USE OF POINT-OF-CARE ULTRASOUND (POCUS) IN THE ASSESSMENT OF FLUID RESPONSIVENESS: PRACTICAL APPLICATIONS AND METHODS

USO DO ULTRASSOM POINT-OF-CARE (POCUS) NA AVALIAÇÃO DA RESPONSIVIDADE VOLÊMICA: APLICAÇÃO PRÁTICA E MÉTODOS

USO DE LA ECOGRAFÍA EN EL PUNTO DE ATENCIÓN (POCUS) PARA EVALUAR LA RESPUESTA AL VOLUMEN: APLICACIÓN PRÁCTICA Y MÉTODOS

https://doi.org/10.56238/sevened2026.020-011

Luan Caimar Fuchs[1], Bruna Turra Aimi[2], Felipe Romão Hatisuka[3], José Henrique Gorgone Zampieri[4], Jaime Javier Garcia Caro[5], Kelen Marques de Souza[6], Lucas Braun Gonçalves[7], João Marcello Fernandes Zanata[8], Júnior Girardi[9], Maria Eduarda Faraldo Calore[10], Filippo Fabi Bez[11], Adriano Pereira Rocha[12], Bráulio Queiros de Andrade[13], Luís Otávio Garcia de Oliveira[14], Lucas Marcos Balduino[15], Débora Vieira de Melo Agra Duarte Nunes[16], Lara Cristine Quaresma Oliveira[17], João Vicente Soares Martins[18], Emily Carboni Silveira Neto[19], Rafael de Cristo[20], Giulia Regina Frangiotti[21], Gabriela Zanardo Sousa[22]

[1] Medicine. Pontifícia Universidade Católica do Paraná (PUCPR). E-mail: drluanfuchs@gmail.com
[2] Medical Doctor. Universidade de Passo Fundo. E-mail: bruunaaimi@gmail.com
[3] Medical Doctor. Universidade do Oeste Paulista (UNOESTE). E-mail: romao_85@hotmail.com
[4] Resident in Radiology and Diagnostic Imaging. Universidade Federal de Pelotas (UFPel). Hospital Moinhos de Vento (HMV). E-mail: jhgzampieri@gmail.com
[5] Postgraduate in General Surgery. Universidade Nacional José Faustino Sánchez Carrión. Universidade Federal de Mato Grosso (UFMT). Santa Casa da Misericórdia do Rio de Janeiro. E-mail: jaimejavier79@hotmail.com
[6] Specialist in Internal Medicine. Universidade do Estado do Amazonas. E-mail: kelen-marques@hotmail.com
[7] Medical Doctor. Universidad Adventista del Plata. Universidade Federal do Rio Grande do Norte (UFRN). E-mail: Lucas.br4un@gmail.com
[8] Undergraduate student in Medicine. Universidade Federal de Pernambuco (UFPE). E-mail: joaomarcellofer@gmail.com
[9] Medical Doctor. Universidade Federal de Santa Maria (UFSM). E-mail: juniorgirardi8@gmail.com
[10] Medical Doctor. Centro Universitário Católico Salesiano Auxilium (UniSALESIANO). E-mail: dudafaraldo@gmail.com
[11] Medicine. Faculdade de Medicina de Santo Amaro (UNISA). E-mail: filippofabi@hotmail.com
[12] Resident in Radiology. Clínica Campimagem. E-mail: dradrianobaldez@gmail.com
[13] Resident in Radiology. Campimagem. E-mail: braulioqueiros@hotmail.com
[14] Medicine. Universidade de Marília. E-mail: luisotavio_garcia@icloud.com
[15] Medicine. Faculdade de Medicina de Marília (FAMEMA). E-mail: balduino.lucas@hotmail.com
[16] Resident in Radiology. UNIFACISA. E-mail: deboravieirademeloagraduarte@gmail.com
[17] Medical Doctor. Universidad Central (UNICEN). E-mail: laraquaresma1995@gmail.com
[18] Medical Doctor. Universidade Federal do Rio Grande do Norte (UFRN). E-mail: jvsmartins@gmail.com
[19] Medical Doctor. ATITUS. E-mail: draemilysn@gmail.com
[20] Medicine. Uniderp. E-mail: rafaelcristomed@hotmail.com
[21] Medical Doctor. Universidade Municipal de São Caetano do Sul. E-mail: giuliafrangiotti@gmail.com
[22] Medicine. UNICID. E-mail: gabizanardo@hotmail.com

ABSTRACT
Fluid responsiveness assessment is essential in the management of critically ill patients, as inappropriate fluid administration is associated with adverse outcomes. In this context, point-of-care ultrasound (POCUS) has emerged as a key tool for hemodynamic monitoring, enabling dynamic bedside evaluation. This study is a structured critical narrative review analyzing 18 studies published between 2015 and 2025, identified through PubMed/MEDLINE, Scopus, and Web of Science databases. Ultrasound-based methods evaluated included left ventricular outflow tract velocity-time integral (LVOT VTI), passive leg raising (PLR), and indices derived from the inferior and superior vena cava. The findings demonstrate the superiority of dynamic over static parameters, with the combination of VTI and PLR representing the most consistent approach. In contrast, vena cava indices show greater variability and context-dependent limitations, while emerging methods such as carotid flow assessment require further validation. In conclusion, no single method is universally applicable, and an integrated, context-based approach is essential, with POCUS playing a central role in clinical decision-making.

Keywords: Point-Of-Care Ultrasound. Fluid Responsiveness. Hemodynamic Monitoring. Critical Care. Echocardiography.

RESUMO
A avaliação da responsividade volêmica é fundamental no manejo de pacientes críticos, uma vez que a administração inadequada de fluidos está associada a desfechos adversos. Nesse contexto, o ultrassom point-of-care (POCUS) tem se consolidado como ferramenta central na monitorização hemodinâmica, permitindo avaliação dinâmica à beira-leito. Este estudo consiste em uma revisão narrativa crítica com abordagem estruturada, que analisou 18 estudos publicados entre 2015 e 2025, selecionados a partir das bases PubMed/MEDLINE, Scopus e Web of Science. Foram avaliados métodos ultrassonográficos como a variação do integral velocidade-tempo do trato de saída do ventrículo esquerdo (VTI do LVOT), o teste de elevação passiva dos membros inferiores (passive leg raising – PLR) e os índices derivados das veias cava inferior e superior. Os achados demonstram superioridade dos métodos dinâmicos em relação aos parâmetros estáticos, com destaque para a combinação entre VTI e PLR como abordagem mais consistente. Em contraste, índices baseados na veia cava apresentam maior variabilidade e limitações contextuais, enquanto métodos emergentes, como o fluxo carotídeo, ainda carecem de validação robusta. Conclui-se que não há método universalmente aplicável, sendo essencial uma abordagem integrada e contextualizada, com o POCUS desempenhando papel central na tomada de decisão clínica.

Palavras-chave: Ultrassom Point-Of-Care. Responsividade Volêmica. Monitorização Hemodinâmica. Terapia Intensiva. Ecocardiografia.

RESUMEN
La evaluación de la respuesta a la fluidoterapia es fundamental en el manejo de pacientes críticos, dado que una administración inadecuada de fluidos se asocia con resultados adversos. En este contexto, la ecografía en el punto de atención (POCUS) se ha convertido en una herramienta central en la monitorización hemodinámica, permitiendo una evaluación dinámica a pie de cama. Este estudio consiste en una revisión narrativa crítica estructurada que analizó 18 estudios publicados entre 2015 y 2025, seleccionados de las bases de datos PubMed/MEDLINE, Scopus y Web of Science. Se evaluaron métodos ecográficos como la integral tiempo-velocidad del tracto de salida del ventrículo izquierdo (LVOT velocity-time integral), la prueba de elevación pasiva de las piernas (PLR) e índices derivados de las venas

cavas superior e inferior. Los hallazgos demuestran la superioridad de los métodos dinámicos en comparación con los parámetros estáticos, destacando la combinación de VTI y PLR como el enfoque más consistente. Por el contrario, los índices basados en la vena cava presentan mayor variabilidad y limitaciones contextuales, mientras que los métodos emergentes, como el flujo carotídeo, aún carecen de una validación sólida. Se concluye que no existe un método universalmente aplicable, y que es esencial un enfoque integrado y contextualizado, donde la ecografía en el punto de atención (POCUS) desempeña un papel central en la toma de decisiones clínicas.

Palabras clave: Ecografía en el Punto de Atención. Respuesta al Volumen. Monitorización Hemodinámica. Cuidados Intensivos. Ecocardiografía.

1 INTRODUCTION

Adequate hemodynamic assessment is one of the main pillars in the management of critically ill patients, especially in the presence of circulatory instability. The administration of intravenous fluids remains one of the first therapeutic interventions in these settings. However, its efficacy is variable and depends on the ability of the cardiovascular system to respond to increased preload. Evidence shows that only a portion of patients have a significant increase in cardiac output after volume expansion, while indiscriminate administration of fluids can result in fluid overload, associated with worse clinical outcomes, including higher morbidity and mortality (MONNET; SHI; TEBOUL, 2022). In this scenario, it is essential to use methods capable of predicting volume responsiveness, defined as the increase in cardiac output after volume replacement, in order to optimize therapy and avoid potentially deleterious interventions (ASOGWA et al., 2024).

Historically, static parameters such as central venous pressure and mean arterial pressure have been widely used to guide volume replacement. However, these measures have low accuracy in predicting responsiveness, as they do not adequately reflect the dynamic interaction between preload, myocardial contractility, and cardiopulmonary conditions (ASOGWA et al., 2024). On the other hand, dynamic methods, based on the evaluation of the cardiovascular response to transient changes in preload, have demonstrated greater predictive capacity and have become preferred in contemporary clinical practice (MONNET; SHI; TEBOUL, 2022). Even so, its applicability may vary according to the clinical context and the physiological conditions of the patient, which reinforces the complexity of volume assessment and the need for more accurate tools.

In this context, point-of-care ultrasound (POCUS) has emerged as a central tool in bedside hemodynamic assessment. It is a non-invasive, portable, and fast-performing method, capable of providing real-time information on cardiac function, volume status, and systemic perfusion (NOOR et al., 2025). In addition, its possibility of serial use allows continuous monitoring of the therapeutic response, favoring a more individualized approach in the management of critically ill patients (PICCIONI et al., 2025). Thus, POCUS has been progressively incorporated into clinical practice in intensive care units, emergency departments, and the perioperative environment.

Among the applications of POCUS, the dynamic methods used in the prediction of volume responsiveness stand out, such as the variation of the integral velocity-time of the left ventricular outflow tract (LVOT VTI), the passive leg raising (PLR) test, and the analysis of respiratory variations of the inferior and superior vena cava. Evidence suggests that the variation of the VTI, especially when associated with the PLR, has high accuracy in predicting

the response to volume, being considered one of the most consistent approaches in clinical practice (PÉREZ-MANJARREZ et al., 2023; BOU CHEBL et al., 2018). On the other hand, parameters based on the vena cava, although widely disseminated, have relevant limitations, particularly in patients with ventricular dysfunction or under different ventilatory conditions, which may compromise their reliability (ZHANG et al., 2019; MA et al., 2022a; MA et al., 2022b). This heterogeneity of performance among the methods highlights the absence of a universally applicable tool.

Despite technological advances and the growing use of POCUS, there is still no definitive consensus in the literature regarding the most accurate, reproducible, and applicable method in different clinical scenarios. In addition, factors such as operator dependence, technical variability, and heterogeneity of the populations studied pose additional challenges for their standardization (HOTZ; VAN GEMMERN; KRIEGE, 2024). In this context, it is essential to critically integrate the available evidence, not only to describe existing methods, but also to understand their limitations and real applicability in clinical practice.

In view of the above, the present study aims to critically analyze the use of point-of-care ultrasound (POCUS) in the evaluation of volume responsiveness in critically ill patients, with emphasis on the main dynamic methods employed, their limitations, and their applications in clinical practice.

2 METHODOLOGY

This is a critical narrative review of the literature, with a structured approach, focused on the analysis of evidence on the use of point-of-care ultrasound (POCUS) in the evaluation of volume responsiveness in critically ill patients. The literature search was carried out in the PubMed/MEDLINE, Scopus, and Web of Science databases, including studies published between 2015 and 2025. English descriptors and keywords were used, combined by Boolean operators AND and OR, including "point-of-care ultrasound", "fluid responsiveness", "hemodynamic monitoring", "passive leg raising", "inferior vena cava", "stroke volume" and "velocity time integral".

Original studies, reviews, and observational studies involving adult patients that addressed sonographic methods applied to the prediction of volume responsiveness, published in English, Portuguese, or Spanish, were included. Case reports, case series with a low level of evidence, studies with an exclusively pediatric population, and those without direct clinical applicability in hemodynamic evaluation were excluded.

The selection of studies was carried out by screening titles and abstracts, followed by reading the eligible articles in full. At the end of the process, 18 studies considered relevant for analysis were included, based on their methodological consistency and clinical applicability.

Data extraction included study design, population evaluated, ultrasound methods used, and parameters analyzed, including variation in the VTI of the left ventricular outflow tract, inferior and superior vena cava indexes, and dynamic tests such as passive leg raising, as well as outcomes related to volume responsiveness.

The analysis was conducted in a qualitative and comparative manner, focusing on the critical evaluation of the diagnostic accuracy, technical limitations, and clinical applicability of the different methods in scenarios such as intensive care unit, emergency, and perioperative environment. No meta-analysis was performed due to the heterogeneity of the designs, populations, and parameters evaluated.

3 RESULTS AND DISCUSSION

The integrated analysis of the studies demonstrates that the use of point-of-care ultrasound (POCUS) in the evaluation of volume responsiveness represents not only a technological advance, but also a conceptual reconfiguration of hemodynamic monitoring in critically ill patients. In this context, the literature converges by evidencing the superiority of dynamic methods in relation to static parameters; However, further comparative analysis reveals that such superiority is not evenly distributed among the different approaches available. In fact, an implicit functional hierarchy is observed, in which methods based on direct flow measurement, such as the VTI of LVOT, tend to present superior performance in relation to indirect indices, such as those derived from vena cava.

Among the methods evaluated, the variation of the LVOT VTI stands out as the parameter most consistently associated with volume responsiveness, especially when analyzed in direct comparison with alternative approaches. Studies such as those by Pérez-Manjarrez et al. (2023) and Maciuliene et al. (2017) demonstrate a strong correlation between VTI variation and classic markers of responsiveness, such as pulse pressure variation, suggesting greater physiological proximity to cardiac output. In contrast, methods based on variations in venous diameter, such as the evaluation of the inferior vena cava, have a more indirect character, predominantly reflecting changes in intrathoracic pressure and venous compliance, which makes them more susceptible to physiological interference. This conceptual distinction contributes to explain the relative superiority of VTI, since it

directly measures the final outcome of the interaction between preload, contractility, and afterload, while CVI represents an intermediate marker of this dynamic.

Nevertheless, this superiority must be interpreted with caution. From an operational point of view, the VTI has relevant limitations, including high operator dependence, the need for an adequate acoustic window, and greater technical complexity, factors that may restrict its applicability in emergency scenarios or in patients with unfavorable clinical conditions (ASOGWA et al., 2024). In contrast, the assessment of CVI, although less accurate from a physiological point of view, is more accessible and less technically demanding, which favors its use in contexts of less complexity. This dichotomy highlights a recurrent tension in the literature between diagnostic accuracy and practical feasibility, which is often underestimated in the interpretation of results.

In this scenario, the passive leg raising (PLR) test assumes a central role as a tool for dynamic modulation of preload, allowing the functional evaluation of the cardiovascular response regardless of the measurement method adopted. When associated with VTI analysis, PLR enhances diagnostic accuracy, configuring the most robust combination described in the literature (MONNET; SHI; TEBOUL, 2022; BOU CHEBL et al., 2018). Compared to indices based exclusively on venous parameters, PLR has a clear advantage, since it induces a measurable physiological change in cardiac output, instead of inferring this response indirectly. However, its efficacy remains strongly conditioned to the adequate technical execution and correct interpretation of hemodynamic variations, being susceptible to relevant operational failures. Recent evidence points to significant discrepancies between the theoretical application and clinical practice of the method, indicating that its accuracy can be substantially reduced in real environments (HOTZ; VAN GEMMERN; KRIEGE, 2024). In addition, conditions such as intra-abdominal hypertension, mechanical ventilation with high parameters, and postural limitations can directly interfere with the response to the test, restricting its applicability in certain contexts.

In turn, indices derived from vena cava, especially CVI, continue to be widely used in clinical practice, mainly due to their ease of obtainment. However, when analyzed comparatively, they demonstrate lower performance and greater variability compared to flow-based methods. The evidence that CVI distensibility has low accuracy in patients with left ventricular dysfunction (ZHANG et al., 2019) constitutes a critical limitation, often neglected in clinical practice. In addition, studies such as those by Ma et al. (2022a) show a wide area of uncertainty in the CVI cut-off values, reducing its usefulness in binary clinical decisions. On the other hand, parameters related to the superior vena cava (SVC) demonstrate superior diagnostic performance in patients under controlled mechanical ventilation (MA et al., 2022b;

BUBENEK-TURCONI et al., 2019), suggesting that the choice between CVI and CVS should be guided by the ventilatory context. Even so, the applicability of CVS remains limited by more complex technical requirements, including the need for transesophageal echocardiography, which restricts its routine use.

Emerging methods, such as the evaluation of carotid flow and carotid VTI, represent an attempt to overcome technical limitations of conventional methods, particularly in scenarios of difficult echocardiographic access. Although studies such as the one by Dai et al. (2024) indicate promising performance, including with accuracy comparable to the VTI of LVOT in specific populations, the generalizability of these findings remains limited. The predominance of highly selected populations and the absence of validation in more heterogeneous clinical contexts introduce important biases, in addition to the scarcity of direct comparisons with consolidated methods, which prevents more definitive conclusions about their relative position in clinical practice.

In a comprehensive way, the comparative analysis of the methods reinforces that the evaluation of volume responsiveness through POCUS should not be based on a single isolated parameter, but rather on an integrated and contextualized approach. The choice of the optimal method should consider not only diagnostic accuracy, but also factors such as technical feasibility, clinical context, and operator experience. This perspective is supported by recent reviews that emphasize the need for multimodal interpretation of sonographic findings (NOOR et al., 2025; PICCIONI et al., 2025), reflecting the pathophysiological complexity of critically ill patients.

In addition, the robustness of the available evidence is limited by recurrent methodological aspects. The predominance of observational studies, often single-center and with small sample sizes, combined with the lack of standardization in the criteria for defining volume responsiveness, compromises the comparability between the findings. The use of different reference methods for measuring cardiac output, associated with the lack of systematic control of the operating factor, introduces relevant biases that should be considered in the interpretation of the results.

In view of this set of evidence, the combination of the passive lower limb elevation test and the measurement of the LVOT VTI is the most consistent and physiologically based strategy for predicting volume responsiveness. However, this superiority must be interpreted relatively, since its applicability remains conditioned by technical and clinical factors. In this sense, POCUS should be understood as a central tool, but dependent on integration with the clinical context and other hemodynamic variables.

In summary, the literature does not support the existence of a universally superior method, but points to the relative primacy of approaches based on direct flow measurement, especially when associated with dynamic tests such as PLR. The consolidation of POCUS as a standard in the evaluation of volume responsiveness will depend on methodological standardization, validation in heterogeneous populations and systematic qualification of operators, and the advancement of the area is more related to the critical and contextualized integration of the available tools than to the introduction of new isolated parameters.

The present review has limitations that should be considered. This is a critical narrative review, with greater dependence on the authors' judgment in the selection and interpretation of studies, which implies a potential risk of selection bias. In addition, the included studies present relevant heterogeneity in terms of methodological design, populations evaluated, and clinical contexts, which limits the generalization of the findings. The predominance of observational studies and the lack of standardization in the criteria of volume responsiveness make direct comparisons difficult. In addition, no formal assessment of the risk of bias of the included studies was performed, which represents an additional limitation in the interpretation of the results.

4 CONCLUSION

Point-of-care ultrasound (POCUS) has established itself as a central tool in the assessment of volume responsiveness, reflecting the transition to dynamic and functionally oriented approaches in hemodynamic monitoring. Among the available methods, the relative superiority of techniques based on direct flow measurement stands out, especially the variation of the VTI of the LVOT associated with the passive elevation test of the lower limbs, configuring the most consistent strategy from the physiological point of view.

However, this superiority is conditioned by technical and contextual limitations, which maintains the relevance of more accessible methods, such as the evaluation of the inferior vena cava, in specific scenarios, while more complex approaches have operational restrictions. Thus, the current evidence does not support the existence of a universal method, reinforcing the need for an integrated and contextualized evaluation.

The consolidation of POCUS in clinical practice depends, therefore, on methodological standardization, validation in heterogeneous populations, and operator qualification. In this sense, the advancement of the area lies in the critical integration of available tools, focusing on the optimization of decision-making and clinical outcomes.

REFERENCES

Asogwa, C., et al. (2024). The utility of echocardiography in estimating fluid responsiveness. Journal of Clinical Medicine Research, 16(2), 85–93. https://doi.org/10.14740/jocmr5050

Bou Chebl, R., et al. (2018). Bedside echocardiography and passive leg raise as a measure of volume responsiveness in the emergency department. Journal of Ultrasound in Medicine, 37(1), 141–150. https://doi.org/10.1002/jum.14338

Bou Chebl, R., et al. (2018). Mitral valve velocity time integral and passive leg raise as a measure of volume responsiveness. Critical Ultrasound Journal, 10(1), 1–8. https://doi.org/10.1186/s13089-018-0097-0

Bubenek-Turconi, S., et al. (2019). The value of a superior vena cava collapsibility index in predicting fluid responsiveness. Journal of Clinical Monitoring and Computing, 33(6), 1027–1033. https://doi.org/10.1007/s10877-019-00282-3

Dai, Y., et al. (2024). Predicting fluid responsiveness in spontaneously breathing patients using carotid blood flow. BMC Pregnancy and Childbirth, 24(1), 1–9. https://doi.org/10.1186/s12884-024-06234-5

Hotz, J., Van Gemmern, J., & Kriege, M. (2024). Are we always right? Evaluation of the performance of passive leg raising in clinical practice. Journal of Clinical Medicine, 13(4), 1–12. https://doi.org/10.3390/jcm13040987

Ishizuka, K., & Su, B. (2023). Critical care echocardiography for fluid responsiveness. Texas Heart Institute Journal, 50(1), e217851. https://doi.org/10.14503/THIJ-21-7851

Ma, X., et al. (2022a). The diagnostic accuracy of inferior vena cava respiratory variation in predicting fluid responsiveness: A systematic review and meta-analysis. BMC Anesthesiology, 22(1), 1–12. https://doi.org/10.1186/s12871-022-01679-5

Ma, X., et al. (2022b). Comparison of superior and inferior vena cava diameter variation in predicting fluid responsiveness: A systematic review and meta-analysis. BMC Anesthesiology, 22(1), 1–13. https://doi.org/10.1186/s12871-022-01678-6

Maciuliene, A., et al. (2017). Variability of left ventricular outflow tract velocity time integral during breathing cycle may predict fluid responsiveness. Medicina, 53(4), 245–252. https://doi.org/10.1016/j.medici.2017.07.003

Monnet, X., Shi, R., & Teboul, J. L. (2022). Prediction of fluid responsiveness: What's new? Annals of Intensive Care, 12(1), 1–10. https://doi.org/10.1186/s13613-022-01057-5

Noor, A., et al. (2025). Point-of-care ultrasound use in hemodynamic assessment. Biomedicines, 13(1), 1–15. https://doi.org/10.3390/biomedicines13010045

Pérez-Manjarrez, A., et al. (2023). Usefulness of the velocity-time integral of the left ventricular outflow tract in predicting fluid responsiveness. Echo Research and Practice, 10(1), 1–9. https://doi.org/10.1186/s44156-023-00045-2

Piccioni, A., et al. (2025). From fluid responsiveness to prognosis: The emerging role of echocardiography in sepsis. Diagnostics, 15(1), 1–14. https://doi.org/10.3390/diagnostics15010067

Rice, J., et al. (2021). The POCUS consult: How point-of-care ultrasound helps guide clinical decision making. International Journal of General Medicine, 14, 3171–3182. https://doi.org/10.2147/IJGM.S307151

Roy, C., et al. (2021). Left ventricular longitudinal strain variations and fluid responsiveness. PLOS ONE, 16(6), e0252812. https://doi.org/10.1371/journal.pone.0252812

Suresh, V., et al. (2020). Fluid responsiveness to passive leg raising in perioperative patients. Annals of Cardiac Anaesthesia, 23(3), 299–304. https://doi.org/10.4103/aca.ACA_72_19

Zhang, Z., et al. (2019). Respiratory variations of inferior vena cava fail to predict fluid responsiveness in patients with left ventricular dysfunction. Annals of Intensive Care, 9(1), 1–9. https://doi.org/10.1186/s13613-019-0527-8