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REVIEW

Passive leg raising

X Monnet[1,2], JL Teboul[1,2]

1 Medical Intensive Care Unit, Bicetre Hospital, Le Kremlin-Bicêtre, France
2 Medical Intensive Care Unit, University Paris-South, Le Kremlin-Bicêtre, France

Abstract - *Objective*: To assess whether the passive leg raising (PLR) test could predict fluid responsiveness and to describe its practical aspects. *Summary of findings:* Raising the legs to 45° transfers blood from the lower part of the body toward the cardiac chambers, increasing the right and left cardiac preload by a significant extent. The PLR test has been recently developed as a transient and reversible endogenous fluid challenge. An increasing number of studies have tested the ability of PLR for predicting the haemodynamic response to fluid in critically ill patients with acute circulatory failure. These studies established that the PLR effects on descending aortic blood flow, on subaortic blood flow or on pulse contour-derived cardiac output allow predicting fluid responsiveness with very good sensitivity and specificity. All the studies are concordant and the cut-off values of the PLR-induced increase in cardiac output or surrogates are quite similar between studies. It is important that prediction remains fully evaluable in patients with cardiac arrhythmias or spontaneous breathing activity. The PLR test is more accurate when it is started from the semi-recumbent rather than the supine position. Its assessment requires a real-time assessment of cardiac output, as enabled by oesophageal Doppler, echocardiography or pulse contour analysis. *Conclusions:* PLR is now well demonstrated to be a reliable test for predicting fluid responsiveness, even in patients with spontaneous breathing activity or arrhythmias.

Keywords - **Fluid Responsiveness; Passive Leg Raising; Volume Expansion, Cardiac Preload**

Introduction

In acute haemodynamic failure, fluid administration is expected to induce a significant increase in cardiac output. Nevertheless, according to the Frank-Starling relationship, this is not always the case [1]: some patients are "non-responders" to fluid therapy. The problem is that in cases where fluid administration does not increase cardiac output, it can still lead to some fluid overload with the inherent risk especially in lung injury [2,3]. Thus, predicting whether fluid therapy will actually increase cardiac output has became a large field of clinical research in intensive care medicine over past years.

The first method that has been proposed for this purpose is to observe the changes in stroke volume induced by mechanical ventilation. A large number of studies have shown that the respiratory variation of many surrogates of stroke volume are able to predict fluid responsiveness with high reliability [1]. Nevertheless, this method cannot be used in patients with cardiac arrhythmias, in patients with spontaneous triggering of the ventilator and in patients who are not being mechanically ventilated. This is a strong limitation since these conditions are frequently found in the intensive care unit. An alternative method for predicting fluid responsiveness is thus mandatory. The passive leg raising (PLR) test has been developed for solving this important clinical problem.

Correspondence

Xavier Monnet
E-mail: xavier.monnet@bct.aphp.fr

Haemodynamic changes during PLR

In a lying subject, raising the legs from the horizontal position passively transfers blood from the lower part of the body to the trunk and, in particular, to the cardiac chambers. Some older physiological works have demonstrated that the blood volume that is so transferred is quite important. In fact, it was shown that a reduction of about 150 mL of the blood volume of the calves was induced by the postural manoeuvre in human subjects [4]. In other words, PLR partially empties the volume reservoir and converts part of the unstressed volume to stressed volume. In turn, PLR increases the mean circulatory pressure and the venous return.

Importantly, if the right ventricle is preload responsive the increase in systemic venous return increases the right ventricular outflow. After the few seconds that are necessary for crossing the pulmonary vasculature, the increased flow is transmitted to the left circulation and the left ventricular preload could theoretically rise.

A number of clinical studies have reported that the blood transfer induced by PLR is of sufficient magnitude to increase the left cardiac preload, assessed either by the pulmonary artery occlusion pressure [5-8], the left ventricular end-diastolic dimension [5,9], the E wave of the mitral flow [5,6,10] or even by the left ventricular ejection time [11].

Eventually, the increase in left cardiac preload should result in an increase in cardiac output depending upon the degree of preload reserve of the left ventricle. Wong and colleagues reported that the increase in stroke volume induced by a 45° leg lifting in healthy subjects was of larger magnitude after withdrawal of 500

mL of blood [12], suggesting that PLR may influence the cardiac output differently according to the central volume status and thus the degree of cardiac preload reserve. Importantly, the increase in cardiac preload induced by PLR totally reverses once the legs are returned to the supine position [8,13-16]. In other words, PLR acts like a reversible and short lived "self" fluid challenge [17].

At this point, it is important to state that the volume of blood transferred to the heart during PLR could vary depending upon the nature of postural change (see below) and upon the ability of the venous reservoir to be recruited. In cases where the veins are constricted, like during hypovolaemic and cardiogenic shock, the venous reservoir is likely to be reduced and the volume recruited by the PLR would be expected to be smaller. By contrast, in a patient in a vasodilatory state such as septic shock, a higher unstressed volume is expected to be recruited by PLR. Based on this hypothesis, PLR should theoretically increase right ventricle preload less in patients with hypovolaemic shock than in those with septic shock. However, in patients with a high degree of volume responsiveness, even a moderate increase in preload can result in a significant change in cardiac output. In support of this, the increase in cardiac output in normal subjects in response to PLR was increased after blood removal [18].

Testing fluid responsiveness with PLR

Due to the curvilinear shape of the Frank-Starling curve, the increase in cardiac preload resulting from fluid loading does not always result in the expected increase in stroke volume and cardiac output. In cases when the heart of a patient is projected onto the initial and steep part of the curve, the increase in cardiac preload by fluid administration will actually result in a significant increase in cardiac output. By contrast, when the patient's heart is projected onto the terminal and flat part of the curve, increasing preload will not affect cardiac output and the patient will be "unresponsive" to fluid therapy [1] (Figure 1). In the latter case, fluid administration could result in an excessive increase in left ventricular filling pressure and hence in worsening of lung oedema in cases of acute respiratory distress syndrome. In this regard, it must be remembered that it is now well demonstrated that a restricted fluid strategy induces beneficial functional effects in acute respiratory distress syndrome [19]. Moreover, the amount of lung oedema was recently shown to be a factor for poor prognosis in critically ill patients [20], particularly in acute respiratory distress syndrome [2, 3]. All these studies that emphasize the risk of fluid loading, along with the observation that some patients are unresponsive to volume expansion, call for methods that could predict fluid responsiveness [21].

Of these methods, observing a given value of any marker of preload such as the central venous pressure is unhelpful. Indeed, there are now a huge number of studies evidencing that neither the central venous pressure, nor the pulmonary artery occlusion pressure, nor the left ventricular end-diastolic area, nor the global end-diastolic volume nor even the flow time of aortic flow enable to predict fluid responsiveness with a sufficient accuracy [1,22]. Indeed, there is not one Frank-Starling curve, but a family of curves describing the relationship between stroke volume and cardiac preload, depending upon the systolic ventricular function [1] (Figure 1). This explains why the same volume expansion with a similar value of initial preload, could lead to either a significant or a negligible response in terms of stroke volume, depending upon the shape of the Frank-Starling curve upon which the heart is actually working.

Beyond the static markers of cardiac preload, the other way to predict fluid responsiveness could be to perform a "preload challenge". It consists simply of observing the resulting effects on stroke volume of any change in preload. If a significant and transient change in preload positively affects the stroke volume or any of its surrogates, fluid administration is likely to have the same significant effect (Figure 1). This concept has been called "functional haemodynamic monitoring" [23].

The first way to change cardiac preload in view of functional haemodynamic monitoring is to observe the haemodynamic effects of mechanical ventilation. Since mechanical ventilation induces cyclic changes in cardiac preload, the respiratory variation of stroke volume has been proposed to assess preload reserve [23] . Accordingly, the respiratory variations in surrogates of stroke volume such as arterial pulse pressure [24,25] , Doppler subaortic flow [26], pulse contour derived stroke volume [27,28], descending aortic blood flow [29] or even pulse oximetry wave [30] have been demonstrated to predict fluid responsiveness in the critically ill. Nonetheless, such heart-lung interaction indices can be utilized only in specific conditions, i.e. in regular sinus cardiac rhythm and full adaptation of the patient to the ventilator as in deep sedation or coma. If not, the irregularity of the cardiac rhythm or of the respiratory cycle also account for variability of the stroke volume such that fluid responsiveness can no longer be predicted by the variations in stroke volume [31].

The PLR, with its "self volume challenge effects", is an alternative way of predicting the haemodynamic response to fluid administration [17] . In mechanically ventilated patients fully adapted to their ventilator, the PLR-induced changes in stroke volume have been found to closely correlate with the changes in stroke volume induced by a subsequent 300 mL colloid infusion [8]. Importantly, since the duration of PLR encompasses several cardiac and respiratory cycles, its haemodynamic effects are not influenced by arrhythmias or by ventilator triggering. Therefore, the PLR can still be utilized in circumstances where heart-lung interaction indices are misleading.

The validation of PLR as a test for predicting fluid responsiveness was first shown by a study including 71 patients in shock monitored by oesophageal Doppler [14]. In these patients, we investigated whether the response of descending aortic blood flow to PLR could predict the response to a 500 mL saline infusion [14]. Interestingly, PLR increased the aortic flow time – a marker of left cardiac preload – in the same proportion in responders and in non-responders, suggesting that this test actually performed like a volume challenge. The changes in the descending aortic blood observed during a PLR test were closely correlated with those induced by the subsequent volume expansion. Moreover, if PLR had increased the aortic blood flow by more than 10%, an increase of aortic blood flow greater than

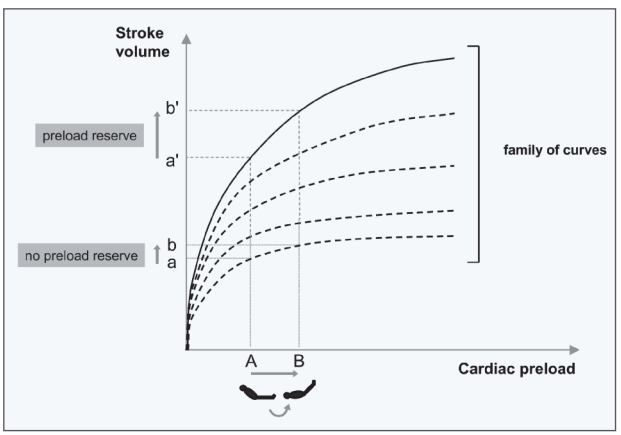
15% could be expected from the subsequent fluid administration with very good sensitivity and specificity [14] (Figure 2). In the subgroup of patients fully adapted to their ventilator, the response to PLR performed equally to pulse pressure respiratory variation in predicting volume responsiveness [14]. Very importantly, in the subgroup of patients who triggered their ventilator or who experienced arrhythmias, we found that the aortic blood flow response to PLR kept its predictive value of fluid responsiveness while pulse pressure variation was no longer reliable [14]. These findings established the PLR test as an alternative for predicting the response to fluid in conditions where the respiratory variations of stroke volume cannot be used for testing the fluid responsiveness. Of course, the PLR test can also be used for predicting fluid responsiveness in patients who have no cardiac arrhythmias and who are fully adapted to the ventilator. In such cases, the PLR test and the respiratory variation of stroke volume might be used together for predicting fluid responsiveness.

These seminal results were confirmed by ensuing studies. In patients that were all fully adapted to mechanical ventilation, a similar prediction of fluid responsiveness was found from the effects of PLR on the aortic blood flow measured by oesophageal Doppler [32]. Two studies performed in patients with spontaneous breathing activity demonstrated that an increase in echocardiographic stroke volume by more than 12% in response to PLR distinguished well between responders and non-responders to fluid administration [33,34]. In addition, the stroke volume response to PLR performed far better than the static ultrasonographic indices of cardiac filling such as left ventricular end-diastolic area or Doppler estimates of left ventricular filling pressure [33,34]. More recently, we demonstrated that the effects of PLR on the pulse contour-derived cardiac index measured by the PiCCO device could be used as well [35]. The cut-off increase in cardiac index was found to be 10% (Figure 2), i.e. no different from the ones found in the above-cited studies [14,32-34]. Compared to oesophageal Doppler or echocardiography, the pulse-contour-derived estimation of cardiac output has the advantage that it is very easy to use. Overall, these studies have contributed to establishing PLR as a reliable and easy way to predict fluid responsiveness at the bedside [17]. Importantly, the cut-off values of PLR-induced increase in cardiac output or surrogates found by these studies were not different from one to another, enhancing the confidence into the test reliability.

Practical aspects of the PLR test

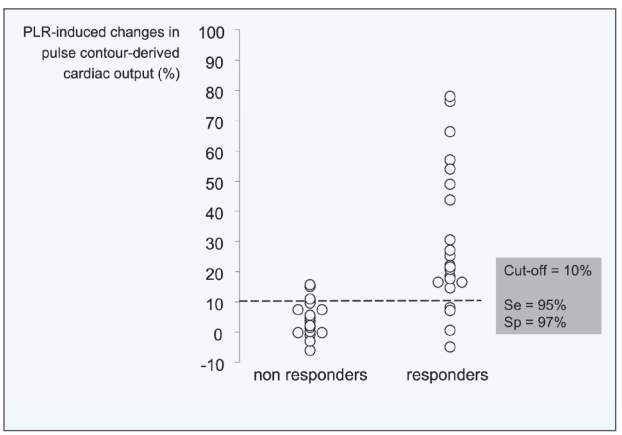
It is important to consider the postural change used in the PLR test [17]. The initial position from which the PLR test is started can be the supine or the semi-recumbent position. In a recent study, we investigated if these two methods could induce different haemodynamic effects [16]. In fact, we observed that if PLR was started from the 45° semi-recumbent position, the induced increase in central venous pressure was significantly higher than if started from the supine position. This was explained by the

Figure 1. Functional assessment of the Frank-Starling curve with the passive leg raising (PLR).



In patients with circulatory failure, it is not possible to predict the response to volume administration because there are numerous curves that relate stroke volume and cardiac preload. PLR induces a change in preload that enables the relationship to be challenged. If the increase in cardiac preload occurring during the test (from A to B) produces a large increase in stroke volume (from a' to b'), the patient should respond to fluid administration. If the increase in stroke volume during the test is of small amplitude (from a to b), preload responsiveness is unlikely and fluid administration should be avoided.

Figure 2. Prediction of fluid responsiveness by the effects of passive leg raising (PLR) on pulse contour-derived cardiac output.



In these 34 patients (all with spontaneous breathing activity or cardiac arrhythmias), observing the effects of PLR on the pulse contour-derived cardiac output measured by the PiCCO device allowed differentiating responders and non responders to fluid infusion. If the PLR-induced changes in cardiac output were larger than 10%, fluid responsiveness could be predicted with accuracy (adapted from ref 35).

fact that starting PLR from the semi-recumbent position enables the mobilization of the splanchnic venous compartment towards the intrathoracic compartment in addition to the leg volume. As a consequence in this study [16], the method starting from the semi-recumbent posture was more sensitive for detecting fluid responsiveness than the method starting from the supine posture. Another advantage of starting PLR from the semi-recumbent position is that it is very easy to perform by using the automatic pivotal motion of the patient's bed [17]. It also allows PLR to be performed without inducing hip flexion and painful femoral catheter motion that could induce some confusing sympathetic activation. Placing the patient in the Trendelenburg position could also induce some blood transfer to the upper part of the body. Nevertheless, this technique might not be ideal due to the risk of gastric regurgitation and because some of the blood transferred might be loosed toward the head.

Another important point concerns the method used for assessing cardiac output changes during PLR. First, it must be a real-time cardiovascular assessment able to track haemodynamic changes in the time frame of PLR effects, i.e. 30-90 sec. Indeed, the effect of PLR on cardiac output - when it occurs - is not always sustained when the leg elevation is prolonged. This is particularly true in septic patients in whom an important capillary leak may account for an attenuation of the PLR effects after one minute, as we have already described [36].

Second, the limits of precision of the technique must be far below the 10-15% increase in cardiac output found as a predicting cut-off [36]. In this regard, it has been proposed that the PLR-induced changes in the descending aorta blood flow [14,37], in the pulse contour-derived stroke volume [35] or in the Doppler-derived velocity-time integral [33,34] be used for that purpose. Importantly, the PLR-induced changes in arterial pulse pressure have been demonstrated to be less accurate than the PLR-induced changes in descending aorta blood flow [14] to predict fluid responsiveness. This is probably explained by the fact that the arterial pulse pressure is only a rough surrogate of stroke volume. It also depends upon arterial compliance, a parameter that might change during the postural manoeuvre. In our practice, the pulse contour estimation of cardiac output is the easiest to use for assessing the PLR effects. Moreover, the reproducibility of this method is very high [38], allowing assessing the cardiac output changes during PLR with a reasonable confidence.

Third, it should be ensured that preload has actually changed in response to PLR before looking for the resulting change in cardiac output. Indeed, if cardiac preload does not change, fluid responsiveness cannot be tested. Thus, significant changes of a marker of cardiac preload should be a prerequisite to the correct interpretation of the PLR test [39]. Central venous pressure, duration of the aortic flow measured by oesophageal Doppler or end-diastolic dimensions on echocardiography, could be used for this purpose.

Finally, PLR can effect both systemic and microvascular haemodynamics. The effects on both circulations might differ [40] such that assessing the response of microcirculatory flow on PLR could become an important diagnostic tool in septic patients, as microcirculatory perfusion problems often persist after restoring systemic haemodynamics.

To summarize the practical aspects of PLR, it is advised that postural change should start from the semi-recumbent position and that during PLR, the head and trunk should be horizontal and not tilted downwards (Trendelenburg position). Another important point is that the haemodynamic effects of PLR should be assessed by a technique able to provide a real-time measure of cardiac output. Finally, it should also be ensured that PLR actually increases central venous pressure. An example of a PLR test can be viewed on a movie accompanying a recent review about PLR [17].

Limitations of the PLR test

Beyond its reliability and the ease with which it can be performed, some limitations of the PLR test must be acknowledged. First, its effects cannot be assessed by observing simple arterial pressure changes and it requires a more or less invasive device for estimating cardiac output. Second, the test requires that the patient be mobilized and the trunk be horizontal. In this regard, the test cannot be carried out in the peri-operative period. It should also be advised to refrain performing the PLR test in cases of head injury or increased intracranial pressure [17]. Finally, elastic compression stockings may also alter the venous volume recruited by the PLR. In such cases, some alternative tests for predicting fluid responsiveness have been recently developed [35].

Conclusion

PLR induces a transient and significant increase in cardiac preload that can be used as an endogenous fluid challenge. It has been well demonstrated that it can predict fluid responsiveness in critically ill patients, including those for whom cardiac arrhythmias, spontaneous breathing activity and low tidal volumes preclude using the respiratory variation of stroke volume for predicting the haemodynamic response to fluid. The optimal utilization of the test requires a real-time assessment of cardiac output capable of detecting the short-term haemodynamic response. Finally, the postural change should be started from the semi-recumbent rather than from the supine position.

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