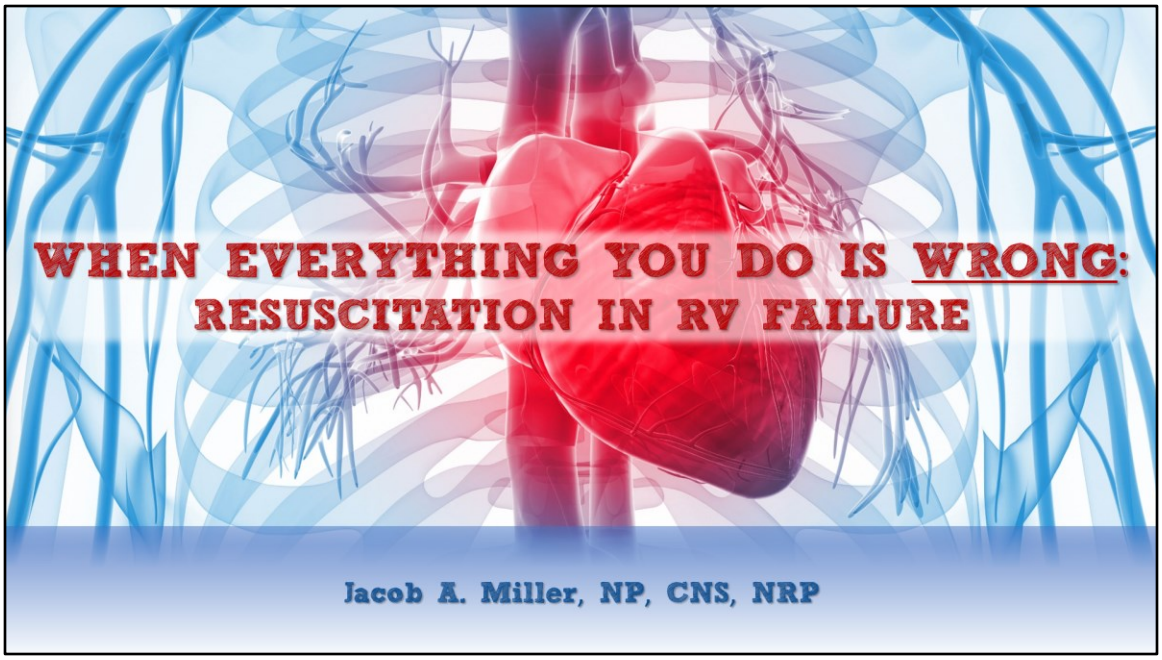


Disclosures & disclaimers:

- This presentation presents general information about a clinical topic, and is not intended to diagnose any condition or to be used as medical advice. Please consult your local policies, protocols, and/or seek expert guidance for actual clinical scenarios.
- I have received a consultation honorarium from Abiomed (a Johnson & Johnson company) within 12 months of creating this presentation, although their products are not discussed in any form during this presentation.
- There will be off-label pharmacotherapy discussion related to nitrates and prostaglandins, and that off-label use will be specifically noted in this presentation

Anatomy and Physiology

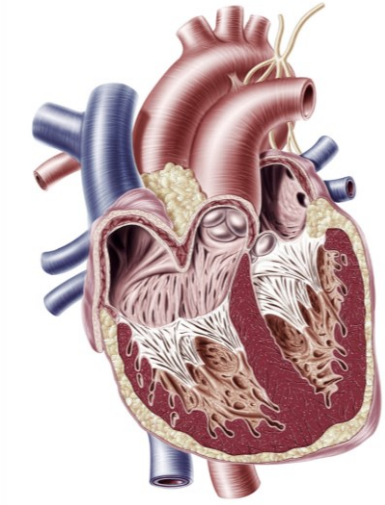


Image: Canva, under License

When we learned about Cardiac A&P in our foundational training, we weren't taught a lie, but we weren't taught a complete truth.

What we were taught about "cardiac anatomy and physiology" can better be re-labeled as "LEFT ventricular anatomy and physiology."

In this image, even the cutaway view of the ventricle makes the right and left sides of the heart look quite similar.

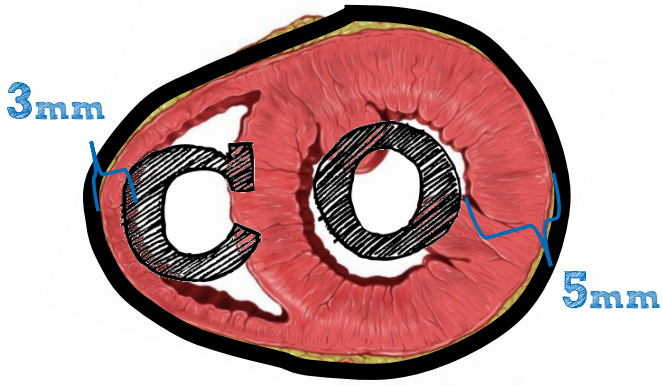


Image: Patrick.lynch via Wikimedia Commons. CC BY 2.5

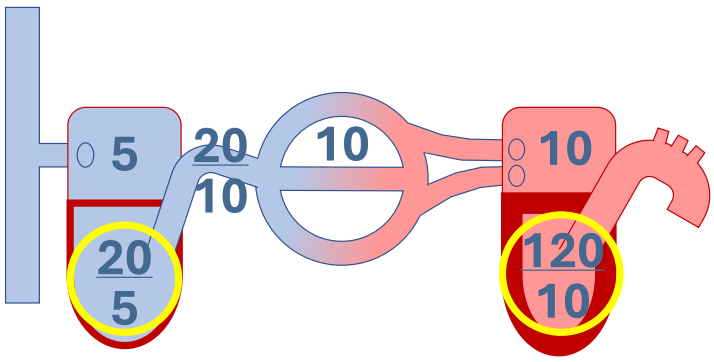
Arq Bras Cardiol 2000;75(2):111
Cardiol Clin 2012;30:167
Heart 2023;109:349

In reality, however, the RIGHT ventricle and the LEFT ventricle are entirely different animals.

The LEFT ventricle is thicker (about 5mm for left vs 3mm for right, on average)

The LEFT ventricle is circumferential (while the RIGHT ventricle is a C-shaped “free wall” that shares the septum with the LV)… however, the septum contributes more to LV ejection than RV ejection.

However, all of this occurs within the relatively fixed space of the pericardial sac (*foreshadowing: this will be important later*)



Cardiol Clin 2013;31:545

Additionally, the LEFT side of the heart is a higher-pressure system, while the RIGHT side is a low-pressure system.

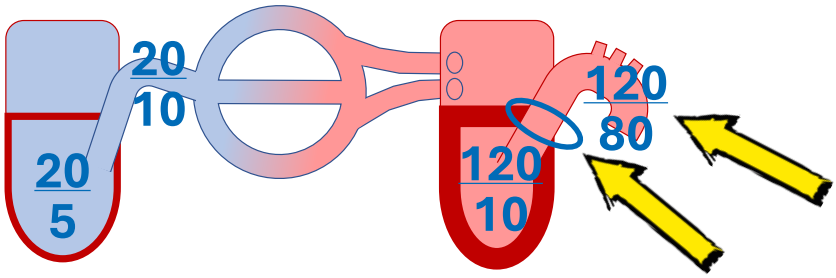
And this has important implications!

DBP - LVEDP = CPP

Cardiol Clin 2012;30:167

Who was taught that the *Coronary Perfusion Pressure (CPP)* is the diastolic blood pressure minus the LV end-diastolic pressure?

Or that the coronary arteries perfuse the myocardium during diastole only?



RV Syst: 120 - 20 = ☺
RV Dias: 80 - 5 = ☺

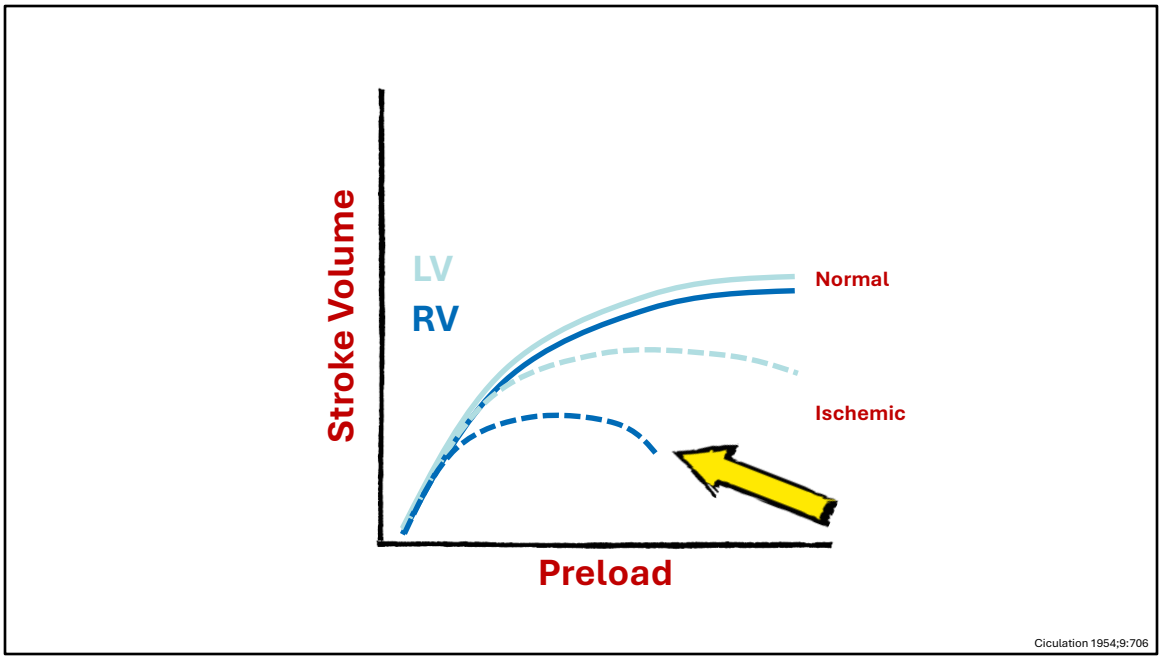
LV Syst: 120 - 120 = X
LV Dias: 80 - 10 = ☺

Cardiol Clin 2012;30:167
Cardiol Clin 2013;31:545

The reality is that the **LEFT** ventricle's CPP is, indeed, the DBP minus LVEDP.
And the **LEFT** ventricle is, indeed, perfused during diastole only.

But on the RIGHT side of the heart, there is a pressure gradient between the vascular pressure (i.e., the systemic "blood pressure") and the pressure/wall tension within the ventricle (remember: it's a low-pressure system!).

This means, the ***RIGHT*** ventricle is used to perfusion during both diastole **AND systole**!

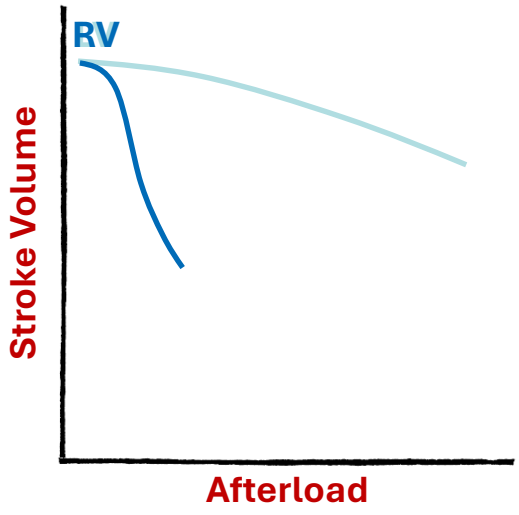


Now, let's look at the ventricular response to preload:

We've heard of the Frank-Starling mechanism, wherein there is an incremental improvement in ejection with additional stretch (i.e., preload, or volume).

However,

(1) There *is* an upper inflection point, where additional volume does not improve, and may worsen, stroke volume,
(2) This response is considerably worse in the setting of ischemia, and
(3) The ischemic response is profoundly worse on the thin-walled, lower-pressured RIGHT ventricle than the left.

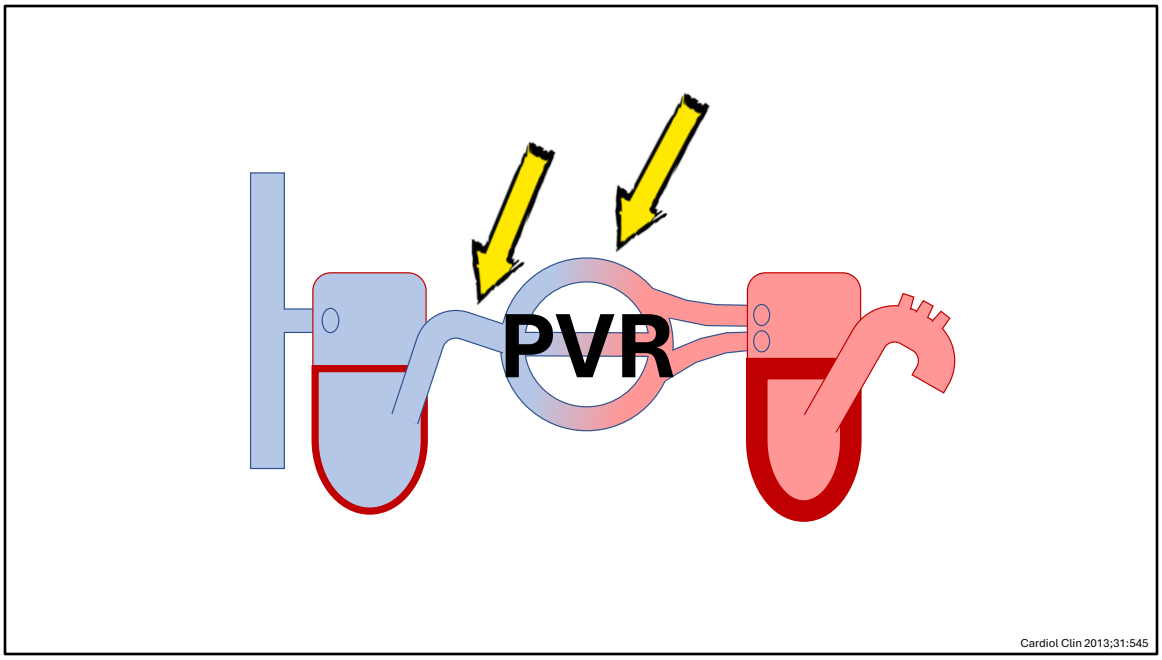


Ann Am Thorac Soc 2014;11:811
Circulation 2018;137:e578
Heart 2023;109:349

And moving from preload to afterload:

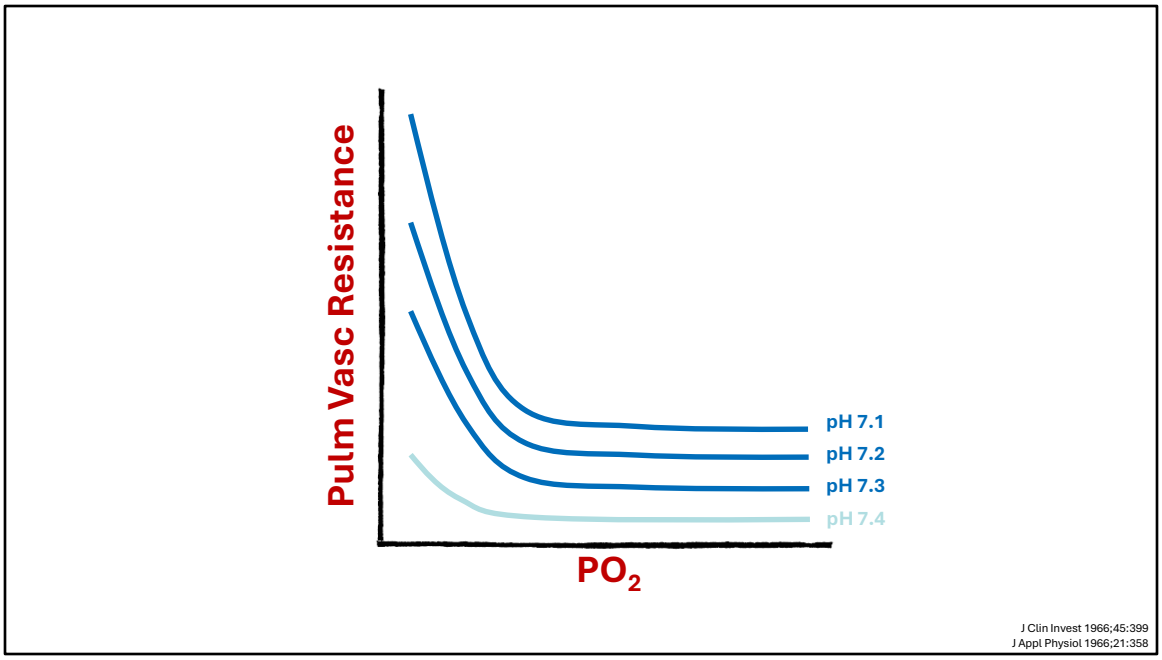
BOTH sides of the heart have a decrease in their stroke volume with increasing afterload (i.e., vascular resistance)

However, the thick, circumferentially muscular LEFT ventricle does a **MUCH** better job at overcoming that afterload than the RIGHT ventricle. The thinner, C-shaped RIGHT ventricle is quickly overwhelmed when its afterload increases.



So what *is* the afterload of the RIGHT ventricle?

Just like how the LV afterload is the *systemic* vascular resistance (i.e., systemic "blood pressure"), the afterload of the RV is the *pulmonary* vascular resistance (PVR, i.e., the pulmonary artery pressure). Changes in PVR or PA pressure can affect the function of the RV, especially when those changes are acute and significant.

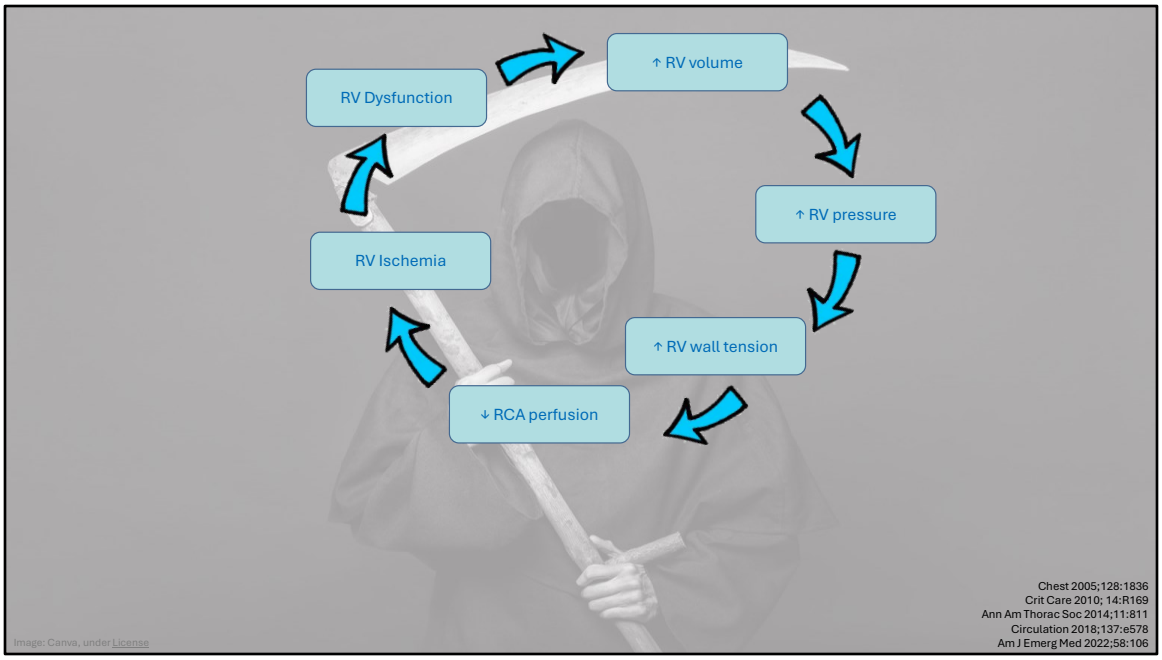


Importantly, PVR is affected by a few different factors:

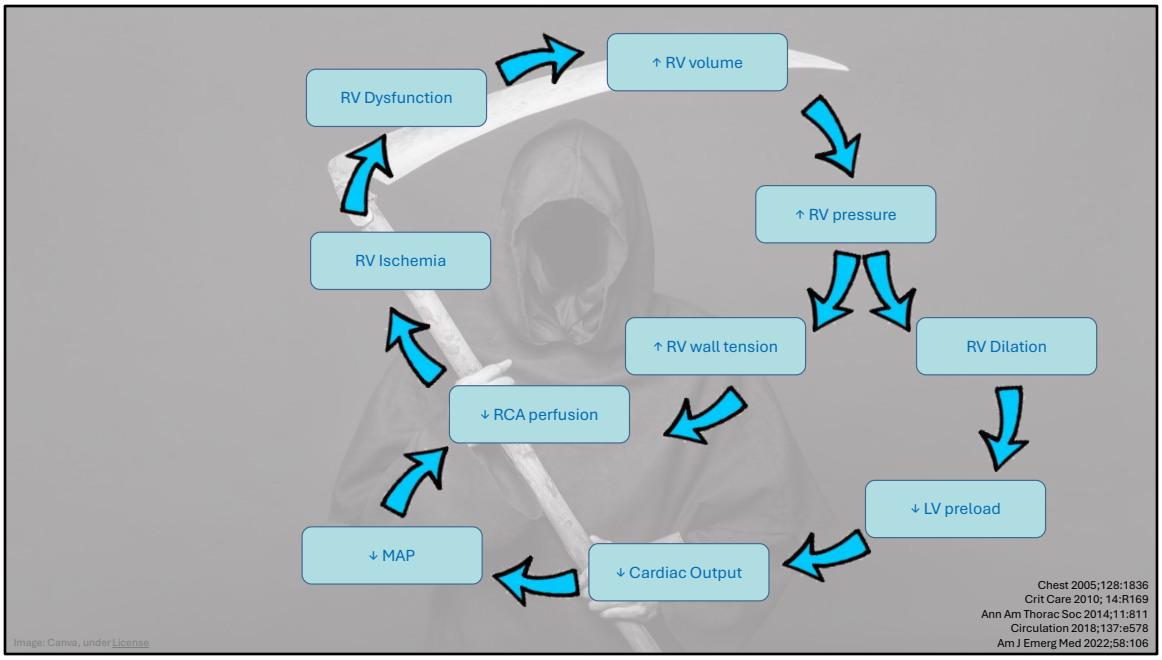
1) Oxygen: as oxygen tension decreases, PVR increases. This is actually functional and beneficial in the right context: you may have heard of “hypoxic vasoconstriction” in the setting of, for example, pneumonia. When there is a decrease in oxygen getting across an area of the lung, there is local vasoconstriction to shunt blood to other areas of the lung that are better functioning. HOWEVER, when there is global hypoxia, this can be more harmful than not.
2) pH: driven largely (but not purely) from rising CO2, acidosis also increases PVR, for a similar reason.

And, these two factors are additive to each other.

So we now have the pieces necessary to understand
[**insert dramatic music here**]
The RV Death Spiral

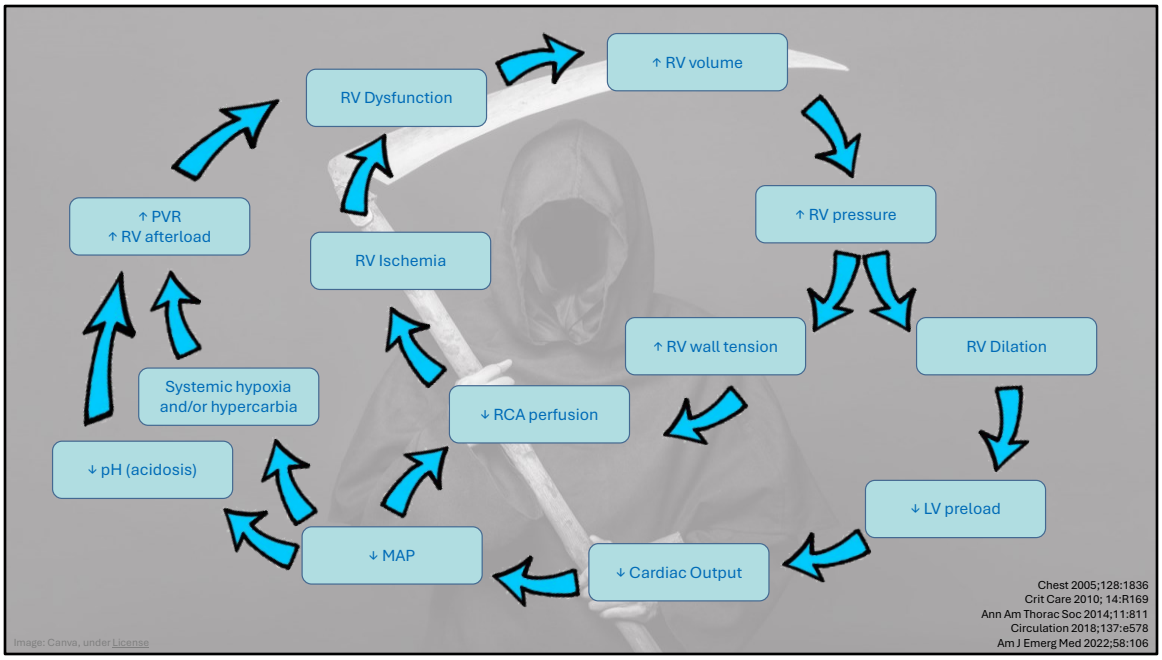


In the first limb, RV dysfunction leads to an increase in RV volume and pressure, which leads to worsening RV wall tension, decreased coronary perfusion to the RV myocardium, worsened RV ischemia, and worsened RV dysfunction.



However, the increased RV pressure also leads to RV dilation.

Because the RV (and LV) are contained within the pericardium, the RV free wall cannot move outward to accommodate this increased volume/pressure, so when the pressure becomes significantly elevated in the RV, the septal wall will move in *toward the LEFT ventricle*, reducing the LV capacity (and, therefore, decreasing the LV preload), decreasing the LV cardiac output, decreasing the systemic blood pressure, and worsening the coronary perfusion pressure. That, in turn, worsens RV ischemia and further propagates the RV dysfunction.

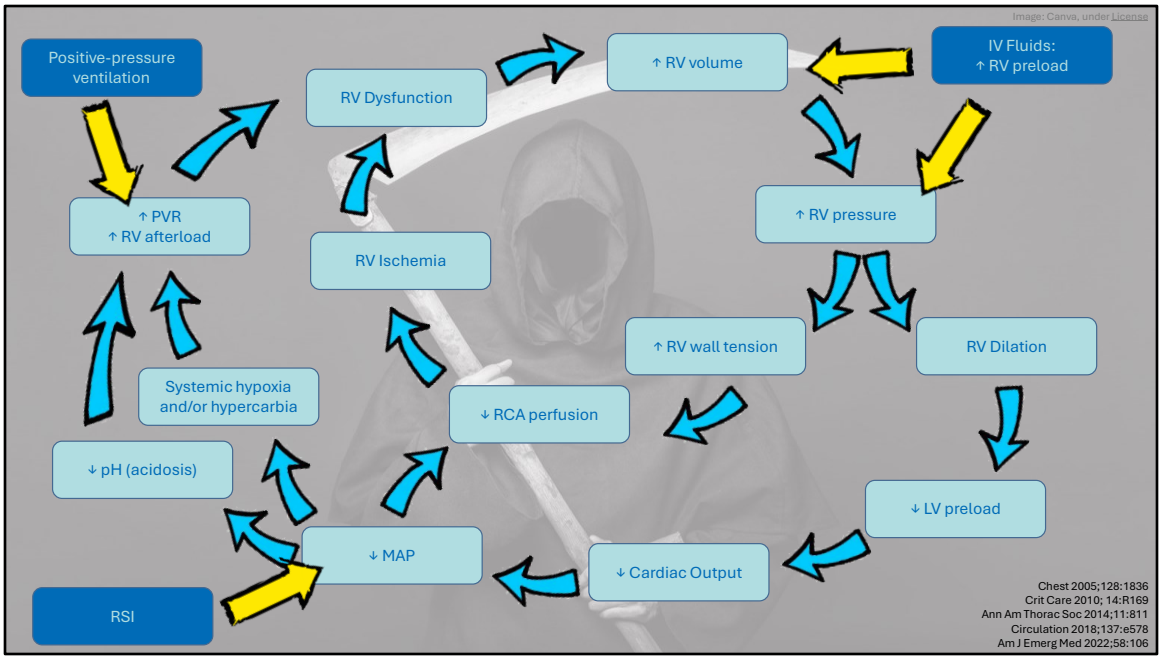


Lastly, the decreasing systemic blood pressure is commonly associated with subsequent hypercarbia, acidosis, and/or hypoxia. These factors increase PVR and RV afterload, again worsening RV dysfunction.

So how do WE, as well-trained healthcare professionals, make things worse?

Surely our typical evidence-based resuscitation practice can't be harmful, right?

….*right?*

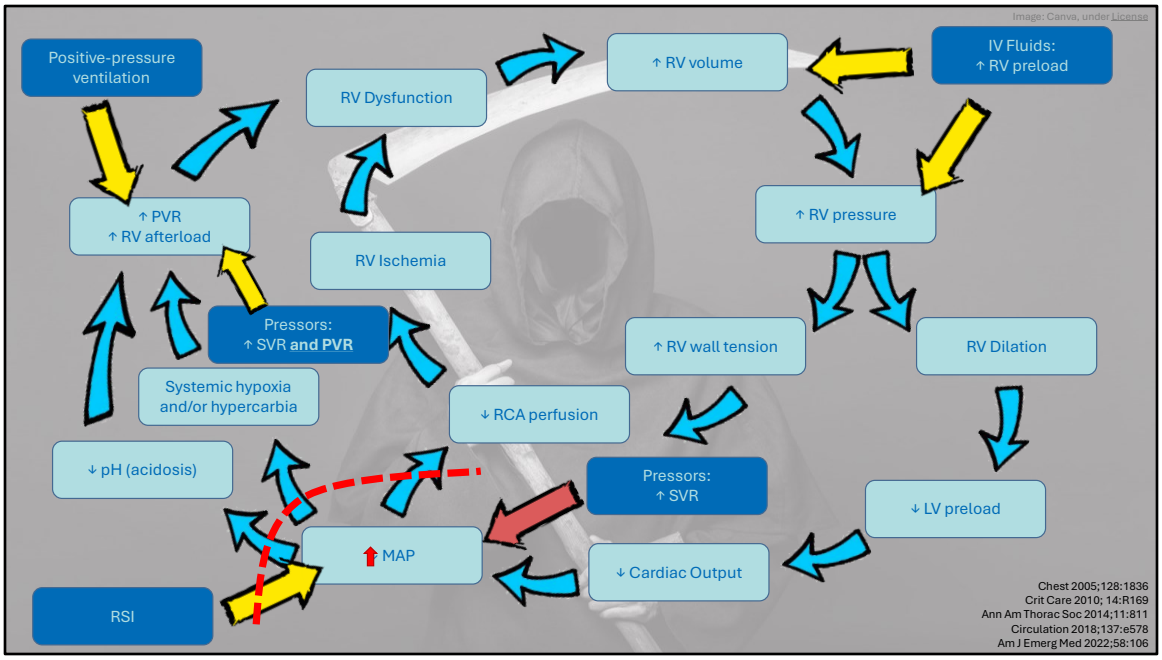


One common intervention for patients in extremis is to perform RSI, secure the airway, and take over the work of oxygenation and ventilation.

Unfortunately, many RSI drugs (yes, even our friend ketamine) can lead to worsened hypotension in the shocked patient (I have a WHOLE other presentation on this!)

The transition to positive-pressure ventilation can also lead to an increase in RV afterload. Basically, the additional pressure distends the alveoli (especially with high peak pressures and additional PEEP) and “smushes” the capillaries, effectively increasing the force (i.e., afterload) needed to circulate blood through those pulmonary capillaries.

Another common intervention is to provide IV fluids to increase preload. Remember, however, that the Frank-Starling response is muted in the setting of ischemia, and an ischemic, dysfunctional RV will quickly become overwhelmed by additional fluids. It’s reasonable to give a *trial* of IV fluids, but perform **frequent** re-evaluation of the patient’s condition after each 100-200 mL aliquot of fluid, as these patients may not be able to tolerate a large-volume fluid bolus.



So, what about giving vasopressors to improve blood pressure and MAP?

That should counteract an entire arm of this Death Spiral, right?

...right?

Vasopressors

	α_1	β_1	β_2	V_1/V_2	D_1/D_2	SVR/ MAP	HR/ CO
Norepinephrine	+++	++	-	-	-	⇧	⇔
Epinephrine	+++	+++	++	-	-	⇧	⇧
Phenylephrine	+++	-	-	-	-	⇧	⇔
Vasopressin	-	-	-	+++	-	⇧	⇔
Dopamine	+*	++*	+*	-	+++	⇧	⇧
Dobutamine	-	+++	-	-	-	⇔	⇧

Crit Care 2010; 14:R169
Intensive Care Med 2019;45:1503

We've probably all seen some form of this chart in the past, with the different receptors and how the different blood pressure agents affect them.

But there's one problem: it's incomplete!

Vasopressors

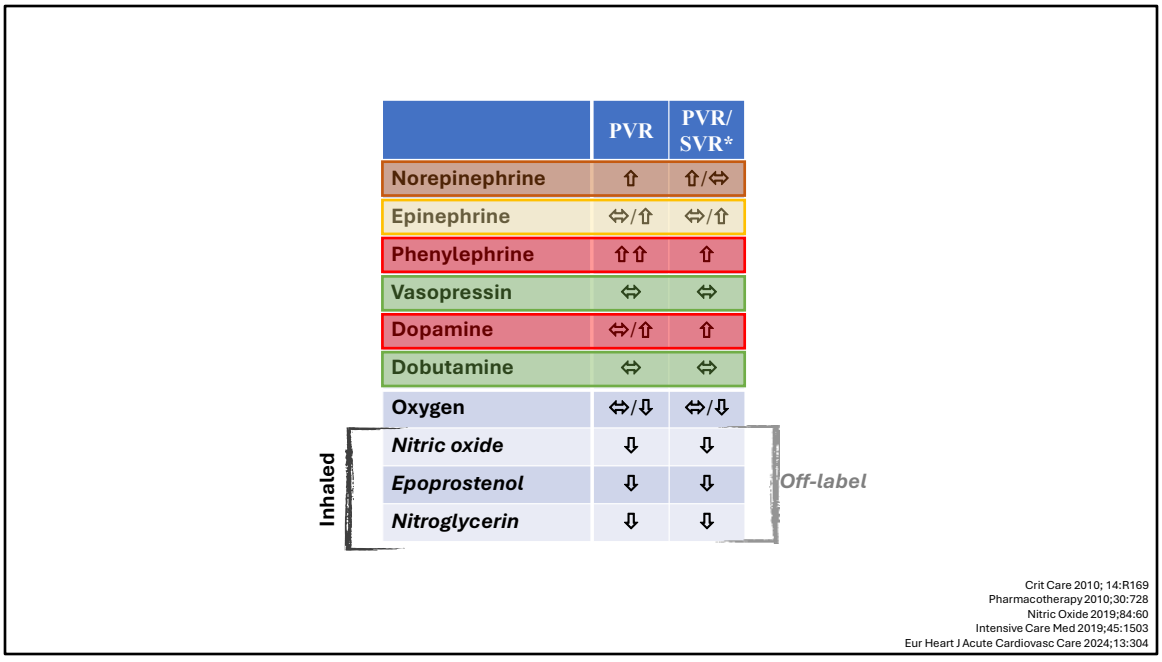
	α_1	β_1	β_2	V_1/V_2	D_1/D_2	SVR/ MAP	HR/ CO	PVR	PVR/ SVR*
Norepinephrine	+++	++	-	-	-	⇧	⇔	⇧	⇧/⇔
Epinephrine	+++	+++	++	-	-	⇧	⇧	⇔/⇧	⇔/⇧
Phenylephrine	+++	-	-	-	-	⇧	⇔	⇧⇧	⇧
Vasopressin	-	-	-	+++	-	⇧	⇔	⇔	⇔
Dopamine	+*	++*	+*	-	+++	⇧	⇧	⇔/⇧	⇧
Dobutamine	-	+++	-	-	-	⇔	⇧	⇔	⇔

Crit Care 2010; 14:R169
Intensive Care Med 2019;45:1503

In the setting of a sick right ventricle, we also need to consider the last two columns: how these agents affect the *pulmonary* circulation, i.e., the PVR, i.e., the RV afterload!

If an RV (even a healthy RV) doesn't deal well with dramatically increased afterload, we probably don't want to increase the afterload (i.e., PVR) on a patient with a weakened RV, if we can avoid it.

So what ***can*** we do to help these patietns?



First of all, use vasopressors that don't drastically increase PVR.

Pure alpha-agents (i.e., phenylephrine) are universally a horrible idea.

Agents with alpha and beta effect, especially where the beta is a bit stronger than the alpha, is probably fine at lower doses. So a low-dose epinephrine or low-dose norepinephrine infusion may be completely appropriate.

Moreover, however, VASOPRESSIN has great systemic vasopressor activity with almost NO effect on the pulmonary circulation. So for a HYPOTENSIVE patient with RV failure, this may be an ideal agent for early initiation.

DOBUTAMINE has great inotropic effects, but remember that it's an *ino**dilator***, so although it has minimal effect on pulmonary circulation, it can lead to worsened **systemic hypotension**, which can worsen RV perfusion.

(Dopamine, in general, just belongs in the trash… There, I said it…)

As far as non-pressor agents are concerned, liberal OXYGEN use in these patients can lead to improved PVR (essentially, reversing that "hypoxic vasoconstriction" discussed previously).

While off-label, agents like inhaled nitric oxide, inhaled epoprostenols, and nebulized nitroglycerin can all have potential improvements in PVR and reduce the RV afterload while having minimal effect on the systemic circulation.

SUMMARY:

- ☑ **The RV is unique**
- ☑ **Avoid hypoxia and acidosis**
- ☑ **Caution with IV fluids**
- ☑ **Low dose epi or NE probably okay**
- ☑ **Consider early vasopressin**
- ☑ **Avoid intubation if possible**
- ☑ **If not – use minimal pressure settings**
- ☑ **Inhaled agents as potential rescue**

In summary, these are our key takeaways:

- The RV is unique
- Hypoxia and acidosis are harmful and should be avoided / aggressively corrected when able
- IV fluids *might* be helpful but may quickly and easily become harmful, so use caution
- Low-dose epinephrine or norepinephrine are reasonable and probably safe first-line pressors
- Consider adding vasopressin early for hemodynamic support
- Avoid intubation (or even positive-pressure) ventilation if possible; if you cannot avoid it, consider short-acting paralytics, early return to spontaneous respirations, and as low pressure as possible to achieve safe oxygenation and ventilation (remember, low oxygen and high CO2 are also bad!)
- Finally, rescue agents may include inhaled nitrates or epoprostenols, if available at your facility (*off-label).

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