1.5 mg/dl OR CrCI < 60 ml/mim
- Age ≥ 75 years
- Diabetes
- Hematocrit < 39% for men, or < 36% for women
- Dehydration
- Concomitant use of nephrotoxic drugs and/or renal perfusion reducing agents
  ACEI’s, Aminoglycosides, Vancomycin, Diuretics, NSAID’s, etc

Steven Dunn, Pharm.D, BCPS, University of Kentucky Chandler Medical Center (UK HealthCare)
Scheme to define contrast-induced nephropathy (CIN) risk score. Anemia = baseline hematocrit value <39% for men and <36% for women; CHF = congestive heart failure class III/IV by New York Heart Association classification and/or history of pulmonary edema; eGFR = estimated glomerular filtration rate; hypotension = systolic blood pressure <80 mm Hg for at least 1 h requiring inotropic support with medications or intra-aortic balloon pump (IABP) within 24 h periprocedurally.

Risk of death (34%) ↑ 6x

Hospitalization ↑ 2x

1 and 2 year mortality ↑ 2x

Increase comorbid complications

HOSPITAL ACQUIRED CIN

7500 Patients

In hospital mortality (22% vs 1.4%)

1 and 5 year mortality 4 x

Rihal et al.
CIN

- Vascular interventional procedures are increasing
- Diabetes is increasing
- Patient population is aging
- CLI and Claudication 45% had RAS, 16% severe, 12% bilateral
- Creatinine clearance subnormal in > 80% of PAOD patients
- Serum Cr is inaccurate in 30% 40-49 yo and 90% > 70 yo
- 30% of Cr Clearance abnormal for > 70 yo
CIN

- Average increased cost of CIN without dialysis
- $10,345 in hospital and $11,812 1st year
ALGORITHM TO AVOID CIN

Figure Legend: Advanced Algorithm for Management of Patients Receiving Iodinated Contrast Media. ACS = acute coronary syndromes; bid = twice daily; Cr = creatinine; DM = diabetes mellitus; IV = intravenous; NAC = N-acetylcysteine; NSAIDs = nonsteroidal anti-inflammatory drugs; PGE\textsubscript{1} = prostaglandin E\textsubscript{1}; po = by mouth; other abbreviations as in Figure 2.

From: Contrast-Induced Acute Kidney Injury
CIN VARIABLES

1. Underlying clinical state (renal insufficiency)

2. Site of administration of contrast

3. Volume of contrast!!!!!!
REDUCE OR PREVENT CIN

LIMIT THE VOLUME OF CONTRAST!!!!!!!
Plastic Bag Delivery System

Plastic Bag Delivery System for Hand Injection of Carbon Dioxide

Irvin F. Hawkins, Jr.¹, James G. Caridi, Scott R. Kerns

Digital subtraction angiography with carbon dioxide as a contrast agent provides images useful in making a diagnosis and occasionally gives information not obtainable with use of iodinated contrast material. However, delivery of the gas is difficult because carbon dioxide is compressible and invisible [1, 2]. Over the past 10 years, we have developed a reliable, user-friendly, computer-controlled injector, which is not yet approved by the Food and Drug Administration. We describe a hand-delivery system designed on the basis of principles learned from the development of the computer-controlled injector system.

Materials and Methods

The system has two major components (Fig. 1): a plastic bag (AngioFill Bag Collection System, AngioDynamics, Queensbury, NY) that is used as a reservoir for the carbon dioxide and a closed fluid (or gas) delivery system (AngioFlush II, AngioDynamics) consisting of multiple check valves, stopcocks, and a connecting tube. The reservoir is a 1500-ml plastic bag with a 100-cm connecting tube. In order to remove residual air from the connecting tubing and the bag, a special female-to-female adaptor is connected to the one-way stopcock. After air is removed from the bag, the stopcock is

AngioFill Bag Collection System and Angioflush 11. AngioDynamics
FLACCID CO$_2$ RECEPTACLE
CO₂ ANGIOGRAPHY
TECHNIQUE
MERIT MEDICAL CUSTOM
WASTE BAG AND CONTRAST
DELIVERY SET

Flaccid reservoir

One way valves

Clamp

Catheter

Delivery syringe
MERITMEDICAL CUSTOM WASTE BAG AND CONTRAST DELIVERY SET
CO$_2$ source

Pre-assembled delivery system with one way valves
DELIVERY SYSTEM

- **Non-compressed** - for accurate volume and prevent explosive delivery
- **Closed system** – to prevent contamination
- **One way valves** - prevent reflux and necessity to remove delivery syringe
- **Glued components** - helps prevent air contamination
- **Hand injection** - purge catheter first to prevent explosive delivery
ARTERIAL DIAGNOSIS
Thicker contrast spuriously suggests distal graft is occluded. CO₂ demonstrates patency
TIPS FOR IMPROVING (RUNOFF) IMAGING

• Reduce motion
• Gentle non explosive delivery
• Faster exposure (6 frames/sec)
• Increase pulse width (60 ms)
• Endhole catheter
• Increase CO$_2$ volume
• (super) Selective injections
• Elevate the extremity or area of interest
• Reflux CO$_2$
• Vasodilator (NTG 100 mcg)
• Stacking software
CO$_2$ DISPERSION PATTERNS FORM WITH DIFFERENT CATHETERS

endhole  halo  pigtail
End hole catheter is best for CO$_2$ providing better bolus and less “bubbling”
STACKING SOFTWARE

Superimposes multiple frames to yield a composite image
STACKING SOFTWARE
VESSELS LESS THAN 10 MM HAVE 1/1 CORRELATION WITH CONTRAST
IMPROVED DETECTION OF BLEEDING / FISTULA

1. CO2 - low viscosity

2. CO2 exits the vessel and expands

3. Little or no capillary phase to obscure CO$_2$

4. CO2 is not diluted by blood

Hashimoto et al, Sem Interven Rad 1997; 14:163-173
Hawkins et al, Sem Interven Rad 1997; 14:175-180
No AVF
Non selective AVF not seen with select liquid contrast
Renal transplant AVF
Renal AVF and bleed post robotic partial nephrectomy not seen with liquid contrast
Bleed post robotic partial nephrectomy not seen with liquid contrast
Post access AVF treated with stent graft
Pre capillary shunting not AVF: a phenomena that can happen with severe peripheral disease.
Phenomena can occur with liquid contrast: popliteal artery entrapment before and after provocative maneuver
VENOUS DX & TREATMENT

- Slow gentle injection of 15-30 cc to avoid pain
- Stretch receptors more sensitive to dilation than artery
- CO2 is not diluted by blood and can opacify central veins more readily from a peripheral approach
- Venous PTA and stent placement
- IVC filter placement
- Ultra fine needle splenoportography
- Portal vein access
Comparison of diluted liquid contrast from antecubital access vs CO₂ using small IV
Low viscosity of CO$_2$ crosses midline to identify collateral again using small peripheral (hand vein) access
SIMON’S UNBREAKABLE RULES OF DIALYSIS

#1 – Every catheter will occlude or become infected

#2 - Every Graft will stenose, occlude, fail, or become infected

#3 - Every Fistula will stenose, occlude, or fail

#4 – Transplants don’t last forever
RENAL FAILURE PATIENT ON DIALYSIS

- + Advantage of maintaining some renal function

- Patients are much easier to manage from their renal failure if they have any kidney function maintained

- If access is lost they tend to tolerate a missed dialysis much better

- Fluid and potassium management is much easier in this group of patients.

- A decrease in GFR of 1 increases mortality by 12%
CO₂ DIALYSIS ACCESS

The mission is to visualize the access without refluxing CO₂ into the cerebral vessels!!!!

Visualize venous limb non-explosively

Alternatively place occlusion balloon toward venous limb inflate balloon and inject

For arterial anastomosis DO NOT forcefully reflux
Place micro catheter in artery and inject gently

If a tilting table is available place in Trendeleburg
Splenoportogram with direct 25 ga spinal needle injection
1/3 rd x-section area of 21 ga
IVC GUIDELINES

• Review CT first if available for size, and congenital variants
• Requires higher volumes: 20-50 cc
• Literature support with almost 1/1 correlation with iodinated contrast
• Right posterior renal vein more posterior and may not be visualized
• May require guide wire or catheter localization for renal vein origins
INTERVENTION
ARTERIAL INTERVENTION

- Reflux - can opacify the entire vessel including ostium for more precise stent placement
- Can inject between guide cath and catheter or wire and catheter to check placement without compromising position for PTA and stenting
- Microcatheter injections for easy opacification
- Can perform repeated injections without the fear of renal failure
EVAR FACTS

- Predisposition for renal dysfunction > open

- Occurs in pts with & without renal insufficiency

- ARF = 7 – 25% with & 2.5% without

- Associated mortality is 30 – 50%
Use of CO2 Angiography for Complex EVAR

J Cross, D Simring, I Morgan Rowe, K Ivanov, P Harris, T Richards

Introduction:
- Incidence of contrast induced nephropathy is proportional to volume of iodinated contrast used
- Complex EVAR: technically challenging requiring multiple images and larger volume of contrast
- Higher incidence of post op renal dysfunction

Aim:
- To assess role of CO2 as primary contrast agent in complex EVAR

Methods:
- Two Cohorts undergoing branched or fenestrated EVAR were compared:
  - Cohort 1: Iodinated contrast only
  - Cohort 2: CO2 primary contrast
- Endpoints: Renal function, Contrast volume, Radiation dose

Results:

<table>
<thead>
<tr>
<th></th>
<th>Iodinated contrast</th>
<th>CO2</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in creatinine (median)</td>
<td>28.5</td>
<td>9.5</td>
<td>0.048</td>
</tr>
<tr>
<td>Post op renal dysfunction*</td>
<td>13/41</td>
<td>8/27</td>
<td>N/S</td>
</tr>
<tr>
<td>Temporary dialysis</td>
<td>7/41</td>
<td>3/27</td>
<td>N/S</td>
</tr>
<tr>
<td>Vol. iodinated contrast (median)</td>
<td>226.25mls</td>
<td>75mls</td>
<td>N/S</td>
</tr>
<tr>
<td>Radiation dose</td>
<td>52005 Gy</td>
<td>41836 Gy</td>
<td>N/S</td>
</tr>
</tbody>
</table>

CONCLUSION
- Useful adjunct for complex EVAR
- Allows ‘unlimited’ images
- Renal dysfunction likely to be multifactorial
- Significant reduction in the median creatinine difference

Technique
- Lab grade CO2
- Standard cylinder attached to filter and 3 way tap
- Attach 50 ml syringe with Floswitch to 3 way tap
- Avoid air contamination and fill using cylinder pressure
- Manually compress syringe of CO2
- Rapidly inject gaseous CO2 into aorta in 30-50ml aliquots

Demographics

<table>
<thead>
<tr>
<th></th>
<th>Iodinated contrast</th>
<th>Primary CO2</th>
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<tbody>
<tr>
<td>Male</td>
<td>32</td>
<td>32</td>
</tr>
<tr>
<td>Female</td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>Median age</td>
<td>75 yrs</td>
<td>74 yrs (P&lt;0.15)</td>
</tr>
<tr>
<td>Age range</td>
<td>60-85</td>
<td>60-85</td>
</tr>
<tr>
<td>Median baseline creatinine</td>
<td>96</td>
<td>180 (P=0.21)</td>
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CLASSIC CONTRAST ASSOCIATED NEPHROPATHY RISKS

- Diabetic nephropathy
- Myeloma
- Large volume contrast
- Intravascular volume depletion
INTERVENTIONAL ONCOLOGY

• Comorbid conditions predisposing to CIN
  - Renal insufficiency, Diabetes, Hepatic insufficiency

• Peri-procedural medications can predispose to renal failure
  - NSAIDS

• Post embolization syndrome can deplete intravascular volume

• Many embolization procedures require high volume contrast

• Tumor lysis syndrome can induce renal failure

• Rare - non-target embolization of kidneys
Prospective study 140 patients for HCC

Pre procedure creatinine 1.1 +/- .2

8.6% developed ARF

2.8% irreversible renal failure (all diabetics)

ARF correlated with the number of procedures, severity of liver disease and presence of post-embolization syndrome

Huo et al, Liver International 2004: 24;210-215
1. Vessels less than 10 mm

2. Low viscosity
   Tumor vessel visualization
   Ease of use with microcatheters

3. Central reflux
Chemoembolization

Contrast

CO₂
Poor opacification attempting contrast through microcatheter
Easy opacification due to low viscosity of CO2
Uterine fibroid embolization
Renal cell carcinoma metastasis
PORTAL VENOGRAPHY

• Diagnostic:
  • When CT/MR is not sufficient or feasible (commonly pediatrics)
  • Portal vein thrombosis
  • Portal vein stricture
  • Venous sampling

• Localization for intervention:
  • TIPS
  • Pre operative portal vein embolization
CONTRAST WEDGED HEPATIC VENOGRAPHY

- Portal vein visualization 40 – 75%
- Main portal vein visualization 40%
- Direct portal venography correlation in only 10%
- Transient elevation of transaminases
- Parenchymal staining with contrast
- Parenchymal scarring and hemorrhagic infarction and congestion of lobules
- When peripheral rarely can result in capsular laceration hemorrhage and death

Culp et al, JVIR 1999; 10:1265-1270
Castaneda-Zuniga et al, Radiology 1978; 126:53-56
CO$_2$ WEDGED HEPATIC VENOGRAPHY

- Portal vein visualization 83% (UF 86%)
- Direct portal correlation in 91%
- No parenchymal staining
- No scarring or hemorrhagic infarction or enzyme changes
- Potential small parenchymal hematomas
- CO$_2$ can linger in vein providing target
- Peripheral injection can still cause capsular laceration hemorrhage and death
- Intraperitoneal extravasation in 1.8%
- It is essential to avoid explosive delivery

DIRECT INTRAPARENCHYMAL CO₂

- Animal studies reveal no hepatic necrosis, infarction, congestion, laceration or extravasation
- Almost 100% portal vein visualization (120 pt’s)
- No complications
- No parenchymal staining
- Eliminates extra step, time and cost
- Uses the needle which is part of the procedure

Hawkins et al, AJR 173; 625-629
Sun et al, Eur Radiol 2003; 13:244-250
Culp et al, JVIR 1999; 10:1265-1270
Intrhepatic parenchymal injection of CO2 20 cc
Liquid contrast only shows peripheral
CO2 demonstrates centrally with reflux
CO2 10-20 cc through 25 ga spinal needle to determine patency of portal vein pre transplant
CO$_2$ GUIDED TIPS

- Hepatic vein evaluation
- Intraparenchymal portal venogram
- Entry site verification
- Portal venogram
- Post procedure portogram
DIRECT INTRAPARENCHYMAL CO$_2$
MEASURING THE TRACT
CARBON DIOXIDE DIGITAL SUBTRACTION ANGIOGRAPHY

- CO₂ angiography is safe when used appropriately
- The delivery system is simple
- CO₂ has unique properties as a contrast agent
- These properties make it a useful tool in both diagnosis and intervention