CHEST

POINT:

Should Acute Fluid Resuscitation Be Guided Primarily by Inferior Vena Cava Ultrasound for Patients in Shock? Yes

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PODCAST

ABBREVIATIONS: CVP = central venous pressure; FR = fluid responsiveness; IVC = inferior vena cava; PLR = passive leg raising

The inferior vena cava (IVC), a capacitance reservoir leading directly to the heart, encodes valuable hemodynamic information. When examined throughout the respiratory cycle, dynamic changes in the IVC diameter (ΔIVC) can guide fluid resuscitation,[1,2] akin to other dynamic predictors such as pulse pressure variation[3] and respiration-related changes in stroke volume,[4] arterial flow velocity,[5] and ventricular outflow tract velocity time integrals.[6] During positive pressure ventilation of the passive patient, inspiration raises the pleural, juxtacardiac, and right atrial pressures much more than abdominal pressure, transiently depressing venous return to the heart and tending to distend the IVC. The magnitude of this cardiopulmonary interaction depends on IVC compliance, the rise in pleural pressure, and whether the heart is on the steep portion of the cardiac function curve.

For passively ventilated patients, four studies have shown a strong correlation between ΔIVC and the change in cardiac output following a fluid bolus, with typical area under the receiver operating characteristic curve of nearly 90%.[1,2,7,8] When combined in a meta-analysis, the diagnostic OR was 30.8, illustrating excellent test performance.[9] Thus, significant dilation of the IVC during tidal ventilation accurately predicts fluid responsiveness (FR) as long as the following conditions hold: (1) the patient is receiving passive ventilation; (2) tidal volume is 8 to 12 mL/kg; and (3) there is an absence of acute cor pulmonale.

For spontaneously breathing patients (including those triggering the ventilator), inspiration tends to collapse the IVC, and the physiology explaining ΔIVC is rather different. Inspiration lowers the pleural pressure (the degree depending on effort, lung compliance, and airways resistance), which lowers the right atrial and ventricular pressures (depending on the compliance of those chambers). At the same time, inspiration raises abdominal pressure. This scenario produces a gradient tending to shift blood from the abdominal IVC to the thorax, but the magnitude of this effect is conditioned by the absolute level of right atrial pressure and IVC compliance. IVC collapse can be seen whenever inspiratory effort is large (eg, with acute asthma or other forms of respiratory failure), not only when the circulation is fluid responsive. For this reason, ΔIVC during spontaneous breathing still predicts FR (diagnostic OR, 13.2)[9] but with less confidence than in passively ventilated patients.[10-12]

In light of the complex underlying physiology, it should be self-evident that IVC diameter and its respiratory variation will never serve as a one-size-fits-all test to guide fluid resuscitation; that would be asking too much. Instead, we should judge its usefulness the way we do other diagnostic tests: when pretest probability and clinical context are integrated, does IVC ultrasound significantly alter the posttest probability of fluid response? Considered this way, the answer is a resounding "yes."

Alternative approaches to fluid resuscitation are seriously flawed. Static predictors such as central venous and wedge pressures are little better than a coin toss.[13-15] Dynamic predictors such as pulse pressure variation

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TABLE 1] Method for Measuring ΔIVC

1. Identify IVC in subcostal window
2. Confirm that the aorta is not being imaged inadvertently (entry of IVC into right atrium; entry of hepatic veins into IVC; or identify aorta separately)
3. Orient transducer in the longitudinal axis
4. Sweep the transducer to identify the largest IVC diameter
5. Measure IVC 2-3 cm from the right atrium through a full respiratory cycle (using M-mode or by capturing a sufficiently long video loop)
6. Calculate ΔIVC: (1) passive, threshold 12%; and (2) spontaneously breathing, threshold 40%-50%

ΔIVC = dynamic changes in the inferior vena cava (IVC) diameter.

and passive leg raising (PLR)[16] are accurate (assuming all of the conditions for validity are met) but require an arterial catheter (pulse pressure variation, stroke volume variation) or significant echocardiographic expertise (velocity time integrals of the left or right ventricular outflow tracts). PLR has the advantage of being accurate even during spontaneous breathing,[17] which is ΔIVC's weakest link. Nevertheless, it is cumbersome to perform (often using a specialized bed) and requires some measure of effect, such as obtaining an apical five-chamber view to estimate the velocity time integral. In carefully conducted clinical trials, investigators can obtain adequate five-chamber views in both the semi-upright and PLR positions without introducing large measurement errors, but I doubt this approach can be utilized as part of usual care.

In practice, using IVC ultrasound to guide fluid resuscitation has significant advantages. The subcostal longitudinal view is readily obtainable in > 90% of patients; it is one of the easiest point-of-care ultrasound techniques to master (Table 1); and the entire examination takes < 3 min. It can be repeated at will (eg, after each fluid bolus or clinical change), is noninvasive, and can be integrated into a more comprehensive ultrasound examination that includes goal-directed echocardiography to exclude tamponade, cardiogenic shock, cor pulmonale, or major valvular lesion; lung ultrasound to rule out tension pneumothorax or diffuse anterior B lines; and (when appropriate) abdominal imaging.[18] Applied this way, point-of-care ultrasound has tremendous value for many patients diagnosed with shock.

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COUNTERPOINT:

Should Acute Fluid Resuscitation Be Guided Primarily by Inferior Vena Cava Ultrasound for Patients in Shock? No

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PODCAST

The goal of fluid resuscitation in shock is to improve organ perfusion while avoiding the harms of excess fluid administration. Fluids lead to harm unless: (1) the tissue hypoxia results from inadequate oxygen delivery rather than mitochondrial or microvascular dysfunction; and (2) fluid administration leads to an increase in tissue oxygen delivery.[1-3] Previous debates and investigations have focused on optimal methods for differentiating between states of inadequate oxygen delivery and mitochondrial dysfunction.[4-6] The role of IVC ultrasound in fluid resuscitation focuses on its ability to predict whether fluids will increase cardiac output, a condition known as fluid responsiveness (FR).

Decades of investigations on tools to identify FR have led to several oft-cited conclusions: (1) only 50% of critically ill patients believed to benefit from fluids actually have FR; (2) traditional clinical and static hemodynamic parameters are poor predictors of FR; and (3) the most accurate predictors are "dynamic measures" (ie, tests that measure changes in cardiac output in response to transient fluid boluses such as pulse pressure variation and PLR).[7-9] Publications regarding these dynamic measures have dominated fluid resuscitation literature since pulse pressure variation was first described > 15 years ago.[9] So why are we debating the utility of IVC ultrasound rather than one of these more established tools? The answer likely has more to do with perceived convenience than diagnostic accuracy. Dynamic measures typically require invasive or sophisticated equipment to insert and calibrate, advanced echocardiographic skills to perform, or unique patient clinical conditions to be met (eg, lack of spontaneous respiratory effort). These limitations render such approaches more difficult for clinicians, particularly in acute care settings such as the ED. In contrast, IVC ultrasound is seen as the "holy grail" of FR predictors: immediately available, easy to learn, quick to perform, and applicable in a wide range of patients. However, diagnostic accuracy must not be sacrificed on the altar of convenience; what good is a convenient tool if it misleads us?

The arguments against IVC ultrasound can be grouped into three categories: (1) technical measurement challenges; (2) inability of filling pressures to predict FR; and (3) difficulties interpreting effects of intrathoracic pressure changes.

Multiple Patient and Operator Factors Limit Accurate Measurement of IVC Parameters

Measuring the IVC is confounded by a host of technical factors, including obesity, abdominal distension, surgical dressings, and intraabdominal hypertension. The abdominal aorta may be mistaken for the IVC. The IVC may be measured at a point that is not the true maximum diameter. IVC measurements have suboptimal interoperator reliability.[10,11] Translational artifacts during inspiration may be incorrectly interpreted as IVC variation.[12] Some of these well-known technical challenges were ignored in studies validating IVC ultrasound.[13]

IVC Parameters Are Determined by Static Filling Pressures That Do Not Predict FR

Two parameters of the IVC have been studied to predict FR: (1) diameter; and (2) variation in diameter during inspiration. In healthy adult subjects, the IVC diameter averages 1.7 ± 0.4 cm and decreases by approximately 50% during tidal breathing.[14,15]

The IVC diameter is determined by the difference between the internal (ie, central venous pressure [CVP]) and external pressure (intraabdominal pressure). When intraabdominal pressure is negligible, a curvilinear positive relationship between CVP and IVC diameter is observed.[16-18] Consequently, "the IVC is the CVP." However, static filling pressures, such as CVP, cannot accurately identify FR in a heterogeneous ICU population composed of significant proportions of patients with septic shock.[7,19]

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Why do we still equate low filling pressures with hypovolemia and/or a need for fluids in septic shock? We forget that low filling pressures are: (1) most often caused by factors other than volume loss in these patients, namely vasodilation and hyperdynamic cardiac function; (2) the normal state of health; and (3) necessary to promote venous return. Although the two main types of hypotensive insults seen in ICUs (bleeding and sepsis) both produce low filling pressures, they require different fluid resuscitation approaches. Blood loss leads to a pure hypovolemic state and requires (and clinically responds to) aggressive repletion of intravascular volume. Sepsis is more complex but, in general, benefits most from initial, modest fluid administration followed by treatment of the associated vasoplegia and/or myocardial dysfunction.

When clinicians do not explicitly identify these disparate clinical contexts, the low filling pressures "seen" on goal-directed echocardiograms (or measured via internal jugular catheters) of patients with sepsis in the ICU after initial fluid resuscitation leads to a conditioned response. This response comprises continued aggressive fluid resuscitation and fluid overload in the > 50% of ICU patients with low filling pressures who do not have FR.[7]

Clearly, in overt hypovolemic insults (eg, after blood donation, after fluid removal during dialysis, bleeding trauma patients), low filling pressures identified by using IVC ultrasound reflect volume loss.[20-22] Is IVC ultrasound really needed to guide our management in these cases, however? Probably not. Assessing and targeting heart rate, blood pressure, or hemoglobin levels during resuscitation represents a sound clinical approach to such cases.

It is when faced with the complex physiology of the patient with septic (or multifactorial) shock that we desire equally robust, simple guides to direct and balance the multiple therapies required. Unfortunately, it is precisely these patients for whom the evidence does not support the use of IVC ultrasound: "where it is useful, it is not needed, and where it is needed, it is not useful." There are two ways to argue why IVC diameter cannot predict FR in critically ill patients: directly and indirectly. The direct argument relies on citing the two studies that report the poor predictive accuracy of IVC diameter in a heterogeneous ICU population. Airapetian et al[23] reported an area under the receiver operating characteristic curve of 0.62 in 58 critically ill shock patients, similar to that of CVP (0.56)[19] and the tossing of a coin, and nowhere near the accuracy of PLR (0.95).[24] Similarly, Feissel et al[25] reported a very weak correlation ($r = 0.46$) of IVC diameter with FR. The indirect argument relies on simply citing the extensive literature demonstrating the near complete inability of the CVP (which largely determines IVC diameter) to predict FR.[19]

Effects of Intrathoracic Pressure Changes on the IVC Are Poorly Understood and Rarely Predictive of FR

There are two types of IVC variation: (1) "collapse" (during inspiration in spontaneously breathing patients); and (2) "distention" (during inspiration in paralyzed patients who are mechanically ventilated).

IVC "Collapsibility"

During inspiration in a spontaneously breathing patient, intrathoracic pressure decreases, the right heart chambers expand, and CVP falls.[16,26] Intraabdominal pressure rises due to descent of the diaphragm and contraction of abdominal muscles. This combination of forces "collapses" the IVC. The amount of collapse observed is thus driven by CVP and the magnitude of inspiratory effort.

To my knowledge, no theory or study has proposed a correlation between the magnitude of inspiratory efforts and presence of FR. Even if we could standardize inspiratory effort among critically ill patients (ie, similar to the "sniff" tests used in the quiet of an echocardiography laboratory), the amount of collapse seen would simply reflect baseline CVP.[27] This fact has not prevented multiple groups from assessing the ability of IVC collapse to predict FR, with predictably and uniformly poor results (Table 1).[28-32] To support the assertion that both IVC collapse and IVC diameter are determined according to CVP, the one study that reported on their predictive accuracy for FR found them to have identical area under the receiver operating characteristic curves of 0.62, similar to that of CVP.[19,25] Of note, the two studies in Table 1 that found even a modest predictive ability of IVC collapse included 38% and 50% of patients, respectively,[29,31] with baseline, overt hypovolemic insults.

IVC "Distensibility"

During insufflation of a paralyzed, intubated patient, the IVC will distend but only in patients whose IVCs are not yet maximally distended. This increase in diameter indicates a "preload reserve" within the vein and has a high correlation with FR ($r = 0.82$).[25] Unfortunately, only 2% of patients in ICUs at a given time will possess the entire set of clinical conditions required to perform this test reliably, making it one of the least generalizable measures described.[33]

TABLE 1] Predictive Accuracy of IVC Collapse for Fluid Responsiveness[a]

Author	Year	No.	Setting	Definition of Fluid Responsiveness	IVC Collapse Measure	Predictive Accuracy of IVC Collapse
Sobczyk et al [28]	2016	35	CTICU	Increase in CO > 15% by echocardiography	None identified	r = 0.16
Airapetian et al[23]	2015	59	ICU	Increase in CO > 10% by echocardiography	None identified	r = 0.20 AUC = 0.62
De Valk et al[29]	2014	45	ED	Increase of SBP > 10 mm Hg	Collapse >36.5%	AUC = 0.74[b]
Corl et al[30]	2012	30	ED	Increase in CO > 10% by IC	None identified	AUC = 0.46
Muller et al[31]	2012	40	ICU	Increase in VTI > 15% by echocardiography	Collapse >40%	AUC = 0.77[c]
Williams et al[32]	2012	15	ED	Increase in SV > 15% by bioreactance	Collapse >40%	Sens-24% Spec-59%

AUC = area under receiver operating characteristics curve; CO= cardiac output; CTICU = cardiothoracic surgery ICU; IC = impedance cardiography; IVC = inferior vena cava; R = correlation coefficient; SBP = systolic blood pressure; SV = stroke volume; VTI = velocity time integral.
[a]Published studies with ≥ 15 patients.
[b]38% of patients with dehydration.
[c]50% of patients with bleeding, dehydration or trauma.

Conclusions

Routine use of IVC ultrasound parameters to guide fluid therapy should be abandoned because they are rarely reliably assessed, are unnecessary in managing patients with overt hypovolemic insults, and are almost completely determined by filling pressures that cannot predict FR in heterogeneous critically ill patient populations. For those who have abandoned CVP in favor of the IVC as a guide to fluid resuscitation, beware of the "wolf in sheep's clothing."

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Rebuttal From Dr Schmidt

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For a patient in shock, ultrasound of the IVC is a fundamental component of the intensivist's assessment. Dr Kory argues that IVC diameter and its variation cannot be reliably assessed,[1] but most intensivists find that the longitudinal, subcostal examination is easily learned. Interrater reliability is known to be high,[2,3] and, with careful attention to methodology,[4] errors are uncommon. Facility with trans-hepatic (and occasionally trans-splenic) sonographic windows makes the examination applicable for nearly every critically ill patient.

Respiratory variation in IVC diameter (ΔIVC) represents far more than a static filling pressure: ΔIVC is no CVP.[5] For spontaneously breathing patients, the theory that links ΔIVC to FR is the physiology of the cardiac function curve.[6] Inspiration lowers the pleural pressure, drawing the cardiac function curve to the left. If the patient's circulation is operating on the flat portion of the cardiac function curve, right atrial pressure will not fall on inspiration, and the IVC will not collapse (Fig 1). Conversely, when operating on the steep limb of the cardiac function curve, inspiration shifts the point at which the cardiac function and venous return function curves intersect, right atrial pressure falls, and the IVC tends to collapse. As long as inspiratory effort is sufficient and the patient is not recruiting accessory muscles at end-expiration, this signal is physiologically sound.[7]

The need to infuse fluid when hypovolemia contributes to shock is not always obvious. Tachycardia may signal pain, ventilator dyssynchrony, systemic inflammation, hypercapnia, pulmonary edema, or a hundred other ills. As a guide to fluid therapy in the bleeding patient, hemoglobin concentration is nearly useless. After all, the exsanguinating patient has similar values at the point of injury and the moment of death. In my own practice, both incomplete and excessive resuscitation are seen regularly; IVC ultrasound often clarifies a hazy picture.

The preconditions for validity of ΔIVC deserve attention. Perhaps I would agree with Dr Kory that a simple snapshot of the IVC could be misleading, especially when devoid of the clinical presentation, examination findings, patient-ventilator interaction, echocardiography, ultrasound interrogation of the lungs, and the clinical trajectory. However, the alert intensivist is attuned to inspiratory effort, abdominal muscle recruitment, intraabdominal pressure, ventricular function, cor pulmonale, and the ventilator tidal volume. Indeed, IVC ultrasound demands an intensivist at the bedside, hand on the belly, in intimate contact with the patient, which is right where he or she belongs.

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Rebuttal From Dr Schmidt

Gregory A. Schmidt, MD, FCCP
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For a patient in shock, ultrasound of the IVC is a fundamental component of the intensivist's assessment. Dr Kory argues that IVC diameter and its variation cannot be reliably assessed,[1] but most intensivists find that the longitudinal, subcostal examination is easily learned. Interrater reliability is known to be high,[2,3] and, with careful attention to methodology,[4] errors are uncommon. Facility with trans-hepatic (and occasionally trans-splenic) sonographic windows makes the examination applicable for nearly every critically ill patient.

Respiratory variation in IVC diameter (ΔIVC) represents far more than a static filling pressure: ΔIVC is no CVP.[5] For spontaneously breathing patients, the theory that links ΔIVC to FR is the physiology of the cardiac function curve.[6] Inspiration lowers the pleural pressure, drawing the cardiac function curve to the left. If the patient's circulation is operating on the flat portion of the cardiac function curve, right atrial pressure will not fall on inspiration, and the IVC will not collapse (Fig 1). Conversely, when operating on the steep limb of the cardiac function curve, inspiration shifts the point at which the cardiac function and venous return function curves intersect, right atrial pressure falls, and the IVC tends to collapse. As long as inspiratory effort is sufficient and the patient is not recruiting accessory muscles at end-expiration, this signal is physiologically sound.[7]

The need to infuse fluid when hypovolemia contributes to shock is not always obvious. Tachycardia may signal pain, ventilator dyssynchrony, systemic inflammation, hypercapnia, pulmonary edema, or a hundred other ills. As a guide to fluid therapy in the bleeding patient, hemoglobin concentration is nearly useless. After all, the exsanguinating patient has similar values at the point of injury and the moment of death. In my own practice, both incomplete and excessive resuscitation are seen regularly; IVC ultrasound often clarifies a hazy picture.

The preconditions for validity of ΔIVC deserve attention. Perhaps I would agree with Dr Kory that a simple snapshot of the IVC could be misleading, especially when devoid of the clinical presentation, examination findings, patient-ventilator interaction, echocardiography, ultrasound interrogation of the lungs, and the clinical trajectory. However, the alert intensivist is attuned to inspiratory effort, abdominal muscle recruitment, intraabdominal pressure, ventricular function, cor pulmonale, and the ventilator tidal volume. Indeed, IVC ultrasound demands an intensivist at the bedside, hand on the belly, in intimate contact with the patient, which is right where he or she belongs.

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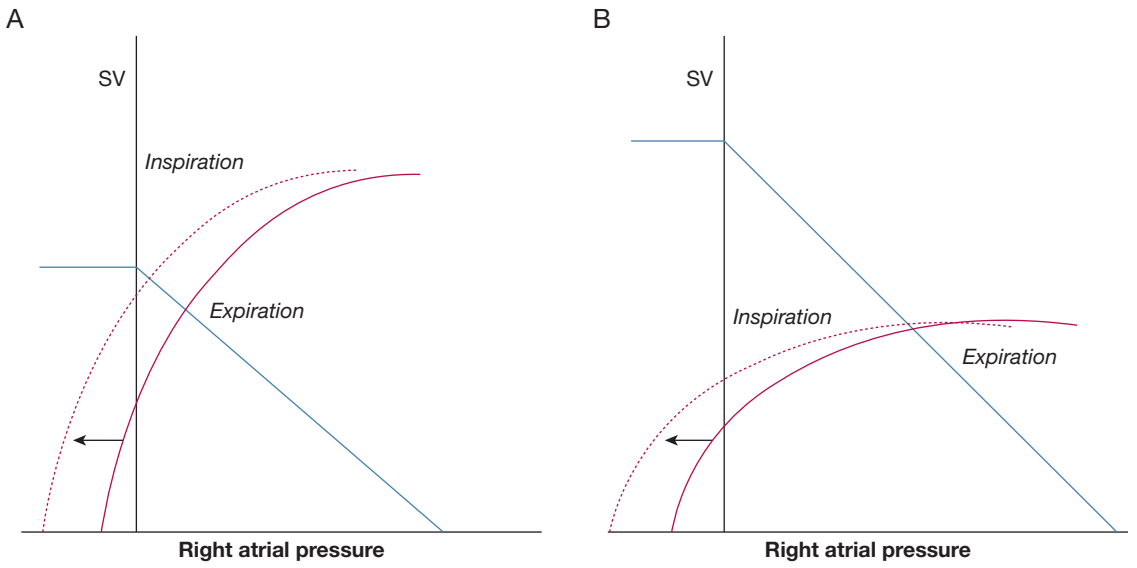

Figure 1 – *A, Represents a fluid-responsive circulation and shows the intersection of the venous return and cardiac function curves at end-expiration (solid cardiac function curve) and end-inspiration (dotted curve). The inspiratory drop in pleural pressure shifts the cardiac function curve to the left, moving the intersection point to a lower right atrial pressure. The IVC tends to collapse accordingly. B, The circulation is characterized by depressed cardiac function and high intravascular volume and would not respond to further fluid loading. Inspiration shifts the cardiac function curve to the left as in A but, because the circulation is operating on its flat portion, the intersection with the venous return function line shifts imperceptibly. Right atrial pressure will not fall measurably, and the IVC will not collapse. SV = stroke volume.*

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Rebuttal From Dr Kory

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I appreciate and commend Dr Schmidt's succinct review[1] of the physiology underlying cardiac filling and output. He accurately observes that IVC distention has a strong correlation with FR. He neglects to mention, however, that IVC distention is found in such rare circumstances, it could never serve as the primary guide to fluid resuscitation unless we heavily sedated, paralyzed, and overinflated our intubated patients, an approach violating some of the most beneficial patient care practices we know of today (ie, low-tidal volume ventilation, avoiding delirium, increasing mobility).[2] Thus, the debate rests almost entirely on the predictive merits of the most common respirophasic IVC variation encountered, which is IVC collapse.

Several of Dr Schmidt's physiologic observations[1] on IVC collapse were identical to those I cited in arguing against its utility to guide fluid resuscitation: (1) that IVC collapse results from spontaneous respiratory effort; and (2) that the magnitude of IVC collapse is almost entirely conditioned by the magnitude of respiratory effort and the level of right atrial pressure. This scenario is precisely the crux of my argument: the amount of IVC collapse (which Dr Schmidt provided instruction in measuring) provides no guidance to answering fluid needs given that: (1) the depth of respiratory effort is a physiologic parameter clearly independent of fluid status; and (2) "right-sided" pressures have been proven to have little utility in predicting FR. I again want to emphasize that the erroneous equating of low right atrial pressure (ie, small IVC) with hypovolemia will persist

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unless we understand that low right atrial pressure in patients with shock most commonly results from vasoplegia and hypercontractile heart function, two physiologic processes that only incompletely respond to fluid. The frequent "incomplete responses" encountered in low right atrial pressure is precisely why a better guide to fluid decisions is needed.

The aforementioned physiology strongly brings into question Dr Schmidt's statement that "ΔIVC during spontaneous breathing predicts FR (diagnostic OR, 13.2)."[1] To be fair, Dr Schmidt admits that this predictive ability is less than in passively ventilated patients and that spontaneously breathing patients is ΔIVC's weakest link. Given the conflicting nature of these statements, a more specific analysis of the cited evidence is warranted.

The OR for FR of 13.2 was taken from a study published in 2014 by Zhang et al.[3] Unfortunately, this "meta-analysis" contains too many limitations to be useful: (1) only a single study of IVC collapse in spontaneously breathing patients was used to calculate the OR (the study by Muller et al,[4] in which 40% of patients were in shock from clinically overt hypovolemic insults); (2) one "negative" study of IVC collapse by Brun et al[5] was excluded after being mischaracterized as not having studied spontaneously breathing patients; (3) another "negative" study by Corl et al[6] was excluded due to incomplete data for meta-analysis; and (4) it was published prior to publication of three more of the largest "negative" studies on IVC collapse.[7-9] The more current summary from Table 1 in my Counterpoint[10] far better demonstrates its actual poor predictability.

In summary, based on the near complete lack of supportive physiology, experimental evidence, or clinical data demonstrating the ability of IVC collapse to reliably predict fluid needs in the critically ill, IVC ultrasound should not serve as the primary guide to fluid resuscitation.

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