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SCIENTIFIC ARTICLE

Does fasting influence preload responsiveness in ASA 1 and 2 volunteers?



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KEYWORDS

Fasting;
Echocardiography;
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Abstract

Introduction: Preoperative fasting was long regarded as an important cause of fluid depletion, leading to hemodynamic instability during surgery should replenishment is not promptly instituted. Lately, this traditional point of view has been progressively challenged, and a growing number of authors now propose a more restrictive approach to fluid management, although doubt remains as to the true hemodynamic influence of preoperative fasting.

Methods: We designed an observational, analytic, prospective, longitudinal study in which 31 ASA 1 and ASA 2 volunteers underwent an echocardiographic examination both before and after a fasting period of at least 6 hours (h). Data from both static and dynamic preload indices were obtained on both periods, and subsequently compared.

Results: Static preload indices exhibited a markedly variable behaviour with fasting. Dynamic indices, however, were far more consistent with one another, all pointing in the same direction, i.e., evidencing no statistically significant change with the fasting period. We also analysed the reliability of dynamic indices to respond to known, intentional preload changes. Aortic velocity time integral (VTI) variation with the passive leg raise manoeuvre was the only variable that proved to be sensitive enough to consistently signal the presence of preload variation.

Conclusion: Fasting does not appear to cause a change in preload of conscious volunteers nor does it significantly alter their position in the Frank–Starling curve, even with longer fasting times than usually recommended. Transaortic VTI variation with the passive leg raise manoeuvre is the most robust dynamic index (of those studied) to evaluate preload responsiveness in spontaneously breathing patients.

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PALAVRAS-CHAVE

Jejum;
 Ecocardiografia;
 Fluidoterapia;
 Hemodinâmica

O jejum influencia a responsividade à pré-carga em voluntários ASA I e II?**Resumo**

Introdução: O jejum no pré-operatório é há muito tempo considerado como uma importante causa de depleção de líquidos, levando à instabilidade hemodinâmica durante a cirurgia, caso a reposição não seja prontamente instituída. Recentemente, esse ponto de vista tradicional vem sendo progressivamente desafiado, e um número crescente de autores agora propõe uma abordagem mais restritiva para o controle de líquidos, embora permaneçam dúvidas quanto à verdadeira influência hemodinâmica do jejum no pré-operatório.

Métodos: Estudo observacional, analítico, prospectivo e longitudinal, no qual 31 voluntários ASA I e II foram submetidos a exame ecocardiográfico antes e após um período de jejum de no mínimo 6 horas. Os dados dos índices de pré-carga tanto estáticos quanto dinâmicos foram obtidos em ambos os períodos e, subsequentemente, comparados.

Resultados: Os índices estáticos de pré-carga mostraram um comportamento acentuadamente variável com o jejum. Os índices dinâmicos, entretanto, foram bem mais consistentes entre si, todos apontando na mesma direção; isto é, não evidenciando nenhuma alteração estatisticamente significativa com o período de jejum. Analisamos também a confiabilidade dos índices dinâmicos para responder a alterações pré-carga intencionais conhecidas. A variação da integral de velocidade-tempo (VTI) aórtica com a manobra de elevação passiva dos membros inferiores foi a única variável que mostrou sensibilidade suficiente para sinalizar de forma consistente a presença de variação na pré-carga.

Conclusão: O jejum não pareceu causar uma alteração na pré-carga de voluntários conscientes nem alterou substancialmente a sua posição na curva de Frank-Starling, mesmo com tempos de jejum mais prolongados que o normalmente recomendado. A variação do VTI transaórtico com a manobra de elevação passiva dos membros inferiores foi o índice dinâmico mais robusto (dos estudados) para avaliar a capacidade de resposta a variações da pré-carga em pacientes respirando espontaneamente.

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Introduction

It is common knowledge that programmed surgical interventions should be preceded by a fasting period.¹⁻³ However, even though recent guidelines allow for the ingestion of clear fluids for up to 2 h before an operation, in daily clinical practice this is seldom performed, at least in adults. In fact, it is not unusual for patients to fast for considerably longer than requested, sometimes even for 10 or 12 h, despite being asked to fast for only six. During this period, fluid depletion from the organism is ongoing – be it in the form of perspiration, breathing or urine production, among other mechanisms – and some authors have actually estimated that a fasting period of approximately 12 h can lead to a fluid depletion of around 1 L,^{4,5} which likely causes some degree of intravascular volume depletion once balance between different body compartments is reached.⁶

According to the Frank–Starling Law, we know that within certain limits, stroke volume is closely dependent on preload,^{7,8} which means that a decrease in preload consequent to hypovolemia will tend to decrease stroke volume. The importance of this mechanism is such that it was actually found to be the main cause of unexplained hypotension with a fall in cardiac output in Intensive Care Unit (ICU) settings.⁸

In the healthy, conscious individual different mechanisms come into play to compensate for fluid loss,^{9,10} with the

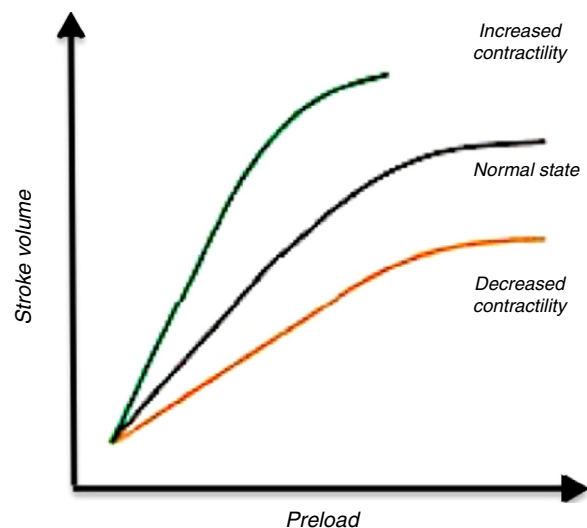


Figure 1 There are different Frank–Starling curves for the same individual, according to his/her hemodynamic state.

potential to shift the patient's own Frank–Starling curve to the left¹¹⁻¹⁵ (Fig. 1) and thus delay clinical manifestations of intravascular volume depletion.^{6,16,17} However, when that same patient undergoes general anaesthesia, the changes in preload, inotropic state, chronotropic response

and afterload caused by the different medications used^{18–26} are likely to disrupt this newly reached balance and predispose a previously stable but fluid depleted individual to hemodynamic decompensation.

For decades, the traditional reaction of Anaesthesiologists to this theoretical mechanism was to estimate the fluid loss caused by fasting²⁷ and systematically replenish it with the intent of restoring intravascular volume and thus the original position of the patient on the Frank–Starling curve. Allegedly, such would help optimize the patients' cardiovascular state and decrease morbidity associated with anaesthesia. Interestingly, though, when real-life studies tried to confirm this, not only were they unable to find evidence for an improved cardiovascular stability profile associated with systematic fluid loading in the intraoperative period, as there were also indications that this practice might actually be associated with a poorer outcome in certain of the settings studied.^{5,10,28–31} In fact, some investigations even found a positive correlation between post-operative weight gain (due to excessive fluid therapy) and an increased mortality in the same period,³² thus challenging what was previously considered to be an absolute truth.

Several studies have addressed the effects of fasting from different perspectives.^{33–35} Because all suffered from limitations that advised caution in the interpretation of results, however, and given the difficulty in actually measuring intravascular volume repeatedly or finding a suitable surrogate for it, the focus of research has recently shifted from studying the hemodynamic effect of fasting itself to focusing on individual management of any given patient according to his/her present hemodynamic state, irrespective of fasting time. With this approach, the so-called goal-directed therapy was born.^{30,36–39} Current goal-directed therapy protocols usually rely on classifying individuals as either fluid-responsive (thus in the ascending limb of the Frank–Starling curve) or fluid non-responsive (already in the flat part of the same curve),²⁹ and have produced significantly positive outcomes, with some studies actually finding evidence of improved survival subsequent to its use in the perioperative period.^{36,40,41}

However, goal-directed therapy protocols tend to rely on data obtained from specific monitoring devices, either too invasive and/or too expensive to become universally adopted, which limits its use to more serious patients and/or more aggressive surgeries. As such, what would be the most appropriate course of action when faced with relatively healthy (ASA 1 or 2) patients scheduled for non-major surgeries? Should fasting time be considered as a guide for routine fluid replenishment? Or should it simply be ignored?

Adopting the rationale behind goal-directed therapy, the true question becomes: does fasting move the patient to the left on the Frank–Starling curve, placing him/her in an optimizable point through an increase in preload (large arrow in Fig. 2), or is its influence only minor in normal circumstances (small arrow)?

Methods

With the objective of ascertaining the true hemodynamic influence of fasting and answering the previous questions,

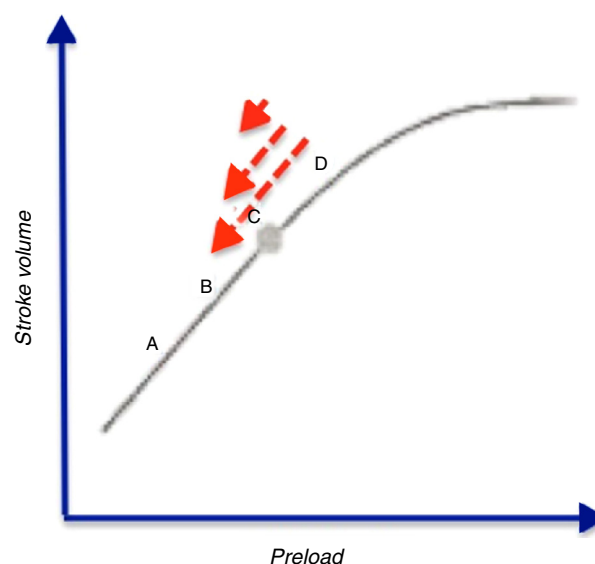


Figure 2 Frank–Starling curve. Does fasting cause a significant change of the individual's position to the left in the curve (big arrow), or is it a more modest influence (medium and small arrows)?

Table 1 Characteristics of the sample.

Parameter	Characteristics
Sex	16 female/15 male
Age	26–67 years old Average = Median = 37 years old
ASA	71% ASA 1 29% ASA 2
Comorbidities in ASA 2 volunteers	Asthma, heavy smoking, obesity; no cardiovascular comorbidities.

we drew on much of the knowledge accumulated with the development of goal-directed therapy to identify different variables that could estimate preload and fluid responsiveness. After ethics clearance and obtaining individual informed consent for every participant, we enrolled in our study 31 volunteers classified as either ASA 1 or 2, without cardiovascular comorbidities, aged 26–67 years old (Table 1). We performed an echocardiographic examination to screen for any abnormalities in the volunteers (which constituted exclusion criteria - Table 2) and subsequently acquired data on three types of variables that were studied both before and after a fasting period of at least 6 h. These were:

“Conventional” variables: weight, heart rate and blood pressure;

Static echocardiographic preload indices: namely telediastolic area of the Left Ventricle (LV) acquired from parasternal short axis images (TD Area_{LV} PSSAx), telediastolic diameter of the LV acquired from parasternal long axis images in M-mode (TD D_{LV} PSLAx); expiratory diameter of the inferior vena cava (IVC_{exp}) and Flow time corrected in the descending aorta (from a suprasternal view) (FTC);

Table 2 Inclusion and exclusion criteria.

Inclusion criteria		Exclusion criteria
Age \geq 18 years old	Refusal of study conditions	Hyperdynamic states (pregnancy, hyperthyroidism, AV fistula, fever, marked anaemia)
ASA 1 or ASA 2	Dysrhythmia and/or pacemaker	Compromised renal function
Acceptance of study conditions (with informed consent)	Systolic dysfunction	Medication interfering with compensatory hemodynamic mechanisms
	Diastolic dysfunction	Osteoarticular pathology preventing proper positioning and PLR
	Valvulopathy	Inadequate echocardiographic images ("bad window")
	Right ventricular dysfunction	Failure to obtain one of the exams

Dynamic echocardiographic preload indices: obtained by making use of an intentional variation of preload, either through:

- Respiratory variation (heart–lung interaction): respiratory variation of IVC diameter ($\Delta\text{res}_{\text{IVC}}$);
- Passive leg raise manoeuvre: more specifically the variation of the transaortic velocity time integral (VTI_{Ao}) with the passive leg raise manoeuvre (PLR) ($\Delta\text{VTI}_{\text{Ao PLR}}$). The PLR manoeuvre is credited with mobilizing 300^{42–44}–500⁴⁵ mL of blood into the circulation and consists in moving the patient from a semi-recumbent position into one with the head of the bed horizontal and the lower limbs raised at a 45° angle. In accordance with the literature, echocardiographic data were acquired between 1 and 3 min after implementing this new position, as it has been estimated that after that time compensatory mechanisms come into play that blunt the effects of the manoeuvre.⁴⁵

All images were acquired by the same operator on the same GE Vivid 7TM echocardiograph, and later analysed by the same individual in a random order through the use of EchoPAC DimensionTM software, in a process later reviewed by an independent observer.

The data extracted were then introduced into an SPSS StatisticsTM database and analysed with the use of either parametric tests (Student's *t* test for paired samples, when there was a normal distribution of the variable in the sample) or non-parametric tests (Wilcoxon test, when the number of observations was under 30 and the distribution of the variable was not normal, but there was a symmetric distribution of differences).

Results

All 31 volunteers underwent a longer fasting period than requested, which varied from 7 to 12.5 h (average=10 h, standard deviation=1.4 h) – in accordance with what happens in clinical practice.

“Conventional” variables (Table 3)

The volunteers were asked to supply data on the evolution of weight between their last meal and after voiding on the pre-fasting day and the following morning (post-fasting), provided that there were no bowel movements in between. In these conditions, any differences between measurements would be attributable to fluid depletion. Even though only 9 of the 31 volunteers supplied valid data, there was a statistically significant reduction in the values obtained, corresponding to 1% of the body weight (approximately 700 g on average).

There were no statistically significant changes in either heart rate or blood pressure between both measurements.

Echocardiographic preload variables

Static parameters (Table 4)

As far as static preload indices are concerned, the behaviour of the different variables studied was markedly dissimilar, with:

- A statistically significant decrease of 6.8% in the telediastolic area of the left ventricle (PSSAx) (pointing to a decreased preload after fasting),
- A statistically significant increase of 9.2% in the Flow time corrected in the descending aorta (pointing to an increase in preload after fasting, considering that peripheral vascular resistance, which is inversely proportional to the $\text{FT}_{\text{Ao d}}$ and could complicate the assessment, also increased in this period)
- No change in the absolute expiratory diameter of the IVC or in the telediastolic diameter of the LV in PSLAx (M-mode), pointing to the absence of change in preload.

Dynamic parameters (Table 5)

As far as the dynamic preload indices studied are concerned, their behaviour was markedly consistent between different indices, with no statistically significant changes on either the respiratory variations of IVC diameter or in the variation of VTI_{Ao} with the PLR manoeuvre. Therefore, they all pointed to the inexistence of a significant preload variation with fasting.

Table 3 “Conventional” variables and their evolution with fasting.

Variable	Δ with fasting, $p < 0.05$	n (valid measurements)	Test	Evolution with fasting
Weight	Yes	9	Wilcoxon's test	↓
HR	No	31	Student's paired	→
BP _{syst}	No	31	samples t test	→
BP _{diast}	No	31		→
BP _{mean}	No	31		→

HR, heart rate; BP, blood pressure; syst, systolic; diast, diastolic.

Table 4 Static preload variables and their evolution with fasting.

Variable	Δ with fasting, $p < 0.05$	n	Test	Evolution with fasting	Degree of change
A _{LV} PSSAx	Yes (with no change in diastolic function)	26	Wilcoxon's test	↓	-6.8%
TDD _{LV} MM PSLAx	No	31	Paired samples t test	→	
IVC (D exp)	No	31		→	
FT _{CAo d}	Yes	31		↑	+9.2%

A_{LV} PSSAx, area of the left ventricle measured in the parasternal short axis window; TDD_{LV} MM PSLAx, telediastolic diameter of the left ventricle using M-mode in the parasternal long axis window; IVC, Inferior Vena Cava; D exp, Diameter in expiration; FT_{CAo d}, Flow time corrected in the descending aorta.

Table 5 Dynamic preload variables and their evolution with fasting.

Variable	Δ with fasting, $p < 0.05$	n	Test	Evolution with fasting
Δ resp IVC (CI _{IVC})	No	31	Paired samples t test	→
Δ VTI _{Ao PLR}	No	31		→

Δ resp IVC (CI_{IVC}), respiratory variation of the inferior vena cava; CI_{IVC}, collapsability index of the IVC; Δ VTI_{Ao PLR}, variation of the transaortic velocity time integral with the passive leg raise manoeuvre.

Discussion

As far as vital signs are concerned (namely heart rate and blood pressure), it was already mentioned that their change is not a sensitive indicator of volaemic state or fluid depletion,^{6,16,17} and thus it came as no surprise that there was no significant change in the values obtained between both periods in our study. Regarding weight assessments, even though the number of valid data obtained was small, there was a statistically significant decrease in this parameter, reaching around 1% of total body weight, which translated into an average loss of 700 g. It is a well known fact that different body compartments are in constant balance with one another, and that means we can calculate how much the loss of this mass means in terms of intravascular plasma volume also lost. Considering that only 1/3 of total body fluid is extracellular and that only about 20% of these constitute plasma volume,^{46,47} then a 700 mL fluid loss in a 70 kg individual would equate to $700 \times 1/3 \times 1/5 = 46.67$ mL plasma volume. Considering the reduced expression of this value, it seems unlikely that there would be a significant preload variation consequent to fasting.

Let us move on to the analysis of echocardiographic indices.

Because preload is defined as the telediastolic dimension (“stretch”) of cardiac fibres, telediastolic dimensions of the ventricles have emerged as a surrogate for preload, with small values signalling a reduction in this important variable. However, it should be noted that static preload indices are considered fallible in the literature, as they compare cardiovascular states without taking into account important covariates that may be instrumental for the results obtained. For instance, telediastolic dimensions depend not only on preload but also on diastolic function, and comparing these indices without knowing whether the diastolic function has been altered between measurements and attributing change to altered preload is incautious, to say the least. Other static variables, such as flow time corrected in the descending aorta are also dependent on cofactors such as peripheral vascular resistance; IVC dimensions are affected by both diastolic function and breathing. Aside from all of this, we have previously addressed the issue that a same preload in the same person can lead to different stroke volumes depending on the contractility state

and afterload at that moment (Fig. 1), because the same individual has different Frank–Starling curves in different moments.^{48,49} Given all of the above, then, it seems only natural that our results from different static preload variables pointed in markedly different directions when used in isolation to assess the cardiovascular effects of fasting.

Consequently, it is important to analyse instead the evolution in dynamic preload variables and fluid responsiveness. These indices focus on the behaviour of a given variable in a small time frame making use of intentional changes in preload, which are usually provoked by either heart–lung interactions (breathing pattern) or the PLR manoeuvre. The quick, intentional, reversible nature of these preload variations allows for the maintenance of other potentially interfering parameters of cardiovascular state to remain constant between measurements, thus making preload the only truly independent variable and lending increased reliability to the data obtained. It should be emphasized, however, that in the literature only IVC inspiratory collapse and variation of VTI_{Ao} with PLR have been validated as a token of fluid responsiveness in spontaneously breathing patients.⁵⁰

In our study, the results obtained with dynamic indices were all coincident: there was no statistically significant change in either of them between before and after a fasting period, even when we considered the subgroup of volunteers who fasted for longer.

Though these data strongly suggest that fasting does not have a significant influence on the hemodynamic state of the patient, we considered it important to prove that the methods used were sensitive enough to detect preload changes, and that a negative result would thus reflect not a lack of sensitivity but rather a true lack of effect. Therefore, we put these variables themselves to the test by analysing their evolution after a PLR manoeuvre. Knowing that this mobilizes 300–500 mL of blood from the lower limbs into the circulation, as previously mentioned, if the variable used was sensitive enough to detect a change of this magnitude, then it should show changes with this test.

The analysis of the results obtained led to interesting conclusions.

Firstly, the respiratory variation of the IVC (and its collapsibility index), a preload index that is widely used in the literature, did not pass this test, failing to consistently change with the use of the PLR. Such raises sensitivity issues for the use of this index in clinical practice.

VTI_{Ao} , however, consistently changed with PLR, making ΔVTI_{Ao} with PLR the preferred variable to evaluate fluid responsiveness (and thus evaluate the position of the individual in the Frank–Starling curve) in our study. Realizing that it did not change after fasting points to a true absence of effect from this entity in the hemodynamic state of the individual.

We can also use this variable to classify our volunteers in terms of fluid-responsiveness, considering that fluid responders are those in which PLR leads to a significant (10–15%)⁵¹ increase in stroke volume (Fig. 3) [and thus in VTI_{Ao} , given that stroke volume (SV) = $VTI_{Ao} \times CSA$ (cross-sectional area – which is considered to be constant)]. In the pre-fasting period 10 individuals (roughly one third) were in the ascending limb of the Frank–Starling curve (i.e., were fluid responders). If the fasting period had caused a

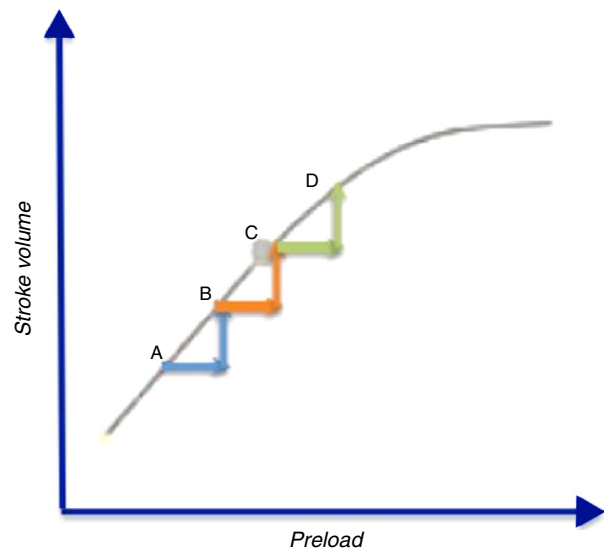


Figure 3 When an individual is in the ascending limb of the Frank–Starling curve an adequate increase in preload (such as that obtained with the PLR manoeuvre) leads to an increase of 10–15% in stroke volume.

reduction in preload, then we would expect the average position of the volunteers to be displaced to the left of the curve, and at least some of those 21 non-responsive individuals before fasting would migrate into the ascending limb of the curve. Such an event, however, did not occur, and after fasting the number of fluid responsive individuals was precisely the same as before fasting: 10, which once again confirms the finding that fasting did not alter the volunteers' position on the Frank–Starling curve, nor did it make them more optimizable by fluid loading – at least in the normal, unanaesthetized setting.

Limitations to the study

There are some limitations to the present study, which should be considered.

Firstly, it is well recognized that echocardiography is a highly user dependent technology, which might skew the results if different operators obtained results that would then be analysed together. To reduce this potential for bias, all scans were performed by the same operator and later reviewed by an independent observer.

We must also acknowledge that this was not a blind study. In order to prevent unintended preconceptions from interfering with the analysis, all measurements were made off-line in a random order as opposed to sequentially, with individual identification encoded so as to prevent an immediate association of results.

The sample size should also be mentioned ($n=31$), as it was relatively small. However, all results were statistically significant, to a p -value < 0.05 . The individuals studied were all ASA 1 and 2, without cardiovascular comorbidities. Therefore, the results obtained should not be directly extrapolated to other patient populations, but rather serve as a reflection for the most appropriate management of those patients not severe enough to merit routine use of invasive monitoring techniques intraoperatively.

We should also consider the possibility that circadian rhythm might have interfered with results, considering that one measurement was made late in the afternoon whereas the other was performed early in the morning. However, the preferential use of dynamic preload variables allows for a greater confidence in the results obtained, decreasing this interference.

Finally, it would be interesting to see how these preoperative results would relate to intraoperative measurements, but such was not possible in this study because it was made with volunteers, not patients undergoing surgery.

Conclusions

The present study showed that in volunteers without cardiovascular comorbidities a period of fasting does not seem to alter their position in the Frank–Starling curve, meaning there is probably no benefit from routine fluid loading in comparable patients presenting for surgery. The fact that the fasting periods actually followed by volunteers was far in excess to the ones requested lends further strength to these results, although further studies relating intraoperative to preoperative data would be welcome.

Finally, we should mention that the velocity time integral variation of trans-aortic flow with the PLR manoeuvre emerged as the most reliable variable to estimate the individual's position in the Frank–Starling curve. Such makes it appropriate not only for investigational purposes, as was the case, but also to guide fluid therapy clinically.

Conflicts of interest

The authors declare no conflicts of interest.

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