Deve Confiar-se no Exame Ecográfico da Veia Cava Inferior para Avaliar a Resposta a Fluidos em Voluntários ASA 1 e 2?

Should Echographic Examination of the Inferior Vena Cava be Trusted to Assess Fluid Responsiveness in ASA 1 and 2 Volunteers?

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Resumo

Introdução: A resposta a fluidos endovenosos é um conceito fundamental na abordagem da fluidoterapia perioperatória, integrando a maioria dos protocolos de fluidoterapia dirigida por objectivos (*goal-directed therapy*). Pode ser avaliada de modo não invasivo utilizando ecocardiografia transtorácica, nomeadamente medindo a variação do integral de velocidade-tempo transaórtico com a manobra de elevação passiva dos membros inferiores ($\Delta VTIA_o$ PLR). Este é o parâmetro ecocardiográfico mais validado em pacientes sob ventilação espontânea, mas outros autores sugerem a avaliação da veia cava inferior (VCI) com esse propósito.

Métodos: Estudo observacional, analítico, prospectivo, em voluntários ASA 1 e ASA 2, em ventilação espontânea, sem comorbilidades cardiovasculares. A relação entre os índices da VCI e a $\Delta VTIA_o$ PLR foi inicialmente estudada através do coeficiente de correlação de Pearson. Os indivíduos foram então estratificados de acordo com as guidelines da ASE/EAE para avaliação da VCI, e a distribuição da $\Delta VTIA_o$ PLR entre cada subgrupo comparada com o teste de Kruskal-Wallis (três subgrupos) e o teste de Mann-Whitney (comparando apenas os dois subgrupos em extremos opostos).

Resultados: Não se verificou relação estatisticamente significativa entre os parâmetros da VCI e a $\Delta VTIA_o$ PLR (p = 0,920 para o diâmetro da VCI e p = 0,248 para o índice de colapsabilidade da VCI). Também não ser verificou diferença estatisticamente significativa na resposta a fluidos endovenosos entre subgrupos com diferentes características da VCI (p = 0,081 para teste de Kruskal-Wallis; p = 0,858 para teste de Mann-Whitney 0,858).

Conclusões: A avaliação da VCI por ecocardiografia transtorácica não se revelou adequada para avaliar a resposta a fluidos em indivíduos ASA 1 e ASA 2 sob ventilação espontânea. À luz dos resultados obtidos sugere-se cautela na utilização de índices da VCI para guiar a fluidoterapia em pacientes não críticos sob ventilação espontânea.

Palavras-chave: Fluidoterapia; Ultrassonografia; Veia Cava Inferior

Abstract

Introduction: *Fluid responsiveness is a fundamental concept in the management of perioperative fluid therapy, and an integrating part of most goal-directed therapy protocols. It can be assessed non-invasively by transthoracic echocardiography, namely by measurement of transaortic velocity time integral variation with the passive leg raise manoeuvre ($\Delta VTIA_o$ PLR). This is the most validated echocardiographic parameter in spontaneously breathing individuals, but other authors suggest using inferior vena cava (IVC) assessment with the same goal.*

Methods: *Observational, analytic, prospective study in ASA 1 and ASA 2 spontaneously breathing volunteers, with no cardiovascular comorbidities. The relationship between isolated IVC indices and $\Delta VTIA_o$ PLR was initially studied using Pearson's correlation coefficient. Individuals were then stratified according to ASE/EAE guidelines for IVC evaluation, and the distribution of $\Delta VTIA_o$ PLR within each subgroup compared with a Kruskal-Wallis test (comparing all three subgroups) and a Mann-Whitney test (comparing only the subgroups at the opposite ends of the spectrum).*

Results: *There was no statistically significant relationship between isolated echocardiographic IVC parameters and $\Delta VTIA_o$ PLR (p value 0.920 for IVC diameter and 0.248 for IVC collapsibility index). There was also no statistically significant difference in fluid responsiveness between subgroups with different IVC characteristics (Kruskal-Wallis test's p value 0.081; Mann-Whitney test's p value 0.858).*

Conclusions: *IVC assessment through transthoracic echocardiography did not prove adequate for assessment of fluid status and fluid responsiveness in ASA 1 and ASA 2 spontaneously breathing individuals. In view of our results caution is advised when relying on IVC indices to guide fluid therapy in non-critical, spontaneously breathing patients.*

Keywords: *Fluid Therapy; Ultrasonography; Vena Cava, Inferior*

INTRODUCTION

In the perioperative period there is often a disruption in patients' homeostasis, with the use of the different drugs and/or interventions routinely altering their preload, contractility, chronotropism and afterload. With the intent of maximizing benefits while at the same time minimizing the possibility of harm, up until a few years ago there was a strong emphasis on fluid loading patients during anaesthesia (provided there were no obvious contraindications nor signs of overload), so as to optimize their cardiovascular state according to the Frank-Starling law.[1,2] However, while such was believed to minimize intraoperative decompensation, more recent studies have shown that excessive fluid replenishment can actually be deleterious,[3–7] and it became necessary to rethink the concept and find ways to better assess the true haemodynamic state of patients on an individual basis.

Goal-directed therapy approaches strive to do precisely that,[6,8–11] usually by classifying individuals according to their position either on the ascending or flat limbs of the Frank-Starling curve.[12] Their implementation has produced favourable outcomes,[8,13,14] but assessing fluid responsiveness is not always easy. Central venous pressure (CVP) measurements are now known to be unreliable markers for the haemodynamic state of the patient,[15–18] and consequently different technologies have evolved to replace it, many of which rely on the analysis of the arterial waveform (like LiDCO™ and FloTrac/Vigileo™, among others[8,19]). Respiratory variations in pulse pressure and systolic pressure were also suggested,[16,17] though presently their use is only validated for ventilated patients. Furthermore, all of these technologies are invasive, and thus not appropriate for simpler patients proposed for minor operations, not meriting such monitoring devices.

More recently, echocardiography has been emerging as a simple, bedside alternative to assess the haemodynamic status of patients noninvasively, and is growingly being used by anaesthesiologists and intensive care physicians worldwide. At the present, and for patients breathing spontaneously, the most validated echocardiographic marker of fluid responsiveness is transaortic velocity time integral variation with the passive leg raise manoeuvre ($\Delta VTIA_o$ PLR).[20] Other authors preconize the use of inferior vena cava (IVC) assessment combining both its diameter and inspiratory collapsibility index.[21] The European Association of Echocardiography (part of the European Association of Cardiovascular Imaging), however, considers the assessment of the IVC as a means to estimate the pressure in the right atrium (i.e., as a means to assess CVP)[22] which, as we previously mentioned, is not an adequate marker for fluid responsiveness.

Given the importance of the subject and that these indices are relied on for important patient management decisions, the authors decided to evaluate whether assessment of the IVC is indeed reliable as an index of fluid responsiveness under spontaneous ventilation.

MATERIAL AND METHODS

After obtaining approval by the local Ethics Commission and informed consent from each participant, we performed an observational, prospective study in 31 spontaneously breathing ASA 1 and ASA 2 individuals, without cardiovascular comorbidities. Table 1 summarizes inclusion and exclusion criteria adopted.

Table 1. Inclusion and exclusion criteria

INCLUSION CRITERIA	EXCLUSION CRITERIA
• Adult, legally competent adults • ASA 1 or ASA 2	• Failure to provide informed consent • Inability to withstand proper positioning • Cardiovascular disease or medication • Inadequate echocardiographic images

Any pre-existing echocardiographic anomalies were excluded by a screening scan, and data on echocardiographic parameters were then collected in two separate examinations per volunteer on separate days, namely:

- Expiratory diameter of the IVC (Dexp IVC);
- Respiratory variation (collapsibility index) of IVC (Δresp IVC);
- Transaortic velocity time integral ($VTIA_o$) variation with the passive leg raise manoeuvre (PLR) ($\Delta VTIA_o$ PLR) – considered as the gold-standard,[20] and used for comparison purposes.

Additional data were also collected and used in satellite studies, previously published,[23] and as such will not be considered here.

All scans were performed by the same operator so as to decrease variability, using the same GE Vivid 7™ echocardiograph, and later analysed off-line in a random order with the software suite EchoPAC Dimension™, in a process reviewed by an independent observer.

The data obtained were then used to build a database in SPSS Statistics™ version 23, and tested for the existence of linear correlation between both types of preload indices (IVC assessment and $\Delta VTIA_o$ PLR) using both Pearson's correlation coefficient and scatter plots. Because this analysis only tested for correlation between isolated IVC indices and fluid responsiveness, not taking into account the possible combined effects of IVC diameter and collapsibility index, we then decided to divide the sample into different classes according to internationally recognized cut-offs[24] for IVC indices, as follows:

- Subgroup 1 – IVCexp ≤ 21 mm and Collapsibility index > 50%;
- Subgroup 2 – IVCexp > 21 mm and Collapsibility index < 50%;
- Subgroup 3 – Individuals not belonging to either of the previous subgroups.

Should IVC expiratory diameter and collapsibility index in combination signal fluid responsiveness, then volunteers in each of the subgroups would differ in $\Delta VTIA_o$ PLR, which we assessed using the Kruskal-Wallis test (due to the existence of three different subgroups).
Finally, because subgroup three included individuals not belonging to either of the traditional subgroups 1 and 2, and as such had a somewhat indeterminate behaviour in terms of fluid responsiveness in the literature, we decided to additionally compare subgroups 1 and 2 against each other in isolation, excluding individuals from subgroup 3 from the analysis, as they might introduce bias. To do so, we performed a Mann-Whitney test.

RESULTS

SAMPLE CHARACTERISTICS

Table 2 summarizes the characteristics of the sample. Forty-eight percent of the volunteers were male, and 71% of the total ASA 2, though without cardiac comorbidities. Existing comorbidities were either respiratory (controlled asthma, with no crisis for over a month and no current medication; smoking) or metabolic (excess weight - BMI 25-29.9 kg/m^2, dyslipidaemia).

Table 2. Sample characteristics

VARIABLE	SAMPLE CHARACTERISTICS
Age	Average of 37 years old (ranging from 26 to 67)
Sex	• 15 male volunteers • 16 female volunteers
ASA Physical Status classification	• ASA 1: 22 volunteers • ASA 2: 9 volunteers

EXPIRATORY DIAMETER OF THE IVC (DEXP IVC)

There was no statistically significant linear correlation between the absolute expiratory dimensions of IVC and $\Delta VTIA_o$ PLR (our gold-standard for fluid responsiveness) (Fig. 1, Table 3), with Pearson's correlation coefficient exhibiting a *p* value of 0.920.

RESPIRATORY VARIATION OF IVC DIAMETER (ΔRESP IVC) (COLLAPSIBILITY INDEX)

There was no statistically significant linear correlation between collapsibility index of the IVC and the gold-standard ($\Delta VTIA_o$ PLR) (Fig. 2, Table 3), with Pearson's correlation coefficient exhibiting a *p* value of 0.248.

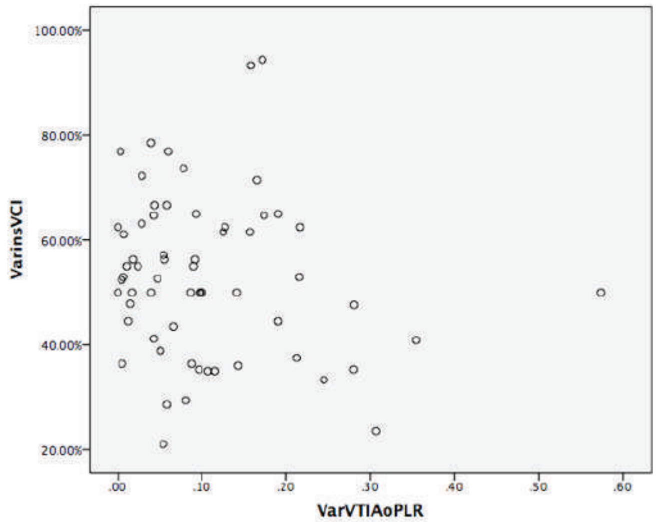

Figure 1. Scatter plot evidencing the relationship between inspiratory variation of IVC (inspiratory collapse – VarinsVCI) and aortic VTI variation with the PLR manoeuvre ($VarVTIA_oPLR$).

Table 3. Pearson's linear correlation coefficient for the relation between different IVC parameters and $\Delta VTIA_o$ PLR (the gold-standard).

VARIABLE	N (NUMBER OF VALID MEASUREMENTS)	CORRELATION WITH $\Delta VTIA_o$ PLR (GOLD-STANDARD)	
		PEARSON'S CORRELATION COEFFICIENT	*p*-value FOR PEARSON'S CORRELATION COEFFICIENT
Dexp IVC	62	-0.013	0.920
Δresp IVC	62	-0.149	0.248

COMBINED IVC INDICES

Dividing the sample into three different subgroups as mentioned in the previous section, we found no statistically significant difference in the distribution of fluid responsiveness in each (Kruskal-Wallis test with a *p*-value of 0.081).
If only the extremes were considered (subgroup 1, with small, readily collapsible IVC *versus* subgroup 2, with dilated,

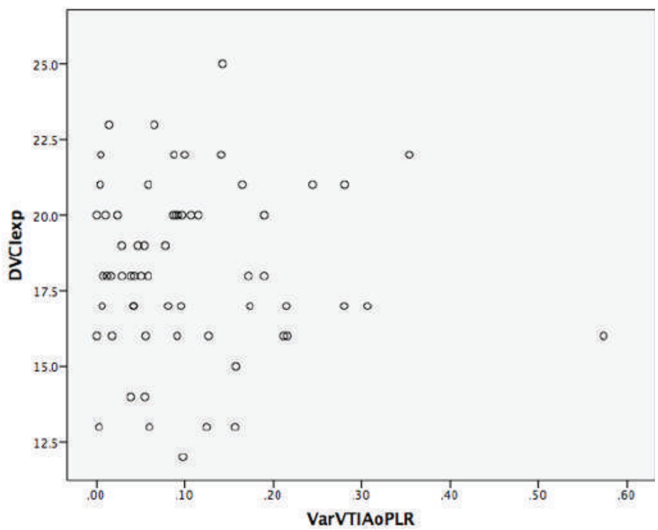

Figure 2. Scatter plot evidencing the relationship between the expiratory dimension of the IVC (DVClexp) and aortic VTI variation with the PLR manoeuvre ($VarVTIA_oPLR$).

non-collapsing IVC), and disregarding individuals with intermediate measurements, we also found no statistically significant difference between $\Delta VTIA_o$ PLR (and thus fluid responsiveness) in each subgroup (Mann-Whitney test with a *p* value of 0.858).

DISCUSSION

All the results obtained point towards the inadequacy of IVC assessment to accurately signal the position of non-critical, ASA 1 or 2 individuals on the Frank-Starling curve and classify them into either fluid-responsive or fluid non-responsive. Not only there was no direct linear correlation between isolated IVC indices and the gold-standard described in the literature for patients breathing spontaneously, but there was also no added advantage from joining absolute expiratory dimensions of the IVC and collapsibility index for this purpose, as no statistical significance was found in fluid responsiveness states in the different subgroups thus formed.

The fact that ASE/EAE guidelines consider IVC indices as a means to calculate CVP[24] and that other authors had already shown that CVP had a predictive value of only 56% in terms of fluid responsiveness[25] already pointed towards the suspicion of a possible non-significance of the index as a good guide for fluid therapy. However, traditional teaching still places a strong emphasis on IVC evaluation,[9,26-31] and the results shown in the present article question such approach.

Clearly, however, this study is not without its limitations.

First and foremost it is a study made with relatively healthy volunteers, and it would be interesting to extend it to include critically ill individuals, as we cannot guarantee that our conclusions will hold true in this important subgroup.

It is also a relatively small study, with data from only 62 exams, though the statistical tests used and the different approaches employed support the validity of the conclusions drawn.

On the other hand, it also uses a very operator-dependent technology – echocardiography. The fact that all exams were performed by the same operator, however, helps decrease any bias in this regard.

Finally, it could also be argued that this was not a blind study, and that the global assessment of the individual by the investigator performing the exam might unwillingly have interfered with the measurements made. To prevent this, all measurements were made off-line and the exams treated in a non-sequential order, so that the investigator did not know who the exam under analysis referred to, when performing measurements.

CONCLUSION

IVC assessment through transthoracic echocardiography was not adequate for assessment of fluid status and fluid responsiveness in ASA 1 and 2 spontaneously ventilating volunteers. In view of our results caution is advised when relying on IVC indices to guide fluid therapy in non-critical, spontaneously breathing individuals. Further, larger trials are needed as it is not possible to guarantee that these results hold true in other patient groups.

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Proteção de Pessoas e Animais: Os autores declaram que os procedimentos seguidos estavam de acordo com os regulamentos estabelecidos pelos responsáveis da comissão de investigação clínica e ética e de acordo com a declaração de Helsínquia da associação médica mundial.

Protection of human and animal subjects: *The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).*

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REFERÊNCIAS

1. Magder S. Fluid status and fluid responsiveness. Curr Opin Crit Care. 2010;16:289-96.
2. Schmidt C, Hinder F, Van Aken H, Poelaert J. Chapter 3 - Global left ventricular systolic function. In: Poelaert J, Skarvan K, editors. Transoesophageal Echocardiography in Anaesthesia and Intensive Care Medicine. London: BMJ Publishing Group; 2004. p. 47-79.
3. Kaye AD. Chapter 23 - Fluid Management. In: Miller RD, Pardo MC, editors. Basics of Anesthesia. Philadelphia: Elsevier Saunders; 2011. p. 364-71.
4. Nygren J, Thorell A, Ljungqvist O. Are there any benefits from minimizing fasting and optimization of nutrition and fluid management for patients undergoing day surgery? Curr Opin Anaesthesiol. 2007;20:540-4.
5. Bamboat ZM, Bordeianou L. Perioperative fluid management. Clin Colon Rectal Surg. 2009;22:28-33.

6. Kirov MY, Kuzkov VV, Molnar Z. Perioperative haemodynamic therapy. Curr Opin Crit Care. 2010;16:384-92.
7. Lowell JA, Schifferdecker C, Driscoll DF, Benotti PN, Bistrian BR. Postoperative fluid overload: not a benign problem. Crit Care Med. 1990;18:728-33.
8. Geisen M, Rhodes A, Cecconi M. Less-invasive approaches to perioperative haemodynamic optimization. Curr Opin Crit Care. 2012;18:377-384.
9. Pinsky MR. Goal-Directed Therapy: Optimizing fluid management in your patient. Initiatives in Safe Patient Care. 20101-12.
10. Bar-Yosef S, Schroeder RA, Mark JB. Chapter 30 - Hemodynamic Monitoring. In: Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish JP, Young WL, editors. Miller's Anesthesia. Philadelphia: Churchill Livingstone - Elsevier; 2010. p. 406-29.
11. Miller TE, Gan TJ. Chapter 11 - Goal-directed fluid therapy. In: Hahn RG, editor. Clinical fluid therapy in the perioperative setting. Cambridge; New York: Cambridge University Press; 2011. p. 91-102.
12. Raghunathan K, McGee WT, Higgins T. Importance of intravenous fluid dose and composition in surgical ICU patients. Curr Opin Crit Care. 2012;18:350-7.
13. Rhodes A, Cecconi M, Hamilton M, Poloniecki J, Woods J, Boyd O, et al. Goal-directed therapy in high-risk surgical patients: a 15-year follow-up study. Intensive Care Med. 2010;36:1327-32.
14. Gil Cano A, Monge Garcia MI, Baigorri Gonzalez F. Evidencia de la utilidad de la monitorizacion hemodinamica en el paciente critico. Med Intensiva. 2012;36:650-655.
15. Benington S, Ferris P, Nirmalan M. Emerging trends in minimally invasive haemodynamic monitoring and optimization of fluid therapy. Eur J Anaesthesiol. 2009;26:893-905.
16. Hamilton M, Chishti A. Advanced cardiovascular monitoring. Surgery. 2013;31:90-7.
17. Joubert I, James MF. The assessment of intravascular volume. SAJAA. 2007;13:33-6.
18. Cecconi M, Parsons AK, Rhodes A. What is a fluid challenge? Curr Opin Crit Care. 2011;17:290-5.
19. Mateu Campos ML, Ferrandiz Selles A, Gruartmoner de Vera G, Mesquida Febrer J, Sabatier Cloarec C, Poveda Hernandez Y, Garcia Nogales X. Técnicas disponibles de monitorización hemodinámica. Ventajas y limitaciones. Med Intensiva. 2012;36:434-44.
20. Ramos FJ, Azevedo LC. Assessment of fluid responsiveness in patients under spontaneous breathing activity. Rev Bras Ter Intensiva. 2009;21:212-8.
21. Dipti A, Soucy Z, Surana A, Chandra S. Role of inferior vena cava diameter in assessment of volume status: a meta-analysis. Am J Emerg Med. 2012;30:1414-19.
22. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, et al. Recommendations for chamber quantification. Eur J Echocardiogr. 2006;7:79-108.
23. Alves DR, Ribeiras R. Does fasting influence preload responsiveness in ASA 1 and 2 volunteers. Braz J Anesthesiol. 2017;67:172-9.
24. Rudski LG, Lai WW, Afilalo J, Hua L, Handschumacher MD, Chandrasekaran K, et al.. Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American Society of Echocardiography endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology, and the Canadian Society of Echocardiography. J Am Soc Echocardiogr. 2010;23:685-713; quiz 786.
25. Marik PE, Baram M, Vahid B. Does central venous pressure predict fluid responsiveness? A systematic review of the literature and the tale of seven mares. Chest. 2008;134:172-8.
26. Atkinson P, Daly C. My patient has no blood pressure: are they empty or full? Point-of-care ultrasound of the inferior vena cava in the hypotensive emergency department patient. Ultrasound. 2011;19: 169-73.
27. Mookadam F, Warsame TA, Yang HS, Emani UR, Appleton CP, Raslan SF. Effect of positional changes on inferior vena cava size. Eur J Echocardiogr. 2011;12:322-5.
28. Labovitz AJ, Noble VE, Bierig M, Goldstein SA, Jones R, Kort S, et al. Focused cardiac ultrasound in the emergent setting: a consensus statement of the American Society of Echocardiography and American College of Emergency Physicians. J Am Soc Echocardiogr. 2010;23:1225-1230.
29. Lyon M, Blaivas M, Brannam L. Sonographic measurement of the inferior vena cava as a marker of blood loss. Am J Emerg Med. 2005;23:45-50.
30. Lyon ML, Verma N. Ultrasound Guided Volume Assessment Using Inferior Vena Cava Diameter. Open Emerg Med J. 2010;3:22-4.
31. Barbier C, Loubieres Y, Schmit C, Hayon J, Ricome JL, Jardin F, . Respiratory changes in inferior vena cava diameter are helpful in predicting fluid responsiveness in ventilated septic patients. Intensive Care Med. 2004;30:1740-6.