

Research Article

Is Fluid Responsiveness A Normal State in Human Beings? A Study in Volunteers

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Abstract

Introduction: The adoption of goal-directed therapy protocols was shown to be beneficial, reducing perioperative morbidity and mortality in certain contexts. It is usually based on the identification of the individual's position on the Frank-Starling curve and on the administration of fluids to patients found to be on its ascending limb to tendentially abolish fluid responsiveness. Different authors, however, state that fluid responsiveness is a physiologic state often found in normal, non-hypovolemic individuals.

Materials and Methods: We performed 62 echocardiograms in 31 ASA I and II volunteers to assess their fluid responsiveness state as shown by the degree of change in transaortic time velocity integral variation (and consequently stroke volume variation) after a passive leg raise manoeuvre.

Results: Depending on the cut-off value used, a third to a half of the normal individuals studied were in a fluid responsive state, i.e., on the ascending limb of the Frank-Starling curve.

Discussion and Conclusions: One should remember that fluid responsiveness is part of the normal physiology of the cardiovascular system, and that the goal behind fluid administration should be to improve haemodynamics and not necessarily try and annihilate this state using closed loop systems. Goal-directed therapy protocols have helped improve prognosis, but are no substitute for an informed, critical approach when choosing to use them.

Keywords: Fluid therapy; Cardiovascular physiology; Hemodynamic; Echocardiography

Introduction

Perioperative fluid therapy has long been a subject of debate, and the way it is handled was shown to impart a substantial influence on perioperative morbidity and mortality [1,2]. Both hypo- and hypervolemia are associated with adverse events [1,3-5] leading to the development of different approaches throughout anaesthesia history to promote more rational and progressively more individualized treatments. Initially, a fluid bolus was often considered beneficial to counteract the haemodynamic effects of anaesthesia and promote cardiovascular stability, leading to the traditional practice of "fasting replenishment" and to fluid administration as a first line therapy whenever target variables such as blood pressure, heart rate or urinary output did not hit the desired values. Today, we know that these indices are not adequate to tailor fluid therapy to the individual patient [6,7] the same happening with traditional measurements such as isolated values of central

venous pressure.

Consequently, most modern goal-directed therapy protocols now rely on specific indicators, called dynamic preload indices [8, 9], that aim to predict a patient's position on the Frank-Starling curve. The rationale behind it is that those individuals in the ascending limb of the curve can have their cardiovascular state optimized (manifested as an increase in stroke volume and ultimately cardiac output) through an increase in preload brought on by fluid administration (Figure 1) [10].

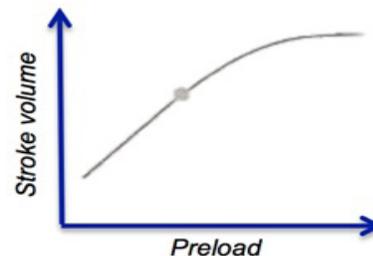


Figure 1: Frank-Starling curve.

On the other hand, those patients shown not to be fluid-responsive (i.e., those already in the flat portion of the Frank-Starling curve), do not benefit from fluid administration to increase preload – and such excessive administration can become detrimental. (Please see Figure 2 for more details on the Frank-Starling curve.)

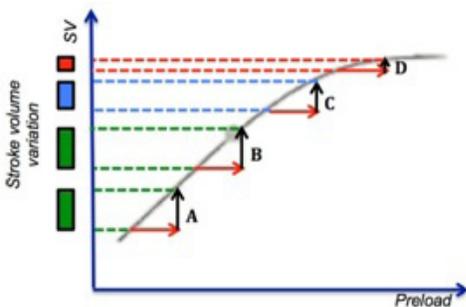


Figure 2: Peculiarities of the Frank-Starling curve.

Depending on the individual's position on the Frank-Starling curve, a same preload variation may lead to markedly dissimilar variations in stroke volume. Please note that the ascending limb is approximately linear, and as such a similar stroke volume variation may be found in individual's whose original position in the curve is relatively far ($A = B$); as we approach the flat portion of the curve, SVV decreases ($D < C < B = A$). (SV – stroke volume; SVV – Stroke Volume Variation).

Goal-directed therapy protocols using this kind of data have been incorporated into guidelines [8] and shown to reduce morbidity [7,8,11-13] while also promoting haemodynamic stability with a smaller total amount of fluids administered in the perioperative period [1]. However, sometimes we see a perhaps excessive reliance on this kind of protocols, without due integration with the patient's global picture. In that sense, it is interesting to realize that some of them now uphold that the patient keep receiving fluids if he/she remains fluid responsive [6,14,15] forcing him/her into the flat part of the Frank-Starling curve.

Faced with that perspective, we hypothesize that by doing so we might be perverting normal physiology, especially if we consider that fluid responsiveness may be part of a normal cardiovascular state – and set out to study the prevalence of fluid responsiveness in relatively healthy, ASA I and II volunteers in basal conditions.

Materials and Methods

This is a satellite study focusing on a sub-analysis of data obtained with a different project previously published [16]. After securing ethical approval and obtaining informed consent from every participant, we enrolled 31 ASA I and II volunteers with no cardiovascular comorbidities, each of which underwent two echocardiographic evaluations (in different days) to exclude baseline anomalies and provide data on transaortic time-velocity

integral variation with the passive leg raise manoeuvre, as a measure of fluid responsiveness. (Please note that a percentual time-velocity integral variation (TVI) is numerically identical to stroke volume variation, considering that stroke volume is calculated as $TVI \times \text{area of the valvular orifice}$, which is constant for a given individual in the study.)

Subjects with a variation $\geq 10\%$ [1,9,15,17] were classified as fluid responders, and the overall distribution of absolute values was analysed using descriptive statistics.

Results

About a third of the examinations (20 out of 62) presented a TVI variation $\geq 10\%$, thus identifying 32.3% of fluid responders. Furthermore, we realized that a significant number of individuals was close to this landmark, so much so that if the cut-off value were to be reduced to 9%, half of all observations (31 out of 62) would correspond to fluid responsive individuals (Figure 3).

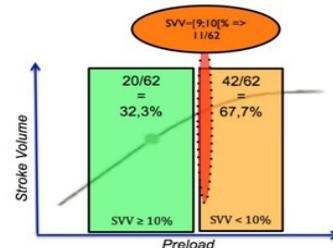


Figure 3: Distribution of the sample per the position on the Frank-Starling curve. 20 exams revealed a $SVV \geq 10\%$, identifying individuals clearly on the ascending limb of the Frank-Starling curve. The remainder had a $SVV < 10\%$ but, interestingly, in 11 of these it was close to the cut-off value (between 9 and 10%). Should these individuals be considered fluid responsive, the division would be 50:50 between fluid responders and non-responders. (SVV – Stroke Volume Variation).

Discussion

From the analysis of the data obtained it stands to reason that fluid responsiveness is a common finding in stable, normal individuals in their basal state – in line with what has been defended by other authors [4,8,19]. We might hypothesize that it becomes even more frequent under anaesthesia, due to its haemodynamic effects, but the design of the study does not allow us to address that issue. It does, however, prompt us to consider that if fluid responsiveness is present in normal conditions in stable individuals, it should not be considered an abnormal state that must necessarily be abolished.

Identifying fluid responsiveness means simply identifying a possible means of increasing stroke volume in our patients, but does not necessarily mean that he/she is hypovolemic or even that he/she needs that optimization. If it did, such would mean that our healthy, stable volunteers would also need to be optimized – which is illogical. Therefore, whether there is a real benefit from fluid

loading a fluid responsive individual must be decided upon on an individual basis, and not as an automatic response to an isolated index.

After thinking about the results obtained and considering their repercussions for understanding fluid therapy and common practice, we came to realize that the real benefit of identifying a patient's position in the Frank-Starling curve lies in the identification of those individuals who, though needing optimization of their cardiovascular state, do not benefit from fluid loading, because that allows us to withhold useless, potentially detrimental therapies.

While all of this may seem natural and self-explanatory, we found that revisiting these concepts was particularly important when automated closed-loop systems have already been developed that administer fluids automatically in fluid responsive patients [8], systematically trying to abolish this state. While frequent re-assessment and small fluid boluses (in the order of 3mL/kg) [20] are instrumental to prevent harm in these contexts, true usefulness should be brought into question by careful individualized analysis. In major surgeries associated with great, sudden fluid shifts or blood loss they may be justified, as there is a strong tendency for a leftward shift in the patient's position on the Frank-Starling curve that may be hard to correct immediately to prevent decompensation. Also in the case of fluid responsive patients in need of haemodynamic stabilization, fluid administration would likewise be useful and indicated [18,19]. However, in some other settings caution is advised.

For example, an apparently stable, relatively healthy patient undergoing inguinal hernia repair found to be fluid responsive should not necessarily be given fluids to abolish that state. And such is only one of many possible scenarios. In fact, herein may lie one of the reasons why goal-directed therapy has not been able to show a significant impact in patient morbid-mortality in fast-track programs comprising less invasive surgeries, as in ERAS (Enhanced Recovery After Surgery) programs [12].

If we consider that new, thus far incompletely validated non-invasive technologies are being perfected to assess fluid responsiveness in patients who don't seem to benefit from the use of invasive monitoring, one such technology being the so-called plethysmography variability index [5], we must realize that if widely adopted it will likely identify many fluid responsive patients intraoperatively who don't really need haemodynamic optimization or fluid administration. Such stresses the relevance of the data obtained with this study and the overall importance of the subject at hand.

Limitations to the Study

Every study has its limitations – and ours is no exception. One might question the choice of technology used – echocardiography. Early goal-directed studies relied on stroke volume or

cardiac output variation data, often obtained invasively, and later evolved to use surrogates such as pulse pressure variation, analysis of invasive arterial pressure curve, among others. The best technology to identify a patient's position in the Frank-Starling curve remains debatable [6], but echocardiography has the advantage of being a non-invasive exam performed at the patient's bedside that has an important track-record of decades of mainstream use clinically, allowing for prompt assessment of stroke volume variation with good patient acceptance. In addition to this, it also allowed us to exclude concomitant structural cardiopathy.

Another point to address is the cut-off value used to define fluid responsiveness. Values between 10%-15% [4] are usually used in the literature, but some authors defend lower values (as low as 5%) when coupled with the passive leg raise manoeuvre (Figure 4), stating that this has a sensitivity of 94% and a specificity of 83% to identify fluid responsive individuals [21]. With that in mind, we did use the more common 10% cut-off value but found it justified to mention that a significant number of individuals were close to this limit, with 50% of measurements $\geq 9\%$.



Figure 4: Passive leg raise manoeuvre (PLR). This manoeuvre mobilizes blood from the extremities, being capable of temporarily increasing venous return and thus preload.

Conclusion

All in all, this study allows us to ascertain that fluid responsiveness is common in stable, normal individuals in their basal state, corresponding to a physiologic condition many of us are likely in right now. Therefore, it should not be considered synonymous with the need for fluid replenishment, probably being more useful as a means of preventing excessive fluid loading in patients unable to benefit from that action (those on the flat part of the Frank-Starling curve) than to systematically indicate the adequacy of fluid administration.

While the adoption of goal-directed therapy protocols has been a significant advance in promoting a more rational, tailored approach to patients, critical thinking is paramount to make the most out of it, integrating different data into the patient's context to appropriately guide therapy.

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