

Agitated Saline Bubble Study

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Outline

- What is a bubble study?
- Indications
- How to perform
- Diagnosis w/ case studies
 - PFO
 - Persistent Left Superior Vena Cava (PLSVC)
 - Pulmonary Arteriovenous Malformation (PAVM)
 - Pericardiocentesis Guidance
- Interesting Case Study – atypical diagnosis with bubble study

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What is a “Bubble Study”

Introduction

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Agitated Saline Imaging

Agitated saline (aka “bubble study”) is used with echo to evaluate for:

- Interatrial shunts
 - PFO
 - ASD
 - Intrapulmonary shunting
- Persistent left SVC

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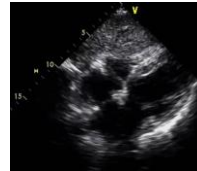
Agitated Saline “Bubble Study”

- Saline is “agitated” and injected via IV to create micro-bubbles
- Micro-bubbles are ultrasound reflective and opacify the right heart
- Looking for any blood flow from RA - LA



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Agitated Bubble Study



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Be Prepared

- Echo labs should be prepared
 - Supplies
 - Trained personnel for IV access
 - Trained sonographer

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Indications

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Indications

Mostly used for the:

- Detection of shunts
- Detection of persistent left superior vena cava
- During echo-guided pericardiocentesis

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Indications

Also used for:

- Central venous line control - after insertion
- Intensifying TR signal
- Delineating right heart borders and masses (including RV wall thickness)
- Thrombi in pulmonary trunk and arteries - appears as contrast filling defects

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Procedure

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Supplies

- 2 10mL syringes with locking mechanism
- Three-way stopcock
- Larger IV size (20 gauge or more)



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Procedure Steps

- Ante-cubital vein
 - Left Arm: Persistent Left SVC
- Prepare Syringe:
 - 8mL of saline / 2mL of air OR
 - 8mL of saline / 1mL of air / 1mL patient's blood
- Flush extension tubing with saline



Agitated Saline with blood

- Enhances contrast / superior results

Research Study

- 8mL of saline, 1mL of patient blood, 1mL of air
- 20 patients (Saline vs. Saline w/blood)
- 3 cardiologists (blinded)
- For all cases (100%), saline w/ blood resulted in greater contrast enhancement



Tips for combining blood with saline

- Fill syringe with 8mL of saline
- Withdraw 0.5-1mL of blood into the *syringe filled with saline*
- Withdraw 0.5 – 1 ml of air in the *other syringe*
 - so you do not disconnect the one with blood in it



Saline Only

- You can withdraw the air in the syringe with the saline already in it
- If no blood - no advantage of withdrawing air in a separate syringe



Agitate Saline

- Stopcock "closed"
 - Positioned between 2 syringes not IV
- Push saline back and forth (from empty to full)
 - Push the stopper to the absolute end of the syringe for maximal agitation (last 2mL)
- Repeat 3–5 times
 - Evenly mix in the air bubbles – ensure smaller bubbles
- This converts clear saline to a whiter, partly opaque air/saline mixture



Procedure

- **Sonographer ready**
- Turn the stop-cock to IV position
- Instantly inject agitated saline into the vein
- Immediately after the injection:
 - Raise patient's arm with the IV OR
 - Squeeze the forearm
 - Enhance saline entrance into venous system and RA
- Agitated saline injection should result in complete opacification of the right atrium



Sonographer Ready



Best Window

- Often apical 4C
- Different views / off axis views used based on indication

Indication	Best Window	Also Used
Detection of Shunts	Apical 4 Chamber (4C)	High PSAX, Subxiphoid, 4C
Persistent Left Superior Vena Cava	PLAX, M-Mode through RVOT and Coronary Sinus. <small>(early phase FCI trial)</small>	Apical 4C with posterior angulation
Intensify TR Jet	Modified Apical 4C, Apical 4C	RVIT, High PSAX
Delineate Right Heart Border & Masses	Apical 4C, Subxiphoid 4C	RVIT, High PSAX
Improved Imaging of Pulmonary Arteries	RVOT Long Axis	PSAX focus on Pulmonary bifurcation
Echo Guided Pericardiocentesis	Para-apical, Subxiphoid	Low Parasternal (long and/or short axis)
Central Venous Line Control	Subxiphoid, Apical 4C	RVIT



Precaution using Subcostal Window

- Good with color Doppler **not with agitated saline**, why?
- Doppler: IAS plane is perpendicular to beam, creating optimal Doppler angle for shunt detection
- Agitated Saline: Right heart is opacified, right heart is in the near field, attenuation artifact



Knobology

- Highest transducer frequency
- Adjust:
 - Dynamic range
 - Compression
 - Reject
- Colorized 2D images
- Use very long loop acquisition of up to 20 cycles / continuous capture



Shunt Assessment

Correct Technique

Resting Study

- Resting study: Bubble study w/o Valsalva
- Resting **shunt**: Agitated saline crosses from right-left without Valsalva
- First inject saline w/out Valsalva to look for a resting shunt
 - Worse outcomes
 - Predictor of stroke recurrence



Valsalva

- If the first injection is positive, no further images are necessary
- If negative: Repeat with Valsalva

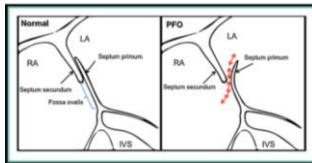


Valsalva - Mechanism

- Valsalva momentarily alters the pressure gradient between the left and right atrium
- This causes the septum primum, on the left side of the atrial septum, to transiently lift up and open the septum - like a door jam
- Bubble Study: Acceptable Valsalva - the interatrial septum is **seen** to shift to the left, most dramatically upon the release phase of Valsalva



Septum Primum



Valsalva Correct Technique

- Patient bears down for 5–10 seconds
- To help patient maintain Valsalva long enough to result in septal shift:
 - Assist the patient by firmly pressing over the abdomen
 - Ask patient to use their abdominal muscles to push back against the examiner's hand
- The patient may need several practice attempts
- Not following criteria has contributed to lower echo detection rates of PFO



Valsalva TEE

- Valsalva during TEE is dependent on the level of sedation
- Ask patient to cough forcefully several times
- Perform the agitated bubble study toward the end of the TEE (patient less sedated)
- Main goal of valsalva it to confirm atrial septal shifting



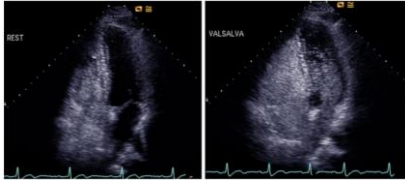
Valsalva Timing with Injection

- Complete opacification of the RA occurs at the end of Valsalva
- Injection: Performed while the patient is bearing down
- Valsalva Release: As contrast enters the RA

pt bears down -> inject saline -> contrast reaches RA -> pt relaxes



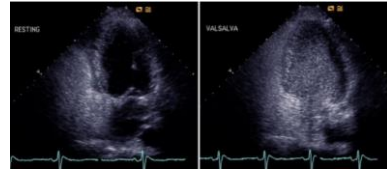
JASE Study: With and without Valsalva



- Left: Bubble study at rest
- Right: Bubble study with Valsalva

CARDIOSERV J Am Soc Echocardiogr 2013;26:96-102
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JASE Study: With and without Valsalva



- Left: Bubble study at rest
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PFO

Description
Case Study

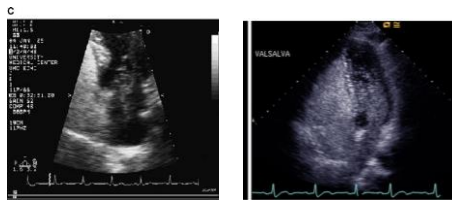
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PFO

- PFO not a true deficiency of atrial septal tissue (space/separation)
- Slit-like defects resulting from incomplete fusion of the foramen ovale with the atrial septum (20-25% of population)
- Risks & Symptoms
 - Migraine headaches
 - TIA, CVA
- Echo bubble studies principal means of diagnosis
- Potential for misinterpretation (false positive and/false negative)

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PFO Examples



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PFO Rule Out Criteria

TABLE II

Findings that Help Exclude Patent Foramen Ovale

1. Right atrial dense opacification (especially adjacent to the septum), and
2. Transient leftward shifting of the interatrial septum, but
3. No bubbles in the left atrium seen to emerge through the interatrial septum, or
4. Bubbles noted in LA only after 3-5 cardiac cycles after the transient septal shift

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False Negative

- If all of the criteria has not been met study a study may be falsely interpreted as negative
- **Especially septal shift** because it reassures the examiner that the mean right atrial pressure has transiently exceeded that of the left atrium
- Even patients with large ASDs - bubbles often remain in RA (Normal right heart pressure)



Septal Bulging



False Negative due to SVC

- MUST have complete RA dense opacification to firmly rule out a PFO
- IVC blood mixes with SVC (non-contrast/bubble study) blood
- “Contrast-free zone” along the septum
- Non-contrast blood may actually “shunt” through a PFO but is not recognized in the LA
- If the RA is not fully opacified- study its indeterminate – repeat with larger dose / faster push



“Contrast-free zone” along the septum



PFO False Positive

- Pulmonary arterial-venous shunt
- Bubbles came from the right superior pulmonary vein NOT the interatrial septum



PFO- Frame by Frame



Timing

- Common viewpoint is that bubbles must appear in the LA within 3–5 cardiac cycles of their appearance in the RA to diagnose a PFO and that bubbles appearing in the LA beyond five cycles suggest transpulmonary shunting

Exceptions

- PFO > 3-5 seconds– dilated fibrillating atria
- Pulmonary shunt < 3-5 seconds – large pulmonary shunt may allow bubbles to get to the LA within the 3–5 cycles



Large pulmonary shunt



PFO Summary

Use Agitated saline bubble study for suspected PFO

- **Correct Valsalva:** Transient leftward bowing atrial septum with Valsalva release
- **Repeat** if failure to demonstrate correct Valsalva



Persistent Left Superior Vena Cava



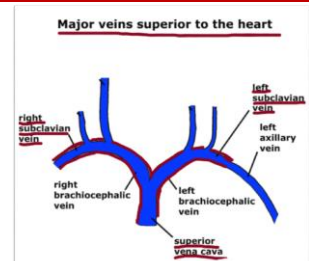
Persistent Left Superior Vena Cava

- 0.5% of the general population
- Isolated anomaly with minimal hemodynamic & clinical significance
- Often discovered follows the finding of an abnormally positioned catheter, pacemaker, or internal defibrillator lead
- If central venous catheter's tip is in the left paramediastinal region – think PLSVC
- Confirm presence of a PLSVC to rule out catheter perforation or migration



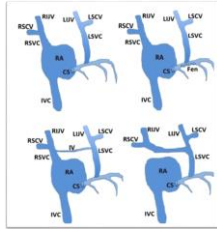
Normal Anatomy

- Right subclavian and left subclavian merge into the Superior Vena Cava (SVC)
- **Normal flow – SVC -> RA**



Persistent Left Superior Vena Cava (PLSVC)

- Various forms of persistent left superior vena cava draining into the coronary sinus
- Left SVC -> coronary sinus



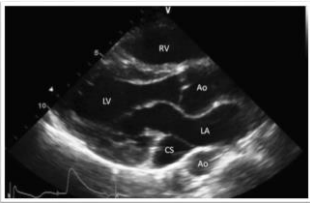
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PLSVC Bubble Study

- **Left Arm:**
 - To R/O PLSVC the IV must be inserted in the left arm
- Dilated coronary sinus
- **Positive Test:**
 - If the agitated saline appears in the coronary sinus before appearance in the right side of the heart.

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PLSVC: Echo- PLAX

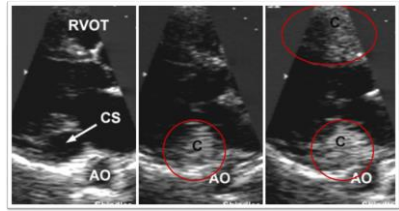


Best Window: Parasternal long axis view.

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PLSVC: Echo

- Contrast travels:
- Left arm - persistent LSCV - the coronary sinus.
 - Bubbles appears first in the coronary sinus, then in the right ventricular outflow (RVOT).

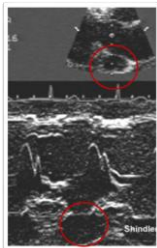


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<http://rwjms1.umdnj.edu/shindler/plsvc.html>

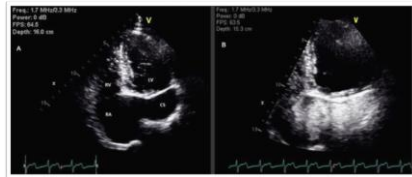
PLSVC: Echo M-Mode

M-mode can be employed for better temporal resolution, with the beam centered on CS and RVOT



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PLSVC: Echo



Angulated A4C with posterior tilt showing CS opening into RA

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Case Study

Persistent Left Superior Vena Cava

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Case Study

- 29M
- Emergency laparotomy for multiple intra-abdominal abscesses
- Postop after central line catheter (placed through left subclavian vein)
- Chest X-ray study showed catheter tip in left paramediastinal position instead of crossing the midline to the superior vena cava
- PLSVC was suspected
- Patient was hemodynamically unstable- needed bedside confirmation
- Echo bubble study ordered

X-Ray

Ordered to confirm correct central line placement of patient in critical condition ...needs meds through central line

Findings:

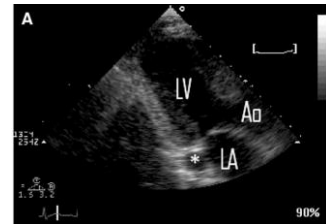
- The chest X-ray study after insertion showed a catheter situated in the left paramediastinal region



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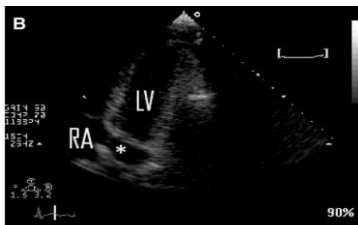
Limited TTE - bedside

Prominent coronary sinus with a diameter of 1.3 cm



Limited TTE - bedside

Off Axis A4C



Bedside bubble study

- Agitated saline injected through the catheter
- Opacification of coronary sinus, RA & RV
- Diagnosis: Anomaly of the venous return, consistent with a persistent left superior vena cava (PLSVC) entering the coronary sinus.
 - Ruled out catheter perforation or migration
 - Medication through central line was deemed to be safe

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Bedside bubble study



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Case Study Conclusion

- A case of a hemodynamically unstable patient w/ a left subclavian catheter placement that was found to be in an abnormal position
- Echo bubble study provided a non-invasive confirmation of the presence of an anomaly of the venous return from the left subclavian vein to the right atrium

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Pulmonary Arteriovenous Malformation (PAVM)

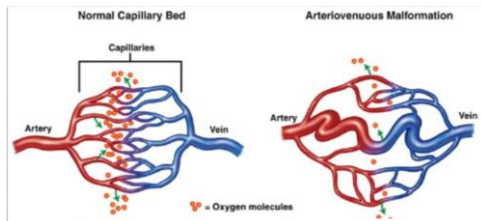
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Pulmonary Arteriovenous Malformations

- **Pulmonary Arteriovenous Malformations (PAVM's):** Rare abnormal connection between the pulmonary vein and pulmonary artery
- Abnormal dilated vessels, right-to-left shunt between the pulmonary and systemic circulation
- The shunt is **extra cardiac**
- Usually congenital

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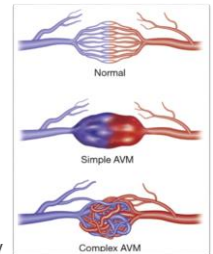
Pulmonary Arteriovenous Malformations



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Pulmonary Arteriovenous Malformations

- **80% Simple**
 - Single feeding artery
 - Single draining vein
 - Empties into bulbous, non-septated aneurysmal segment
- **20% Complex**
 - 2 or more feeding arteries
 - 2 or more draining veins
 - Empties into septated, aneurysmal segment



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Pulmonary Arteriovenous Malformations

- Most patients are asymptomatic
- Manifest in adult life (3rd/4th decade)
 - Nose bleeds, dyspnea on exertion, hemoptysis (rupture)
- Bruit over lesion > with inspiration
- Complications
 - Hypoxemia
 - Migraine headaches
 - TIA, CVA
 - Pulmonary HTN



PAVM: Hemodynamics

- PAVMs do NOT affect cardiac hemodynamics
- Normal Limits: Cardiac Output, cardiac index, pulmonary capillary wedge pressure, HR, BP, ECG
- Degree of right to left shunt determines clinical effects on patient

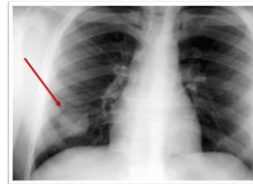


PAVM: Diagnostic Testing, X-ray

- Round or oval sharply defined mass or uniform density (80%)
- 1-5 cm in diameter
- Enlarge with advancing age
- 2/3rd located in lower lobes
- May show connecting vessel radiating from the hilum



PAVM: Diagnostic Testing, X-ray



Posteroanterior chest xray: Large, single PAVM in right lower hemithorax.



Lateral chest xray: Large, single PAVM in right lower hemithorax.



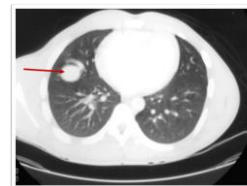
Khurshid I, Downie GH
Pulmonary arteriovenous malformation
Postgraduate Medical Journal 2002;78:191-197.

PAVM: Diagnostic Testing, CT

- Contrast CT is used for diagnosing/defining the vascular anatomy of PAVM
- However, angiography is better able to determine the angioarchitecture of individual PAVMs and remains the gold standard in diagnosis of PAVM



PAVM: Diagnostic Testing – CT



CT: Well circumscribed density in right lower lobe connected by a blood vessel.



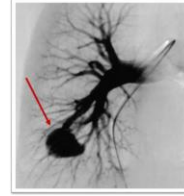
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PAVM: Diagnostic Testing, Pulmonary Angiogram

- Angiography should be performed on all portions of the lung
- Look for any unsuspected PAVM and source of *intrathoracic or extrathoracic* vascular communications
- Necessary before therapeutic embolization or surgical resection
- CT & MRA should be used for those patients who cannot undergo angiography or for the follow up of patients with a proved PAVM

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PAVM: Diagnostic Testing, Pulmonary Angiogram



Angiogram showing large, single PAVM of right lower lobe with a single artery.

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PAVM: Diagnostic Testing, Echo Bubble Study

Common protocol:

- CT w/contrast once chest x-ray suspicious of PAVM
- Contrast echocardiography is done to determine the presence of right-to-left shunt
- If the patient is eligible for further intervention, pulmonary angiography is done to define anatomical details of the lesion

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PAVM: Diagnostic Testing, Echo Bubble Study

- Do NOT inject agitated saline through intrapulmonary catheters in wedge position, as microbubbles may then cross the pulmonary capillary bed.
- PAVM: Micro-bubbles appear in the left side of the heart **after 4-5 cardiac cycles "late bubbles"**.
- **PAVM = Late bubbles**

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PAVM: Late Bubbles

- Pulmonary shunting may be diagnosed on the basis of a delay
- **4-5 cardiac cycle delay** before bubbles appear in the **left atrium** after their first appearance in the right atrium
- Delay depends on the quantity, anatomic locations, and sizes of PAVMs - delay of 2-8 cycles have been noted
- Cautious about depending solely on the timing (Large RA, etc.)

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PAVM and Valsalva

- The diagnosis of PAVM-related pulmonary shunting depends on a saline contrast injection **without** the Valsalva maneuver
- Why?

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Intracardiac hemodynamics

- Inspiration: Intrathoracic pressure decreases
 - Augmented flow into the right atrium and ventricle
 - Decreased flow out of the pulmonary veins into the left atrium and ventricle
- Expiration: Intrathoracic pressure increases
 - Mild decrease in right ventricular diastolic filling and subsequent increase in left ventricular filling.
- **These respiration-related variations influence the timing of intracardiac & pulmonary shunting on saline bubble studies**



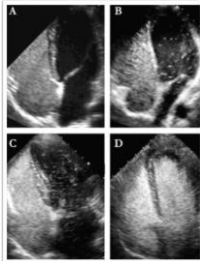
Intracardiac versus Pulmonary R-to-L Shunting

- Perform saline bubble study both with and without the Valsalva maneuver during normal respiration to help determine intracardiac v. pulmonary
- PAVM will have delayed bubbles w/out Valsalva



Pulmonary Shunts: Grading

- No shunt
- Grade 1
- Grade 2
- Grade 3



PAVM: Treatment

- Treatment modalities have evolved from invasive surgeries to catheter-based interventions
 - Embolization
 - Pushable coils
 - Detachable plug to occlude
- The intended site of occlusion is the feeding artery, not the actual fistula or draining vein.
- High technical success rate for the treatment of PAVMs



Pericardiocentesis

Echo Guided Pericardiocentesis

- During pericardiocentesis; agitated saline could be used during the procedure to differentiate if the needle is within the pericardium or in one the cardiac chambers (mostly RV)
- Push agitated saline and look for the microbubbles either in the pericardium or within a chamber.



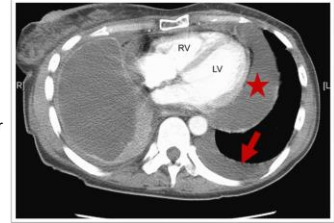
Echo Guided Pericardiocentesis

- 43-year-old African American woman
- Recurrent breast cancer
- Increasing shortness of breath
- Lower extremity edema
- Known recurrent pleural effusions
- CT ordered

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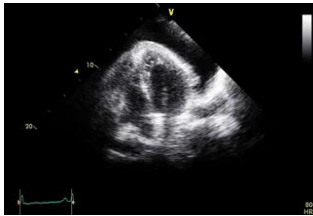
Case Study: CT

- Large, circumferential pericardial effusion ★
- Moderate sized pleural effusion →
- Referred to cardiology for consultation and consideration for pericardiocentesis.



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Case Study: Echocardiogram



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Case Study: Echo Findings / Action Plan

- Large pericardial effusion
- Partial collapse of right sided chambers
- No clinical tamponade
- Pericardiocentesis ordered to ease symptoms
- Allow for diagnostic evaluation

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Case Study: Bubble Study Plan

- To prevent the inadvertent placement of the catheter in the right heart, agitated saline was injected through the tip of the pericardiocentesis needle to determine its location prior to tract dilation and insertion of a drainage catheter.

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Case Study: Pericardiocentesis Bubble Study

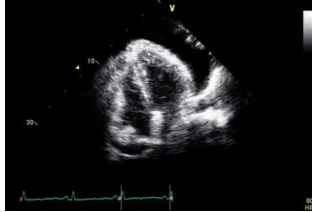
- The initial bubble injection clearly demonstrated opacification of the right-sided cardiac chambers



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Case Study: Pericardiocentesis Bubble Study

- The needle was pulled back, and a second bubble injection demonstrated localization in the pericardial space



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Case Study: Outcome

- The guidewire was inserted
- Tract was dilated
- Pericardial drainage catheter was successfully placed in the pericardial space
- Approximately 800 cm³ of pericardial fluid was removed.

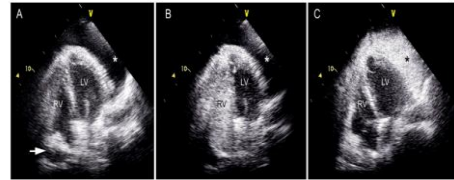
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Case Study: Echo Findings / Action Plan

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- Partial collapse of right sided chambers
- No clinical tamponade
- Pericardiocentesis ordered to ease symptoms
- Allow for diagnostic evaluation

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Echo Guided Pericardiocentesis



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Central Venous Line Control

Central Venous Line Control

- Contrast should appear immediately in RA after forceful push through one of the central line ports
- If bubbles do not appear at all this means arterial cannulation
- If bubbles appearing late this means coiling of the catheter
- When using a central venous line port and forceful saline push some agitation takes place even without air, so you can skip the step with 0.5 – 1 ml of air.

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Safety



Safety

Potential complications

- Risk for systemic air emboli
- Safety of saline bubble study well documented in a large retrospective survey
 - 363 physicians
 - 27,000 bubble studies
 - Over 16-year period
- (0.062%), Transient side effects: Lightheadedness, visual sparks, flashing lights, blind spots, central and peripheral numbness, nausea, vagal symptoms, anxiety
- Low risk and NO residual side effects or complications were reported



Safety

- Agitated saline injection is safe with very few (if any) side effects that are mostly related to injection site.
- Safety Tips:
 - Point syringe tip down / plunger up during injection
 - Air stays up near the plunger
- You can not empty the syringe completely - stop the injection when close to the last 2ml
- You can use less air (0.5 instead of 1mL)



Is it Safe NOT to perform Bubble Studies?

PFO:

ASE study shows color flow alone is not enough to accurately detect PFOs

PAVM:

- CT produces **negative results** in 55% of PAVM patients with grades 2 and 3 pulmonary shunts
- Echo - **negative results** in 8%



Unusual Diagnosis

Echo Bubble Study



Superior Vena Cava Syndrome

Echo Bubble Study



Superior Vena Cava Syndrome

- SVC Syndrome
- Obstruction of blood flow through the SVC
- Often manifests in pts with malignant disease: Lymphoma & lung cancer
- Complete occlusion = Bypass of head, neck, and upper limbs venous drainage
- Medical emergency – requires immediate diagnostic evaluation and treatment



Shunt Mechanism

- SVC occlusion can cause opening of unusual collaterals between systemic and pulmonary veins
- Driven by increased venous pressures
- Results in right to left shunt
- These unusual shunts can cause hypoxemia and systemic embolism



Case study

- 26F
- Chronic illness
- Previous pulmonary embolism
- Currently taking blood thinners
- Episode of slurred speech after a routine flushing of her central venous line port
- Head CT excluded an acute brain pathology
- Echo ordered and a transthoracic



TTE

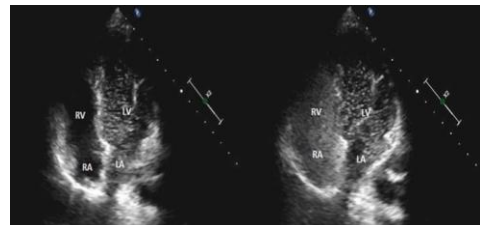
- Normal LV size and function
- Normal RV size and function
- No evidence of valvular abnormalities
- No Pulmonary hypertension
- No intracardiac shunts

Agitated Saline Study

- Performed to exclude an PFO/ASD due to her symptoms of TIA)
- Left arm injection
 - **demonstrated bubbles entering the left atrium (LA) before their appearance in the right atrium (RA)**
- The patient complained of a transient headache immediately after the agitated saline (bubbles) injection, although she did not have any focal neurological symptoms

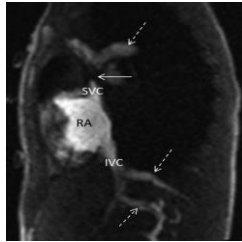


Bubbles enter LA before RA!



MRI

- Cardiac MRI showed occlusion of SVC
- Dilated azygos venous system
- Azygos → IVC → RA



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Cardiac MRI Findings

- Structurally normal heart
- Occluded SVC
- MRI Contrast: **Flowing into LA before RA**, bypassing the pulmonary arterial circulation
- Azygos venous system dilated → draining into IVC → into RA

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Why/How??

- Remember echo showed bubbles entering the left atrium (LA) before their appearance in the right atrium (RA)
- MRI confirmed venous → venous shunting
- Why/how are bubbles entering LA before RA

- CT ordered

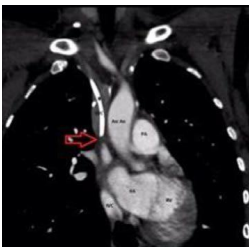
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Chest CT with Contrast

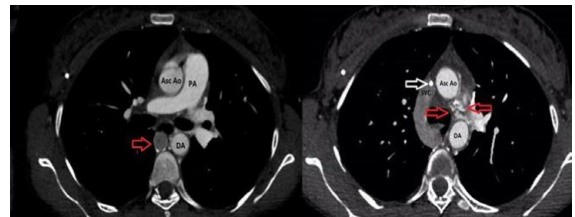
- Occlusion of the SVC at the level of the **central line tip**
- Azygos venous system dilated → draining into IVC → into RA
- **Multiple mediastinal collateral vessels → into the pulmonary veins**

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SVC Occlusion



Dilated Azygos Venous System



Treatment: Angioplasty

- Angioplasty of the occluded SVC was performed and her port was replaced



Case Study Review

- “SVC syndrome” is a well-known clinical entity characterized by SVC occlusion causing the bypass of head, neck, and upper limbs venous drainage through the azygos venous system
- In this case, **the systemic-to-pulmonary venous shunt was formed by multiple mediastinal collateral vessels**
- Causing bubbles to appear in the LA before the RA



Discussion

- Traditionally, echo bubble studies are used to assess the existence of an interatrial communication
- In this case, it played a pivotal role in the diagnosis of an extracardiac shunt
- The diagnosis was suspected based on the timing of bubbles
 - LA before the RA, which represents a very unusual pattern
- Multimodality imaging demonstrated the unusual etiology and pathophysiology



Bubble Study Conclusion



Conclusion

- Agitated saline is cheap, easy to perform and safe - with lots of added information when properly used
- Mostly used to R/O PFO

Findings that Help Exclude Patent Foramen Ovale
1. Right atrial dense opacification (especially adjacent to the septum), and
2. Transient leftward shifting of the interatrial septum, but
3. No bubbles in the left atrium seen to emerge through the interatrial septum, or
4. Bubbles noted in LA only after 3–5 cardiac cycles after the transient septal shift



Slides/Meeting Handout available at:

www.cardioserv.net/MCSS



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