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**EDITORIAL**

# Assessing fluid responsiveness during spontaneous breathing

**Koichi Suehiro**[1]

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## Introduction

Fluid administration is the first-line intervention for increasing stroke volume (SV) and blood pressure (BP) in hemodynamically unstable patients [1]. In a previous study, approximately 70% and 30% of critically ill patients responded and did not respond to fluid challenges, respectively [2]. The lack of response to fluid challenges could lead to excessive fluid administration. Since hemodynamically unstable patients do not always respond to fluid challenges, various hemodynamic indices have been developed for predicting fluid responsiveness [3–7]. Dynamic indices using minimally invasive hemodynamic monitoring are commonly used to measure the SV and predict fluid responsiveness [8–10]. Goal-directed fluid therapy using dynamic indices can decrease complications in various clinical settings [11–15].

However, the clinical utility of dynamic indices in patients with low tidal volume, spontaneous breathing, and arrhythmias is limited [16]. Although lung-protective ventilation with low tidal volume (< 7 ml/kg) is frequently used for intra-operative respiratory management, the predictive utility of dynamic indices in such settings remains poor [17]. Accordingly, the utility of dynamic indices, especially in critically ill patients, is reduced [18]. Mechanical ventilation induces cyclic changes in intrathoracic pressure, which affects the right and left ventricular preload. The lower tidal volume ventilation leads to smaller changes in intrathoracic pressure and ventricular preload. Although the heart–lung interaction differs between spontaneously breathing and mechanically ventilated patients, the respiration during spontaneous breathing also induces the changes in the ventricular preload, which allows the use of dynamic indices to predict fluid responsiveness. However, the predictive utility of dynamic indices for fluid responsiveness is poor in normal spontaneously breathing patients [19]. Since spontaneous breathing induces small variations in the ventricular preload, dynamic indices cannot accurately detect fluid responsiveness. Additionally, because the effect of spontaneous breathing on hemodynamic conditions is dependent on several factors, including the respiratory rate and effort, which vary across breaths [20], the utility of dynamic indices during spontaneous breathing is limited. Accordingly, there is a need for novel interventions for assessing fluid responsiveness in patients with spontaneous breathing. This article summarizes an update regarding the prediction of fluid responsiveness during spontaneous breathing.

## Diameter of the inferior vena cava

Measuring the diameter of the inferior vena cava (IVC) using ultrasonography is commonly used to assess the volume status in critically ill patients. Especially, the collapsibility index [(maximum expiratory diameter − minimum inspiratory diameter)/maximum expiratory diameter] of the IVC could be a good predictor of fluid responsiveness in spontaneous breathing patients [21]. A recent meta-analysis revealed that respiratory variations of the IVC could reliably predict fluid responsiveness during spontaneous breathing (pooled sensitivity: 80%, pooled specificity: 79%, area under the curve [AUC] by a receiver operating characteristic [ROC] analysis: 0.857). Respiratory interventions, including deep and standardized breathing, could improve the accuracy of the collapsibility index of IVC in predicting fluid responsiveness [22, 23]. Furthermore, the IVC measurement site is an essential factor for successful measurement. Caplan et al. [21] investigated the effect of the IVC measurement site on the predictability of fluid responsiveness and concluded that

✉ Koichi Suehiro
suehirokoichi@yahoo.co.jp

[1] Department of Anesthesiology, Osaka Metropolitan University Graduate School of Medicine, 1-5-7 Asahimachi, Abenoku, Osaka City, Osaka 545-8586, Japan

measuring the IVC diameter at 4 cm caudal to the IVC-right atrium junction allowed the best accuracy for discriminating fluid responders. At this site, standardized breathing also significantly improved the predicted power with an AUC of 0.98 compared with non-standardized breathing (AUC: 0.85) [21].

## Passive leg raising

Passive leg raising (PLR) involves raising the lower limbs of the patient at 30–45 degrees from a horizontal position. It induces an increase in the preload by transferring a portion of the venous blood from the lower limbs to the central compartment [24]. To maximize the PLR-induced preload increase, the patient is usually (especially in the intensive care unit) set at a semi-recumbent rather than a horizontal position at baseline [24]. The PLR-induced preload increase is similar to the effect of a fluid challenge, with the difference being that PLR is reversible when returning to the baseline position [17]. Dynamic indices, including SV and cardiac output (CO), measured through minimally invasive CO monitoring or transthoracic echocardiography, are commonly used to assess the effect of PLR. A PLR-induced increase in SV or CO (thresholds: approximately 10–15%) could reliably predict fluid responsiveness (AUC: 0.74–0.94) in patients with spontaneous breathing [1]. Recently, Hamazaoui et al. [25] reported that a PLR-induced decrease in pulse pressure variation (PPV) could predict fluid responsiveness even in mechanically ventilated patients with spontaneous breathing activity. Specifically, a 1% decrease in PPV induced by PLR discriminated fluid responders with good sensitivity (87%) and specificity (68%). Further, an ROC analysis revealed that the AUC of PPV decreased by PLR was significantly higher than that of PPV without PLR procedures (0.78 vs. 0.61, $P = 0.04$). Although PLR can discriminate fluid responders even among spontaneously breathing patients, it has several limitations. First, it requires direct measurement of SV or CO, which is not feasible in some clinical situations [17]. Second, it cannot be used in patients with intracranial hypertension. Finally, intraabdominal hypertension can cause false PLR test results since the PLR-induced blood transfer from the lower limbs may be limited in this condition [17].

## Changing the breathing technique

Changing the breathing technique is among the methods for improving the predictability of dynamic indices, even in spontaneous breathing. A previous study [26] reported that forced inspiratory breathing could increase the predictive utility of PPV (threshold: 13.7%) for fluid responsiveness during spontaneous breathing (AUC 0.910). Bronzwaer et al. [27] showed that paced breathing involving six breathing cycles per minute with additional expiratory resistance could improve the reliability of PPV with relatively high accuracy (AUC 0.46 vs. 0.92). Additionally, deep breathing is effective. Mukai et al. [19] investigated the effect of deep breathing on the reliability of the stroke volume variation (SVV) in patients with spontaneous breathing. They concluded that the difference (threshold: 4%) in SVV between normal and deep breathing showed excellent reliability in predicting fluid responsiveness (AUC 0.850, 95% CI 0.672–0.953), whereas SVV during normal breathing could not (AUC 0.579, 95% CI 0.386–0.756). The pre-anesthetic SVV during deep breathing is a good predictor of hemodynamic fluctuation after anesthetic induction in patients undergoing general anesthesia [28]. As aforementioned, respiratory interventions can enhance the predictability of dynamic indices even during spontaneous breathing and standardizing the breathing pace (including tidal volume) is essential for successful measurement.

## Mini-fluid challenge

The optimal means of assessing fluid responsiveness is actually administering fluids and evaluating the response. However, the traditional 500-ml dose for the fluid challenge is excessive and can harm critically ill patients. Therefore, a small 100-ml dose is recently used to discriminate fluid responders [7]. A meta-analysis [29] revealed that a mini-fluid challenge (50–100 ml) could effectively predict fluid responsiveness with an AUC of 0.91 and an optimal threshold of 5% (pooled sensitivity: 82%, pooled specificity: 83%).

Mini-fluid challenge can effectively evaluate fluid responsiveness even in patients with spontaneous breathing. Guinot et al. [30] investigated the effectiveness of mini-fluid challenge during spontaneous breathing. They concluded that an increase in SV after a mini-fluid challenge (100 ml over 1 min) could predict an increase in SV after a 500-ml volume expansion (AUC 0.93, threshold: 7%). Mini-fluid challenge can effectively predict the fluid response of arterial pressure in patients under spinal anesthesia [31]. A recent study [32] found that a fluid challenge < 100 ml might be insufficient for yielding significant changes to discriminate fluid responders. Furthermore, it is important to consider the duration of the fluid challenge. The rate of fluid responders depends on the duration of the fluid challenge [33]. A rapid fluid bolus increases the proportion of fluid responders. Future studies are warranted to standardize the protocol of the mini-fluid challenge, including the fluid amount and duration.

## Conclusion

Excessive fluid infusion, especially in critically ill patients, can be harmful. Therefore, volume expansion should be carefully performed. Dynamic indices could be used as indicators of fluid responsiveness with some interventions, even in patients with spontaneous breathing. Anesthesiologists should be aware of the strengths and limitations of each technique for clinical use. It is crucial that the decision of volume expansion is not solely based on the values of dynamic indices; rather, it should also consider the patients' requirements (tissue hypoperfusion and hemodynamic instability) [7].

## Declarations

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