



THE CARDIORENAL SYNDROME

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Disclosures

- **I have no financial disclosures**
- **I will not discuss off-label drug or device use**
- **I am not a heart failure specialist**
- **Some of my slides are taken from presentations given at Cardiology at Cancun 2015 by Dr. Barry Boilson and Dr. Paul McKie
Cardiology at Cancun 2020**

Division of Cardiovascular Diseases



20th Annual

2015 Cardiology at Cancun

Topics in Clinical Cardiology

February 23 – 27, 2015



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Evil Easter Bunny



Case Report

- **80 yo female with chronic HFpEF (first name is a flower)**
- **Admitted from CHF Clinic with 7 lb. weight gain and increased SOB after drinking a jar of pickle juice**
- **Oxygen sat 75% on RA**
- **Chronic AFib**
- **Decreased breath sounds at bases and coarse wheezes**
- **2+ edema**

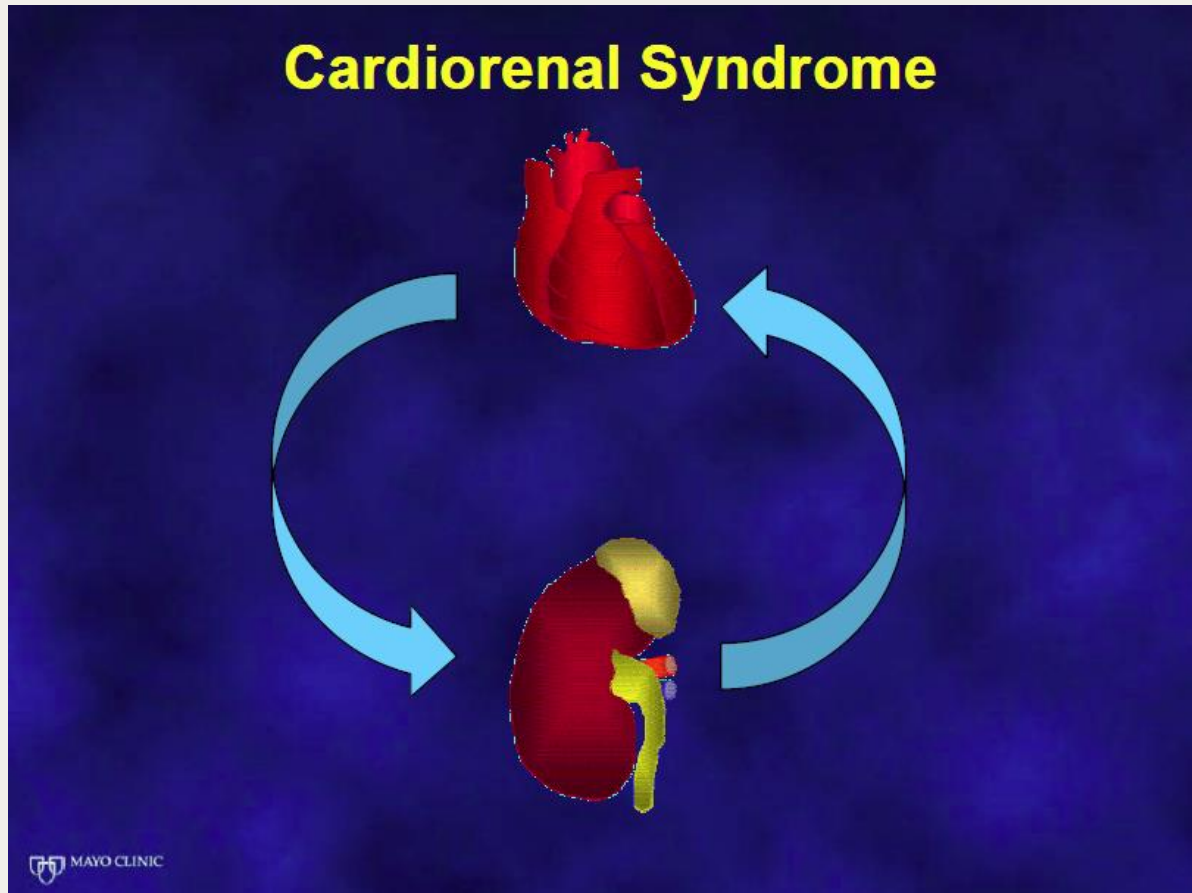
Case Report

- **LVEF 50%-55% with mild LVH and BiAE – AFib present**
- **Chest X-ray with diffuse patchy infiltrate**
- **Sodium 133**
- **Potassium 3.3**
- **BUN 43/Creat. 1.2 (21/0.8)**

Case Report

- **Antibiotics and diuretics**
- **Sodium 124/Potassium 6.3**
- **BUN 51/Creat. 1.5**
- **Chest X-ray and edema no better**
- **Diuretics stopped and normal saline started**
- **“Dr. Farrar, I feel awful. I can’t breathe.”**

Cardiorenal Syndrome



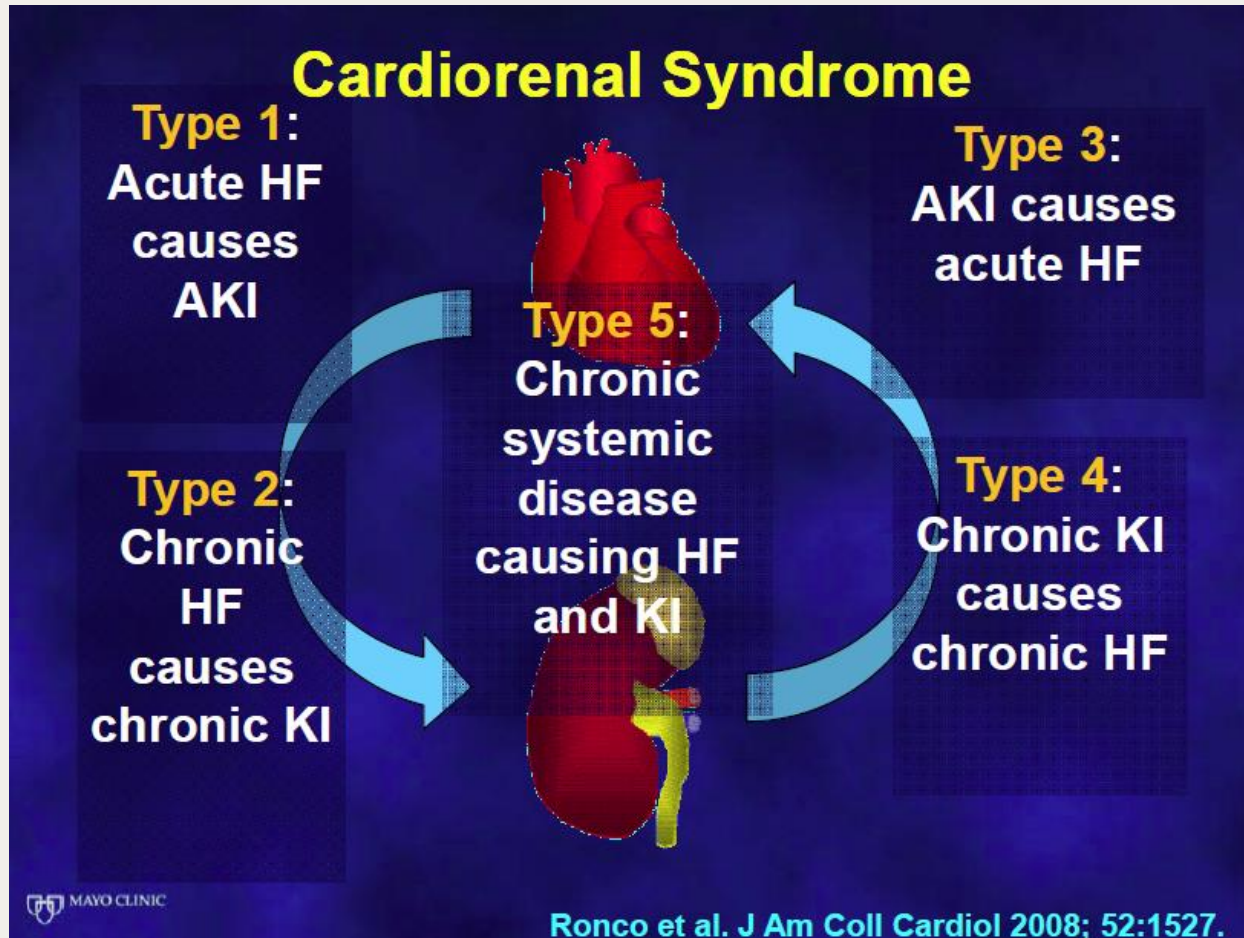
Cardiorenal Syndrome

- **A condition in which therapy to relieve congestive symptoms of heart failure is limited by a decline in renal function as manifested by a reduction in GFR**
– www.nhlbi.nih.gov
- **A spectrum of acute or chronic disorders of heart and kidney function characterized by mutual deterioration**

Cardiorenal Syndrome

- **Very common – 30%-60% of patients**
- **ADHERE – 30% creatinine >2 mg/dl**
- **20%-30% increase in creatinine >0.3 mg/dl**
- **Risk factors**
 - Diabetes mellitus
 - Admission creatinine >1.5 mg/dl
 - Uncontrolled hypertension

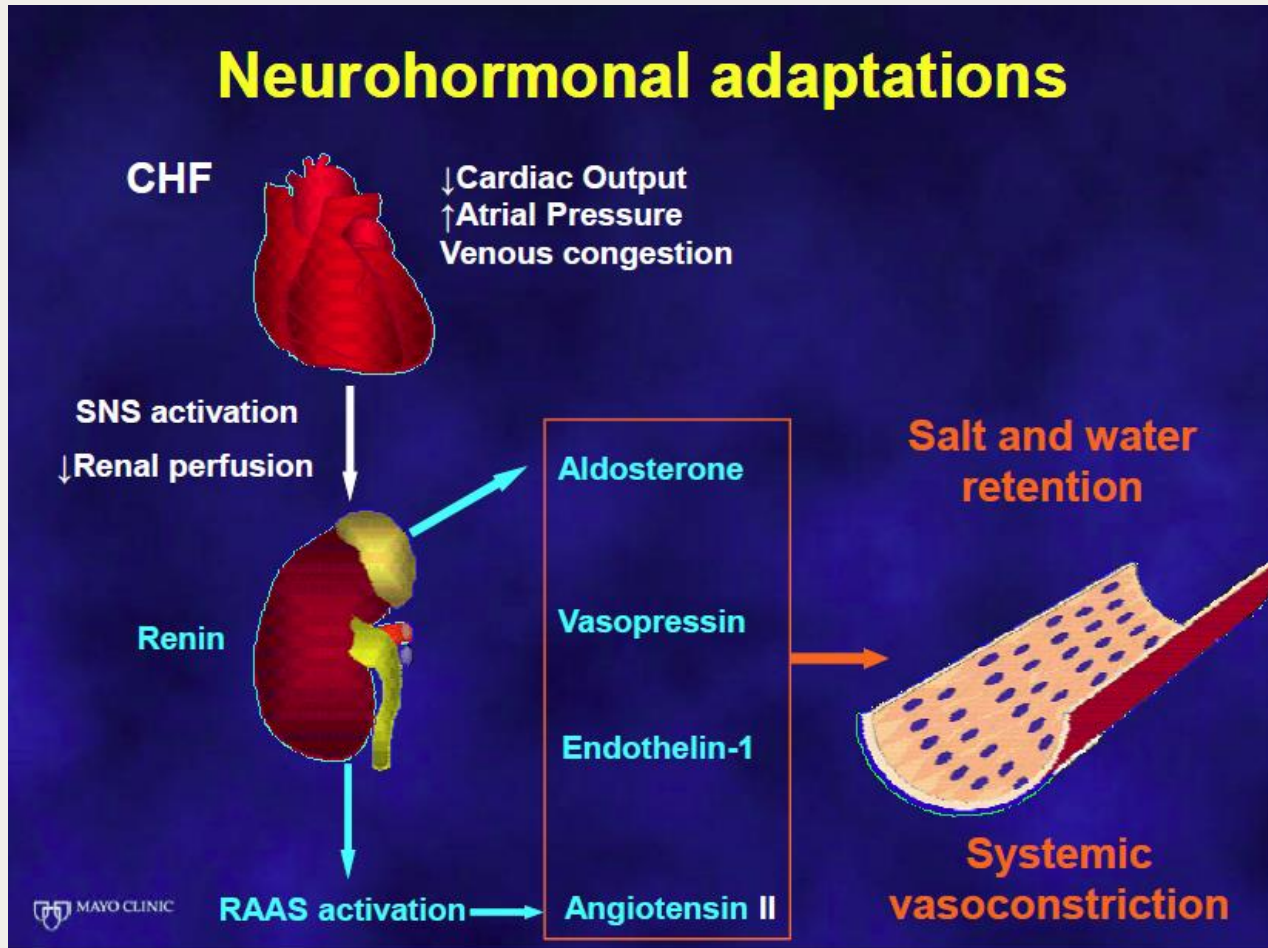
Cardiorenal Syndrome



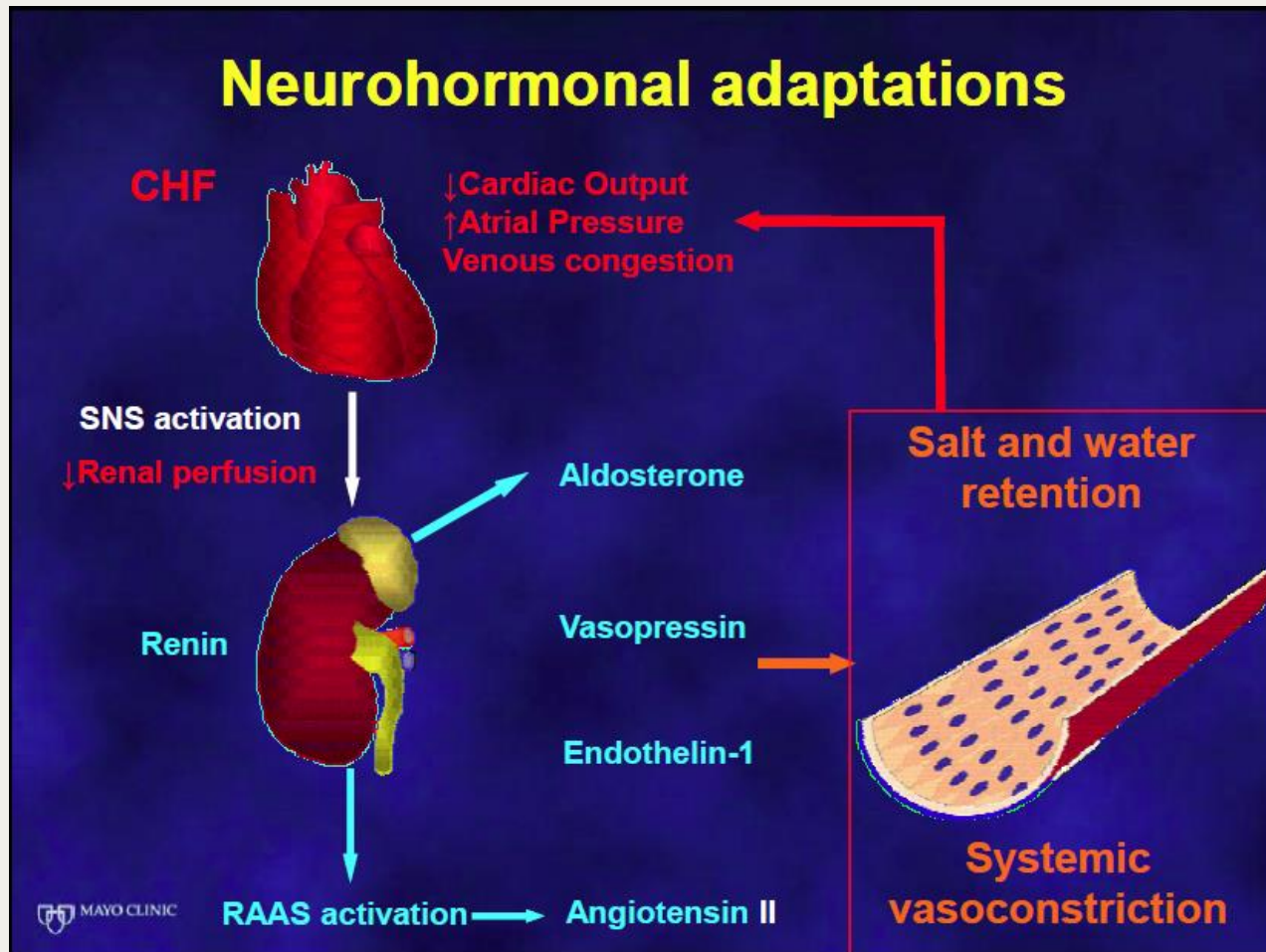
Pathophysiology

- **Complex**
- **Neurohormonal adaptations**
- **Reduced renal perfusion**
- **Renal congestion**
- **Right ventricular dysfunction**

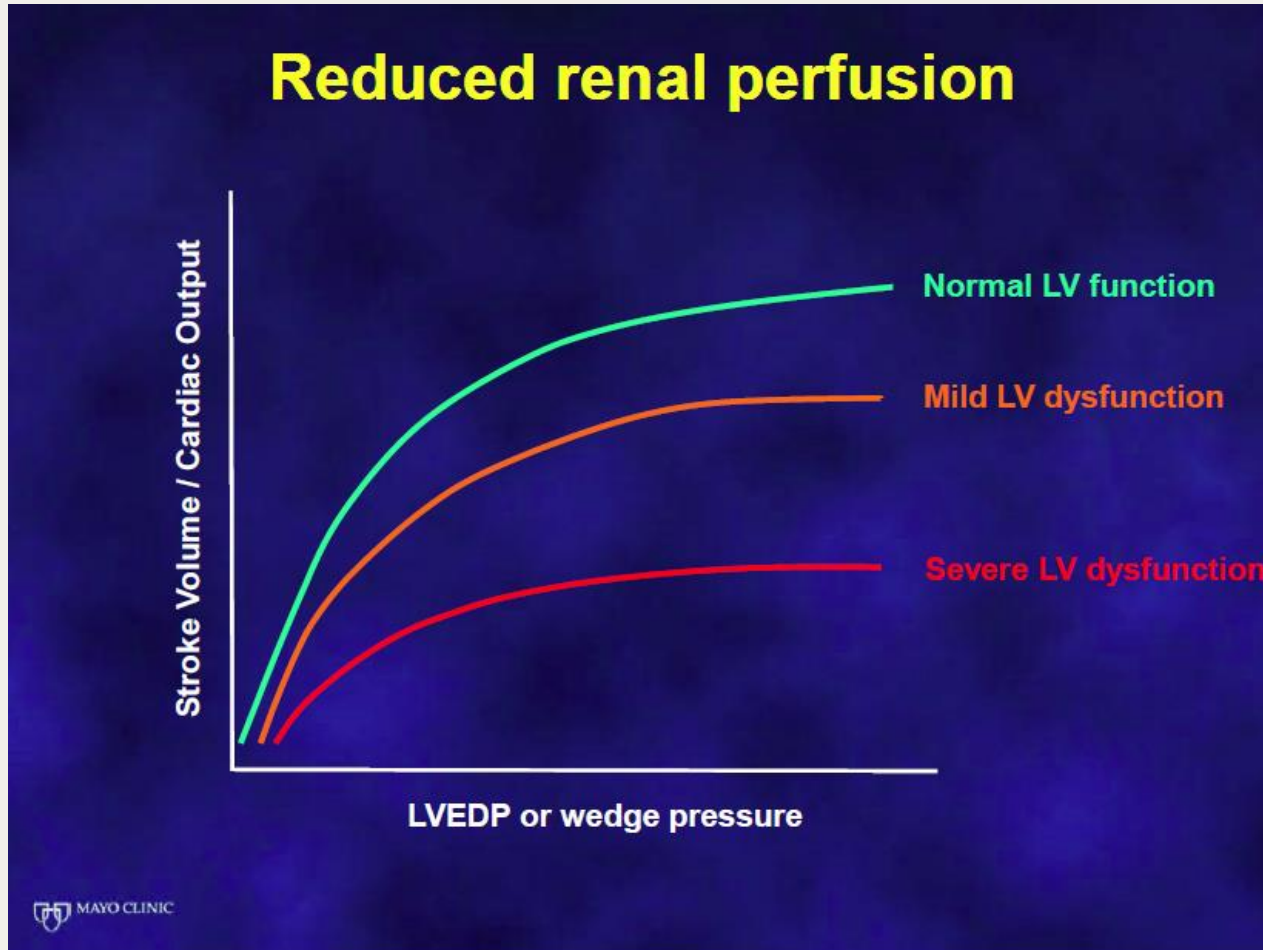
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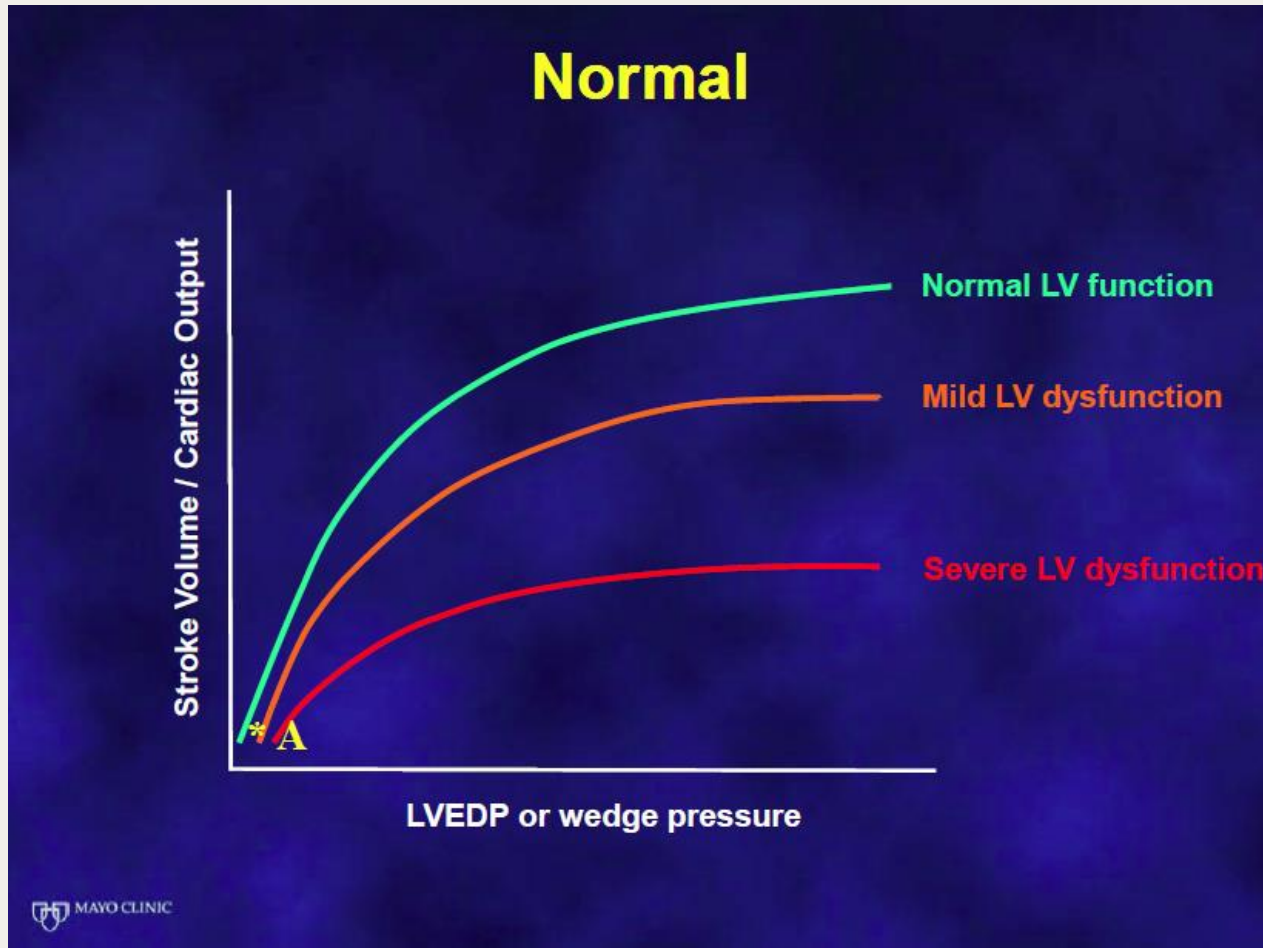
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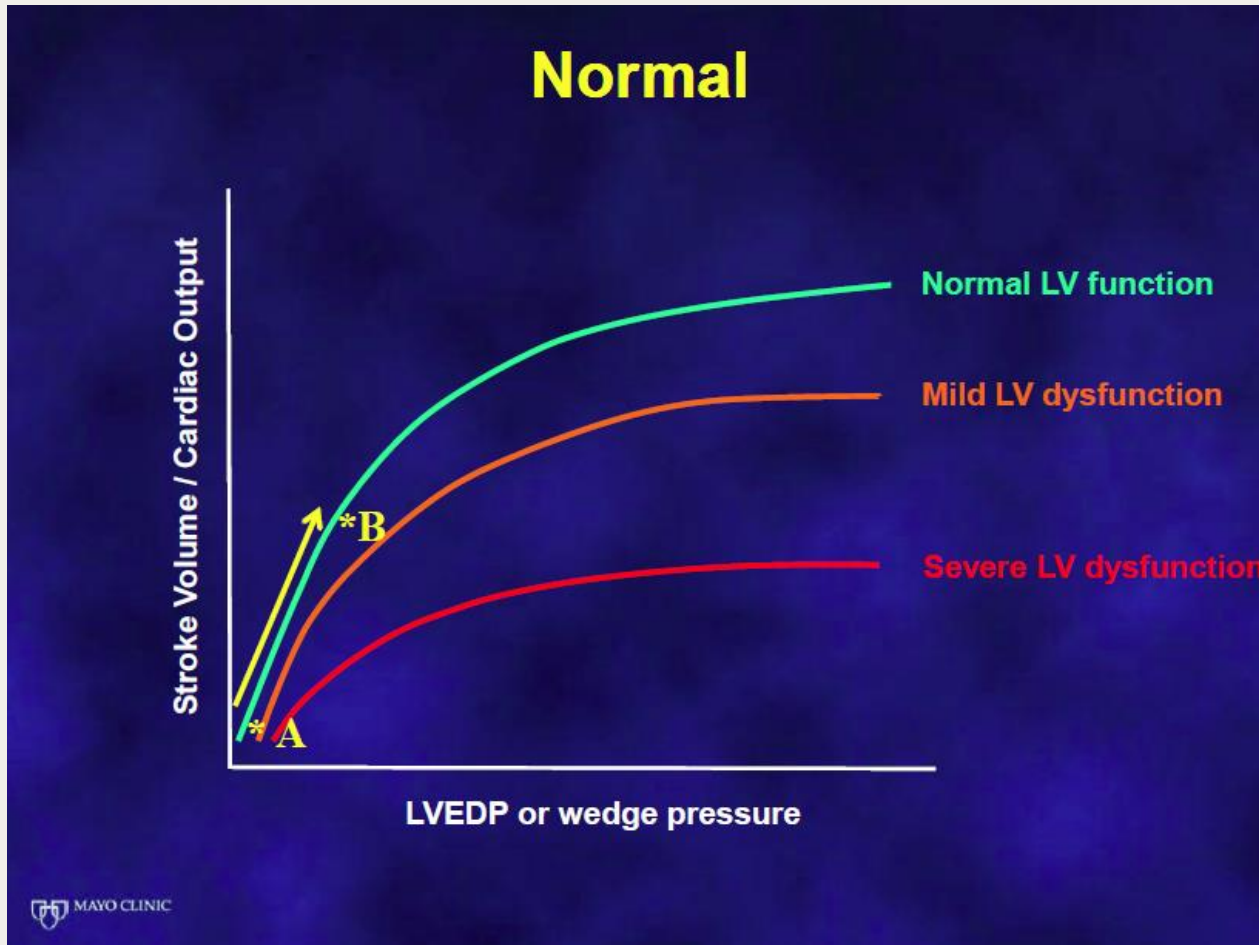
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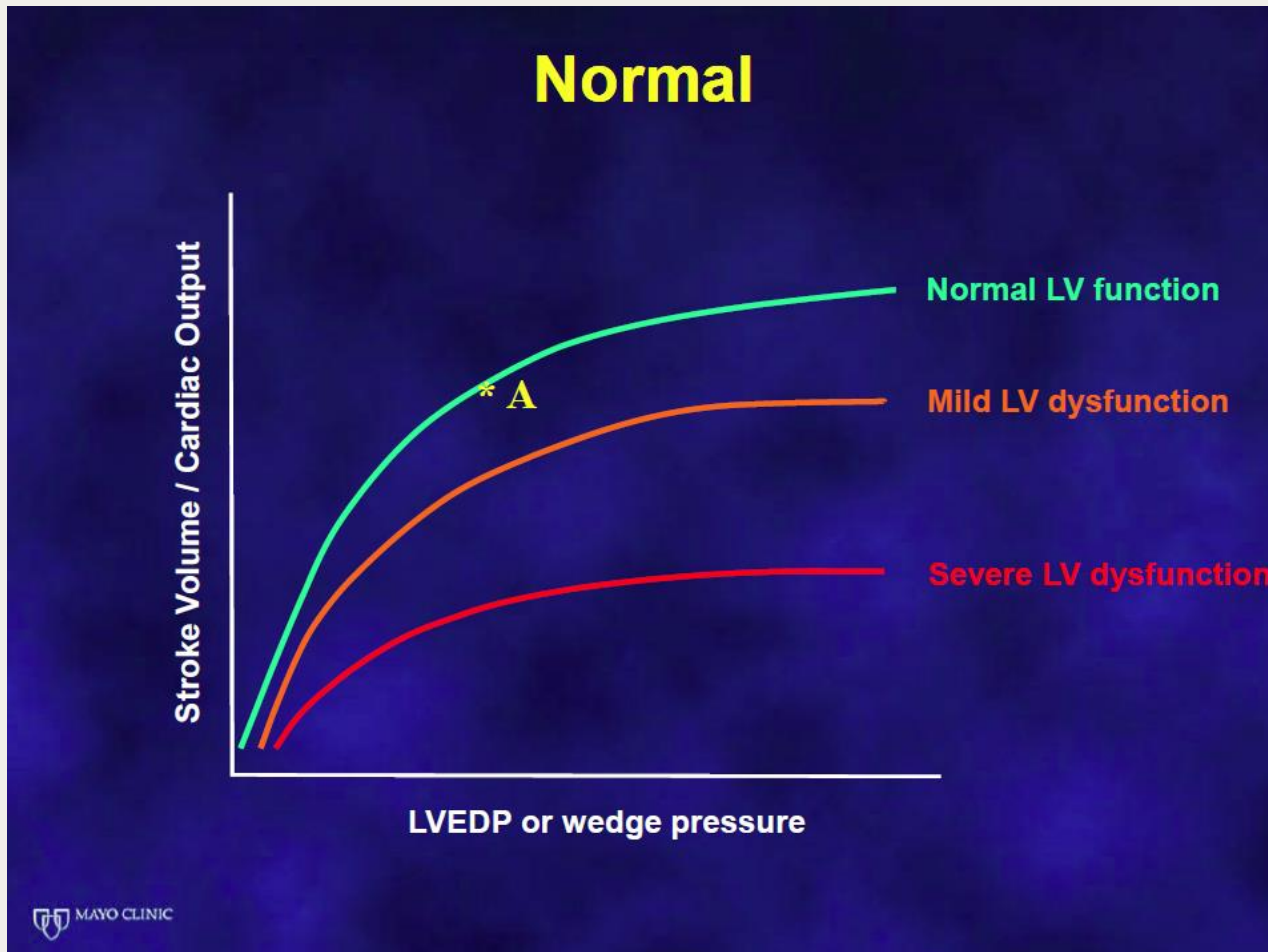
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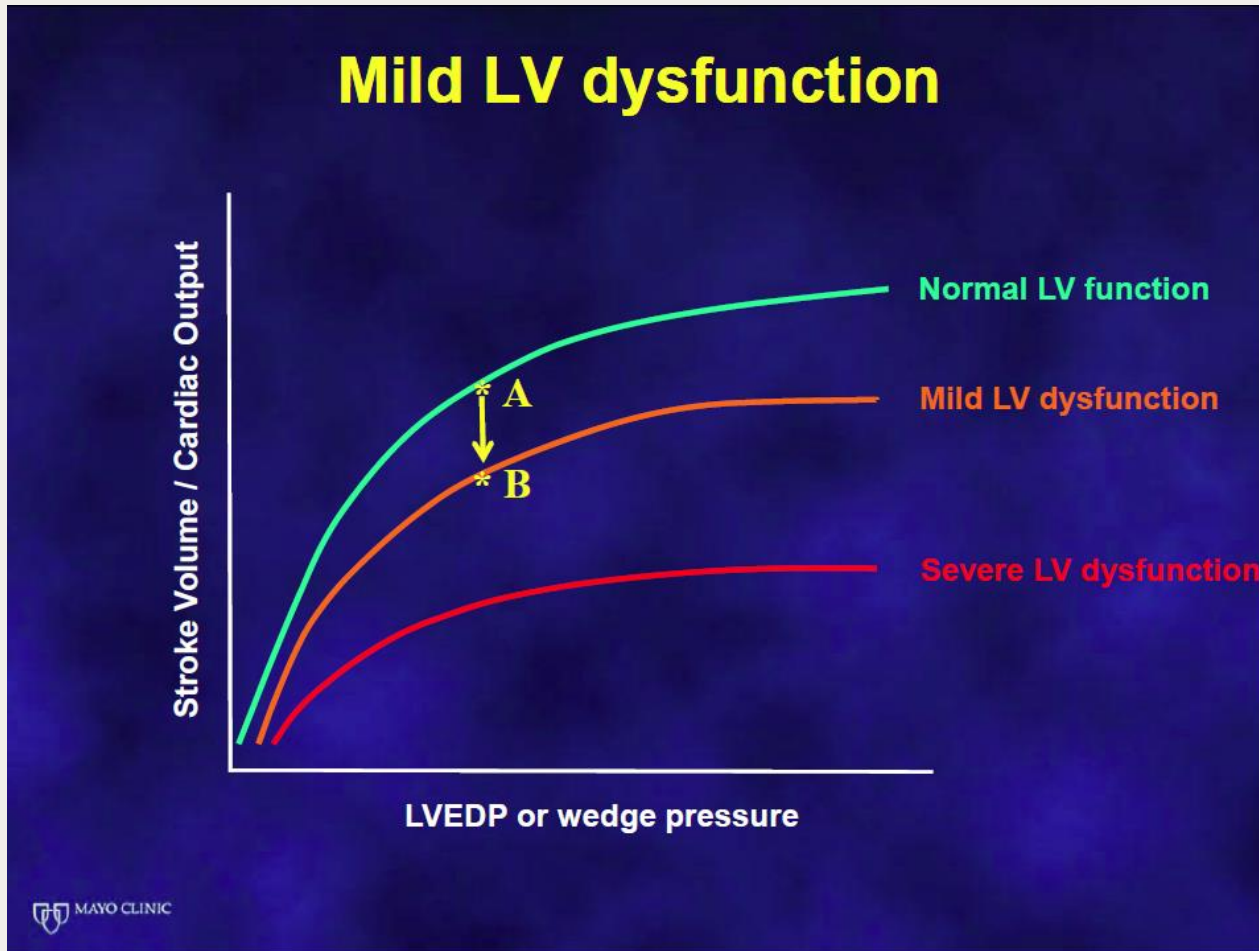
Cardiorenal Syndrome



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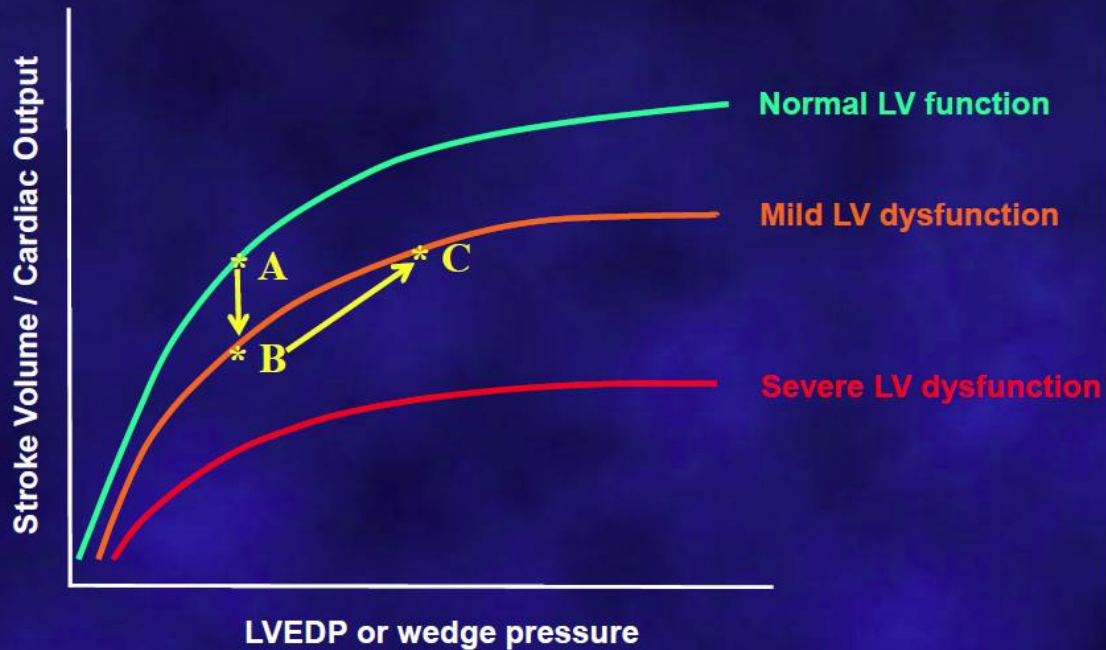


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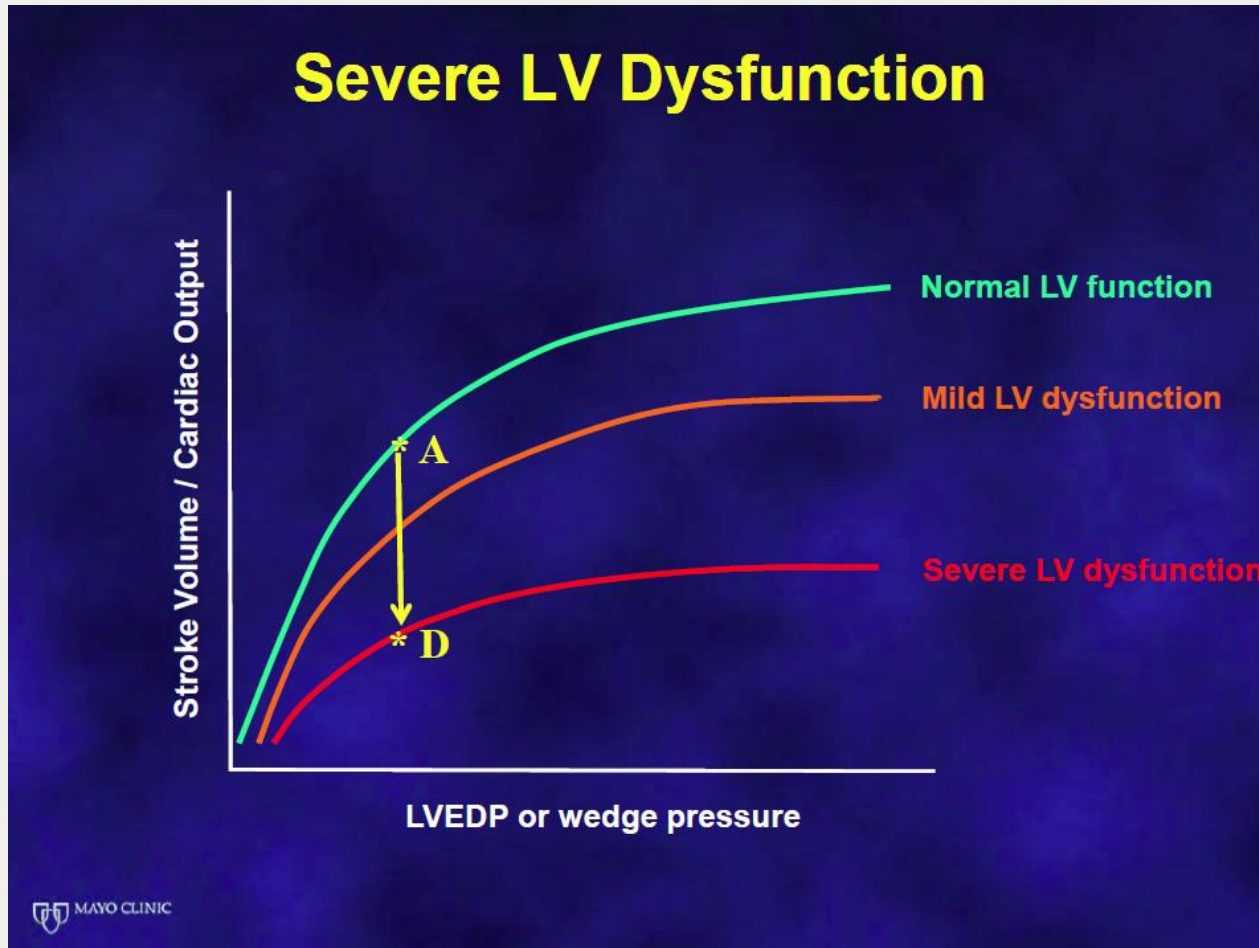
Cardiorenal Syndrome

Mild LV dysfunction - compensation

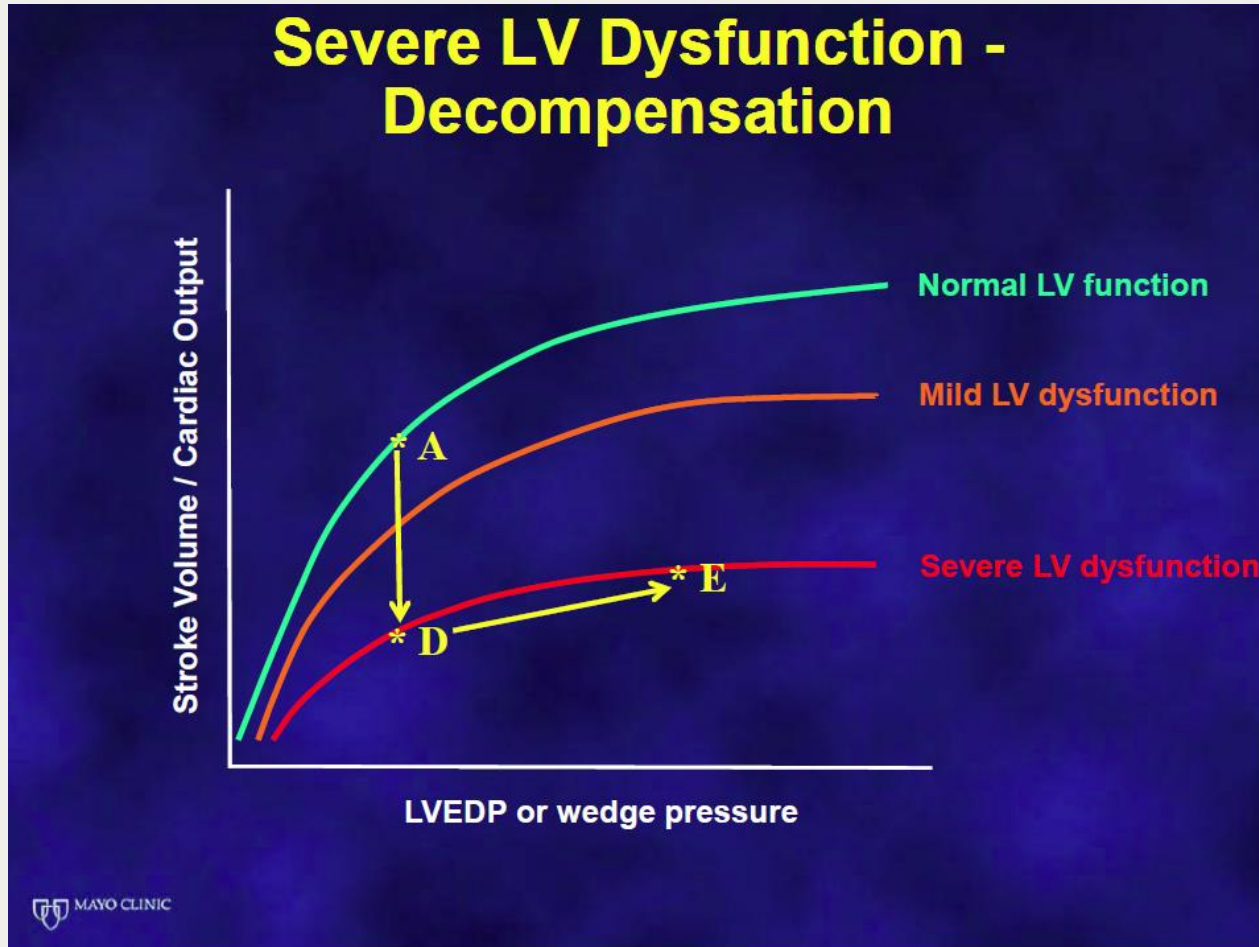


MAYO CLINIC

Cardiorenal Syndrome

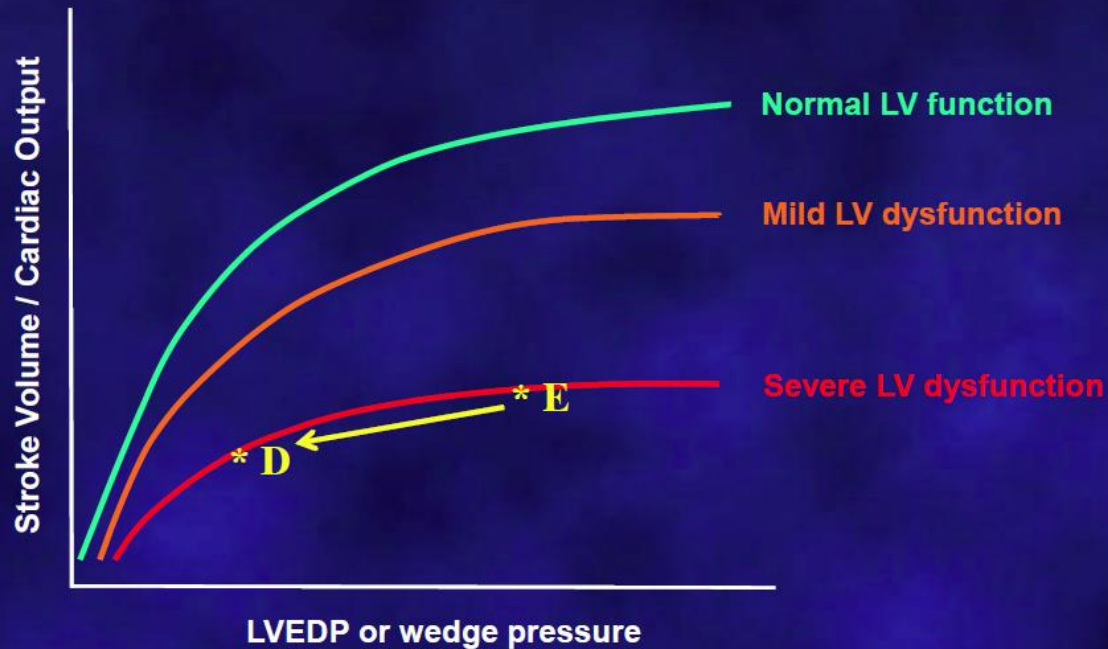


Cardiorenal Syndrome



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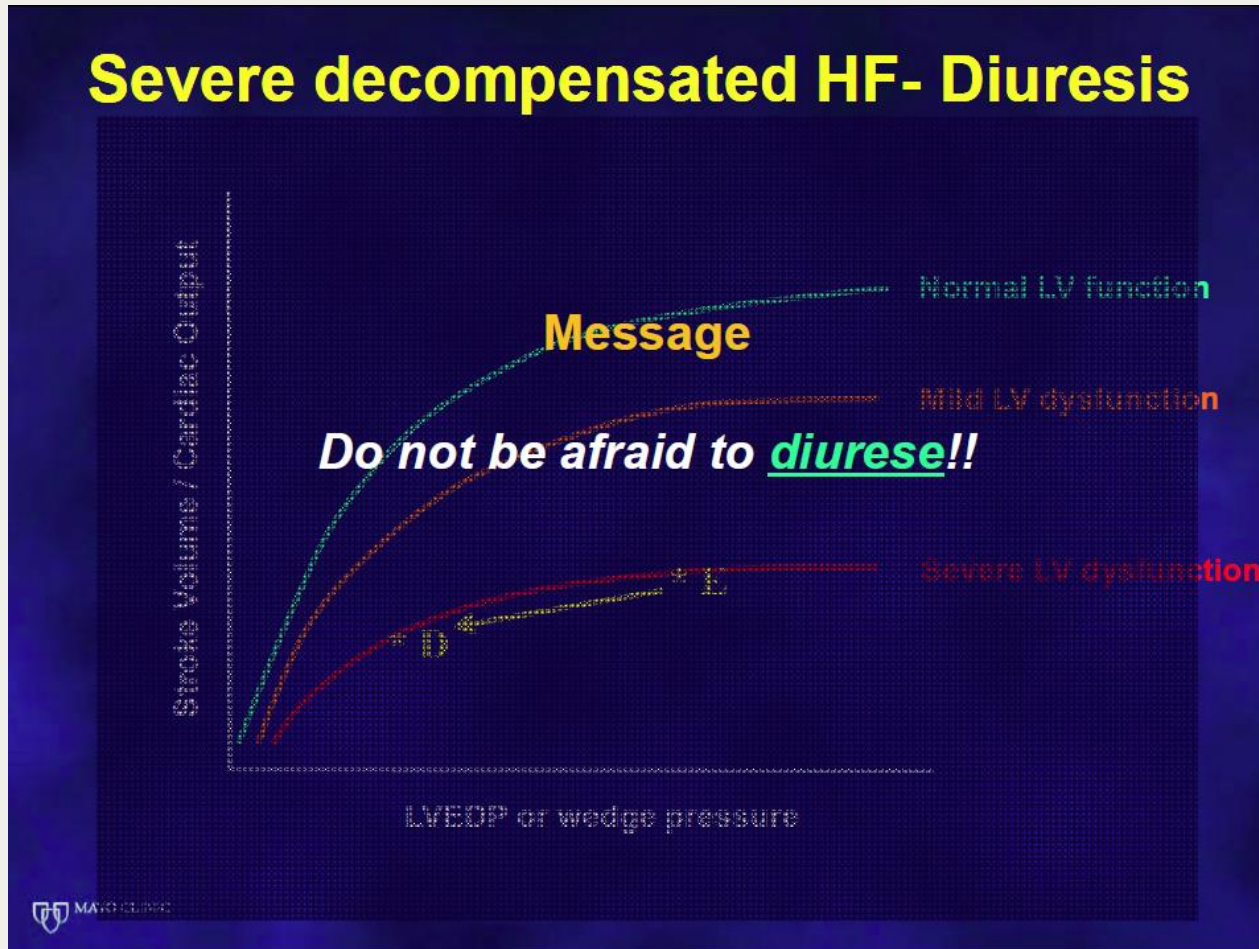
Severe decompensated HF- Diuresis



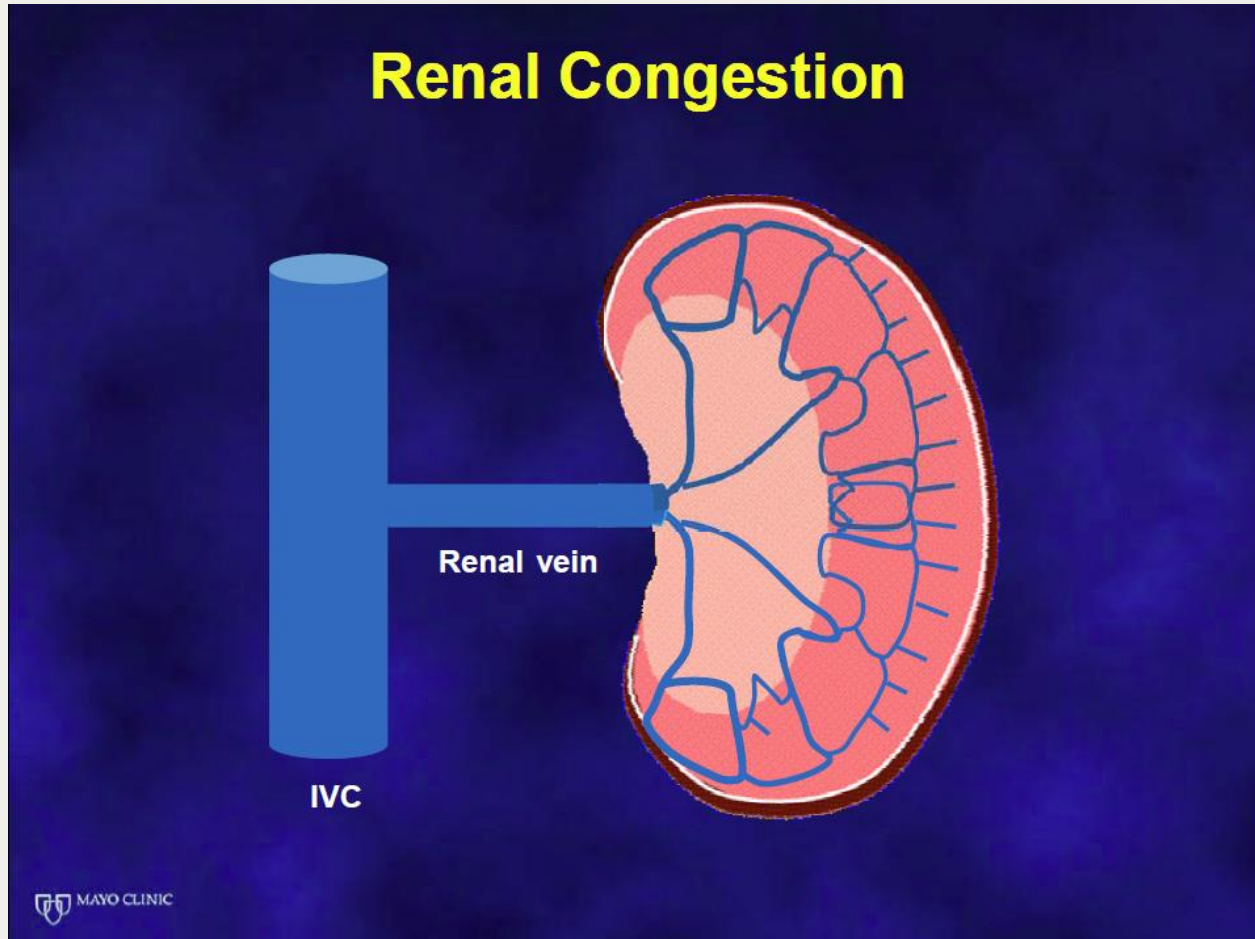
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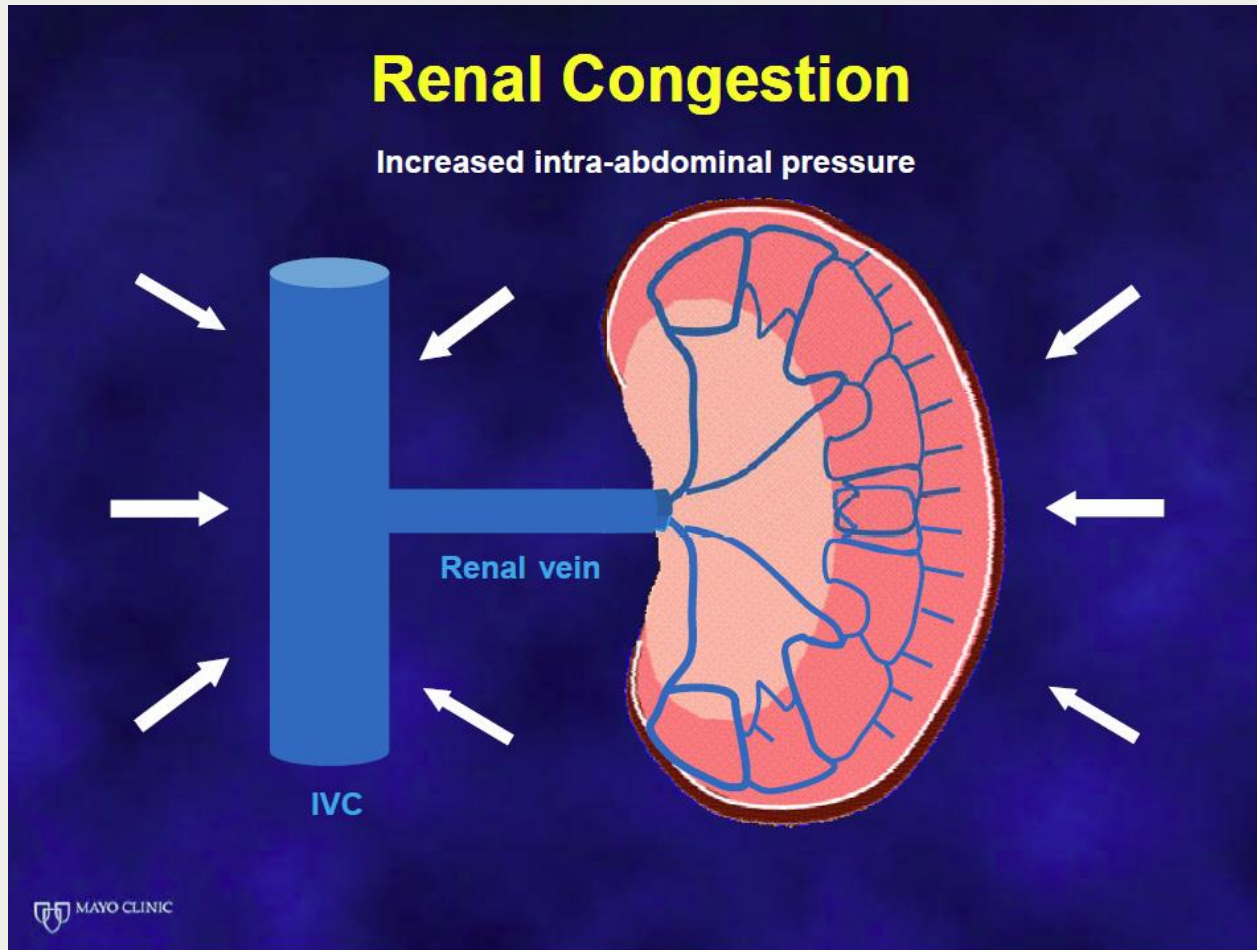
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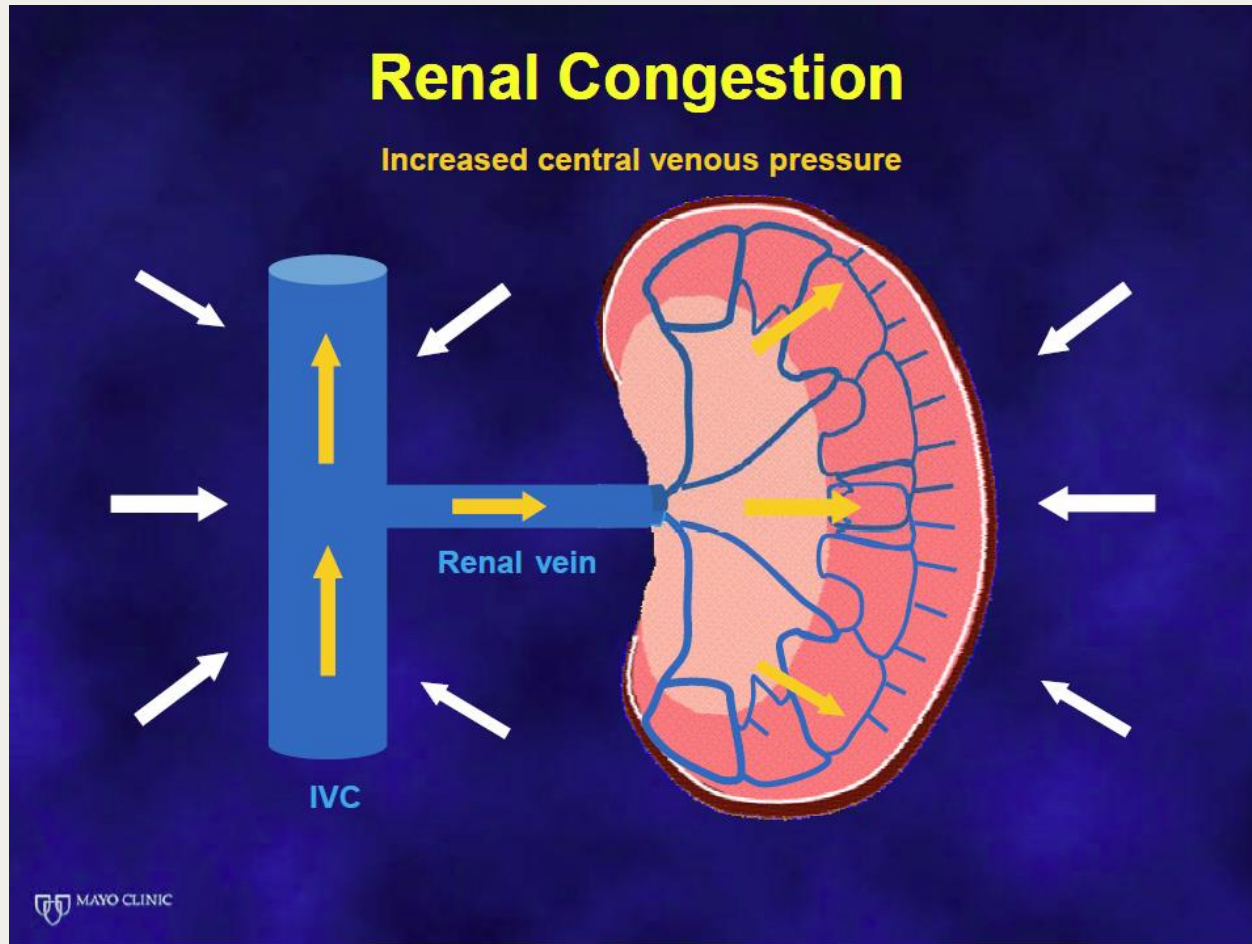
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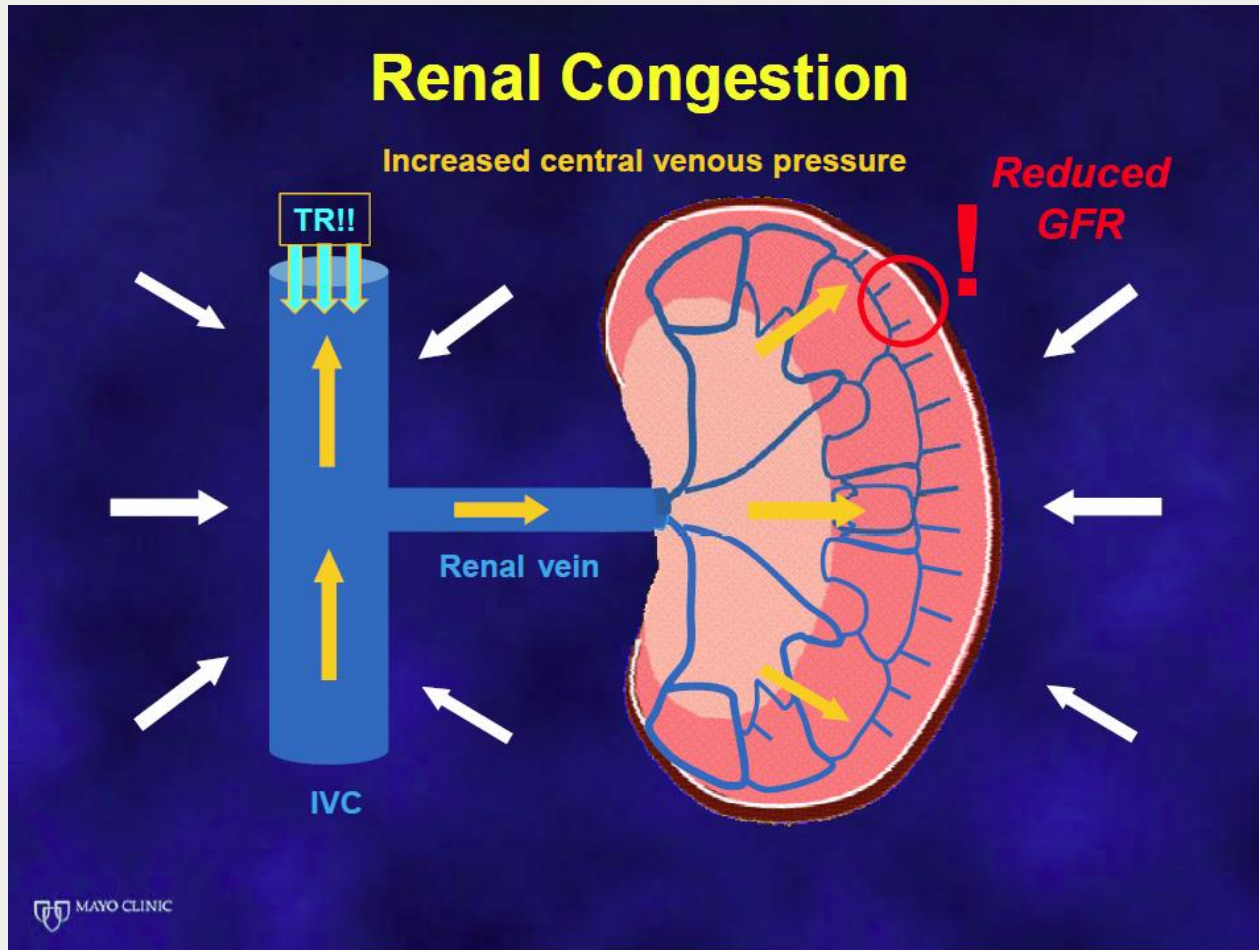
Cardiorenal Syndrome



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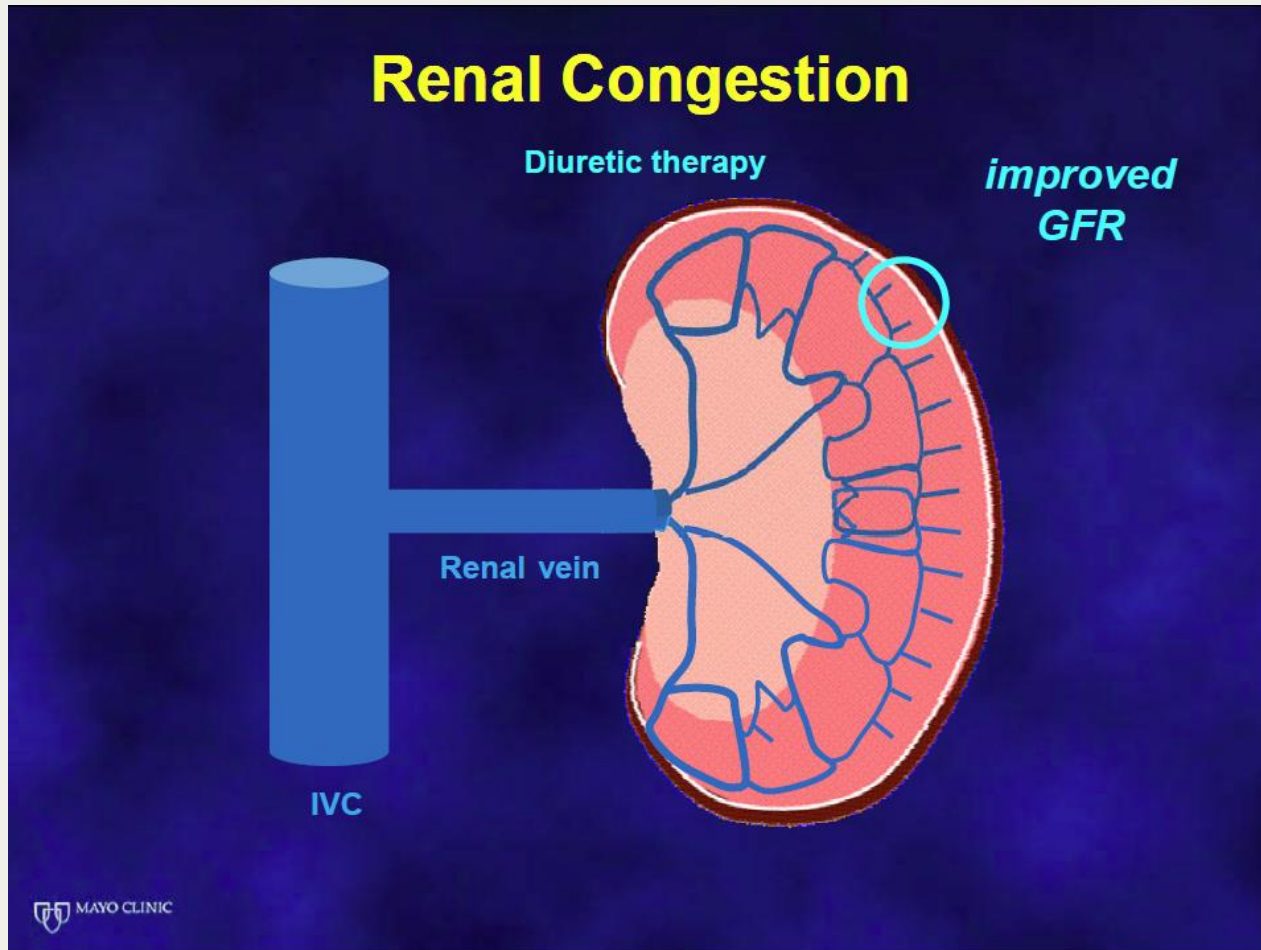


Cardiorenal Syndrome



MAVO CLINIC

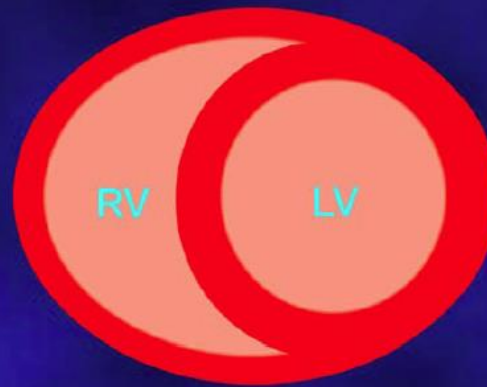
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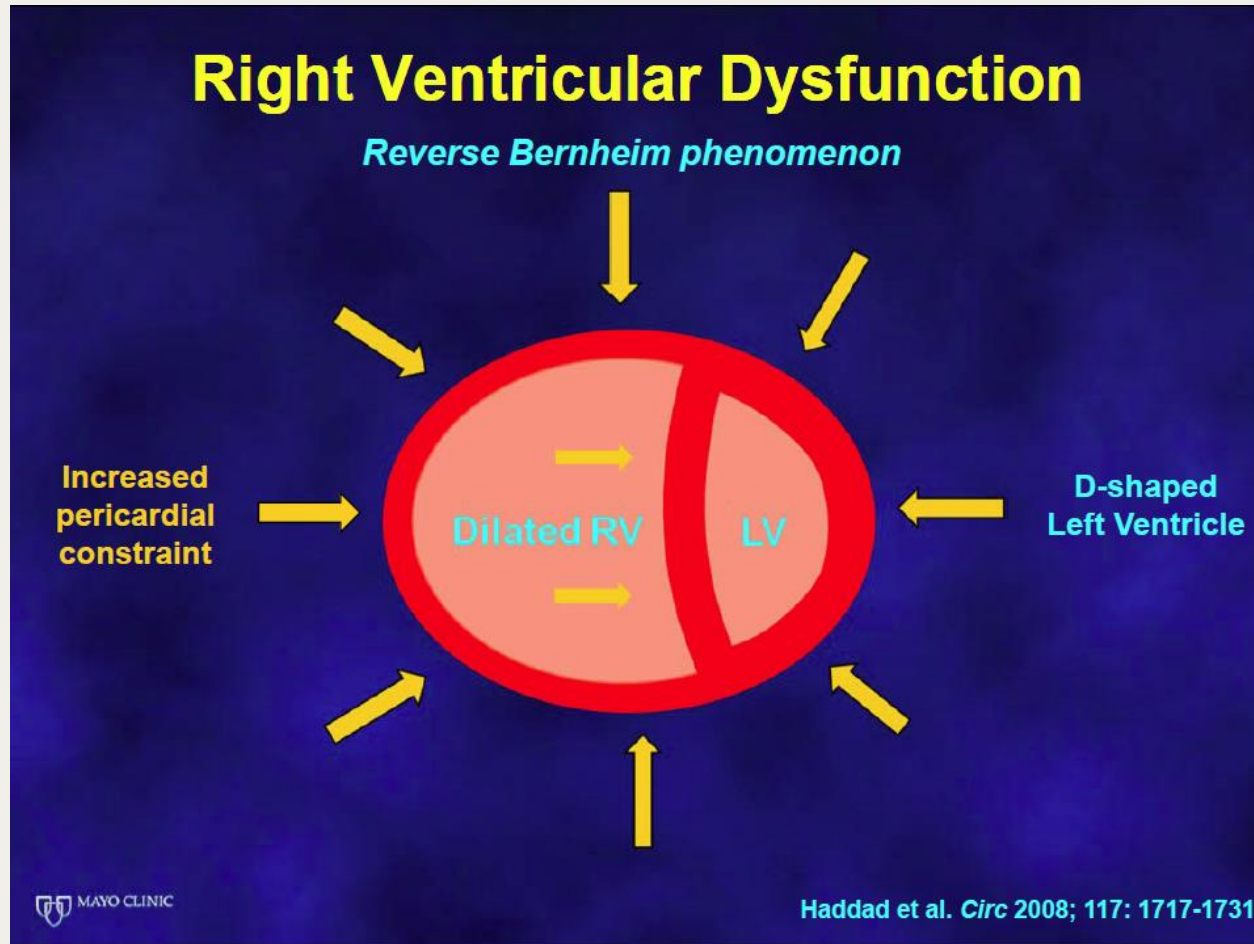
Cardiorenal Syndrome

Right Ventricular Dysfunction

- Increased central venous pressure
- *Reverse Bernheim phenomenon*



Cardiorenal Syndrome



Clinical Importance

- **First-line therapy should be diuretics/volume removal**
 - Diuretic resistance is common
- **CVP is a major driver and predictor**
- **Cardiac index is secondary**

Clinical Evidence

- **ESCAPE: No correlation between cardiac index and either the baseline GFR or worsening renal function**
 - Nohria et al. JACC 2008;51(13):1268
- **CVP is a major predictor of worsening renal function, independent of systemic BP, PCWP, cardiac index and estimated GFR**
 - Mullens et al. JACC 2009;53(7):589

Congested Patient Treatment

- **Diuretics are first-line treatment**
 - Elevated BUN/creatinine ratio should not deter diuretics, if congestion is present
 - ESCAPE and EVEREST
 - Negative effect on renal function with aggressive diuresis, but survival improved
 - Testani et al. Circ 2010;122:265
 - Greene et al. Eur J Heart Fail 2013;15:1401

Congested Patient Treatment

- **ACC/AHA Heart Failure Guidelines**

- Eliminate clinical evidence of fluid retention, such as elevated JVP and peripheral edema
- Goal of diuretic therapy is to eliminate fluid retention even if this leads to mild to moderate reductions in blood pressure or renal function

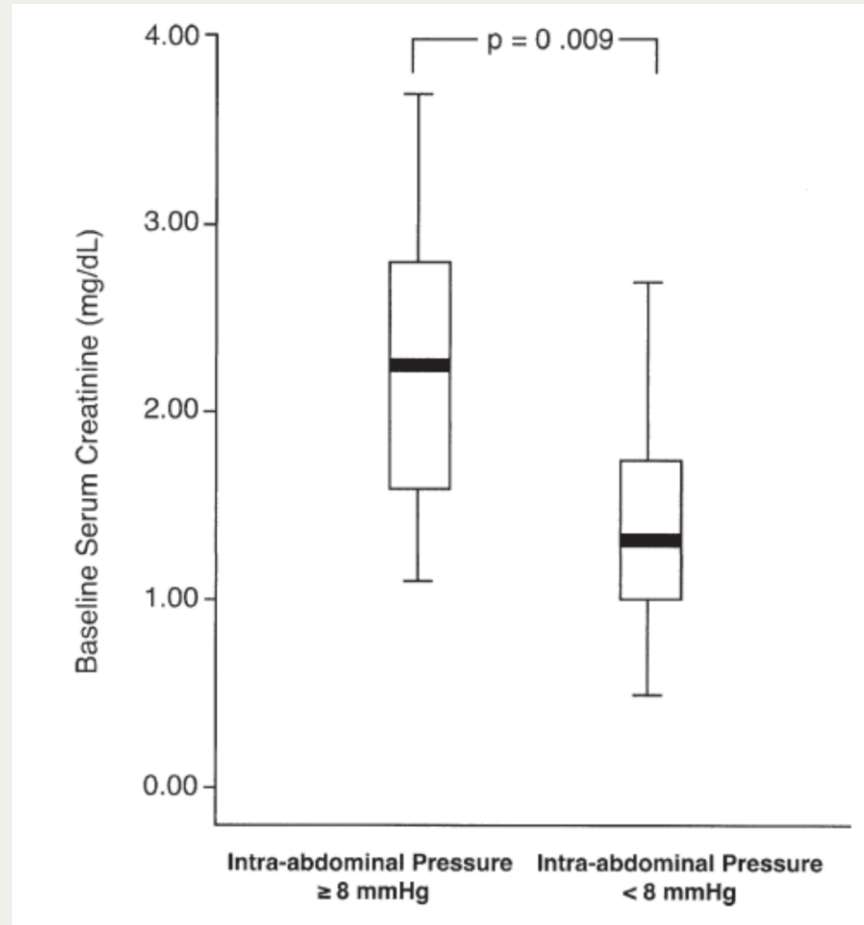
- Yancy et al. Circ 2013;128:1310

Therapeutic Paracentesis

- **Rapid symptom improvement**
- **Decompress kidneys and renal veins**
- **Increase diuretic responsiveness**
- **Relatively low risk**
- **No routine replacement of albumin**



Therapeutic Paracentesis



Congested Patient Treatment

- **Ultrafiltration role**
 - Conflicting data
 - UNLOAD and RAPID-CHF
 - Significantly greater rate of fluid loss than diuretic therapy, but no difference in serum creatinine
 - » Costanzo et al. JACC 2007;49:675
 - » Bart et al. JACC 2005;46:2013

Congested Patient Treatment

- **Ultrafiltration role**
 - Conflicting data
 - CARESS-HF
 - Weight loss was similar in ultrafiltration and stepped pharmacologic therapy groups
 - Ultrafiltration therapy caused an increase in serum creatinine and a higher rate of adverse events
 - » Bart et al. N Engl J Med 2012;367:2296

Congested Patient Treatment

- **Ultrafiltration may be helpful for fluid removal in acute decompensated heart failure in patients unresponsive to diuretic therapy**
- **Not first-line therapy**

Diuretic Resistance

- **Precipitants**
 - Exogenous fluids/sodium
 - Arrhythmias
 - Anemia
 - Ischemia
 - Infection
 - Drugs

Diuretic Resistance Tools

- **High-dose loop diuretics**
- **Double dose if poor response**
- **Max dose (FDA) = 600 mg/day**
- **NHS: 1500 mg/day**
- **Probably limited benefit over 720 mg/day**



Loop Diuretics

- **Equivalent doses**
 - Furosemide 40 mg
 - Torsemide 20 mg
 - Bumetanide 1 mg
- **Bioavailability**
 - Furosemide 10%-100%
 - Torsemide 80%-100%
 - Bumetanide 80%-100%
 - Ethacrynic acid 100%?

DOSE Study

- **IV BID bolus**
 - Low dose = 1.0 x outpatient dose
 - High dose = 2.5 x outpatient dose
- **High-dose bolus versus low-dose bolus**
- **Bolus versus continuous infusion**

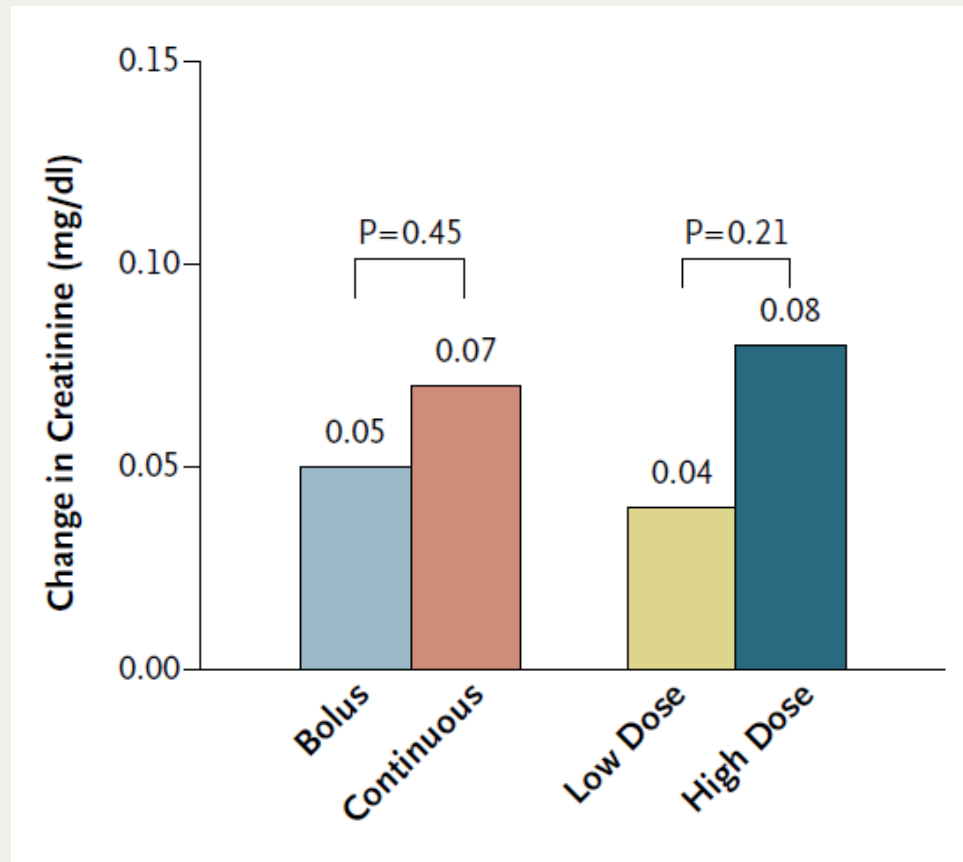
DOSE Study

- **No difference between high-dose bolus versus continuous infusion IV loop diuretics**
 - Length of stay
 - Renal function
 - NT-proBNP

DOSE Study

	Low Dose	High Dose	
AUC for dyspnea at 72 hr (higher = better)	4478±1550	4668±1496	0.04
Change in weight at 72 hr – lb	–6.1±9.5	–8.7±8.5	0.01
Net fluid loss at 72 hr — mL	3575±2635	4899±3479	0.01
Change in NT-proBNP at 72 hr	–1194±4094	–1882±4105	0.06
Increase in creatinine of >0.3 mg/dL within 72 hr — no./total no. (%)	20/147 (14)	35/154 (23)	0.04
Median stay in hospital – days	6	5	0.55

DOSE Study



Diuretic Resistance Tools

- **Thiazides**

- Classic teaching: 30-60 minutes prior to loop diuretic?
- Chlorothiazide (Diuril): 250-1000 mg IV
- Metolazone (Zaroxolyn): 2.5-10 mg PO
- Highly variable response
- Can significantly worsen electrolyte abnormalities

Diuretic Dosing

Outpatient furosemide equivalent daily dose	Continuous IV infusion strategy		Twice daily IV bolus dosing strategy
mg/day	Initial bolus	hourly rate	
<40	40 mg	2.5 mg/hr	40 mg twice daily
40 to 80	40 mg	5 mg/hr	60 mg twice daily
81 to 120	80 mg	7.5 mg/hr	100 mg twice daily
121 to 160	80 mg	10 mg/hr	140 mg twice daily
161 to 240†	80 mg	20 mg/hr	180 mg twice daily
>240†	80 mg	30 mg/hr	200 mg twice daily

Diuretic Dosing

Level	Furosemide		Metolazone†	
	Previous Oral Dose‡	Bolus	Infusion Rate	Oral Dose
1	≤80 mg	40 mg	5 mg/hr	NA
2	81–160 mg	80 mg	10 mg/hr	5 mg daily
3	161–240 mg	80 mg	20 mg/hr	5 mg twice daily
4	>240 mg	80 mg	30 mg/hr	5 mg twice daily

Low Cardiac Output Patients

- **Pharmacologic therapy**
 - Inotropes
 - Cardiogenic shock
 - Selected ADHF patients but not routinely
 - No survival benefit

Low Cardiac Output Patients

- **Pharmacologic therapy**

- Renal dose dopamine?

- Conflicting data – Insufficient evidence to recommend routine use

- DAD-HF: Enhanced diuretic effect of dopamine 5 mcg/kg/min combined with low-dose furosemide infusion similar to high-dose infusion

- » Giamouzis et al. J Card Fail 2010;16:922

Low Cardiac Output Patients

- **Pharmacologic therapy**
 - Renal dose dopamine?
 - ROSE: 2 mcg/kg/min combined with furosemide showed no benefit
 - » Chen et al. JAMA 2013;310:2533

Low Cardiac Output Patients

- **Device therapy**

- LVAD

- INTERMACS registry

- Improvements in BUN and creatinine among patients with moderate or severe renal dysfunction
 - Improvements in estimated GFR were noted within one month of LVAD implantation
 - Persisted over a two-year follow-up period
 - » Kirklin et al. J Heart Lung Transplant 2013;32:1205

Low Cardiac Output Patients

- **Device therapy**

- CRT

- MIRACLE

- eGFR improved in selected patients with GFR 30-59 ml/min

- » Adelstein et al. Pacing Clin EP 2010;33:850

- » Boerrigter et al. J Card Fail 2008;14:539

Clinical Assessment

Assessment: Summary

Congestion?

Orthopnea, rales, JVD, ascites, edema, weights, I/O

No

Yes

**Adequate
perfusion?** Yes

Pulse pressure,
cool extremities,
altered mentation

No



Summary

- **First-line approach is diuretic therapy if the patient is congested, even if elevated BUN/creatinine ratio**
- **If diuretic resistant or severe renal dysfunction is present, consider ultrafiltration**

Summary

- **Don't forget paracentesis**
- **Low cardiac output state/cardiogenic shock:
Short-term inotropes may be helpful as a bridge to stability for conventional therapy or cardiac replacement therapy**

Summary

- **These are not patients that the hospitalists should treat without cardiology consultation**
- **These patients are sick, complex and difficult to manage**
- **A team approach involving a good nephrologist is recommended**

JACC September 1, 2020

THE PRESENT AND FUTURE

JACC COUNCIL PERSPECTIVES

Contemporary Management of Severe Acute Kidney Injury and Refractory Cardiorenal Syndrome

JACC Council Perspectives

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Thank you!



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