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EDITORIAL

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Combined analysis of cardiac output and CVP changes remains the best way to titrate fluid administration in shocked patients

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Predicting fluid responsiveness is a topic of major interest. The passive leg raising (PLR) manoeuvre has been recently proposed and tested [1–8]. PLR is based on the principle that it can induce an abrupt increase in venous return secondary to auto-transfusion of peripheral blood from capacitive veins of the lower part of the body [9]. The attractiveness of PLR relates to the apparent simplicity of its physiology, but it presents some limitations [5, 6]. In particular, the increase in preload is not predictable and may be insufficient to challenge the right cardiac function curve [1, 2, 6]. Also, the definitive technique to perform PLR—i.e., supine (PLR_{SUPINE}) or semi-recumbent ($PLR_{SEMIREC}$)—remains a matter of debate [1, 5, 6, 9].

In the present issue, Lakhal et al. [10] present the results of a multicenter study testing the predictive value of PLR for fluid responsiveness. They used thermodilution techniques to assess cardiac output (CO) changes during PLR (PLR-CO) and arterial pulse pressure (PP) changes during PLR (PLR-PP) as a surrogate for stroke volume (SV) [1, 2]. Lakhal et al. described a physiological approach to the problem of random effect of preload induced by PLR: cardiac preload was assumed to be increased during PLR if central venous pressure (CVP) increased $\geq$2 mmHg.

The main results are interesting and somewhat conclusive. Lakhal et al. demonstrated that predictive performance of PLR-CO was acceptable in the whole population as evidenced by the area under the ROC curve [AUC: 0.89 (0.81–0.94)], which confirmed previous findings [2, 7, 8]. But the performance of its surrogate PLR-PP was clinically inconsistent as already suggested [2, 8]. Therefore, generalised use of PLR-PP as a marker of SV change induced by PLR cannot be supported [10]. Although only half of the included patients increased $\geq$2 mmHg in CVP during PLR, the PLR-PP test performed better among these patients than in the overall population [AUC: 0.91 (0.79–0.97)]. Importantly, 98% of the fluid challenges were well tolerated and all gave definitive information about fluid responsiveness.

The PLR test described by Lakhal et al. may be less useful than hoped for. Indeed, the proposed PLR-PP could be depicted as follows: (1) To detect an eligible patient within the whole ICU population (free of cardiac arrhythmias and deeply sedated). (2) To analyse CVP correctly as recommended [11]. (3) To perform PLR by leg elevation to 45°. (3) While continuously checking possible adrenergic stimulation, to detect a CVP increase $\geq$2 mmHg. (4) And finally, if CVP increases, to measure the averaged PP in order to minimise respiratory related variation.

These practical aspects must be kept in mind before implementing these results in daily practice. However, the PLR manoeuvre used in this study (PLR_{SUPINE}) is controversial [5, 6, 9]. Instead, $PLR_{SEMIREC}$ may be used to reduce adrenergic and nociceptive stimulation and to increase the venous return induced by PLR [6].

Only half of the selected population was accurately discriminated with PLR-PP. In this sub-population, the best cut off value was an 8% increase in PP compared to baseline. This represented an approximate change of 3.8 mmHg in PP. This is small and close to the error of measurement experienced with the available pressure monitors. This practical point seems crucial, as even the results of the present study were physiologically interesting and statistically significant; this small 8% threshold could largely reduce the reproducibility and efficiency of the manoeuvre at bedside.

Preload modification was deduced by CVP course by testing the hypothesis that the cardiac function curve is challenged when CVP $\geq$2 mmHg during PLR. A large increase in CVP can be at least explained by two different mechanisms: either end-diastolic ventricle volume increased without increase in stroke volume (flat part of Starling relationship) or end-diastolic ventricle volume failed to increase because the patient was already on the steep part of the pressure–volume relationship. Indeed, the right auricular pressure–volume relationship has a curvilinear shape. In its steep part, a small increase of volume produces a marked increase in pressure at high distending volume. In such a scenario (e.g. ARDS [12]), an increase in CVP could be associated with a critical cardiac preload reserve breaking-point and thus depressed volume responsiveness. This point was suggested in the study of Lakhal et al. by two times more nonresponsive patients in the CVP $\geq$ 2 mmHg group. Hence the results of the present study underline again that assessment of CVP changes during fluid challenge (or PLR) is recommended both to detect increase in right heart preload and to assess the tolerance to fluid loading [13].

Finally, this study underscores that the characteristics of patients included in studies of fluid responsiveness remain conceptually questionable. Indeed, statistical significance of dynamic indices depends on the population screened and tends to be reduced in mixed large sized ICU populations [14–16]. From a physiological point of view, the quest of a test to suit every situation is in vain. Benefit from fluid responsiveness predictive tests may be mostly relevant when focused in risk patients such as hypoxemic or cardiac failure. In these pathophysiological situations, accuracy of predictive tests as PLR-PP remains to be validated. On the other hand, the good tolerance of volume expansion advocates again that a cautious fluid challenge, with coupled assessments of CO and CVP is a clinical acceptable option which makes sense most of the time to detect and correct hypovolemia [13]. In the future, assessment of volume responsiveness should not only deal with a macro-hemodynamics response, but should include attempts to predict global benefit from fluid taking into account the impact of fluid on pulmonary capillary hydrostatics, ventilation–perfusion relationships and tissue oxygenation [17, 18]. Fluid response in itself needs probably to be conceptually enlarged and refined.

In summary, the results presented by Lakhal et al. of PLR-PP in the sub-group of patients who increased CVP $\geq$2 mmHg during PLR are attractive but need to be confirmed, especially in high risk patients. As demonstrated by this study, a combined analysis of CVP and CO changes remains actually the best way to titrate fluid administration. In sedated patients with persistent shock invasiveness for a better diagnostics cannot be disputed.

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