Shock and Awe: A dynamic approach to resuscitation

Critical Care Symposium
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Anna Perrello, RPA-C, MPAS
Brian Kersten, PharmD, BCCCP, BCPS

Disclosures

- Brian Kersten
  - Nothing to disclose
- Anna Perrello
  - Nothing to disclose

Objectives

- Identify and explain the physiology of various shock states including distributive, cardiogenic, obstructive and hypovolemic.
- Discuss advantages and limitations to static and dynamic predictors of volume responsiveness.
- Recognize techniques related to visualization of basic structures and medium identification during bedside ultrasonography.
- Evaluate treatment options for shock states using dynamic measures for fluid resuscitation

Shock

- A heterogenous syndrome best defined as circulatory failure
  - Originates from mismatch between oxygen delivery (DO_2) and oxygen consumption (VO_2)

- Often becomes apparent in setting of arterial hypotension

Differentiating Shock

	Wedge pressure	Cardiac output	Systemic vascular resistance	Mixed venous oxygen
Hypovolemic - Hemorrhage - Dehydration	↓	↓	↑	↓
Cardiogenic - Myocardial infarction - Arrhythmia - Cardiomyopathy	↑	↓	↑	↓
Obstructive - Pulmonary embolism - Tension pneumothorax - Cardiac tamponade	↑↔	↓	↑	↓
Distributive - Septic shock - Anaphylaxis - Neurogenic - Myxedema coma - Post-cardiopulmonary bypass	↑↔	↑	↓	↑

Goals of Therapy in Shock

- Restore effective tissue perfusion and normalize cellular metabolism by ensuring systemic oxygen delivery by
    1. Aggressive and appropriate fluid resuscitation
    2. Supporting CO and MAP
- Above are titrated to individual endpoints and used together to assess adequacy of resuscitation
    1. Markers suggesting adequate tissue perfusion
    2. Markers suggesting adequate intravascular volume
    3. Target MAP

Shock and Awe

- Military doctrine of rapid dominance

Question

- Global (macrocirculatory) oxygen delivery (DO_2) can be best approximated by which variable?
  1. Arterial partial pressure of oxygen (PaO_2)
  2. Arterial oxygen saturation (SaO_2)
  3. Hemoglobin
  4. Systemic vascular resistance (SVR)
  5. Stroke volume (SV)

Global Tissue Perfusion

- 'Macrocirculation'
  - DO_2 = CO x CaO2
  - DO_2 = (SV x HR) x ([0.0138 x Hgb x SaO2] + [0.0031 x PaO2])
    - Increasing hemoglobin and oxygen produce minimal changes in oxygen delivery
    - Heart rate is generally at maximum compensation, therefore
  - **DO_2 = SV** ~~x (HR) x ([0.0138 x Hgb x SaO2] + [0.0031 x PaO2])~~
- Regional tissue perfusion (microcirculation)
    - Not predicted by DO_2

Assessing perfusion

Physical Exam

- Mean arterial pressure
- Mentation
  - Cerebral perfusion
- Urine output (>0.5ml/kg/hr)
- Capillary refill
- Skin perfusion/mottling
- Cold (or warm) extremities
- Generalized edema
  - Pulmonary edema
- Intra-abdominal pressure

Laboratory

- Lactate
- pH, pCO_2 and HCO_3
- $SCVO_2$ or SVO_2

Volume Challenge

- Reserved for hemodynamically unstable patients with three advantages
  1. Opportunity to quantitate response during infusion
  2. Prompt correction of fluid (preload) deficits
  3. Minimizing risk of volume overload

- Only ~50% of hemodynamically unstable patients are fluid responsive after initial resuscitation
  - Aggressive and overzealous fluid administration can lead to severe tissue edema and compromised organ function

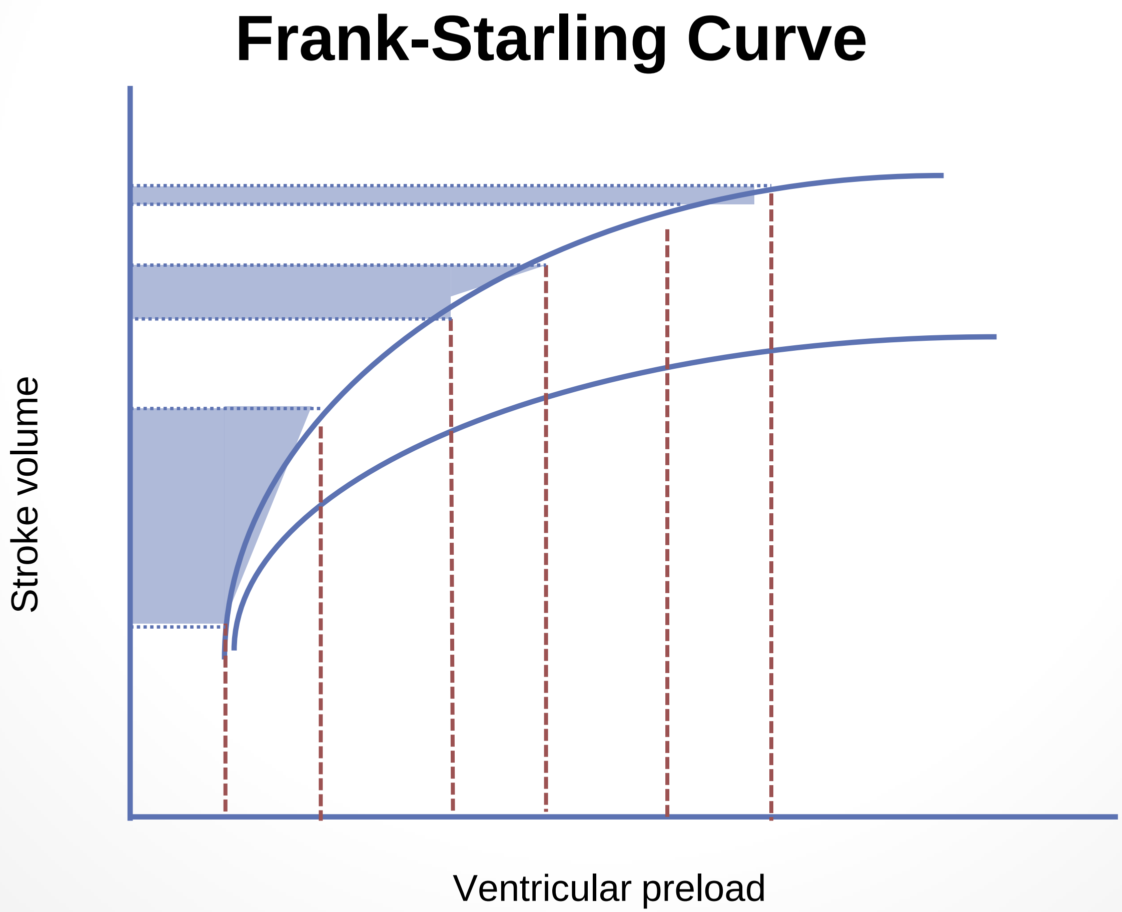
Vincent JL. Crit Care Med 2006; 34:1333-1337
Marik PE. Crit Care Med 2013; 41:1774-1781

Question

- Which of the following is best to utilize for quantifying a response to a volume challenge?
  1. Central venous pressure (CVP)
  2. Mean arterial pressure (MAP)
  3. Pulmonary capillary wedge pressure (PCWP)
  4. Pulse pressure variation (PPV)
  5. Urine output

Stroke Volume

- Dependent on preload and contractility in shock



Volume responsiveness - Static

CVP = RAP = RVEDP = RVEDV = RV Preload ≈ PCWP = LVEDP = LVEDV = LV Preload

Measure*	Premise	Limitations	Takeaway
Central venous pressure (CVP)	CVP surrogate for PCWP & PCWP = LVEDP (and thus stroke volume)	CVP or ΔCVP does not correlate with intravascular volume or stroke index/cardiac output	DO NOT USE 
Pulmonary capillary wedge pressure (PCWP)	PCWP = LVEDP	LVEDP can be altered independently of LVEDV; does not	DO NOT USE

*Other measures: left ventricular end diastolic area (LVEDA), right ventricular end diastolic volume (RVEDV) similar concerns

Kumar A. Crit Care Med 2004; 32:691-699.
Marik PE. Chest 2008; 134:172-178
Marik PE. Crit Care Med 2013; 41:1774-1781

CVP & PCWP and Cardiac Output

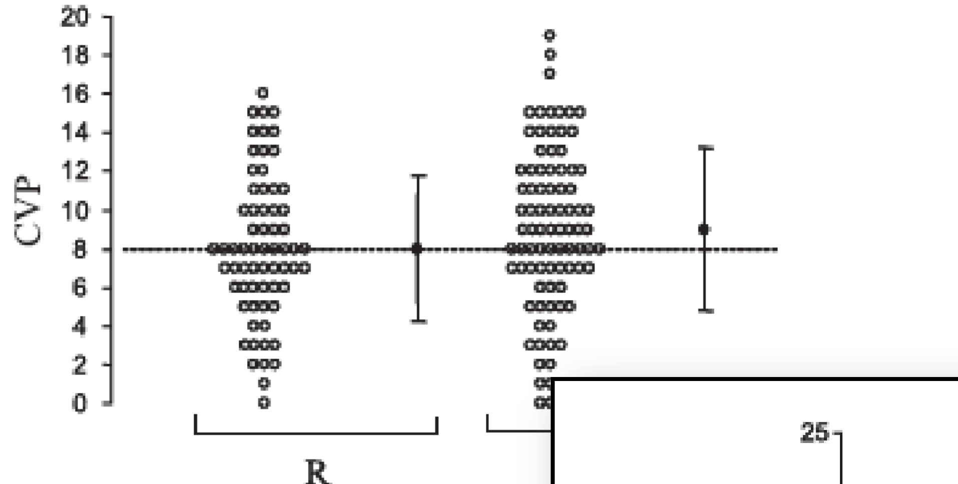


Figure 2. Individual values (*open circles*) and mean ± SD (*closed ci*
pressure (*CVP*) (both expressed in millimeters of mercury) in resp

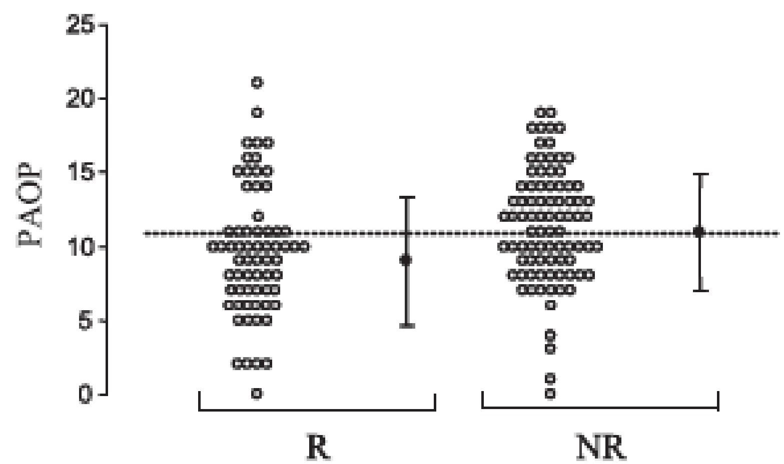


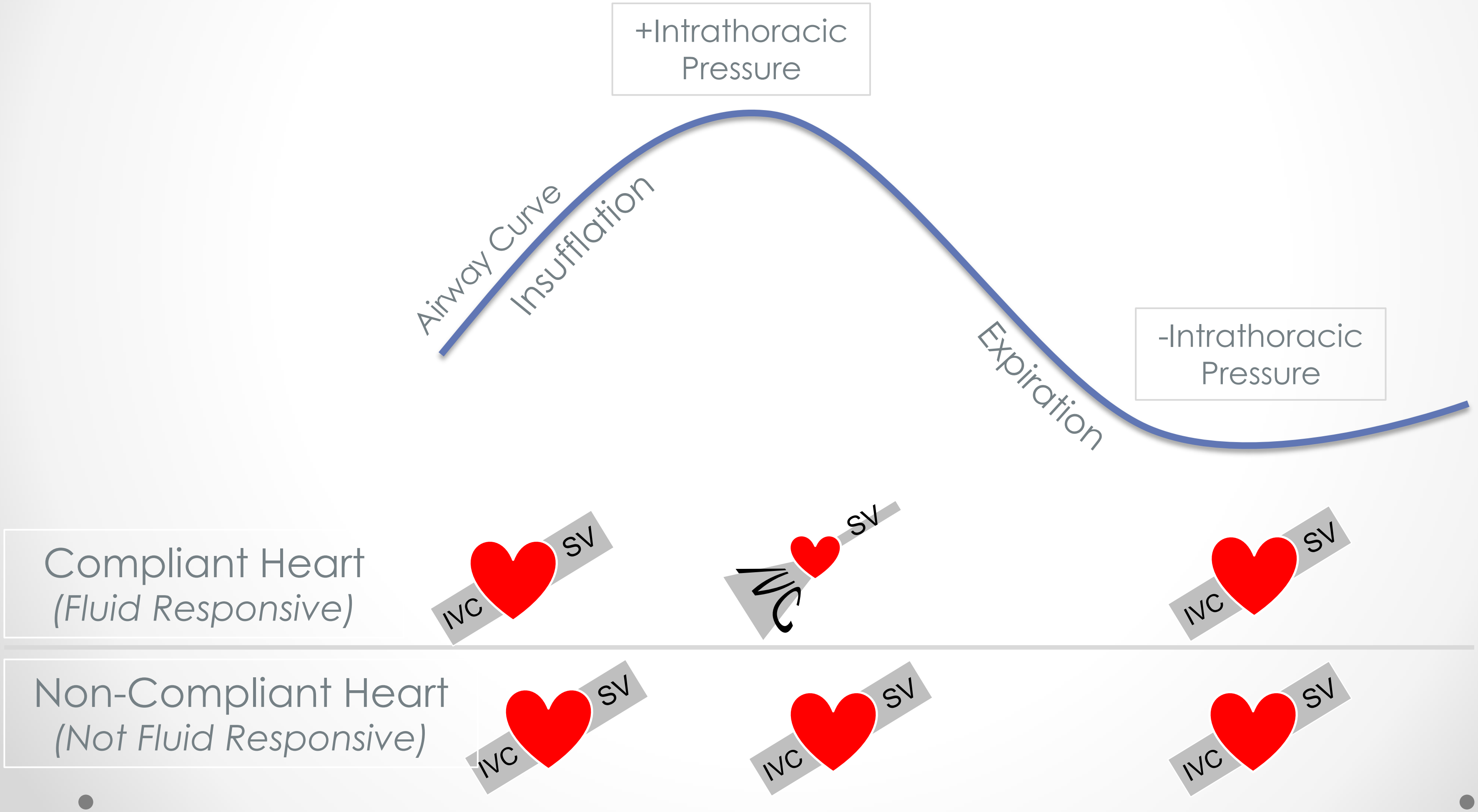
Figure 3. Individual values (*open circles*) and mean ± SD (*closed circles*) of pre-infusion pulmonary artery occlusion pressure (*PAOP*) (both expressed in millimeters of mercury) in responders (*R*) and nonresponders (*NR*).

Osman D. Crit Care Med 2007; 35:64-68

Dynamic Measurements of Fluid Responsiveness

- Dynamic measures are used to exploit the existing relationship between heart and lungs during mechanical ventilation
- To evaluate a patient's location on the Frank-Starling curve, the following dynamic measures can be used:
  - Stroke Volume Variation (SVV)
  - Pulse Pressure Variation (PPV)
  - IVC Diameter Variation (ΔD_{IVC})

Effects of Mechanical Ventilation on Intrathoracic Structures



Stroke Volume Variation (SVV)

- Procedure:
  - Arterial line is placed, and the change in area under the arterial wave form during respiratory variation is compared

- **ΔSVV 12-13%** correlated with an increase of CO ≥ 15% after volume expansion, was highly predictive of fluid responsiveness[1]

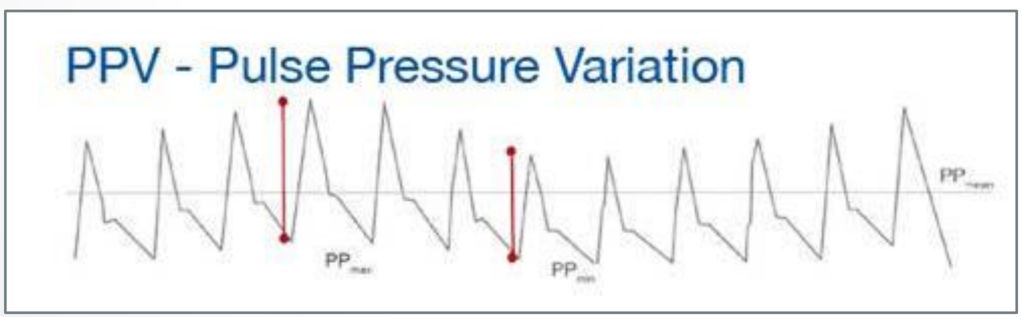
	SVV
Sensitivity	0.82
Specificity	0.86

[1]Marik, PE, et al. Stroke volume variation and fluid responsiveness. A systematic review of the literature. *Critical Care Med 2009; 37; 2642-7.*
"Advanced Monitoring Parameters: SVV, PPV." *Change Region*, Maquet Getinge Group, www.maquet.com/uk/services/advanced-monitoring-parameters/svv-ppv/. September 2 2017.

Pulse Pressure Variation (PPV)

- Procedure:
  - Arterial line is placed, calculated difference (%) of pulse pressure between inspiration and expiration

- **ΔPPV 12-13%** correlated with an increase of CO ≥ 15% after volume expansion, was highly predictive of fluid responsiveness[1]



	PPV
Sensitivity	0.89
Specificity	0.88

[1]Marik, PE, et al. Stroke volume variation and fluid responsiveness. A systematic review of the literature. *Critical Care Med 2009; 37; 2642-7.*

"Advanced Monitoring Parameters: SVV, PPV." *Change Region*, Maquet Getinge Group, www.maquet.com/uk/services/advanced-monitoring-parameters/svv-ppv/. September 2 2017.

IVC Variation

- Non-invasive measure to assess for fluid responsiveness in *mechanically ventilated* patients
- Procedure:
  - 2D Echocardiography is used, IVC visualized in subxiphoidal view, measurements made in M-Mode during respiratory cycle at ~3cm from right atrium
  - Difference calculated as ΔD_{IVC} as a percentage

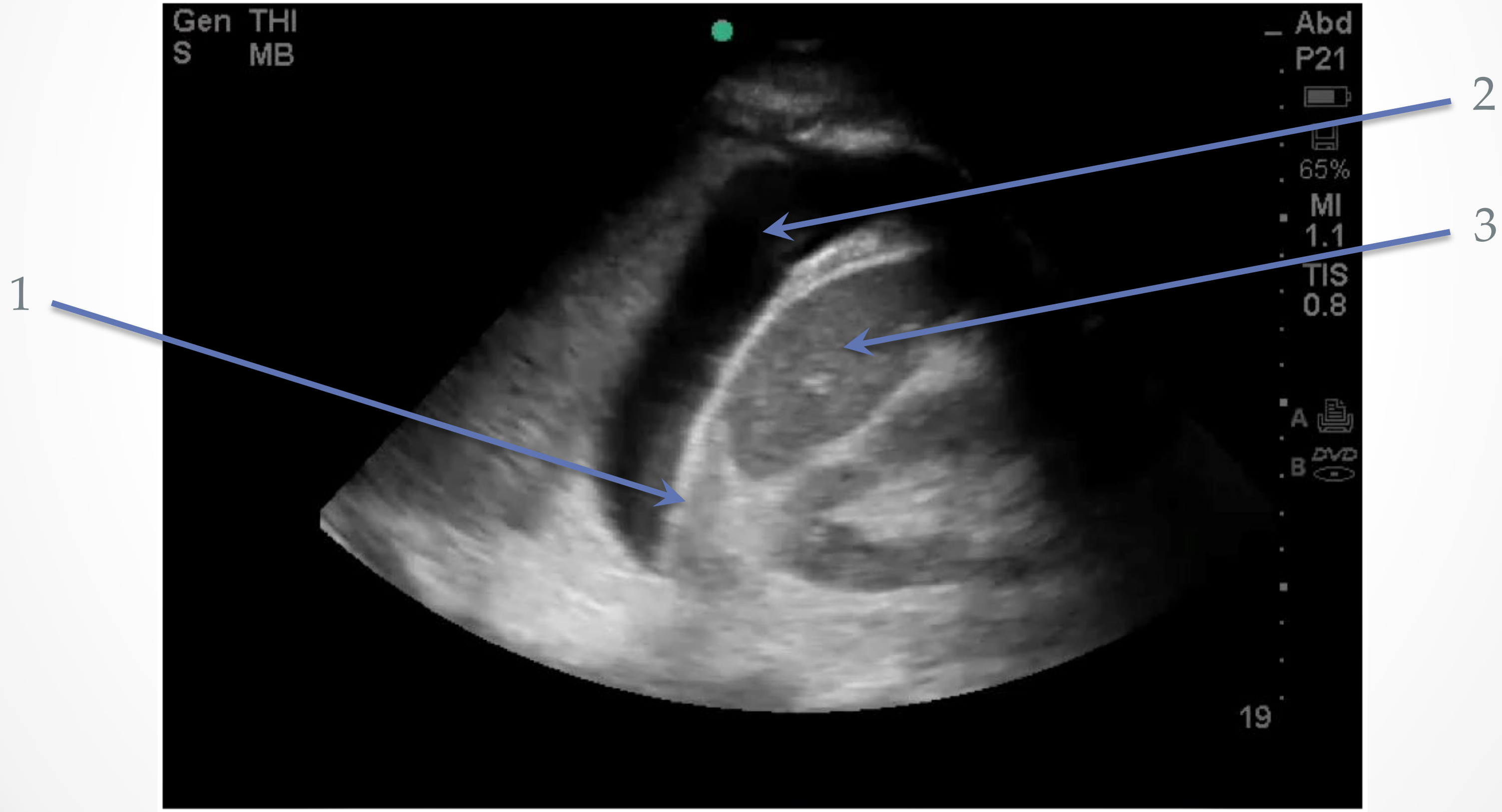
- ΔD_{IVC} 12-18% with subsequent increase of CO ≥ 15% after volume expansion, correlated with fluid responsiveness[3,4]
  - Positive Predictive Value: 93%
  - Negative Predictive Value: 92%

[3]Feissel, M. et al. Intensive Care Med (2004) 30: 1834.http://doi-org.gate.lib.buffalo.edu//100.1007/s00134-004-2233-5
[4]Barbier, C. et al. Intensive Care Med(2004) 30:1740. Http://doi-org.gate.lib.buffalo.edu/10.1007/s00134-004-2259-8

Identification of Structures and Mediums on Ultrasound

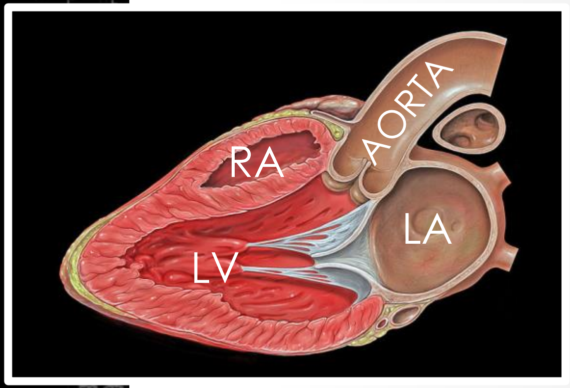
- **White:** Hyperechoic, often dense/calcified tissue; pericardium, diaphragm
- **Black:** Anechoic; **fluid;** blood, pleural fluid
- **Light/Dark Gray:** Hypoechoic, isoechoic; organs or structures, soft tissue, may indicate sluggish blood flow, thrombus
- **Air:** White/gray, STRONG reflector of sound waves, impedes visibility, often a limitation during bedside evaluation

Identification of Structures and Mediums on Ultrasound



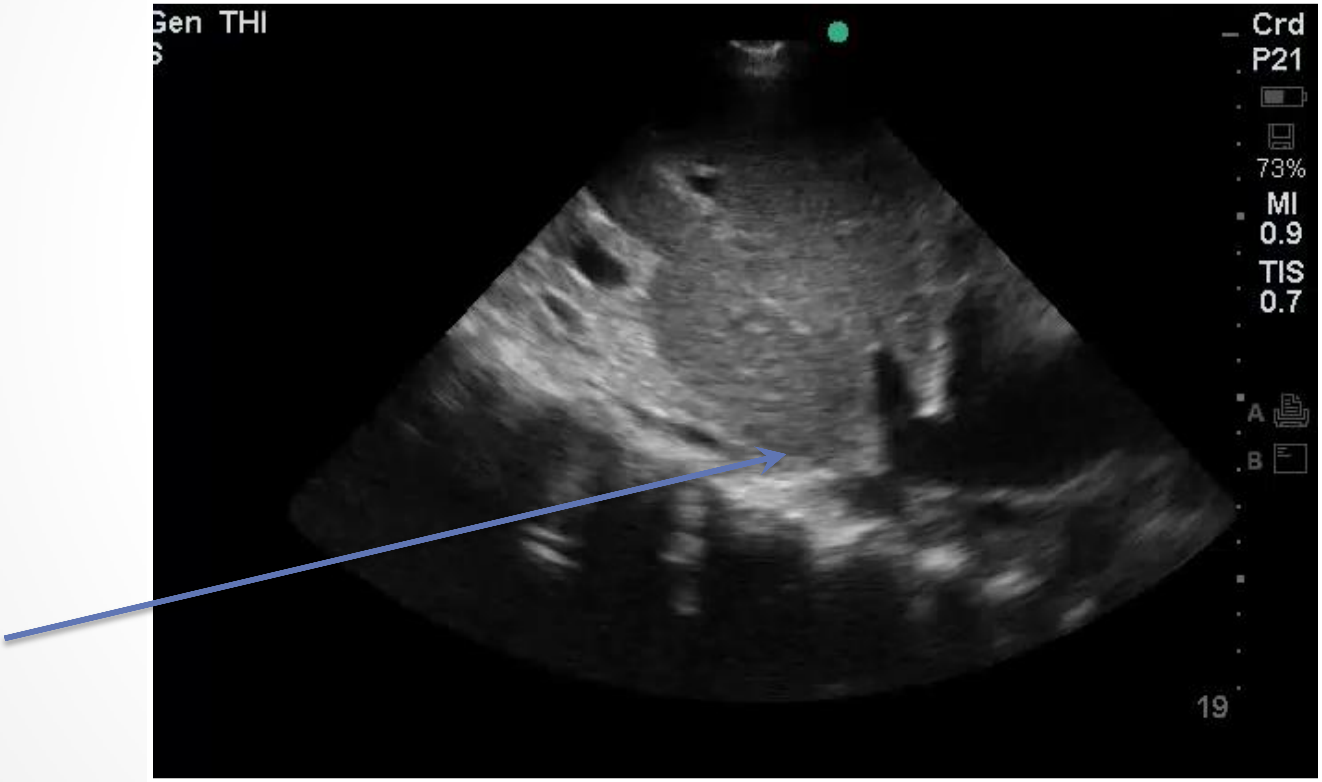
Transducer placed on left chest, along midaxillary line

Identification of Structures and Mediums on Ultrasound



Parasternal Long Axis

Identification of Structures and Mediums on Ultrasound



Transducer placed subxiphoid view

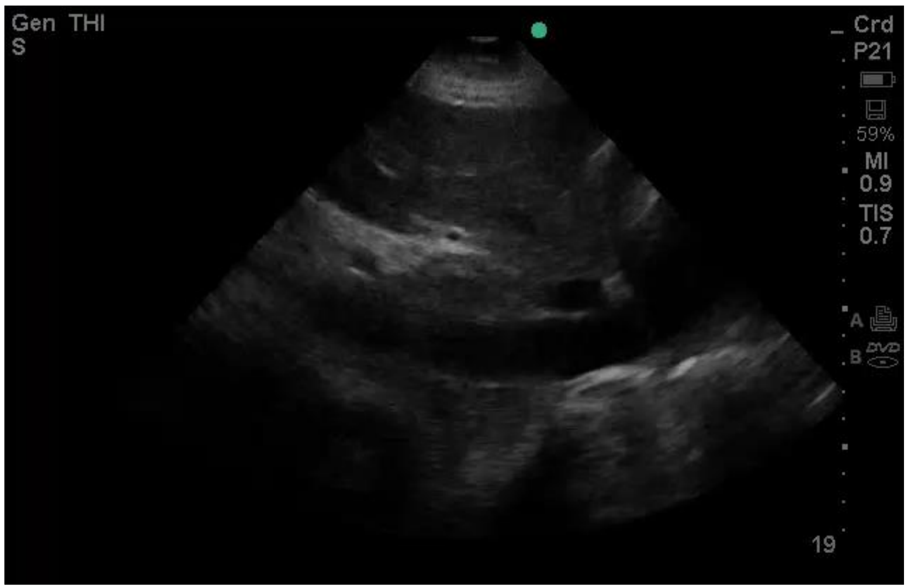
IVC Variation

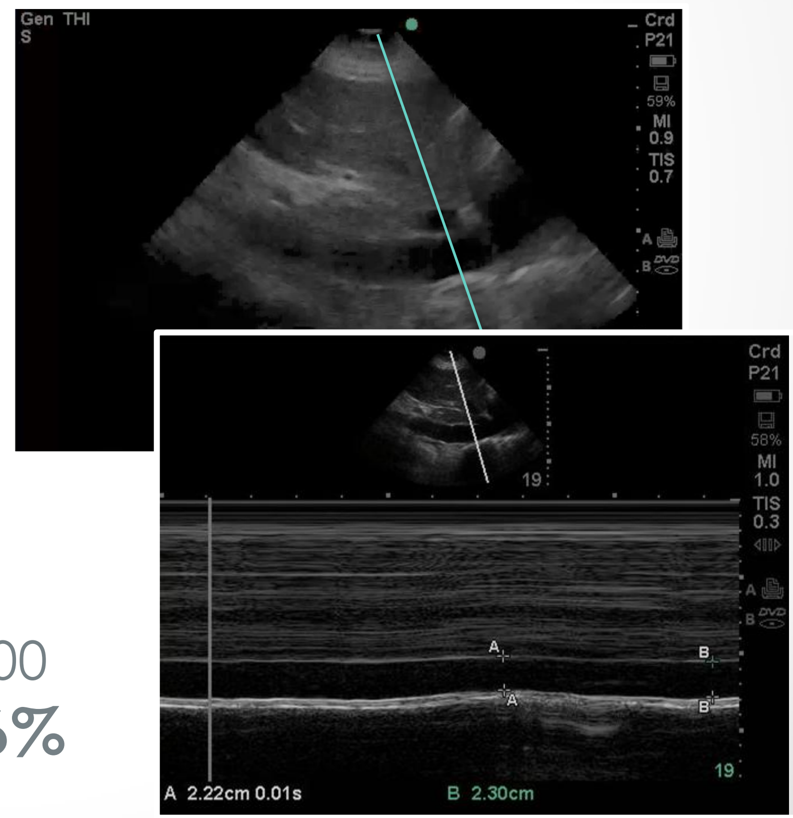
ΔD_{IVC}

ΔD_{IVC}

Inferior Vena Cava Variation to Assess for Fluid Responsiveness

Is this patient likely to be fluid responsive?





$\Delta D_{IVC}(\%)=[(IVCD_b\text{-}IVCD_a)/IVCD_b]\text{x}100$

$\Delta D_{IVC}(\%)=[(2.30\text{-}2.22)/2.22]\text{x}100=\mathbf{3.6\%}$

Limitations of PP, SV and IVC Variation

- Limitations:
  - Patient must be mechanically ventilated with a V_t of at least 8ml/kg of IBW
  - No arrhythmias present
  - Passive ventilation
  - No increase in IAP or open chest
  - Requires arterial line placement (PPV and SVV)
  - Required Hemodynamic Monitoring Device (SVV)
  - Experience of ultrasonographer (IVC Variation)

Passive Leg Raise

- Non-invasive measure to assess for fluid responsiveness in *spontaneously breathing* patients
- PLR to 30˚ simulates ~300cc fluid bolus to the patient that is easily reversible

- Procedure:
  - Patient is placed in a supine position, passive leg raise of 30˚, returned to supine position, administered 500cc NS
  - HR, BP and aortic flow velocity measured at each interval

Passive Leg Raise

- Aortic Flow Velocity (marker of SV) measured with bedside echocardiography, an increase of **CO and SV >12%** was noted to be significant and correlated with fluid responsiveness[2]

	Sensitivity	Specificity
CO	63%	89%
SV	69%	89%

- Limitations:
  - Good echocardiographic widows required for evaluation of SV and CO
  - Advanced echocardiographic skills
  - Technically difficult in many ICU patients

[2]Maizel, J. et al. Intensive Care Med (2007) 33: 1133. http://doi.org.gate.lib.buffalo.edu/10.1007/s00134-007-0642-7

Summary of Static and Dynamic Measures

Method	Technology	Sensitivity, Specificity, AUC
Pulse pressure variation (PPV)	Arterial waveform	Sensitivity 89% Specificity 88%
Stroke volume variation (SVV)	Pulse contour analysis	Sensitivity 82% Specificity 86%
IVC Variation (ΔD_{IVC})	Echocardiography	Sensitivity 93% Specificity 92%
Passive Leg Raise	Echocardiography	Sensitivity 63% Specificity 89%
Central venous pressure (CVP)	Central venous catheter	AUC: 0.55 (0.48-0.62)

1 Case Study

Case Study One

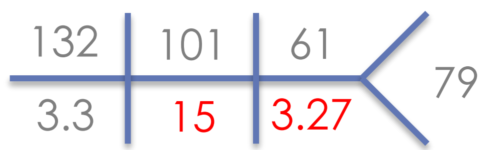
- 44 y/o F presents with SOB and 10/10 extremity pain with subsequent difficulty ambulating, and decreased urine output

- PMHx:
    - IVDA, currently on Suboxone
    - Anxiety
    - Fungemia ~6 months ago s/p full treatment course
    - H/o Empyema requiring thoracentesis

Case Study One

- Vitals on admission :
  - HR: 154, Sinus Tachycardia
  - BP: 96/79, on 10mcg of Levophed infusion
  - Temperature: 36.6˚
  - RR: 35-47
  - Spo2: 97% on 50% Venti-Mask

Initial Labs:



VBG: 7.25/38/74/17
Lactate: 2.9

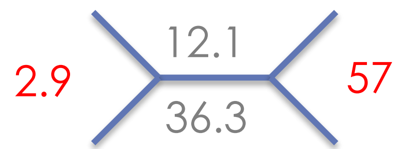
Mg: 1.4
AST/ALT: 48/17
Albumin: 2.5
Calcium: 8.2

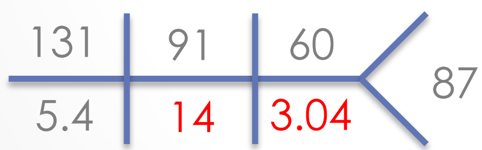
U/a w/ Micro: 1+ leuk esterase, +26-100 leukocytes, +26-100 erythrocytes, few bacteria

Case Study One

- Given additional 2L NS
- Patient was intubated for respiratory failure
- Started on Vanco, Zosyn, and Micafungin

- **Repeat Labs:**

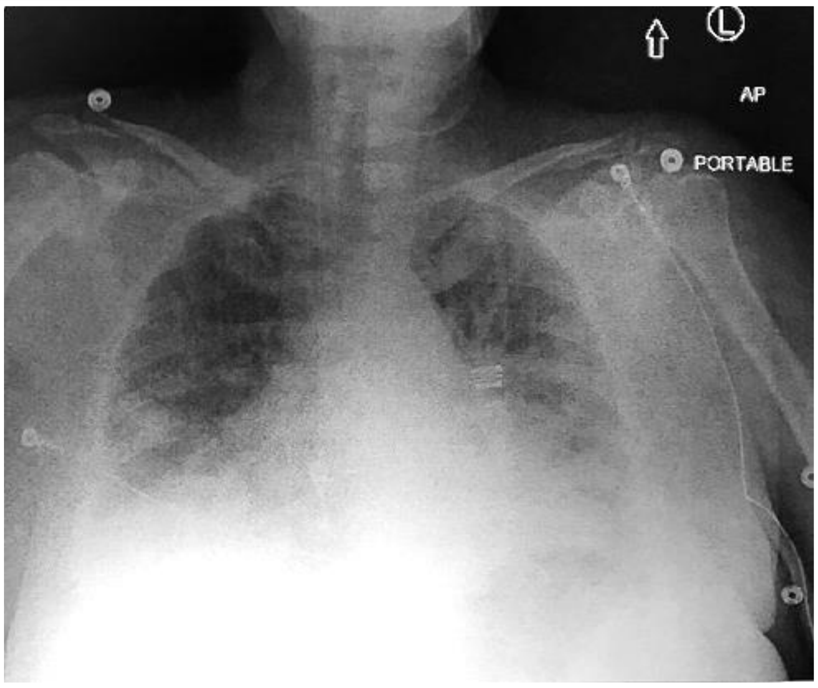




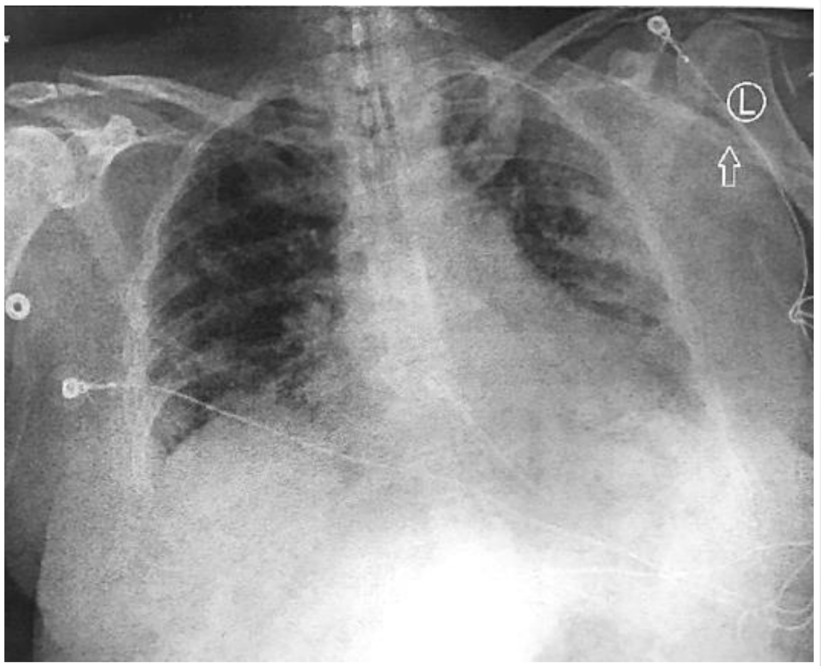
ABG: 7.19/38/65/14
Lactate: 4.3

Case Study One

- Chest portable on admission :

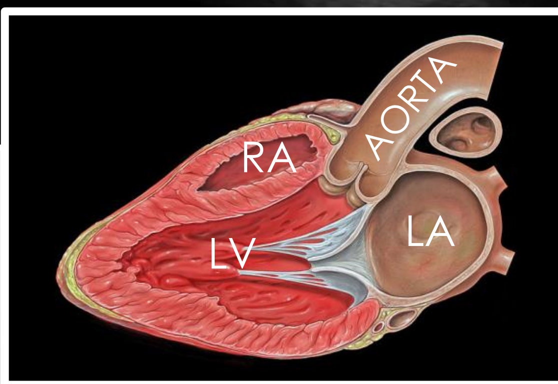


Chest portable post-intubation:



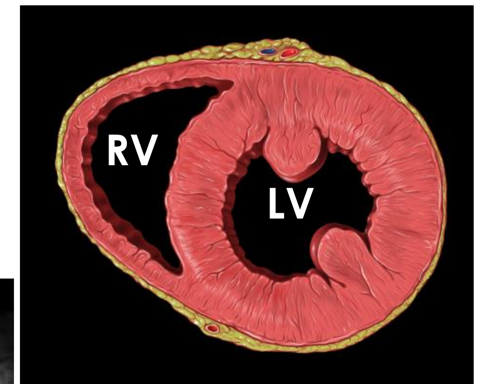
Case Study One

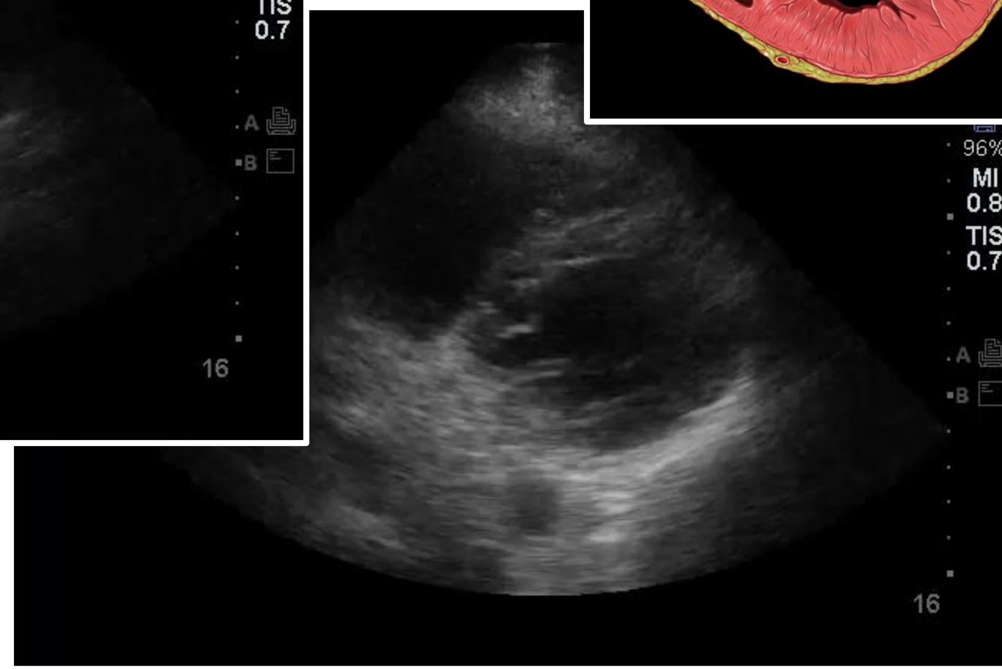
- Bedside US:



- Parasternal Long Axis

Parasternal Short Axis





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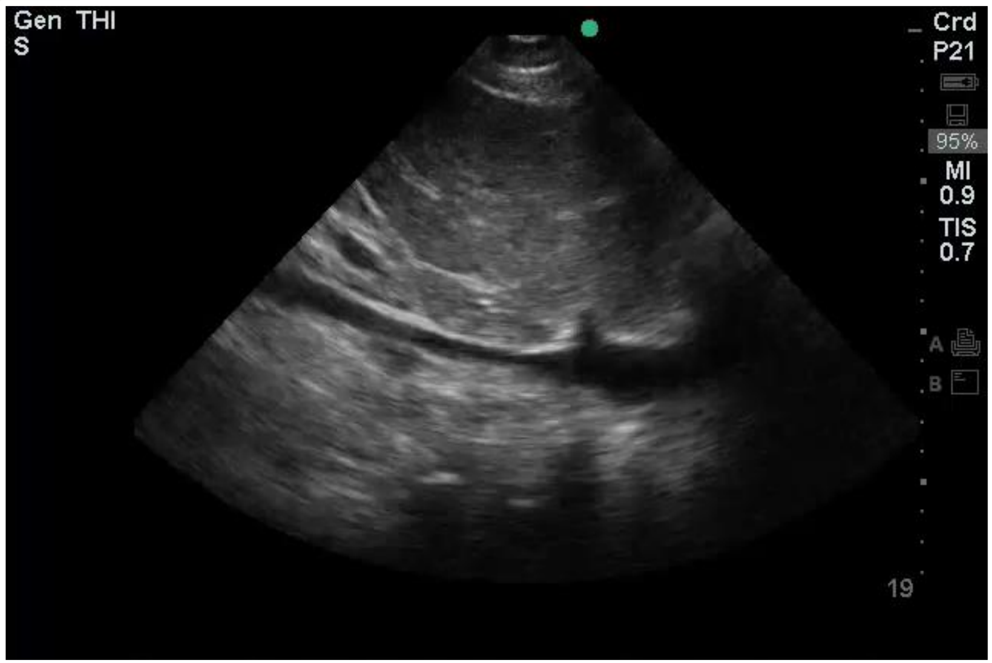
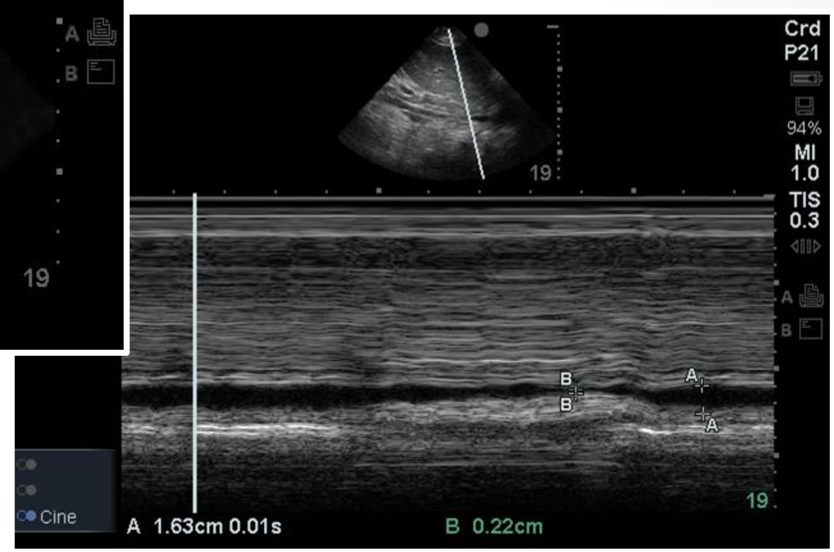
Case Study One

- Bedside US:



$\Delta D_{IVC}(\%)=$ **640%**



Is the patient likely to be fluid responsive?

Case Study One: Diagnosis

- Patient was treated for severe septic shock, additional 4L IVF given
- Vasopressin added to Levophed gtt
- Patient grew +2/2 Blood cultures for Gram Positive Cocci in clusters within 8 hours of admission

Crystalloid vs colloid

Trial	Design	Population	Interventions	Results	Conclusion
SAFE 2004	Multicenter, randomized, double-blind	Medical, surgical intravascular volume ICU resuscitation	4% albumin (n= 3497) 0.9% sodium chloride (n=3500)	RR death at 28 days 0.99 (95%CI; 0.91-1.09); Trends in sepsis and trauma for and against albumin	No mortality difference in heterogeneous population
CHEST 2012	Multicenter, randomized, blinded, parallel-group	Medical and surgical patients w/ hypovolemia in ICU	HES 130/0.4 (n=3358) vs 0.9% NaCl (n=3384)	RR mortality at 90 days 1.06 (95%CI; 0.96 -1.18).	No mortality difference, but increased AKI and RRT in HES
6S 2012	Multicenter, randomized, blinded, parallel-group	Medical and surgical patients with severe sepsis in ICU	HES 130/0.4 (n=398) vs Ringer's acetate (n=400)	RR 90-day mortality 1.17 (95% CI; 1.01-1.36) favoring Ringer's	Increased mortality and RRT with HES
CRISTAL 2013	Multicenter, randomized, open-label	Sepsis, trauma, hypovolemic shock in ICU	Colloids (n=1414); Crystalloids (n=1443)	No difference (25.4 vs 27%) in 28-day mortality. Decreased 90-day mortality	No difference in mortality for hypovolemia in ICU patients
ALBIOS 2014	Multicenter, randomized, open-label	Severe sepsis medical/surgical ICU	20% albumin & crystalloid (n=903) vs crystalloid alone (n=907)	RR death at 28 days 1.0 (95% CI; 0.87-1.14); no difference at 90 days	No mortality benefit

Crystalloid vs colloid

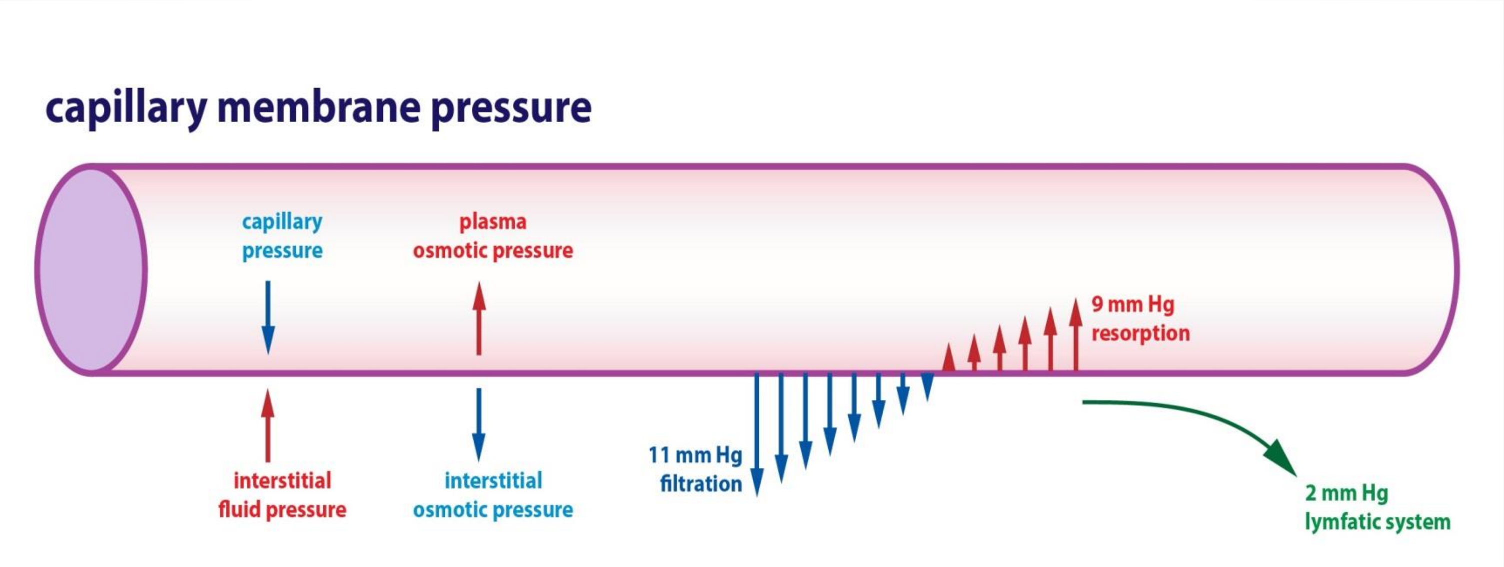
- No evidence from randomized trials that resuscitation with colloids reduces mortality compared with crystalloids
  - HES solutions may increase mortality and AKI
- Avoid albumin and hypotonic solutions in TBI
  - Potential increased mortality due to increased intracranial pressure

Cochrance Database Syst Rev. 2013: 28;2 CD00D567
NEJM 2004; 350:2247-56

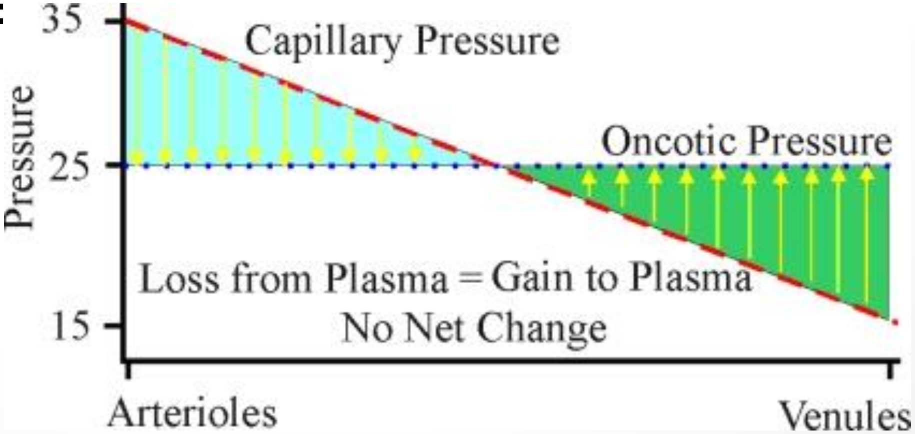
Question

- In microcirculatory models interstitial edema ('third-spacing') is influenced mainly by
    1. Low capillary oncotic pressure (π_P)
    2. High capillary hydrostatic pressure (P_C)
    3. High interstitial oncotic pressure (π_I)
    4. High interstitial hydrostatic pressure (P_I)

Starling Forces



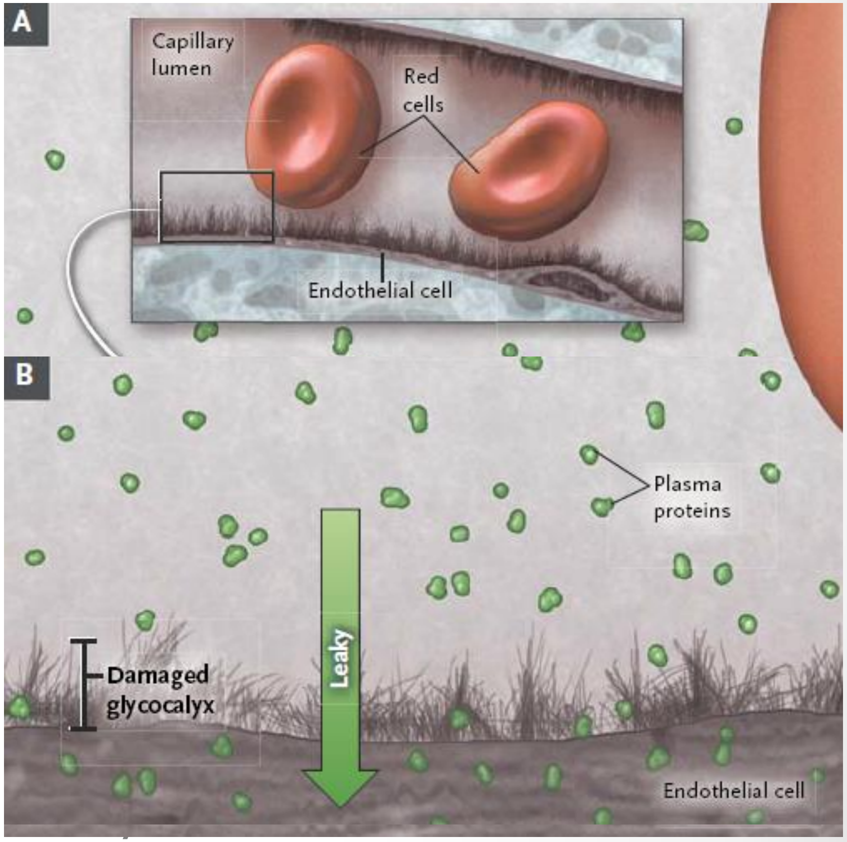
Net filtration pressure = $(P_C - P_I) - (\pi_P - \pi_I)$



Endothelial Glycocalyx

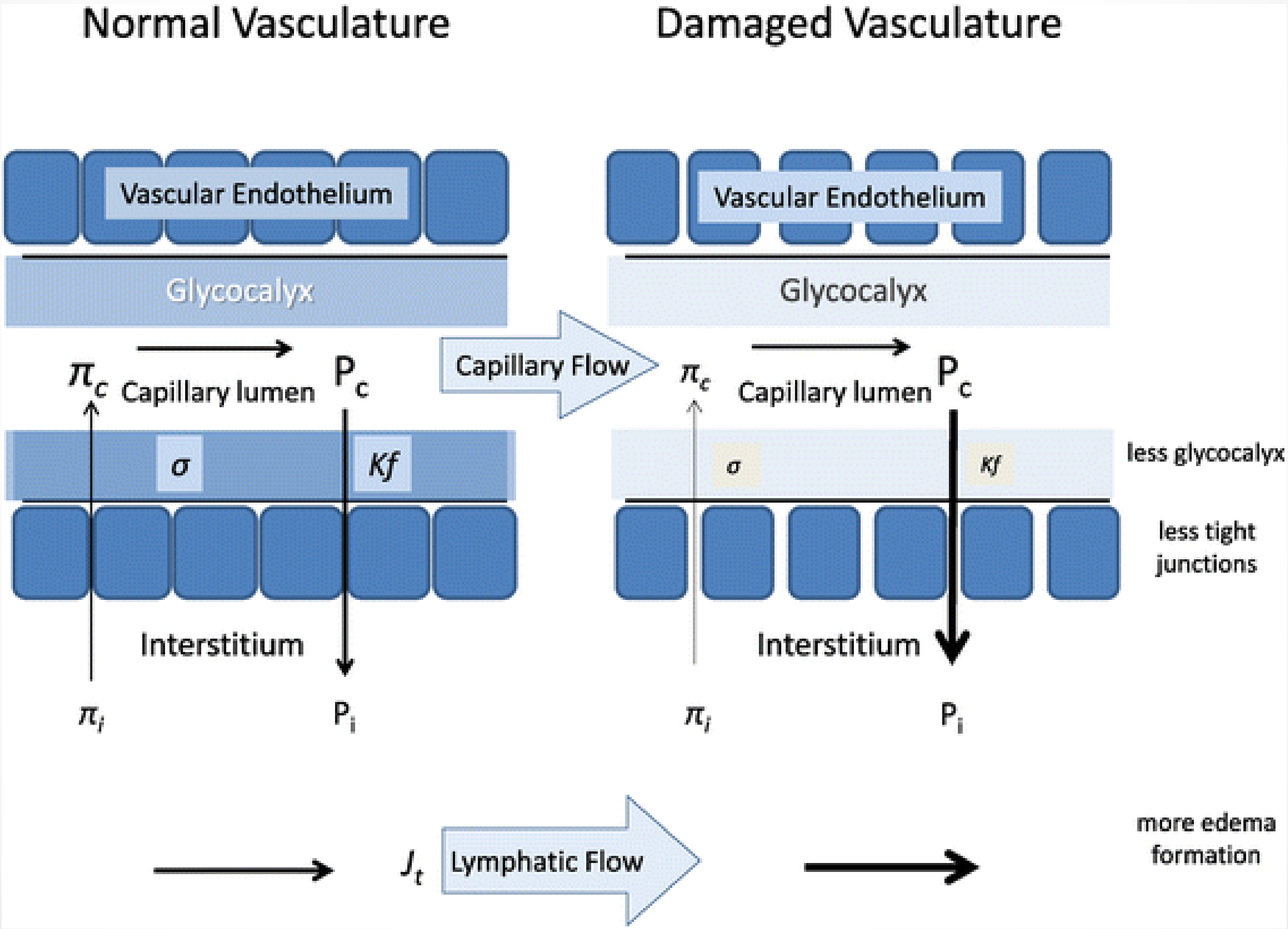
- Acellular layer lining the intravascular endothelium
  - Web of membrane-bound glycoproteins and proteoglycans
  - Hydrophilic and anionic

- Colloid oncotic pressure across the EGL opposes, *but does not reverse*, filtration rate by transfusion colloids



Myburg N Engl J Med 2013; 369(13):1243-51.
Woodcock Brit J Anaesth 2012; 108 (3); 384-94.

Endothelial Damage



Glycocalyx Implications

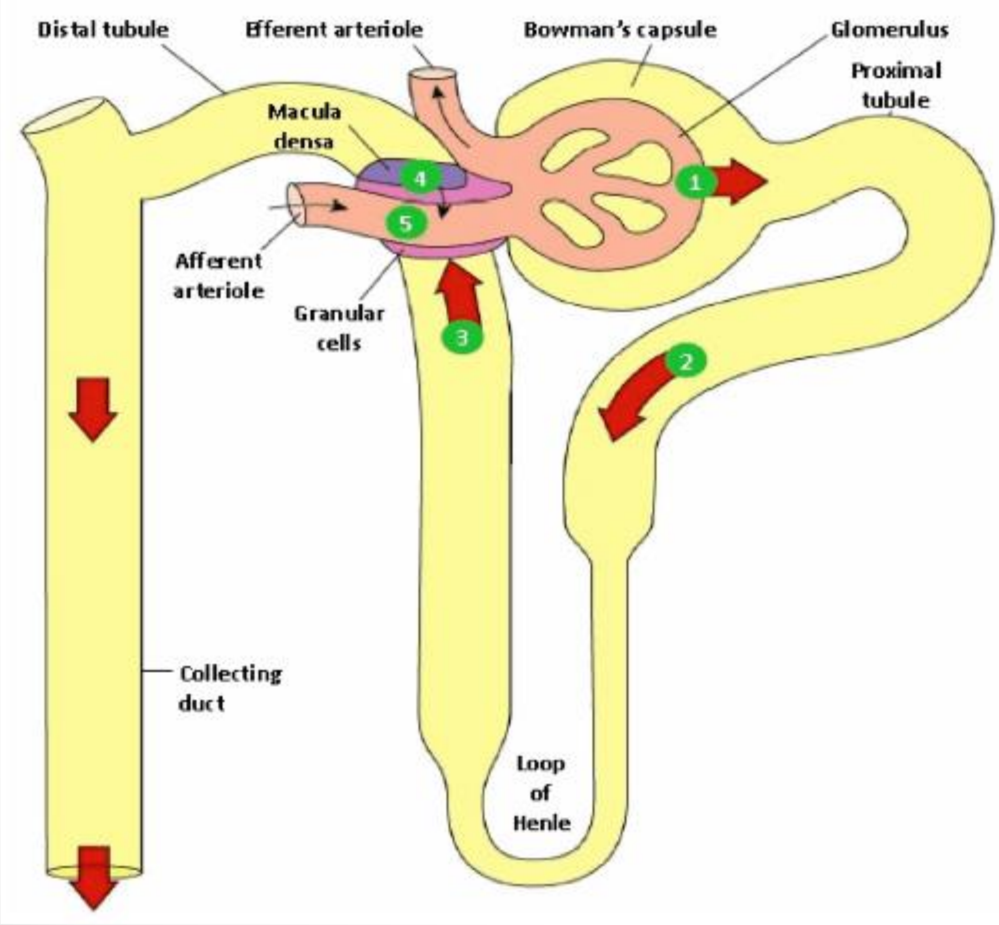
1. Glycocalyx 'traps' plasma water in hydrophilic composition
   - Crystalloid : colloid is ~1.3:1
   - Colloid administration likely 'dehydrates' glycocalyx increases plasma volume (transiently)
2. Fluid extravasation predominately dependent on capillary hydrostatic pressures
   - Minimize rapid increases in P_C
     - Small boluses
     - Alpha agonists – constricts pre-capillary arterioles attenuating P_C
3. Hypoalbuminemia correction is of no clinical benefit
   - Indicator of disease severity
4. Hyperoncotic albumin solution doesn't improve pulmonary edema

Myburg N Engl J Med 2013; 369(13):1243-51.
Woodcock Brit J Anaesth 2012; 108 (3); 384-94.

Crystalloids

	Plasma	0.9% NaCl	Lactated Ringer's	Plasma-Lyte & Normosol
Sodium (mmol/L)	140	154	130	140
Chloride (mmol/L)	102	154	109	98
Potassium (mmol/L)	4	-	4	5
Calcium (mmol/L)	5	-	3	-
Magnesium (mmol/L)	2	-	-	3
Buffer (mmol/L)	Bicarbonate (24)	-	Lactate (28)	Acetate (27) Gluconate (23)
pH	7.4	5.7	6.4	7.4
Osmolality (mOsm/L)	290	308	273	295

Hyperchloremia



1. High chloride concentration filtered across glomerulus
2. Increased chloride concentration in tubule
3. Macula densa senses increased chloride concentration
4. Macula densa releases local mediators stimulating afferent arteriole
5. Afferent arteriole constricts

Decreased hydrostatic pressure and GFR

0.9% NaCl vs Chloride restrictive

Trial	Design	Population	Interventions	Results	Conclusion
Yunos 2012	Single center, prospective, open-label, before-and-after	22-bed mixed med-surg ICU	Chloride-liberal vs chloride-restrictive in 6 months periods 2008 and 2009, respectively	Restrictive associated with less RIFLE-defined AKI and RRT and lower serum creatinine rise	Restricting IV chloride decreases incidence of AKI and RRT
SPLIT 2015	Double-blind, cluster randomized, double cross-over	4 New Zealand ICUs (3 mixed med-surg, 1 cardiothoracic and vascular)	Alternating 7-week blocks of Plasma-Lyte or 0.9% saline with two crossovers	AKI at 90 days was 9.6% PL and 9.2% NS with a RR 1.04 [95% CI 0.80-1.36]. No difference in RRT	Buffered crystalloid did not reduce the risk of AKI compared to saline
PLUS *Recruiting*	Multicenter, blinded, randomized	ICU patients requiring fluid resuscitation	Plasma-Lyte vs 0.9% NaCl	Expected completion 2021	N/A

2 Case Study

Case Study Two

- 67 y/o F presents s/p PEA arrest for 10 minutes, presumed septic shock secondary to unknown source. Patient ventilated and sedated upon admission, on Levophed gtt at 15mcg/hr.
  - Family denies prodrome of fevers/chills/n/v/d, or CP, but reported +general malaise and increased SOB x3 days.

- PMHx:
  - Hyperlipidemia
  - DM
  - HTN
  - CAD

Case Study Two

- Vitals on admission :
  - HR: 72, NSR
  - BP: 101/54 on Levophed gtt at 15mcg/hr
  - Temperature: 37.5˚
  - RR: 22
  - Ventilated, Spo2 96% on Fio2 of 80%, PEEP of 8

Initial Labs:

144	109	65	83
4.6	17	2.25	

18.9	10.3	225
	30.9	

VBG: 7.25/34/61/16
Lactate: 2.4

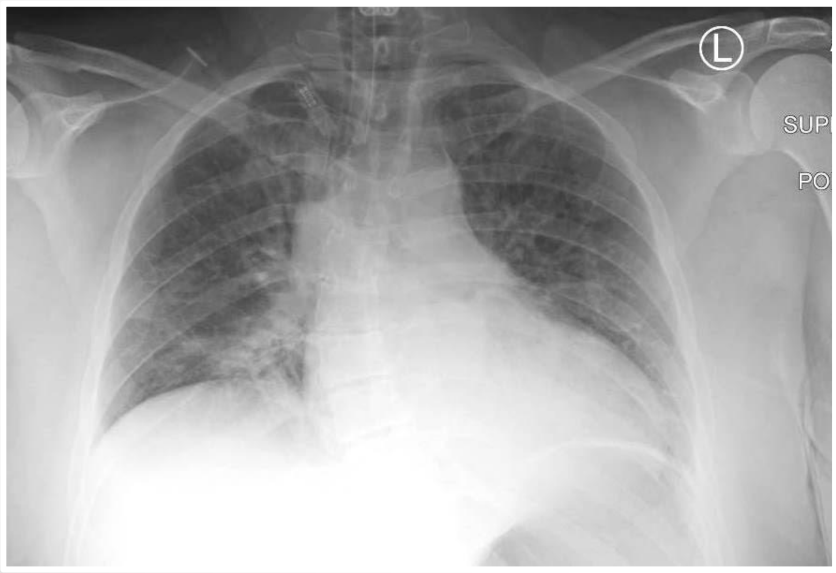
Troponin: 1.31
CK-MB: 8
Mg: 1.2
AST/ALT: 101/132
Calcium: 8.2

U/a w/ Micro: -6-25, -Nitrites, -Bacteria, +Small protein
U/o: 20cc since admission

Case Study Two

- Patient given 2L IVF in the Emergency Department
- Started on Vanco and Zosyn for severe septic shock

Chest portable on admission:

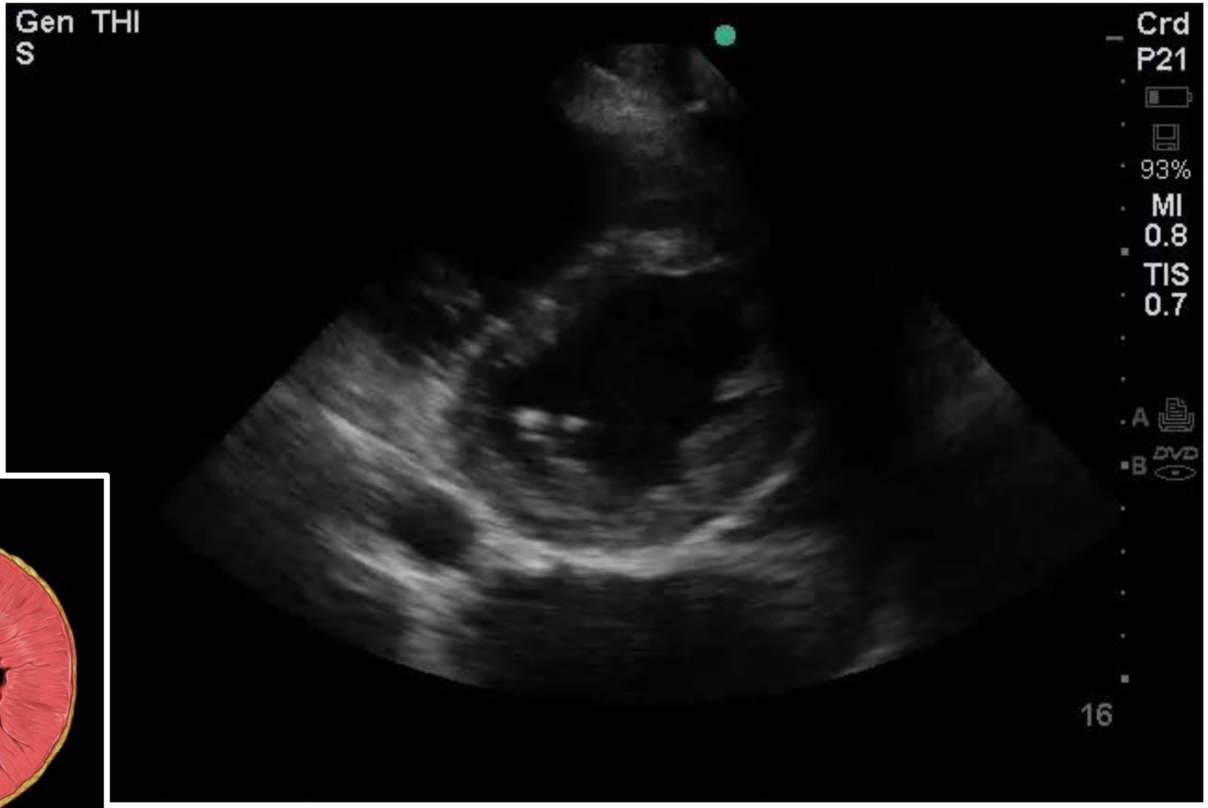


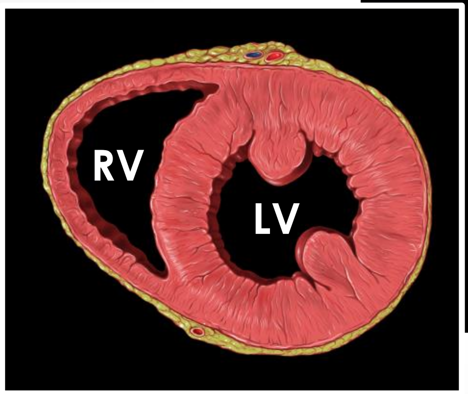
ECG on admission: *ST depressions in II, II and aVF with TWI in* V_5 *and* V_6

Repeat labs:
Troponin(8hr): 16.31
CK-MB: 25

Case Study Two

- Bedside US continued:

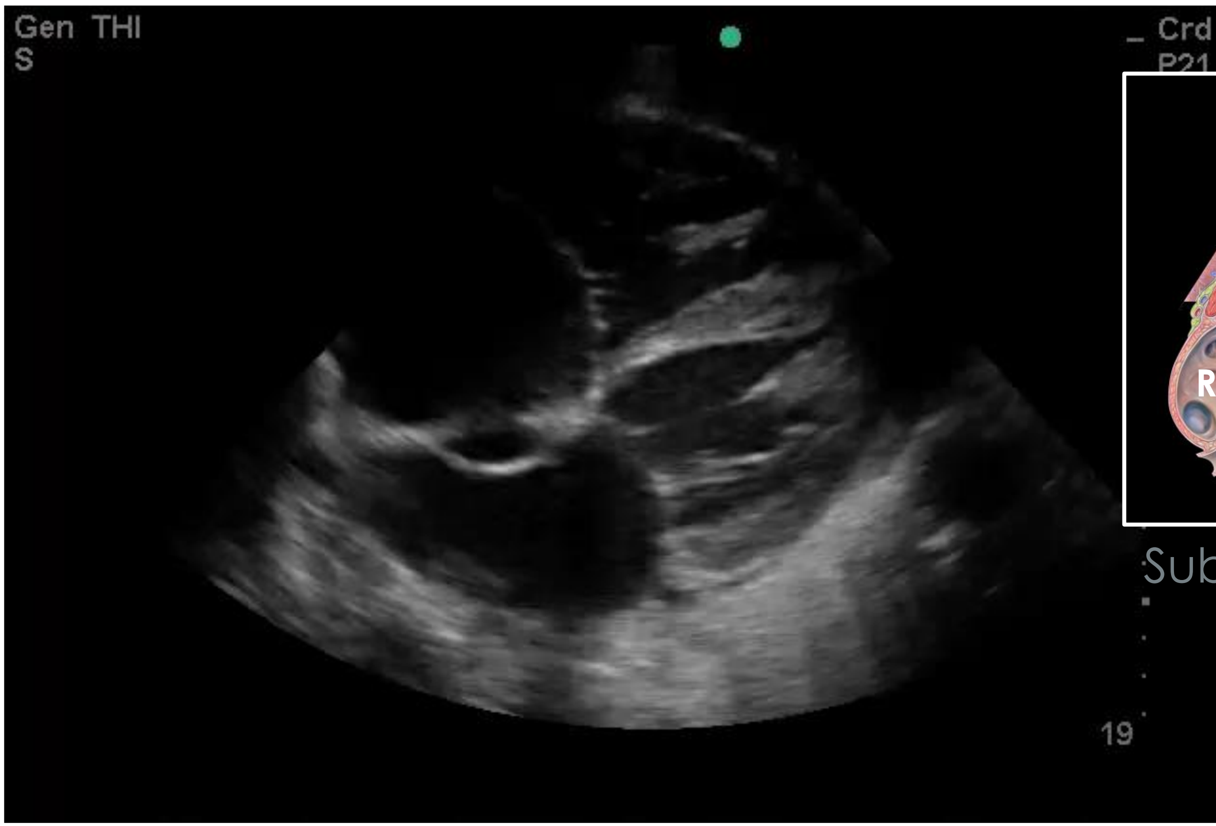


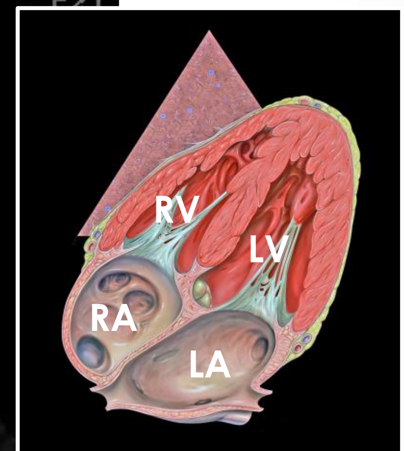


Parasternal Short Axis

Case Study Two

- Bedside US was completed :



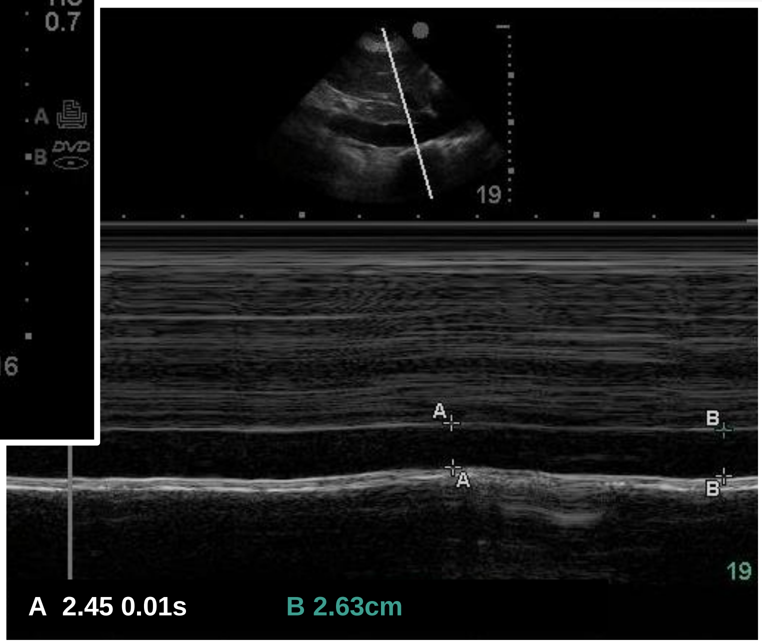


Subcostal view

Case Study Two

- Bedside US:

$\Delta IVC_D(\%)=$**6.8%**



Is the patient likely to be fluid responsive?

Case Study Two: Diagnosis

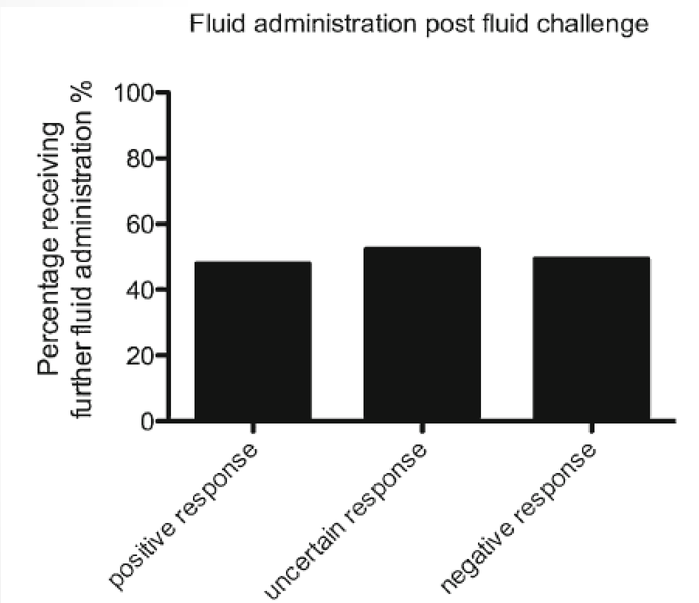
- Patient diagnosed with cardiogenic shock secondary to acute myocardial infarction
- Additional IVF administration was stopped
- Vasopressin was added for to Levophed infusion

"Fluid Safety"

- Earlier initiation of vasopressors may be warranted
- Volume overload compromises organ blood flow
- Most clinicians would likely support conservative therapy once 'adequate resuscitation' achieved
- Interestingly, recent trials SSSP-2 and FEAST suggest bolus fluid is harmful
    - Both in sub-Saharan Africa, one in children

What is practiced?

- FENICE Study
- Half of patients with negative response to fluid challenge received further fluid



- Clinicians relied heavily on hypotension and BP response
- Half of patients had no hemodynamic value to measure response
    - CVP used most often

- Authors conclude *"current practice and evaluation of fluid challenge in critically ill patients seems to be arbitrary"*

Cecconi Intensive Care Med; 2015(41):1529-37.

3 Case Study

Case Study Three

- 58 y/o M presents with chief complaint of SOB x 3 weeks, progressively worsening in the past 3 days
  - ROS: +cough with white sputum production, +chest pressure, +intermittent chills, +dyspnea on exertion.

- PMHx:
  - HTN
  - Raynaud's Disease
  - Tobacco use; quit 30 years ago

Case Study Three

- Vitals on admission :
    - HR: 107, NSR
    - BP: 121/74
    - Temperature: 36.3˚
    - RR: 19-26
    - Spo2: 80% on Room air

Initial Labs:

118	84	44	110
5.9	17	1.74	

	14.7	
14.8		339
	41.3	

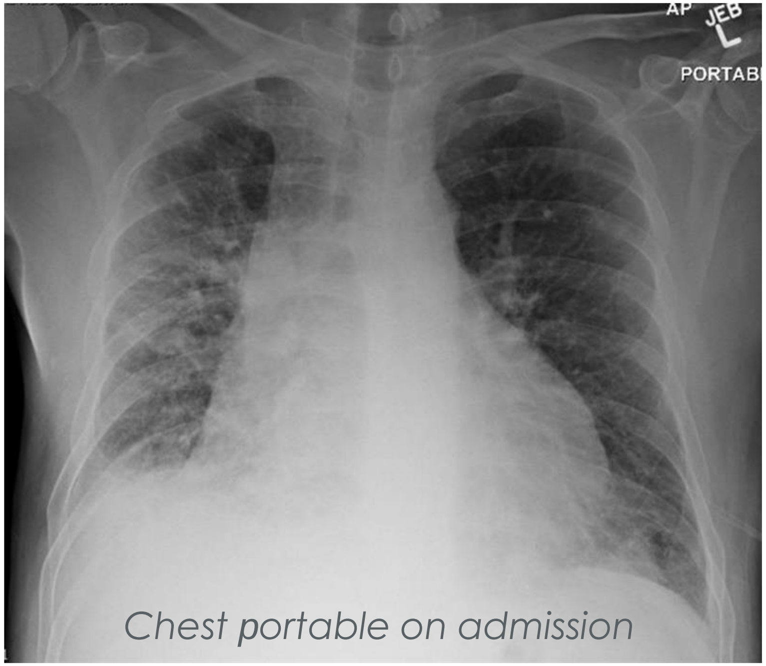
ABG: 7.47/24/62/21
Lactate: 2.4

Mg: 2.2
AST/ALT: 23/17
Albumin: 3.9
Calcium: 9.7

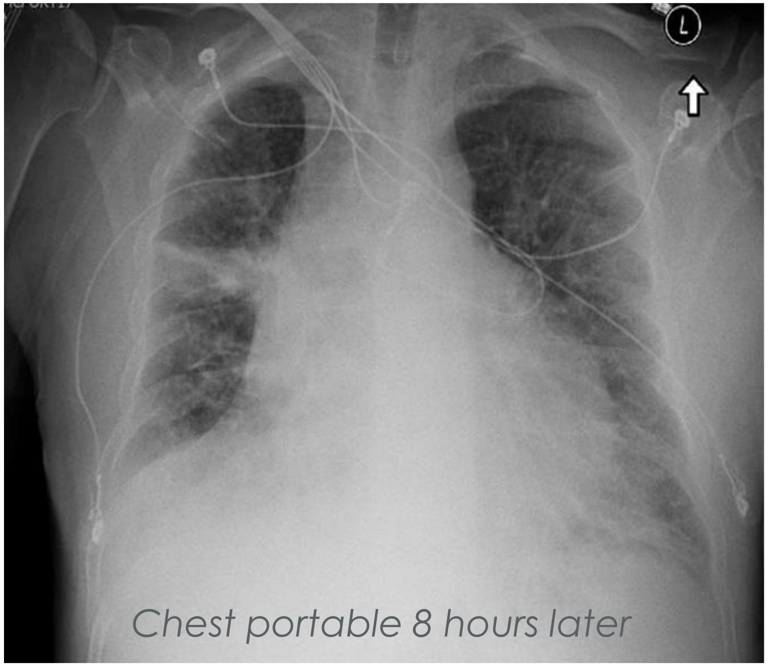
Troponin: 0.02
BNP: 69

Case Study Three

- Given 3L NS, placed on4L NC, Spo2 improved to 96%
- Started on Ceftriaxone and Azithromycin for CAP
- Developed worsening SOB overnight

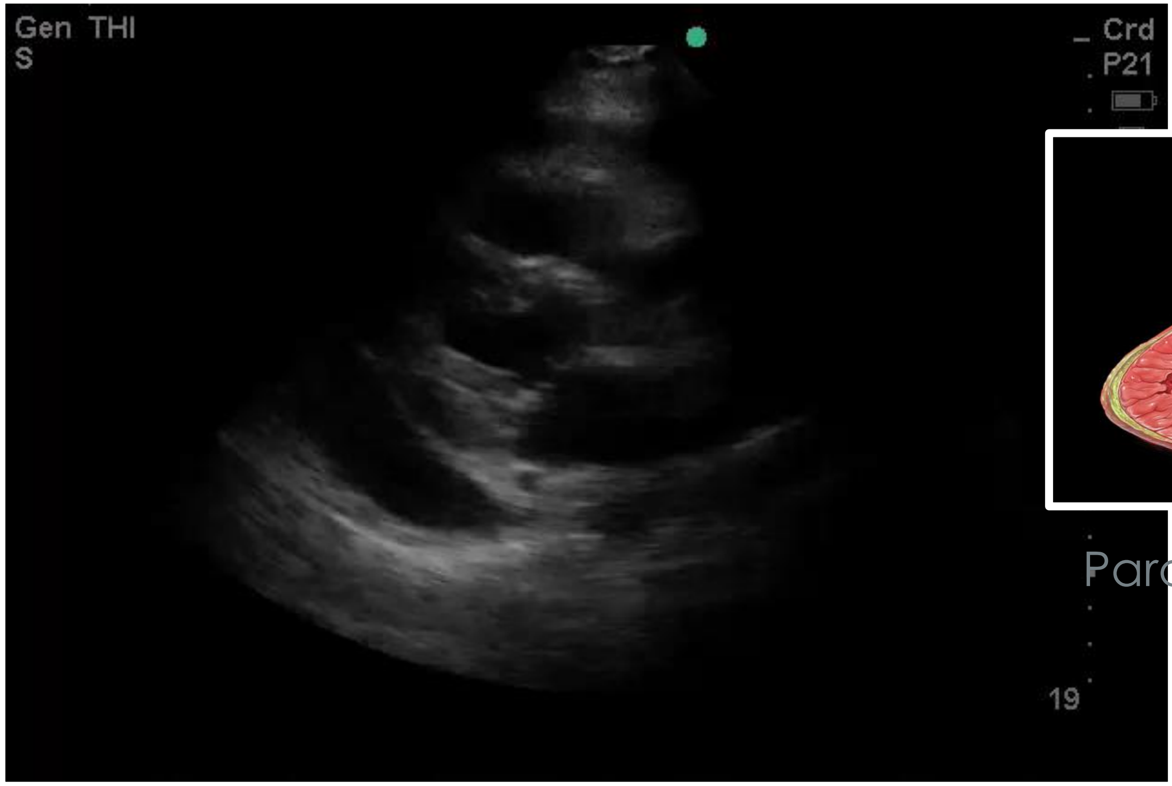


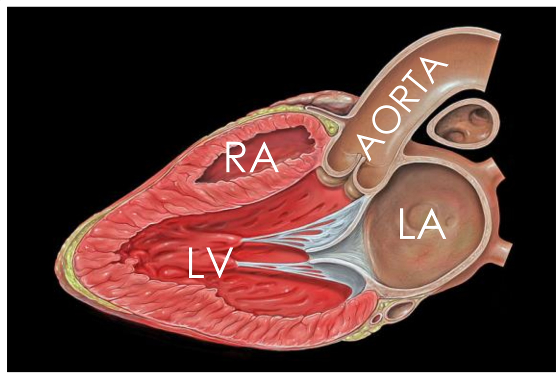
Chest portable on admission


Chest portable 8 hours later

Case Study Three

- Bedside US was completed :



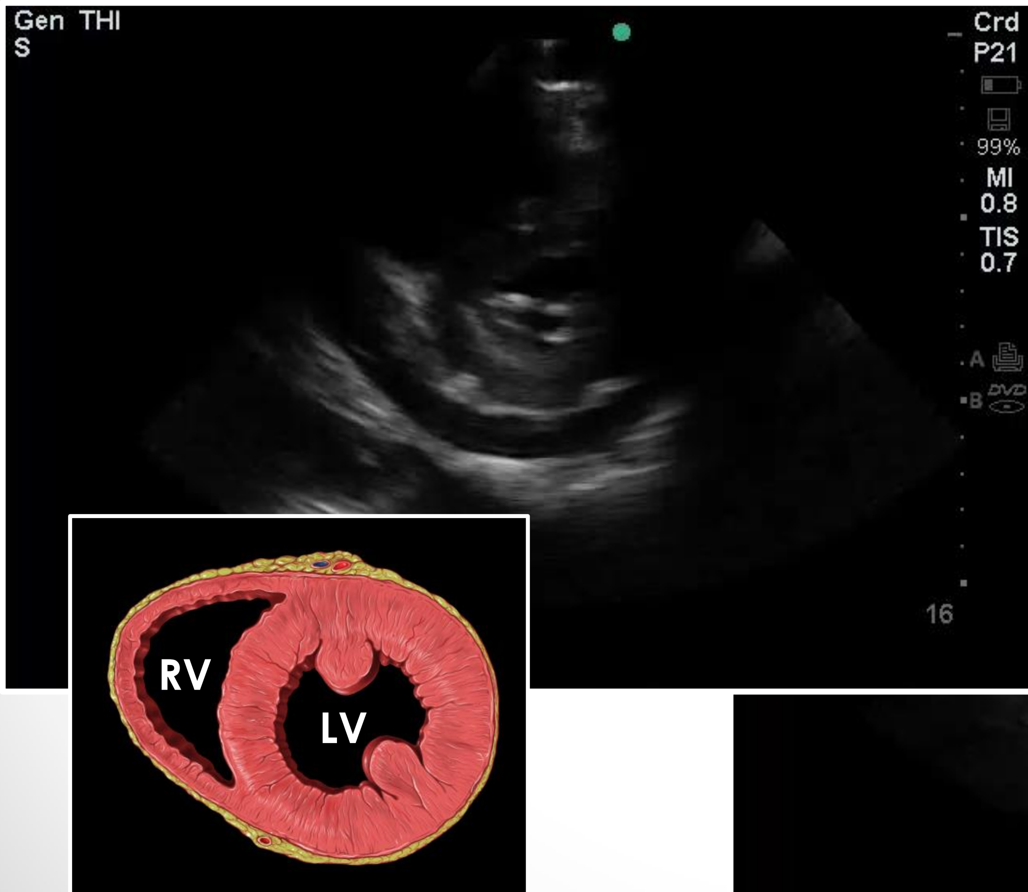


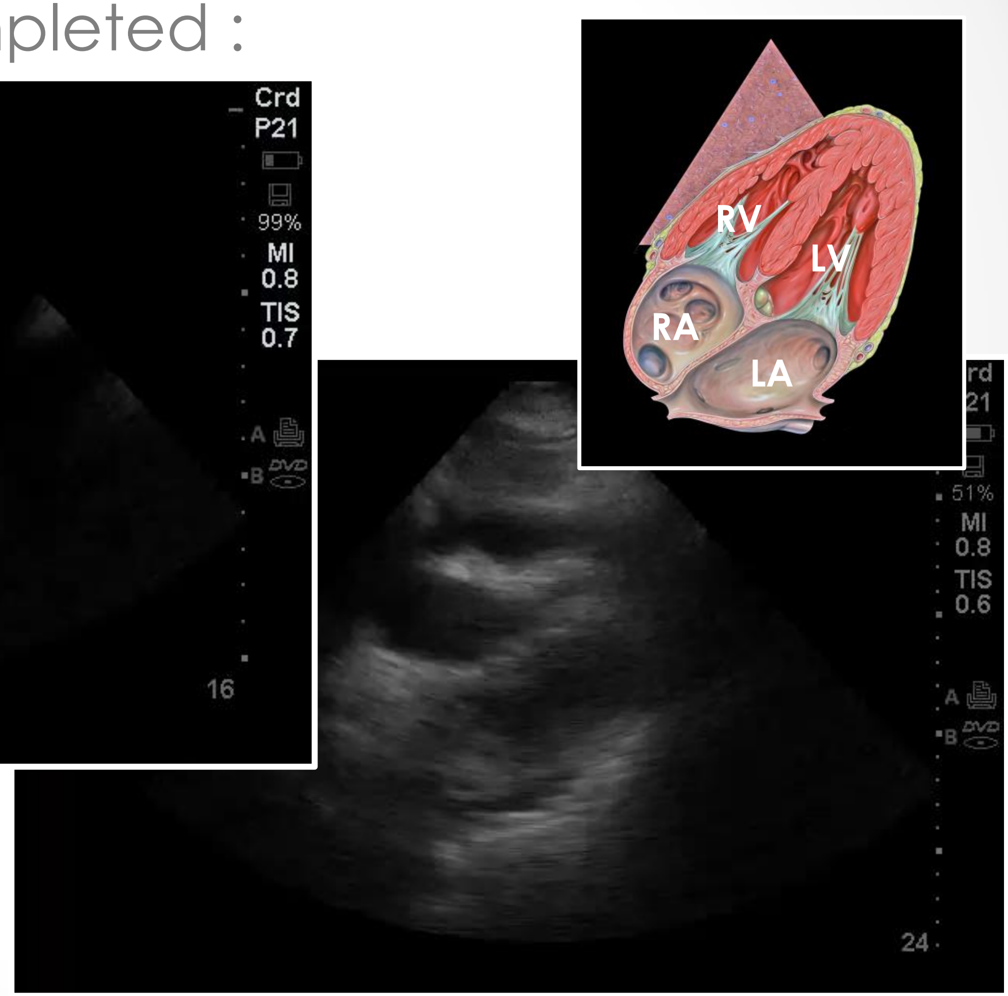
Parasternal Long Axis

Case Study Three

- Bedside US was completed :

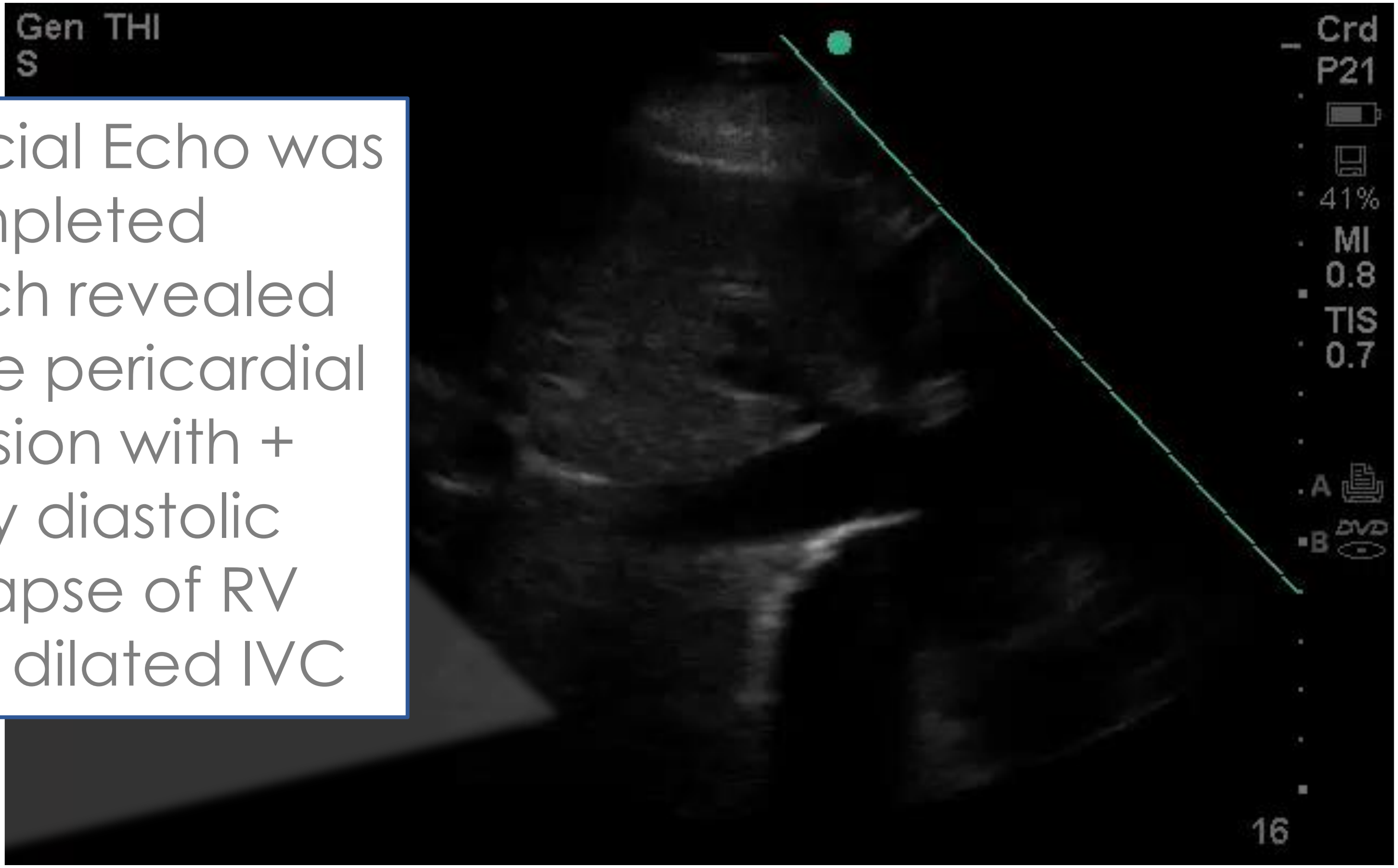
Subcostal view





- Parasternal Short Axis

Case Study Three



- Official Echo was completed which revealed large pericardial effusion with + early diastolic collapse of RV and dilated IVC

Case Study Three: Diagnosis

- Cardiac Tamponade
  - Pericardial Window; 750cc of serosanguineous fluid was removed
  - Pericardial fluid revealed malignant cells

*Remember, a patient in tamponade is *preload dependent*, but when using IVC variation to assess for volume status, would show a dilated IVC with little variation due to obstructive shock.

Summary

- Goal of shock is to restore effective tissue perfusion beginning with fluid challenge
  - Assessing response is crucial
    - Dynamic >> static
- Ultrasonography is an excellent modality for undifferentiated shock as it can provide data regarding type of shock, need for therapeutic intervention and response to resuscitation
- Crystalloids are reasonable first-line agents for fluid resuscitation in most patients